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Universidad del País Vasco Euskal Herriko Unibertsitatea

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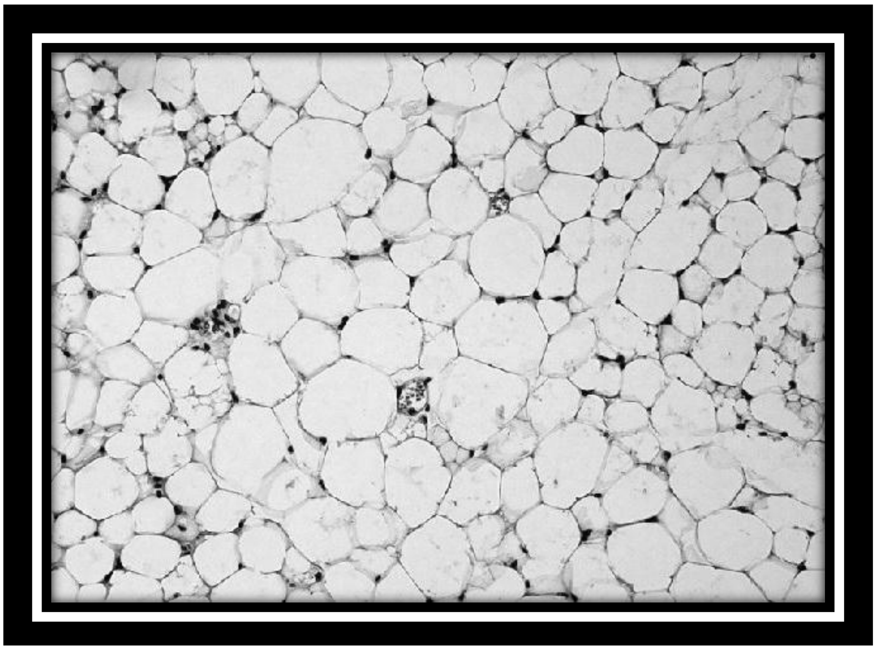

María Eugenia

Ibáñez Pérez-Zamacona

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BIOANTROPOLOGÍA DE LA OBESIDAD EN POBLACIÓN DE LA COMUNIDAD AUTÓNOMA DEL PAÍS VASCO

Tesis Doctoral dirigida por:

Dra. Esther Rebato Ochoa

Dra. Alaitz Poveda Zabala

Memoria para optar al grado de Doctora en Ciencias Biológicas presentada por:

María Eugenia Ibáñez Pérez-Zamacona

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A todas las personas
que considero mi familia

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RESUMEN

En la mayoría de los países, la prevalencia de sobrepeso y obesidad se ha incrementado enormemente en los últimos años. En 1997, la Organización Mundial de la Salud (OMS) reconoció la naturaleza global de la obesidad y hoy en día se considera que la obesidad es una pandemia a nivel global. Este incremento en la prevalencia de sobrepeso y obesidad, tiene un gran impacto en la salud pública, ya que está ligado al aumento de la prevalencia de una serie de enfermedades crónicas no contagiosas entre las que se encuentran la diabetes tipo 2, las enfermedades cardiovasculares o incluso ciertos tipos de cáncer. Además, debido a los prejuicios y a la discriminación que existe hacia las personas con obesidad, esta condición también se asocia a ciertos tipos de problemas psicológicos, sobre todo relacionados con la imagen corporal y la autoestima. A parte de tener efectos perjudiciales sobre la salud, el sobrepeso y la obesidad suponen también un impacto importante a nivel económico, ya sea por costes directos relacionados con el tratamiento y el cuidado de estos pacientes, o por costes indirectos debidos a la pérdida de productividad asociada a la morbilidad y mortalidad que conlleva la obesidad.

La OMS define la obesidad como una acumulación anormal o excesiva de grasa que puede ser perjudicial para la salud. Desde un punto de vista energético, la obesidad es simplemente el resultado de un balance energético positivo mantenido en el tiempo, donde la ingesta de energía supera el gasto energético y donde dicha energía es acumulada en forma de triglicéridos en los adipocitos del tejido adiposo. Sin embargo, existen muchos factores que influyen en dicho desequilibrio energético y que se consideran en parte responsables del desarrollo del sobrepeso y la obesidad. Entre ellos, los factores ambientales y genéticos juegan un papel importante a la hora de explicar el incremento de la prevalencia de obesidad en determinados países, sobre todo en los industrializados. Por una parte, en las sociedades actuales predomina un ambiente "obesogénico" que promueve una ingesta excesiva de energía a la vez que promueve también un estilo de vida sedentario. Por otra parte, determinadas variantes genéticas que hace tiempo pudieron promover una mayor acumulación de energía y que por lo tanto pudieron suponer una ventaja frente a periodos de hambruna, podrían hoy en día facilitar el desarrollo de sobrepeso y obesidad.

Por todo lo anterior resulta de gran importancia el estudio de la obesidad; esto es, entender los efectos que puede tener sobre la composición, morfología e imagen corporal, así como determinar los factores ambientales y genéticos que contribuyen al desarrollo de sus diversos fenotipos. Todo lo anterior es objeto de estudio en este trabajo.

La presente Tesis Doctoral está basada en un diseño retrospectivo de caso-control, donde los participantes se seleccionaron en base a la característica de estudio, en este caso la obesidad. De esta forma los casos son sujetos que presentan dicha característica en el momento del muestreo (sujetos obesos), mientras que los controles son sujetos sanos dentro de la misma población, es decir, individuos con las mismas probabilidades de estar expuestos a la/s causa/s del evento pero que no han desarrollado la enfermedad (sujetos no obesos). Este tipo de estudios son adecuados para estimar el riesgo de la enfermedad, pero no pueden proporcionar prevalencias absolutas o tasas de incidencia de la enfermedad. Además, debido a la dificultad y al sesgo a la hora de recolectar la muestra en este tipo de estudios bioantropológicos, este diseño asegura un número suficiente de individuos con obesidad para poder estudiar la etiología de esta condición desde una perspectiva antropológica, psicológica, ambiental y genética. En esta investigación hemos usado de forma habitual el Índice de Masa Corporal (IMC) para definir la obesidad siguiendo los criterios establecidos por la OMS. Además, en determinados capítulos también se han usado, para definir otros fenotipos de obesidad, la circunferencia de la cintura (CC), el índice cintura cadera (ICC) o el porcentaje de masa grasa (%MG) según los criterios de la OMS o de la Sociedad Española para el Estudio de la Obesidad (SEEDO).

En el presente trabajo, se empleó una muestra de 524 individuos adultos (320 mujeres y 204 varones) con diferentes estados nutricionales, todos ellos residentes en el País Vasco. A todos los participantes, previo consentimiento informado, se les tomaron diversas medidas antropométricas (estatura; peso; anchura biepicondilar del húmero y del fémur; circunferencias de la cintura, la cadera, el brazo relajado, el brazo contraído y la pantorrilla; pliegues subcutáneos del bíceps, tríceps, subescapular, suprailíaco, abdominal y de la pantorrilla). Además se les realizó una encuesta personal para recabar datos acerca del sexo, edad, características biodemográficas, nivel socioeconómico, imagen corporal y diversas variables ambientales y del estilo de vida. Por último, se les pidió una muestra de saliva para la posterior obtención de ADN.

Además del capítulo introductorio, del referido a Hipótesis y Objetivos y a la descripción de los Materiales y Métodos, esta Tesis se ha organizado en cuatro capítulos principales de Resultados y Discusión, que analizan diferentes aspectos de la obesidad. En el primer capitulo de Resultados y Discusión (Capítulo IV) se estudia la variabilidad en la morfología y composición corporal debida al sexo, la edad y la práctica de deporte, en los diferentes estados nutricionales. Para ello se ha analizado la variabilidad del somatotipo antropométrico de Heath-Carter (1990), tanto en su conjunto como en cada uno de sus componentes: endomorfia (adiposidad relativa), mesomorfia (masa magra relativa o componente músculo esquelético) y ectomorfia (linealidad relativa). Las distancias de dispersión del somatotipo (SDD) se han usado para estudiar las diferencias del somatotipo global, mientras que las pruebas estadísticas de ANOVA, Kruskal-Wallis o ANCOVA han permitido estudiar las diferencias de cada componente por separado. Los resultados de este capítulo nos muestran claramente cómo las personas con sobrepeso y obesidad tienen una mayor masa corporal y una menor linealidad que las personas en normo-peso y que esto se debe a un aumento tanto de la masa grasa como de masa libre de grasa. El aumento de ambos componentes (endomorfia y mesomorfia) al aumentar el grado de obesidad se observa en ambos sexos y grupos de edad, e incluso en los individuos que practican deporte. Aunque en la población general no se observan diferencias claras con la práctica deportiva, en individuos con normopeso aumenta el predominio de la mesomorfia mientras, que en individuos con sobrepeso y obesidad únicamente se observa una reducción de masa corporal acompañado de un aumento de la linealidad (ectomorfia). Sin embargo, en una sub-muestra analizada de deportistas (jugadores de rugby) aumenta claramente el predominio del componente muscular sobre el adiposo a medida que aumenta el estado nutricional (basado en el IMC). Por último, el dimorfismo sexual en la composición corporal, donde existe un claro predominio del componente muscular en los varones y del adiposo en las mujeres, se mantiene en casi todos los estados nutricionales, aunque se pierde en la obesidad mórbida. Sin embargo, los cambios con la edad no son tan significativos, aunque si se aprecia un descenso de la linealidad.

Las variaciones en la morfología y composición del cuerpo suelen ir acompañadas de cambios en la imagen corporal, que a su vez pueden influir en la percepción de la propia imagen, la autoestima y ciertas actitudes en relación con la imagen corporal. En el Capítulo V se analiza la percepción del tamaño corporal, la consistencia entre el tamaño percibido y el estimado mediante técnicas antropométricas, la imagen ideal de mujeres y varones para sí mismos y para el sexo opuesto y el grado de satisfacción con la propia imagen corporal. Para ello se ha utilizado la colección de siluetas de Stunkard et al. (1983), donde aparecen nueve siluetas de cada sexo representando diferentes imágenes corporales desde la más fina a la más corpulenta. No sólo se han estudiado las diferencias entre mujeres y varones mediante el test de Mann-Whitney, sino que también se ha analizado su asociación con el estado nutricional mediante el coeficiente Gamma. Este capítulo nos muestra cómo, generalmente, la imagen percibida se corresponde con el estado nutricional de los sujetos; los individuos con mayores grados de obesidad eligen siluetas mayores. Sin embargo, generalmente las mujeres desean para sí mismas cuerpos más delgados que los que desean los varones para sí mismos. Este ideal social hacia una imagen más estilizada en las mujeres también se aprecia en la imagen que se escoge como la más atractiva para el sexo opuesto; a los varones también les resultan más atractivas las siluetas de mujeres más delgadas que las que les resultan atractivas a las mujeres en los varones. La imagen ideal está claramente influenciada por el estado nutricional de forma que las personas con mayor grado de obesidad también tienen imágenes ideales más corpulentas. Sin embargo, por alguna razón esto deja de ser importante cuando los adultos en rangos de edad más mayores eligen la silueta ideal para el sexo opuesto.

En el Capítulo VI de esta Tesis Doctoral se ha querido determinar la contribución relativa de algunas variables ambientales (relacionadas con el historial personal, la actividad o inactividad física, los hábitos alimentarios y de sueño y el consumo de tabaco y alcohol) a la obesidad, definida mediante distintos puntos de corte establecidos para el IMC, CC, ICC y el %MG, lo que representa diferentes fenotipos de obesidad. Los resultados de la regresión logística utilizada para lograr este objetivo han confirmado la influencia de los factores ambientales en la obesidad, no solo en la obesidad generalizada, sino también en la obesidad abdominal, en la distribución central de grasa y en el excesivo porcentaje de masa grasa. Sin embargo, el efecto de cada variable ambiental sobre los distintos fenotipos de obesidad no ha sido siempre igual. Una distribución de grasa central, que está a su vez asociada a diversas comorbilidades, está claramente influenciada por la actividad o inactividad física (sedentarismo) así como por el consumo de tabaco; sin embargo, los hábitos alimentarios o de sueño parecen no tener tanto efecto en este fenotipo. Por el contrario, el número de ingestas y la calidad del sueño afectan tanto a la obesidad general como a la abdominal (ambas muy correlacionadas entre sí), aunque tampoco afectan de forma significativa a un exceso exclusivo de masa grasa. Este último fenotipo de obesidad se muestra sin embargo claramente asociado con una mala percepción del estado físico, con el mayor tamaño del efecto encontrado en este análisis.

En el último de los cuatro capítulos de Resultados y Discusión, el Capítulo VII, se analiza la asociación de 21 polimorfismos de un único nucleótido (SNPs) con diferentes fenotipos de obesidad y variables antropométricas relacionadas con la obesidad. Además, también se ha estudiado la asociación de estos SNPs con la morfología y la composición corporal mediante su asociación con cada uno de los tres componentes del somatotipo. Los resultados obtenidos han confirmado un efecto modesto en la obesidad y la composición corporal de 12 de los 21 SNPs estudiados, localizados en los *loci* de 9 genes diferentes (*NEGR1*, *TMEM18*, *GNPDA2*, *BDNF*, *UCP2*, *NRXN3*, *FTO*, *KCTD15* and *MAP2K5*). Entre ellos, el alelo de riesgo del SNP rs925946 (*BDNF*) es uno de los que presenta un mayor efecto, no sólo en el desarrollo de obesidad general, sino también en la de tipo abdominal, en la distribución central de la grasa, en la obesidad mórbida y en la suma de los seis pliegues subcutáneos. Por otra parte, aunque también se ha confirmado la asociación del SNP rs10146997 (*NRXN3*) con la obesidad, al contrario que en otras poblaciones, en la muestra analizada el alelo de riesgo se encuentra asociado de forma negativa con la obesidad. Por último, teniendo en cuenta que hasta donde sabemos nunca hasta ahora se había estudiado la asociación de estos SNPs con los componentes del somatotipo, este trabajo ha sido el primero en demostrar la asociación de cuatro de estos polimorfismos (rs925946, *BDNF*; rs10146997, *NRXN3*; rs4776970, *MAP2K5* y rs9939609, *FTO*) con la forma y la composición del cuerpo calculado mediante la técnica del somatotipo antropométrico.

Esta Tesis Doctoral ofrece datos interesantes sobre la morfología, composición e imagen corporal en diferentes estados nutricionales (incluida la obesidad mórbida), así como sobre la influencia del ambiente (modo de vida) y la genética en diferentes fenotipos de obesidad; estos datos, junto con los obtenidos en otras poblaciones, podrán ser utilizados en un futuro a la hora de desarrollar y diseñar nuevas estrategias para el control y la prevención del sobrepeso y la obesidad.

LIST OF PUBLICATIONS

The following publications were a result of work conducted during doctoral study:

I. Poveda, A., Jelenkovic, A., **Ibáñez, M.E.**, Rebato, E. (2010). Obesity in ethnic minorities and low-income populations: social and public policy considerations from a comparative study. In: Global food security: ethical and legal challenges. Romeo, C.M., Escajedo, L., Emaldi, A. (Eds.). Wageningen Academic Publishers. The Netherlands, 198-201 pages.

II. Poveda, A., **Ibáñez, M.E.**, Rebato, E. (2012). Heritability and genetic correlations of obesity-related phenotypes among Roma people. Annals of Human Biology 39:183-189.

III. Poveda, A., Jelenkovic, A., Salces, I., **Ibañez, M.E.**, Rebato, E. (2012). Heritability variations of body linearity and obesity indicators during growth. HOMO Journal of Comparative Human Biology 63: 301–310.

IV. Poveda, A., **Ibáñez, M.E.**, Rebato, E. (2012). Obesidad y modo de vida en población gitana. Inguruak. Revista Vasca de Sociología y Ciencia Política 57: 2294-2309

V. Poveda, A., **Ibánez, M.E.**, Rebato, E. (2013). Obesity and Body Size Perceptions in a Spanish Roma Population. Annals of Human Biology 41: 428-35.

VI. Poveda, A., **Ibánez, M.E.**, Rebato, E. (2014). Common Variants in BDNF, FAIM2, FTO, MC4R, NEGR1, and SH2B1 Show Association with Obesity-Related Variables in Spanish Roma Population. American Journal of Human Biology 26:660-669.

VII. Bufa, R., Mereu, E., Comandini, O., **Ibáñez, M.E.**, Marini, E. (2014). Bioelectrical impedance vector analysis (BIVA) for the assessment of two-compartment body composition. European Journal of Clinical Nutrition 68:1234-1240.

VIII. **Ibáñez, M.E.**, Poveda, A., Goñi, F., Rebato, E. (2014). Análisis del somatotipo y estado nutricional en adultos de Vizcaya. España. Revista Española de Antropología Física 35: 22-33.

IX. **Ibáñez, M.E.**, Mereu, E., Buffa, R., Gualdi-Russo, E., Zaccagni, L., Cossu, S., Rebato, E., Merini, E. (2015). New Specific Bioelectrical Impedance Vector Reference Values for Assessing Body Composition in the Italian-Spanish Young Adult Population. American Journal of Human Biology 27: 871-876.

CONTENTS

Chapter I- INTRODUCTION

Chapter II- MOTIVATION HYPOTHESIS AND OBJECTIVES

Chapter III- MATERIALS AND METHODS

Chapter IV- SOMATOTYPE VARIABILITY ACCORDING TO SEX AGE AND SPORT PRACTICE IN DIFFERENT NUTRITIONAL STATUS

Chapter V- BODY SIZE PERCEPTION AND SATISFACTION IN INDIVIDUALS OF DIFFERENT NUTRITIONAL STATUS

Chapter I

Introduction

1. THE HUMAN BODY

1.1. BODY MORPHOLOGY AND COMPOSITION

Body composition refers to all components (from elements to tissues and organs) that provide mass, shape and function to all living beings. It reflects the accumulation of nutrients and other substrates acquired from the environment and retained by the body during the entire life of an organism (Shen et al. 2005).

Human body composition can be studied at five different levels of increasing complexity in which the sum of all components at each level is equivalent to the total body mass. The five levels are: atomic, molecular, cellular, tissue-system and whole body (Figure 1.1).

The **atomic level** is composed by atoms or elements. Approximately 50 of the 106 elements are distributed in the various tissues and organs of the human body. Six elements (oxygen, carbon, hydrogen, nitrogen, calcium, and phosphorus) account for >98% of total body weight. The 11 principal elements are incorporated into molecules that form > 100000 chemical compounds found in the human body. At **molecular level**, chemical compounds are considered in six major categories of closely related molecular species: water, lipid, protein, carbohydrates, bone minerals, and soft tissue minerals. To explore body composition at this level, there are various models that range from two to six components. One of the most widely used models in body composition studies is the two-component model in which total body weight is divided in two components: fat mass (FM) and fat-free mass (FFM) (e.g. Maron et al. 2001; Forsum, Henriksson, and Löf 2014). Other models with three or more components are obtained by splitting the FFM into additional components. At the **cellular level**, the different components from the molecular level (chemical compounds) are assembled into cells. There are three main compartments at this level: cells, extracellular fluid, and extracellular solids. The cellular component can be additionally partitioned into two components: fat and body cell mass. The three components from the cellular level are further organized into tissues, organs, and systems, which constitute the **tissue-system level**. Three specific tissues are of particular importance in body composition: bone, muscular, and adipose. The fifth and last level corresponds to **whole body level**, and concerns to body size, shape, and exterior and physical characteristics. It can be divided into appendages, trunk and head.

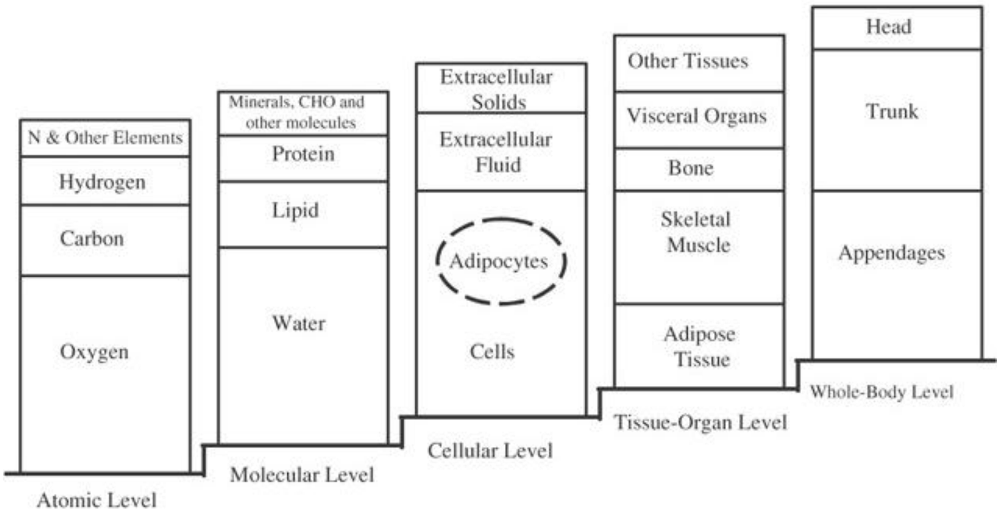

Figure 1.1. Representation of the five different levels of body composition: atomic, molecular, cellular, tissue-organ, and whole-body. Source: Modified from Wang, Pierson, and Heymsfield (1992).

All levels can be considered separately but they are also biochemically and physiologically integrated. Any major changes in body composition on the first four levels will manifest on the whole-body level; and most differences at the whole-body level are related to changes in composition on the other levels. This relation is the basis of many researches since most indicators at the whole-body level are simpler and easier to perform than the ones performed at the other levels. Thus, measurement techniques at this level are widely used for large-scale studies or for field work (Wang, Pierson, and Heymsfield 1992). Variations in body composition involve changes related to physiological or pathological conditions. Due to this the study of body composition is very important in many areas such as growth, development, aging, race, nutrition, physical activity or some diseases (Heymsfield 2005).

1.2. ASSESSMENT OF BODY COMPOSITION

The only way to directly measure body composition is cadaver dissection. Therefore, when living humans are the subject of the research, other strategies to evaluate body composition are needed. Many indirect methods are available, from the simplest to the more complex ones, but all of them have strengths and limitations. Below some of these methods are described.

1.2.1. Anthropometry

Anthropometry is the science that deals with the measurement of the size, shape, proportions, and composition of the human body (Abernethy et al. 2013). Some measurements are directly obtained on the human body. These direct measurements can be combined to obtain derived measurements, which can be used to define population characteristics or to assess individuals with respect to some physical parameter.

Although the assessment of body composition through anthropometric measures can be less accurate than those from newer techniques, anthropometry is still a simple, inexpensive, portable and non-invasive technique with a substantial literature available (Weiner and Lourie 1981; Lohman, Roche, and Martorell 1988; Hayward and Stolarczyk 1996; Roche, Heymsfield, and Lohman 1996; Frisancho 2008), which make it easily and accurately applicable in epidemiologic and population studies. Due to this, anthropometry is still one of the most widely used methods (Moreno et al. 2003).

1.2.1.1. Simple measures

Anthropometric simple measurements are taken directly on the human body, and they can be classified into different categories: lengths, bone breadths, body weight, skinfold thicknesses and circumferences. Almost all anthropometric measures include a variety of tissues, and the influence of each of these tissues on the recorded values is not always clear. So, it is normally assumed that tissues included in the measurements are in a "standard" state, which means that muscles are relaxed and that soft tissues are normally hydrated.

Lengths. Among lengths, height is a major indicator of general body size and bone length. It is one of the most important and useful anthropometric parameters used in bioanthropological studies. It also has a considerable relevance in screening for disease or malnutrition and in the interpretation of weight. Height is a composite measurement including several segments: lower extremities, trunk, neck, and head.

Bone breadths. Even though the distances between the two bony landmarks are also influenced by the overlying muscle, fat, and skin, these measures are considered skeletal dimensions. In order to minimize the effect of soft tissue, firm pressure can be applied during the measurements. Biepicondylar breadth of the humerus (elbow) and biepicondylar breadth of the femur (knee) are generally used as indicators of frame size and skeletal mass. However, knee breadth is less useful than elbow breadth in the prediction of skeletal mass probably because of a greater amount of intervening soft tissue at this site (Frisancho 1990; Gibson 2005).

Body weight. Body weight is the most commonly recorded anthropometric variable, and it is relatively easy to measure it accurately. Strictly speaking, this variable measures the mass rather than weight. However, the term is widely spread and its application is easily accepted. This variable has a considerable importance in screening for unusual growth, obesity or undernutrition.

Skinfolds. Skinfolds are thickness measurements comprising a double layer of skin and the underlying subcutaneous adipose tissue, but not the muscle. They are considered a good fatness indicator, as about 40-60% of total body fat is in the subcutaneous region of the human body (Wang et al. 2000). They can be used to estimate general FM, from which FFM can also be estimated by using different prediction equations available in literature (Siri 1961; Lohman et al. 1984). However, measuring skinfolds thicknesses consistently is difficult and a standardized methodology is needed to improve the measures. Furthermore, these measures are affected by individual and regional differences in compressibility that vary with age, gender, and recent weight loss.

Circumferences. Circumferences are measurements of the cross-sectional and circumferential dimensions of the body and are used for estimating skeletal muscle mass and fat distribution. Mid-arm, mid-thigh, waist, and hip circumferences are used more frequently than others, because they indicate differences among people in major regions of the body. Although circumferences are easy to collect, they are difficult to interpret because they include skin, subcutaneous adipose tissue, muscle, bone, blood vessels and nerves (trunk circumferences also include organs). Waist circumference (WC) has shown to be a very useful measure of increased intra-abdominal fat. According to the WHO, WC is a good indicator of overweight and obesity, and can also properly predict the risk for weight-related health problems such as hypertension, dyslipidaemia or insulin resistance.

1.2.1.2. Derived variables

Derived measures are obtained by combining simple ones. There are many of them, but some of the most important ones are: body mass index (BMI), waist to hip ratio (WHR) the sum of six skinfolds (SF6) and FM%.

Body mass index (BMI). This index is used to express weight in relation to height. In general population BMI is a robust but indirect measure of body fatness, and it allows individuals to be classified into nutritional categories. The use of BMI to make this classification is based on the premise that variation between individuals is fundamentally due to differences in FM. However, body weight is influenced not only by FM but also by FFM (Boileau and Horswill 2000).

Waist to hip ratio (WHR). This ratio evaluates the distribution of body fat. According to fat distribution, two different shapes could be appreciated in humans. On the one hand, android fat distribution is characterized by the distribution of adipose tissue mainly around the trunk and upper body; it is also called "apple" shaped distribution or central obesity and it is more common in males than in females. On the other hand, gynoid fat distribution is characterized by the distribution of adipose tissue mainly on thighs, hips and bottom; it is also called "pear" shaped distribution and it is more common in females than in males. Fat in the waist and abdomen is metabolically more active than fat in the thighs, hip and buttocks and it is positively associated with increased risk of heart diseases and premature death. Even though central obesity is more common in men, both men and women could show a central fat distribution.

Sum of six skinfolds (SF6). The SF6 is considered to be an indicator of the total amount of subcutaneous adipose tissue (SAT). The use of SF6 as a complement of BMI is very interesting; for example in athletes where BMI values are compromised by muscle mass (Garrido-Chamorro et al. 2012).

Fat Mass Percentage (FM%). The use of FM% as a complement of BMI is also very interesting as it allows evaluating total body fat mass independently of body weight.

1.2.1.3. Somatotype of Heath-Carter

Heath-Carter somatotype assesses human physique variation and classifies it into different body types as a mixture of three basic components (endomorphy, mesomorphy and ectomorphy). Heath-Carter somatotype method is a modification of the original Sheldon's method of somatotyping (1940), with some important modifications that allows changes over time, makes it applicable to both sexes at all ages and also permits the inclusion of obese individuals with extreme values.

Heath-Carter method defines somatotype as a quantitative description of the present shape and composition of the human body. Even though Heath-Carter somatotype is not equivalent to body composition, it is closely related to it. The somatotype provides a general summary of body shape, from which estimates of body composition can be deduced.

Heath-Carter somatotype is expressed as three sequential numbers that represent the three components of physique: endomorphy, mesomorphy and ectomorphy. Endomorphy is dominated by tissues derived principally from the endodermal embryonic layer (Figure 1.2) such as digestive viscera, and it represents the relative fatness. Mesomorphy is dominated by tissues derived from the mesodermal embryonic layer such as muscle, bone and connective tissue, this component represents the musculoskeletal robustness relative to stature. And finally, ectomorphy is dominated by tissues derived from the ectodermal embryonic layer such as skin and the nervous system, it represents the relative linearity.

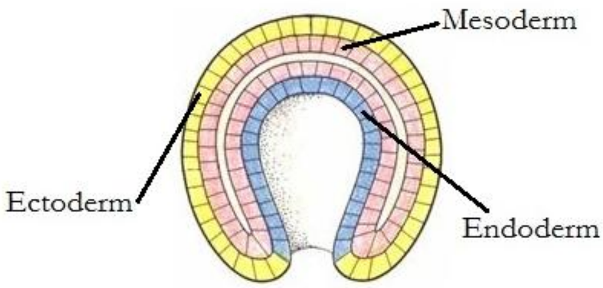

Figure 1.2. The three embryonic layers in triblastic organisms.

Since its development somatotype method was principally used in athletes, so the number of works carried out in this field are numerous (e.g. Fidelix et al. 2014; Noh et al. 2014; Purenović-Ivanović and Popović 2014) but somatotype has been also used in other areas, such as in auxology or to characterize different populations (Monyeki et al. 2002; Lizana, Olivares, and Berral 2015). Only more recently, somatotype has begun to be used in nutritional status research (e.g. Galić et al. 2016).

1.2.2. <u>Newer techniques</u>

During the last years, researchers have developed new techniques in an attempt to find more accurate ways to assess body composition. These techniques differ in their basis as well as in the body compartments they quantify. Even though they are generally considered more accurate than anthropometric assessment, they also differ in their results and are so laborious, expensive and time consuming, that are normally impractical in large scale surveys.

Bioelectrical impedance analysis (BIA). BIA measures the impedance of the body to a small electric current. The theoretical model treats the body as a single cylinder. A small alternating current flows between the two electrodes. The current passes more rapidly through hydrated fat-free tissues and extracellular water than through fat or bone tissue because of the greater electrolyte content of the fat-free component. Therefore as impedance to the electrical current (adjusted for height), is related to the amount of total body water (TBW), which it is also related to the amount of FM and FFM, this measurement can be used to estimate body composition. This technique is very sensitive to physical conditions, especially to hydration status, recent food and drinks intake, skin temperature, and recent physical activity.

Hydrostatic weighing. This method is based on the two-component model (FM and FFM) and on the difference of density between them. According to Archimedean principle when a body is immersed in water, the mass can be estimated by measuring the amount of water displaced or by comparing the differences between the underwater and dry weighing. Immersed in water, a person with a high percentage of FFM will weigh more than a person of equal volume but with a large amount of FM, which will make the body lighter in water due to its lower density. The major problem of this technique is the amount of gas in the body, especially the air in the lungs and the air in the gastrointestinal tract, because it has a very low density and can increase the floatability of the body.

Isotope dilution technique. Dilution of ^{2}H in body water is also used to determine body composition. A known dose of water labelled with deuterium is given orally to the subjects and, after an equilibrium period, deuterium enrichment of the body water pool is measured using saliva, urine, or blood samples. FFM is determined based on the calculation of TBW. This estimation of FFM from TBW requires an assumed value for FFM hydration (730g H_2O/kg FFM) (Wang et al. 1999; Westerterp 1999; Lee and Gallagher 2008). Subsequently, FM is calculated by subtracting the FFM from the total body mass (Walker, Thaden, and Deutz 2015).

Dual-energy X-ray absorptiometry (DEXA). This method uses an energy source that generates photons at two different energy levels. When the photons pass through tissues, the differential attenuation of the two energies is used to estimate the bone mineral content and the soft tissue composition. This technique can estimate three body components: fat, lean and bone mass. However, it presents some limitations, such as the weight limit of the scanning bed or the effect of hydration of FFM. An additional drawback is that participants are exposed to a small amount of radiation.

Computed tomography (CT). This technique consists in thin cross-sectional radiographies that allow a computerized measurement of the total fat area, and even the differentiation of subcutaneous fat from intra-abdominal fat. It also offers the possibility to measure just a single section or a complete volume. From the obtained volumes and knowing the density of the different tissues, mass can be calculated. Limitations in CT method include the radiation exposure, which is substantially higher than with other techniques and the inability to measure large individuals.

Magnetic resonance imaging (MRI). It is an imaging technique where magnetic fields and radio waves are used to produce images of the body. It generates imaging slices that can then be summed to calculate the volume of the tissues. Based on those tissues' volumes and knowing the density of the different tissues, mass can be calculated. MRI can only assess FM in adipose tissue, so this technique is not useful for determining lipids in other specific tissues. Conversely to CT, MRI does not use ionizing radiation. However, it is expensive and large individuals cannot be measured either.

1.3. DETERMINANTS OF BODY MORPHOLOGY AND COMPOSITION

Body morphology and composition are under the control of multiple factors that could be constitutive (inherent to ourselves) such as genetic factors, sex, age; or facultative (developed in response to environmental events) such as socioeconomic status (SES), nutrition, diseases, and physical activity. All these factors interact with each other in complex ways that are not completely understood.

Genetics. The importance of genetics in body composition has been widely studied, and the research based in twins, family and adoption studies found a significant effect of genetic factors (i.e. heritability) on body components (Silventoinen et al. 2008; Bryan et al. 2014; Bonnet et al. 2015; Stone et al. 2015). Besides, body composition is influenced by complex interactions between genetic and environmental factors.

Sex. Women and men differ considerably in body composition and morphology. On average, adult women are shorter and lighter than adult men. For a given BMI, women present greater amounts of FM, whereas FFM is greater in men. In addition, distribution of fat deposits is also different between both sexes. Men have generally more central fat distribution, whereas in women peripheral fat distribution is predominant (Geer and Shen 2009). Sexual dimorphism in body composition can be attributed, to a great extent, to the effects of sex hormones, especially during pubertal development.

Age. Human body morphology and composition vary from the beginning as it grows, maturates and develops. Major changes take place since birth and during childhood until adolescence. Although changes decrease, body composition and morphology continue changing during adulthood. Many men and women continue to gain weight throughout adulthood due to an increase of the total amount of adipose tissue. Often, there is also an age-related reduction of FFM, with a decrease of muscle mass and a reduction of bone mass (Burr 1997). In addition, fat distribution changes from a peripheral to a more central distribution and there is also a progressive reduction of height with increasing age, especially in elderly population.

Ethnicity. In relatively small (and isolated) populations some genetic combinations may disappear by mere chance (genetic drift), and others may be favoured (natural selection). As a result of those evolution mechanisms in response to some specific habitats, differences in body composition and morphology may arise in different populations or ethnic groups, and thus each one could have a particular genetic background.

Socioeconomic status (SES). SES encompasses multiple and important dimensions of social standing of individuals. However, some studies support the primacy of education and income as SES indicators (Thorpe et al. 2011). Higher SES has been associated with better health and longer life (Tyrrell et al. 2016). SES has also been associated with some body composition measures, such as height, BMI or fat distribution. However, the relationship between SES, health and body composition measures vary depending on the degree of development of the country. In developed countries, tall stature, low BMI and peripheral fat distribution are associated with higher SES and better health (Skrzypczak et al. 2008; Grabner 2012; Lundborg, Nystedt, and Rooth 2014). One possible explanation for the relationship between SES, body composition and health in developed countries may be an easier access to physical activity facilities and to high-quality foods by individuals with high SES.

Nutrition and physical activity. Body composition is maintained at a constant level when there is a condition of energy balance (i.e. energy expenditure matches energy intake from food). When energy expenditure exceeds the energy intake, people lose body mass. Conversely, if energy intake exceeds energy expenditure, people will gain body mass.

Diseases. The effects of disease are generally similar to those of malnutrition; they may act, in part, by inducing a disturbance of energy balance that may influence body composition and morphology. In some cases, short periods of disease are followed by a later catch-up phase. On the other hand, some chronic diseases can lead to a permanent stunting of the adult. In general, resistance to disease is increased by substantial body reserves of protein, fat and fluid (Shephard 1991).

Secular changes. Secular changes in body composition refers to the increase or decrease of body measurements in populations over time, and it is one of the best examples of environmental effects on body composition during the last one and a half centuries. Although secular trends could be seen in maturation age or in weight, according to Cole (2003) the increase in adult height is the most noticeable expression of secular trend since the mid-19th century, as body height has been increasing by about one to three centimetres per decade (Kołodziej et al. 2015). In Europe, secular trends are clearly linked to industrialization and changes related to lifestyle (INSERM Collective Expertise Centre 2000).

2. <u>BODY IMAGE AND SATISFACTION</u>

2.1. CONCEPTS AND DEFINITIONS

Schilder introduced psychology and sociology in the concept of body image, and in 1950, in his book “the Image and Appearance of the Human body” (Schilder 2013), he defined it as “the picture of our own body which we form in our mind, that is, the way in which the body appears to ourselves”. Later in 2007, in her book titled “Body Image: Understanding Body Dissatisfaction in Men, Women and Children”, Grogan defined body image as “A person’s perceptions, thoughts, and feelings about his or her body” (Grogan 2017).

It is beyond argument that body image is a complex concept, since personal perception of self and reactions of the others interact to construct a subjective ideal of one´s physical appearance. There has been a significant increase in popular interest on body image in the twenty-first century. As body shape and composition changes a lot during childhood and adolescence (Jones 2001) when individuals are also socially and psychologically vulnerable, body image perception has been deeply studied in these periods (Abalkhail, Shawky, and Ghabrah 2002; Agras et al. 2007; Abraham et al. 2009; Abbott et al. 2010; Almeida et al. 2012). However, although adulthood is characterised by a higher physical stability, during adulthood and aging until death the body is also continuously changing. Besides, westernized countries are under the effect of the obesity epidemic at the same time in which thinness is an idyllic social value. This background may have a lot of implications in body morphology and composition. Individuals must adapt their selves to those changes and respond to them, in order to maintain their identity balance incorporating information about the aging process or morphologic changes into their sense of self.

2.2. THEORETICAL PERSPECTIVES

In order to properly understand body image concept, some conceptual approaches and perspectives must be taken into consideration. Below, some of these perspectives are shown.

2.2.1. Sociocultural Perspective

The sociocultural perspective explains how cultural values influence individual values and behaviours. Thus, cultural ideals are important to understand how individuals are perceived by others and how they perceive themselves (Cash and Pruzinsky 2004). This concept proposes that societies have body shape ideals, which are communicated (through media, family and peers) to individuals, who internalize them (Tiggemann 2011). When cultural values develop, also body ideals do, which generates differences among cultures as well as within cultures across groups and time.

2.2.2. Cognitive-Behavioral Perspective

According to the cognitive-behavioral perspective there is a mutual relationship between environmental events, cognitive, affective and physical processes, and the individual’s behaviours in the determination of body image (Cash 2002). There are two kinds of body image attitudes: "body image evaluation", which refers to body satisfaction or dissatisfaction; and "body image investment", which refers to the cognitive, behavioural and emotional importance of the body for self-evaluation. Additionally, historical events refer to past experiences that influence how people feel, and act in relation to their body. Whereas proximal events refer to more immediate body image experiences such as internal dialogues, body image emotions, and self-regulatory actions (Cash and Pruzinsky 2004).

2.2.3. Information-Processing Perspective

This perspective considers disturbed body images as one type of cognitive bias that comes from a self-schema composed by memories related to body size, shape and eating behaviour. The model assumes that cognitive biases occur without conscious awareness and that the person experiences the cognition as "real". Besides, negative emotions interact with the self-schema to increase the probability of certain cognitive biases of body image.

2.2.4. Objectification Perspective

The objectification perspective (Fredrickson and Roberts 1997) focuses on women, and considers that women's body dissatisfaction is not an individual pathology but a systematic social phenomenon. Western societies construct a duality between mind and body where women are associated with the body and men with the mind. Besides men's bodies are defined as the standard, against which women's bodies are compared (e.g. the body considered attractive by the media is slim and muscular, which is a more common body type in men than in women). This social construction impacts girls and women, who learn that they are judged by how they appear to others and encourages them to view their bodies as objects to be watched.

2.2.5. Positive Body Image Perspective

Positive body image perspective aims to enable people to recognize their strengths and nurture them (Tylka and Wood-Barcalow 2015). It tends to take the view that positive body image is not just the inverse of negative body image but has unique elements that require understanding (Tylka 2011). This elements are: having a favorable opinion of the body irrespective of its actual appearance; acceptance of the body in spite of weight, imperfections and body shape; respect for the body involving engaging in healthy behaviours and responding to its needs; and rejection of media imagery, which helps to protect the body.

2.3. OBESITY STIGMA

Obesity or weight stigma is defined as the social devaluation and denigration of people perceived to carry excess weight that leads to prejudice, negative stereotyping and discrimination toward those people (Tomiyama 2014). Negative attitudes and inequities against people with obesity are widely spread in our society in many aspects of life, including employment, education, healthcare facilities, mass media, and even in interpersonal relationships with friends and family members. Nowadays the prevalence of weight discrimination is increasing. For example, according to Andreyeva et al. (2008), the prevalence of weight discrimination in US has reached similar levels to those of race and age discrimination.

Obese individuals are considered lazy, weak-willed, unsuccessful, unintelligent, lacking in self-discipline, poor will-powered. Furthermore, overweight and obesity are commonly considered to be under personal control, which make most people to attribute responsibility and blame to overweight or obese individuals for their weight status. This view is the prevailing message in the media as well as in general society. Besides, the fact that humans must eat everyday makes weight stigma unique, as eating itself may be a propitious situation for stigmatization and provides multiple, daily opportunities for suffering weight stigma (Tomiyama 2014). It is the internalization of this concept what could make obese people think that they are actually responsible for their body shape. However, this is not exactly this way, as there are many other significant contributors to obesity beyond the control of individuals, such as the important role of genetic and biological factors regulating body weight (Lee 2009) or the multiple social and economic influences that have significantly altered the environment to promote and reinforce obesity (Finkelstein, Ruhm, and Kosa 2005).

Fat stigma or weight discrimination has been associated with negative psychosocial outcomes such as low body satisfaction, depression, anxiety, low self-esteem, emotional eating, or psychological stress (Chondronikola et al. 2013; Barlösius and Philipps 2015). According to Tomiyama (2014), it may undermine weight loss attempts and in some cases can even contribute to increase weight gain.

2.4. BODY IMAGE (DIS)SATISFACTION

Body image satisfaction or dissatisfaction depends on the experience of body as a social and cultural construct. The level of satisfaction is influenced by many factors, however the most important one would be the way the body is experienced and evaluated by the subject himself. Grogan (2017) defined body image dissatisfaction as a person's negative thoughts and feelings about his or her body. Thus, dissatisfaction with the own body image appears when there is a discrepancy between the biological characteristics of the body and the satisfaction towards them.

As the perceptual component of body image refers mainly to body size (Neagu 2015), distortion between the perceived and desired body size as well as between the actual and perceived body size are of great importance in body image satisfaction or dissatisfaction. Indeed, both concepts are considered predictor factors in the development of eating disorders such as anorexia, bulimia or binge eating disorder.

However, body dissatisfaction is not a phenomenon unique to those with eating disorders or obesity; normal weight individuals are also becoming increasingly dissatisfied with their body image (Padgett and Biro 2003). Subjects with a body image disorder manifest upsetting preoccupation with their appearance, unrealistically believe their appearance proves something negative about their personal worth, avoid too many social situations because of their weight, and are overly concern about hiding their body.

Although almost everyone is exposed to social prejudices about obesity, not all of them develop body image dissatisfaction. In agreement with Rosen (2013), having good experiences in sports or receive positive self-esteem messages from family or friends, such as "Accept yourself for who you are", are associated with positive body image, whereas being teased or persuaded by parents to lose weight is associated with negative body image.

3. THE OBESITY EPIDEMIC

3.1. DEFINITION AND TRENDS

World Health Organization (World Health Organization 2016b) defines overweight and obesity as abnormal or excessive fat accumulation that may impair health. Obesity is caused by a positive energy balance, when energy intake exceeds energy expenditure. The consequence of this imbalance, is an increase in body mass when the energy excess is stored as fat, generally in the adipose tissue (Hill, Wyatt, and Peters 2012). Differences between overweight and obesity are due exclusively to the amount of stored fat. Accordingly, obesity would suppose a higher accumulation of fat than overweight.

As mentioned above, the use of direct measures of body fat in living populations or in epidemiological studies is unfeasible. Nowadays, the most widely spread method to measure the excess of fat in adults, is the body mass index (BMI), which is based on simple measurements of weight and height. Even though this index cannot distinguish between FM or FFM, it is reasonably well correlated with total body fat in adult humans (Deurenberg, Weststrate, and Seidell 1991; Romero-Corral et al. 2008). Besides, it allows us to classify the excessive fat storage into different nutritional categories based on epidemiological data indicating the risk of morbidity and premature mortality. On that basis, overweight is defined as a BMI from 25 kg/m^2 to 29.9 kg/m^2 as it is around these values where health risks usually begin to increase; whereas obesity is defined as a BMI of 30 kg/m^2 or above where health risks are further increased.

3.1.1. Adipose tissue

The principal characteristic of obesity is an excess accumulation of adipose tissue. Due to this and in order to understand its influence in obesity condition, it is important to know the characteristics and physiological functions of this tissue. Historically the adipose tissue has been considered exclusively an inert depot that stores fat; however, nowadays it is known that it is also a metabolically active endocrine organ that is involved in the regulation of glucose and lipid metabolism, insulin sensitivity, inflammatory response, non-shivering thermogenesis, and vascular endothelial function (Kwok, Lam, and Xu 2016).

Adipose tissue is considered a specialized connective tissue that consists mainly of adipocytes surrounded by a matrix of collagen. This tissue contains blood vessels, nerves, and the usual complement of connective tissue cells. In mammals, there are two main types of adipose tissue that differ in morphology and function: white adipose tissue (WAT) and brown adipose tissue (BAT).

Adipocytes from BAT are characterized by a relatively abundant cytoplasm with several lipid droplets, a round nucleus, and many mitochondria (Coelho, Oliveira, and Fernandes 2013). This tissue is specialized in producing heat (thermogenesis) by the oxidation of fatty acids through the action of uncoupled protein 1 (UCP-1), in mitochondria. The high amount of these organelles (mitochondria) together with the dense vascularisation of this tissue, are responsible of its typical brown colour. In humans, BAT deposits are presented principally in new-born infants, situated mostly on the back between scapulas and around the neck (Figure 1.3). The principal role of BAT is thought to be related to non-shivering thermogenesis, which is an adaptive response to the transition from uterus, considered a warm environment, to the cold outside environment (Cannon and Nedergaard 2004; Symonds, Pope, and Budge 2015). BAT was considered to be practically absent in adults until Nedergaard et al. (2007) pointed to the presence of functional BAT in adults too. Nowadays it is known that the capacity of BAT to oxidize fatty acids and glucose without ATP production could be stimulated by cold exposure (u Din et al. 2016), which contributes to energy expenditure and glucose homoeostasis. Due to this, BAT has been considered in many studies as a new target in the fight against obesity (Poekes, Lanthier, and Leclercq 2015).

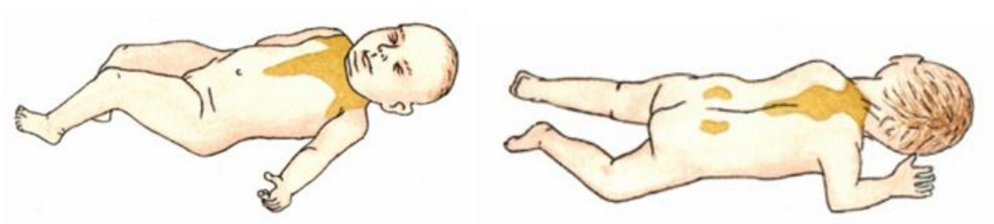

Figure 1.3. BAT distribution in new-born and children

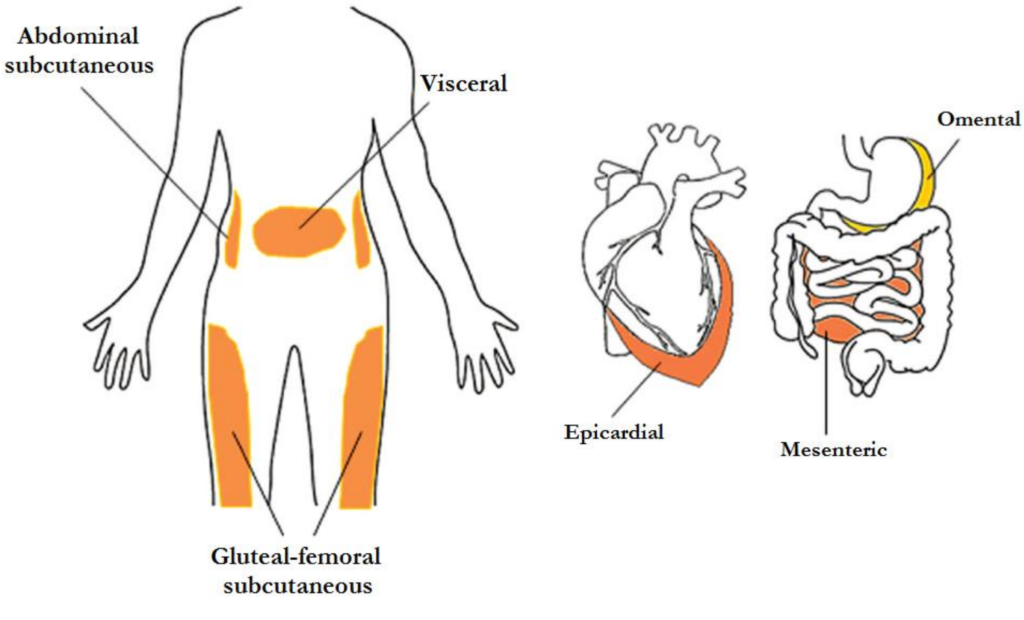

Figure 1.4. WAT distribution. Source: Kwok et al.(2016).

The principal features of adipocytes in WAT are the single large central lipid drop encircled by a peripheral thin circumference of cytoplasm and a flattened nucleus located peripherally (Ahmad and Imam 2016; Sorisky 2017). WAT is widely distributed in human body. It is located subcutaneously principally in the abdominal and gluteo-femoral regions, as well as in the visceral region (omental, mesenteric and epicardial regions) (Kwok, Lam, and Xu 2016) (Figure 1.4). Functional capacities of WAT are extensive. It provides mechanical protection against external impacts and work as an excellent thermal insulator participating in the maintenance of a stable body temperature. However, the primary role of WAT is to accumulate and provide energy when necessary through two metabolic processes called lipogenesis (process by which glycerol is esterified with free fatty acids to form triglyceride) and lipolysis (process by which triglycerides are hydrolyzed to free fatty acids and glycerol). These two processes are mediated by changes in diet as well as by hormonal signals. In short, in state of feeding, insulin allows the uptake of glucose from bloodstream to adipocytes; through glycolysis glycerol-3-phosfate is obtained, which is needed along with fatty acids from liver and chylomicrons to form lipid drops of triacylglycerols. On the other hand, in fasting state, lipase is activated for lipolysis and the resulted free fatty acids travel to other organs in order to be oxidized and get energy (Coelho, Oliveira, and Fernandes 2013).

However, due to the establishment of the adipose tissue as an endocrine organ, when leptin was identified and characterized by Zhang et al. (1994), adipose tissue is also considered now as one of the largest endocrine tissues in human beings, which is implicated in multiple functions. WAT secretes many hormones, growth factors, enzymes, cytokines, and complement factors that work as endocrine, paracrine and autocrine signals and influence the response of many tissues. It also expresses receptors for most of these factors which gives it an important role on regulating processes such as food intake, energy expenditure, metabolism homeostasis, immunity or blood pressure homeostasis (Coelho, Oliveira, and Fernandes 2013). It is important to highlight the heterogeneity of WAT in order to understand obesity related diseases. Subcutaneous and visceral adipose tissues present some differences, mostly related to their unique adipocytokines production profile. For example subcutaneous fat presents greater synthesis of leptin and adiponectin, which show beneficial effects on insulin action and lipid metabolism; whereas visceral fat has higher concentrations of interleukin-6, which is associated with CVD.

Finally from another point of view, adipose tissue may be seen as a protection against detrimental disorders from obesity rather than the cause of them. However, when adipose tissue capacity is exceeded (due to an excess of fat accumulation or to a poor capacity of this tissue), fat is redistributed to skeletal muscle and liver and it is this ectopic fat what seems to underlies detrimental effects such as severe insulin resistance, fatty liver, diabetes or hypertriglyceridemia (Grundy 2015).

3.2. PREVALENCE OF OBESITY

As overweight and obesity are linked to many health risks, they have emerged as one of the most serious public health concerns in the 21st century. Indeed, according to the WHO (2016b), this condition was responsible of more deaths worldwide than underweight.

Prevalence of overweight and obesity has been increasing worldwide and it has more than doubled since 1980. The global nature of the obesity epidemic was formally recognized by a World Health Organization consultation in 1997 (World Health Organization 2000; Caballero 2007). Nowadays due to the increasing prevalence of obesity in many countries it is considered a global pandemic.

However, this rate of obesity increase has apparently slowed down over the last decade, particularly in some developed countries (Ng et al. 2014). For example, there is a recent study carried out in Swedish population (Bygdell et al. 2017) showing that this downward trend has begun.

3.2.1. <u>Prevalence of obesity worldwide</u>

According to WHO (2016b), in 2014 more than 1.9 billion adults were overweight, and of these over 600 million were obese. Prevalence of both, overweight and obesity has risen by 27.5% for adults between 1980 and 2013 (Ng et al. 2014). In 2014, 13% of adults aged 18 years and over were obese ($BMI \geq 30$ kg/m^2), 11% of men and 15% of women. Childhood obesity has also increased. In 2015, approximately over 42 million children under the age of 5 years were overweight or obese (World Health Organization 2016b). Obesity in children is particularly alarming, as it is associated with persistence of obesity in adulthood and with higher chances of premature death and disability in the future.

Although the prevalence of obesity has more than doubled between 1980 and 2014 (World Health Organization 2016b), according to the WHO (2014) estimations, there are extreme differences between countries in the prevalence of obesity. The highest prevalence of obesity is observed in Pacific island populations with rates exceeding 40% in males and

50% in females. Beyond this, prevalence of obesity usually increases with the income level of countries. As it can be seen in Figure 1.5 and Figure 1.6, there are high percentages of obesity in oil-rich Arabian Countries, such as Qatar (39.4%), Kuwait (37.8%) or United Arab Emirates (34.45%), as well as in United States of America (34.25%) or New Zealand (29.15%). There are also relatively high percentages of obesity in Central and South America, such as Mexico (28.05%) or Argentina (28.4%). In Europe, obesity rates vary markedly from country to country. However, according to Gallus et al. (2015), northern countries have the highest obesity prevalence, such as United Kingdom (27.3%); whereas Western/Southern European countries have the lowest prevalence of obesity, such as Italy (21.5%) or France (21.95%), low obesity rates in these countries could be explained by the Mediterranean dietary habits (Schroder et al. 2004). On the other hand, there are some countries worldwide, such as Japan, that do not follow the worldwide trend and no remarkable increase on obesity prevalence has been observed (3.35%).

As it could be seen in Figure 1.5 and Figure 1.6, Asian and the African Sub-Saharan countries, present some of the lowest rates of obesity, with the exception of South Africa (26.3%), where the obesity rates in black women often exceed 30%. Some examples of low obesity rates in Africa would be Burundi (3%), Ethiopia (3.6%) or Rwanda (3.75%). And in Asia: Timor-Leste (1.95%), Vietnam (2.45%) or Republic of Korea (2.85%) (World Health Organization 2014).

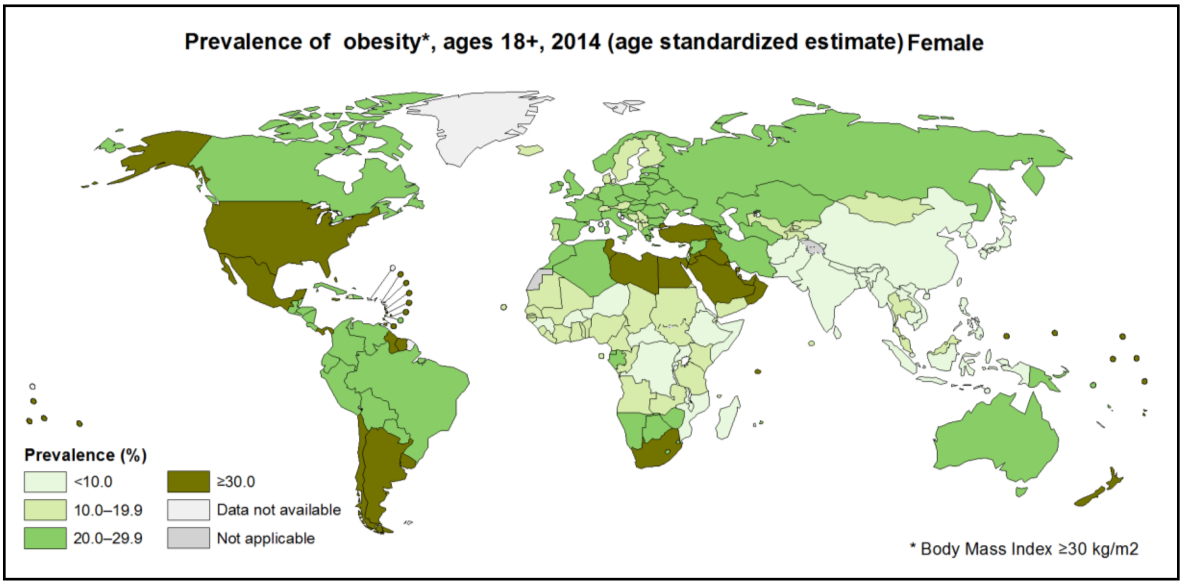

Figure 1.5. Prevalence of obesity in adult women. Source: World Health Organization (World Health Organization 2014)

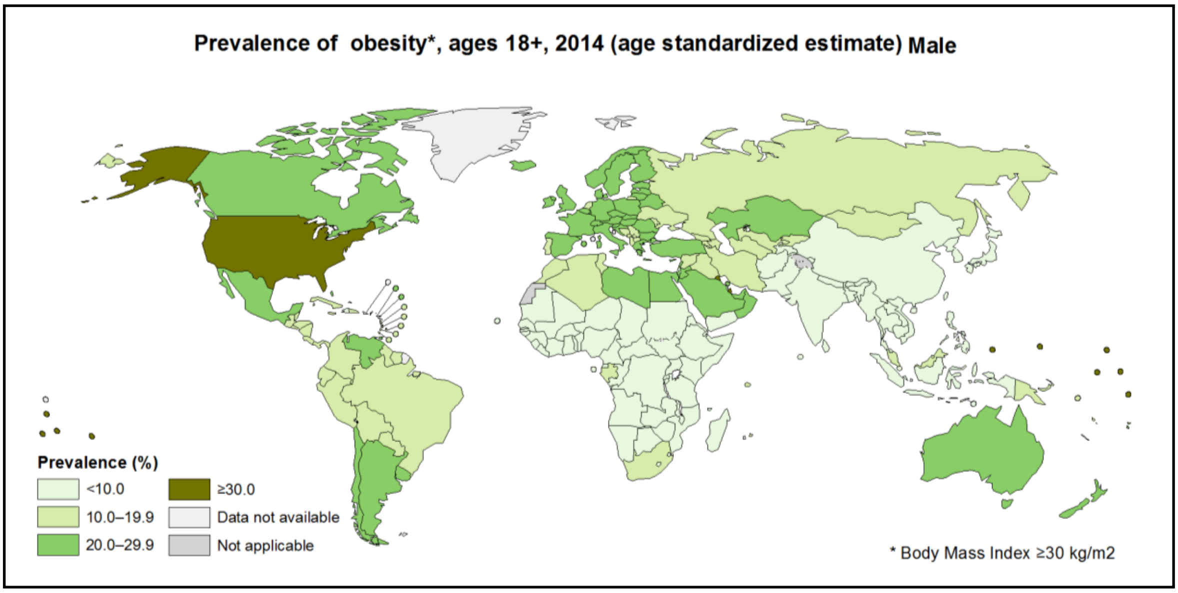

Figure 1.6. Prevalence of obesity in adult men. Source: World Health Organization (World Health Organization 2014)

3.2.2. Prevalence of obesity in Spain

Obesity rate in Spain is situated in an intermediate position in relation to world's obesity prevalence; between countries with low obesity rates (e.g. Italy), and countries with high obesity rates (e.g. EE.UU.). According to the ENRICA study (2008-2010), in Spanish adult population (≥18 years), the prevalence of overweight was 39.4% (46.4% in men and 32.5% in women), and the prevalence of obesity was 22.9% (24.4% in men and 21.4% in women) (Gutiérrez-Fisac et al. 2012). Overweight rate was very similar to the one estimated by DORICA study in 2004 (39.2%), but from that date, obesity rate has apparently increased as the obesity prevalence estimated in DORICA (in 2004) was 15.56% (Aranceta-Bartrina et al. 2005; Rubio et al. 2007).

DORICA study divided Spain in eight regions (Northwest, North, Northeast, Central, East, Murcia, South and Canarias). According to this, some geographic differences could be observed. There are high obesity proportions in the Autonomous Communities of north-west and south of Spain (Figure 1.7); whereas the Basque Country, together with the Autonomous Communities of north and northeast regions, presents the lowest proportion of obesity (Aranceta-Bartrina et al. 2005). These regional variations in the Spanish obesity prevalence (mainly observed in a north-south gradient) were traditionally explained by differences in the socioeconomic level, which is lower in Canary Islands and Southern Spain than in other regions of Spain (Gutiérrez-Fisac et al. 1999).

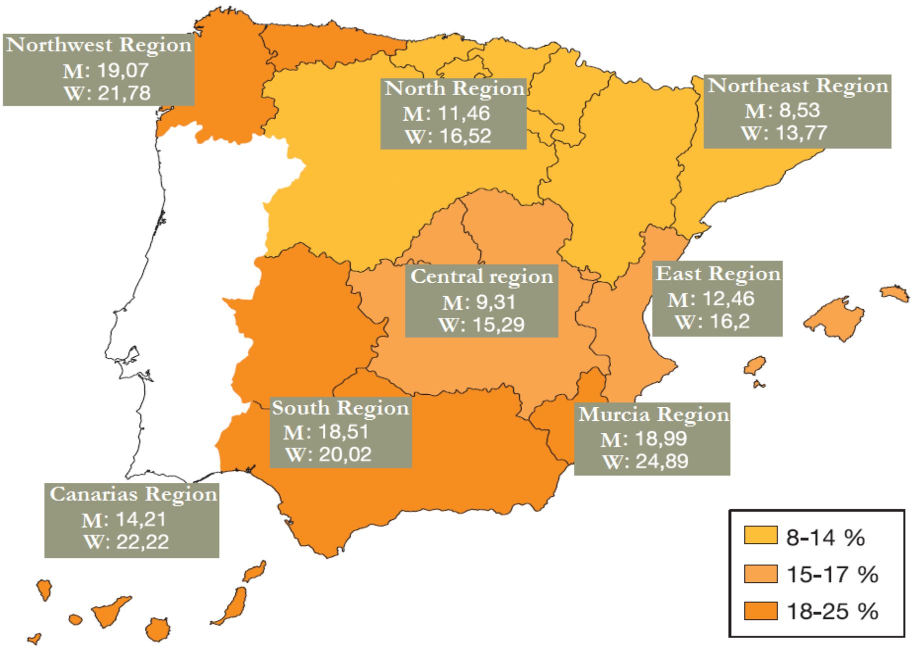

Figure 1.7. Prevalence of obesity in different regions of Spain. Source: Modified from Aranceta-Bartrina et al. (2005)

3.3. CAUSES OF OBESITY

Obesity is caused by a positive energy balance prolonged in time, thus from a simple perspective, it would be easy to think that obesity is the result of an over-consumption of calories relative to the amount of calories needed by the body to live. However, the aetiology of obesity is more complicated, as it is known that most adults present a relatively stable body weight in spite of the daily variation in energy intake and expenditure. Body weight stability suggests active regulation in order to achieve homeostatic control of weight, but the increases of overweight and obesity rates in the last decades indicate the inability to regulate body weight beyond a fixed point (Keijer et al. 2014). Many factors may favour this positive energy balance.

3.3.1. <u>Environmental causes of obesity</u>

Diet and exercise

Total daily energy expenditure (TEE) is mainly the sum of three basic components: resting metabolic rate (RMR), which is the amount of energy necessary to maintain normal physiological functions when the body is at rest; the thermal effect of food (TEF), which is the amount of energy consumed during the digestion, absorption, and metabolism of nutrients; and activity energy expenditure (AEE), which is the amount of energy necessary to physical exertion (Panini 2013). Among them, AEE is the only component of TEE that is under voluntary control; due to this it is a very important aspect of body weight regulation. AEE is further subdivided in two components: exercise activity thermogenesis (EAT), which corresponds to active exercise; and non-exercise activity thermogenesis (NEAT), which represent the energy expenditure associated to free-living daily activities (von Loeffelholz 2000; Levine et al. 2008; Hamasaki et al. 2015). According to von Loeffelholz (2000), EAT is a small contributor to TEE variance, since at industrialized countries the level of exercise is generally very low, while NEAT is the main component of daily activity thermogenesis and varies by up to 2000 kcal/day between subjects (Hamasaki, Ezaki, and Yanai 2016). Anyway, the contribution of EAT and NEAT to the total AEE may differ from one individual to another and may play different roles in obesity development.

Increases in physical activity will stimulate energy expenditure and favour a negative energy balance. In addition physical exercise will specifically enhance fat oxidation, which can help to reduce fat deposits. However, westernized societies present a sedentary physical activity pattern characterized by the use of cars, labour-saving devices, many sedentary jobs and sedentary leisure time such as television or computer games.

Usually, when physical activity levels decrease, appetite and consequently calories intake will spontaneously reduce as well (Moore and Pi-Sunyer 2012). However, other factors especially in industrialized countries may interfere with this physiological regulation of appetite by stimulating the ingestion of high amounts of calories. Palatability was identified by the WHO as one of the most powerful influences in inducing calories overconsumption. Fat is a major contributor to food palatability, thus some combinations of fat and sugar or fat and salt have been proposed as particularly palatable, and encourage individuals to further consumption (Moore and Pi-Sunyer 2012). As fat (9 kcal/g) contains more than twice the calories of carbohydrate (4 kcal/g) or protein (4 kcal/g), it makes that the most delicious foods are precisely the most caloric ones. Besides, sugar-sweetened beverages and the increasing portion sizes are ones of the many external cues that promote overeating in our societies.

Psychological factors

The connection between body weight and mental disorders remain still unclear (Lykouras and Michopoulos 2011). However, some psychopathologies such as stress, anxiety, and depression have been associated with body weight (Egger and Dixon 2014). Psychopathologies can be both, the cause or the consequence of obesity, and in many cases they show a bidirectional relationship between each other. In some cases, individuals may develop dysfunctional strategies to deal with emotional problems, developing abnormal eating behaviour instead of a proper emotional regulation, which may lead to weight gain (Lazarevich, Irigoyen-Camacho, and Velázquez-Alva 2013).

Pharmaceutically induced weight gain

Weight gain and hunger are also associated with some of the most commonly used medications (Egger and Dixon 2014), including psychotropic medications, diabetic treatments, antihypertensives, steroid hormones and contraceptives, antihistamines, and protease inhibitors (Wright and Aronne 2012). The full contribution of prescribed legal drugs to the obesity epidemic remains difficult to estimate. However, the significant weight gain caused by some of the most widely prescribed medications supports the hypothesis of the drug-induced weight gain (Wright and Aronne 2012).

Alcohol and tobacco consumption

On the other hand, there are some licit drugs, mainly alcohol and tobacco that, for different reasons, could lead to weight gain. Large amount of extra calories are consumed when large amount of alcohol (7.1kcal/gr.) is ingested (Suter and Tremblay 2005), or when the cigarette craving supposes an increase of food intake (Ogden and Fox 1994). Besides, interaction of alcohol and tobacco consumption with body metabolism regulation could be implicated in body composition changes and obesity (Harris, Zopey, and Friedman 2016).

Sleep debt

Sleep is a state of restorative resting characterized by altered consciousness, decreased sensory activity, cessation of any voluntary movement and reduced response to stimuli. In today's modern society, along with obesity increase, there has been a reduction in the duration and quality of sleep (Bayon et al. 2014). According to different studies (Cappuccio et al. 2008), sleep deprivation has been associated with obesity.

Sleep reduction or deprivation may modify the secretion of several hormones involved in body metabolism and energy balance (Bayon et al. 2014). For example a reduction of leptin and an increase of ghrelin have been observed during sleep restriction (Stern et al. 2014; Broussard et al. 2016). The imbalance between these hormones involved in the control of feeding, may explain changes in hunger (Bayon et al. 2014). In addition, sleep restriction may suppose more time to eat and a decrease in energy expenditure (Knutson et al. 2007).

Socioeconomic Factors

In developed countries, obesity prevalence is influenced by socioeconomic level, with lower rates of obesity in high socioeconomic levels. For example in US and Canada, lower socioeconomic levels present higher obesity prevalence than more elevated socioeconomic levels (Siddiqi et al. 2015). Lower SES groups, due to limited financial resources, have easier access to cheaper food high in energy density, which could contribute to excess weight, instead of healthier but more expensive food (Conklin et al. 2013). In addition the access to supportive environments that encourage physical activity are also limited among these groups (Nogueira et al. 2013).

Other contextual environmental factors

According to Williams et al. (2015) there are some features in the urban environment that could influence body size and weight, such as walkability, presence of sidewalks, proximity to green space, and traffic density. Besides, some physiological and behavioural changes, such as increased hunger, have been attributed to small pollution particles as well as to a wide range of chemicals in the air, water, soil, and households (Egger and Dixon 2014).

There are also some sociocultural influences and traditions that last from historical times, which have been related to obesity development. Although these traditions could have been suitable in those moments, they are not compatible in a western culture any more. For example, some cultural practices that serve to promote social connection between family, friends or workmates, such as feasting, are often characterized by low-nutrient but high-caloric foods (Egger and Dixon 2014). Social relationships may also contribute to obesity epidemic. In their review Pachucki and Goodman (2015) indicate that a person's chance of becoming obese increases if he or she had a friend, a sibling or a marriage couple who had become obese.

In their book "Planet Obesity: How We Are Eating Ourselves and the Planet to Death", Swinburn and Egger (2011) explain how the modern unrestrained economic growth model (characterized by "over-consumption") could be the underlying cause of obesity. Indeed, this hypothesis is supported by global data where it could be seen how as a country develops economically its population becomes fatter (Egger, Swinburn, and Islam 2012).

3.3.2. Genetic causes of obesity

Apart from environmental factors, genetics is also a major contributor in obesity development. Indeed, there are several studies that reveal moderate to high heritability for BMI and other fat related measures (Pena et al. 2014). A number of genetic variants have been associated with common forms of obesity and there is also a group of rare genetic syndromes or disorders that result in monogenic forms of obesity. These facts highlight the influence of genetics in obesity.

Monogenic forms of obesity

Monogenic forms of obesity are originated from a single dysfunctional gene and are rare among population. Some of this obesity cases are part of a syndrome and occur associated with other clinical phenotypes, such as, for example, WAGR, Prader-Willi, Bardet-Bield, Altröm and Cohen syndromes (Bray and Bouchard 2014; Albuquerque et al. 2015). Additionally, there are also non-syndromic forms of monogenic obesity due to autosomal recessive or dominant mutations that are involved in the control of food intake (González Jiménez et al. 2012). Some well-known genes implicated in this kind of monogenic obesity are: LEP, LEPR, POMC, PCSK1, MC4R, BDNF, NTRK2 and SIM1 (Albuquerque et al. 2015).

Polygenic (or common) obesity

On the other hand, common obesity is considered a polygenic disease where each DNA polymorphism required the additional presence of other variants as well as environmental factors to develop obesity.

One of the most widely known hypotheses with genetic base to explain the increase in common obesity prevalence in the last decades is the so called "thrifty genotype" hypothesis. According to this hypothesis, some specific alleles were historically advantageous as could have helped individuals to extract and store energy during food abundance periods in order to increase survival chances in times of famine. Nowadays, in societies where food availability is not a problem anymore, these alleles would be responsible of obese phenotypes (Neel 1962).

3.3.2.1. Genetic study of common obesity

Common obesity (usually estimated through BMI) is a polygenic and multifactorial trait with continuous distribution in natural populations. Two individuals may be differentiated in smaller or greater degree in relation to traits that follow this kind of distribution, but taken the whole population together the entire spectrum of trait (obesity in our case) will be covered. These features can be measured on a metric scale and its distribution is often approximated to statistical normal distribution.

For a long time it was thought that traits with discrete or continuous distributions were defined by different laws in nature, until 1918 when Sir Ronald Fisher integrated Mendel's law into the transmission of continuous traits (in such a way that Mendel's law were no longer exclusive of discrete traits).

The continuous distribution of these traits is due to genetic and environmental factors. Its variance is controlled by multiple *loci*, where each allele often has a relatively small and additive effect over the trait. The effect of each gene can also be influenced by environmental factors (gene x environment interaction) as well as by genetic background (gene x gene interactions). Because of this complexity, in two different individuals, the same genotype may result in different phenotype and conversely different genotypes may provide the same phenotype.

A first step to understand the genetic contribution on complex traits is carried out with studies that make inference about the influences of the genes based on the phenotype distribution (e.g. heritability studies and complex segregation analyses). After confirming the significant contribution of genetic factors in a multifactorial trait, the next goal is the identification of the principal underlying genes (Bouchard, Malina, and Pérusse 1997; Lee, Gould, and Stinchcombe 2014). However, the discovery of any *locus* is very difficult since these kinds of qualities are influenced by many different genes with probably small effects.

In order to properly find genes implicated in quantitative traits variation, research approaches are focused on genetic mapping (Wu, Ma, and Casella 2007). These methods are based on the coinheritance of close DNA sequences and uses molecular markers, which are known sequences used to track a nearby gene that has not yet been identified. Markers could be of many different types, such as restriction fragment length polymorphisms (RFLP), microsatellites, also called simple sequence repeats (SSR), short tandem repeats (STR) or single nucleotide polymorphism (SNP) among others.

Two main approaches have been adopted in molecular dissection of complex phenotypes: linkage studies and association studies. The premise of linkage analysis is that the alleles of two *loci* will be more likely to be inherited together when they are physically close to each other (Cameron and Bogin 2012). In this sense, the chromosomal location of the gene influencing a trait is searched by monitoring co-segregation of several genetic markers with the trait in multi-generation families or extensive groups of sibpairs. On the other hand, association studies seek to identify particular variants associated with the phenotype at the population level and rely on the fact that particular DNA markers can remain together on ancestral haplotypes for several generations, leading to linkage disequilibrium (Bouchard and Bray 2004). These kinds of studies may be based principally on candidate gene approaches or in genome wide association scan (GWAS).

3.3.2.2. Molecular genetics of human obesity

In relation to the discovery of genetic factors that could predispose to obesity, first studies were mostly **genetic linkage studies** performed in families, which were used to identify wide genomic regions that might contain a disease gene, even in the absence of a previous biological hypothesis. Several chromosomal areas were linked with obesity by this method. In accordance with Bouchard (1997), by 1997 almost all chromosomes but 4 (chromosomes: 9, 18, 21 and Y) were represented in the obesity map. Unfortunately, the vast majority of these positive results were not confirmed in independent studies. Subsequently, **candidate gene studies** looked at variants in genes that already have an important implication in the pathogenesis of the disease, based in different criteria including a particular biological hypothesis or positive results performed in animal models. Some of the polymorphisms discovered by this method are in genes participating for example in dietary intake (i.e. *LEP*, *LEPR* or *MC4R*), in energy expenditure (i.e. *UCP2* or *ADBR3*) or in adipose tissue growth and development (i.e. *PPARG*) (Moleres, Martinez, and Marti 2013). However, this approach was limited to a previous knowledge about the gene function, so a more global and non-hypothesis approach was necessary. Finally, **GWAS** allowed scientists to scan associations between a wide range of single nucleotide polymorphisms (SNPs), spread all over the human genome, and a given phenotype, without any prior knowledge of their function. This last technique has turned out to be a very successful approach and many variants associated with obesity have been discovered through this method. The first obesity associated gene identified through GWAS was the fat mass and obesity associated gene" (*FTO*) (Dina et al. 2007; Frayling et al. 2007; Scuteri et al. 2007), which was associated with BMI, hip circumference and body weight. Since then several further studies have replicated the association of different variants of this gene (*FTO*) with polygenic obesity, especially in European derived populations (e.g. Peeters et al. 2008). Later studies identified additional genes harbouring common SNPs that associate with obesity or obesity traits. In 2008, Loos et al. (2008) established common variants near *MC4R* that influence fat mass, weight and obesity; and in 2009, Willer et al. (2009) identified six additional *loci* as genome-wide significantly associated with BMI: *TMEM18*, *KCTD15*, *GNPDA2*, *SH2B1*, *MTCH2* and *NEGR1*. Thorleifsson et al. (2009) reported two additional new *loci*: *ETV5* and *BDNF*, and Speliotes et al. (2010) identified 18 new *loci* associated with BMI. By 2013, GWAS in populations of European ancestry have identified at least 54 obesity-susceptibility *loci* (Lu and Loos 2013). And later, Locke et al. (2015) identify 97 *loci* associated with BMI. Nevertheless, most polymorphisms variants associated with obesity or obesity related traits have relatively small effect sizes and explain a relatively little obesity genetic variation. Therefore, it is possible that many variants influencing obesity, with small effect sizes, which have not reach genome-wide significance, were still undetected; in addition to other sources of variation, such as gene-gene or gene-environment interactions, copy number variation or epigenetic effects, that should be included in those models (Peterson et al. 2011).

3.4. CONSEQUENCES OF OBESITY

3.4.1. Health consequences

Obesity is a major risk factor for numerous adverse health outcomes such as: cardiovascular diseases, hypertension, type 2 diabetes, some types of cancers or musculoskeletal disorders among others, which have important impact on the public health.

Cardiovascular diseases

Cardiovascular disease (CVD) is the primary cause of death globally (World Health Organization 2016a) and it includes conditions such as hypertension, coronary heart disease or stroke. Cardiovascular function may be compromised by obesity. The expansion of adipose and lean tissues associated with obesity (Ibáñez et al. 2014), increases total body oxygen consumption, which in turn increases the total volume of blood and the cardiac output (Kopelman 2000). This may lead to structural changes in heart, which in some cases may progress to heart failure.

Hypertension is defined as elevated blood pressure, which is the measure of the strength that the heart requires to pump blood around the body. It is a treatable condition; however it is difficult to notice and when it is left untreated, it can increase the risk of many other severe conditions such as coronary heart disease (CHD) or strokes. Blood pressure is very susceptible to changes in body weight but the exact mechanism through which obesity causes hypertension is yet unknown. Hyperinsulinemia and increased activity of the sympathetic nervous system in obese individuals could be implicated in some of these hypertension development pathways (Neter et al. 2003).

Congestive cardiac failure, especially in the presence of left ventricular hypertrophy (due to hypertension), increases the risks of morbidity and mortality from CHD (Kahan and Bergfeldt 2005). It is, indeed, the leading cause of morbidity and mortality among adults in Europe and North America (Wilson et al. 1998). Several epidemiological studies have revealed that coronary heart diseases (CHD) are more likely between overweight or obese adults than between their leaner peers. Hyperlipidaemia (especially with high levels of low density lipoproteins cholesterol (LDL-C)) is also one of the mechanisms through which obesity increases the risk of CHD (Bray 1996), as it contributes to the formation of atherosclerosis.

Type 2 Diabetes

According to the WHO (2016c), diabetes is a metabolic disorder that occurs either when the pancreas does not generate enough insulin, or when the body cannot efficiently use this insulin, which lead to high levels of glucose in blood (hyperglycaemia). There are three main types of diabetes: Type 1 diabetes, Type 2 diabetes and Gestational diabetes, but the vast majority of the world diabetes cases are Type 2 diabetes (World Health Organization. 2016c).

Obesity is one of the most important risk factors for developing Type 2 Diabetes (Schienkiewitz et al. 2006) as overall fatness influences glucose metabolism. However, body fat distribution is also very important as abdominal adipose tissue presents usually a more marked response toward lipolytic stimuli such as catecholamines (noradrenaline) than gluteal and femoral fat (Nielsen et al. 2014). An elevated release of free fatty acids due to high lipolysis, contribute to hepatic glucose release (via gluconeogenesis), and inhibits insulin uptake by the liver, which lead to a down-regulation of insulin receptors and the subsequent decrease of skeletal insulin sensitivity. Initially it could be a compensatory hiperinsulinemia but eventually, the compensatory mechanism does not work anymore and hyperglycemia appears (Kopelman 2000).

Diabetes increases the risk for developing heart disease, stroke, blindness, neuropathy, kidney disease and amputations (Nayak et al. 2014).

Respiratory dysfunction

The increased amount of fat in chest and abdomen observed in obese individuals, leads to a reduction of the lung volume and alters ventilation pattern. An extra respiratory muscle force is needed to compensate the extra FM in these individuals. All this is particularly important when the person lies down (Kopelman 2000). During sleep voluntary muscle tone is decreased, especially in obese individuals where irregular respiration and occasional apnoeic episodes are more frequent than in lean individuals. All this may drive to a reduction in arterial oxygen saturation and to an increase in carbon dioxide (severe hypoxia) in addition to cardiac arrhythmias (Kopelman 2000).

Cancers

According to the National Cancer Institute (NCI 2015), cancer is the summarizing name for a collection of related diseases characterized by the division without stopping of body cells and its spread into surrounding tissues. Numerous epidemiological studies have shown that excessive weight is associated with an increased risk of different varieties of cancer, including oesophagus, pancreas, colon and rectum, breast (post-menopause), endometrium, and kidney (World Cancer Research Fund. American Institute for Cancer Research 2007)

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There are many mechanisms proposed for explaining the development of obesity related cancer. One of these mechanisms is related with inflammation and angiogenesis. Development and growth of adipose tissue requires new blood vessels supply (angiogenesis), for this purpose adipose tissue generates several angiogenic and angiostatic factors that confer plasticity to adipose vasculature. Furthermore, obesity has been considered a chronic inflammatory condition. The hypoxia found in the adipose tissue of many obese individuals is a common stimulus for chronic inflammation and angiogenesis (Tahergorabi et al. 2016). These processes were also suggested to be involved in tumour biology and progression (Jain 2013).

Alterations in hormone production by obese individuals may also play a role in cancer development. It is now accepted that adipose tissue works, in part, as an endocrine organ. Different mechanism could be implicated according to the type of cancer. For example, high amounts of adipose tissue increases oestrogen levels in obese individuals, which may be involved in the development of some kinds of sex-dependent cancers such as breast, endometrium or prostate (Tahergorabi et al. 2016). In addition, elevated insulin levels associated with obesity reduce apoptosis and promote cell growth, which are implicated in cancer development (González Svatetz and Goday Arno 2015). Several cytokines, such as some interleukins or tumour necrosis factor α (TNFα), related with the chronic inflammatory process in obesity are also related with insulin resistance and apoptosis, and thus, with cancer. Finally, leptin is a hormone secreted by subcutaneous adipose tissue with a key role in the regulation of food intake and energy balance. However, it is also a potent angiogenic factor that acts through with mitogenic, antiapoptotic and proinflamatory properties contributing to carcinogenesis (Tahergorabi et al. 2016).

Gallstones (Gall bladder disease)

Gallstones are hardened deposits usually made of undissolved cholesterol or bilirubin. They could be very painful but some of them could be asymptomatic; however, if any stone accommodates in a duct it can lead to inflammation in the gallbladder, the ducts or even the liver, which can have severe consequences (Wadden and Stunkard 2002).

They could be formed in both lean and obese individuals and are more common in women; however obesity is a strong factor associated with the development of cholesterol gallstones. In obese individuals hepatic secretion of cholesterol is increased and gallbladder motility is impaired, thus bile saturates with cholesterol, which contributed to the aggregation of solid cholesterol crystals and stones growth (Bonfrate et al. 2014). In addition, rapid weight lost increases the risk of gallstones development due to high amounts of biliary cholesterol secretion and reduced biliary bile salts.

Osteoarthritis (Musculoskeletal diseases)

Osteoarthritis is a rheumatic disease characterized by the degeneration of cartilage in joints. In the absence of cartilage, bones rub together, which makes osteoarthritis considerably painful. Compared with normal weight individuals, subjects with obesity present more severe joint deterioration (Bliddal, Leeds, and Christensen 2014) since an excessive body weight involves additional pressure on the joints. Due to this, the most common sites for osteoarthritis development are the joints that support body weight such as knees, hips or spine. However, along with the development of obesity prevalence, an increase of osteoarthritis in sites that do not bear body weight such as hands or mandible has also been observed (Sartori-Cintra, Aikawa, and Cintra 2014). This indicates that other mechanisms related with obesity are also implicated in osteoarthritis development (Sartori-Cintra, Aikawa, and Cintra 2014). Indeed, leptin and other inflammatory cytokines secreted by adipose tissue are involved in the inflammatory process of joints that lead to osteoarthritis.

Osteoarthritis development in obesity is of great importance since it can initiate a vicious cycle: osteoarthritis reduces mobility, which may cause weight gain (due to a lack of energy expenditure), and this in turn increased joint problems. (Bliddal, Leeds, and Christensen 2014).

Non-alcoholic fatty liver disease (NAFLD)

The principal characteristic of this disease is steatosis (fatty infiltration of the liver). It is related to inflammatory changes and fibrosis (steatohepatitis), which can progress into cirrhosis and hepatocellular carcinoma (Cotrim et al. 2016). It is important to note that individuals with this condition do not have a history of alcohol abuse or other hepatic diseases to explain the steatosis.

Although it is common that NAFLD go undetected for years before the first appearance of symptoms, it is know that its prevalence has grown parallel to obesity development in this society. However its pathogenesis is still controversial. According to Barros et al. (2016), NAFLD is not directly related to patient size (weight or BMI), but its relation with obesity is probably due to some shared comorbidities. For example some characteristics such as excess of adipocytes, altered metabolism or insulin resistance are common in both conditions.

Dyslipidaemia

Obesity has been typically related to increased rates of dyslipidaemia, which is characterized by increased triglycerides (TG) and free fatty acids (FFA), decreased high-density lipoprotein cholesterol (HDL-C) and slightly increased low-density lipoprotein cholesterol (LDL-C) (elevated LDL-C/HDL-C ratio), it has also been observed increased concentration of plasma apolipoprotein B (Apo B) (Klop, Elte, and Cabezas 2013). These lipid and lipoprotein abnormalities characterized by the combination of high levels of TG and low levels of HDL were also known as atherogenic dyslipidaemia and support a causal relationship between the phenotype and atherosclerosis and CVD (Valensi et al. 2016; Xiao et al. 2016).

The pathophysiology of this condition in obese individuals involves hepatic overproduction of very low density lipoproteins (VLDL), decreased circulating TG lipolysis and impaired peripheral trapping of FFA, increased FFA fluxes from adipocytes to the liver and other tissues and the formation of small dense LDL (Klop, Elte, and Cabezas 2013).

Metabolic syndrome

Metabolic syndrome, also known as insulin resistance syndrome, is a common and complex disorder comprised of multiple interconnected factors that increase the risk of cardiovascular disease and type 2 diabetes. Its pathogenesis is complicated as it includes a great heterogeneity of features such as central adiposity, dyslipidaemia, atherosclerosis, insulin resistance or hypertension. Although all affected individuals do not need to have all the factors to develop this syndrome (Ricci et al. 2017), resistance to the action of insulin and central adiposity seem to be the key components of the metabolic syndrome (Kassi et al. 2011).

The clustering of these all closely related risk factors into the metabolic syndrome has become one of the major difficult challenges worldwide since there is not a clear concept to support and define this syndrome. Many different opinions have arisen related to metabolic syndrome, such as if it should be defined to mainly indicate insulin resistance, the metabolic consequences of obesity, risk for CVD, or simply as a collection of statistically related factors (Alberti, Zimmet, and Shaw 2005). However, due to its increasing prevalence and its importance in the design of novel therapeutic strategies, the metabolic syndrome remains under intense investigation.

Psychological problems

As mentioned above, there is a link between psychological problems and obesity which could be both the cause and the consequence of obesity. According to Lykouras and Michopoulos (2011), the way of thinking of obese patients is characterized by cognitive distortions such as dichotomous and catastrophic ways of thinking that could be connected with anxiety disorders.

3.4.2. Other consequences

Economic consequences of obesity

In addition to health consequences, overweight and obesity result in a significant economic impact in society. Indeed, as BMI increases, the healthcare costs also increase, as well as the cost due to the loss of productivity; in fact obesity account for much higher costs than overweight (Dee et al. 2014).

In order to properly analyse the cost associated to obesity it is usually necessary to separately consider direct costs, indirect costs and intangible costs. Direct costs refer mainly to medical and health services and consist mainly on prevention, diagnosis, and therapy, including among others, pharmaceuticals, physician, surgeon, and hospital costs (Moore and Pi-Sunyer 2012; Ricci et al. 2017). Indirect costs refer to the lack of wealth production due to both morbidity and mortality. It includes the value of income lost from the illness due to decreased productivity, absenteeism, bed days, early retirement or even the time relatives or caregivers devoted to health care; as well as the value of future income lost because of premature death (Moore and Pi-Sunyer 2012; Ricci et al. 2017). Finally intangible costs are difficult to estimate as they are related with pain, anxiety, physical, and psychological suffering of the patient and its relatives (Ricci et al. 2017). They might suppose missed opportunities, psychological problems and poorer quality of life.

Overweight and obesity prevalence as well as total healthcare expenditures vary widely across Europe. Due to this, it is difficult to establish the relative economic burden in this continent. However, according to a European letter against obesity signed by Akdag and Danzon (2006), overweight and obesity in adult population account for as much as 6% of total healthcare expenditure in the European Region. Furthermore, data from Vazquez and López (2002), indicate that the economic cost of obesity in Spain (direct and indirect) is about 7% of the total health cost.

Chapter II

Motivation, Hypothesis and Objectives

1. MOTIVATION, HYPOTHESIS AND OBJETIVES

Common obesity is a widespread condition in westernized countries; however, its incidence is variable between and within populations. Therefore, it is of great importance to study obesity in many different populations to help understand the underlying causes of this condition.

Obesity development is influenced by many modifiable and non-modifiable factors. Genetic profile, sex, age and environmental factors such as lifestyle (e.g. sleep patterns, physical activity), socioeconomic status (e.g. education, professional occupation) or psychological circumstances (e.g. body image perception and satisfaction) are considered key elements in obesity development, as they are involved in energy balance and adiposity accumulation.

Although common obesity is a widespread problem in industrialised populations, the research on this area is frequently complicated due to the difficulties of obtaining an adequate sample size. Obesity, due to its impact in health and physical appearance, is usually a highly stigmatized condition, which might limit the participation of obese individuals in epidemiologic studies. However, a well-represented obese sample is necessary in order to characterize all dimensions of the condition.

The general hypothesis of the present Thesis is that genetic factors, sex, age, environmental and psychological factors influence adiposity and energy expenditure and in turn are significantly associated with several phenotypes of overweight and obesity in the Basque Country population.

The **main objective** of the present work was to explore the role of different modifiable and non-modifiable factors in obesity aetiology from a bioanthropological approach. To achieve this major purpose some key factors, including body morphology and composition, body image, environmental context, and genetic profile were analysed and discussed in relation to obesity, in a sample from the Basque Country population based in a case-control design. The **specific aims** of this work were the following:

I. To determine the body morphology and composition of women and men of different ages in several nutritional categories **(Chapter IV)**.

II. To analyse the changes in body morphology and composition in relation to sex and age in different nutritional categories **(Chapter IV)**.

III. To analyse the changes in body morphology and composition in relation to sex and sport practice in each nutritional category **(Chapter IV)**.

IV. To determine sexual differences in body image perception, and satisfaction on the analysed population **(Chapter V)**.

V. To analyse the relation of body image perception and satisfaction with nutritional status **(Chapter V)**.

VI. To characterize the environmental context of obese and not obese individuals in a sample of the Basque Country population **(Chapter VI)**.

VII. To determine the relative effect of several environmental factors on obesity by using different obesity phenotypes **(Chapter VI)**.

VIII. To provide information about the frequencies of obesity-related single nucleotide polymorphisms (SNPs) in normal-weight and obese populations **(Chapter VII)**.

IX. To explore associations between some previously obesity-related SNPs and several obesity phenotypes as well as their association with some obesity related traits **(Chapter VII)**.

X. To explore association between some previously obesity-related SNPs with body morphology and composition (somatotype components) **(Chapter VII)**.

XI. To compare the results obtained on the analysed sample to those reported on other populations.

Chapter III

Materials and Methods

1. POPULATION SAMPLE

1.1. STUDY AREA

The sample used in the present study was recruited in the autonomous community of The Basque Country in Spain, more specifically in the province of Biscay (Bizkaia).

1.1.1. The Basque Country

The Basque Country is one of the 19 autonomous communities and cities of Spain, and is located in the northeast area of the Iberian Peninsula. Its surface area is 723,492 Ha (Eustat 2017) and comprises three provinces: Araba (304,179 Ha), Bizkaia (221.485 Ha) and Gipuzkoa (197.828 Ha) (Figure 3.1). The Basque Country borders the Bay of Biscay to the north, La Rioja to the south, Cantabria and Burgos provinces to the west and France and Navarre to the east.

Figure 3.1. Geographic location of the Basque Country. Source: Modified from Wikipedia. EspañaLoc.svg, de HansenBCN (Mutxamel).

The territory of the Basque Country has three distinct areas defined by two parallel ranges of mountains: the "Montes Vascos" and the "Sierra de Cantabria". These three differentiated areas, from north to south, are the Atlantic Basin, which is formed by many valleys with short rivers that flow from the mountains to the Bay of Biscay; the Middle section, which is principally occupied by a high plateau; and the Ebro Valley, which stretches from the southern mountains to the Ebro River.

There are also three climate areas (Figure 3.2). In the northern area, the climate is characterised by moderate temperatures and much rain (i.e. Atlantic climate), whereas in the southern area, the climate is characterised by hot and dry summers and cold winters with low rainfall (i.e. Mediterranean climate). In the middle area there is a transition between these two climate areas (Euskalmet 2011).

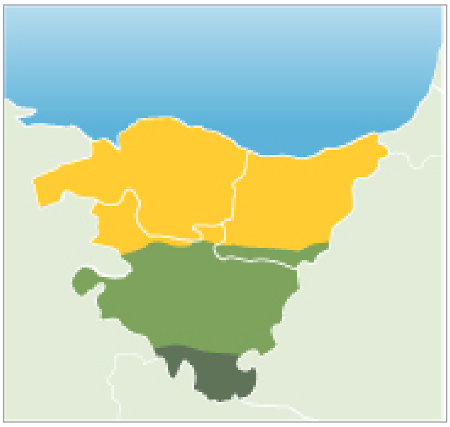


Figure 3.2. Climate zones of the Basque Country. Source: Basque meteorological agency (Euskalmet 2011).

The autonomous community of the Basque Country has a population of 2,171,886 inhabitants, with a slightly lower proportion of males (48.6%) than females (51.4%), and with a population density of 300.4 inhab/km^2 (Eustat 2017).

The Basque Country reflects the characteristics of an ageing population, where the number of people in their old age increases and the number of children decreases (Figure 3.3). Indeed, the percentage of population aged 65 or over is 21.1% while the percentage of population aged 19 or less is 18.1%. The Basque Country has also one of the lowest birth rates in Europe (8.9 births per 1,000 inhabitants).

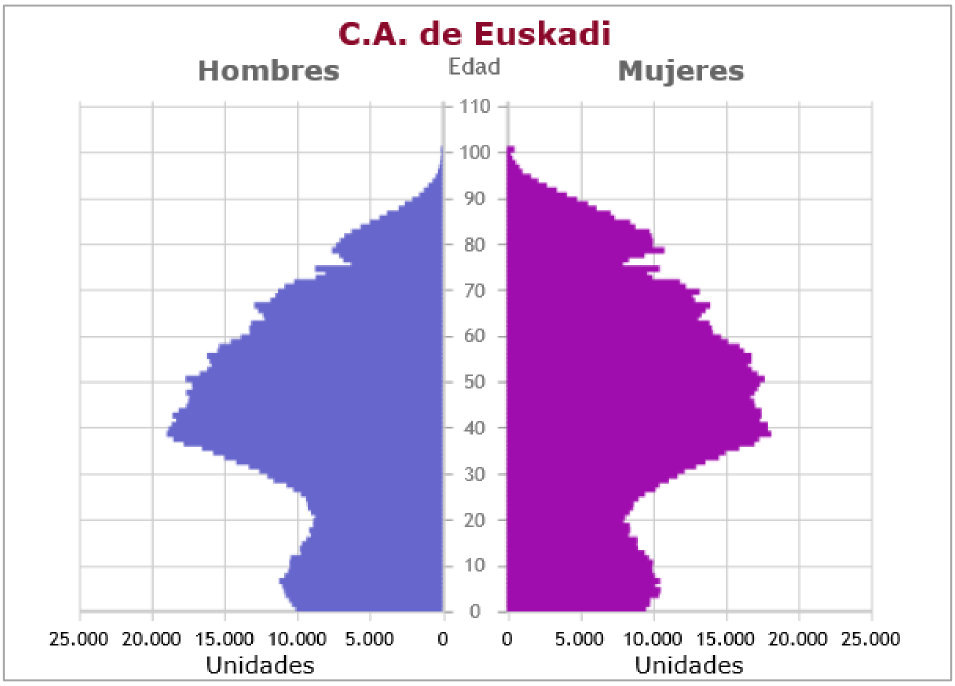


Figure 3.3. Population pyramid of the autonomous community of the Basque Country (2015). Source: Basque Statistics Institute (Eustat 2017).

According to the Basque Statistics Institute (Eustat 2017), the life expectancy at birth in 2010/2011 was 85.4 years for women and 78.9 years for men, which situates the Basque Country in the upper range of life expectancy in Spain. This autonomous community is also one of the wealthiest regions in Spain. Industrial sector is the main driver of the economy in the Basque Country. However, services sector has experienced a great increase in the last years, being trade, transport and hospitality sectors the largest ones, with the 37.9% of all the establishments (Eustat 2017).

1.1.1.1. The province of Bizkaia

Most of the sample was recruited in the province of Bizkaia, which is located in the North West area of the Basque Country (Figure 3.4). It borders the autonomous community of Cantabria to the west, Burgos and Araba provinces to the south, Gipuzkoa province to the east and the Cantábrico Sea (Bay of Biscay) to the north. The surface area of Bizkaia is 221,485 Ha (Eustat 2017), and comprises seven regions (comarcas): Encartaciones (42,950 Ha), Gran Bilbao (37,558 Ha), Uribe (20,836 Ha), Busturialdea (27,857 Ha), Lea-Artibai (20,596 Ha), Arratia-Nervión (40,053 Ha) and Duranguesado (31,635 Ha).

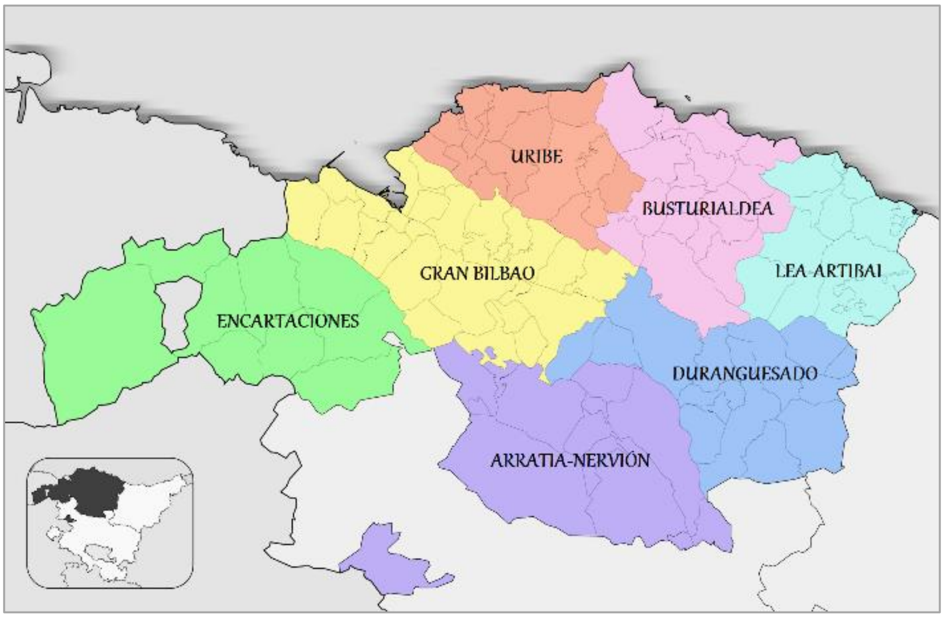


Figure 3.4. Comarcal division of the province of Bizkaia. Source: Modified from Wikipedia. Own Work (Time Zones Boy).

Bizkaia is the province with the largest population of the Basque Country with 1,138,852 inhabitants (Eustat 2017), which represents a 52.44% of the total population of the Basque Country. The population density of Bizkaia is 515.4 inhab/km^2. While most of the regions have a population density that ranges from 59.3 inhab/km^2 (Arratia-Nervión) to 309.71 inhab/km^2 (Duranguesado), Gran Bilbao has 2,297.28 inhab/km^2. Bilbao is the capital of Bizkaia, and it is the largest city in both the province and the autonomous community.

The Greater Bilbao

The study area was almost limited to the Gran Bilbao (Greater Bilbao), one of the seven regions of Bizkaia. Greater Bilbao could be divided into six subregions along both sides of Nervión River: Bilbao, Margen Izquierda (Left bank), Margen derecha (Right bank), Txoriherri, Zona minera (Mining zone) and Alto Nervión (High Nervion).

The Greater Bilbao has a population of 857,044 inhabitants but the city of Bilbao has almost 40% of this population (342,481 inhabitants) (Eustat 2017). Apart from Bilbao (4,059 Ha) there are other 25 municipalities that comprise the Greater Bilbao (Eustat 2017).

In terms of economy, Bilbao has been considered the main economic area of the Basque Country since XIX with the development of iron mines and metallurgical industry, which promoted port activity. Since 90's decade a deindustrialization process has taken place in Bilbao, which has centred its activities in the services sector.

1.1.1.2. The province of Araba

Part of the sample was also recruited in the province of Araba, which is located in the South area of the Basque Country (Figure 3.5). It borders the Basque provinces of Bizkaia and Gipuzkoa to the north, the community of La Rioja to the south, the province of Burgos to the west and the community of Navarra to the east. Araba is the largest of the three provinces in the Basque autonomous community with a surface area of 304,179 Ha (Eustat 2017), and comprises seven regions (comarcas): Ayala (33,212 Ha), Zuia (41,040 Ha), Salvatierra (39,699 Ha), Añana (64,567 Ha), Vitoria-Gasteiz (40,564 Ha), Campezo (53,512 Ha) and Laguardia (31,585 Ha).

Figure 3.5. Comarcal division of the province of Araba. Source: Modified from Wikipedia. Trabajo propio (Time Zones Boy).

Araba is the least populated province in the Basque Country with 321,777 inhabitants, which represents a 14.80% of the total population of the Basque Country (Eustat 2017). The population density of Araba is 105.8 inhab/km^2. Vitoria is the capital of Araba, and it is also the capital of the autonomous community of the Basque Country.

1.2. SUBJECT RECRUITMENT

1.2.1. Case-control methodology

Case-control studies have a retrospective design in which subjects are deliberately chosen according to the presence or absence of the study characteristic (obesity in this case). This means that case subjects are recruited at the time of or after having developed obesity. Control subjects are recruited from the same population so that they have had the same probability of exposure to the cause of the event, but they have not developed the disease. Additional data concerning risk factors, external (e.g. environmental factors) or internal (e.g. genetic factors), are collected to look back toward the possible causes of the event.

Due to the sampling strategy followed, case control studies are designed to provide relative estimates of disease risk and they are not designed to provide absolute prevalence or incidence rates of diseases.

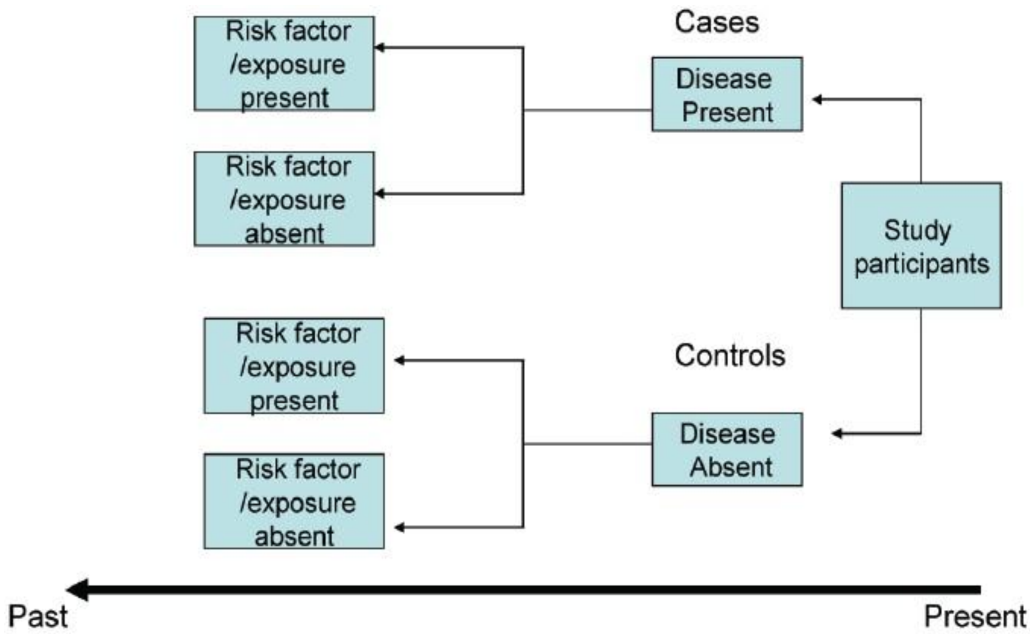


Figure 3.6. Structure of case-control study recruitment

1.2.2. Organization. Sampling places

The data collection was carried out between 2009 and 2013 in eight different locations that can be grouped into health centres, residences, educational centres and work centres (Table 3.1). The vast majority of the centres were located in Bizkaia and just one in the province of Araba (Lascaray Ikergunea Research Center). Most of the recruitment locations were public centres; only two of them were private (Indautxu Clinic and the doctor's office). In addition, a relative small number of participants were measured in their private houses.

Even though BMI restrictions were not considered during recruitment in each place, some of them were selected specifically for their high probability of finding obese participants. These places were Indautxu Clinic, Basurto Hospital and the private doctor's office.

Table 3.1. Summary of the centres sampled.

Types of Centres	Centre	Municipality	Province
Health Centres	Basurto Hospital	Bilbao	Bizkaia
	Indautxu Clinic	Bilbao	Bizkaia
	Doctor's office	Bilbao	Bizkaia
Residences	Miguel de Unamuno Residence (UPV/EHU)	Bilbao	Bizkaia
	Private homes	Getxo/Bilbao	Bizkaia
Educational centres	Faculty of Science and Technology	Leioa	Bizkaia
	Public Sport Education Centre, Kirolene	Durango	Bizkaia
Work centre	Lascaray Ikergunea Research Centre	Vitoria	Araba
Sport Centre	Municipal Sports Centre Fango	Bilbao	Biscay

Permission to carry out the study in the different centres was requested from the head of each centre. An information letter explaining the objectives and procedures of the study was given to all potential participants through the responsible of each centre or the author of this thesis. In the first stage of the sampling process, the objectives and procedures of the study were explained to each participant and all questions were correctly and comprehensively answered. All study participants were adults and written informed consent was obtained from all of them.

The project was approved by the Ethics Committee for Research Involving Human beings of the University of the Basque Country (CEISH). All research included in this thesis was conducted according to the international guidelines for biomedical research outlined in the declaration of Helsinki (World Medical Association 2013).

1.3. SAMPLE DESCRIPTION

As part of the sample was collected in medical centres, any individual with type 1 diabetes or with an untreated endocrine disorder were excluded from the beginning of the collection process, as well as individuals with any known eating disorder. The sample was initially composed by 626 individuals residing in the Basque Country. However, the sample size was reduced when applying the following exclusion criteria: foreign non-European origin (38 individuals excluded), pregnancy (1 individual excluded), growth disorders (1 individual excluded), and family relatedness (27 individuals excluded; only one of each set of related persons remained in the sample).

Additionally, 33 individuals from a rugby team were also excluded in the majority of the analyses in order to avoid the variability of body composition due to the practice of a professional sport. This subsample was only included in a section of Chapter 4, precisely to observe the relation of body morphology and composition with professional sport practice.

1.3.1. Nutritional status

The present case-control study was conducted on 524 unrelated individuals (204 men and 320 women) with different nutritional status. The definition of the different nutritional status for epidemiological surveys is mainly based on BMI. A description of the nutritional status in the analysed sample is shown in Table 3.2. BMI was categorized in two different ways in order to characterize cases (obesity) vs. controls (no obesity) or to do it in a more accurate nutritional status classification. Three individuals have missing values for nutritional status (based on BMI).

In the analysed sample, the number of non-obese participants is higher than obese participants. However, as it was expected due to the sampling methodology of this study, the percentage of obesity is relatively higher than the percentage of obesity in Spain general population, which is of about 17.5% (women) and 13.2% (men) according to the DORICA study (Aranceta et al. 2004).

The most represented nutritional status in both men and women are: normal weight, overweight and obesity. However, although extreme nutritional status are not highly represented, a relatively important number of participants were classified as morbid obese (11.3% of men and 12.9% of women).

Table 3.2. Number and percentage of individuals by sex and nutritional status.

Nutritional status	Men		Women		All	
	N	%	N	%	N	%
*No obesity (controls)	124	61.1	176	55.3	300	57.6
Underweight	1	0.5	5	1.6	6	1.2
Normal-weight	58	28.6	98	30.8	156	29.9
Overweight	65	32.0	73	23.0	138	26.5
*Obesity (cases)	79	38.9	142	44.7	221	42.4
Obesity	56	27.6	101	31.8	157	30.1
Morbid obesity	23	11.3	41	12.9	64	12.3
Total	203	100	318	100	521	100

*No obesity: BMI<30 kg/m²; Obesity: BMI≥30 kg/m².
Underweight: BMI<18.5 kg/m²; Normal-weight: BMI=18.5-24.9 kg/m²; Overweight: BMI=25-29.9 kg/m²; Obesity: BMI=30-39.9 kg/m²; Morbid obesity: BMI≥40 kg/m².

1.3.2. Age distribution

Age distribution for each sex and for the whole sample at the time of the study is shown in Table 3.3 for non-obese participants and in Table 3.4 for obese participants. Age ranges from 18 to 82 years in the non-obese group (men: 18 to 76 years, women: 18 to 82) and from 19 to 79 years in obese group (men: 21 to 72 years, women: 19 to 79 years). Higher number of women than men can be seen in almost all age ranges, with two exceptions for men in ranges of 18-24 and 55-64 of the non-obese group.

In non-obese individuals, the most frequent age range was from 25 to 34.9 years old for both sexes. In obese individuals the highest participation rate was found between 45 to 54.9 years of age. However, while the majority of obese women are in this age range (45-54.9 years old), in obese men the most frequent age group was the previous one (35-44.9 years).

Table 3.3. Number and percentage of non-obese individuals in each age group by sex and in the whole sample.

Age group (years)	Men		Women		All	
	N	%	N	%	N	%
18-24.9	26	21.0	17	9.7	43	14.3
25-34.9	32	25.8	49	27.8	81	27.0
35-44.9	16	12.9	34	19.3	50	16.7
45-54.9	19	15.3	43	24.4	62	20.7
55-64.9	23	18.5	21	11.9	44	14.7
≥65	8	6.5	12	6.8	20	6.7
Total	124	100	176	100	300	100

N: number; %: percentage.

Table 3.4. Number and percentage of obese individuals in each age group by sex and in the whole sample.

Age group (years)	Men		Women		All	
	N	%	N	%	N	%
18-24.9	2	2.5	5	3.5	7	3.2
25-34.9	13	16.5	16	11.3	29	13.1
35-44.9	22	27.8	24	16.9	46	20.8
45-54.9	19	24.1	43	30.3	62	28.1
55-64.9	12	15.2	37	26.1	49	22.2
≥65	11	13.9	17	12.0	28	12.7
Total	79	100	142	100	221	100

N: number; %: percentage.

1.3.3. Environmental circumstances

Information about environmental circumstances that constitute the everyday life of the studied individuals was obtained through an extensive questionnaire, including demographic, socioeconomic and lifestyle information. Next, a description of all these environmental circumstances is presented with the exception of the lifestyle description, which will be mentioned in the analysed variables section of this chapter and will be also discussed in Chapter 6.

1.3.3.1. Demographic origin

The demographic origin of the studied subjects as well as that of their parents and grandparents is shown in Table 3.5 and Table 3.6. The majority of the study participants were born in the Basque Country (77.7%) as their parents and grandparents. However, a substantial number of the studied subjects were born out of the Basque Country, in other autonomous communities of Spain (20.8%), especially in the autonomous community of Castilla y León. There is also a small group of participants that was born outside Spain (1.5%).

The immigration pattern that took place during the early 20th century can be easily appreciated in the studied sample. The percentage of people born in the Basque Country is higher in the studied participants compared to their parents and it is also higher in the parents compared to the grandparents; whereas the percentage of people born in other autonomous communities, increases from participants to their parents and to their grandparents. It can also be appreciated how this migration phenomenon was more intense from Castilla y Leon to the Basque Country than from other autonomous communities. However, there are other autonomous communities where the migration was also relatively high such as Galicia, Cantabria or Andalucía.

Table 3.5. Number and percentage of participants in the study according to the place of birth of the subject, and of their father and mother.

	Subject		Father		Mother	
	N	**%**	**N**	**%**	**N**	**%**
Basque Country	407	77.7	273	52.1	267	51
Bizkaia	357	87.7	230	84.2	220	82.4
Guipuzkoa	33	8.1	28	10.3	27	10.1
Araba	17	4.2	15	5.5	20	7.5
Navarra	5	1	11	2.1	10	1.9
La Rioja	5	1	7	1.3	13	2.5
Cantabria	12	2.3	23	4.4	22	4.2
Principado de Asturias	5	1	5	1	12	2.3
Galicia	12	2.3	23	4.4	25	4.8
Cataluña	5	1	5	1	3	0.6
Aragón	5	1	5	1	4	0.8
Castilla y León	39	7.4	112	21.4	102	19.5
Comunidad de Madrid	8	1.5	6	1.1	9	1.7
Comunidad Valenciana	2	0.4	1	0.2	1	0.2
Castilla-La Mancha	3	0.6	7	1.3	9	1.7
Extremadura	3	0.6	17	3.2	20	3.8
Región de Murcia	0	0	0	0	0	0
Andalucía	4	0.8	19	3.6	21	4
Islas Baleares	1	0.2	0	0	1	0.2
Islas Canarias	0	0	1	0.2	0	0
Melilla	0	0	2	0.4	0	0
Europe	6	1.1	6	1.1	4	0.8
Asia	0	0	0	0	1	0.2
America	2	0.4	1	0.2	0	0
Total	524	100	524	100	524	100

N: number; %: percentage.

Table 3.6. Number and percentage of participants in the study according to the place of birth of the subjects' paternal and maternal grandparents.

	Paternal Grandfather		**Paternal Grandmother**		**Maternal Grandfather**		**Maternal Grandmother**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Basque Country	209	40.6	217	42.4	194	37.7	210	40.6
Bizkaia	169	80.9	176	81.1	145	74.7	168	80.4
Guipuzkoa	27	12.9	25	11.5	26	13.4	18	8.6
Araba	13	6.2	16	7.4	23	11.9	23	11
Navarra	20	3.9	19	3.7	16	3.1	10	1.9
La Rioja	14	2.7	14	2.7	20	3.9	17	3.3
Cantabria	23	4.5	26	5.1	32	6.2	30	5.8
Principado de Asturias	6	1.2	9	1.8	10	1.9	12	2.3
Galicia	28	5.4	29	5.7	30	5.8	30	5.8
Cataluña	2	0.4	1	0.2	3	0.6	4	0.8
Aragón	8	1.6	9	1.8	7	1.4	6	1.2
Castilla y León	142	27.6	127	24.8	135	26.3	137	26.5
Comunidad de Madrid	5	1	5	1	4	0.8	4	0.8
Comunidad Valenciana	0	0	2	0.4	3	0.6	1	0.2
Castilla-La Mancha	9	1.7	9	1.8	12	2.3	7	1.4
Extremadura	18	3.5	17	3.3	20	3.9	22	4.3
Región de Murcia	2	0.4	1	0.2	0	0	0	0
Andalucía	21	4.1	20	3.9	21	4.1	23	4.4
Islas Baleares	0	0	0	0	1	0.2	0	0
Islas Canarias	1	0.2	1	0.2	0	0	0	0
Melilla	0	0	0	0	0	0	0	0
Europe	7	1.4	6	1.2	6	1.2	4	0.8
Asia	0	0	0	0	0	0	0	0
America	0	0	0	0	0	0	0	0
Total	515	100	512	100	514	100	517	100

N: number; %: percentage.

1.3.3.2. Biodemographic characteristics

Three biodemographic characteristics were considered in the present sample: maternal and paternal age of marriage, maternal age at first birth and number of siblings.

As it is shown in Table 3.7 most of the participant's parents got married between 18 and 29.9 years (85.8% of mothers and 72.2% of fathers). Fathers tended to marry at an older age compared to mothers; the majority of fathers got married between 25 and 29.9 years (43.5%), whereas more than half of mothers got married between 18 and 24.9 years (52.7%). Besides, there are 27.6% of fathers who got married with 30 years or more and only 12.2% of mothers got married at this age. Although the majority of mothers got married between 18 and 24.9 years, most of them had their first child at 25-29.9 years (40.1%).

Table 3.7. Number and percentage of participants' mothers and fathers at each marriage age group and number and percentage of participants' mothers at each group of age at first birth.

Age at marriage	Mother		Father		Age at first birth	Mother	
	N	%	N	%		N	%
≤17	10	2.0	1	0.2	≤17	6	1.2
18-24.9	258	52.7	139	28.7	18-24.9	184	37.6
25-29.9	162	33.1	211	43.5	25-29.9	196	40.1
30-34.9	50	10.2	97	20.0	30-34.9	89	18.2
35-39.9	8	1.6	24	4.9	35-39.9	10	2.0
≥40	2	0.4	13	2.7	≥40	4	0.8
Total	490	100	485	100	Total	489	100

N: number; %: percentage

In the next table mothers were divided according to their age at the first birth and by the subject age group (Table 3.8). The analysed data clearly shows a delaying of the age at maternity, which has also been noticed in the Spanish general population (INE 2015). For the mothers of the youngest participants, the most common age at first child birth was between 30 and 34.9 years. However, as the age of participants increases, their mothers' age at first maternity decreases (25-29.9 years for the mothers of the second younger group of participants and 20-29.9 years from here backwards).

Table 3.8. Number and percentage of participants' mothers, according to maternal age at first birth and participants' age.

Maternal age at first birth (years)	Measured subjects' age (years)													
	≤25		25-34.9		35-44.9		45-54.9		55-64.9		65-74.9		≥75	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
≤19.9	1	2.0	7	6.5	7	7.6	3	2.5	6	6.8	2	7.1	1	33.3
20-24.9	4	8.0	38	35.2	40	43.5	37	30.8	32	36.4	10	35.7	2	66.7
25-29.9	19	38.0	47	43.5	36	39.1	52	43.3	32	36.4	10	35.7	0	0.0
30-34.9	24	48.0	14	13.0	7	7.6	23	19.2	17	19.3	4	14.3	0	0.0
35-39.9	2	4.0	1	0.9	2	2.2	3	2.5	1	1.1	1	3.6	0	0.0
≥40	0	0.0	1	0.9	0	0.0	2	1.7	0	0.0	1	3.6	0	0.0
Total	50	100	108	100	92	100	120	100	88	100	28	100	3	100

N: number; %: percentage

Families with two siblings (including the participant) were clearly predominant in the present sample, followed by families with three and four siblings. The percentage of participants who were only children was of 9.1% while there were 18.7% of individuals with 5 or more siblings (Figure 3.7).

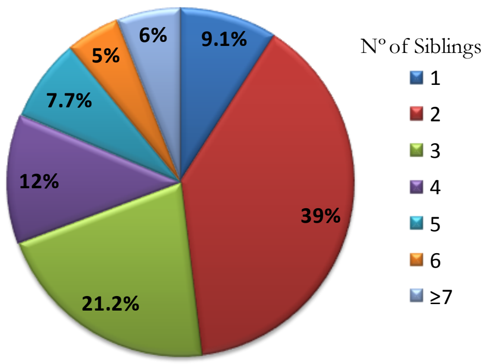


Figure 3.7. Percentage of individuals according to the number of siblings in the family (including the participant).

When the sample was divided by participants' age range, a remarkable tendency towards a decrease in sibship size was observed (Figure 3.8). In almost all age groups, the predominant sibship size was of two siblings. However, a homogeneous diversity could be seen in the oldest groups of participants, whereas in the youngest groups the percentage of participants with higher number of siblings decreases. In fact, there are no participants with 25 years or less and more than three siblings (including the participant).

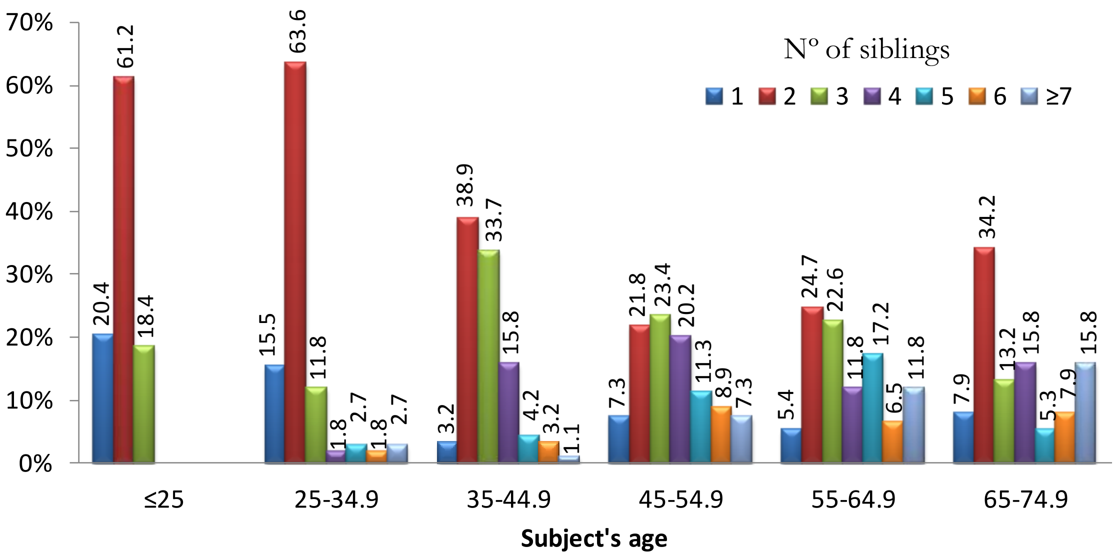


Figure 3.8. Percentage of individuals in each age group according to the number of siblings (including the participant).

1.3.3.3. Socioeconomic status (SES)

Although there are a variety of methods to classify individuals by socioeconomic status, the most widely used for urban populations is the one proposed by Kuppuswamy (1976), which includes three indicators: education, occupation and income. However, obtaining income information is difficult and it is considered a rather volatile indicator. In this study, SES was assessed through educational and occupational levels.

Education

Six categories were employed to describe the educational characteristics of the studied sample: primary school, secondary school, vocational training, baccalaureate, general degree and honours degree (Table 3.9). University educated subjects represent the 40.4% of the studied subjects, 21.8% of participants chose a vocational training education and just a 4% are not graduated from Secondary School. In Figure 3.9 the sample was divided in obese and non-obese participants. The highest educational categories are predominantly composed of non-obese individuals, whereas in the lowest educational categories the highest percentages of participants correspond to obese persons.

Table 3.9. Number and percentage of participants in each educational level.

Educational level	N	%
Primary school	21	4.0
Secondary school	88	16.9
Vocational training	114	21.8
Baccalaureate	88	16.9
General degree	54	10.3
Honours degree	157	30.1
Total	522	100

N: number; %: percentage

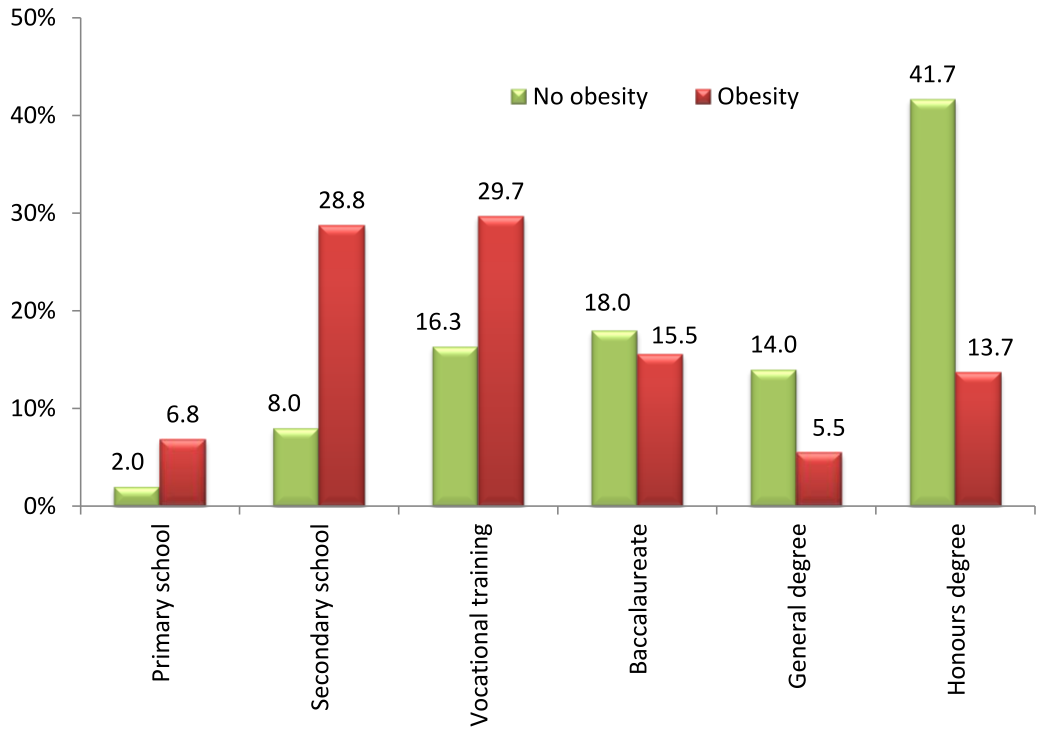


Figure 3.9. Percentage of individuals according to their educational level in non-obese and obese participants.

Occupation

Initially, the professional occupation of participants were classified based on the occupational categories of the Census of the City Council of Bilbao in 1990, but then this classification was re-organized in order to adapt it to this sample. As a result eight professional categories were used to assess the occupational level of the studied population: (1) retired, pensioners, off work or unemployment, (2) students, (3) homemakers, (4) skilled workers, (5) sailors or agriculture and livestock farming, (6) hospitality sector and services, (7) commercial sector and self-employers, (8) administrative officers, (9) professionals, technicians, directors or managers (Table 3.10). The category with the highest percentage of participants was "professionals, technicians, directors or managers", followed by "homemakers" and persons with no occupation. The only occupational category, in which no individual was included, was the category of "sailors or agriculture and livestock farming". When the sample was divided in obese and non-obese individuals (Figure 3.10), a similar trend to that described for the educational level was observed. Higher percentages of obesity are found in lower occupational categories (with the exception of the student category), whereas the highest occupational categories present higher percentages of non-obese participants.

Table 3.10. Number and percentage of participants in each occupational category.

Occupations	N	%
Retired, pensioners, off work or unemployment	70	13.4
Students	54	10.3
Homemakers	71	13.6
Skilled or unskilled workers	37	7.1
Sailors or agriculture and livestock farming	-	-
Hospitality sector and services	58	11.1
Commercial sector and self-employers	24	4.6
Administrative officers	55	10.5
Professionals, technicians, directors or managers	154	29.4
Total	523	100

N: number; %: percentage

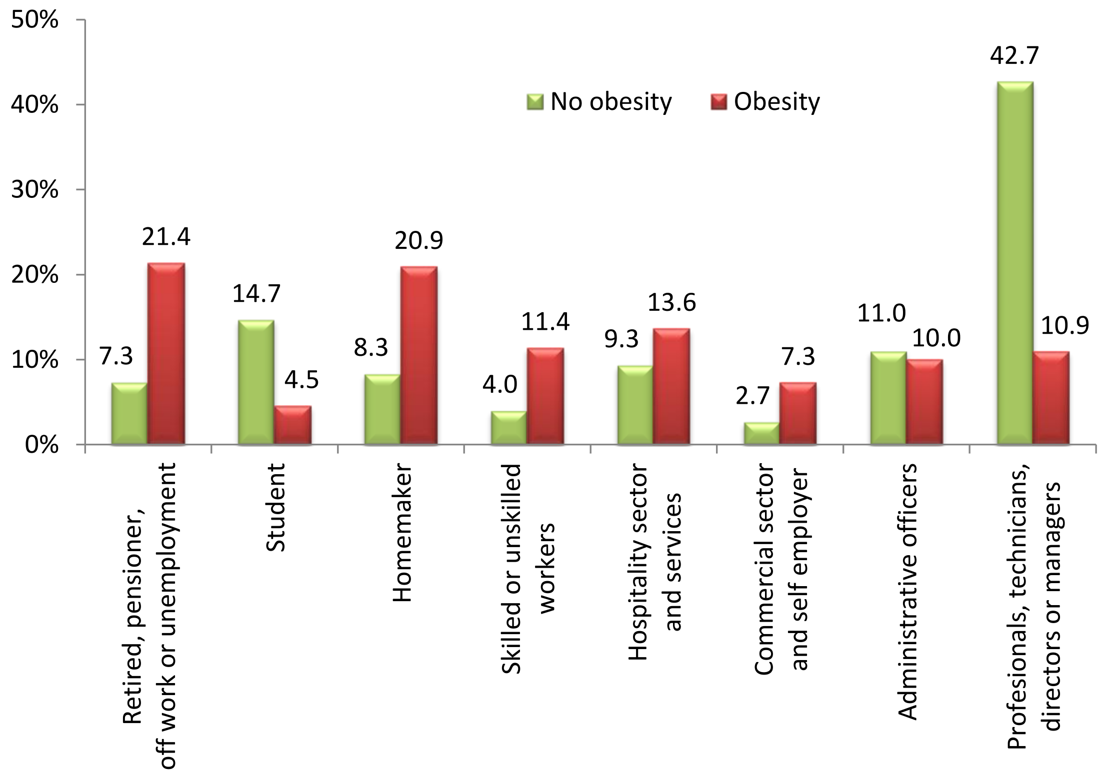


Figure 3.10. Percentage of individuals according to their occupational category in non-obese and obese participants.

2. ANALYSED VARIABLES

2.1. ANTHROPOMETRIC PHENOTYPES

2.1.1. Anthropometric measurements

Anthropometric measurements were taken from each participant following standard anthropometric techniques (Lohman, Roche, and Martorell 1988) with a simple modification: bilateral measures were taken on the left side of the body as this side is supposed to be the less modified by physical activity. All participants were asked to wear light clothing and to stand without shoes. All measures were taken by the same investigator (the author of this Doctoral Dissertation) as a way to reduce inter-observer error. The anthropometric measures included in this work are: height, weight, two breadths (biepicondylar breadth of the humerus and of the femur), five circumferences (upper arm relaxed, upper arm contracted, waist, hip, and medial calf) and six skinfold thicknesses (biceps, triceps, subscapular, suprailiac, abdominal and medial calf).

Height was measured with a Siber-Hegner anthropometer (GPM, Zurich, Switzerland) accurate to 1 mm. The subject was standing with the back as straight as possible and, wherever possible, the heels of the feet were placed together with the weight of the participant distributed on both feet. The head was aligned in the Frankfort Horizontal Plane position (Figure 3.11) and the subject was asked to inhale deeply as a way to compensate the shortening of intervertebral discs.

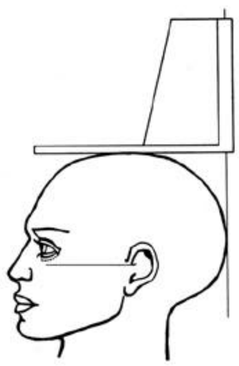


Figure 3.11. The head in the Frankfort plane. Source: International Society for the Advancement of Kinanthropometry (ISAK).

Weight was measured with a digital balance (accuracy of 0.1 kg) with the participant standing on the centre of the weight scale platform. If the participant´s weight was higher than 150 kg (limit of the balance), the participant was asked to report his/her last weight measured in a medical consultation.

Breadth measurements were performed with a Siber-Hegner spreading calliper with rounded edges (GPM, Zurich, Switzerland) accurate to 1 mm (Figure 3.12). For the biepicondylar breadth of the humerus (elbow breadth) measurement, the subject was standing with the arm extended forward (perpendicular to the body). Then the arm was flexed until it formed a 90° angle and the measure was taken across the epicondyles of the humerus, with the calliper at a slight angle because the medial condyle is more distal than the lateral condyle. For the biepicondylar breadth of the femur (knee breadth), the subject was sitting on a chair with the knee also flexed in a 90° angle. In this case, the measure was taken across the condyles of the femur. In both measures, pressure was exerted to compress the tissues.

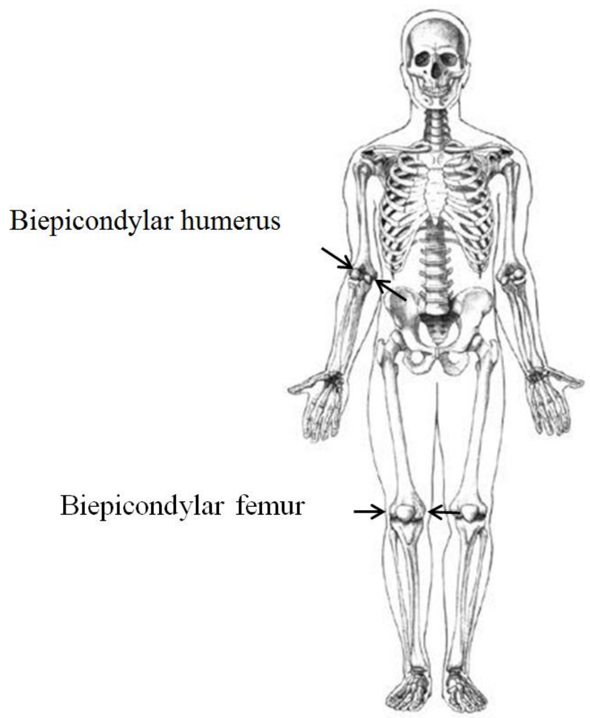


Figure 3.12. Location of breadths measurements sites. Source: International Society for the Advancement of Kinanthropometry (ISAK)

Circumferences were measured with a Harpenden anthropometric tape to the nearest mm (Holtain Ltd., Crymych, Pembrokeshire, UK). The subject was in a standing position with arms hanging freely to the side and relaxed. Circumferences were measured horizontally at their specific points (Figure 3.13). The tape rested on the skin surface, but was not pulled tight enough to compress the skin. For the waist circumference the tape was placed around the trunk at the desired level, between the lower costal border and the iliac crest. For hip circumference, the tape was placed at the maximum extension of the buttocks. For calf circumference, the tape was placed around the medium height of the calf. For arm circumference, the tape was placed around the upper arm perpendicular to the long axis of the upper arm. For flexed arm circumference, the participant was asked to bend the elbow and flex the muscles of the upper arm; the tape was placed at the same point as for the relaxed arm measurement.

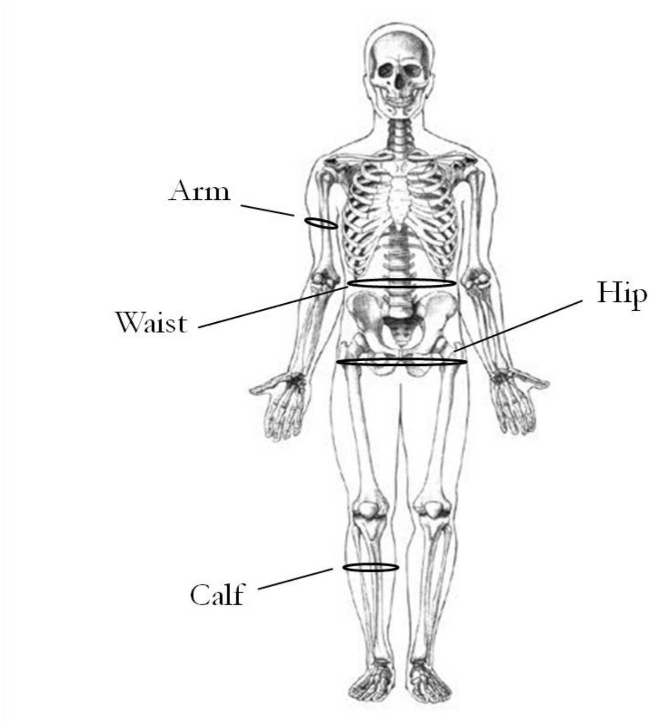


Figure 3.13. Location of circumference measurements sites. Source: International Society for the Advancement of Kinanthropometry (ISAK).

Skinfolds were measured with a 10g/mm^2 constant pressure Lange calliper (Cambridge Scientific Industries, Cambridge, MA). In order to measure skindfolds (biceps, triceps, subscapular, suprailiac, abdominal and medial calf), the fold of skin and the underlying subcutaneous adipose tissue (without the underlying muscle) should be gently grasped between the left thumb and forefingers (Figure 3.14). The jaws of the calliper were placed perpendicular to the length of the fold. Medial calf skinfold was measured with the subject sitting.

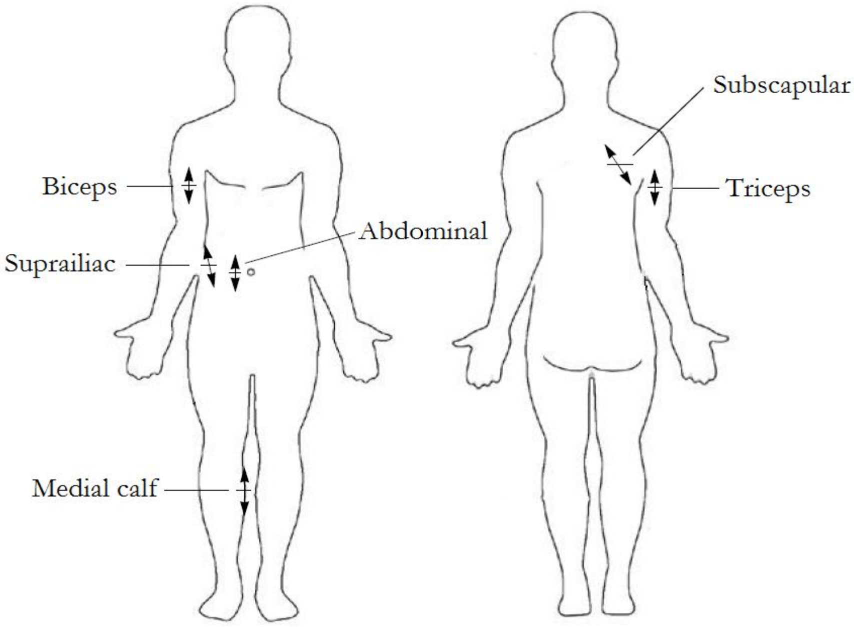


Figure 3.14. Location of skinfold measurements sites: anterior view (left panel) and posterior view (right panel) Source: International Society for the Advancement of Kinanthropometry (ISAK).

2.1.1.6. Technical error of measurement

Variability on measures occur due to biological variation, which cannot be avoided and is the issue of interest, or due to variations in the execution of the anthropometric technique, which are responsible for the higher incidence of error (Perini et al. 2005). Due to this, verification of the accuracy and reliability of the measurements are necessary in all studies including anthropometric data. In this work, appropriate equipment, which was carefully maintained and calibrated, was used to ensure high quality of data. On the other hand, Technical Error of Measurement (TEM) was also employed as a way to obtain a measure of anthropometric data accuracy (Perini et al. 2005). TEM is defined as a measure of the extent of agreement between two repeated measurements recorded for the same individuals. As the measurements were recorded by the same researcher, only intra-observer TEMs were calculated employing the following equation:

$$TEM = \sqrt{\frac{\sum d^2}{2n}}$$

Where "d" is the difference between measurements and "n" is the number of individuals measured.

In the present study two repeated measurements were taken on 15 randomly selected subjects. The obtained intra-observer TEMs fell within the range of the observed in other studies (Ulijaszek and Kerr 1999).

2.1.2. Indexes

From the simple anthropometric measurements four obesity or adiposity related indexes were calculated: body mass index (BMI), the sum of all 6 skinfolds (SF6), the waist to hip ratio (WHR) and the fat mass percentage (FM%).

$$BMI = \frac{weight\ (kg)}{height\ (m^2)}$$

$$SF6 = triceps\ (mm) + subscapular\ (mm) + suprailiac\ (mm) + medial\ calf\ (mm) + abdominal\ (mm) + biceps\ (mm)$$

$$WHR = \frac{waist\ circumference\ (cm)}{hip\ circumference\ (cm)}$$

Fat mass percentage (FM%) was calculated through Siri's equations and using Durnin and Womersley's density (D) equations (Siri 1961; Durnin and Womersley 1974).

$$D = c - [m \times Log(Bic. + Tric. + Sub. + Supra.)]$$

Where the used skinfolds are: Bic: biceps (mm), Tric: triceps (mm), Sub: subscapular (mm), Supra: suprailiac (mm). c and m are specific values corresponding to each sex and age groups (see Table 3.11 and Table 3.12).

Table 3.11. "c" and "m" values for women in the Durnin and Womersley's equation.

	Women				
	16-19 years	**20-29 years**	**30-39 years**	**40-49 years**	**+50 years**
c	1.1549	1.1599	1.1423	1.1333	1.1339
m	0.0678	0.0717	0.0632	0.0612	0.0645

Table 3.12. "c" and "m" values for men in the Durnin and Womersley's equation.

	Men				
	16-19 years	**20-29 years**	**30-39 years**	**40-49 years**	**+50 years**
c	1.1620	1.1631	1.1422	1.1620	1.1715
m	0.0630	0.0632	0.0544	0.0700	0.0779

$$FM\% = [(4.95/D) - 4.50] \times 100$$

2.1.3. Obesity definition

In the present study four variables were used to define obesity (BMI, WC, WHR and FM%). The cut-off points established by the WHO (World Health Organization 2011) or by the SEEDO (Campillo et al. 2000) were used for this purpose (From Table 3.13 to Table 3.16). Classification of obesity on different categories based on BMI was done in two ways: i) obesity and no obesity and ii) a classification including five different nutritional status (i.e. under-weight, normal-weight, overweight, obesity and morbid obesity).

Table 3.13. Cut-off points for nutritional status based on BMI. According to WHO criteria (World Health Organization 2011).

Nutritional status		**BMI**
No obesity	Under-weight	<18.5 kg/m^2
	Normal-weight	18.5 – 24.99 kg/m^2
	Overweight	25 – 29.99 kg/m^2
Obesity	Obesity	30 – 39.99 kg/m^2
	Morbid obesity	≥40 kg/m^2

Table 3.14. Cut-off points for central obesity classification based on WC. According to WHO criteria (World Health Organization 2011).

Nutritional status	**WC**	
	Women	Men
No central obesity	≤88 cm	≤102 cm
Central Obesity	>88 cm	>102 cm

Table 3.15. Cut-off points for adiposity distribution classification based on WHR. According to WHO criteria (World Health Organization 2011).

Nutritional status	**WHR**	
	Women	Men
Peripheral fat distribution	<0.85	<0.90
Central fat distribution	≥0.85	≥0.90

Table 3.16. Cut-off points for excess of adiposity based on FM%. According to SEEDO criteria (Campillo et al. 2000).

Nutritional status	**FM%**	
	Women	Men
No excessive adiposity	20-33%	12-25%
Excessive adiposity	>33%	>25%

2.1.4. Heath-Carter anthropometric somatotype

The three components of the Heath-Carter anthropometric somatotype were calculated according to the equations described in Carter and Heath (1990).

Endomorphy (Endo.) was obtained from three skinfolds (triceps, subscapular and suprailiac) according to the following equation:

$$Endo = -0.7182 + 0.1451\,(A) - 0.00068\,(A^2) + 0.0000014\,(A^3)$$

Where:

$$A = (triceps\ skf + subscapular\ skf + suprailiac\ skf) \times \frac{170.18}{height\ (cm)}$$

Mesomorphy (Meso.) was obtained based on height, humerus and femoral breadths, as well as flexed arm and calf circumferences corrected for triceps, and calf skinfolds, according to the following equation:

$$Meso = [(0.858 \times humerus\ breadth) + (0.601 \times femur\ breadth) + (0.188 \times corrected\ arm\ girth) + (0.161 \times corrected\ calf\ girth)] - (height \times 0.131) + 4.50$$

Where:

$$Corrected\ arm\ girth = arm\ circumference - triceps\ skf$$

$$Corrected\ calf\ girth = calf\ circumference - medial\ calf\ skf$$

Ectomorphy (Ecto.) was obtained from three different equations according to the height-weight ratio (HWR):

$$HWR = \frac{height}{\sqrt[3]{weight}}$$

If HWR ≥ 40.75 then:

$$Ecto = HWR \times 0.732 - 28.58$$

If HWR < 40.75, but > 38.25 then:

$$Ecto = HWR \times 0.463 - 17.63$$

If HWR ≤ 38.25 then:

$$Ecto = 0.1$$

Compograms were used to represent the means of the three somatotype components (Araujo, Gomes, and Moutinho 1979). In the horizontal axis the three somatotype components are represented whereas the somatotype ratings appear in the vertical axis. Several examples of compograms could be seen in Appendix I.

Somatoplot coordinates were also calculated from the three somatotype components using the following equations:

$$X = ectomorphy - endomorphy$$

$$Y = 2(mesomorphy) - (endomorphy + ectomorphy)$$

Somatotypes were plotted in two dimensions somatocharts (Figure 3.15) using the X, Y coordinates.

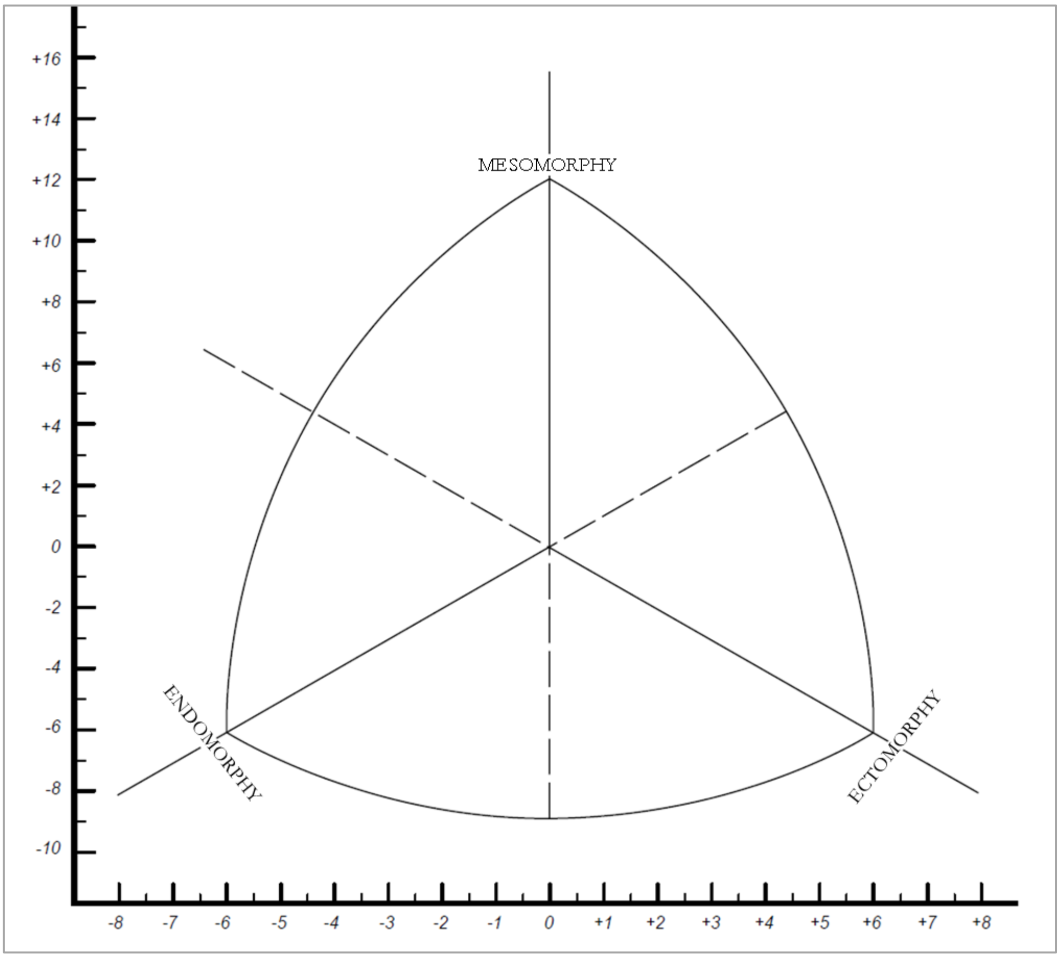


Figure 3.15. Example of a somatochart used to display the distribution of somatotypes in two dimensions.

Somatotype dispersion distance (SDD) indicates the difference between two somatoplot in a two dimension somatochart. Distances are considered as statistically significant (p≤0.05) when SDD is equal or greater than 2 (Hebbelinck, Carter, and De Garay 1975). SDDs were calculated using the following equation:

$$SDD_{1,2} = \sqrt{[3(X_1 - X_2)^2 + (Y_1 - Y_2)^2]}$$

Although the information obtained by somatotypes represented in two dimensions is somewhat diminished, two-dimensional somatocharts and SDDs are widely used by the scientific community as they are convenient and useful for visual display of the somatotype information.

2.3. ENVIRONMENTAL FACTORS

All environmental factors were assessed through a personal interview, in which in addition to the information corresponding to age, biodemographic characteristics and SES, some attitudes and lifestyle information was also collected. These environmental variables were used to assess the association between environment and obesity in Chapter 6 and are collected as follow:

Background. The variables included in this group reflect the personal and familial health status in relation to obesity. Three variables are included in this group:

i) "Family history of obesity" indicates if the participant has any relative with obesity and its degree of relatedness (Categories: No; 1^{st} Degree; 2^{nd} Degree).

ii) "Obesity related diseases" indicates if the participant is free of any obesity related disease or if he/she presents any of the following diseases: type 2 diabetes, hypertension, hypercholesterolemia, cardiovascular diseases or respiratory diseases (Categories: No; Yes).

iii) "Perceived physical condition" indicates how the participant perceives his/her physical health but it does not give any indication of the aesthetic perception (Categories: Good; Regular; Bad).

Physical (In)Activity. The variables included in this group provide information about some habits related to activity energy expenditure (AEE). Five variables are included in this group:

i) "Physical activity" indicates if the participant practices any sport or not (Categories: None; Walking; Regular sport). A distinction between sport practice and walking was made in this variable: participants were classified into walking category when they walk as a mean to exercise the body; whereas they were classified into regular sport category when any other sports are regularly practice.

ii) "Since how long" indicates when the participant started practicing sports regularly (Categories: None; Less than a year; 1-2 years ago; 3-6 years ago; >6 years ago).

iii) "Daily walking" indicates the minutes per day the participant walks in order to realise his/her daily activities. (Unit: Minutes/day).

iv) "Work intensity" indicates the perceived intensity of the work performed by the participant (Categories: Light; Moderate; Intense).

v) "Television" reflects the number of hours per week that the participant dedicates to watch television (Unit: Hours/week).

Sleep patterns. The two variables included in this group evaluate participants' sleep:

i) "Sleep duration" indicates the sleeping hours calculated through the difference between bedtime and waking-up time. This variable was categorized due to the hypothesis of a U-shaped effect on BMI (Taheri et al. 2004) (Categories: 6-8 h; <6 h; >8 h).

ii) "Sleep quality" indicates participant's quality of sleep (Categories: Good; Regular; Bad).

Eating patterns. The three variables included in this group of variables reflect subject's eating habits:

i) "Main meal duration" indicates the time that the participant expends eating the main meal of the day. This variable was categorized in order to take into account the hypothesis about the time needed to develop the biological signalling of hunger and satiety (Andrade, Greene, and Melanson 2008)(Categories: ≤20 min; >20 min).

ii) "The place of the main meal" indicates if the participant eats the main meal of the day at home or outside it, and in the latter case if the participant eats home-made food or if he/she eats at the company's dining room or in a restaurant (Categories: Home; Tupperware; Restaurant; Company dining room).

iii) "Meals frequency" indicates the number of eating episodes in a day (Categories: 3 times; 4 times; 5 times; 6 times; 1 or 2 times).

Smoking and alcohol consumption. The variables included in this group reflect the participants' habits towards tobacco and alcohol.

i) "Smoking" indicates if the participant currently smokes or not, and if he/she has previously smoked (Categories: Non-smokers; Ex-smokers, Smokers).

ii) "Number of cigarettes" indicates the quantity of cigarettes smoked by the participants who declared to be smokers (Units: Number of cigarettes/week).

iii) "Alcohol" indicates if the participant consumes alcohol or not. Participants who consume alcohol infrequently (see next variable) were classified in the same category as those who do not consume alcohol (Categories: No/infrequently; Yes).

iv) "Alcohol frequency" indicates the frequency of alcohol consumption (Categories: Never/infrequently; Occasionally; Weekends; Some days a week; Every day). In this classification "Infrequently" grouped participants that drink some days during a year; "Occasionally" grouped participants that drink some days during a month; "Weekends" grouped participants that drink exclusively during the weekends; "Some days a week" grouped participants that drink during the week, but not every day, and finally "Every day" grouped participants that drink some alcoholic beverage every day.

2.4. BODY IMAGE

In the present work, participants' current body image perception, ideal body image perception, satisfaction degree and inconsistency degree were assessed through Stunkard et al. (1983) silhouettes collection (Figure 3.16). This collection consists of 18 schematic drawings of human body (silhouettes), 9 of them representing adult men, and the other 9 adult women. The silhouettes range in size from very thin (silhouette 1) to very fat (silhouette 9). The standards connecting body silhouettes to weight categories were established by Bulik et al. (2001) in a large Caucasian population-based sample.

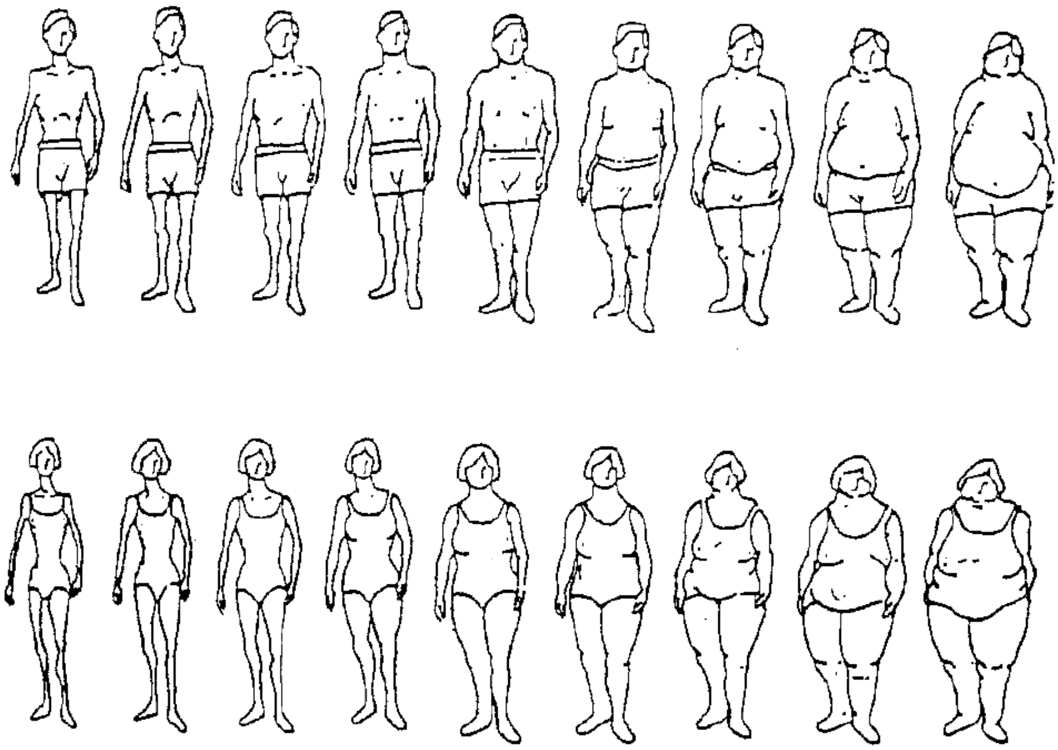


Figure 3.16. Silhouettes collection. Source: Stunkard, Sorensen, and Schulsinger (1983).

Three variables were obtained directly from this silhouettes collection:

1. Current body size. Participants were asked to identify the figure that best represented their current body size.

2. Ideal body size. Participants were asked to identify the figure that best represented their desired body size

3. Most attractive body size. Participants were asked to identify the figure that best represented their preferred body size in the opposite gender.

From these variables, two more indexes were calculated:

1. Body size dissatisfaction score (DS): This index was computed by subtracting the preferred silhouette from the current silhouette.

$$DS = Current\ body\ image - Ideal\ body\ image$$

DS is a measure of satisfaction/dissatisfaction with the current body size where "0" indicates full satisfaction with the current body size and larger numbers indicate greater dissatisfaction between the current body size and the ideal body size. Positive numbers indicate dissatisfaction by excess (i.e. the participant wishes his/her body to be smaller than his/her actual body size) whereas negative numbers indicate dissatisfaction by default (i.e. the participant wishes his/her body to be bigger than his/her actual body size). Based on this, seven categories were created:

(3) Severe dissatisfaction by excess

(2) Moderate dissatisfaction by excess

(1) Slight dissatisfaction by excess

(0) Full satisfaction

(-1) Slight dissatisfaction by default

(-2) Moderate dissatisfaction by default

(-3) Severe dissatisfaction by default

2. Body size inconsistency score (IS): This index was proposed by Zaccagni et al. (2014) and it is calculated by subtracting the nutritional status assessed through BMI from the nutritional status estimated based on the silhouette chosen by the participant to represent his/her current body size.

$$IS = Status\ based\ in\ current\ silhouettes - Status\ based\ on\ BMI$$

Nutritional status based on the current silhouette selection was obtained using the standards published by Bulik et al. (2001) and nutritional status based on BMI was obtained using the thresholds from WHO classification (World Health Organization 2011) (Table 3.17)

Table 3.17. Correspondence between the nutritional status based on the current silhouette selection and based on the BMI classification

Silhouettes	BMI (kg/m²)	Nutritional status
1-2	<18.5	Under-weight
3-4	18.5-24.99	Normal-weight
5	25-29.99	Overweight
6-7	30-39.99	Obesity
8-9	≥40	Morbid obesity

IS is a measure of inconsistency between the perception of the current body size and the actual nutritional status, where "0" indicates full consistency and larger numbers (negative or positive) indicate greater inconsistency. Negative values indicate an under-estimation of the real body size whereas positive values indicate an over-estimation of the real body size. Based on this, five categories were made:

(2) Moderate inconsistency by over-estimation

(1) Slight inconsistency by over-estimation

(0) Full consistency

(-1) Slight inconsistency by under-estimation

(-2) Moderate inconsistency by under-estimation

2.5. GENETIC DATA

2.5.1. SNP selection

A review of literature was done through PubMed (NCBI 2017) in order to choose SNPs that have shown to be associated with obesity development. Based on the information gathered, 24 SNPs were selected in 13 different genes, which have been shown to have a significant influence on BMI or on other obesity-related traits (LEPR, NEGR1, TMEM18, GNPDA2, BDNF, UCP2, FAIM2, NRXN3, MAP2K5, SH2B1, FTO, MC4R and KCTD15). Those SNPs were selected either from GWAS or candidate gene studies. The characteristics of the selected SNPs for this study are listed in Table 3.18.

Table 3.18. Characteristics of the selected SNPs.

Gene	Location	SNP	Basepair Position	Alleles	Minor Allele	MAF* CEU	MAF* IBS
LEPR	1p31	rs1137101	65831101	G/A	A	0.52	0.63
NEGR1	1p31.1	rs3101336	72523773	C/T	T	0.36	0.34
		rs2568958	72537704	A/G	G	0.36	0.34
		rs2815752	72585028	A/G	G	0.36	0.34
TMEM18	2p25.3	rs6548238	624905	C/T	T	0.17	0.15
		rs7561317	634953	G/A	A	0.16	0.15
GNPDA2	4p12	rs10938397	44877284	A/G	G	0.42	0.37
ADRB2	5q31-q32	rs1042719	148187640	G/C	C	0.26	0.28
BDNF	11p13	rs4923461	27613486	A/G	G	0.24	0.24
		rs925946	27623778	G/T	T	0.34	0.27
UCP2	11q13	rs660339	73366752	G/A	A	0.40	0.36
		rs659366	73372402	C/T	T	0.36	0.33
FAIM2	12q13	rs7138803	48533735	G/A	A	0.32	0.34
NRXN3	14q31	rs10150332	79006717	T/C	C	0.25	0.17
		rs10146997	79014915	A/G	G	0.25	0.17
MAP2K5	15q23	rs4776970	65867940	T/A	A	0.64	0.60
		rs2241423	65873892	G/A	A	0.20	0.29
SH2B1	16p11.2	rs7498665	28790742	A/G	G	0.36	0.29
FTO	16q12.2	rs9939609	52378028	T/A	A	0.44	0.37
		rs8049235	52578510	G/A	A	0.37	0.39
MC4R	18q22	rs17782313	56002077	T/C	C	0.26	0.26
		rs12970134	56035730	G/A	A	0.29	0.29
KCTD15	19q13.11	rs29941	39001372	G/A	A	0.31	0.36
		rs11084753	39013977	G/A	A	0.30	0.38

MAF: Minor allele frequency; CEU: European Ancestry; IBS: Iberian Population in Spain.
* Minor allele frequencies were obtained from 1000 Genomes Project (Phase 3) (1000 Genomes 2015).

2.5.2. Saliva samples

Oragene DNA sample collection kit OG-500 (DNA Genotek, 2 Beaverbrook Road Kanata, ON Canada) was used to collect saliva samples from participants. This is an all-in-one system for the collection, stabilization, transportation and purification of DNA from saliva. To successfully carry out the saliva collection, participants were asked not to eat, drink, smoke or chew gum 30 minutes before collecting the saliva sample. The sample was collected as it is shown in the following schema (Figure 3.17):

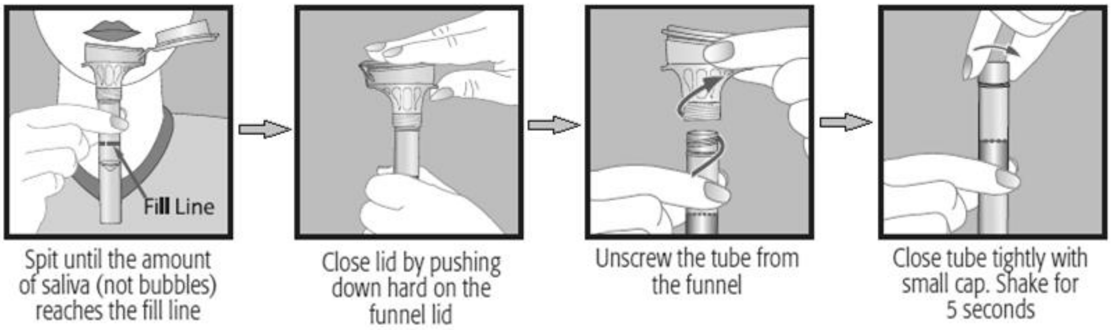


Figure 3.17. Steps on the collection of the saliva sample. Source: (DNA Genotek 2017).

2.5.3. DNA extraction

After the collection of saliva samples, the tubes were stored in a freezer at -20ºC until the DNA extraction, as recommended by the manufacturer of the Oragene DNA (OG-500) Kit for long term storage.

Saliva samples were thawed before DNA extraction. For the purification of genomic DNA an ethanol precipitation protocol with OG-L2P-5 Purifier (purification reagent) was used, which is a step-by-step protocol provided by the manufacturer for manual purification of DNA from 0.5 ml of sample (PD-PR-006 Issue, DNA Genotek Inc.).

2.5.4. DNA quality control

After the DNA extraction the quantity and purity of the DNA samples was determined. This was carried out by assessing samples' optical densities at three different wavelengths (230nm, 260nm, 280nm). In this study a Nanodrop Spectrophotometer (NanoDrop Technologies, USA) was used to quantify DNA and assess its purity, according to the manufacturer's instructions. The micro volume capability of this system (1μl) allows to quickly and easily run quality control checks of nucleic acid, since the sample directly wets the system optics, reducing the variations and contaminations resulting from changing or repositioning the cuvettes.

Purity

Nucleic acids absorb ultraviolet light specifically at 260nm (A260), proteins absorb light at a specific wavelength of 280nm (A280), and finally, there are other contaminants (e.g. salts or some solvents) that absorb light at 230nm (A230). Based on this it is possible to check the DNA purity through two ratios: A260/A280 and A260/A230. The

A260/A280 ratio indicates principally the presence of proteins but also of residual phenol or other reagent associated with the extraction protocol. A ratio of around 2.1 and 1.8 is generally accepted as "pure" for DNA. The studied samples presented a mean value for A260/A280 ratio of 1.85. The A260/A230 ratio indicates the presence of other contaminants such as salts, phenols, carbohydrates or other aromatic compounds. This ratio should be close to 2.0 in pure samples. The samples in the present study showed a mean value of 1.31 for A260/A230 ratio.

Quantity

According to the Beer-Lambert law, DNA shows a direct correlation between its absorbance at 260nm and its concentration (only linear for absorbance between 0.1 and 1.0). Thus, the quantity of DNA in the samples could be determined by the OD (optical density) measured at 260nm. The samples in the present study showed a mean concentration of 308.22ng/μl.

2.5.5. SNP genotyping

Selected SNPs were genotyped using TaqMan OpenArray™ Genotyping system (Applied Biosystems). This system uses polymerase chain reaction (PCR) reagents based on fluorescence to provide a qualitative detection of targets using post-PCR analysis. Thus, two steps are needed to conduct this kind of analysis: thermal cycling (PCR amplification) and detection of the resulting fluorescence signals. The genotyping process was performed by professionals at the General Genomics Service, Sequencing and Genotyping unit of UPV/EHU, following the TaqMan OpenArray™ Genotyping System User Guide and with starting DNA concentrations of 50 ng/μl. Two duplicate samples as positive controls and two negative controls were included on each genotyping plate following the standard protocol.

This genotyping system allows the differentiation of the two alleles of a single nucleotide polymorphism (SNP) of unknown samples. The PCR includes a specific fluorescent-dye-labelled probe for each allele of the target SNP. In order to differentiate each allele, the probes have two different fluorescent reporter dyes at 5´-end of the oligonucleotide. VIC™ dye is linked to the allele 1 probe and FAM™ is linked to the allele 2 probe. TaqMan probes also have a minor groove binder (MGB), which increases the melting temperature of probes allowing greater differences in melting temperatures values between matched and mismatched probes, and thus providing accurate genotyping. In addition to the reporter dye and the MGB, probes also have a non-fluorescent quencher (NFQ) at the 3´-end, which inhibits any fluorescence signal emitted by the reporter dye as long as the reporter dye and the quencher are in proximity (Figure 3.18).

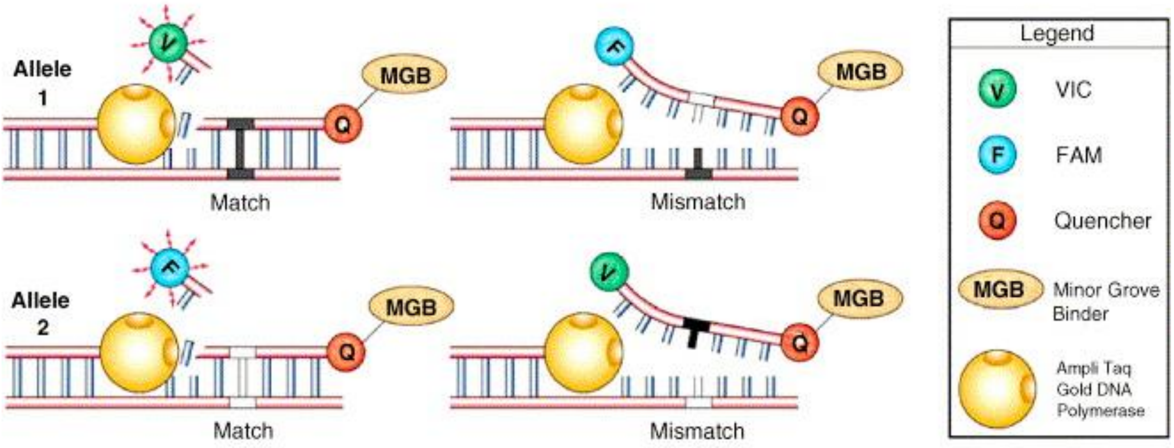


Figure 3.18. SNP genotyping with TaqMan. Source: TaqMan OpenArray™ Genotyping System User Guide

During PCR, each probe anneals specifically to its complementary sequence. DNA polymerase can cleave only probes that have hybridized to its specific SNP allele, separating the reporter dye from the quencher and increasing fluorescence of the reporter dye. A mismatch greatly reduces the efficiency of hybridization, so the DNA polymerase displaces the probe and the reporter dye is not release.

After performing the PCR, fluorescence data are collected and transferred to genotyping software that translated them into genotypes (Figure 3.19). In this case, TaqMan™ Genotyper Software Version 1.3 (Applied Biosystem) was employed for this purpose.

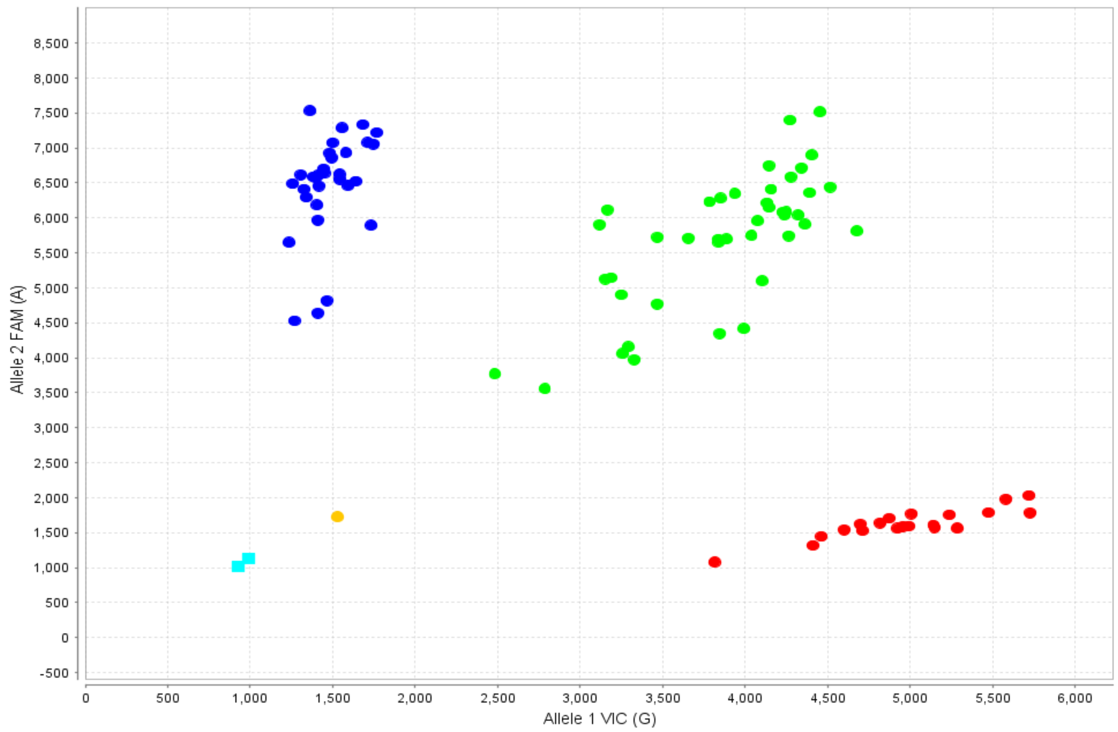


Figure 3.19. Typical scatter plot from TaqMan SNP Genotyper Software.

2.5.6. <u>Genotyping quality control</u>

As expected, minor allele frequencies (MAF) were higher than 0.05 for all analysed SNPs. Two SNPs with a call rate (i.e. successful genotyping frequency) <90% were excluded from the analyses (rs1042719 and rs8049235). Likewise, 33 individuals with individual call rate <90% were also excluded.

Hardy-Weinberg equilibrium (HWE) is other of the requirements in the quality control of SNPs. This equilibrium states that allele and genotype frequencies in an infinite and panmictic population will remain constant from one generation to the next in the absence of mutation, selection, genetic drift, gene flow or crosses between different generations. The genotype frequencies in the studied population are compared with the ones predicted by the Hardy-Weinberg equilibrium using a Chi-square test. As in case-control studies genotypic frequencies of cases could be different than expected according to HWE just due to the implication of the polymorphisms in the disease, only control genotypic frequencies were tested for HWE, using PLINK. After checking HWE, another SNP (rs10150332) was excluded from the analysis since it was not in HWE ($p<0.05$).

3. ANALYTICAL METHODS

3.1. DATABASE MANAGEMENT

All the acquired data during the collection period were stored in a database created with IBM SPSS Statistics program. Exact decimal age for each individual was calculated from the date of birth and the date of measurement, following these steps:

(1) Calculate the birth day from the birth date as follows:

$$(Year\ of\ birth \times 365.25) + [(Month\ of\ birth - 1) \times 30] + (Day\ of\ birth)$$

(2) Calculate the measurement day from the measure date as follow:

$$(Year\ of\ measure \times 365.25) + [(Month\ of\ measure - 1) \times 30] + (Day\ of\ measure)$$

(3) Calculate lived years from the lived days as follow:

$$\frac{(Day\ of\ measure - Day\ of\ birth)}{365.25}$$

3.1.1. Outliers

Outliers are atypical values that lie distant from the overall pattern of distribution. This kind of values usually indicates abnormal values of the traits or an error in measurement. Whatever the reason, their inclusion in a study may drastically affect many statistical analyses. For this reason, the presence of outliers was checked by visual inspection with the help of box whisker plots for each sex separately, and these data points were excluded from the analyses.

3.2. PRELIMINARY STATISTICAL ANALYSIS

3.2.1. Normality and homoscedasticity of data

In the present work, normality and homocedasticity (equality of variances) of data were checked, as some statistical test can only be applied when trait's values follow a multivariate normal distribution.

There are several ways to detect significant departures from normality of quantitative traits. In this work Kolmogorov-Smirnov was generally used to check normality, as the sample or the sample subgroups were composed of more than 50 individuals. In a few specific cases it was necessary to use Shapiro-Wilk, when subgroups were composed of 50 individuals or less. On the other hand, Levene test was employed to assess equality of variances.

In some cases the data did not fulfil Kolmogorov-Smirnov or Shapiro-Wilk tests' criteria of normality. However, in this kind of studies a distribution with a kurtosis and skewness <2 could be reasonably analysed under the assumption of a multivariate normal distribution (deCarlo 1997; Kim 2013). Thus, kurtosis was also calculated to verify the normality of the data.

3.2.2. Descriptive statistics

Basic descriptive statistics in this thesis were performed as a first step to describe the sample. Mean and standard deviation were used to describe continuous variables, whereas, percentage was used to describe categorical variables.

In Chapter IV, mean and standard deviation were calculated for each somatotype component separately. Somatotype Dispersion Mean (SDM) and Somatotype Attitudinal Mean (SAM) with their correspondent standard deviations were obtained for the somatotype as a whole, which indicates the homogeneity of each group in two and three dimensions respectively. Mean BMI and obesity percentage for all the categories in each image related variable were also calculated for Chapter V and shown in Appendix II. Descriptive statistics for all the variables analysed in Chapter VI are also shown in appendix III.

3.3. STATISTICAL ANALYSES

3.3.1. Partial correlations

This procedure is a measure of the strength and direction of a linear relationship between two continuous variables whilst controlling for the effect of one or more continuous confounding variables. It differs from Pearson correlation in that the latter does not allow controlling for any covariate. The null hypothesis (H_0) is that the partial correlation coefficient is "0", which means that there is no lineal relation between the two variables. In this study a p-value lower than 0.05 was considered significant. Thus, when the p-value is less than 0.05, the H_0 can be rejected which indicates that a lineal relation exists between the two variables. Partial correlations coefficients range between -1 and 1; negative values indicate a negative lineal relation, whereas positive values indicate a positive lineal relation.

In Chapter IV partial correlations between somatotype components as well as between these components and some anthropometric measures were calculated controlling for sex and age.

3.3.2. ANOVA

The one-way analysis of variance (ANOVA) is used to determine whether there are any statistically significant differences between several independent groups, on the mean of a continuous dependent variable. In order to perform this analysis, the dependent variable needs to be normally distributed for each category of the independent variable. Besides, F statistic can only be used when variance homogeneity is assumed and Welch statistic must be used when variance homogeneity cannot be assumed. ANOVA tests the null hypothesis (H_0) of no statistically significant differences between group means. This hypothesis is accepted when the p-value is equal to or greater than 0.05. When the p-value is less than 0.05 the alternative hypothesis (H_A), which indicates that there are at least two group means that are statistically and significantly different from each other, should be accepted. However, this test cannot point to what specific groups are statistically and significantly different from each other. Therefore, when significant differences are shown by the ANOVA, a post hoc test should be performed to obtain this information. These tests perform multiple pair wise tests while they control for multiple comparisons error. If the data met the assumption of homogeneity of variances, "Tukey" post hoc test will be used; whereas, if the data do not meet this assumption, "Games Howell post hoc test will be used instead.

The ANOVA test was used in Chapter IV to compare each somatotype component between four groups created based on sex and age in each nutritional category.

3.3.3. Kruskal-Wallis

The Kruskal-Wallis H test is used to determine if there are statistically significant differences on the medians or mean ranks of a continuous or ordinal dependent variable between several groups of an independent variable. It is the nonparametric alternative to the ANOVA test when the normality assumption is not met. This analysis also tests the H_0, of no difference between mean ranks of the groups. When the p-value is less than 0.05, the H_0 is rejected, and statistically significant differences between at least two groups are assumed. This test cannot also identify what specific groups show statistically and significantly differences between each other. Thus, when overall statistically significant differences are shown, Mann-Whitney U test should be performed in order to find between which groups are the differences.

The Kruskal-Wallis H test was used in Chapter IV, when the dependent variable was not normally distributed, to compare each somatotype component between four groups created based on sex and age in each nutritional category.

3.3.4. ANCOVA

The one-way analysis of covariance (ANCOVA) is used to determine whether there are any significant differences between several independent groups, on a continuous dependent variable. However, whereas the ANOVA looks for differences in the group means, the ANCOVA looks for differences in the means adjusted for a covariate (i.e. a third variable that is believed to affect the results). The dependent variable only needs to be approximately normally distributed for each category of the independent variable because this test is quite "robust" to violations of normality. When the p-value is less than 0.05 the H_0 can be rejected, indicating that there are at least two group means that are statistically significantly different from each other when controlling for a covariate. Just like in ANOVA, another test is needed to check between which groups are the differences; T tests for comparisons in pairs is used for this purpose and in order to control for multiple comparisons Bonferroni correction is used.

The ANCOVA test was used in Chapter IV to compare each somatotype component between five groups created based on sex and sport practice in each nutritional category and controlling for age effect.

3.3.5. Mann-Whitney U test

The Mann-Whitney U test is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed. When the distribution of the two groups has the same shape, the comparison is between medians; but, when their shape is different, the comparison is between mean ranks.

The H_0 is rejected when the p-value is less than 0.05, indicating that there are significant differences between the two groups.

The Mann-Whitney U test was used in Chapter V to assess differences in the current body image, ideal body image, ideal body image for the opposite sex, dissatisfaction score and inconsistency score between women and men. In the same chapter, this test was also used to assess BMI differences between women and men as well as between two groups based on age (<45 years, ≥45 years).

3.3.6. Chi square

The Chi-square test is usually used to assess relationship between two independent nominal variables. The null hypothesis of independence should be rejected when the p-value is less than 0.05, concluding that the two variables are related. However, this test can also be used to test for equality of proportions between two populations, in this case when the p-value is less than 0.05 the H_0 is rejected, indicating different proportions between the two populations.

In Chapter V, Chi-square test was used to compare the obesity % between women and men as well as between the two age groups (<45 years, ≥45 years). Chi-square test was also used to check HWE in Chapter VII.

3.3.7. Gamma

Gamma is a common measure of association between two ordinal variables. Unlike the Chi-square, Gamma can also reveal the direction of the relationship between the two variables. This measure ranges between -1.0 to +1.0, with a value of 0 indicating no relationship.

Gamma measure is used in Chapter V to assess association between the nutritional status and the body image related variables (current body image, ideal body image, ideal body image for the opposite sex, dissatisfaction score and inconsistency score).

3.3.8. Logistic regression

A logistic regression, predicts the probability that an observation falls into one of the two categories of a dichotomous dependent variable based on one or more independent variables that can be either continuous or categorical. Simple logistic regression is used when there is just one independent variable and multiple logistic regression, when there are several independent variables. The strength of association between the binary outcome and the exposure variables are expressed in term of odds ratios, which measures the effect size. The odds are defined as the ratio of the probability that the event of interest occurs to the probability that it does not; taking into account another variable, the odds ratio can be computed.

$$odds = \frac{P(the\ event\ occurs)}{P(the\ event\ does\ not\ occurs)}$$

$$odds\ ratio = \frac{odds\ (if\ the\ corresponding\ variable\ is\ incremented\ by\ 1)}{odds\ (if\ the\ corresponding\ variable\ is\ not\ incremented)}$$

Odds ratio ranges between 0 and infinity. An odds ratio equal to 1 indicates that there is no relationship between the two variables. An odds ratio higher than 1 indicates that the two variables are positively associated; the greater the odds ratio, the stronger is the association. An odds ratio lower than 1, indicates that there is a negative association between the two variables. In logistic regression, Wald statistic is used to assess the significance of the coefficients in the model. When the p-value associated to Wald statistics is less than 0.05, the H_0 of independence can be rejected and it can be concluded that both variables are significantly associated.

Multiple logistic regression was used in Chapter VI to assess the association between 17 environmental factors and obesity. Multiple logistic regression was also used in Chapter VII in order to assess the effects of 21 genetic polymorphisms (SNPs) and obesity. In both situations obesity was considered as a dichotomous variable. In order to control the confounding effects of sex, age and SES, these variables were introduced as covariates in the multiple logistic regressions performed in both chapters.

3.3.9. Linear Regression

Linear regression predicts the value of a continuous variable (dependent variable) based on the value of another continuous variable (independent variable). Simple linear regression is used when there is just one independent variable and multiple linear regression, when there are more than one independent variable. Beta coefficient indicates the change in the dependent variable for one unit increase in the independent variable. Thus, the higher the beta value the greater the influence. A positive beta coefficient is indicative of a positive relation between variables, while a negative beta coefficient is indicative of a negative the relation between variables. A beta coefficient equal to "0" indicates no relationship between the variables. When the p value associated to the beta coefficient is less than 0.05 it can be concluded that the independent variable is significantly associated to the dependent variable.

Multiple linear regression was used in Chapter VII in order to assess the influence of the 21 selected SNPs in obesity related continuous variables. In order to control the confounding effects of sex, age and SES, these variables were also introduced as covariates in the multiple linear regressions performed in this chapter.

3.4. MULTIPLE COMPARISON CORRECTION

Bonferroni correction method reduces the chances of obtaining type I errors when multiple pair wise tests are performed on a single set of data. This method controls the error of multiple comparison tests, adjusting the critical p-value (α) by the number of performed comparisons (k) as follows: $\alpha_c=\alpha/k$.

When the applied test does not directly correct for multiple comparisons, Bonferroni correction was used for this purpose (Chapter VI and Chapter VII).

3.5. SOFTWARE PACKAGES

SNP genotyping was performed using TaqMan™ Genotyper Software Version 1.3 (Applied Biosystem). Logistic and linear regression analyses as well as Hardy-Weinberg equilibrium tests used in Chapter VII were performed in PLINK (v1.07), which is a toolset for whole-genome association and population-based linkage analysis (Purcell S. et al., 2007). The other statistical analyses from this thesis were performed in IBM SPSS Statistics, version 23 for Windows (SPSS Inc., Chicago, IL). Microsoft Office Excel 2007 was used for data management and graphics construction.

Chapter IV

Somatotype Variability According to Sex Age and Sport Practice in Different Nutritional Status

1. SUMMARY

OBJECTIVES: Obesity development is due to an imbalance in energy metabolism, which alters body composition and as consequence modifies body morphology. In this chapter variability of body shape and composition due to sex, age and sport practice was analysed in each nutritional category. Understanding changes in body morphology and composition in each nutritional category may help to improve the attention of obese subjects.

METHODS: The sample was composed by 483 adults (291 women and 192 men) from the Basque Country, and it was divided in four groups based on sex and age, or on sex and sport practice in each nutritional category. Three more groups (based on nutritional categories) from a sample of 33 men rugby players were also used in this chapter. Body morphology and composition was estimated through the Heath-Carter's anthropometric somatotype. Somatotype dispersion distances (SDD) were calculated between sex, age and sport practice groups in each nutritional category. For each somatotype component, ANOVA or Kruskal-Wallis was used to assess differences between groups based on sex and age; and ANCOVA (with age as a covariate) was used to assess differences between groups based on sex and sport practice in each nutritional category.

RESULTS: Endomorph and mesomorph components increased as ectomorphy decreased with BMI. High sexual dimorphism for somatotype could be seen in these results, being women more endomorphic and less mesomorphic than men. Ectomorphy was the somatotype component that showed the highest differences by age group. In overweight and obese nutritional status, no-professional sport practice leaded to a reduction on body mass (endomorphy and mesomorphy).

CONCLUSIONS: The obtained results indicate that not just fat mass (FM) but also fat free mass (FFM) is involved in obesity development. Sexual dimorphism is more remarkable in normal-weight category and is minimal in morbid obesity. Besides, the ageing process is related with a progressive reduction in body linearity. On the other hand no-professional sport practice may help to reduce body mass, especially in men; whereas, professional sport practice may help to reduce FM more specifically.

2. BRIEF INTRODUCTION

Somatotype is one of the most useful tools in the study of body morphology and composition. It was originally defined by Sheldon et al. (1940) as the quantification of the major components of human beings (adiposity, musculoskeletal component and linearity) and subsequently modified by Heath and Carter (1967). This technique has been mainly used for studies in the field of sports, primarily in kinanthropometry and also in the area of auxology (e.g. Ghosh and Malik 2010; Sanchez-Martinez et al. 2017; Sanchez-Munoz, Muros, and Zabala 2017). However, the use of somatotype for the study of obesity and related phenotypes or the study of nutritional status has been weakly developed.

Body morphology is influenced by the amount of each body component. Many constitutive factors, such as age and sex, are known to be of great importance on body composition. For example, according to Mobbs and Hof (2010) an increase in adiposity and a decrease in muscle mass constitute an almost universal feature of animal aging. Also, the differences in the hormonal mechanism between men and women, due to differences in physiological and metabolic requirements, influence body components (Buffa, Marini, and Floris 2001). Body morphology can also be affected by external or environmental factors (Buffa, Marini, and Floris 2001; Gutnik et al. 2015), being nutrition one of the most important ones as body composition is strongly related to food consumption (Serairi Beji et al. 2016). Low energy intake may cause muscular mass loss or conversely, an excess of energy intake could promote the increase in body fat, potentially leading to obesity (Serairi Beji et al. 2016). On the other hand, practice of sports increases energy expenditure, which in turn could as well influence body morphology.

3. BRIEF METHODOLOGY

In order to undertake the analyses in this chapter, the general sample was divided in four groups based on sex (men, women) and age (<45 years, ≥45 years) in each nutritional category. Nutritional categories were created based on BMI and according to the WHO criteria (normal-weight, overweight, obesity, morbid obesity). As only six participants were in the under-weight category (all of them in the upper limit), they were included in the normal-weight group in order to conduct the specific analysis of this chapter.

Subjects' somatoplots or mean somatoplots for the studied groups in each nutritional category were represented in two-dimensional somatocharts. In addition, in order to complete graphical information, compograms comparing the mean values of the three somatotype components in each group were presented in the Appendix I (from Figure A.4.1. to Figure A.4.4.).

In order to test for differences in somatotype between age and sex groups, the somatotype dispersion distances (SDD) between the somatoplots of both sexes in each age group, and between both age groups in each sex were calculated in the different nutritional categories. This method assess the distances between two somatoplots from a two dimensional somatochart. According to Hebbelinck et al. (1975) when SDD is equal to or greater than 2, the distance is considered as statistically significant ($p<0.05$), which means that both groups have actually different somatoplots.

The study of each somatotype component separately may be helpful to complement the information of the somatotype as a whole. For this reason, ANOVA or Kruskal-Wallis test were used to compare the means (or medians) of each somatotype component between the four age and sex groups, in each nutritional category, followed by post-hoc analyses (i.e. Tukey, Games-Howell or Mann Whitney) to check which specific groups caused the differences and control for multiple comparisons.

Besides age and sex, practice of sports also modifies body composition. Thus, another section was included in this chapter, where in addition to the general population sample, a little sample of rugby players was included in order to assess the changes in body shape and composition related to sport practice in a sample heavily exposed to it.

For the analyses conducted on this section, five groups based on sex and sport practice (i.e. men- no sport, men-sport, men-rugby players, women-no sport, women-sport) were used for each nutritional category created as in the analyses above based on BMI and WHO recommendations. Only one rugby practice group was created since all the rugby players of the sample were men.

Each somatotype component means were compared by ANCOVA between the above mentioned groups, with decimal age included as a covariate in order to remove the effect of age. The mean somatoplots as well as the mean values of the three somatotype components, previously adjusted for age within the ANCOVA, were also represented in a two dimensional somatochart and in compograms, respectively (Compograms are shown in Appendix I: Figure A.4.5 and Figure A.4.6). SDD were also calculated between groups that do not practice sports and those who do (general population or rugby players). Bonferroni test was used to adjust for multiple comparisons in post-hoc analyses within ANCOVA test. In this section morbid obesity was not included due to the low number of morbid obese individuals who perform any sport.

Partial correlations controlled for sex and age, between the three somatotype components were calculated. In Appendix I (Table A.4.1) the correlation between somatotype components and some anthropometric variables can be also seen.

In order to make more clear explanations, SDD between nutritional categories, in each group based on sex and age were also performed and shown in Appendix I (Table A.4.2). Comparisons between nutritional categories for each somatotype component were performed in each group based on sex and age, these results are shown in Appendix I (from Table A.4.3 to Table A.4.6). Finally, comparisons between nutritional categories for each somatotype component were also performed in each group based on sex and sport practice (previously adjusted for age) and the results are shown in Appendix I (from Table A.4.7 to Table A.4.11).

4. RESULTS

4.1. DESCRIPTIVE STATISTICS

Somatotype characteristics of the examined subjects are presented in Table 4.1 for men and in Table 4.2 for women. In these tables, somatotype means and standard deviations in each nutritional category could be seen for each of the four groups (based on sex and age) as well as somatotype dispersion means (SDM) and somatotype attitudinal means (SAM). In general, women presented higher values of SDM and SAM indicating that women were more heterogeneous than men in all nutritional categories with the exception of obesity in the older group where men were slightly more heterogeneous.

Table 4.1. Descriptive statistics of somatotype components in men.

	<45 years							≥45 years						
	N	Somatotype components		SDM		SAM		N	Somatotype components		SDM		SAM	
		M	S.D	M	S.D	M	S.D		M	S.D	M	S.D	M	S.D
NW	49	3-4-3	1.0-0.9-0.8	3.2	1.8	1.4	0.7	13	4-4-2	0.9-0.7-0.6	2.3	1.4	1.1	0.5
OW	26	5-5-1	1.0-0.6-0.5	2.6	1.3	1.1	0.6	38	4-5-1	0.9-0.7-0.4	2.2	1.4	1.1	0.6
OB	19	7-7-0	1.4-1.3-0.1	3.1	1.6	1.6	0.9	33	6-7-0	1.5-1.0-0.0	3.0	1.7	1.6	0.8
MO	9	9-10-0	0.6-1.0-0.0	1.6	0.9	0.9	0.5	5	8-9-0	1.1-0.6-0.0	2.2	1.3	1.0	0.4

NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity; M: mean; SD: standard deviation; SDM: somatotype dispersion mean; SAM somatotype attitudinal mean.

Table 4.2. Descriptive statistics of somatotype components in women.

	<45 years							≥45 years						
	N	Somatotype components		SDM		SAM		N	Somatotype components		SDM		SAM	
		M	S.D	M	S.D	M	S.D		M	S.D	M	S.D	M	S.D
NW	68	5-4-2	1.4-1.0-1.1	4.1	2.1	1.8	0.9	34	5-4-2	1.3-0.9-1.0	4.0	2.0	1.7	0.8
OW	31	7-5-1	1.2-0.9-0.4	3.0	1.8	1.4	0.7	40	7-5-0	1.3-1.0-0.2	3.2	1.6	1.5	0.7
OB	26	8-7-0	0.9-1.7-0.0	3.5	1.9	1.7	0.8	64	8-7-0	1.0-1.3-0.0	2.8	1.6	1.4	0.8
MO	9	10-11-0	0.6-2.4-0.0	3.4	2.2	1.7	1.1	19	9-10-0	1.0-1.9-0.0	3.3	2.7	1.7	1.2

NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity; M: mean; SD: standard deviation; SDM: somatotype dispersion mean; SAM somatotype attitudinal mean.

4.2. CORRELATIONS BETWEEN SOMATOTYPE COMPONENTS

Partial correlations between somatotype components controlled for age and sex are presented in Table 4.3. There was a positive correlation between the endomorphic and mesomorphic components, whereas these two components had a negative correlation with ectomorphy. Additionaly, correlations between somatotype components and some anthropometric measures, including BMI, were shown in the Appendix I (Table A.4.1). Height was the only antropometric meassurement that showed a positive correlation with ectomorphy (r=0.15). Circumferences as well as weight and biepicondilar measures of humerous and femur presented their highest positive correlations with mesomorphy, whereas all the skinfolds presented their highest positive correlations with endomorphy. Finally, BMI had a negative correlation with ectomorphy (r=-0.72) and a relatively high and positive correlation with endomorphy (r=0.82) and mesomorphy (r=0.89).

Table 4.3. Pearson correlations between somatotype components controlled for sex and age

	Endomorphy	Mesomorphy	Ectomorphy
Endomorphy	1		
Mesomorphy	0.67 ***	1	
Ectomorphy	-0.75 ***	-0.66 ***	1

*** Estimate significant at p<0.001

4.3. SEXUAL DIMORPHISM AND AGE EFFECT

4.3.1. Representation in two dimensional somatochart and SDDs

Figure 4.1 shows all the somatoplots (men and women) represented in the somatochart. Somatoplots appeared to be distributed along the ectomorphy axis from the central region to the northwest, which indicates that participants had similar values for endomorphy and mesomorphy as ectomorphy changes. Although there was an overlap between men and women, primarily in the endomorph-mesomorph region, men were mostly distributed in the endomorphic mesomorph area (showing a predominance of the mesomorphic component over the endomorphic one), whereas women were mostly distributed in the mesomorphic endomorph area (showing a predominance of the endomorphic component over the mesomorphic one).

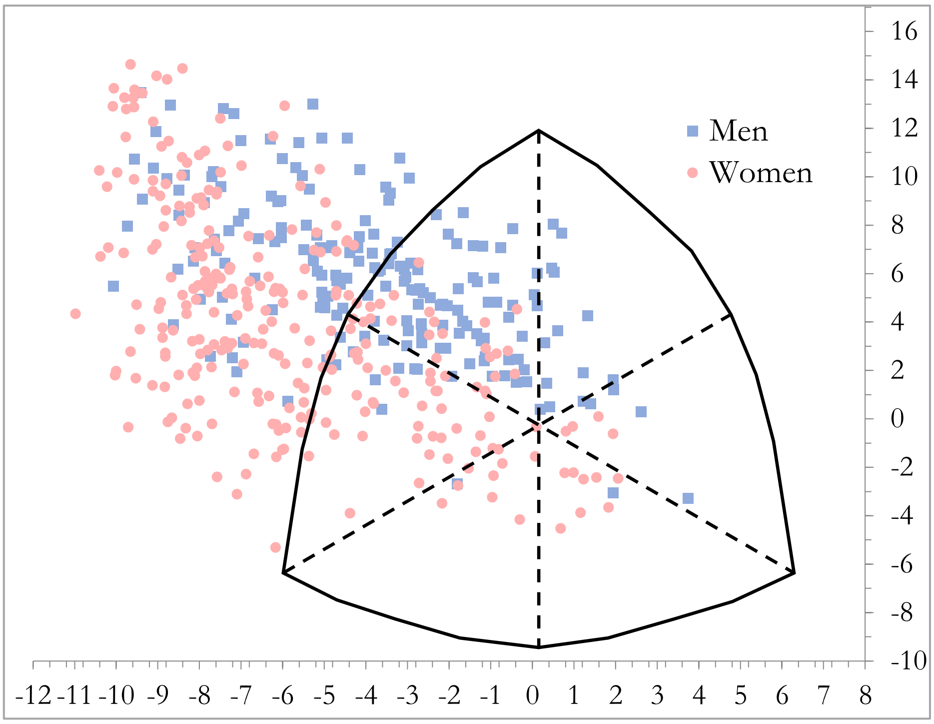


Figure 4.1. Somatochart showing the somatoplots for men and women.

Mean somatoplots for each sex, age and nutritional status groups are displayed in Figure 4.2. Normal-weight individuals were close to central somatotype, especially younger adults. From here, the higher the nutritional status was, the more extreme the values for endomorphy and mesomorphy were (see Appendix I. From Table A.4.2 to Table A.4.5). All somatoplots representing obesity or morbid obesity categories were located outside the arc-sided triangle (Figure 4.2.), which identified them as extreme cases for their particular somatotype category. On the other hand, overweight groups were close to the arc-sided triangle (men were inside it while women were outside of it), which marks the limit between normal and extreme morphotypes. The mean values for each somatotype components and their comparison between nutritional status in each studied group together with the compograms with the mean values for each somatotype component can be seen in Appendix I (From Table A.4.2 to Table A.4.5 and from Figure A.4.1. to Figure A.4.4.). Significant differences in the three somatotype components between nutritional status could be seen along obesity development in the four studied groups.

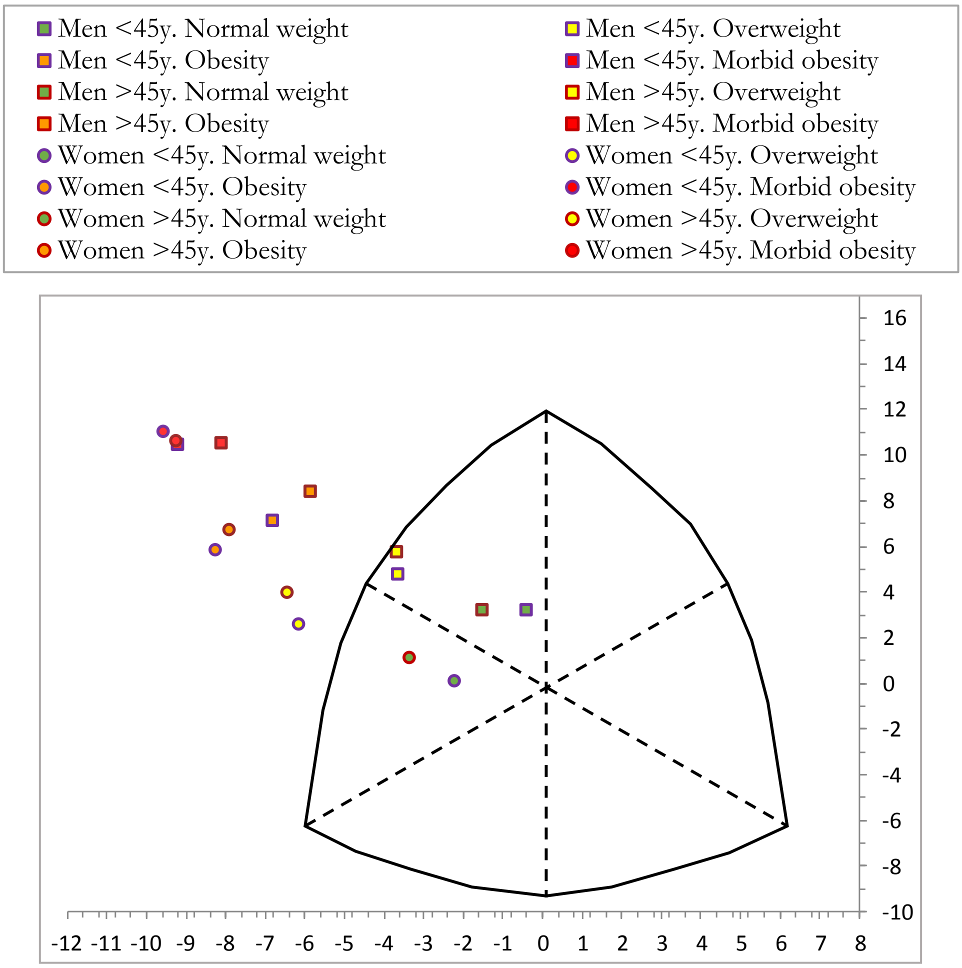


Figure 4.2. Somatochart showing the mean somatoplots for the sixteen groups based on sex, age group and nutritional status.

SDDs could be represented as imaginary lines connecting two somatoplots. SDDs between mean somatoplots of men and women of different age groups in each nutritional status are shown in Table 4.4 and SDDs between mean somatotypes of younger and older individuals of each sex in each nutritional status are shown in Table 4.5. The imaginary lines between men and women were situated across the ectomorphic axis and roughly parallel to each other, whereas the ones between the different age groups were above and under the ectomorphic axis in men and women respectively (Figure 4.2). A significant sexual dimorphism was found in both age groups (i.e. SDD≥2 between males and females) in all nutritional status with the exception of morbid obesity where sexual dimorphism was attenuated and the SDD did not reach statistical significance. Distances between the different age groups were generally lower than between sexes, pointing to a higher similarity in body morphology between individuals of different age group than between individuals of different sex. In normal-weight and overweight categories, distances between the two age groups were higher for women than for men while for obesity and morbid obesity the distances between age groups were higher in men than in women. The SDD between consecutive nutritional status (Appendix I, Table A.4.6) were clearly significant (i.e. SDD ≥2) in each of the four groups based on sex and age. Those distances were always larger in the younger age groups, compared with the older groups.

Table 4.4. Distances between somatoplots of men and women in each age group.

SDD	<45years Men vs. Women	≥45years Men vs. Women
NW	**4.42**	**3.81**
OW	**4.86**	**5.11**
OB	**2.81**	**3.93**
MO	0.85	1.98

NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity
Significant SDD at $p<0.05$ are shown in **bold**.

Table 4.5. Distances between somatoplots of younger and older adults in each sex group.

SDD	Men <45years vs. ≥45years	Women <45years vs. ≥45years
NW	1.93	**2.22**
OW	0.97	1.48
OB	**2.09**	1.07
MO	1.91	0.69

NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity
Significant SDD at $p<0.05$ are shown in **bold**.

.4.3.2. Somatotype components' mean comparison between groups

The results of the ANOVA or Kruskal-Wallis together with the results for the post-hoc analyses, for each somatotype component, between the four age and sex groups in each nutritional category are shown from Table 4.6 to Table 4.9. Endomorphy ~~is~~ was the only somatotype component that showed significant differences among the four groups in all nutritional status. However, it is important to highlight that these differences were between sexes and not between the two age categories. Besides, these differences in endomorphy were a little bit attenuated in morbid obesity status compared to other nutritional status since only a significant difference between older adult men and younger adult women was found. Mesomorphic component only presented significant sex differences in normal-weight category and showed an overlap between older adult women and men. Finally, ectomorphic component presented significant differences in almost all nutritional categories, with the exception of morbid obesity where this somatotype component reached its minimum value and remained constant in all the individuals. Besides, in contrast to the differences found for endomoprhy and mesomorphy, differences found in this component were mostly between age groups especially in normal weight and overweight categories.

Table 4.6. Means of each somatotype component and differences between the four groups based on sex and age in **normal weight** category.

	Men 18-44 y.		**Men 45-83 y.**		**Women 18-44 y.**		**Women 45-83 y.**		**Statistic**		**p-value**
Endomorphy	3.07	**a**	3.64	**a**	4.61	**b**	5.16	**b**	F	24.57	**3.8E-13**
Mesomorphy	4.47	**a**	4.49	**a**	3.56	**b**	4.05	**ab**	F	10.59	**2.1E-06**
Ectomorphy	2.65	**a**	2.11	**bc**	2.38	**ab**	1.79	**c**	Welch	6.28	**9.6E-4**

a, b, c: there are significant differences between values with different bold letters.

Table 4.7. Means of each somatotype component and differences between the four groups based on sex and age in **overweight** category.

	Men 18-44 y.		**Men 45-83 y.**		**Women 18-44 y.**		**Women 45-83 y.**		**Statistic**		**p-value**
Endomorphy	4.81	**a**	4.43	**a**	6.78	**b**	6.72	**b**	F	41.29	**7.5E-19**
Mesomorphy	5.37	**a**	5.47	**a**	5.00	**a**	5.49	**a**	Welch	2.03	0.117
Ectomorphy	1.15	**a**	0.74	**b**	0.61	**b**	0.26	**c**	Welch	37.18	**8.5E-14**

a, b, c: there are significant differences between values with different bold letters.

Table 4.8. Means of each somatotype component and differences between the four groups based on sex and age in **obesity** category.

	Men 18-44 y.		**Men 45-83 y.**		**Women 18-44 y.**		**Women 45-83 y.**		**Statistic**		**p-value**
Endomorphy	6.94	**a**	5.97	**a**	8.37	**b**	8.02	**b**	Welch	22.84	**9.1E-10**
Mesomorphy	7.10	**a**	7.25	**a**	7.16	**a**	7.43	**a**	Welch	0.44	0.723
Ectomorphy	0.12	**a**	0.10	**ab**	0.10	**bc**	0.10	**c**	$\chi2$	18.23	**3.9E-04**

a, b, c: there are significant differences between values with different bold letters.

Table 4.9. Means of each somatotype component and differences between the four groups based on sex and age in **morbid obesity** category.

	Men 18-44 y.		**Men 45-83 y.**		**Women 18-44 y.**		**Women 45-83 y.**		**Statistic**		**p-value**
Endomorphy	9.32	**ab**	8.22	**a**	9.58	**b**	9.34	**ab**	Welch	3.13	**0.047**
Mesomorphy	9.95	**a**	9.43	**a**	11.32	**a**	10.11	**a**	$\chi2$	4.03	0.259
Ectomorphy	0.10	**a**	0.10	**a**	0.10	**a**	0.10	**a**	$\chi2$	0.00	1.000

a, b: there are significant differences between values with different bold letters.

4.4. EFFECTS OF SPORT PRACTICE

4.4.1. Representation in two dimensional somatochart and SDDs

Somatochart presented in Figure 4.3 shows the mean somatoplots of participants who practiced some sport (general population or the rugby team) and participants who did not practice any sport in both sexes and in each nutritional category. Even taking into account sport practice, women and men continued to be under and above the ectomorphy axis respectively. However somatoplots showed some differences in their somatotypes, especially in rugby players. Indeed the SDDs shown in Table 4.10 indicated statistically significant distances (i.e. SDD≥2) between individuals who did not practice any sport and rugby players; these distances were higher as the nutritional category represented a higher BMI. Distances between individuals who did not practice any sport and non-professional sportsmen or women were not significant. Yet, these distances were higher in men than in women and almost reached significance threshold in normal-weight men.

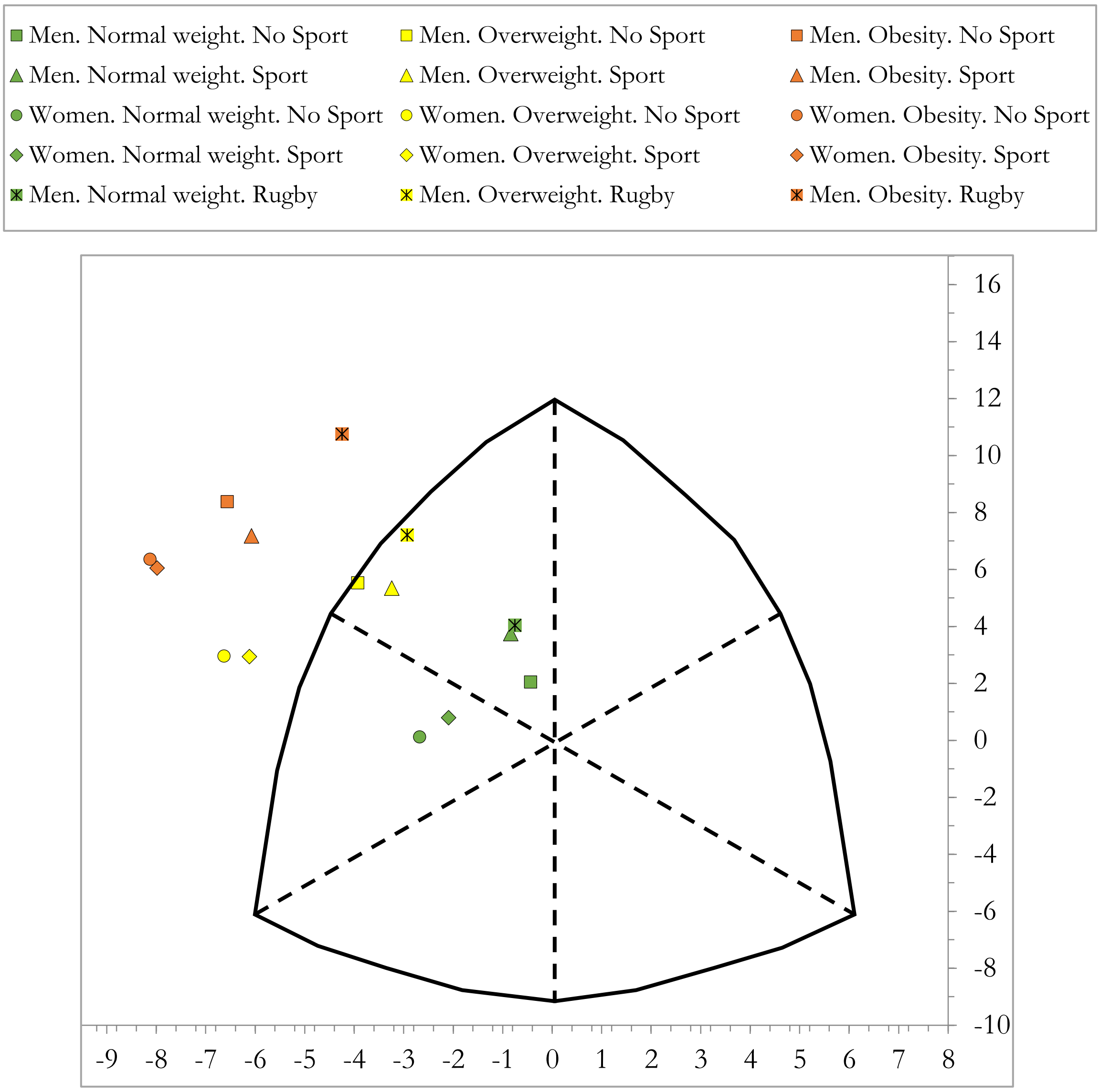


Figure 4.3. Somatochart showing the mean somatoplot for the fifteen groups based on sex, physical activity and nutritional status.

Table 4.10. Distances between the somatoplots of participants that practice and do not practice sports in each sex and nutritional category.

SDD	Men No Sport vs. Sport	Men No Sport vs. Rugby	Women No Sport vs. Sport
NW	1.83	**2.06**	1.21
OW	1.21	**2.41**	0.90
OB	1.47	**4.66**	0.40

NW: normal weight; OW: Overweight; OB: obesity
Significant SDD at $p<0.05$ are shown in **bold**.

4.4.2. Somatotype components' mean comparison between groups

Differences in the means (adjusted for age) of each somatotype component between groups based on sex and sport practice in each nutritional category are presented from Table 4.11 to Table 4.13. Very little differences could be seen in somatotype components between sportswomen and non-sportswomen; there was no nutritional category where these differences reached statistical significance. On the other hand, some differences were seen between non-sportsmen and sportsmen, especially concerning rugby players. Endomorphy presented lower values in sportsmen groups compared to non-sportsmen groups, however differences were significant just between rugby players and non-rugby players in obesity category. Mesomorphy was higher in sportsmen than in non-sportsmen but just in normal-weight category; however, the significance was lost with the correction for multiple comparison. In overweight and obesity categories, mesomorphy decreased with the practice of sports except for rugby players who maintained higher values of mesomorphy (however, possibly due to the small sample of rugby players, significance could not be appreciated). Ectomorphy did not change significantly between men groups in normal-weight category but in obesity its value was higher in the group of rugby players compared with non-rugby players men. The comparison of the mean values for each somatotype component between nutritional status in each studied group together with the compograms representing the mean somatotype components could be seen in Appendix I (From Table A.4.7 to Table A.4.11 and Figure A.4.5 and Figure A.4.6). All somatotype components presented significant differences between consecutive nutritional status in the five studied groups (i.e.: men, no sport; men, sport; men, rugby; women, no sport; women, sport), with the exception of ectomorphy, which had no significant differences between overweight and obesity in women groups.

Table 4.11. Differences in mean somatotype components between the four groups based on sex and sport in **normal-weight** category.

	Men; No sport		Men; Sport		Men; Rugby		Women; No sport		Women; Sport		Statistic		p-value
Endomorphy	3.29	**a**	3.22	**a**	3.06	**ac**	4.88	**b**	4.45	**bc**	F	13.76	**1.4E-09**
Mesomorphy	4.09	**ab**	4.68	**a**	4.70	**ab**	3.60	**b**	3.79	**b**	F	8.48	**3.4E-06**
Ectomorphy	2.85	**a**	2.38	**a**	2.31	**a**	2.20	**a**	2.35	**a**	F	1.53	0.195

a, b, c: there are significant differences between values with different bold letters.

Table 4.12. Differences in mean somatotype components between the four groups based on sex and sport in **overweight** category.

	Men; No sport		Men; Sport		Men; Rugby		Women; No sport		Women; Sport		Statistic		p-value
Endomorphy	4.81	**a**	4.34	**a**	3.81	**a**	7.06	**b**	6.67	**b**	F	38.46	**1.2E-20**
Mesomorphy	5.61	**ab**	5.39	**ab**	5.95	**a**	5.23	**b**	5.08	**b**	F	4.28	**0.003**
Ectomorphy	0.88	**a**	1.10	**a**	0.88	**ac**	0.43	**b**	0.56	**bc**	F	12.77	**1.1E-08**

a, b, c: there are significant differences between values with different bold letters.

Table 4.13. Differences in mean somatotype components between the four groups based on sex and sport in **obesity** category.

	Men; No sport		Men; Sport		Men; Rugby		Women; No sport		Women; Sport		Statistic		p-value
Endomorphy	6.67	**b**	6.18	**b**	4.50	**a**	8.23	**c**	8.08	**c**	F	28.36	**1.1E-16**
Mesomorphy	7.58	**a**	6.73	**a**	7.75	**a**	7.34	**a**	7.12	**a**	F	1.29	0.278
Ectomorphy	0.11	**b**	0.11	**b**	0.25	**a**	0.10	**b**	0.10	**b**	F	15.73	**1.6E-10**

a, b, c: there are significant differences between values with different bold letters.

5. DISCUSSION

The overarching aim of this chapter was to analyse somatotype differences between subgroups based on sex and age, discussed in relation to different nutritional categories. Additionally the effect of sport practice in somatotype components was also examined in each nutritional category. For this last purpose a small sample of rugby players were included in the analyses. In summary the results of this chapter showed that there was an increase in endomorphy and mesomorphy and a decrease in ectomorphy as nutritional status increases. Clear sexual differences were also detected along all nutritional categories being endomorphy the predominant somatotype component in women and mesomorphy in men. Concerning age associated changes, ectomorphy decreased with age at least in normal-weight and overweight categories. Finally, the practice of non-professional sports in general population showed a tendency towards a reduction of body mass; endomorphy as well as mesomorphy are lower when the participant practices any sport (except in normal-weight status where mesomorphy is higher). Whereas, a lower endomorphy but a higher mesomorphy was observed in rugby players compared to non-sports men in all nutritional status.

Ectomorphy usually shows a negative correlation with both endomorph and mesomorph components (e.g. Dey, Khanna, and Batra 1993); result that was also found in our sample. This relationship between somatotype components was logical since while endomorphy and mesomorphy represent the relative mass of the subject, ectomorphy represents the linearity of the body and as body mass increases linearity decreases. On the other hand, several studies conducted in different populations and compiled in Carter and Heath (1990) showed that correlations between endomorphy and mesomorphy are highly variable and relatively small, with coefficients ranging from -0.33 to 0.47 and close to 0 in many samples. This indicates the existence of little mutual predictive value between endomorphy and mesomorphy which entails that subjects with high values of mesomorph could have both high and low values of endomorphy and vice versa. However, in the present study a relatively high positive correlation (0.67) was found between endomorphy and mesomorphy, which was in disagreement with previous studies and indicates that in this sample either of the two somatotype components (i.e. mesomorphy or endomorphy) increase or decrease in similar proportions. The difference between the correlation obtained in the present work and the range described in Carter and Heath (1990) could be explained by the wide range of BMIs included in the present sample. Variability in body mass could be due to many factors such as sex, ethnicity, practice of any sport… and these factors could affect body morphology changing a particular component of the body (i.e. FM or FFM, in the two compartments model). As it was shown in this thesis, differences in nutritional status (based on BMI) also resulted in body morphology changes. But in this particular study, the high and similar correlations shown between endomorphy and mesomorphy with BMI could be indicating that body morphology differences among different nutritional status are a consequence of changes in both components and not just due to changes in the adipose tissue. Other studies also found higher FFM in obese subjects than in normal weight ones (Lafortuna et al. 2005). This suggests a "training effect" where the excess of FM could act as a chronic extra-load, resulting in muscles development to support it. Indeed, Bosco et al. (1986) observed that subjects loaded with external extra load presented a greater development of the musculature. On the other hand, it should be taken into account that fat is initially stored in the subcutaneous adipose tissue, but when the capacity of this tissue reaches its limit, fat begins to be stored in visceral and intramuscular depots, which could lead to an overestimation of FFM (Palmer and Clegg 2015; Galic et al. 2016).

Although several studies have reported a clear sexual dimorphism in human body morphology and composition (Gris, Giacchino, and Lentini 2004; Wells 2012; Palmer and Clegg 2015), this thesis confirmed the existence of sexual dimorphisms in somatotype, not only in general, but also in each nutritional category. However, sexual dimorphism in high nutritional categories was reduced since somatotype distances between men and women somatoplots were lower in obesity and morbid obesity compared to their immediately previous nutritional category.

Mean somatotype distributions represented in the somatochart indicated dominance of musculo-skeletal component in men and of adipose tissue in women, which agrees with previous works on body composition in both sexes (Wells 2007). The relationship between these two somatotype components is consistent across all nutritional status. However, it is the endomorph component the clear responsible for the maintenance of sexual dimorphism in all nutritional categories.

Among normal-weight participants, the group of young adults presented the highest sexual dimorphism, as both endomorph and mesomorph components showed clear gender differences. This fact is in agreement with other body composition studies which indicate that across all ethnic groups and populations, younger adulthood groups are characterized by considerable dimorphism in body composition with greater mean percentage of fat and less lean mass in women than in men (Wells 2007). However, in higher nutritional categories, mesomorphic differences disappeared, which means that both men and women had similar musculo-skeletal component and only the differences in the endomorphic component remained (excerpt in morbid obesity category).

Regarding age effect on somatotype, SDDs did not always show significant differences between age groups in all nutritional categories. In women, somatotype differences between older and younger women were reduced as nutritional category increases; indicating a reduction of the age effect on body morphology with increasing BMI. However, this pattern could not be seen in men. Although, in this study age differences were lower than sex differences, body morphology was also influenced by age, especially due to ectomorph component. In normal-weight women, there was a significant reduction on body linearity accompanied by a very similar but not significant, increase of endomorphy and mesomorphy in the older group compared to the younger group. In men, body linearity was also reduced in the older age group; however, there was only a non-significant increase in endomorphy while mesomorphy remained almost stable. Differences in the ectomorph component between age groups could be seen from normal-weight to overweight categories but were absent in obesity and morbid obesity. Ectomorphy acquired a minimum value (0.1) in high nutritional categories. Therefore, the absence of ectomorphy differences in these nutritional categories may be related to a limitation of the method and not to the absence of real differences in ectomorph component between age groups. Decreasing stature with ageing has been observed in many populations, such as Mexican (Lopez-Ortega and Arroyo 2016), English (Fernihough and McGovern 2015), or Austrian (Peter et al. 2014) populations. As it can be seen in this study, ectomorphy was positively correlated with height, which could be related to the ageing associated decrease of ectomorphy. The reduction of height seen in older age groups was not only due to intrinsic ageing processes such as postural changes, thinning of the disks of the spinal column, diminution in the height of the vertebrae or conditions such as scoliosis, but also due to the concomitant effect of secular trends where younger generations are taller than previous ones (Cline et al. 1989).

Although changes in endomorph and mesomorph components were not significant between age groups, different patterns could be seen between ageing in normal-weight and in higher nutritional status. As it has been mentioned above, in this study endomorphy (somatotype component mainly representing FM) tended to increase with age in normal-weight category which was in agreement with other studies where an increase in FM with age was shown, even if BMI did not increase (e.g. Ohkawa et al. 2005; Andreenko and Mladenova 2015). Surprisingly, this is not the case in high nutritional categories (overweight, obesity and morbid obesity), where endomorphy decreases with age, especially in men. In agreement with this, Herrera et al. (2001), also detected a reduction in endomorph component with age. A possible explanation for this effect could be a worse life expectancy in individuals with high FM%, which could reduce the presence of this kind of individuals at advanced ages in the population. Another explanation is possible, as the reduction in endomorphy matches with an increase in mesomorphy. This relationship between endomorph and mesomorph components seems to contradict with the typical condition of sarcopenia (reduction in lean mass) in advanced age (Edwards et al. 2015). However, it is important to highlight that the redistribution of subcutaneous fat in the elderly as well as in postmenopausal women (Tchernof, Poehlman, and Despres 2000; Gavin, Cooper, and Hickner 2013) could be responsible of an overestimation of mesomorphy in older groups because a greater proportion of body fat in older than in young people is intrahepatic, intramuscular and intra-abdominal (Mobbs and Hof 2010);

and so, part of the fat could be considered as muscularity. On the other hand, this effect in endomorph and mesomorph components could also be explained by other reasons. The older adult group is composed of a wide range of ages and not only of elderly, so that the reduction of mesomorphy on this group could be attenuated by the high mesomorphy in the younger age range of this group. Indeed, in Kalichman et al. (2006), the authors explained that mesomorphy continues to increase until the end of the fifth decade. Finally, changes in endomorph and mesomorph components may just be due to changes in ectomorph component, as it is a predictive variable for the other two components. In agreement with this, Peter et al. (2014) showed that BMI changes in older individuals were offset to some degree by height loss.

Along with sex and age, sport practice is another factor that can also modify body morphology. Until now, the analyses of the relation between body morphology and nutritional status in this chapter pointed out that throughout obesity development the extra energy supplies seems to be directed towards a general increase in body mass, affecting FM as well as FFM. However practice of sports may somehow redirect this extra energy. In general population (excluding rugby players), sport practice exerted a slight effect on body morphology in each nutritional category, with the highest differences shown in normal-weight category between sport and non-sport men and women. However, these differences were not enough to be translated into significant distances between somatotypes. In normal-weight men and women, endomorphy tended to decrease and mesomorphy tended to increase with sport practice, which was in agreement with the previously reported concept that exercise reduces body fat (Tan, Wang, and Cao 2016) and increases FFM (Wilkinson et al. 2017). In sportsmen of this nutritional category, changes in FFM were responsible of the increase in general body mass, verified by the reduction of the ectomorph component. Something similar was found in Drenowatz et al. (2015) where exercise in participants with a normal level of fat affected lean mass, while there was not significant effect on FM. In women, the reduction in endomorphy due to sport practice was higher than the increase in mesomorphy, which was not enough to increase body mass but reduced differences between both components, making sportswomen a little bit more mesomorphic compared with non-sportwomen. In high nutritional categories, both endomorphy and mesomorphy were lower in sport groups than in non-sport groups, which could point to a slight reduction of body mass (FM and FFM) due to an increase in total energy expenditure (Sculthorpe, Herbert, and Grace 2017). It is important to highlight, that due to the idiosyncrasy of this population (i.e. a considerable sector of the sample was collected in health centers), individuals in high nutritional status that practice sport were very probably obese before starting to practice the sport. In King et al. (2012), it was explained that lean individuals who perform long term exercise increased energy intake as a compensatory mechanism, but overweight and obese adults were less likely to do it. Although this compensatory behavior was not checked in our sample, something similar could have happened. Anyway, these results provided evidence of the beneficial effects of practicing sports in overweight and obese subjects, as it tends to reduce BMI.

A curious observation that could be made from our results was that somatotype distances between sportswomen and non-sportswomen were always smaller than between sportsmen and non-sportsmen. As suggested by Buffa et al. (2001), this result may be due to a lower influence of sports in women than in men, which is in agreement with the theory stating that females are less influenced by environment (Stini 1982), including the practice of sport.

A small sample of individuals from a rugby team was also analyzed in relation to the effect of sport practice in the different nutritional categories. This sample differs from the general one in the intensity and time spent practicing sport, since the members of the rugby team follow a rigorous training schedule for competition. Rugby is a team sport where players perform periods of high-intensity activity separated by short periods of lower-intensity activities (Till et al. 2016). Additionally there are also periods of wrestling and physically demanding collisions. Due to the complex demands of the game, rugby players require a wide range of physical qualities. As it was observed in general population, in rugby players both endomorph and mesomorph components increased as ectomorph component decreased along with the increase of nutritional status (based on BMI). This confirmed the positive correlation between these two components when nutritional status is considered, not just for the general population but also in sportsmen. However, in rugby players (as opposed to general sportsmen), mesomorphy increased more compared to endomorphy when nutritional categories represented higher BMIs and as a consequence there was a higher dominance of mesomorph component as BMI increases in this population. Thus, in contrast to what was described in general population, distances between not-sportsmen and rugby players were significant in all nutritional categories, and the differences between the two groups were enhanced in overweight and obesity subjects. On the other hand, the high dominance of mesomorphy over endomorphy observed in rugby players compared with non-sportsmen (and even with general sportsmen) was due to a lower increase in the endomorph component in rugby players compared to non-sportsmen as the nutritional category increases. Indeed, the difference in endomorphy was significant between rugby players and non-sportsmen in obesity category. Mesomorphy was also increased in both groups in higher nutritional status, but although the increase was higher in rugby players than in non-sportsmen, the difference between the groups was low and not significant. These results seemed to be in agreement with de Gouvêa et al. (2017), where more skilled sports men, even with higher body mass, presented less relative body fat than the less skilled ones do. Furthermore, Johnston et al. (2014) mentioned that low skinfold thickness, which represent low body fat, is associated with improved vertical jump, agility and maximal aerobic power, which indicate that low body fat is even more important than high body mass to discriminate between more and less skilled sport men.

6. CONCLUSION

There is a general tendency in relation to changes in body morphology and composition, which points to a general increase in body mass along obesity development, characterized by the increase of both endomorphy and mesomorphy (representing FM and FFM, respectively) and the decrease in ectomorphy (representing body linearity). Even though obesity definition was commonly expressed as the increase in body mass due to an increase almost exclusively of FM (Sørensen, Virtue, and Vidal-Puig 2010), these results points to the importance of FFM in obesity development, since most of the time they increase together. The use of BMI in obesity assessment is still recommended, since it measures the total body mass. However, this method does not allow us to evaluate each component separately, but this limitation could be compensated by the use of complementary techniques. The commonly observed differences in body morphology and composition due to the effect of sex and age could be affected by the nutritional status of the compared subjects. In this way, in high nutritional status the typical increase of endomorphy with age (due to higher amount of FM in older adults), is not observed, and also with regard to sexual dimorphism, it seems to be reduced from overweight to morbid obesity. Fuethermore, in skilled sport men, represented by men from a rugby team, although both components (endomorphy and mesomorphy) also increase with obesity, the increase of body mass in high BMI categories is characterized by higher dominance of the mesomorph component due precisely to lower endomorphy compared with non-sport men from the same nutritional category. This confirms the precaution that should be taken when BMI is used in sports men. However, sports in general population (low skilled sport individuals) may help to reduces body mass, especially in men.

Chapter V

Body Size Perception and Satisfaction in Individuals of Different Nutritional Status

1. SUMMARY

OBJECTIVES: Overweight and obesity involve changes in body composition and morphology that influence the perception of body image and general health status. Body dissatisfaction could be influenced, among other factors, by socio-cultural environment, which promotes a thin image in women and a strong and muscular image in men. The study of body human dissatisfaction in different nutritional status is of great importance as it is also related with image and eating disorders. The aims of this chapter are to analyse the body size perceptions and preferences among men and women, and to assess their relationship with nutritional status.

METHODS: The analyses were carried out on 405 individuals (178 men and 227 women) with ages from 18 to 80 years, all of them living in the Basque Country (Spain). Stunkard et al. (1983) silhouettes collection was used to evaluate current and ideal body image perceptions as well as dissatisfaction with the own body image and inconsistency between the body image and BMI. WHO criteria for BMI were used to categorize the nutritional status of the participants (World Health Organization 2000). Mann-Whitney U test was used to analyse sexual differences in the perceived images or in the dissatisfaction or inconsistency scores for each age group. Gamma coefficient was used to assess the association between the nutritional status and the selected image or the dissatisfaction or inconsistency score.

RESULTS: Most people selected the silhouette corresponding to their nutritional category. The ideal images chosen by women were less corpulent than the ideal images chosen by men, but young women chose more corpulent bodies as ideal for the opposite sex compared to young men. People with greater BMI tended to prefer partners with bigger silhouettes; however, it was only significant in men and women under 45 years old. Even if they had higher BMI, men were more satisfied than women with their body image.

CONCLUSIONS: Body image perception does not show gender differences but it is strongly associated with nutritional status. Body dissatisfaction affects both sexes. Dissatisfaction by excess (wish their body size to be smaller than their actual body size) is more common in women, while dissatisfaction by default (wish their body size to be bigger than their actual body size) is more common in men. The body size seen as ideal differs between men and women and reflects the body image model shown in mass media.

2. BRIEF INTRODUCTION

Body image is a subjective and multidimensional construct (Cash and Pruzinsky 2004), defined by Grogan (2017) as "a person's perception, thoughts and feelings about his or her body".

Nutritional status differs from one individual to another due to many different factors such as sex, age, or even a personal lifestyle, modifying the size and shape of the person, and therefore also modifying body image. Thus, obesity and overweight may play an important role in self-perceptions.

Cultural influences are also a powerful determinant of body size and morphology since cultural values unequivocally influences how members of the culture think about and behave toward other individuals (Cash and Pruzinsky 2004). Thereby body preferences highly depend on the cultural background of each population. Body ideals vary among cultures as well as within cultures, across groups and time (Cash and Pruzinsky 2004). In Contemporary Western cultures, sociocultural influences known as "culture of thinness" can be appreciated in many mass media. Cultural influences are specifically targeted to each sex, and have an important role in the increase of body dissatisfaction. For women, attractiveness is associated with being thin, whereas what it is considered attractive for men, is a more muscular appearance (Brennan, Lalonde, and Bain 2010). All this can generate unrealistic ideal body images, which influence the perception of our own image and lead to a conflict between the ideal beauty and the actual image. An obsessive behaviour related to our body image (e.g. try to reach to what is beautiful in our society), can lead to low self-esteem, body image disorders or even to eating disorders (such as anorexia, bulimia, bigorexia…).

3. BRIEF METHODOLOGY

BMI was categorized in five nutritional groups following the cut-off points established by the WHO for adult population: underweight (UW), normal weight (NW), overweight (OW), obesity (O) and morbid obesity (MO) (World Health Organization 2000).

Self-perceived and desired body sizes as well as most attractive body sizes for the opposite sex were assessed directly using the figural scale developed by Stunkard et al. (1983). Body size dissatisfaction and inconsistency scores were derived from these variables.

Body size dissatisfaction score was computed by subtracting the ideal silhouette from the current silhouette. This score is a measure of dissatisfaction with current body size where "0" indicates full satisfaction and the larger the score, the greater dissatisfaction with the current body size. Based on this, seven categories were obtained. Positive numbers indicate dissatisfaction by excess (i.e. wish their body size to be smaller than their actual body size) whereas negative numbers indicate dissatisfaction by default (i.e. wish their body size to be bigger than their actual body size). On the other hand, body size inconsistency index was computed by subtracting the nutritional status based on BMI from the nutritional status based on the current chosen silhouette (Zaccagni et al. 2014). This score is a measure of inconsistency between the current image perception and the actual nutritional status. Thus, "0" indicate full consistency, whereas larger numbers (negative or positive) indicated greater inconsistency. Based on this, five categories were obtained. Negative values indicate an under-estimation of the real size whereas positives ones indicate an over-estimation.

In order to perform the statistical analyses in this chapter, the sample was divided in four groups based on sex (women and men) and age (<45 years, ≥45 years). Differences between women and men in each age group were tested for each studied variable (current body image, ideal body image, ideal body image for the opposite sex, dissatisfaction score and inconsistency score) using a non-parametric Mann-Whitney U test for ordinal data. Differences between age groups in each sex for each studied variable were also tested using Mann-Whitney U test (Appendix II. From Figure A.5.1 to Figure A.5.10). On the other hand, the associations among nutritional categories and the above mentioned body image variables were tested using Gamma coefficient for ordinal data. To perform those test, the categories of the body image related variables with less than 10% of representation were excluded, as they were considered not enough representative of the category. In order to clarify the results, the outcomes of the performed analyses are presented over the graphics with the values of each studied variable. Besides, tables showing men and women percentages of each age group who chose each silhouette or who were in each dissatisfaction or inconsistency score, as well as their mean BMI and obesity percentage, are presented in the Appendix II (from Table A.5.1 to Table A.5.5). Together with these data, comparisons between sexes and between age groups in each image category were performed: Chi-square test was use to compare obesity percentages; whereas, as groups did not meet the requirement of normality, Mann-Whitney U test was used for BMI comparisons.

4. RESULTS

4.1. CURRENT SILHOUETTES

The percentages of women and men who chose each of the 9 silhouettes as best representing their current body image (i.e. perceived appearance) are shown in Figure 5.1 for participants with less than 45 years old and in Figure 5.2 for participants with 45 years or more. There were no gender differences for the chosen current silhouettes in neither of the two age groups. The most frequently chosen silhouette in the youngest group was number 4 (20.4% of men and 33.0% of women) whereas in the older group bigger silhouettes were chosen (31.3% of men chose silhouette 6 and 25.0% of women chose silhouette 5). No one chose silhouette 1 as their actual body image with the exception of 1% of women from the youngest group. Significant differences between the younger and the older groups were found in both sexes ($p<0.05$) (Appendix II. Figure A.5.1 and Figure A.5.2).

U-Mann Whitney *p= 0.317*

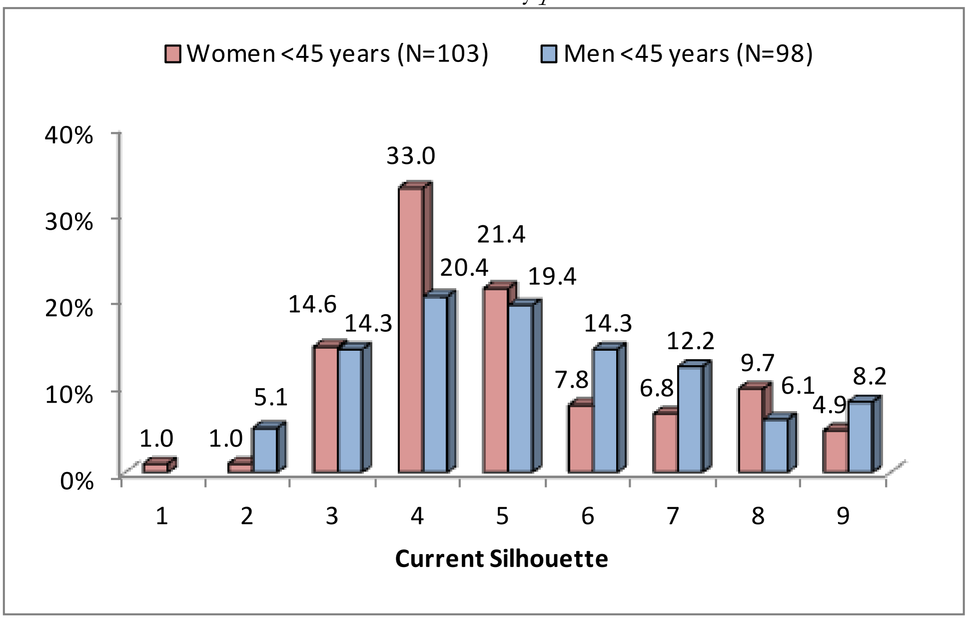


Figure 5.1. Percentage of women and men with less than 45 years who chose each of the silhouettes as the best representing their current body image.

U-Mann Whitney *p= 0.731*

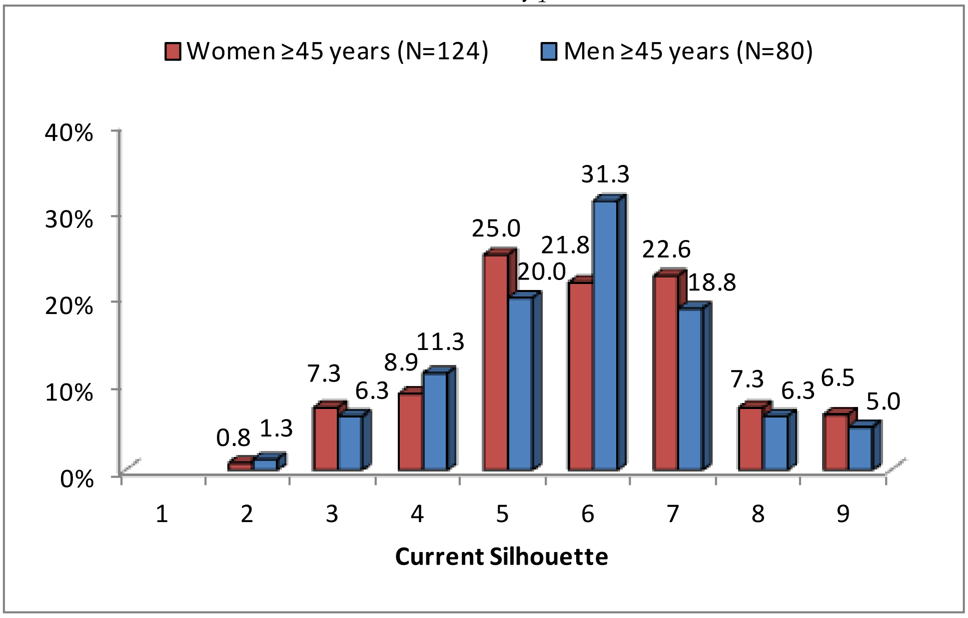
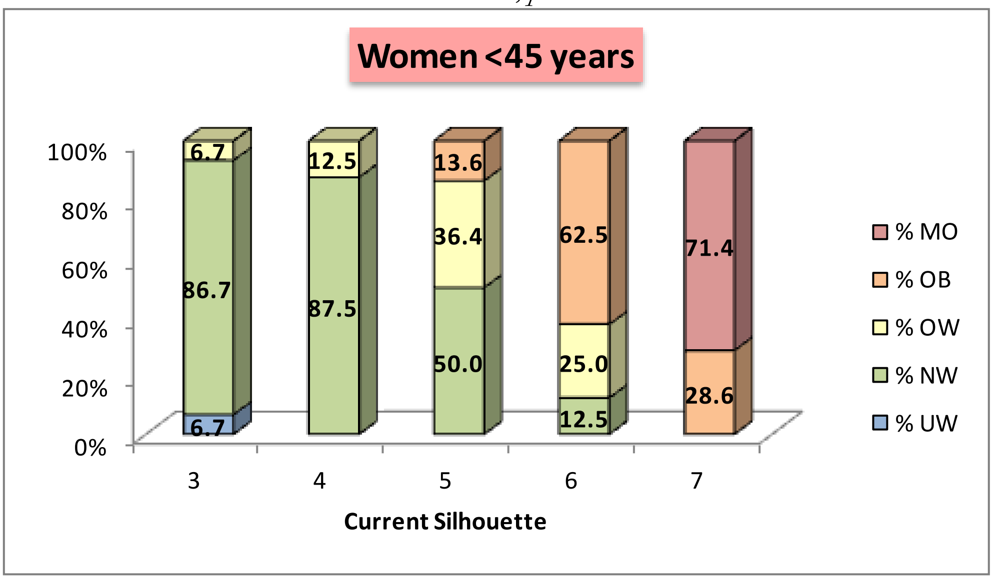


Figure 5.2. Percentage of women and men with 45 years or more who chose each of the silhouettes as the best representing their current body image.

Nutritional status was significantly associated (*p<0.001*) with the perceived current silhouette in all groups (from Figure 5.3 to Figure 5.6). Individuals with lower BMI chose smaller silhouettes, whereas the ones with higher BMI, chose bigger silhouettes.

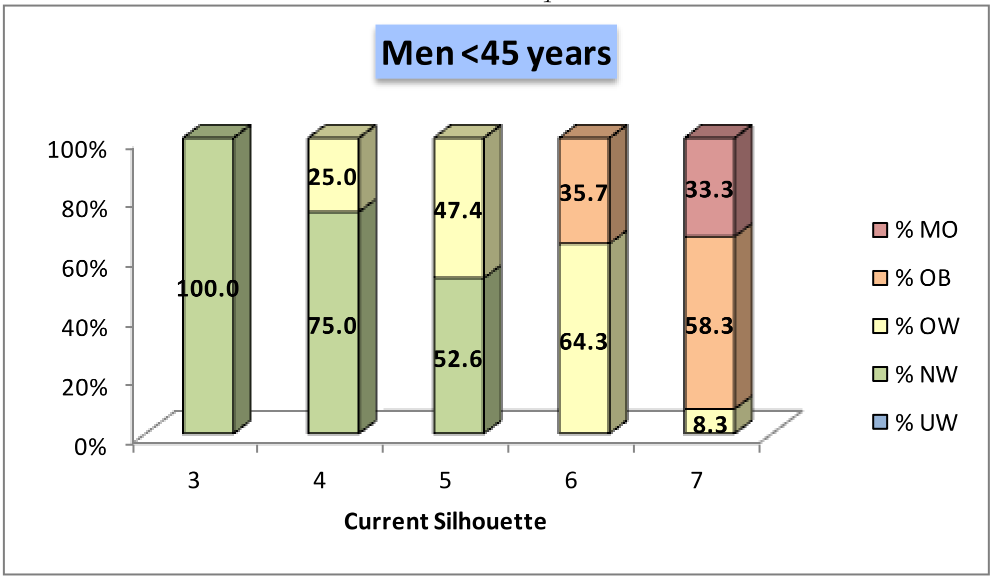
Gamma= 0.882; *p=4.44E-16*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.3. Percentage of the nutritional categories presented in each silhouette representing current body size for women with less than 45 years.

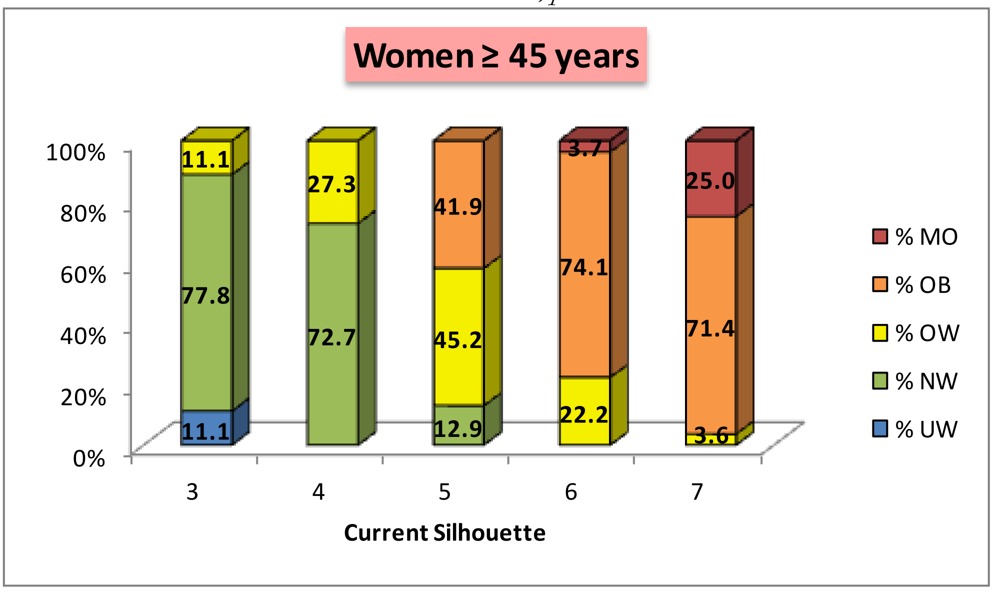
Gamma=0.903; *p=0.000*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.4. Percentage of the nutritional categories presented in each silhouette representing current body size for men with less than 45 years.

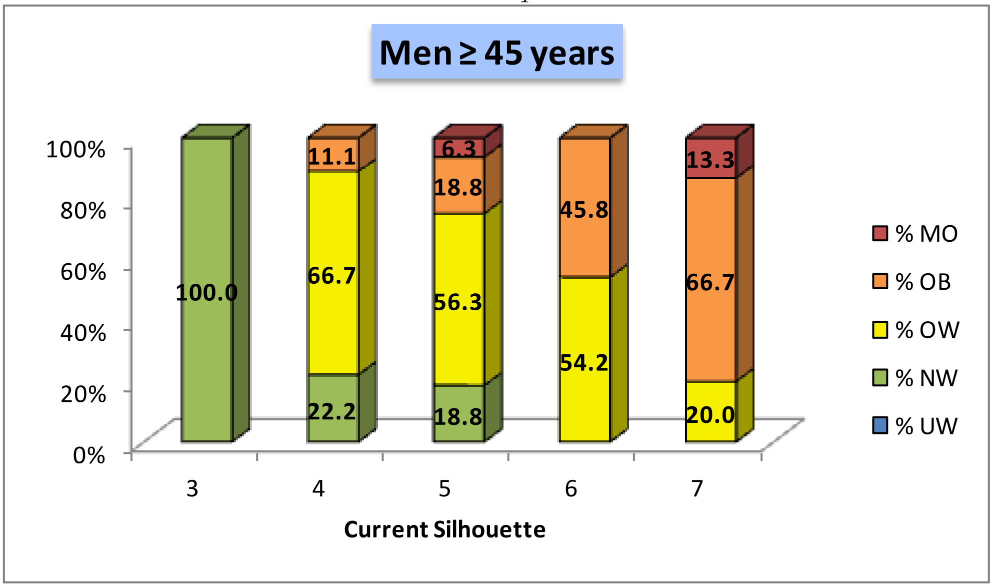
Gamma= 0.895; *p=0.000*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.5. Percentage of the nutritional categories presented in each silhouette representing current body size for women with 45 years or more.

Gamma= 0.752; *p= 7.06E-12*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.6. Percentage of the nutritional categories presented in each silhouette representing current body size for men with 45 years or more.

4.2. IDEAL SILHOUETTES

The distributions of desired silhouettes for young men and women are presented in Figure 5.7, and for older adults in Figure 5.8. In both cases there were significant gender differences between silhouettes chosen as ideal by men and by women. For individuals under 45 years old, the most often chosen silhouette was number 4 (41.8% for men and for 49.5% women). Silhouette number 5 was also highly chosen in younger men (39.8%) whereas silhouette number 3 was the second most frequently chosen by younger women (36.9%). For people with 45 years or more, silhouettes 3, 4 and 5 continued to be the most often chosen silhouettes, 3 (26.8%) and 4 (44.7%) for women and 4 (35.0%) and 5 (36.3%) for men. However, in this case, the number of women who chose number 5 (14.6%) is higher compared with the number of women who chose it in the younger group. In the same way, the number of men who chose the silhouette number 3 (20.0%) was also higher compared with men in the younger group. Few participants chose silhouettes 1, 2 and 6 as ideal body image, especially in the younger group. No significant differences were found between age groups in any sex (Appendix II. Figure A.5.3 and Figure A.5.4).

U-Mann Whitney *p= 3.4E-08*

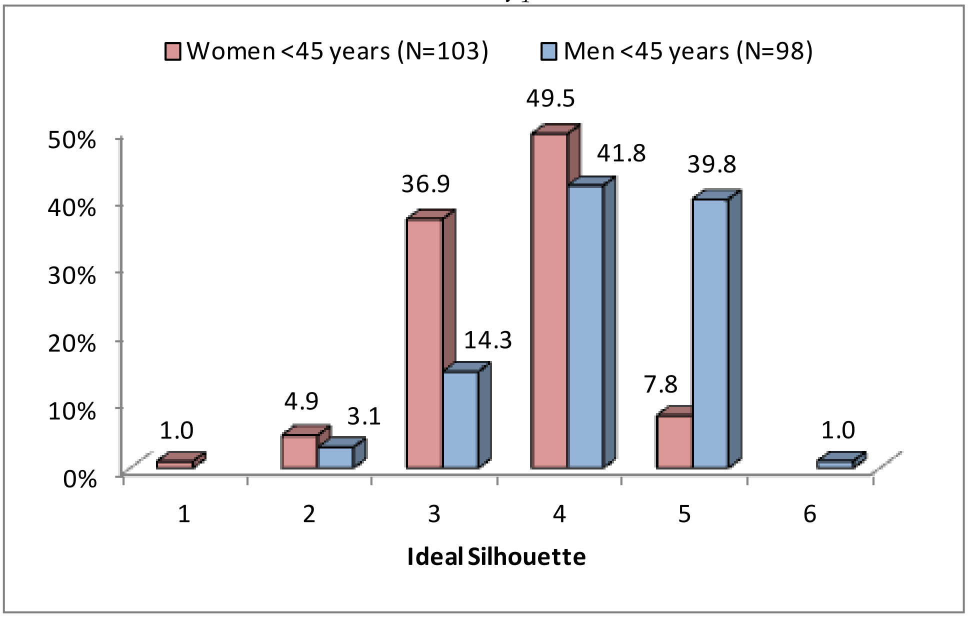


Figure 5.7. Percentage of women and men with less than 45 years who chose each of the silhouettes as their ideal body image.

U-Mann Whitney *p= 8.1E-04*

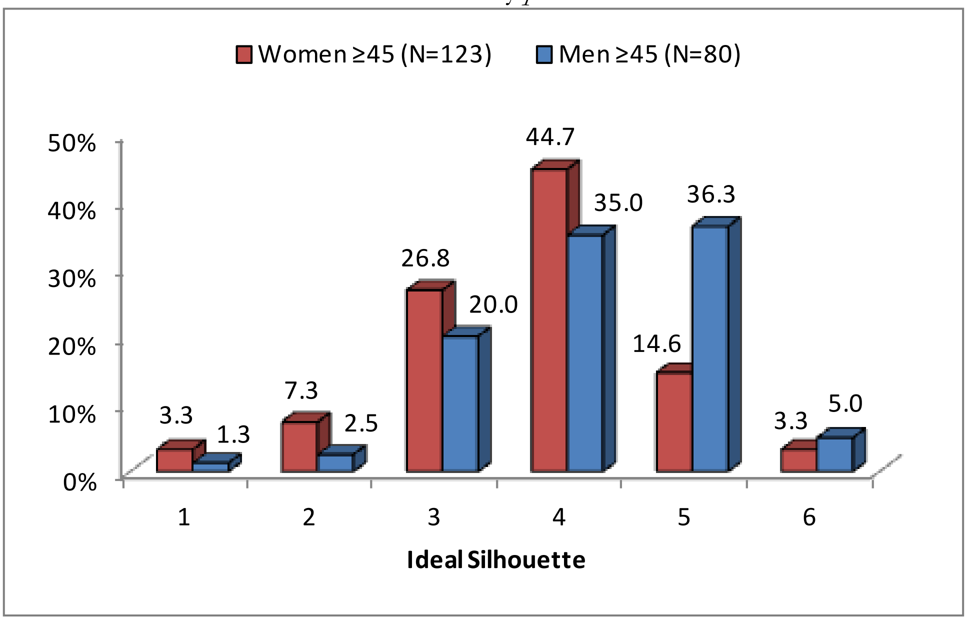
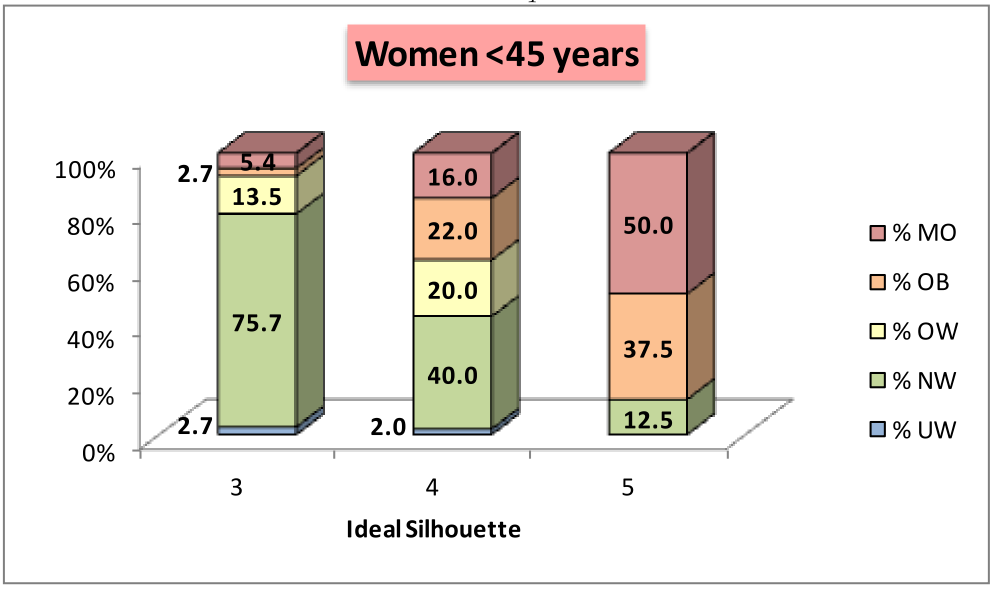


Figure 5.8. Percentage of women and men with 45 years or more who chose each of the silhouettes as their ideal body image.

Nutritional status showed a positive association with the chosen ideal silhouettes, which was significant in all studied groups, but stronger in individuals under 45 years (from Figure 5.9 to Figure 5.12). Slightly higher silhouettes were chosen by individuals with higher BMI. Among the group with less than 45 years, more than 75% of women and 71% of men who chose solhouette 3 had a normal weight, whereas around 85% of people who chose silhouette 5 were obese or overweight. In individuals with 45 years or more the prevalence of obesity was higher than in the younger groups in each chosen ideal silhouette.

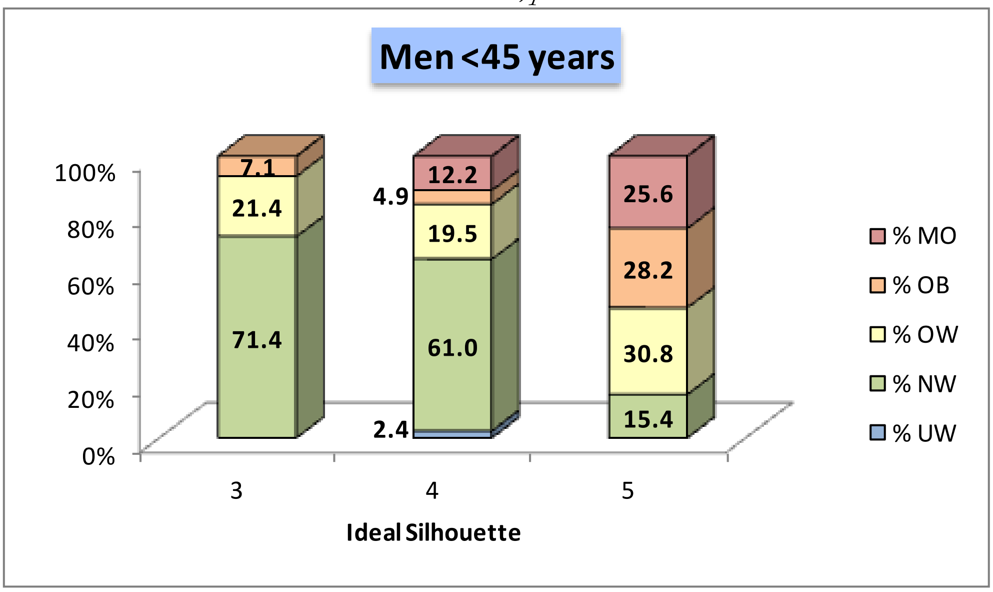
Gamma= 0.627; *p= 4.63E-7*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.9. Percentage of the nutritional categories presented in each ideal silhouette for women with less than 45 years.

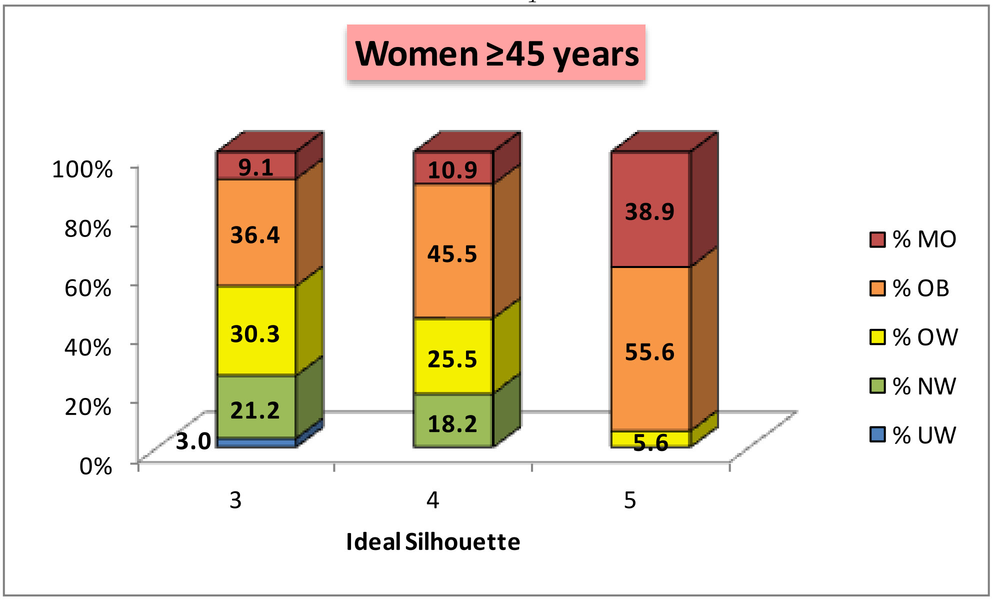
Gamma= 0.571; *p= 7.23E-8*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.10. Percentage of the nutritional categories presented in each ideal silhouette for men with less than 45 years.

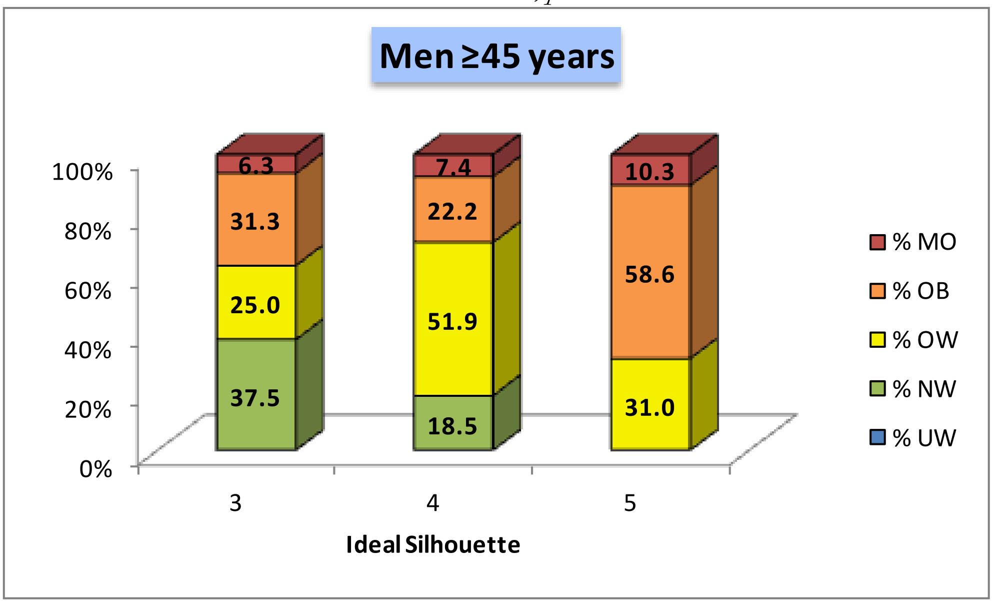
Gamma= 0.437; *p= 3.33E-4*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.11. Percentage of the nutritional categories presented in each ideal silhouette for women with 45 years or more.

Gamma= 0.456; *p= 0.001*



UW: under-weight; NW: normal weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.12. Percentage of the nutritional categories presented in each ideal silhouette for men with 45 years or more.

4.3. MOST ATTRACTIVE SILHOUETTES

Men and women from both age groups agreed to consider silhouette 4 as the most attractive silhouette for the opposite sex. In regard to individuals under 45 years (Figure 5.13), significant differences between silhouettes chosen by men and women could be seen. Even though silhouette 4 was the most frequently chosen silhouette by both sexes, women preferred silhouettes between 4 (56.3%) and 5 (27.2%) while men preferred silhouettes between 4 (67.4%) and 3 (20.4%) as the most attractive silhouette for the other sex. Individuals with 45 years or more (Figure 5.14) showed no gender differences in the silhouette chosen as the most attractive for the opposite sex, but the same tendency seen in the youngest age group could be also appreciated in this group. In any case, no men chose silhouettes bigger than number 6, and no women chose silhouettes bigger than number 5 as the most attractive for the opposite sex. No significant differences were found between age groups in any sex for the most attractive silhouette for the opposite sex (Appendix II. Figure A.5.5 and Figure A.5.6).

U-Mann Whitney *p= 0.014*

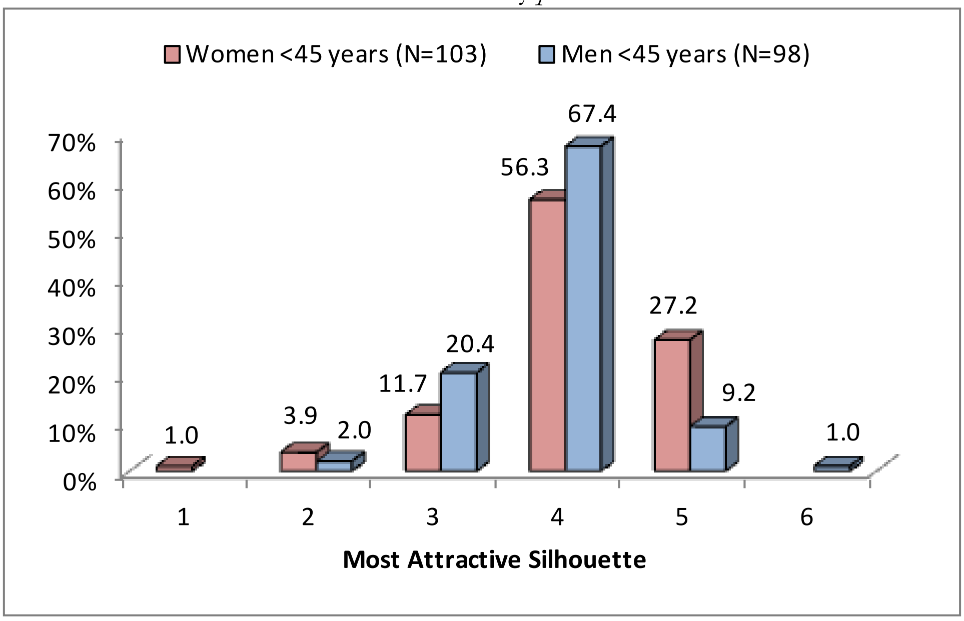


Figure 5.13. Percentage of women and men with < 45 years who chose each of the silhouettes as the ideal body image for the oposite sex.

U-Mann Whitney *p= 0.105*

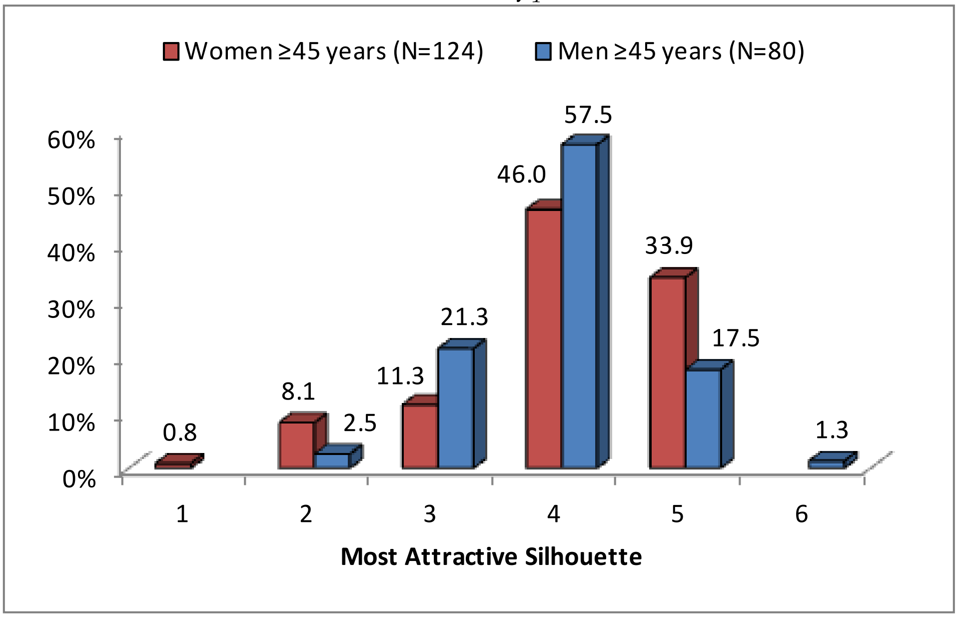
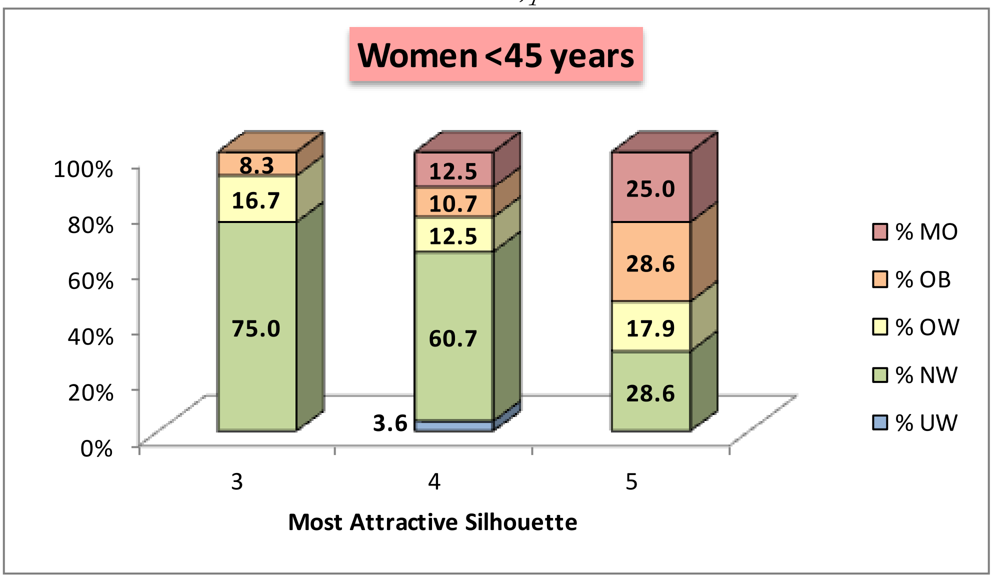


Figure 5.14. Percentage of women and men with ≥45 years who chose each of the silhouettes as the ideal body image for the oposite sex.

The asociation between nutritional status and the chosen silhouettes as most attractive in the opposite sex (from Figure 5.15 to Figure 5.18) was only significant in the younger group. Individuals of 45 years or more, chose the ideal silhouettes for the oposite sex independently of their own nutritional status.

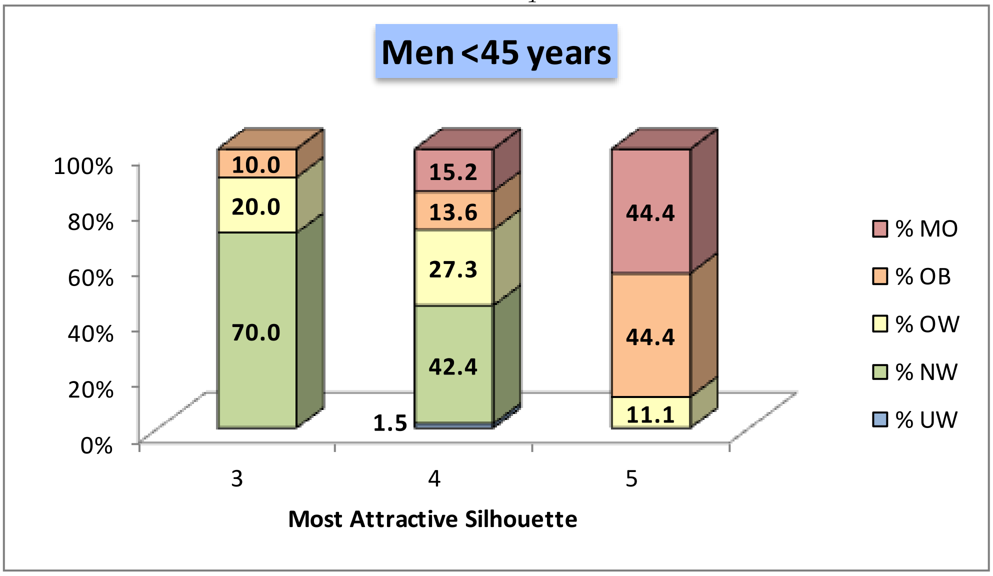
Gamma= 0.506; *p= 2.60E-5*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.15. Percentage of the nutritional categories presented in each ideal silhouette chosen as the most attractive for the oposite sex, for women with less than 45 years.

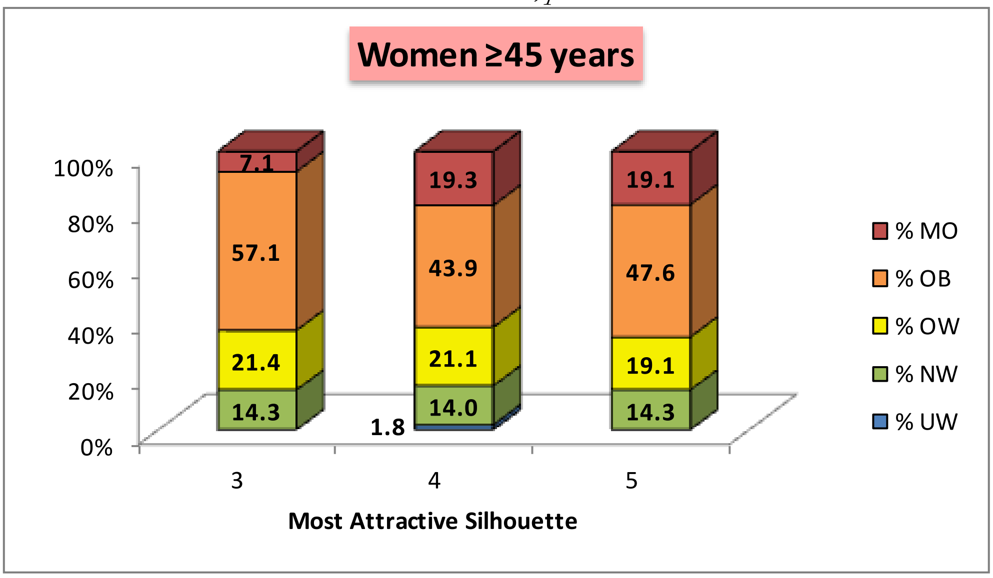
Gamma= 0.590; *p= 2.10E-5*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.16. Percentage of the nutritional categories presented in each ideal silhouette chosen as the most attractive for the oposite sex, for men with less than 45 years.

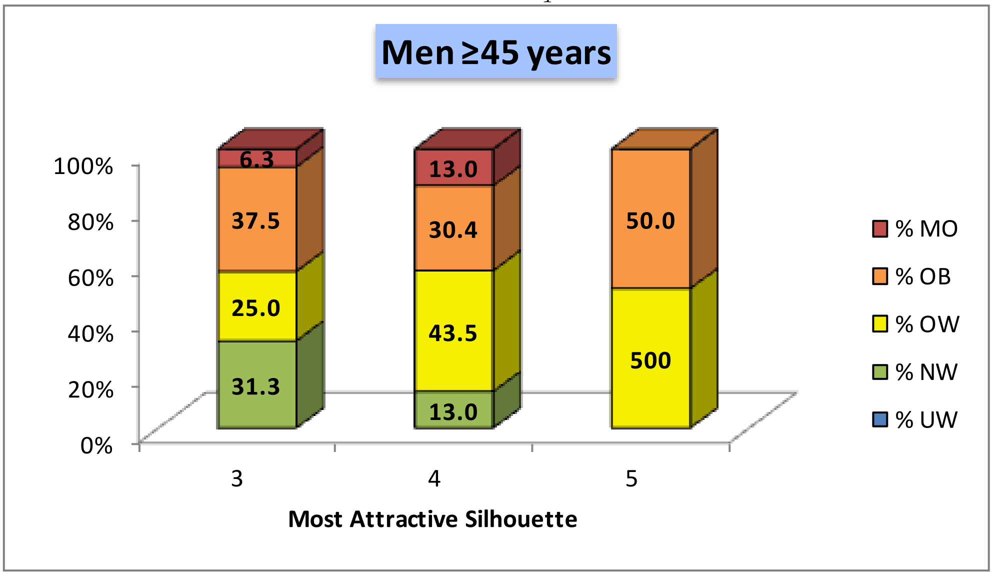
Gamma= 0.081; *p= 0.523*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.17. Percentage of the nutritional categories presented in each ideal silhouette chosen as the most attractive for the oposite sex, for women with 45 years or more.

Gamma= 0.165; *p= 0.287*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.18. Percentage of the nutritional categories presented in each ideal silhouette chosen as the most attractive for the oposite sex, for men with 45 years or more.

4.4. BODY SIZE DISSATISFACTION SCORE (DS)

Both age groups were dominated by a slight dissatisfaction by excess, followed by full satisfaction in the younger group (Figure 5.19) and by a higher level of dissatisfaction by excess (moderate) in the older one (Figure 5.20). Dissatisfaction score showed differences between sexes in both age groups ($p<0.05$). Women had a higher percentage of dissatisfaction by excess than men, whereas men had higher percentages of satisfaction. Although dissatisfaction by default was not highly represented, it was also higher in men than in women and in the younger age group compared to the older one. Significant differences in the dissatisfaction score between the younger and the older groups were found in both sexes ($p<0.005$) (Appendix II. Figure A.5.7 and Figure A.5.8).

U-Mann Whitney *p= 0.040*

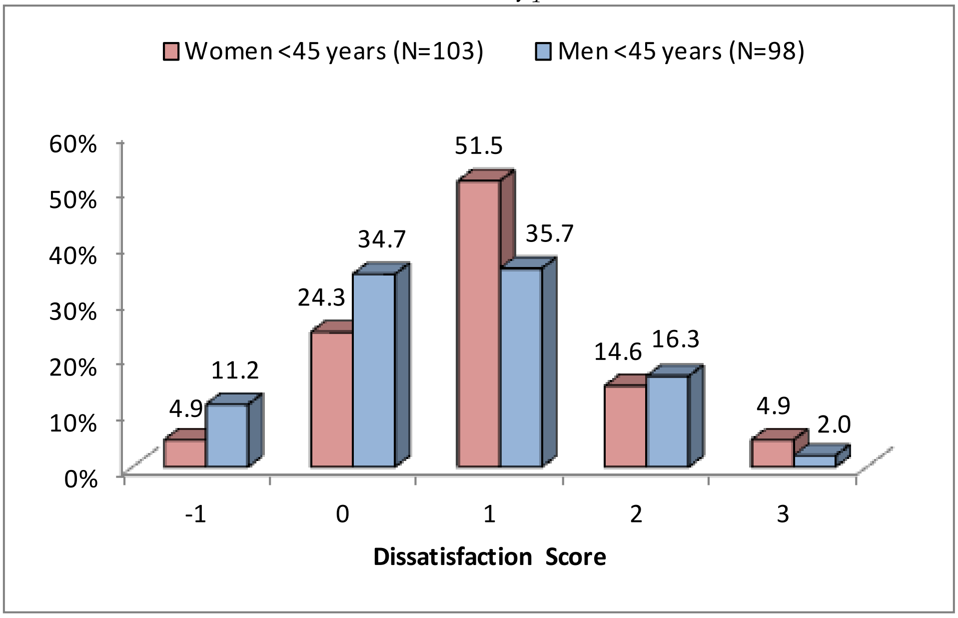


Figure 5.19. Percentage of women and men with less than 45 years in each dissatisfaction score.

U-Mann Whitney *p= 0.047*

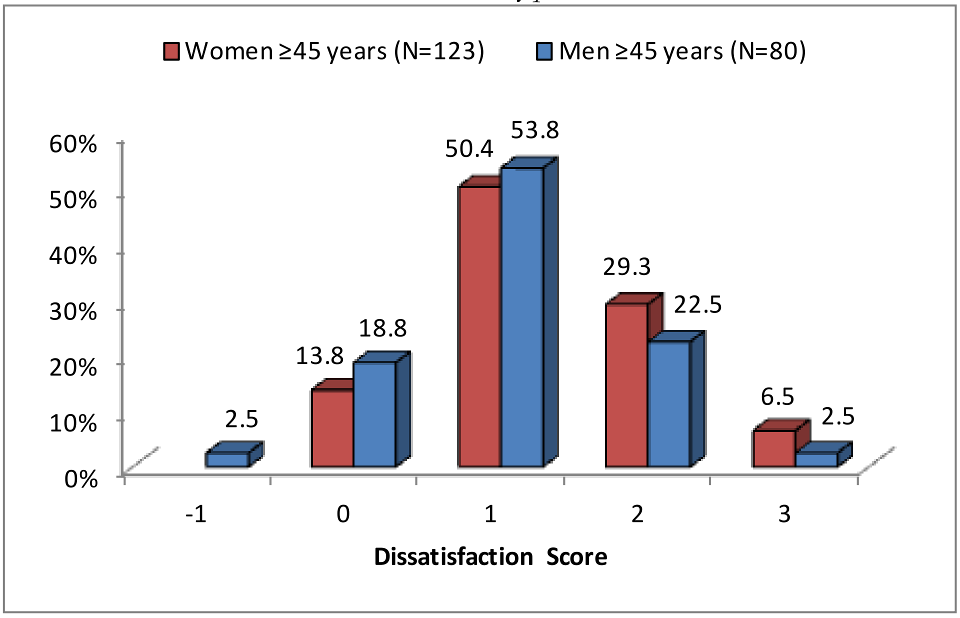
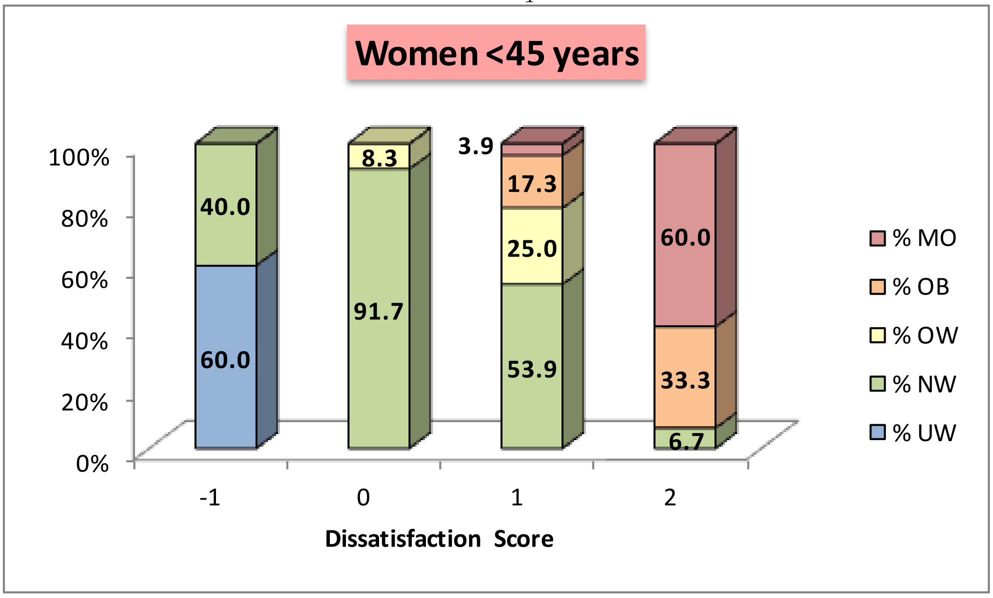


Figure 5.20. Percentage of women and men with 45 years or more in each dissatisfaction score.

Body size dissatisfaction score showed a significant association with nutritional status in the four groups based on sex and age (from Figure 5.21 to Figure 5.24). The higher the degree of dissatisfaction by excess was, the higher the nutritional category of the individual.

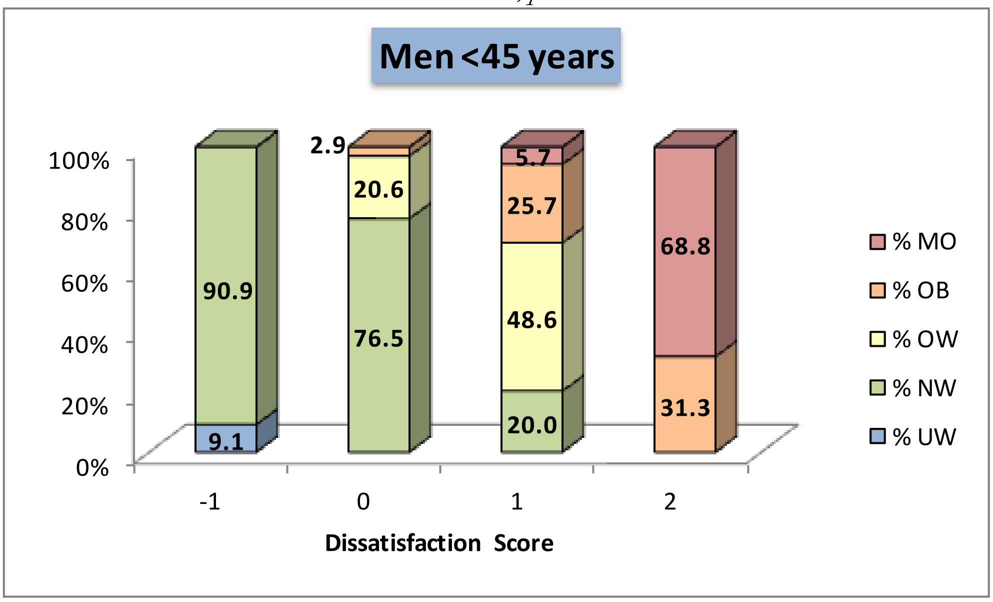
Gamma= -0.897; *p= 9.48E-16*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.21. Percentage of the nutritional categories presented in each dissatisfaction score for women with less than 45 years.

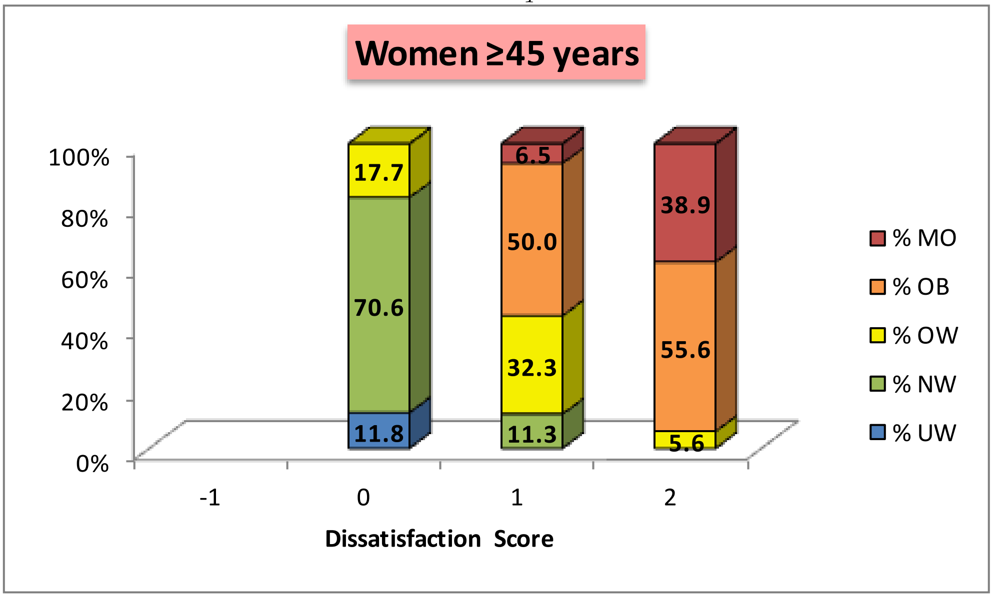
Gamma= -0.934; *p= 1.05E-40*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.22. Percentage of the nutritional categories presented in each dissatisfaction score for men with less than 45 years.

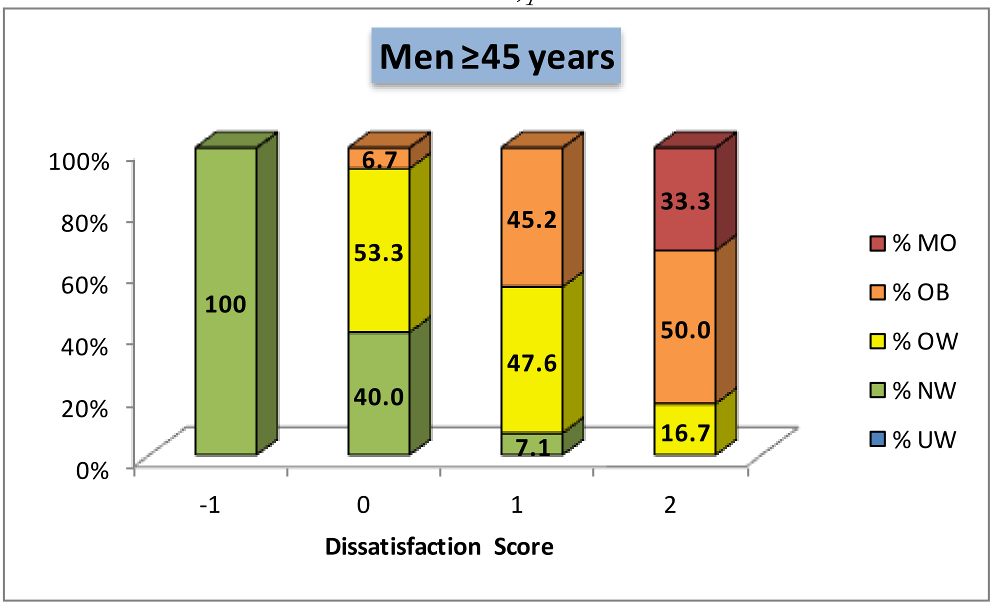
Gamma= -0.885; *p= 2.42E-24*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.23. Percentage of the nutritional categories presented in each dissatisfaction score for women with 45 years or more.

Gamma= -0.848; *p= 2.88E-13*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.24. Percentage of the nutritional categories presented in each dissatisfaction score for men with 45 years or more.

4.5. BODY SIZE INCONSISTENCY SCORE (IS)

In both age groups, more than 60% of individuals showed good consistency between their actual nutritional status and the silhouette selected as representative of their current status; except for men with 45 years or more where this percentage was just a little bit higher than 50% (Figure 5.25 and Figure 5.26). In the youngest group there were no significant differences between sexes. A slightly higher percentage of both men and women overestimated rather than underestimated their body size. Among individuals with 45 years or more there were sexual differences ($p<0.05$). Full consistency was lower for men in the older age group compared to the younger group (63.3% vs. 51.9%), while both body size under and overestimation were higher. In women from the older group and compared to de younger group, body size overestimation decreased in favour of body size underestimation. No significant differences were found between age groups in any sex for the inconsistency score, although in women those differences were close to signification ($p=0.063$) (Appendix II. Figure A.5.9 and Figure A.5.10).

U-Mann Whitney *p= 0.702*

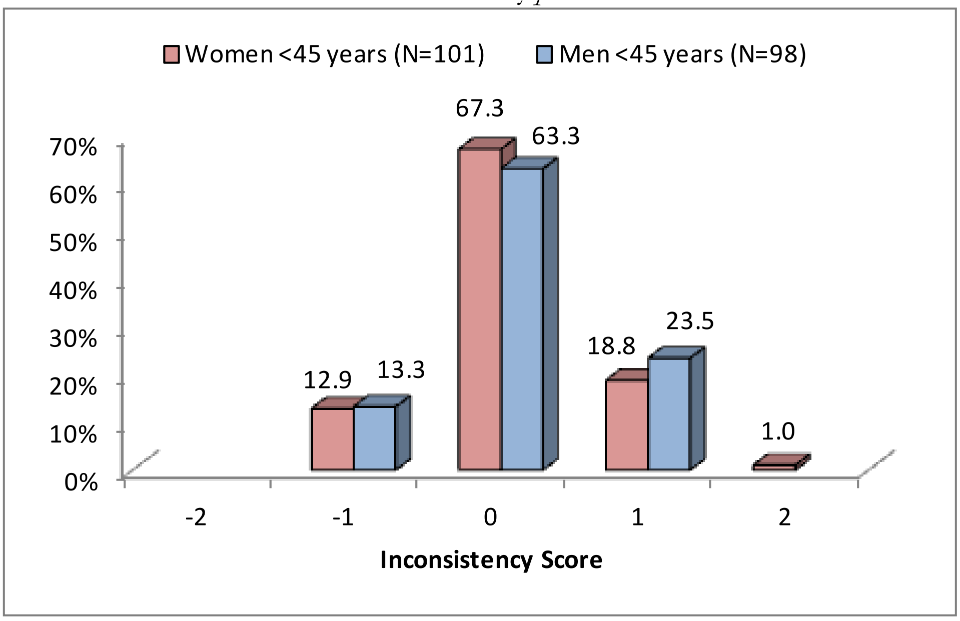


Figure 5.25. Percentage of women and men with less than 45 years in each inconsistency score.

U-Mann Whitney *p= 0.032*

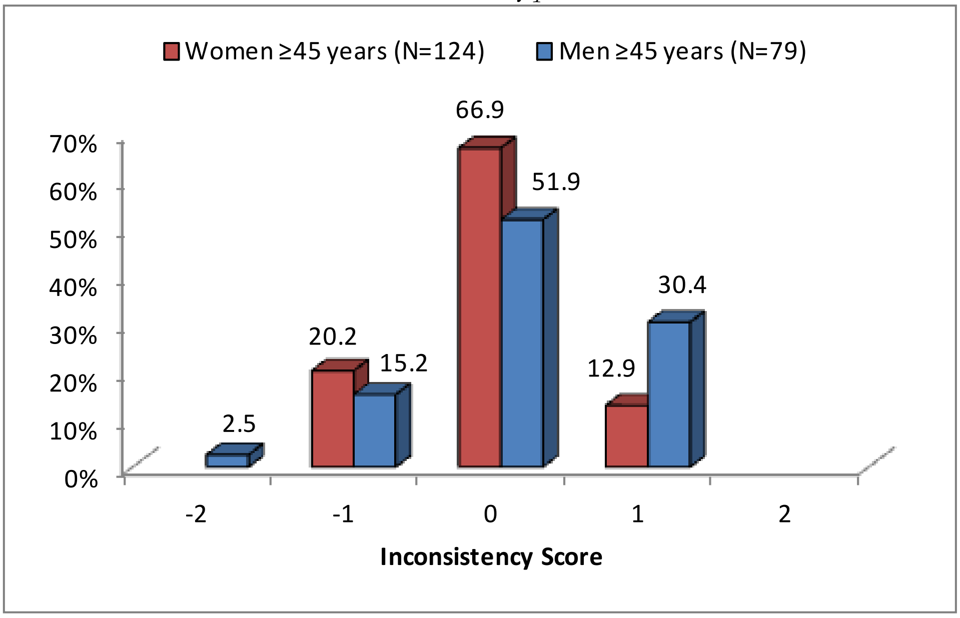
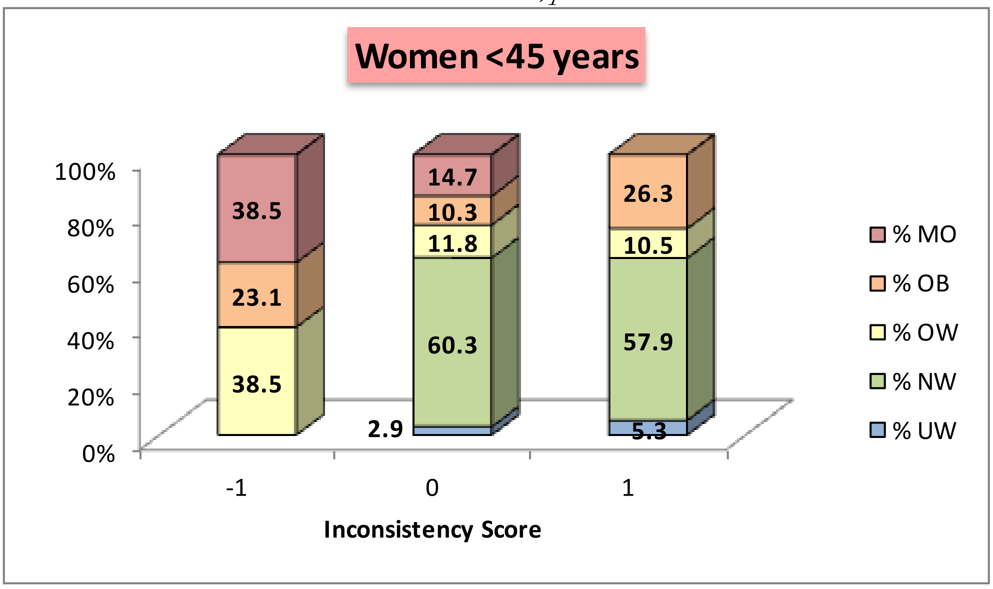


Figure 5.26. Percentage of women and men with with 45 years or more in each inconsistency score.

Asociation between inconsistency score and nutritional status could be seen in the four studied groups (from Figure 5.27 to Figure 5.30). Those who understimate their body image were the ones with higher nutritional category and viceversa.

Gamma= -0.393; *p= 0.004*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

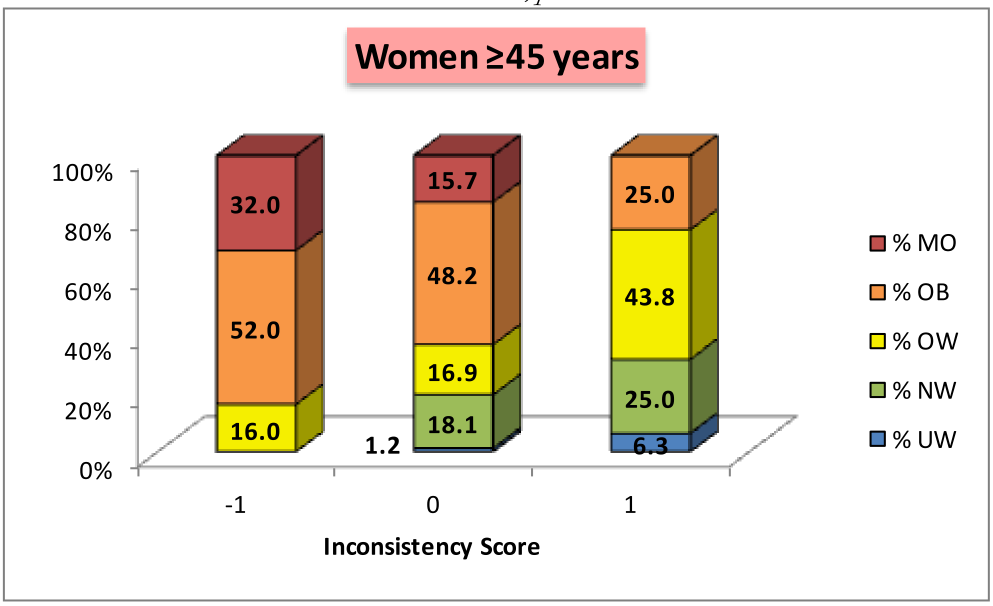
Figure 5.27. Percentage of the nutritional categories presented in each inconsistency score for women with less than 45 years.

Gamma= -0.170; *p= 0.166*

UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.28. Percentage of the nutritional categories presented in each inconsistency score for men with less than 45 years.

Gamma= -0.531; *p= 2.00E-6*



UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.29. Percentage of the nutritional categories presented in each inconsistency score for women with 45 years or more.

Gamma= -0.243; *p*= *0.070*

UW: under-weight; NW: normal-weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure 5.30. Percentage of the nutritional categories presented in each inconsistency score for men with 45 years or more.

5. <u>DISCUSSION</u>

Prevalence of obesity is increasing worldwide and is a major public health concern, not only due to their associated comorbidities but also to its psychological impact (Onyike et al. 2003). Individuals who are considered attractive are usually viewed more favourably than unattractive persons. This response is called the "halo effect" (Thorndike 1920). Western societies generally consider thinness as an ideal of beauty, and obese individuals suffer social rejection and negative judgments. As a result, obese people tend to have poorer body image perception and self-esteem (Kindes 2006).

5.1. BODY IMAGE PERCEPTION

Body image perception through silhouettes was proposed as a good method to detect nutritional status (Kaufer-Horwitz et al. 2006; Nagasaka et al. 2008). In Bulik et al. (2001), some standards in Caucasians were proposed to link BMI to Stunkard's silhouettes collection. In the analysed population the highest percentage of individuals from the youngest group declared themselves as a 4 on Stunkard's body silhouettes and had a mean BMI corresponding to normal weight (men: 23.5 kg/m^2; women: 22.3 kg/m^2; see Appendix

II, Table A.5.1), which was similar to the BMI associated to this silhouette in adults of 18 to 40 years old (men: 23.2 kg/m^2; women: 22.6 kg/m^2) in Bulik et al. (2001). Body size inconsistency score was also assessed, indicating that more than 60% of men and women in this age group showed full consistency between the perceived and the actual nutritional category. Some works highlight sexual differences in perceived image. For example, in Fallon et al. (1985) women were more susceptible to overestimate their weight, whereas men tended to underestimate it, and in Zaccagni et al. (2014) higher consistency scores were found in females than in males from a student university population. However, even though in the studied younger group overestimation was higher than underestimation; sexual differences could not be appreciated.

In the older group, the highest percentages of men and women choosing their current body image were found for silhouettes 6 and 5, respectively. The mean BMIs found in the groups that chose these silhouettes were a little higher (men: 30.7 kg/m^2; women: 29.5 kg/m^2; see Appendix II, Table A.5.1) than the ones found in Bulik et al. (2001) (men: 28.2 kg/m^2; women: 26.3 kg/m^2), yet in both cases the BMI was always >25 kg/m^2. There were no sexual differences in the older group either. However, the significant differences between the age groups for both men and women in the chosen silhouette as best representing their current body size ($p<0.05$) (Appendix II. Figure A.5.1 and Figure A.5.2), pointed to higher prevalence of obesity in the older group, which was consistent with Deurenberg et al. (1991) who indicated that the amount of body fat tends to increase with age (even if muscular component decrease). Therefore, older populations should be considered a risk group, susceptible for overweight and obesity and thus, vulnerable to body image dissatisfaction. The percentage of women with full consistency between the actual and the perceived body size was high and very similar in both age groups. However, although they were not significant, some differences could be seen between ages (Appendix II. Figure A.5.9). In the younger group body size overestimation was more common than underestimation, whereas in the older group underestimation was more common. Other works also confirmed that underestimation of weight by women is a common pattern across different cultures (Kirk, Cockbain, and Beazley 2008; Barrett and Huffman 2011). Although in the older group underestimation was higher in women, both men and women seemed to underestimate their actual body size more than their younger peers did (Appendix II. Figure A.5.9 and Figure A.5.10). Not only underestimation, but also overestimation was increased in the older men group compared with the younger one, simultaneously with a decrease in full consistency. Indeed, in men from the older group overestimation was higher than underestimation. In agreement with other studies, women ≥45 seemed to classify their own nutritional category better than men (Sánchez-Villegas et al. 2001; Zaccagni et al. 2014). In fact, according to Sanchez-Villegas et al. (2001), men of the European Union are apparently less aware of their body size than women. Misperceptions of body size could be considered a sign for image disorders, and are of particular importance with regard to weight control and obesity prevention. However, the multidimensional nature of body image could make difficult the interpretation of these results (Muñoz-Cachón et al. 2009).

The silhouette perceived by the subjects as their current image was positively associated with the nutritional category, which means that in both sexes nutritional status was determinant of how a person perceives him or herself. Values of the gamma coefficient were high, indicating a positive strong association. Other studies also reported relatively high correlations between BMI and perceived silhouettes, in those works women presented higher correlations than men (Bulik et al. 2001; Kaufer-Horwitz et al. 2006; Nagasaka et al. 2008). Nevertheless, in this study a higher correlation in women than in men could only be slightly observed in participants with ≥45 years. An interesting thing that could be appreciated in this work is that until silhouette 4, the mean BMI associated to each silhouette was higher in men than in women (Appendix II, Table A.5.1). The pattern changed from silhouette 5 onwards, where BMI was higher in women. It happened in both age groups and it could also be seen in Bulik et al. (2001). Differences were not very high and were not always significant, but they could point to sexual differences in body composition, such as the usually higher prevalence of lean mass in men than in women (Wells 2007). In figures lower than 5, which represent silhouettes with a low percentage of fat mass, differences in BMI due to fat free mass would be easily appreciated, and men will have higher BMI due to a higher percentage of muscle mass. A study in Japanese population also noticed this effect but slightly shifted (it did not happen until silhouette 7) (Nagasaka et al. 2008). An explanation for this could be that body composition is slightly different in Asian populations and in the silhouettes collection used for the study of Nagasaka et al. (2008), overweight did not appear until silhouette 7. However, there are others studies where this effect could not be seen (Kaufer-Horwitz et al. 2006) and more studies will be necessary to confirm if this tendency is actually significant.

There was also a significant association between inconsistency score and nutritional status, but just in women and especially in the older group. In agreement with Easton et al.

(2017), individuals who underestimated their nutritional status presented higher percentages of overweight and obesity in comparison with the individuals who overestimated it. Some authors agree with this and say that specially, overweight women are more prone to underestimate their weight status as a protective factor for self-esteem (Madrigal et al. 2000; Muñoz-Cachón et al. 2009; Barrett and Huffman 2011). Appropriate self-esteem could be helpful in our society. But, if overweight and obese individuals do not have an accurate perception of their real size, they probably won't see the need to control their weight and obesity prevention and treatments will be ineffective (Schuler et al. 2008). It is important to note here that although misperception seemed to be greater among older men, it was in women where the association between inconsistency score and nutritional status seemed to matter. This could somehow reflect the different reactions that both sexes have to body image perception, being the nutritional status less important in men than in women. For example, according to Sanchez-Villegas et al. (2001) men from the European Union are less conscious of the potential problems associated with BMI. And women could be more prone to change their body image by changing their BMI, which agrees with the higher prevalence of eating disorders found in women (Neumark-Sztainer et al. 2011; Lundahl et al. 2015; Holland et al. 2016).

5.2. THE OWN IDEAL IMAGE AND THE MOST ATTRACTIVE IMAGE FOR THE OPPOSITE SEX

All silhouettes (except silhouette 1) were represented in the four age and sex groups as the current image perceived by participants, but ideal body image was represented by silhouettes from 1 to 6, excluding silhouettes representing the most corpulent body configurations. Moreover, only silhouettes 3, 4 and 5 showed a percentage of individuals higher than 10% in almost all groups, with exception of women less than 45 years where just silhouettes 3 and 4 were represented with more than 10%. These results seems to reflect the restrictions on the sociocultural acceptance of beauty, especially in the young groups and even more in women, which has been always the most susceptible group to body image diseases (Ramos-Valverde, Rivera-de-los-Santos, and Moreno-Rodríguez 2010). These results were consistent with the work performed by Rand et al. (2000), where also mid-range silhouettes were chosen as ideal image. The authors found that individuals of all ages were more restrictive selecting acceptable body sizes than which would be acceptable based on medical perspective. As it could be seen in our results, they also found a more restrictive image selection in younger groups and propose that this could be due to an increased concern about dating and appearance.

In the section above, we saw that there were no differences in perceived body images between men and women. Nevertheless, ideal body image showed a clear sexual dimorphism in both age groups. In the younger group, silhouette 4 was the most usually chosen silhouette by both sexes; however, silhouettes 3 and 4 were the most chosen ones in women, while men chose silhouettes 4 and 5. This indicates that women prefer smaller silhouettes than men, which is in agreement with Barret (2011) work, and confirms the usually observed conduct in women derived from the socio-cultural pressure that emphasize a thin ideal for women (Morrison, Kalin, and Morrison 2004; Zaccagni et al. 2014). On the other hand, the fact that men chose bigger silhouettes might have nothing to do with higher amount of fat, but with fat free mass, since men usually associate bigger silhouettes with a bigger amount of muscle instead of fat mass (Muñoz-Cachón et al. 2009). Under this hypothesis, men would prefer a more muscular image than women.

As it has been mentioned in the introduction, body image ideals have changed throughout history, from the first human beings until now. There are many reasons for these changes and for the sexual differences concerning ideal body image. It is possible that the ideal body image men and women have for themselves could be conditioned by the ideal body image they have for the opposite sex. This theory has a clear evolutionary perspective, according to which, men would prefer a female body shape that points to a mate's high potential to contribute to his reproductive success (Meltzer et al. 2014; Bovet and Raymond 2015). Thus, an appropriate image would improve matching probabilities and biological fitness. In past, men could have sought women with a more robust silhouette as a sign of health and fertility, and women could have sought more well-built men as indicative of strength and ability. However, as we have already seen ideal image has changed in our days, especially in women. Does this mean that the most attractive image for the opposite sex has changed too? Results showed how in all cases the most attractive silhouette for the opposite sex was silhouette number 4. However, in the same way as it happens with ideal image, women preferred men with silhouettes between 4 and 5 whereas men preferred women with slightly lower silhouettes (between 3 and 4). Differences between what was chosen by men and by women was statistically significant just for individuals under 45 years old; in individuals over 45 years, even though this tendency could be easily appreciated, the difference was not significant. There may be several explanations for this. On one hand, significant differences showed up in young people whose ages were more appropriate to match and produce offspring and where participants were more susceptible to external influences. On the other hand, it might be related to differences in sexual dimorphism of human's morphology at different ages. Sexual dimorphism in body composition has its higher peak in young adults (Wells 2007). Since people often choose partners of similar age, these differences would be reflected in the chosen silhouette for the opposite sex.

Many authors argue that changes in ideal body image could be due to mass media impact (Grabe, Ward, and Hyde 2008; Chang et al. 2013). According to this theory mass media can influence the internalization and perception about what the ideal body is, and bodies that do not match this ideal are thought to be unattractive (Morrison, Morrison, and Hopkins 2003; Dye 2016). However, according to Bovet et al. (2015) body size preferences had already changed before the appearance of mass media. According to one of his studies (Bovet and Raymond 2015), the preferred WHR began to decrease since the 15th century, explained by a change of environment in western societies, when life expectancy, food availability and gross domestic product increased in these populations. Thus, with a more clement environment, with higher resources and better health, men's preferences could have evolved towards a lower WHR (Bovet and Raymond 2015). In line with this suggestion, the ideal body image would be related to a representative image of prosperity. But prosperity has been associated to different shapes through years, and so the ideal image has also changed. Long time ago or even nowadays in underdeveloped societies, where food is scarce and can be a source of illness and death, higher BMI would be preferred as indicative of good nutrition and therefore good health. Nowadays, in our society the access to food is not a problem anymore. In fact, overfeeding has become a source of illness and social problems. This may be the reason why high nutritional status were rejected, and the low ones suggested prosperity and welfare. In spite of this, it cannot be denied that mass media has an important presence in our society and has the ability to reach many people. Thereby both theories could have an important role nowadays, since TV will reflect the environmental changes and will associate those improvements in quality of life with thinness. It must be noted that not only women are affected by sociocultural environment and mass media, but also men are susceptible to their influence (since the ideal image for the opposite sex has also changed and it is in agreement with what women choose for themselves). However, it has been the body image of women which has experimented a higher change, at a morphological level, in mass media and in our society.

We may think that as the body image shown in media is the same for all women, and it is also the same for all men (although different between each other), men and women would choose similar silhouettes among them. However, research suggests that inspecting one's self in comparison to those who are more or less attractive, that is, comparing our body image which the ones shown in TV and promoted in our society, affects self-perceptions (Morrison, Kalin, and Morrison 2004). Thereby, our ideal body image for our-self or for the opposite sex would be affected by our own body image too. Thus, it is worth asking if our nutritional status may affect our preferences about the ideal body image and how it might affect those preferences. In regards to the most attractive body image for the opposite sex, in the group with <45 years, there was a higher percentage of obesity in subjects who chose slightly bigger silhouettes, than in subjects who chose smaller ones, where normal-weight was predominant. According to other studies, there may be assortative matting for body fatness (Speakman et al. 2007; Fisher et al. 2014). Thereby, results might reflect the preference of young individuals for a partner with a similar nutritional status. It is not clear why this happens. Speakman et al. (2007) say that assortative mating might happen because physically attractive persons pair off with each other first, decreasing the available attractive subjects, so that the remaining has to pair off with each other. We cannot confirm this with our results, since in our case we had data of body preferences and not of a real partner choice. In any case, as Fisher (2014) mentioned, people seem to realign their preferences so that they match with partner characteristics, so that cognitive dissonance is reduced. One possible interpretation could be a low self-esteem of subjects with high BMI, who do not dare to approach thinner individuals afraid of what they might think. On the other hand, in people ≥ 45 years this association could not be found in the present study. It seems that in this age group the own nutritional status was no longer important since at this age the social or biological pressure for an appropriate matching has decreased, and in addition external influences or suggestibility generally decreases with age (Marple 1933; Umanath 2016). Concerning the ideal body image chosen for oneself, it would be logical to think that obese people would like to be just as thin as normal-weight or overweight individuals are. However, as shown in the results, a higher percentage of obese participants chose silhouettes that represented slightly larger bodies. This association was not limited to a particular group; since, even though association was higher in young individuals, it was also appreciated in the older ones. In their study, Naghshizadian (2014) also found that the higher the subject's BMI–was, the higher they think their ideal weight was supposed to be. One possible explanation for this effect is that, as it happens with underestimation of current body image, a misperception of body image can lead a person to think that the ideal body image is smaller than it really is. This may provide protection against low self-esteem, but it can also interfere with weight control. On the other hand, it is possible that obese individuals who are aware of their obesity choose slightly larger silhouettes as a more realistic goal in their attempt to reduce obesity.

5.3. BODY IMAGE DISSATISFACTION

Body image dissatisfaction affects the feelings we have about ourselves. Many variables, such as psychological components, family, peers, ethnicity…, play a role in body image dissatisfaction (Brennan, Lalonde, and Bain 2010), which is associated with depression (Noles, Cash, and Winstead 1985), low self-esteem (Mendelson, Mendelson, and White 2001), feelings of shame (McKinley and Hyde 1996), body surveillance (McKinley and Hyde 1996), diminished quality of life (Cash and Fleming 2002), and avoidance of body exposure during sexual activity, which can lead to impaired sexual functioning (Cash, Maikkula, and Yamamiya 2004). Discrepancy between self-perceived body image and ideal body image could be used as an indicator of body image dissatisfaction and it has been used previously in many works (Tiggemann 2004; Solomon-Krakus et al. 2017).

In the present study, the pattern of body image dissatisfaction was very similar in men and women, but with significant differences between them. Consistent with Bibiloni et al. (2017), a slight desire to be thinner was predominant in the entire sample. Although, neither of the two age groups had sexual differences in the perceived silhouette chosen as their current image, the ideal body image was clearly different in both groups, and this was reflected in body image dissatisfaction. Consistent with other studies (Mendelson, Mendelson, and White 2001; Johnstone et al. 2008; Ramirez-Molina et al. 2015; Bibiloni et al. 2017), in our sample women were always more dissatisfied than men.

In accordance with other studies, in the older group the desire to be thinner was higher than in the younger one (McCabe and Ricciardelli 2004; Bibiloni et al. 2017). This is logical in our results, as this group also selected larger silhouettes as their current image. As previously argued, fat mass increases with age and this makes older individuals more susceptible to obesity which can increase their body dissatisfaction. However, even though full satisfaction was higher in the younger group compared with the older one, especially in men, dissatisfaction by excess was still predominant. Dissatisfaction by default was relatively small, but in young men it reached an important percentage, which was also in agreement with the results found in Bibiloni et al. (2017) where the younger men group also presented the highest proportion of subjects dissatisfied due to being underweight. Probably these results reflect the desire of a more muscular body in young men.

Both images, the one perceived as current and the one perceived as ideal, were associated with nutritional status, in consequence we may suppose that body dissatisfaction is also associated with it. In fact, as it is shown in the results, it was. Nevertheless, some differences between groups could be seen in the percentages of the different nutritional status for each dissatisfaction score. In women ≥45 years, a logical pattern could be seen in relation to nutritional status. Normal-weight was predominant in satisfaction category whereas overweight and obesity were predominant in a slight dissatisfaction by excess category, and obesity and morbid obesity were predominant in moderate dissatisfaction by excess category. In younger women, the percentage of normal-weight in each dissatisfaction score is higher than in the older women group. (e.g. in the younger group, more than 50% of normal weight women were in the slight dissatisfaction by excess category, whereas just 11.3% of older women were in that category). In the light of these results, we can state that although dissatisfaction was higher in older women, it seemed to be in concordance with nutritional status. So at this age group, strategies for weight control would be useful not only for health but also for self-esteem. However, in the younger women group weight control strategies could help with health problems related to obesity, but if problems related to body image dissatisfactions want to be eradicated, new strategies focused on stereotypes and self-perception are needed. For men of both age groups dissatisfaction by excess was also higher as BMI increases, but full satisfaction categories had higher percentages of overweight than the women groups with equivalent age. As it has been mentioned above, this may be related to a higher prevalence of fat free mass in men and their preference for muscular bodies, which was discussed by Johnstone et al. (2008), who found that body image dissatisfaction in men is affected by perceived muscle and by perceived excess weight (Brennan, Lalonde, and Bain 2010).

Individuals deal with body image dissatisfaction in many different ways. A common way of coping with it is to limit the number of calories consumed. According to Gough (2007) dieting is more frequent among women than among men, but both sexes deal with body dissatisfaction, and its handling also include excessive exercise, cosmetic surgery, and using diet pills, steroids or protein supplements (Brennan, Lalonde, and Bain 2010). All these activities may be dangerous if the subject who wants to lose weight or change his or her body image has already a proper nutritional status. In this study, although dissatisfaction was higher in older than in younger groups, in most cases it was in concordance with the nutritional status. It was the young women group which was at higher risk as a slight displacement between dissatisfaction score and nutritional status was observed.

6. CONCLUSION

Results from this thesis confirm the relation of nutritional categories, based on BMI, with body size perception and satisfaction. Most people are able to choose the appropriate silhouette according to their nutritional status. However, misperception seems to be greater among older men, but unrelated to nutritional categories. Although women tend to classify themselves properly, underestimation is more common among high nutritional categories whereas overestimation is more common among lower ones. This is a matter of concern as obese women could not see the need to control their weight whereas already normal-weight women could try to reduce their BMI.

Following the tendency shown in society and in mass media, the ideal image most individuals have for women is smaller than for men, either if it was the image chosen for themselves or the one chosen for the opposite sex. Nevertheless individuals with higher nutritional categories also prefer bigger silhouettes for themselves or for the opposite sex, with the exception of older subjects who do not seem to care for the image of the opposite sex. The desire to be thinner is common in the studied sample, but in most cases it is consistent with the nutritional status of the individuals. However, young women are a group at risk as a high percentage of normal-weight women desire thinner bodies.

Chapter VI

Association between Obesity and Environmental Factors

1. SUMMARY

OBJECTIVES: Obesity has experienced a dramatic rise, reaching epidemic proportions over the last decades. Although genetic factors clearly contribute to individual differences in adiposity, they cannot fully explain the obesity pandemic. Lifestyle, socioeconomic, biodemographic and environmental factors may also play, in general, an important role in the development of obesity and related diseases. The aim of this chapter is to determine the relative contribution of environmental factors upon four obesity indices representing overall obesity, abdominal obesity, central fat distribution and excessive adiposity.

METHODS: The study includes 521 adults between 18 and 80 years (203 men and 318 women). Information about 17 environmental factors in addition to biodemographic and socioeconomic information were obtained by personal interview. Obesity was defined in four different ways, based on each of the four indexes: BMI ≥30 kg/m^2, WC >102 cm for men and WC >88 cm for women, WHR ≥0.90 for men and WHR ≥0.85 for women and FM% >25% for men and FM% >33% for women. Multiple logistic regressions were used to identify predictive factors of obesity in a case-control study design, and SPSS Statistics 23 was the statistical program used to conduct the analyses.

RESULTS: Multiple logistic regressions showed that obesity was positively associated with personal background, sedentary lifestyle, bad sleep quality, low number of eating episodes and smoking, whereas physical activity, main meal duration and moderate alcohol consumption were found to be protective factors against obesity.

CONCLUSIONS: This study confirms the influence of environmental factors on obesity. However, it suggest that this influence is a little different depending on the index used to evaluate obesity (BMI, WC, WHR or FM%).

2. BRIEF INTRODUCTION

Concern about the growing prevalence of obesity during the last few decades has increase since it is one of the main risk factors for several non-communicable diseases. Besides, general and abdominal adiposity are associated with increased dead rate (Pischon et al. 2008). According to the WHO, worldwide in 2014, 13% of adults were obese (World Health Organization 2016b).

In simple words, obesity develops when energy intake exceeds energy expenditure (Hill and Peters 1998). Although genetic factors are determinant in individual susceptibility to obesity, they cannot explain, the population growth to pandemic levels of obesity in the last years, as our genes have not changed substantially during the past two decades (Hill and Peters 1998). As recent reviews have pointed out, this scenario is best explained by adding to the equation the contribution of obesogenic environments (Giles-Corti et al. 2003).

Since industrialization, the high prevalence of energy-dense diets and the arise of labour-saving technologies have led to an excessive energy intake and a decline in energy expenditure in favour of an increase in sedentary lifestyle in the daily living (Giles-Corti et al. 2003). Therefore, some conditions or attitudes in relation to the new environment around us, and even the own society where we live and work, may increase or decrease the risk of developing obesity. The relationship between environmental factors and obesity is complex and still a subject of investigation.

The main aim of this study is to determine the relative contribution of environmental factors (i.e. background, (in)activity, sleep patterns, eating patterns, smoking and alcohol consumption) upon four obesity indices (BMI, WC, WHR and FM%).

3. BRIEF METHODOLOGY

The basic descriptive statistics were computed for environmental factors. The number and percentage of subjects with obesity (BMI ≥30 kg/m^2) as well as BMI mean and standard deviation were calculated for each category of the studied qualitative variables separately for age group (<45 years and ≥ 45 years) and sex (men and women). The number of subjects and BMI mean and standard deviation were also calculated for continuous variables in each nutritional category (no obesity and obesity), and also separately by age group and sex. Tables for these descriptive statistics are presented in Appendix III (From Table A.6.1 to Table A.6.17)

Multiple logistic regressions were used to study the association between environmental factors and obesity indices (BMI, WC, WHR and FM%). Each obesity index was dichotomized following the OMS criteria for BMI (obesity: BMI $\geq$30 kg/m^2; no obesity: BMI <30 kg/m^2), WC (abdominal obesity: WC >102 cm. for men and WC >88 cm. for women; no abdominal obesity: WC $\leq$102 cm. for men and WC $\leq$88 cm. for women) and WHR (central fat distribution: WHR $\geq$0.90 for men and WHR $\geq$0.85 for women; peripheral fat distribution: WHR <0.90 for men and WHR <0.85 for women) (World Health Organization 2011) and the SEEDO criteria for FM% (excessive adiposity: FM% >25% for men and FM% >33% for women; no excessive adiposity: FM% $\leq$25% for men and FM% $\leq$33% for women) (Campillo et al. 2000). The four obesity indexes were used as dependent variables while environmental factors were used as independent variables in the multiple logistic regressions, in which decimal age, sex and socioeconomic status (SES) were used as covariates. Most of the environmental variables were qualitative, but five of them were quantitative. In order to conduct the statistical analyses, two of the quantitative variables (sleep duration and main meal duration) were categorized, since a homogeneous response to obesity along all the range of those variables could not be assumed. Bonferroni correction for multiple comparisons was also calculated. Taking into account the 17 variables analysed and the 4 phenotypes, the new critic value for "p" would be α=0.05/68=0.0007; however, as the used sample is not very big and Bonferroni correction could be too much conservative, the significance threshold in discussion was set at $p<0.05$.

4. RESULTS

In this study the association between 17 environmental factors and 4 obesity related indices (BMI, WC, WHR and FM%) were explored. Results have been divided into 5 sections for a better comprehension (i.e. Background, (In)Activity, Sleep patterns, Eating patterns and Tobacco/Alcohol).

4.1. BACKGROUND

Participants with obese first-degree relatives had between 2.19 and 3.96 times more odd to be obese (based on BMI, WC and FM% classifications) compared with individuals who did not have obese relatives (Table 6.1). The odd of being obese based on BMI and WC was almost 2 fold higher in participants having obesity related diseases than in those free of disease. However, the odd was 3.44 fold higher in individuals with central fat distribution, also compared with subjects free of diseases. The four studied obesity indices were associated with a bad perception of the physical condition. Among them, the one based on FM% had the higher association, whereas the one based on WHR had the lowest association.

Table 6.1. Odd Ratios for association between background and obesity indices.

	Background							
	Overall obesity		**Abdominal obesity**		**Central fat distribution**		**Excessive adiposity**	
	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig
Family history of obesity								
No	1.00		1.00		1.00		1.00	
1st Degree	3.62 (2.2-6.0)	**6.2E-07**	3.96 (2.4-6.7)	**2.0E-07**	1.62 (0.9-2.8)	0.080	2.19 (1.3-3.7)	**0.004**
2nd Degree	1.13 (0.5-2.8)	0.790	1.21 (0.5-2.9)	0.676	1.59 (0.7-3.7)	0.282	1.15 (0.5-2.5)	0.724
Obesity related disease								
No	1.00		1.00		1.00		1.00	
Yes	1.83 (1.0-3.3)	**0.039**	1.99 (1.1-3.6)	**0.025**	3.44 (1.7-7.1)	**7.1E-04**	0.81 (0.4-1.7)	0.578
Perceived physical condition								
Good	1.00		1.00		1.00		1.00	
Regular	0.98 (0.6-1.7)	0.941	1.01 (0.6-1.8)	0.970	0.94 (0.5-1.7)	0.834	0.98 (0.6-1.7)	0.932
Bad	6.60 (3.6-12.0)	**7.2E-10**	5.91 (3.2-10.9)	**1.1E-08**	2.64 (1.4-5.0)	**0.003**	10.42 (4.5-24.3)	**5.3E-08**

Adjusted for age, gender, educational level and professional level (multivariable-adjusted).
OR: odd ratio; CI: confidence interval. Bonferroni correction ($p < 0.0007$).
Overall obesity, abdominal obesity, central fat distribution and excessive adiposity were respectively based on the cut off points established by the WHO or the SEEDO for BMI, WC, WHR and FM%.

4.2. (IN)ACTIVITY

Practicing regular sport and more than 6 years practicing it were protective factors against overall obesity, abdominal obesity, central fat distribution and excessive adiposity (Table 6.2). Concerning overall and abdominal obesity, walking and practicing sport since 3 to 6 years also had a protective effect against obesity (OR: 0.29 and 0.40, respectively). Work intensity and daily walking had no effect on obesity (with the exception of a weak positive association with central fat distribution). On the other hand, the time spent watching TV was positively associated with obesity for any of the four obesity phenotypes.

Table 6.2. Odd Ratios for association between (in)activity and obesity indices.

	(In)Activity							
	Overall obesity		**Abdominal obesity**		**Central fat distribution**		**Excessive adiposity**	
	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig
Physical activity								
Nothing	1.00		1.00		1.00		1.00	
Walking	0.29 (0.2-0.6)	**5.1E-04**	0.40 (0.2-0.8)	**0.010**	0.95 (0.4-2.1)	0.909	1.03 (0.4-2.6)	0.947
Regular sport	0.33 (0.2-0.6)	**4.1E-05**	0.33 (0.2-0.6)	**3.9E-05**	0.42 (0.2-0.7)	**0.002**	0.45 (0.3-0.8)	**0.003**
Since how long								
Nothing	1.00		1.00		1.00		1.00	
< 1 year ago	0.91 (0.3-2.5)	0.852	0.63 (0.2-1.8)	0.382	0.61 (0.2-1.9)	0.398	0.75 (0.2-2.3)	0.615
1-2 years ago	0.53 (0.2-1.3)	0.152	0.45 (0.2-1.1)	0.076	1.94 (0.7-5.2)	0.187	1.02 (0.4-2.5)	0.967
3-6 years ago	0.18 (0.1-0.5)	**4.2E-04**	0.15 (0.1-0.4)	**1.5E-04**	0.67 (0.3-1.6)	0.368	0.52 (0.2-1.3)	0.154
> 6 years ago	0.23 (0.1-0.4)	**3.3E-06**	0.34 (0.2-0.6)	**3.3E-04**	0.30 (0.2-0.6)	**2.8E-04**	0.39 (0.2-0.7)	**0.002**
Daily walking								
Minutes/day	1.00 (1.0-1.0)	0.502	1.00 (1.0-1.0)	0.154	1.01 (1.0-1.0)	**0.016**	1.00 (1.0-1.0)	0.999
Work intensity								
Light	1.00		1.00		1.00		1.00	
Moderate/busy	0.89 (0.6-1.4)	0.618	0.99 (0.6-1.6)	0.954	1.22 (0.7-2.0)	0.445	0.75 (0.5-1.2)	0.258
Television								
Hours/week	1.04 (1.0-1.1)	**2.9E-04**	1.05 (1.0-1.1)	**4.7E-05**	1.04 (1.0-1.1)	**0.002**	1.03 (1.0-1.1)	**0.016**

Adjusted for age, gender, educational level and professional level (multivariable-adjusted).
OR: odd ratio; CI: confidence interval. Bonferroni correction ($p < 0.0007$).
Overall obesity, abdominal obesity, central fat distribution and excessive adiposity were respectively based on the cut off points stabilised by the WHO or the SEEDO for BMI, WC, WHR and FM%.

4.3. SLEEP PATTERNS

Table 6.3 presents the results from the multiple logistic regressions between sleep patterns (i.e. sleep duration and sleep quality) and obesity indices. Only sleep quality but not sleep duration seemed to be a risk factor for obesity. Regarding overall and abdominal obesity, based on BMI and WC, both regular and bad sleep qualities increased the odd of obesity by 1.78 to 2.73 fold. However, bad sleep quality did not modify the odd for high central fat distribution, based on WHR, or excessive adiposity, based on FM%.

Table 6.3. Odd Ratios for association between sleep patterns and obesity indices.

	Sleep patterns							
	Overall obesity		**Abdominal obesity**		**Central fat distribution**		**Excessive adiposity**	
	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig
Sleep duration								
6-8 h	1.00		1.00		1.00		1.00	
<6 h	0.90 (0.5-1.8)	0.765	0.82 (0.4-1.7)	0.590	1.24 (0.6-2.6)	0.576	0.91 (0.4-2.1)	0.817
>8 h	1.51 (0.7-3.3)	0.290	1.46 (0.7-3.3)	0.364	1.51 (0.6-3.9)	0.397	1.15 (0.4-3.0)	0.773
Sleep quality								
Good	1.00		1.00		1.00		1.00	
Regular	2.02 (1.2-3.4)	**0.008**	1.78 (1.1-3.0)	**0.032**	1.26 (0.7-2.3)	0.431	1.68 (0.9-3.0)	0.079
Bad	2.73 (1.4-5.2)	**0.002**	2.09 (1.1-4.1)	**0.030**	0.96 (0.5-2.0)	0.913	2.08 (0.9-4.7)	0.076

Adjusted for age, gender, educational level and professional level (multivariable-adjusted).
OR: odd ratio; CI: confidence interval. Bonferroni correction (p< 0.0007).
Overall obesity, abdominal obesity, central fat distribution and excessive adiposity were respectively based on the cut off points stabilised by the WHO or the SEEDO for BMI, WC, WHR and FM%.

4.4. EATING PATTERNS

Main meal duration was inversely associated with overall obesity (OR: 0.54) and abdominal obesity (OR: 0.50), but it was not associated with central fat distribution or excessive adiposity (Table 6.4). Having lunch in a company´s lunchroom was a protective factor against central fat distribution (OR: 0.45) in comparison with having lunch at home. Participants who reported less than 3 meals per day showed a higher odd for both, overall obesity and central obesity, compared to participants that eat 3 meals per day.

Table 6.4. Odd Ratios from multiple logistic regression test for association between eating patterns variables and obesity indices.

	Eating patterns							
	Overall obesity		**Abdominal obesity**		**Central fat distribution**		**Excessive adiposity**	
	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig
Main meal duration								
≤ 20 min	1.00		1.00		1.00		1.00	
>20 min	0.54 (0.3-0.9)	**0.010**	0.50 (0.3-0.8)	**0.004**	0.79 (0.5-1.3)	0.372	0.66 (0.4-1.1)	0.100
The place of the main meal								
Home	1.00		1.00		1.00		1.00	
Tupperware	0.85 (0.4-1.9)	0.703	0.98 (0.4-2.2)	0.955	1.04 (0.5-2.4)	0.928	1.11 (0.5-2.4)	0.795
Restaurant	1.15 (0.5-2.6)	0.726	1.11 (0.5-2.5)	0.802	1.17 (0.5-2.9)	0.739	0.84 (0.4-2.0)	0.696
Company dining room	0.53 (0.2-1.2)	0.114	0.53 (0.3-1.1)	0.098	0.45 (0.2-1.0)	**0.041**	0.71 (0.4-1.4)	0.313
Number of eating episodes								
3 times	1.00		1.00		1.00		1.00	
4 times	0.76 (0.4-1.4)	0.372	0.69 (0.4-1.3)	0.221	1.69 (0.9-3.2)	0.107	0.86 (0.5-1.6)	0.616
5 times	1.03 (0.6-1.8)	0.910	1.18 (0.7-2.1)	0.590	1.17 (0.6-2.3)	0.634	1.08 (0.6-2.0)	0.806
6 times or more	1.32 (0.4-4.0)	0.620	0.88 (0.3-2.8)	0.832	0.79 (0.2-2.7)	0.714	0.58 (0.2-2.2)	0.415
1 or 2 times	6.16 (1.4-28.1)	**0.019**	5.38 (1.2-24.7)	**0.031**	1.67 (0.4-8.0)	0.525	1.27 (0.2-8.3)	0.804

Adjusted for age, gender, educational level and professional level (multivariable-adjusted).
OR: odd ratio; CI: confidence interval. Bonferroni correction ($p< 0.0007$).
Overall obesity, abdominal obesity, central fat distribution and excessive adiposity were respectively based on the cut off points stabilised by the WHO or the SEEDO for BMI, WC, WHR and FM%.

4.5. SMOKING AND ALCOHOL CONSUMPTION

As shown in Table 6.5, only former smokers (but no current smokers) were more likely to have abdominal obesity in comparison with those who had never smoked (OR: 1.88). Whereas both, former and current smokers were more likely to present central fat distribution (OR: 2.46 and 1.99, respectively). The increase in just one the number of cigarettes smoked per day was also associated with an increase in the odd ratios of being obese for three of the four studied indices (based on BMI, WC and FM %). On the other hand, alcohol consumption was inversely associated with excessive adiposity (OR: 0.52). When the frequency of alcohol consumption was taken into account, it could be seen that occasional drinking was inversely associated with obesity, based on BMI and on FM%.

Table 6.5. Odd Ratios for association between smoking, and alcohol variables and obesity indices.

	Smoking/Alcohol consumption							
	Overall obesity		**Abdominal obesity**		**Central fat distribution**		**Excessive adiposity**	
	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig	OR (95% CI)	Sig
Smoking								
No	1.00		1.00		1.00		1.00	
Before, not now	1.56 (0.9-2.6)	0.093	1.88 (1.1-3.2)	**0.021**	2.46 (1.4-4.4)	**0.002**	1.05 (0.6-1.9)	0.862
Yes, now	1.29 (0.7-2.4)	0.415	1.77 (1.0-3.3)	0.073	1.99 (1.0-3.9)	**0.047**	0.87 (0.5-1.6)	0.670
Number of cigarettes								
Cigarettes/week	1.06 (1.0-1.1)	**5.2E-05**	1.05 (1.0-1.1)	**3.7E-04**	1.03 (1.0-1.1)	0.120	1.04 (1.01-1.07)	**0.010**
Alcohol								
No/infrequently	1.00		1.00		1.00		1.00	
Yes	0.62 (0.4-1.0)	0.058	0.69 (0.4-1.2)	0.160	0.80 (0.5-1.4)	0.452	0.52 (0.3-0.9)	**0.030**
Alcohol frequency								
No/infrequently	1.00		1.00		1.00		1.00	
Occasionally	0.51 (0.3-1.0)	**0.050**	0.66 (0.3-1.3)	0.230	0.71 (0.3-1.5)	0.361	0.43 (0.2-0.9)	**0.022**
Weekends	0.54 (0.3-1.0)	0.061	0.58 (0.3-1.1)	0.101	0.56 (0.3-1.1)	0.100	0.51 (0.3-1.0)	0.052
Some days/week	0,78 (0,3-1,9)	0.578	0.83 (0.3-2.0)	0.685	2.65 (1.0-7.2)	0.055	1.30 (0.5-3.7)	0.629
Every days	0.87 (0.4-1.8)	0.711	0.89 (0.4-1.9)	0.761	0.97 (0.4-2.3)	0.948	0.51 (0.2-1.2)	0.125

Adjusted for age, gender, educational level and professional level (multivariable-adjusted).
OR: odd ratio; CI: confidence interval. Bonferroni correction ($p< 0.0007$).
Overall obesity, abdominal obesity, central fat distribution and excessive adiposity were respectively based on the cut off points stabilised by the WHO or the SEEDO for BMI, WC, WHR and FM%.

5. DISCUSSION

5.1. BACKGROUND

According to the results of this study and in agreement with other studies (Neutzling, Taddei, and Gigante 2003; Ochoa et al. 2007), a family history of obesity was a risk factor for obesity development. This association typically illustrate two underlying processes. On one hand, familial clustering of obesity has a clear genetic component (Ukkola and Bouchard 2001), so that genetic material related with obesity is transmitted from obese parents to offspring (Wannaiampikul et al. 2015; Singh, Kumar, and Mahalingam 2017) (Genetic factors of obesity will be discussed on Chapter VII). On the other hand, parents not only provide genes, but also environmental experiences (Birch and Fisher 1998), which may modulate children behaviour and attitudes. For example, eating patterns and food preferences are conditioned by the number of exposures to a particular food (Birch and Marlin 1982), the work cost required to obtain food (Epstein and Saelens 2000), or the limitation of food or food variety (Fisher and Birch 1999). Shared environment is also a very important contributing factor to physical activity in children (Franks et al. 2005; Fisher et al. 2010). According to Beets et al. (2010), parents serve as reference guides and are often responsible of children's leisure time activities, thus their behaviour is a strong influence on children's attitude toward exercise (Huppertz et al. 2012). However, environment provided by parents might depend on their own attitudes, which could be different in obese and in non-obese individuals. According to this, Deforche et al. (2006) found that overweight and obese individuals had less positive attitude toward physical activity than normal-weight subjects. It is important to note that this study was carried out in adults, who usually are less influenced by parents than children. However, the significant association found between obesity and first degree obese relatives may be somehow reflecting the influence received as children, since obesity during childhood increased significantly the risk of obesity in adulthood (Jung et al. 2009). In agreement with this, Whitaker et al. (1997) also found that parental obesity increased the risk of adult obesity. Besides, it should not be forgotten that the genetic background remains during all life, and it may predispose to obesity development in adulthood.

Obesity is clearly associated with health disturbances. In this study type 2 diabetes, hypertension, cholesterol, cardiovascular diseases or respiratory diseases were considered obesity related diseases, and consistently with other studies (Canoy et al. 2007; de Mutsert et al. 2014) were significantly associated with obesity. The highest positive association was found with central fat distribution (defined by WHR), and although weaker but significant association could also be found for overall and abdominal obesity (defined by BMI and WC, respectively) no association were found when obesity was defined by FM%. Consistently with these results, Canoy et al. (2007) found that WHR, WC and BMI were directly related to coronary heart disease development, but WHR was more consistently associated than WC or BMI. The stronger association found between obesity related diseases and fat distribution could reveal differences in metabolic characteristics between central and peripheral body fat. In fact, increased abdominal obesity could indicate increased visceral fat (Canoy et al. 2007), which has been demonstrated to be associated with insulin resistance and a worse lipid profile (Carr et al. 2004) than peripheral fat.

In their constitution, the World Health Organization (1946) defined health as not only the absence of diseases but also a state of physical, mental and social well-being (World Health Organization 2006), and the Secretary of State for Health in London (1998) also said that a good health is the base of a good life. Thus, a proper evaluation of health should include the health perceived by the own patient, and not only the diseases diagnosed by doctors (Okosun et al. 2001). In our study the perceived physical condition was asked to the participants and results showed significant associations between it and obesity defined by BMI, WC, WHR and FM%. This finding supports the idea that obesity is associated with reduced self-rated health (Okosun et al. 2001); however, the OR obtained for fat distribution was smaller than the ones obtained for overall or abdominal obesity, while excessive adiposity presented the highest positive association with a bad perceived physical condition. As it has been said above, central fat distribution is related to metabolic and cardiovascular diseases, which may influence the physical condition perceived by subjects, but general obesity could also affect health trough non-metabolic conditions. According to Després et al. (1990), individuals with peripheral fat accumulation are prone to varicose veins and other problems commonly associated with excess body weight, such as lung volume reduction that hinders ventilation, osteoarthritis or low back pain. In several works, obesity has also been associated with depression or mental issues (Abou Abbas et al. 2015; Pereira-Miranda et al. 2017). Besides, obese individuals are highly stigmatized in our society (Fruh et al. 2016; Latner and Stefano 2016). All this contribute to a bad health perception, and as obesity assessed by FM%, or even by BMI or WC provides a better idea of the excess of adiposity than just fat distribution, it could explain the higher OR found in these variables.

5.2. (IN)ACTIVITY

Obesity is caused, from the simplest point of view, by an imbalance between energy intake and energy expenditure. However, according to Prentice et al. (1995), in some populations experiencing an increase in obesity prevalence, the usually increase in total energy intake was not demonstrated. Thus, variables related to energy expenditure are considered to play an important role in obesity development.

Non-exercise activity thermogenesis (NEAT) has a significant interindividual variation and it is considered important in obesity development by many authors (Villablanca et al. 2015; Hamasaki, Ezaki, and Yanai 2016). According to Levine et al. (2008) walking is the main component of NEAT. In addition to this, as most adults spend a lot of time at work, the intensity of the performed work may also be considered as an important NEAT component. In agreement with Gutiérrez-Fisac et al. (2002), our study did not find association between work intensity and obesity. Besides, contrary to expectations, a small but significant positive association was found between daily walking minutes (along daily activities and not as sport) and central fat distribution. Walk and work are considered low intensity activities that do not require great energy expenditure and, contrary to what happens in high intensity aerobic exercise, basal metabolism rate is not increased with these kinds of activities (Bernstein, Costanza, and Morabia 2004). This, together with the possibility that the extra energy expenditure caused by walking and work activities could be neutralized by higher or additional intake in more active individuals (Gutiérrez-Fisac et al. 2002), may explain the results obtained in this work. Furthermore, as mentioned in Deforche et al. (2003), inactive or obese individuals tend to over-report their exercise practice in an effort to cover their inability to meet with the activity level expectations perceived by them. However, there are studies where associations between walking or work intensity and obesity were found (Jeffery, Adlis, and Forster 1991; Levine et al. 2008), so the association between NEAT and obesity remains controversial and more research is needed.

In industrialized countries, energy intake is based in occidental high caloric diets, and the energy expended in our daily living activities is very low. As a result, energy balance between energy intake and energy expenditure is most commonly positive than in no-industrialized countries. In agreement with the review performed by Füzéki et al. (2017), in our work regular sports practice seemed to work as a protective factor against obesity, whatever the index used to assess obesity, possibly because it could result in extra energy expenditure that otherwise would not be spent. Furthermore, oxygen consumption remains elevated above resting levels for some time after the end of a high intensity exercise such as sports, due to the need to restore energy reserves, especially glycogen levels in liver and muscles (Bernstein, Costanza, and Morabia 2004). This may help maintain a proper energy balance even if additional energy is consumed after the sport practice. Walking, not just during daily activities but as sport, has also shown a positive effect in obesity control; however, this association could be seen just when obesity was defined by BMI or WC. Although the amount of energy necessary to perform this activity is lower than in other sports, activities of lower intensities can be sustained for much longer periods of time than higher intensity activities, so the overall energy expenditure might be enough to influence metabolic balance and protect against weight gain (Füzéki, Engeroff, and Banzer 2017).

On the other hand "sedentariness" has been proposed as one of the main responsible factors of the obesity epidemic, and it has been associated with a variety of health risks (United States. Department of Health and Human Services 1996). Sedentary behavior is not just the absence of exercise, but actually performing activities that do not considerably increase energy expenditure (Pate, O'Neill, and Lobelo 2008). In this work we had considered the time spent watching TV as an indicator of sedentariness and, in agreement with many other studies (Inoue et al. 2012; Xie et al. 2014), our results confirmed its association with obesity. Since the emergence of TV, the use of leisure time has profoundly changed. In the early 90s, Tucker et al. (1991) showed that the typical adult spent on average nearly four hours per day viewing TV. Nowadays, watching TV takes a lot of our daily time and there are really few people who do not watch TV. The mechanisms through which TV is related to obesity are not entirely clarified. The main disadvantage seems to be the physical inactivity that accompanies TV viewing (Tucker and Bagwell 1991), as the time spent on watching TV displaces the time spent in other physical activities. However, according to some studies the association between TV watching and obesity is independent from physical activity (Rey-López et al. 2012; Xie et al. 2014), which suggest that other possible mechanisms could also be playing a role on this association. In this way, a reduction in resting energy expenditure during TV watching, may also contribute to the reduction of total energy expenditure (Klesges, Shelton, and Klesges 1993), making even harder to spend enough energy to maintain a proper energy balance. Furthermore, both snaking and high-density food consumption are increased during TV viewing (Tucker and Bagwell 1991; Hernández et al. 1999; Blass et al. 2006), which increases the energy intake and also hinders energy balance.

5.3. SLEEP PATTERNS

Sleep comprises about one third of a person's life (Lauderdale et al. 2006), but it was not until recently that it has received more attention in epidemiology. According to many studies, sleep deprivation could affect obesity trough changes in hunger regulation hormones (i.e. decrease in leptin and increase in ghrelin), which lead to an increase in energy intake (Spiegel et al. 2004a; Spiegel et al. 2004b; Schmid et al. 2008). Besides, according to Sivak et al. (2006) sleep reduction also supposes an amplified opportunity to eat. Additionally, conversely to what it might be thought, sleep deprivation could suppose a reduction in energy expenditure during day due to feelings of tiredness, which could lead to a decrease in voluntary exercise (Patel 2009). Results from this thesis could not confirm the relation between sleep hours and obesity. However, the lack of association could be due to a limitation of the sample, as the majority of the participants slept between 6 to 8 hours per day (77.5%) and few slept less than 6 or more than 8 hours. So the statistical analysis could not have had enough power to find this association and further analyses should be performed to clarify this.

Since some disparities between time in bed and the actual time slept have been found (Lauderdale et al. 2006), sleep quality, which involves problems such as difficulty in falling asleep, waking up frequently during the night or difficulty in returning to sleep, was also assessed in this work. A clear association was obtained between sleep quality and overall and abdominal obesity (defined by BMI and WC, respectively). Additionally, the association with excess adiposity (defined by FM%) was relatively close to signification. However, no association was found between sleep quality and central fat distribution (defined by WHR). These results could mean that a bad quality of sleep is more related with overall obesity than with fat distribution. However, the present study cannot show the cause-effect direction of the association, so it is possible that the detrimental effects of overall obesity in many aspects of the subject's health and life, such as respiratory problems (St-Onge and Shechter 2014) or even mental disturbances could make it harder to fall asleep or to have an undisturbed sleep than the ones caused by metabolic disturbances more related with central fat distribution.

5.4. EATING PATTERNS

Nutrition transition has involved a lot of changes in our dietary habits. In Europe, diet fat content as well as simple carbohydrate intake are greater than recommended by

WHO; additionally, sugar-rich and alcohol beverages consumption has increased during the past decade, while fruit and vegetable consumption has decreased (Branca, Nikogosian, and Lobstein 2007). However, not only has the diet content changed, but also people's dietary habits (Bertéus-Forslund et al. 2002), such as the temporal distribution of eating events across the day or the frequency of meals eaten away from home. As these changes might also influence obesity development, some variables related to eating patterns were also analyzed in the present study.

In this study it was found that individuals who spent more than 20 minutes eating their principal meal of the day had lower odds of being obese (defined by BMI or WC) than individuals who ate in 20 minutes or less. It could be thought that the longer the time a person spends on having a meal, the more the amount of food he or she will eat. However, energy intake is regulated by circulating factors and gut hormones (e.g. after food ingestion: Ghrelin ↓, Peptide tyrosine-tyrosine (PYY) and glucagon-like peptide-1 (GLP-1) ↑) that play important roles in the control of hunger and satiety feelings (Angelopoulos et al. 2014). When meal duration is prolonged, physiological signals have more time to develop before the ingestion of an excessive amount of food (Andrade, Greene, and Melanson 2008), which could explain the obtained results. Indeed, according with Andrade et al. (2008) the physiological feedback from ingested food takes at least 20 minutes to develop, independently from the amount of food ingested, and people who spend more time on eating ingest fewer calories. Additionally, when meals last longer, there could be more time for drinking water along with the meal, and this may induce satiety by increasing stomach distention (Kissileff et al. 2003).

Nowadays the increase in the number of women participating in the labor market as well as the increase in the time dedicated in commute or in work have led to a decrease in the time spent on meal preparation (Bes-Rastrollo et al. 2010), and consequently, food consumption outside home has been increased (Lin, Guthrie, and Frazao 1999). However, the association or the absence of association between the frequency of meals eaten outside home and obesity is still unclear. For example, Bes-Rastrollo et al. (2010) found a positive association, whereas Marín-Guerrero et al. (2008) found no association at all. A possible explanation for these discrepancies is that several studies did not take into account the place or the kind of food eaten outside home. In our study, we had assessed the place where the main meal was eaten and almost no significant associations were found with the exception of a protective factor against central fat distribution (defined by WHR) when the main meal was eaten in the company dining room. Although there are many works (Guthrie, Lin, and Frazao 2002; Bes-Rastrollo et al. 2010) where eating at restaurants are considered a risk factor for obesity, due to oversized portions and energy-dense foods that promotes weight gain, our results could not confirm this association, whatever the index used to assess obesity. It should be taken into account that, in the present study, only the place where the main meal was eaten on ordinary days was analyzed. Thus, it is also possible that eating breakfast or dinner away from home have a greater impact on obesity development than eating lunch away from home (Ma et al. 2003).

Finally, some studies pointed out that increasing number of eating episodes reduces weight gain (Drummond et al. 1998; Ma et al. 2003), since small but multiple intakes may reduce feelings of hunger and serum insulin concentrations (Speechly and Buffenstein 1999). Additionally, according to Le-Blanc et al. (1993), multiple eating episodes also increase thermogenesis and fat utilization. However, conversely to those studies but in agreement with others (Kant et al. 1995), our study did not find a protective or a risk effect for obesity when eating more than 3 times a day. A higher eating frequency might protect against obesity if the calories consumed do not increase; however, as it was said by Bertéus-Forslund et al. (2002), it might be difficult to increase the number of meals without increasing energy intake. Besides, supporting these results, Belko et al. (1987) did not find changes in the thermic effect of food due to meal frequency. On the other hand, the effect size was increased when eating less than three times per day. In relation to this, many studies also indicated that individuals who do not eat breakfast have a greater overall daily energy intake compared to individuals that eat breakfast (Wyatt et al. 2002). Suggesting that, individuals who skip a meal might probably overeat at subsequent meals, which may also explain our results.

5.5. SMOKING AND ALCOHOL CONSUMPTION

Several studies have investigated the relation between cigarette smoking and body weight, but its association is controversial as smoking has been associated with low as well as with high BMI (Saarni et al. 2009). In this work, ex-smokers presented higher effect sizes for abdominal obesity and central fat distribution. These results were in agreement with the idea that smoking cessation is commonly followed by an increase in weight (Flegal et al. 1995; Chiolero et al. 2008). The mechanisms that lead to weight gain in former smokers are not completely understood. Smoke quitting is frequently related to changes in palatability perceptions (Wack and Rodin 1982), which could be responsible of the increase in energy intake. However, according to Stamford et al. (1986), former smokers could increase their energy intake just by replacing cigarettes with food as a means of oral gratification. Other works explained the body weight increase in former smokers by a shift in metabolism due to the loss of nicotine's effect that would result in a tendency to increase caloric storage and add weight (Wack and Rodin 1982). On the other hand, numerous studies indicated that obesity was lower in smokers (Albanes et al. 1987; Molarius et al. 1997). In this case nicotine from tobacco would stimulate the autonomic nervous system, increasing catecholamines secretion, which would lead to lower insulin secretion (Wack and Rodin 1982), and thus, glucose levels would remain high over a longer period of time. These metabolic changes would result in the storage of fewer calories or in them being stored via less energy conserving pathways (Wack and Rodin 1982). However our results did not support this idea. Indeed smoking (now or before) did not suppose higher odds for overall obesity (defined by BMI) or excess adiposity (defined by FM %), but instead the associations found between obesity and smoking variable were more related with abdominal obesity and central fat distribution, which was in agreement with the work of (Bamia et al. 2004). This agrees with some metabolic changes observed in smokers. Cigarettes smoking stimulate sympathetic nervous system activity, which could be responsible of the increase in cortisol concentrations; this could explain our results, as visceral adipose tissue is influenced by cortisol concentrations (Chiolero et al. 2008). On the other hand, in agreement with other works (Bamia et al. 2004; Chiolero et al. 2008), this thesis confirmed a positive association between the amount of smoked cigarettes and obesity, among smokers. These results were unexpected due the above mentioned metabolic effect of smoking; however, smoking is associated with other unhealthy behaviours (Castro et al. 1989; Tobias et al. 2007), which could explain the obtained results.

The energy required by our body comes mainly from macronutrients; 1 gram of carbohydrates or proteins provides 4 kcal, whereas 1 gram of lipids provides 9 kcal. But, apart from that, the recreational intake of alcohol is very common around the world (Traversy and Chaput 2015); according to Jequier (1999), among adult consumers of ethanol the average intake of alcohol is ≈ 10% of the total daily energy intake in several developed countries. Alcohol has relatively high caloric content (1 gram of alcohol provides 7.1 kcal) (Traversy and Chaput 2015), which has been shown to be efficiently used by body (Suter, Schutz, and Jequier 1992; Jequier 1999). Thus, it could be thought that alcohol supposes an extra energy source to the diet that is not necessary to our body maintenance. Due to this, alcohol intake has been proposed as a possible factor in obesity development.

However, our results did not show a positive association between alcohol and obesity. Even more, alcohol consummation showed a protective effect against excessive adiposity. This effect has been shown in many studies and it has been called the "alcohol paradox" (Yeomans 2010). Several experimental studies have been conducted to examine the effect of alcohol intake on appetite control. However it seems that alcohol have no effect reducing appetite. Indeed it may amplify appetite perception in response to food stimuli (Yeomans 2010). A possible explanation for the "alcohol paradox" could be the high thermogenic effect of alcohol, which could be responsible of an increase in energy expenditure (Traversy and Chaput 2015). In a study carried out by Raben et al. (2003) it was found that diet-induced thermogenesis was a 27% higher after an alcohol-rich meal than after carbohydrate-rich and fat-rich meals. However, this paradox could also be the product of many factors beyond the individual habits of ingestion and metabolism. Considering the frequency of alcohol consumption, the negative association between alcohol and excessive adiposity (defined by FM%) as well as overall obesity (defined by BMI), was only significant when individuals drank occasionally, indicating that the protective effect that alcohol seemed to have against obesity was just for a moderate consumption of alcohol. Indeed there are some works showing that the positive association between alcohol consumption and obesity or waist circumference is a dose-dependent association, so that heavy alcohol consumption may be more of a risk factor than light-to-moderate alcohol consumption (Vadstrup et al. 2003). However, this work did not provide alcohol quantity data, so more studies are needed to assess a possible positive association between alcohol amount and obesity.

6. CONCLUSION

Findings on the present study confirm the association between several environmental factors and obesity, not just with overall obesity, defined by BMI, but also with more specific obesity phenotypes such as abdominal obesity (defined by WC), central fat distribution (defined by WHR) or excessive adiposity (defined by FM%). However, in many cases, the effect sizes of the obtained associations with the environmental variables are different for each obesity phenotype, suggesting that all of them are interesting elements for obesity assessment.

Although a family history of obesity is a clear risk factor for obesity development in adults, fat distribution is not associated with it. However, central fat distribution, which is positively associated with obesity related diseases, is also highly influenced by (in)activity and smoking. Physical activity shows a protective effect against central fat distribution, but just when it is a sport other than walking and when it is practiced during a relatively long period of time. Besides, the detrimental effect of a sedentary lifestyle over fat distribution can also be confirmed. On the other hand, the merely act of smoking (now or some time ago), but not the amount of cigarettes, supposes a risk factor for a central fat distribution. These variables are of great importance in health due to their influence over central fat distribution, which is of great importance in the development of obesity comorbidities. The positively association found for the bad perceived physical condition with central fat distribution is lower than the one found with excessive adiposity or even with overall and abdominal obesity. However, central fat distribution has a higher influence in the development of cardiovascular and metabolic diseases.

The results found for overall and abdominal obesity are very similar, possibly due to a higher correlation between each other than with the other obesity phenotypes. Meanwhile excessive adiposity, although similar, has its own characteristics. Due to the stronger association of these three obesity variables with a poor perception of the physical condition than with the obesity related diseases (excessive adiposity is not associated with them), it could be said that the amount of adipose tissue rather than its distribution affects the perception of the own health. The health problems associated to overall obesity could be also reflected in a bad sleep quality. Concerning eating patterns, both main meal duration and the number of eating episodes are associated with overall and abdominal obesity but not with excessive fat mass, indicating that their contribution is probably not just in adipose tissue, but also in other body components involved in BMI and WC. Physical activity is a protective factor and a sedentary lifestyle is a risk factor for overall and abdominal obesity as well as for an excessive adiposity. A lighter physical activity, such as walking or less time practicing a sport, can also help against overall and abdominal obesity development. Finally, although the act of smoking does not have relation with these three obesity variables (except abdominal obesity and ex-smokers), the influence of the amount of cigarettes among smokers with obesity is clear. However, due to the metabolic effect of nicotine, this association is probably pointing to some behavioral attitudes related with the amount of cigarettes smoked that influence obesity risk and the amount of fat but not fat distribution.

On the other hand, alcohol consumption seems to have a protective effect against obesity but not against central fat distribution, and just when it is consumed occasionally.

Chapter VII

Replication Study of the Association of 21 SNPs with Obesity

1. SUMMARY

OBJECTIVES: Obesity is a globally prevalent heritable condition. Candidate gene studies and especially Genome-Wide Association Studies (GWAS) have identified novel BMI/obesity associated *loci*. However genetic factors predisposing to obesity are yet poorly understood. The purpose of this study is to investigate the association between 24 single nucleotide polymorphisms (SNPs), previously reported in GWAS or candidate genes studies, and obesity in a population from the Basque Country (Spain). Additionally, the association of these SNPs and different somatotype components describing body morphology and composition was also analysed.

METHODS: 24 SNPs were genotyped in 476 adults living in the Basque Country. Multiple logistic regression and multiple linear regression were used to assess the association between SNPs and obesity phenotypes, obesity related traits and body morphology variables. PLINK program was used for this purpose.

RESULTS: 12 SNPs in or near *NEGR1*, *TMEM18*, *GNPDA2*, *BDNF*, *UCP2*, *NRXN3*, *MAP2K5*, *FTO* and *KCTD15* were associated with obesity, obesity related traits and/or body morphology in the Basque country population. The most significantly associated SNPs with obesity were rs925946 (*BDNF*; p=0.001 with extreme obesity and p=0.008 with overall obesity), rs9939609 (*FTO*; p=0.007 with morbid/extreme obesity) and rs7561317 (*TMEM18*; p=0.008 with morbid/extreme obesity); rs10146997 (*NRXN3*; p=0.003) with BMI and rs925946 (*BDNF*; p=0.001) with endomorphy.

CONCLUSIONS: In conclusion, the results of this study replicate previously reported associations of 12 genetic variants and obesity and/or obesity related traits in a Basque Country population and shed some light on the possible implication of these SNPs in the different components of body morphology.

2. BRIEF INTRODUCTION

Obesity is a complex trait affected not only by behavioural and environmental factors, but also by genetic factors. Nowadays, obesity is a globally prevalent condition and it is a major cause of morbidity and mortality. However, according to the thrifty genotype hypothesis proposed by Neel (1962), during human evolution there were times when food was restricted (i.e. times characterized by feast or famine) and physical activity was predominant among population. In those times, individuals with a "thrifty genotype" could have had a higher success on the transmission of their particular genotype to future generations, due to a survival advantage provided by a more efficient use of calories. This previously successful genotype could be nowadays predisposing individuals to obesity and some cardiometabolic diseases when exposed to the prevalent obesogenic environment.

Nowadays, a substantial genetic contribution to obesity risk has been demonstrated by different heritability studies based on families or twins, with heritabilities (h^2) that ranged from 40% to 70% (Elks et al. 2012; Feng 2016). Genetic contribution to obesity risk may explain why, within a particular population, where all the individuals are exposed to the same particular environment, there are individuals who are most likely to develop obesity than the rest of the population. However, the specific underlying genetic factors predisposing to obesity are poorly understood and remain largely elusive.

Many studies with different methodologies have been performed to discover genetic factors that could predispose to obesity. Thanks to those studies and especially to GWASs several variants have been associated with obesity related traits. The first obesity associated gene identified through GWAS was the "fat mass and obesity associated gene" (*FTO*) (Dina et al. 2007; Frayling et al. 2007; Scuteri et al. 2007). Since then several studies have demonstrated that variants in *FTO* have the strongest associations with polygenic obesity, especially in European derived populations (e.g. Peeters et al. 2008). Other recent analyses identified additional genes harbouring common SNPs that associate with obesity or obesity related traits. Loos et al (2008) established common variants near *MC4R* influencing fat mass, weight and obesity. Willer et al. (2009) identified six additional *loci* as genome-wide significantly associated with BMI: *TMEM18*, *KCTD15*, *GNPDA2*, *SH2B1*, *MTCH2* and *NEGR1*. Thorleifsson et al. (2009) reported two additional new *loci* *ETV5* and *BDNF*. Speliotes et al. (2010) identified 18 new *loci* associated with BMI. By 2013, GWAS in populations of European ancestry have identified at least 54 obesity-susceptibility *loci* (Lu and Loos 2013). And later, Locke et al. (2015) identify 97 *loci* associated with BMI.

Although, until recently, the majority of the studies have been conducted in European ancestry populations (Xia and Grant 2013), studies in Africans (Adeyemo et al. 2010) and in East Asians (Okada et al. 2012; Wen et al. 2012; Wang et al. 2016) have begun to appear in recent years. Several SNPs previously discovered in European populations have also been replicated in these non-European populations, in addition to the discovery of some novel SNPs that were previously undetected. Due to the differences found in the SNPs associations with obesity traits between studies with different sampled populations, it is important to further investigate and compare those associations across populations, even within European territory, as it can shed light on the physiology of obesity susceptibility.

The aim of this study was to replicate some previously reported genetic associations, from GWAS or candidate gene studies, with obesity and obesity related traits in a case control sample from the Basque Country (Spain). On the other hand, few studies have focused on determining the differential effects of these SNPs on body morphology and composition. Thus, the associations of these SNPs with the three somatotype components were also assessed in this work.

3. BRIEF METHODOLOGY

In order to perform the present analyses, 24 SNPs from GWAS and candidate gene studies were selected in or near thirteen different genes: *NEGR1*, *TMEM18*, *GNPDA2*, *BDNF*, *FAIM2*, *NRXN3*, *MAP2K5*, *SH2B1*, *FTO*, *MC4R*, *KCTD15*, *LEPR* and *UCP2*. All the 24 SNPs were genotyped by TaqMan technology (Applied Biosystems, Calif., USA). At quality control, two SNPs were excluded, as more than 10% of individuals were not properly genotyped for them (i.e. genotype call rate <90%; rs1042719 and rs8049235). Another SNP was excluded as it was not in Hardy-Weinberg equilibrium (rs10150332). On the other hand, 33 individuals were also excluded as more than 10% of the proposed SNPs were not properly genotyped for them (i.e. sample call rate <90%). After quality control, 21 SNPs and 476 individuals remained to conduct association analyses.

Associations between selected SNPs and obesity phenotypes (defined by three different indices: BMI, WC and WHR), were tested through multiple logistic regression analyses, while the associations of the selected SNPs with the continuous obesity related traits (BMI, weight and SF6) and the somatotype components (endomorphy, mesomorphy and ectomorphy) were tested, by multiple linear regression analyses. Obesity definitions used in this study were obtained by the dichotomization of the different obesity related indices: BMI was used to define overall obesity (obesity: BMI≥30 kg/m^2; no obesity: BMI<30 kg/m^2), WC was used to define abdominal obesity (abdominal obesity: WC>102 for men and WC>88 for women; no abdominal obesity: WC≤102 for men and WC≤88 for women) and WHR was used to define central fat distribution (central fat distribution: WHR≥0.90 for men and WHR≥0.85 for women; peripheral fat distribution: WHR<0.90 for men and WHR<0.85 for women). Additionally, BMI was also used to define extreme obesity, where only upper and down extreme phenotypes were considered from both tails of the BMI distribution (extreme obesity: BMI≥40 kg/m^2; no extreme obesity: BMI<25 kg/m^2). This approach allows improving the power of the analysis, but it should not be forgotten that the obtained results are just for the upper extreme phenotypes (Price, Li, and Zhao 2008). The analyses were performed under the assumption of an additive model of inheritance in which the genotype was coded as 0, 1 or 2, depending on whether the subject was homozygous for the non-effect allele (genotype= 0), heterozygous (genotype= 1), or homozygous for the effect allele (genotype= 2). In all cases age, sex and socio-economic status were introduced as covariates in the regression models. The effect alleles (the allele that shows a positive effect in obesity associated traits) were established based on previous studies in order to facilitate further comparisons (e.g. Chambers et al. 2008; Sandholt et al. 2011; Lu and Loos 2013; Robiou-du-Pont et al. 2013). These association tests were performed using PLINK software. Bonferroni correction for multiple comparisons was also calculated. Taking into account the 21 considered SNPs and the 10 analysed variables, the new critic value for "p" would be α=0.05/210= 0.0002 . However, as this correction is too conservative, discussion were made based on α= 0.05.

4. RESULTS

4.1. GENOTYPIC CHARACTERISTICS

A total of 21 SNPs were included in the association analyses. Minor allele frequencies (expressed in percentages) in cases and controls as well as in the whole sample, and Hardy-Weinberg analyses results can be seen in Table 7.1. Minor alleles in the studied population and in a European ancestry population from 1000 Genomes (CEU), were concordant. Minor allele frequencies in the studied population were similar to those in CEU population. Biggest differences were found in rs1137101 (controls 40% vs. CEU 48%), rs925946 (controls 24% vs. CEU 34%) and rs12970134 (controls 23% vs. CEU 29%). In 12 SNPs, minor allele frequencies were higher in controls (non-obese individuals; BMI<30kg/m^2) than in cases (obese individuals; BMI≥30kg/m^2), whereas in 7 SNPs, the highest frequencies were in cases. The highest differences between minor allele frequencies in controls and in cases were in rs925946 (*BDNF*) and rs9939609 (*FTO*).

Table 7.1. Genotypic characteristics of cases and controls for each of the analysed SNPs.

GEN	CHR	SNP	Alleles	MA	EA	MAF	MAF (%) controls	MAF (%) cases	MAF (%) (CEU)	HWE
LEPR	1	rs1137101	G/A	G	A	39	40	38	48	0.40
NEGR1	1	rs3101336	C/T	T	C	35	35	35	36	0.23
	1	rs2568958	A/G	G	A	35	36	35	36	0.13
	1	rs2815752	A/G	G	A	35	35	34	36	0.20
TMEM18	2	rs6548238	C/T	T	C	18	20	15	17	0.53
	2	rs7561317	G/A	A	G	18	20	15	16	0.44
GNPDA2	4	rs10938397	A/G	G	G	44	42	48	42	0.45
BDNF	11	rs4923461	A/G	G	A	23	24	21	24	0.87
	11	rs925946	G/T	T	T	27	24	32	34	0.95
UCP2	11	rs660339	G/A	A	G	38	40	36	40	0.93
	11	rs659366	C/T	T	C	35	37	33	36	0.71
FAIM2	12	rs7138803	G/A	A	A	37	36	38	32	0.36
NRXN3	14	rs10146997	A/G	G	G	20	22	18	25	0.06
MAP2K5	15	rs4776970	T/A	T	A	37	37	38	36	0.72
	15	rs2241423	G/A	A	G	25	24	26	20	0.18
SH2B1	16	rs7498665	A/G	G	G	33	34	32	36	0.23
FTO	16	rs9939609	T/A	A	A	43	39	48	44	0.23
MC4R	18	rs17782313	T/C	C	C	22	22	22	26	0.57
	18	rs12970134	G/A	A	A	23	23	24	29	0.32
KCTD15	19	rs29941	G/A	A	G	25	27	22	31	0.74
	19	rs11084753	G/A	A	G	28	28	27	30	0.85

CHR: chromosome; MA: minor allele; EA: effect allele; MAF: minor allele frequency; CEU: European ancestry population of 1000 Genomes; HWE: Hardy-Weinberg equilibrium.
Hardy-Weinberg analyses were performed only in control population.
Cases and controls are defined by the WHO criteria for BMI.

4.2. REPLICATION OF PREVIOUSLY OBESITY ASSOCIATED SNPs

BMI differences between homozygotes for the effect allele and homozygotes for the non-effect allele at each SNP are shown in Figure 7.1. The homozygosis for the effect allele led to an increase of BMI in 18 of the 21 studied SNPs, 7 of which presented a difference on BMI greater than 2 kg/m^2; among them, rs925946 (*BDNF*) was the SNP with the greater difference between effect allele and non-effect allele homozygotes (4.60 kg/m^2). On the other hand, there were 3 SNPs that presented a reduction in BMI for the effect allele homozygotes, but just one of them had a difference greater than 2 kg/m^2, rs2241423 (*MAP2K5*).

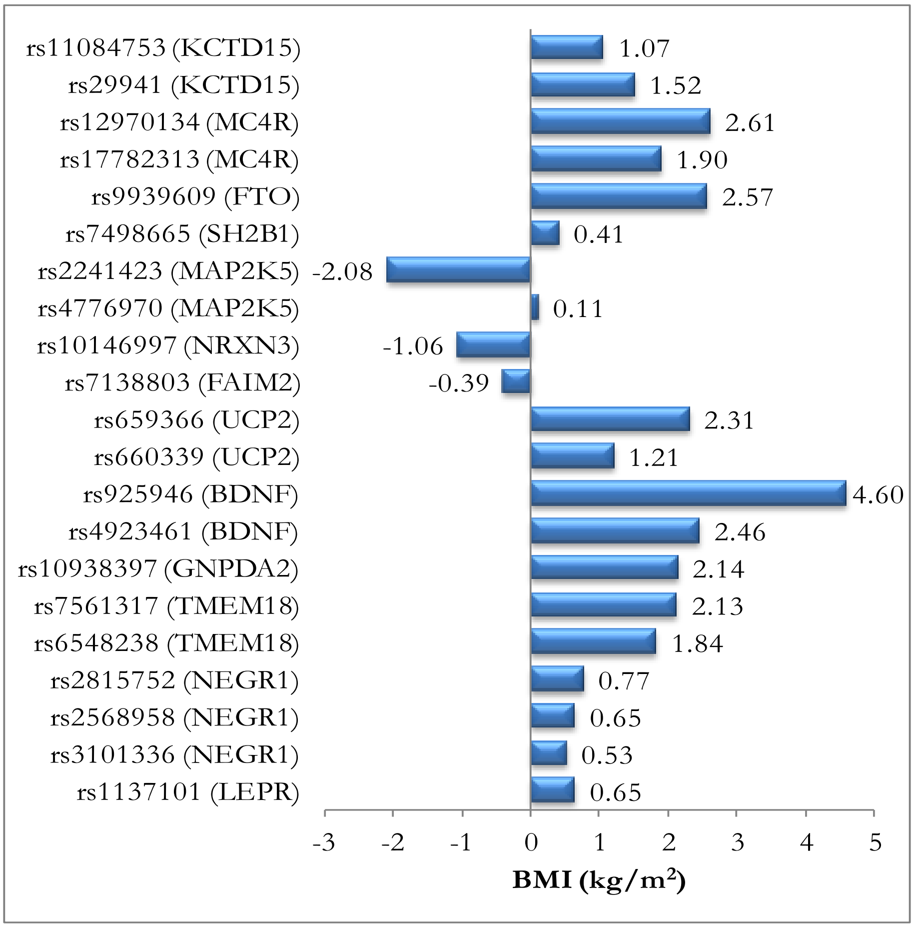


Figure 7.1. Differences in BMI (kg/m^2) between effect and non-effect allele homozygotes at selected SNPs.

4.2.1. SNPs associated with obesity

Of the 21 SNPs studied for association with obesity, there were four that showed significant association with at least one of the three obesity definitions utilized in this study (overall obesity, abdominal obesity and central fat distribution): rs10938397 (*GNPDA2*), rs925946 (*BDNF*), rs10146997 (*NRXN3*) and rs11084753 (*KCTD15*) (Table 7.2).

When BMI was used as the criteria to define overall obesity, the "T" allele of rs925946 (*BDNF*) was positively associated (OR=1.60; p=0.008) with obesity, whereas the

"G" allele of rs10146997 (*NRXN3*) provided a protective effect against obesity, with an OR of 0.62 (p=0.022). The same two SNPs were also associated with abdominal obesity (based on the cut-off points stabilised for WC), with the same association directions and similar effect sizes (rs925946: OR=1.56, p=0.016; rs10146997: OR=0.62, p=0.026). When WHR was used to define obesity, results, showed 3 SNPs with significant association with central fat distribution: rs10938397 (*GNPDA2*), 925946 (*BDNF*) and rs11084753 (*KCTD15*). All of them were associated with an increased probability of central fat distribution; being their ORs 1.61 (p=0.032), 1.65 (p=0.020) and 1.57 (p=0.036), respectively. Additionally, genetic variants at *TMEM18* showed results close to statistical significance for its association with overall obesity.

Table 7.2. Results of the association analyses between the selected SNPs and three different obesity definitions

			Overall obesity		Abdominal obesity		Central fat distribution	
GEN	**SNP**	**EA**	**OR (CI 95%)**	**p**	**OR (CI 95%)**	**p**	**OR (CI 95%)**	**p**
LEPR	rs1137101	A	1.29 (0.84/1.98)	0.242	0.96 (0.63/1.47)	0.857	1.07 (0.67/1.68)	0.788
NEGR1	rs3101336	C	1.14 (0.82/1.58)	0.431	1.03 (0.74/1.45)	0.858	0.98 (0.67/1.43)	0.908
	rs2568958	A	1.20 (0.86/1.67)	0.276	1.10 (0.78/1.54)	0.588	0.93 (0.64/1.36)	0.711
	rs2815752	A	1.18 (0.85/1.64)	0.329	1.07 (0.76/1.51)	0.684	0.97 (0.66/1.42)	0.865
TMEM18	rs6548238	C	1.49 (0.98/2.25)	0.061	1.38 (0.90/2.11)	0.139	0.83 (0.51/1.35)	0.446
	rs7561317	G	1.50 (0.99/2.26)	0.056	1.41 (0.92/2.15)	0.113	0.86 (0.53/1.40)	0.552
GNPDA2	rs10938397	G	1.24 (0.86/1.77)	0.255	1.33 (0.91/1.93)	0.139	1.61 (1.04/2.48)	**0.032**
BDNF	rs4923461	A	1.16 (0.81/1.68)	0.416	1.36 (0.93/1.99)	0.116	1.24 (0.80/1.91)	0.337
	rs925946	T	1.60 (1.13/2.25)	**0.008**	1.56 (1.09/2.24)	**0.016**	1.65 (1.08/2.51)	**0.020**
UCP2	rs660339	G	1.31 (0.95/1.80)	0.097	1.22 (0.87/1.70)	0.247	1.32 (0.91/1.92)	0.142
	rs659366	C	1.18 (0.85/1.64)	0.316	1.17 (0.83/1.65)	0.372	1.17 (0.80/1.71)	0.433
FAIM2	rs7138803	A	0.98 (0.70/1.37)	0.903	0.88 (0.62/1.26)	0.489	1.38 (0.92/2.08)	0.122
NRXN3	rs10146997	G	0.62 (0.42/0.93)	**0.022**	0.62 (0.41/0.94)	**0.026**	0.67 (0.41/1.09)	0.104
MAP2K5	rs4776970	A	1.19 (0.78/1.82)	0.428	1.03 (0.67/1.57)	0.911	1.11 (0.71/1.76)	0.643
	rs2241423	G	0.94 (0.66/1.33)	0.709	1.05 (0.73/1.51)	0.791	1.38 (0.88/2.15)	0.157
SH2B1	rs7498665	G	0.83 (0.59/1.16)	0.272	0.90 (0.63/1.27)	0.543	1.06 (0.70/1.59)	0.795
FTO	rs9939609	A	1.26 (0.94/1.70)	0.126	1.14 (0.84/1.55)	0.406	0.80 (0.56/1.15)	0.225
*MC4*R	rs17782313	C	1.10 (0.75/1.61)	0.619	1.02 (0.69/1.51)	0.924	0.98 (0.62/1.55)	0.944
	rs12970134	A	1.11 (0.76/1.61)	0.588	1.10 (0.74/1.62)	0.639	0.95 (0.60/1.50)	0.810
KCTD15	rs29941	G	1.13 (0.79/1.62)	0.491	1.06 (0.73/1.53)	0.758	1.39 (0.91/2.13)	0.126
	rs11084753	G	0.97 (0.69/1.37)	0.865	1.10 (0.77/1.57)	0.616	1.57 (1.03/2.39)	**0.036**

Adjusted for age, gender, educational level and professional level (multivariable-adjusted). Overall obesity is defined by BMI; Abdominal obesity is defined by WC; Central fat distribution is defined by WHR. SNP: single nucleotide polymorphism; EA: Effect allele; OR: odds ratio; CI: confidence intervals. Significant results at $p<0.05$ are shown in **bold**. Bonferroni correction ($\alpha<0.0002$).

In order to improve the power to detect association with obesity, multiple logistic regressions were also performed with cases and controls from both extremes of BMI. Table 7.3 shows the results of these analyses. There were eight SNPs positively associated with extreme obesity. Among them, there were three SNPs in or near *TMEM18* and *BDNF* with ORs>2: rs6548238 (OR: 2.46, p=0.012), rs7561317 (OR: 2.58, p=0.008), and rs925946 (OR: 2.56, p=0.001). The SNP in the *FTO* region also had a relatively high effect (OR: 1.94 p=0.007), followed by two SNPs in *NEGR1*: rs2568958 (OR: 1.85, p=0.030) and rs2815752 (OR: 1.81, p=0.036). Finally, rs660339 and rs659366 in the *UCP2* region had ORs of 1.79 (p=0.034) and 1.74 (p=0.044), respectively. Additionally, there were two other SNPs in or near *LEPR* and *NEGR1* that were closed to statistical significance.

Table 7.3. Results of the association analyses between the selected SNPs and extreme obesity.

			Extreme obesity	
GEN	**SNP**	**EA**	**OR (CI 95%)**	**p**
LEPR	rs1137101	A	2.94 (0.99/8.68)	0.052
NEGR1	rs3101336	C	1.72 (1.00/2.96)	0.052
	rs2568958	A	1.85 (1.06/3.22)	**0.030**
	rs2815752	A	1.81 (1.04/3.13)	**0.036**
TMEM18	rs6548238	C	2.46 (1.22/4.97)	**0.012**
	rs7561317	G	2.58 (1.28/5.20)	**0.008**
GNPDA2	rs10938397	G	1.36 (0.80/2.31)	0.262
BDNF	rs4923461	A	1.24 (0.70/2.21)	0.462
	rs925946	T	2.56 (1.47/4.47)	**0.001**
UCP2	rs660339	G	1.79 (1.05/3.05)	**0.034**
	rs659366	C	1.74 (1.02/3.00)	**0.044**
FAIM2	rs7138803	A	1.06 (0.62/1.81)	0.841
NRXN3	rs10146997	G	0.68 (0.36/1.28)	0.233
MAP2K5	rs4776970	A	0.78 (0.32/1.92)	0.593
	rs2241423	G	0.76 (0.44/1.32)	0.331
SH2B1	rs7498665	G	0.97 (0.57/1.67)	0.923
FTO	rs9939609	A	1.94 (1.20/3.13)	**0.007**
MC4R	rs17782313	C	1.08 (0.60/1.97)	0.793
	rs12970134	A	1.28 (0.70/2.33)	0.416
KCTD15	rs29941	G	1.29 (0.75/2.21)	0.365
	rs11084753	G	1.11 (0.67/1.85)	0.682

Adjusted for age, gender, educational level and professional level (multivariable-adjusted). Extreme obesity is defined by BMI. SNP: single nucleotide polymorphism; EA: Effect allele; OR: odds ratio; CI: confidence intervals. Significant results at $p<0.05$ are shown in **bold**. Bonferroni correction ($\alpha <$ 0.0002)

4.2.2. SNPs associated with obesity related traits

Table 7.4 shows the associations between the studied SNPs and three anthropometric traits (SF6, weight and BMI). Two of these SNPs presented significant association with at least one of these continuous anthropometric variables. rs10146997 (*NRXN3*) was negatively associated with SF6 (p=0.014), weight (p=0.021) and BMI (p=0.003). Whereas, rs925946 (*BDNF*) was positively associated with SF6 (p=0.009). This SNP, along with two other SNPs in the *UCP2* region, approached statistical significance in their association with BMI.

Table 7.4. Results of the association analyses between the effect allele of the selected SNPs and obesity related anthropometric traits.

			SF6 (mm)		Weight (kg)		BMI (kg/m²)	
GEN	**SNP**	**EA**	**β (CI 95%)**	**p**	**β (CI 95%)**	**p**	**β (CI 95%)**	**p**
LEPR	rs1137101	A	-3.96 (-11.85/3.93)	0.326	1.75 (-1.02/4.52)	0.216	0.63 (-0.34/1.60)	0.207
NEGR1	rs3101336	C	-0.65 (-8.76/7.46)	0.875	1.10 (-2.02/4.21)	0.491	0.47 (-0.65/1.59)	0.409
	rs2568958	A	-0.25 (-8.42/7.93)	0.952	1.17 (-1.96/4.30)	0.465	0.51 (-0.62/1.64)	0.377
	rs2815752	A	-0.77 (-8.88/7.34)	0.853	1.24 (-1.87/4.35)	0.434	0.50 (-0.62/1.62)	0.381
TMEM18	rs6548238	C	5.09 (-5.00/15.19)	0.324	3.04 (-0.88/6.96)	0.129	0.74 (-0.67/2.15)	0.307
	rs7561317	G	5.18 (-4.89/15.26)	0.314	3.15 (-0.76/7.06)	0.115	0.72 (-0.68/2.13)	0.315
GNPDA2	rs10938397	G	2.10 (-7.25/11.45)	0.660	-0.67 (-4.18/2.84)	0.709	0.04 (-1.22/1.30)	0.949
BDNF	rs4923461	A	-1.11 (-10.03/7.80)	0.807	1.56 (-1.87/4.99)	0.373	0.40 (-0.84/1.63)	0.529
	rs925946	T	11.86 (3.06/20.66)	**0.009**	3.06 (-0.31/6.44)	0.076	1.20 (-0.02/2.42)	0.055
UCP2	rs660339	G	5.99 (-1.93/13.91)	0.139	2.76 (-0.27/5.78)	0.075	1.08 (-0.01/2.17)	0.053
	rs659366	C	7.63 (-0.54/15.79)	0.068	2.73 (-0.38/5.84)	0.086	1.08 (-0.04/2.20)	0.059
FAIM2	rs7138803	A	-1.44 (-9.63/6.75)	0.731	-0.49 (-3.71/2.73)	0.765	-0.60 (-1.75/0.56)	0.313
NRXN3	rs10146997	G	-12.58 (-22.56/-2.60)	**0.014**	-4.57 (-8.45/-0.69)	**0.021**	-2.10 (-3.50/-0.71)	**0.003**
MAP2K5	rs4776970	A	3.88 (-3.72/11.48)	0.318	1.08 (-1.65/3.80)	0.439	0.44 (-0.51/1.40)	0.366
	rs2241423	G	2.44 (-6.55/11.43)	0.595	-0.33 (-3.84/3.18)	0.854	0.08 (-1.19/1.34)	0.907
SH2B1	rs7498665	G	-5.67 (-13.99/2.65)	0.183	-2.15 (-5.39/1.09)	0.193	-0.90 (-2.06/0.26)	0.130
FTO	rs9939609	A	4.85 (-2.66/12.37)	0.206	1.41 (-1.49/4.32)	0.341	0.91 (-0.14/1.95)	0.090
MC4R	rs17782313	C	-2.43 (-12.04/7.18)	0.620	-1.21 (-4.88/2.46)	0.520	-0.45 (-1.78/0.87)	0.502
	rs12970134	A	-3.03 (-12.64/6.58)	0.538	-0.53 (-4.16/3.11)	0.777	-0.36 (-1.67/0.95)	0.592
KCTD15	rs29941	G	-4.66 (-13.43/4.11)	0.298	0.49 (-2.89/3.88)	0.776	0.23 (-0.98/1.45)	0.707
	rs11084753	G	-3.92 (-12.54/4.70)	0.374	0.48 (-2.86/3.81)	0.779	0.21 (-0.99/1.41)	0.730

Adjusted for age, gender, educational level and professional level (multivariable-adjusted). SNP: single nucleotide polymorphism; EA: Effect allele; OR: odds ratio; CI: confidence intervals. Significant results at p<0.05 are shown in **bold**. Bonferroni correction (α< 0.0002).

4.2.3. SNPs associated with somatotype components

Four SNPs were associated with at least one somatotype component (Table 7.5). Among them, two SNPs were associated with endomorphy; rs925946 (*BDNF*), was associated with increased endomorphy values (β=0.54; p=0.001), while the risk allele of rs10146997 (*NRXN3*) was associated with lower endomorphy values (β: -0.54; p: 0.004). On the other hand, the effect allele of rs9939609 (*FTO*) showed a positive association with mesomorphy (β=0.45; p=0.003), while rs10146997 (*NRXN*) also showed a negative association with mesomorphy (β= -0.60; p=0.003). Finally, only one SNP (*NRXN3*: rs10146997) was positively associated with ectomorphy (β=0.26; p=0.006), whereas two SNPs (*BDNF*: rs925946 and *MAP2K5*: rs4776970) were negatively associated with this somatotype component (β=-0.19; p=0.025 and β=-0.19; p=0.028, respectively).

Table 7.5. Results of the association analyses between the selected SNPs and the three somatotype components.

			Endomorphy		Mesomorphy		Ectomorphy	
GEN	**SNP**	**EA**	**β (CI 95%)**	**p**	**β (CI 95%)**	**p**	**β (CI 95%)**	**p**
LEPR	rs1137101	A	-0.11 (-0.42/0.19)	0.471	0.13 (-0.15/0.42)	0.367	-0.04 (-0.22/0.13)	0.635
	rs3101336	C	0.09 (-0.21/0.38)	0.573	-0.04 (-0.36/0.28)	0.801	-0.06 (-0.21/0.09)	0.436
NEGR1	rs2568958	A	0.11 (-0.18/0.41)	0.452	-0.06 (-0.38/0.27)	0.727	-0.06 (-0.21/0.09)	0.454
	rs2815752	A	0.09 (-0.20/0.39)	0.542	-0.03 (-0.35/0.29)	0.845	-0.06 (-0.21/0.09)	0.419
TMEM18	rs6548238	C	0.18 (-0.19/0.55)	0.336	0.28 (-0.12/0.69)	0.167	-0.01 (-0.20/0.18)	0.943
	rs7561317	G	0.18 (-0.19/0.55)	0.344	0.26 (-0.14/0.66)	0.202	-0.02 (-0.21/0.17)	0.838
GNPDA2	rs10938397	G	0.08 (-0.25/0.40)	0.646	0.06 (-0.29/0.42)	0.732	0.09 (-0.09/0.26)	0.332
BDNF	rs4923461	A	-0.01 (-0.33/0.32)	0.975	0.10 (-0.26/0.45)	0.600	0.03 (-0.13/0.20)	0.689
	rs925946	T	0.54 (0.22/0.86)	**0.001**	0.32 (-0.04/0.67)	0.082	-0.19 (-0.35/-0.02)	**0.025**
UCP2	rs660339	G	0.26 (-0.03/0.55)	0.077	0.25 (-0.07/0.56)	0.124	-0.14 (-0.28/0.01)	0.073
	rs659366	C	0.28 (-0.01/0.58)	0.062	0.26 (-0.06/0.58)	0.112	-0.12 (-0.27/0.03)	0.130
FAIM2	rs7138803	A	-0.05 (-0.35/0.25)	0.723	-0.27 (-0.59/0.06)	0.115	0.03 (-0.12/0.18)	0.696
NRXN3	rs10146997	G	-0.54 (-0.91/-0.18)	**0.004**	-0.60 (-1.00/-0.20)	**0.003**	0.26 (0.08/0.45)	**0.006**
MAP2K5	rs4776970	A	0.17 (-0.13/0.46)	0.275	0.12 (-0.16/0.40)	0.398	-0.19 (-0.36/-0.02)	**0.028**
	rs2241423	G	0.10 (-0.23/0.43)	0.544	-0.01 (-0.37/0.35)	0.971	-0.03 (-0.20/0.14)	0.692
SH2B1	rs7498665	G	-0.15 (-0.46/0.15)	0.332	-0.23 (-0.56/0.10)	0.179	0.08 (-0.08/0.23)	0.346
FTO	rs9939609	A	0.16 (-0.12/0.43)	0.267	0.45 (0.16/0.75)	**0.003**	-0.12 (-0.26/0.02)	0.102
MC4R	rs17782313	C	-0.05 (-0.40/0.30)	0.780	-0.19 (-0.57/0.20)	0.338	-0.09 (-0.26/0.09)	0.325
	rs12970134	A	-0.04 (-0.38/0.31)	0.843	-0.22 (-0.60/0.17)	0.269	-0.08 (-0.26/0.09)	0.367
KCTD15	rs29941	G	-0.09 (-0.41/0.23)	0.591	0.14 (-0.21/0.49)	0.427	0.06 (-0.10/0.23)	0.448
	rs11084753	G	-0.11 (-0.42/0.21)	0.504	0.16 (-0.18/0.50)	0.361	0.05 (-0.11/0.21)	0.553

Adjusted for age, gender, educational level and professional level (multivariable-adjusted). SNP: single nucleotide polymorphism; EA: Effect allele; OR: odds ratio; CI: confidence intervals. Significant results at p<0.05 are shown in **bold**. Bonferroni correction (α< 0.0002).

5. DISCUSSION

All the studied SNPs were previously identified as genetic variants associated to obesity, but not all of them were replicated in other works. Additionally, most of the association analyses performed to date between genetic variants and obesity have used BMI to define it. However, BMI cannot distinguish between FM and FFM, and therefore the use of other obesity and body composition related variables, could be of great interest in the study of genetic variants associated to obesity. The present study conducted on a Basque Country population attempts to confirm the association between 21 of the previously identified SNPs and obesity, defined by three different criteria (BMI, WC and WHR). In the same way, the study also aimed to elucidate the association of these genetic variants with obesity-related traits and with body morphology and composition assessed through somatotype components. Four of the 21 analyzed SNPs located in or near *GNPDA2*, *BDNF*, *NRXN3* and *KCTD15* genes showed association with obesity. Whereas, eight SNPs located in or near *NEGR1*, *TMEM18*, *BDNF*, *UCP2* and *FTO* genes could be confirmed as positively associated with extreme obesity. Additionally, two SNPs (in or near *BDNF* and *NRXN3* genes) were associated with SF6 and only one (*NRXN3*) with weight and BMI. Finally four SNPs were associated with body morphology: two (in *BDNF* and *NRXN3* regions) with endomorphy, two (in *NRXN3* and *FTO* regions) with mesomorphy and three (in *BDNF*, *NRXN3* and *MAP2K5* regions) with ectomorphy.

5.1. ASSOCIATION WITH OBESITY AND OBESITY RELATED TRAITS

In the current study, a significant contribution of the minor allele of rs925946 (*BDNF*) to obesity was found, regardless of the classification parameter used to assess obesity (i.e. BMI, WC or WHR). Furthermore, this SNP was also associated with the total amount of subcutaneous adiposity, estimated through SF6 and its association to BMI was close to significance (p=0.055). In 1995, the brain derived neurotrophic factor gene (*BDNF*) was proposed as a candidate gene for obesity, since rodent models with *BDNF* disruption manifest increased food intake and obesity (Pelleymounter, Cullen, and Wellman 1995). Later, Gray et al. (2006) also provided evidence of the consequences produced by the loss of one copy of this gene in humans, but it was not until 2009, when the association of this SNP with obesity was confirmed through a GWAS (Thorleifsson et al. 2009). *BDNF* encodes a protein of the nerve growth factor family that is necessary for survival of striatal neurons in the brain (Zuccato et al. 2001). Additionally, this protein also plays an important role in food intake and energy homeostasis (Motamedi, Karimi, and Jafari 2017). Several

SNPs located in or near *BDNF* have been associated with neurological and psychiatric disorders (Hall et al. 2003) and in her work Nakazato et al. (2003) suggested its role in eating behaviour and BMI. According to Thorleifsson et al. (2009), the two studied SNPs located near *BDNF* (rs4923461 and rs925946) represent independent signals of association with BMI and weight. However, in this study rs925946, but not rs4923461, showed a significant association with obesity. Moreover, rs925946 presented the highest effect size (OR) and the highest significance among all studied SNPs, which makes its association with obesity the strongest found in this population.

A genetic variant in *NRXN3* gene (rs10146997) showed not only a significant effect on the three analysed obesity related traits (i.e. SF6, weight and BMI) but also on overall obesity and abdominal obesity (defined by BMI and WC, respectively). The three parameters used to assess obesity were correlated, but the correlation was higher between BMI and WC (r=0.9) than between BMI and WHR (r=0.4) (analysis not shown). The lack of association of rs10146997 with WHR and its association with BMI and WC may indicate that this SNP is mostly associated with overall adiposity and not with fat distribution. A study performed by Heard-Costa et al. (2009) also found that this SNP in *NRXN3* was associated with WC and BMI. In further analyses, they showed that the association with WC was attenuated after adjusting for BMI, suggesting as in the present study that this SNP is most likely involved in overall adiposity rather than in specific abdominal fat deposition. Neurexin 3 gene (*NRXN3*), encodes a presynaptic cell adhesion protein from neurexines family that exerts its function in the nervous system playing a role in the formation and function of synapses (Wolock et al. 2013). This gene has been previously implicated in the pathogenesis of drug addiction (Bierut et al. 2007; Hishimoto et al. 2007; Lachman et al. 2007). According to Rapaka et al. (2008), compulsive eating and compulsive drug use, may converge and share some biological mechanisms that play a role in compulsive behaviour. Indeed, according to Woods et al. (2006) organism eats not just to provide nutrients, but also to derive pleasure and abate negative sensations (Rapaka, Schnur, and Shurtleff 2008). Therefore, this gene could be implicated in obesity development through some brain controlled mechanism involved in addiction behaviours. Most studies conducted to date, have demonstrated a positive association between the "G" allele of rs10146997 (*NRXN3*) and obesity (Heard-Costa et al. 2009). However our results showed negative associations with overall and abdominal obesity, as well as with SF6, weight and BMI. There are other populations where the usually obtained positive associations between the "G" allele of rs10146997 and obesity were neither observed. For example in a population of the

Netherlands, from the EUROSPAN consortium, no association was found between this gene and obesity (Heard-Costa et al. 2009). Results from this thesis confirm the implication of this SNP in obesity, but they also shed some doubts regarding the direction of the association, which seems to be reverse in the studied population. This fact highlights the importance of conduct similar investigations in different populations.

Two SNPs were associated exclusively with central fat distribution (i.e. rs10938397 in *GNPDA2* region and rs11084753 in *KCTD15* region). These genetic variants have been previously reported as obesity-related SNPs (Willer et al. 2009; Speliotes et al. 2010; Felix et al. 2016), but their functions are yet poorly understood. Glucosamine-6-phosphate deaminase 2 (*GNPDA2*) encodes an enzyme that catalyzes the deamination of the glucosamine-6-phosphate (Gutierrez-Aguilar et al. 2012). Potassium channel tetramerization domain containing 15 (*KCTD15*) is a voltage-gated potassium channel (Gutierrez-Aguilar et al. 2012) that interferes with neural crest formation during embryonic development, and inhibits binding protein 2 (AP-2) transcriptional activities by interaction with its activation domain (Zarelli and Dawid 2013). As in this study these two SNPs were only associated to central fat distribution and not to overall or abdominal obesity or any obesity related trait, these genetic variants could play a more significant role in fat distribution rather than in overall adiposity. However, further association studies of these SNPs with fat distribution variables as well as adjusting WHR for BMI would be necessary to ascertain the contribution of these SNPs in obesity and in fat distribution.

5.2. ASSOCIATION WITH EXTREME OBESITY

Analyses conducted only on extremes cases (BMI $\geq$40 kg/m^2) and controls (BMI <25 kg/m^2), increase substantially the power to detect associations (Price, Li, and Zhao 2008) and allow to detect variants with small effects. By these means, we could replicate, in this sample from the Basque Country population, the association of eight SNPs previously identified in other independent studies. In agreement with those studies, the results from this thesis showed significant positive associations between the effect allele, and extreme obesity for: rs2568958 and rs2815752 (in *NEGR1* region), rs6548238 and rs7561317 (in *TMEM18* region), rs925946 (in *BDNF* region), rs660339 and rs659366 (in *UCP2* region) and rs9939609 (in *FTO* region).

Among the eight associated SNPs, rs925946 (in *BDNF* region) had one of the greatest effect sizes and the lowest p-value of all the performed analyses, which underscored the importance of this genetic variant as one of the most strongly associated with obesity in this population.

In agreement with other study where SNPs from *TMEM18* were associated with BMI (Liu et al. 2014), in this study, there were two SNPs in *TMEM18* (rs6548238 and rs7561317) that also presented a relatively high effect on extreme obesity. *TMEM18* encodes a sequence-specific DNA-binding protein (Jurvansuu and Goldman 2011). Concerning its role in obesity development, this gene was shown to be expressed in brain, including the hypothalamic region, which is responsible for the control of energy homeostasis, and therefore some authors have hypothesized that it could influence feeding behaviour (Almén et al. 2010; Jurvansuu and Goldman 2011). However, it is also expressed in many other human tissues (e.g. skeletal muscle, liver and adipose tissue) (Jurvansuu and Goldman 2011; Rohde et al. 2014). Due to this and to some works where this gene showed differential expression between the adipose tissue of obese and lean participants (Bernhard et al. 2013) and even between subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) (Rohde et al. 2014), it has been speculated about a possible participation of this gene in fat distribution. The results of this thesis did not support this hypothesis, as no association was found between these SNPs and central fat distribution. However, results obtained until now by other authors were contradictory. Some works found positive associations between some genetic risk variants in this gene and waist circumference (Rask-Andersen et al. 2012); while others, including the results of this study, did not detect significant associations of *TMEM18* risk variants with measurements related to fat distribution (Hotta et al. 2011). Therefore, more researches are needed to elucidate this effect.

Rs99399609 from the *FTO locus*, showed an OR of almost 2, which makes it one of the three genes with the highest effect sizes on extreme obesity. *FTO* was the first obesity associated gene discovered by GWAS (Dina et al. 2007; Frayling et al. 2007; Scuteri et al. 2007), and it has been replicated in several studies since then. This gene encodes a 2-oxoglutarate-dependent nucleic acid demethylase (Gerken et al. 2007), however its physiological function is not completely understood. Fredriksson et al. (2008) proposed that this gene could have a role in the neuronal network regulating feeding. However, a direct connection between obesity associated SNPs and *FTO* expression has not been made yet. Smemo et al. (2014) postulated that *FTO* and *IRX3* are two overlapping genes and that some genetic variants within *FTO*, previously associated with increased BMI, are actually associated with *IRX3* expression, but not with *FTO* expression. Other study performed by Srivastava et al. (2016) in North Indians, also confirmed the connexion between *FTO* and *IRX3* genes. *IRX3* is a coding protein gene, and according to Smemo et al. (2014) its hypothalamic expression regulates energy homeostasis and body composition. However, some genetic variants in *IRX3* and *FTO* can also interact, independently or cooperatively, with other genes close to this *locus* and therefore further investigations are still needed.

In agreement with other studies (Thorleifsson et al. 2009; Willer et al. 2009), two SNPs in the *NEGR1* region (rs2568958 and rs2815752) also showed a significant association with extreme obesity, while the other studied SNP in this gene (rs3101336) was close to significance. The neuronal growth regulator 1 gene (*NEGR1*) encodes a member of the immunoglobulin superfamily protein that is also expressed at high levels in brain and hypothalamus. These proteins serve as cell-adhesion molecules and regulate synapse formation (Hashimoto, Maekawa, and Miyata 2009). The association of these SNPs with obesity supports and highlights the role of the central nervous system on body weight regulation. However, the mechanisms of action are not totally elucidated. Recently, Boender et al. (2014) proposed the contribution of this gene (Negr1) in the regulation of energy balance in rodents by controlling the intake of specific macronutrients and the regulation of energy expenditure. In addition, Walley et al. (2012) demonstrated that *NEGR1* was also expressed in human subcutaneous adipose tissue (SAT) where it was differentially expressed between lean and obese subjects. The contribution of this gene to obesity was clear, yet further investigations are required to understand which the mechanisms of action are.

The uncoupling protein 2 (*UCP2*) is a mitochondrial membrane transporter, and its function is to transfer the anions and protons through the mitochondrial membrane. Due to its location in several mammalian tissues, including white adipose tissue (Chevillotte et al. 2007) and to its function on energy metabolism, it was proposed as a candidate gene involved in obesity. Fleury et al. (1997) linked this gene to obesity and hyperinsulinemia. Later, other studies have also demonstrated that rs660339 and rs659366 (in *UCP2* region) were associated to obesity (Oktavianthi et al. 2012). A meta-analysis carried out by Liu et al. (2013) confirmed the association of rs659366 polymorphism and obesity. In their study the T allele had a significant protective effect on the risk of obesity development in Europeans, which is in agreement with the result shown in the present study. Furthermore, another SNP in the *UCP2* gene (rs660339) was also significantly associated with morbid obesity with the G allele increasing the risk of morbid obesity. This SNP was previously associated with energy expenditure; according to Buemann et al. (2001), basal metabolic rate and energy cost of exercise are raised in subjects carrying the "A" allele. A decrease in energy expenditure in individuals carrying the other allele ("G" allele) may explain the association of this allele with extreme obesity in this population.

5.3. ASSOCIATION WITH SOMATOTYPE COMPONENTS

Finally, as nutritional status affects body morphology and composition, the same SNPs were analysed to find a possible association between them and somatotype components. Two SNPs were associated with endomorphy: the "T" allele from rs925946 (in *BDNF* region) was associated with an increase in endomorphy, whereas the "G" allele from rs10146997 (in *NRXN3* region) was associated with a decrease in it. These results were in agreement with the previously reported results obtained for overall obesity (defined as BMI≥30 kg/m^2). These results were expected, since endomorphy is the somatotype component more related with adiposity, and therefore obese individuals have high endomorphic values and rounded shapes (Carter and Heath 1990). These two SNPs were also associated with ectomorphy but the direction of association was the opposite of what was presented for endomorphy. This was also expected, as ectomorphy refers to the relative predominance of linearity, and persons with high ectomorphy tend to be tall and lean (Carter and Heath 1990). In this way the allele of a SNP that is positively associated with endomorphy, will be negatively associated with ectomorphy and vice versa.

In addition, there was another SNP exclusively associated with ectomorphy: rs4776970 (in *MAP2K5* region). The protein encoded by this gene is a dual specificity protein kinase that belongs to the MAP kinase family. The signal cascade mediated by this kinase is involved in growth factor stimulated cell proliferation and muscle cell differentiation. The two studied SNPs in this gene were previously associated with increased BMI (Speliotes et al. 2010; Wen et al. 2012; Wen et al. 2014), so the negative association found between the effect allele of this SNP and ectomorphy could be reflecting the negative correlation between this component and the other two components of somatotype (i.e. endomorphy and mesomorphy), which are positively correlated with BMI (see Chapter 4). However, the lack of association of this SNP with obesity in the present study and its negative association with ectomorphy, may be indicating that the previously obtained associations of this SNP with obesity could be mediated by its association with other characteristics instead of directly with obesity. For example, there are other works where this *locus* has been associated with the restless legs syndrome (RLS) (Rask-Andersen et al. 2012), which is a sensory-motor neurological disorder (Varim et al. 2016).

Finally, mesomorphy reflects the relative predominance of muscle, bone and connective tissue. In this study, two SNPs were associated with this body morphology component: rs10146997 (in *NRXN3* region) and rs9939609 (in *FTO* region). Interestingly, both SNPs were also associated with obesity. This might seem contradictory at first, but as mentioned in Chapter 4 of this thesis, both components: endomorphy and mesomorphy increase with BMI; and thus, this association with mesomorphy could be pointing out changes in morphology that happen along obesity development.

6. CONCLUSIONS

In summary, the results obtained in the present study suggest a modest contribution to obesity variation as well as to body morphology and composition, of 12 SNPs in or near *NEGR1*, *TMEM18*, *GNPDA2*, *BDNF*, *UCP2*, *NRXN3*, *FTO*, *KCTD15* and *MAP2K5* genes in the Basque Country population.

Many of the associated SNPs in this study are in or near genes with a function or differential expression in neuronal system, which may highlight the importance of this system in the development of obesity. Among them the genetic variant in *BDNF* is one of the most significantly associated SNP to most of the obesity related traits. On the other hand, some of these SNPs are also expressed in adipose tissue. As a high amount of adipose tissue is one of the main characteristics of obesity, the study of new candidate SNPs with differential expressions in this tissue could help in obesity research. Additionally, one unexpected result was found, as the effect allele of rs10146997 in *NRXN3* is negatively associated to obesity in this sample of the Basque Country population. However, although the implication of *NRXN3* is confirmed in this study, due to the limitations of this work, new researches in different populations within the European territory, are need to assess possible differences in the genetic association patterns of this gene.

Chapter VIII

General Discussion

1. GENERAL DISCUSSION

Obesity has increased to global epidemic proportions in the last decades and morbid obesity has also been reported to increase even at a faster rate (Lavie, Milani, and Ventura 2009). Overweight and obesity have a great impact on today's society due to their influence on the development of major chronic diseases such as type II diabetes or cardiovascular diseases (CVDs) among others, but also due to their contribution to an impaired quality of life, a general sense of fatigue and major decrease of functional motor status (Han et al. 1998).

In order to address the problem of the increasing worldwide prevalence of obesity, research studies based on body morphology and composition have acquired a notable importance during last years. The WHO (World Health Organization 2017) defined overweight and obesity as an "abnormal or excessive fat accumulation that may impair heath". Indeed, several detrimental effects of overweight and obesity are attributed to some metabolic characteristics of adipose tissue and thus, many studies are focused on this body component (e.g. Sakurai et al. 2017; Schlecht et al. 2017). However, in the studied population as well as in other populations (Galic et al. 2016), the increase in FM that occurs in the development of obesity was usually accompanied by an increase in FFM. There are also other studies that point to a decrease of muscle and bone mass associated with intentional or unintentional weight loss (Backx et al. 2016; Mason et al. 2016). Due to the simultaneously increase or decrease of FFM with FM in relation to obesity status and to the role of muscle mass in glucose metabolism (i.e. major site of insulin-stimulated glucose uptake) (Glouzon et al. 2015), the results of this thesis emphasized the importance of studying the implication of FFM in obesity, together with the study of FM. In the same way, endomorphy (body component related to adiposity) and mesomorphy (body component related to muscularity) also increased simultaneously with the increase of the nutritional category in sport men according to our results (**Chapter IV**). However, the regular practice of sport, as that performed by professional sport men, may help redirect some of the extra energy to a particular somatotype component, which resulted in a greater dominance of mesomorphy over endomorphy as the nutritional category increases, indeed obese rugby players presented similar values of endomorphy to overweight men. In non-professional sport men the increase in the mesomorph component only happened in normal-weight category, whereas in higher nutritional status sport practices meant a decrease in both components FM and FFM. Sport practice had similar but slight effects in women; nevertheless, the effect of sports in body morphology seemed to be higher in men than in women. On the other hand, differences in body morphology and composition, typically observed between sexes and between younger and older individuals, depended on the nutritional status. Compared with high nutritional status, sexual dimorphism in both endomorphy and mesomorphy was more marked in normal-weight participants, and the usual decrease in ectomorphy with age was also more clearly seen in this nutritional status.

Body image encompasses perceptions, emotions, cognitions and behaviours towards physical appearance (Muth and Cash 1997) and plays an important role in the aetiology of overweight and obesity. In accordance with the obtained results (**Chapter V**) perceived body image usually reflects subjects' actual body size. A correct perception of body size is essential personal well-being, but the discrepancies between perceived body image and desired body image are what leads to body dissatisfaction, and in turn to many health problems such as low self-esteem, eating disorders or risky behaviours related to image changes attempts (Garrusi, Garousi, and Baneshi 2013). Although in this study the highest inconsistency between the perceived body image and the actual nutritional status were appreciated among older men, it was in women where the inconsistency score was significantly associated with the nutritional category. In fact, women with a higher body size tended to underestimate it, which has been proposed as a mechanism to self-esteem protection (Barrett and Huffman 2011). However, this underestimation could also make obese people not to see their need to lose weight and makes difficult to follow attitudes to control weight (Duncan et al. 2011). On the other hand overestimation of the actual body size was more common among women with lower nutritional status. The results of this thesis, in agreement with other studies (McCabe and Ricciardelli 2004; Garrusi, Garousi, and Baneshi 2013), indicate that higher body image dissatisfaction by excess is usually associated with greater nutritional status in men and women. Dissatisfaction by default was also detected in the studied sample, especially among young men, who in spite of being normal-weighted desired greater body sizes. This preference usually reflects the desire of more muscular bodies in men. Preferences in body image have a clear sexual dimorphism; women preferred for themselves slightly smaller body sizes than men. Although the environmental context (mass media messages, society ideals…) was quite homogeneous in this sample, inter-individual differences in the choice of the ideal silhouette were appreciated. The ideal silhouettes chosen by participants were positively associated with their nutritional status and reflected the influence of the own perception in individuals' body image preferences. Regarding preferences for the opposite sex, the great majority of subjects chose a silhouette representing normal-weight (silhouette number 4). However, also on this occasion, body images chosen for women were slightly smaller than the ones chosen for men, which reflects that social influences usually directed to promote a small body image of women (Grabe, Ward, and Hyde 2008), affected both sexes. On the other hand, an assortative choice, where bigger subjects prefer bigger mates, seems to be important only in young. It is not clear why this happens, but it points to a decrease in the importance of body image in older adults, possibly due to a decrease in social or biological pressure for an appropriate matching.

The results of the present research confirm the environmental contribution to obesity (Giskes et al. 2011) (**Chapter VI**). Several environmental factors were associated not only to overall obesity (assessed through BMI) but also to abdominal obesity (assessed through WC), central fat distribution (assessed through WHR) or excessive adiposity (assessed through FM %). The different methods used to assess obesity represent different obesity phenotypes. However, according to the results of this thesis overall and abdominal obesity were usually influenced by the same environmental factors, probably due to their high correlation, whereas central fat distribution followed a slightly different pattern, influenced by some of the same factors that influence overall obesity, but also by some additional factors. First of all, the obtained results, confirmed the impact of obesity in health; but, while central fat distribution was more related to the usually called "obesity related diseased", overall and abdominal obesity were more related with the perception of poor physical condition. Daily walking, eating in the company's dining room and smoking were almost only associated with central fat distribution. However, it is not clear yet how these factors can influence a more central fat distribution. Meanwhile, a poor quality of sleep, some eating patterns (main meal duration and the number of eating episodes) and the number of cigarettes smoked per day were only associated with overall and abdominal obesity, and seemed to have no influence on fat distribution. On the other hand, excessive adiposity was the obesity phenotype most strongly associated to a bad perception of physical condition, but it was not associated with any sleeping or eating patterns. Additionally, in agreement with other works (González-Gross and Meléndez 2013; Goedecke and Micklesfield 2014), results from this study confirmed the strong benefits of sport practice, especially regularly sport practice throughout life, in order to maintain a proper nutritional status. TV watching was also validated as a sedentary lifestyle indicator that is importantly involved in obesity development (Maher et al. 2013).

Although environmental factors are clearly involved in the population-development of obesity, genetic factors are thought to influence an individual susceptibility to obesity given a particular level of energy intake and expenditure. Evidences of the relatively strong genetic influence on the development of obesity have been established by many studies (Elks et al. 2012; Nan et al. 2012; Poveda et al. 2012; Silventoinen et al. 2016). However, the identification of genetic variants contributing to common obesity has been largely controversial. Many SNPs in different genes were found to be associated with obesity in several studies but the replication of those results is scarce. In **Chapter VII**, the association between 21 SNPs, identified through GWAS or candidate genes studies, and obesity phenotypes, obesity-related traits and somatotype components was investigated in a population from the Basque Country. Significant associations with obesity and obesity related traits were found in or near 4 genes (*GNPDA2*, *BDNF*, *NRXN3*, *KCTD15*), suggesting that these genetic variants contribute to obesity variation in the Basque Country population. Among them, rs925946 located on chromosome 11p13 in *BDNF* showed the most significant association with the three obesity phenotypes and SF6. Besides, there were two SNPs rs10938397 (in *GNPDA2* region) and rs11084753 (in *KCTD15* region) that only showed association with central fat distribution, but not with overall or abdominal obesity. The associations between 8 SNPs in 5 different genes (*NEGR1*, *TMEM18*, *BDNF*, *UCP2* and *FTO*) with extreme values of obesity were replicated in this population, and rs925946 was confirmed as one of the most significantly associated SNPs with obesity. The association between obesity-related SNPs and somatotype components has been poorly investigated in these kinds of works. However, in this thesis, a significant association between four SNPs in different genes (BDNF, NRXN3, MAP2K5 and FTO) and at least one of the three somatotype components was found, pointing to a possible influence of these genetic variants also in body morphology and composition.

The present research provides interesting findings on body morphology, composition and image of obesity as well as on the genetic and environmental influences on several obesity phenotypes. These findings could open new possibilities in the development and design of future strategies to prevent and control obesity. However, this work has some limitations. First, the relative small number of individuals included in the sample limits the power of the statistical analyses. However, the case-control methodology recruitment provided a good representation of obese subjects with varying degrees of obesity. Although an individually matched design was not possible (to avoid a sample size loss), when necessary, sex age and SES were included as covariates in order to eliminate confounding effects. The results obtained were generally significant and the values concordant with those estimated in other populations. Nevertheless, inclusion of more individuals in the present sample will be recommendable in order to obtain stronger results, as it will be the replication of the present analyses in other samples of the Basque Country as well as in other population samples. Second, the case-control design of the present study does not allow inferring causality of the associations between obesity and the environmental or genetic studied factors. Third, environmental factors were assessed through a questionnaire, and thus they could be imprecise and prone to bias. However, in order to reduce the variability due to different interpretations to the questionnaire, all the questions were performed by the author of this thesis and some guidance was given to avoid misinterpretations. Similarly, all the measures were taken by the same person, which reduces considerably the total measurement error. Finally, the results of the present research are population, setting and time-specific, and thus, they could not be generalized to other populations.

Chapter IX

General Conclusions

GENERAL CONCLUSIONS

The main conclusions of this research have been extracted from each of the individual chapters and are the following:

I. Body morphology and composition vary along obesity development. Both endomorphy and mesomorphy increase with obesity while ectomorphy decreases, which reflects the increase in body mass due to both FM and FFM together with a body linearity reduction.

II. Sexual dimorphism of somatotype is evident in almost all nutritional categories with the exception of morbid obesity. The dominance of endomorphy over mesomorphy is characteristic in women; whereas in men, mesomorphy is the predominant somatotype component. Sexual differences in ectomorphy are less marked.

III. Age changes in somatotype are unclear. The typical reduction in ectomorphy with age is only evident in normal weight category, where endomorphy and mesomorphy are increased. In high nutritional categories there is not a clear pattern related to changes in body morphology with age.

IV. Somatotype differences between individuals who practice or do not practice sports are relatively small; however they are always higher in men than in women. Additionally, the practice of a sport in a more professional way (in this work as a member of a rugby team) clearly modifies body composition, with a higher dominance of mesomorphy as the nutritional category increases.

V. The own identification with the image that better represent the own BMI is common among the studied population. Despite this, adult men must be taken with concern, due to the relatively high inconsistency found between their most representative silhouette and their BMI. However, it is in women where the nutritional category is closely related to the inconsistency score; women with higher nutritional status usually underestimate their body size more than women with lower nutritional categories.

VI. There are clear differences between the ideal body image that women and men choose for themselves. Women tend to choose small silhouettes, whereas men choose more corpulent ones. However, for both sexes, the ideal image is influenced by the own nutritional status. More corpulent images are chosen as the ideal one by individuals in high nutritional categories whereas smaller silhouettes are chosen by individuals in low nutritional categories.

VII. The most attractive silhouette for the opposite sex follows the same tendency as the ideal image: men choose smaller silhouettes for women and women choose bigger silhouettes for men. This points to a similar social influence shared by both sexes. However, these sexual differences are only important enough in the youngest groups, where the most attractive silhouette for the opposite sex is also conditioned by nutritional category, so that silhouettes representing bigger bodies are often chosen by individuals in high nutritional categories.

VIII. Although the wish to be thinner is common in the studied sample, full satisfaction with body image is always more common in men than in women. Nevertheless, younger adults are the most concerning groups, as normal weight is quite common among women who wish to be thinner and among men who wish to be more corpulent.

IX. In this sample of the Basque Country population, both environmental and genetic factors play important roles in the development of different obesity phenotypes.

X. A bad perception of the own physical condition has one of the highest effect sizes for excessive adiposity as well as a relatively high one for overall and abdominal obesity in comparison with central fat distribution. However, the effect size of obesity related diseases is higher for central fat distribution than for other obesity phenotypes.

XI. All obesity phenotypes are affected by sport practice and TV watching. The sport practice is a protective factor against all obesity phenotypes, but just walking (as a sport) is only a protective factor against overall and abdominal obesity. Too much time watching TV represents a sedentary lifestyle, which is a risk factor for obesity development, whatever the phenotype considered.

XII. In this study sleep duration has no effect on obesity. However, there is a clear association between sleep quality and overall and abdominal obesity, since these two obesity phenotypes are more common among individuals with a regular or bad sleep quality than among the ones with a good sleep quality. On the other hand, longer main meal duration has a protective effect against overall and abdominal obesity, possibly due to the time needed for the regulation of hunger and satiety sensations.

XIII. Smoking has an influence in fat mass distribution, especially in former smokers. However, the increase in the number of smoked cigarettes affects overall and abdominal obesity, as well as excessive adiposity.

XIV. Although due to its toxicity alcohol cannot be recommended, in the analysed sample it has a protective effect against overall obesity and excessive fat mass, but just when its consumption is occasional.

XV. Genetic variants in eight genes (*GNPDA2*, *BDNF*, *NRXN3*, *KCTD15*, *NEGR1*, *TMEM18*, *UCP2* and *FTO*) contribute to variation in obesity and obesity related traits.

XVI. Four genetic variants in or near *BDNF* (rs925946), *NRXN3* (rs10146997), *MAP2K5* (rs4776970) and *FTO* (rs9939609) contribute to body morphology and composition (anthropometric somatotype).

XVII. Although the association between the “G” allele of rs10146997 (NRXN3) and obesity is usually positive, in the studied sample from the Basque Country population this allele shows a negative association with obesity.

Chapter X

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Chapter XI

Supplementary Material

Appendix I

Table A.4.1. Pearson correlations (r) between somatotype components and anthropometric measures controlled for sex and age.

	Endomorphy (r)	**Mesomorphy (r)**	**Ectomorphy (r)**
Height	-0.08	-0.16***	0.15***
Weight	0.76***	0.79***	-0.67***
Arm rel. c.	0.79***	0.85***	-0.69***
Arm cont. c.	0.77***	0.87***	-0.68***
Waist c.	0.78***	0.78***	-0.69***
Hip c.	0.75***	0.80***	-0.65***
Medial calf c.	0.66***	0.84***	-0.66***
Biceps s.	0.82***	0.56***	-0.60***
Triceps s.	0.80***	0.46***	-0.53***
Subscapular s.	0.91***	0.66***	-0.68***
Suprailiac s.	0.91***	0.66***	-0.63***
Abdominal s.	0.86***	0.53***	-0.61***
Medial calf s.	0.68***	0.35***	-0.50***
Humerus b.	0.16***	0.44***	-0.17***
Femoral b.	0.51***	0.84***	-0.43***
BMI	0.82***	0.89***	-0.72***

rel: relaxed; cont: contracted; c: circumference; s: skinfold; b: breadth.
*** Estimate significant at $p<0.001$.

Table A.4.2. Means of each somatotype component and differences between the four groups based on nutritional category in the group of **Men <45 years**.

	NW		OW		OB		MO		Estatistic		**p-value**
Endomorphy	3.11	**a**	4.81	**b**	6.94	**c**	9.32	**d**	F	165.957	**1.7E-39**
Mesomorphy	4.58	**a**	5.37	**b**	7.10	**c**	9.95	**d**	Welch	91.532	**1.3E-14**
Ectomorphy	2.55	**a**	1.15	**b**	0.12	**c**	0.10	**c**	$\chi 2$	94.331	**2.6E-20**

a, b, c, d: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.3. Means of each somatotype component and differences between the four groups based on nutritional category in the group of **Men >45 years**.

	NW		OW		OB		MO		Estatistic		**p-value**
Endomorphy	3.64	**a**	4.43	**a**	5.97	**b**	8.22	**c**	F	31.494	**6.4E-14**
Mesomorphy	4.49	**a**	5.47	**b**	7.25	**c**	9.43	**d**	$\chi 2$	62.575	**1.7E-13**
Ectomorphy	2.11	**a**	0.74	**b**	0.10	**c**	0.10	**c**	$\chi 2$	82.162	**1.1E-17**

a, b, c, d: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.4. Means of each somatotype component and differences between the four groups based on nutritional category in the group of **Women <45 years**.

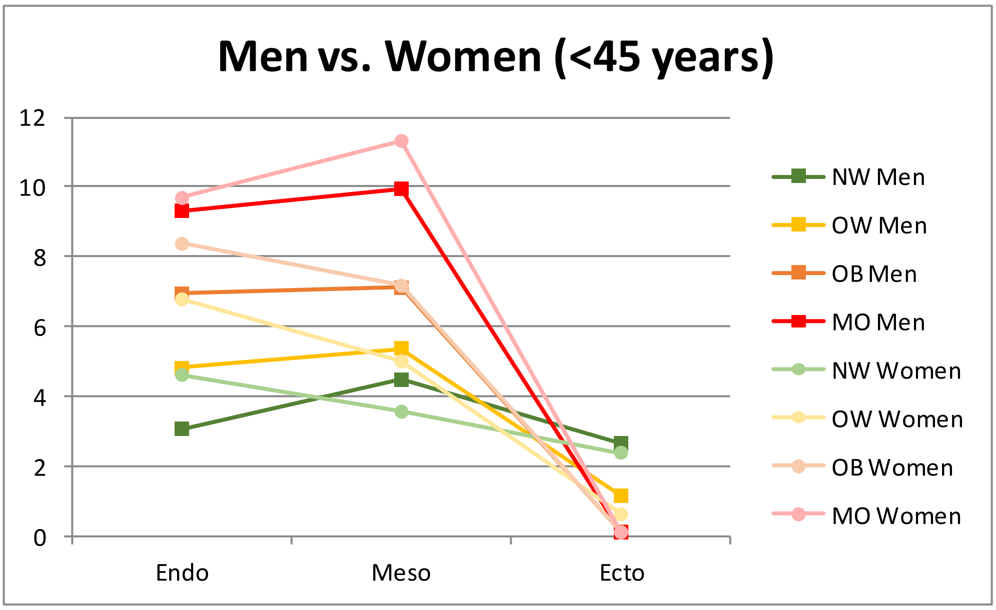
	NW		OW		OB		MO		Estatistic		p-value
Endomorphy	4.82	**a**	6.78	**b**	8.37	**c**	9.58	**d**	Welch	148.034	**4.6E-26**
Mesomorphy	3.75	**a**	5.00	**b**	7.16	**c**	11.32	**d**	Welch	68.256	**3.5E-14**
Ectomorphy	2.16	**a**	0.61	**b**	0.10	**c**	0.10	**c**	$\chi 2$	112.934	**2.6E-24**

a, b, c, d: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.5. Means of each somatotype component and differences between the four groups based on nutritional category in the group of **Women >45 years**.

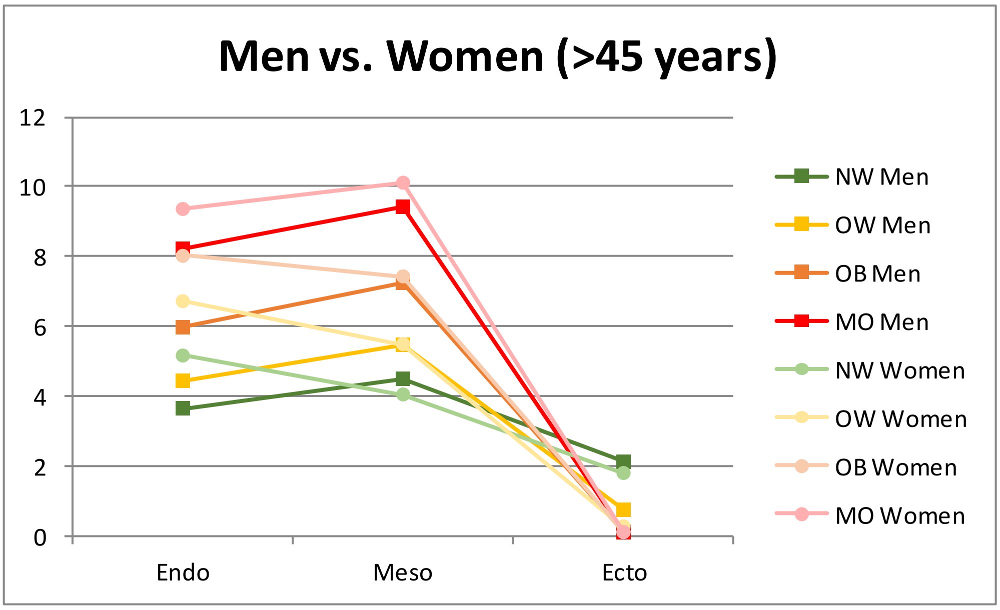
	NW		OW		OB		MO		Estatistic		p-value
Endomorphy	5.33	**a**	6.72	**b**	8.02	**c**	9.34	**d**	F	73.925	**8.4E-30**
Mesomorphy	4.10	**a**	5.49	**b**	7.43	**c**	10.11	**d**	$\chi 2$	110.542	**8.4E-24**
Ectomorphy	1.65	**a**	0.26	**b**	0.10	**c**	0.10	**c**	$\chi 2$	138.314	**8.7E-30**

a, b, c, d: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.



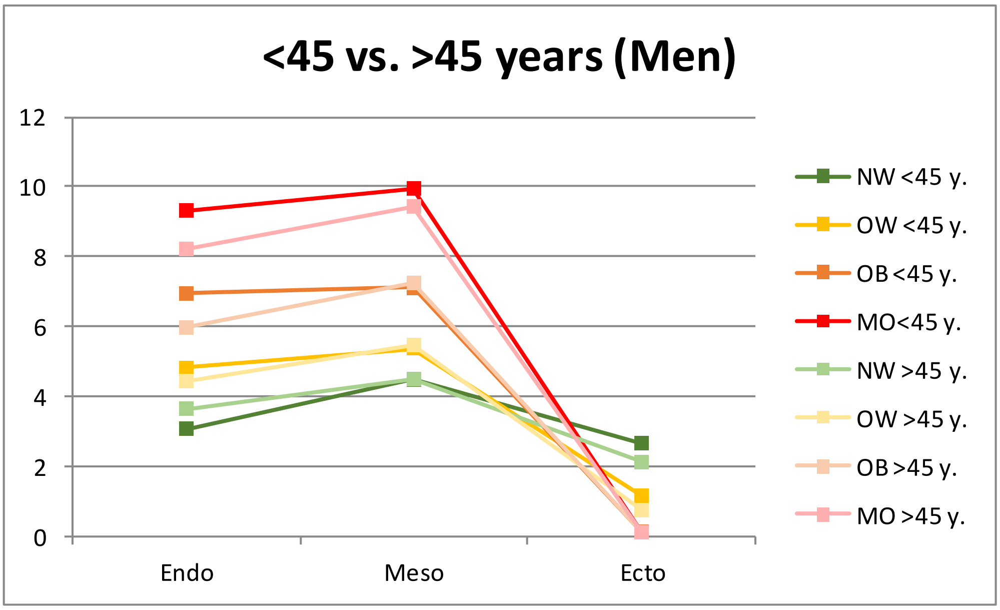
Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure A.4.1. Comprogram representing the three somatotype components means for men and women in the younger group.



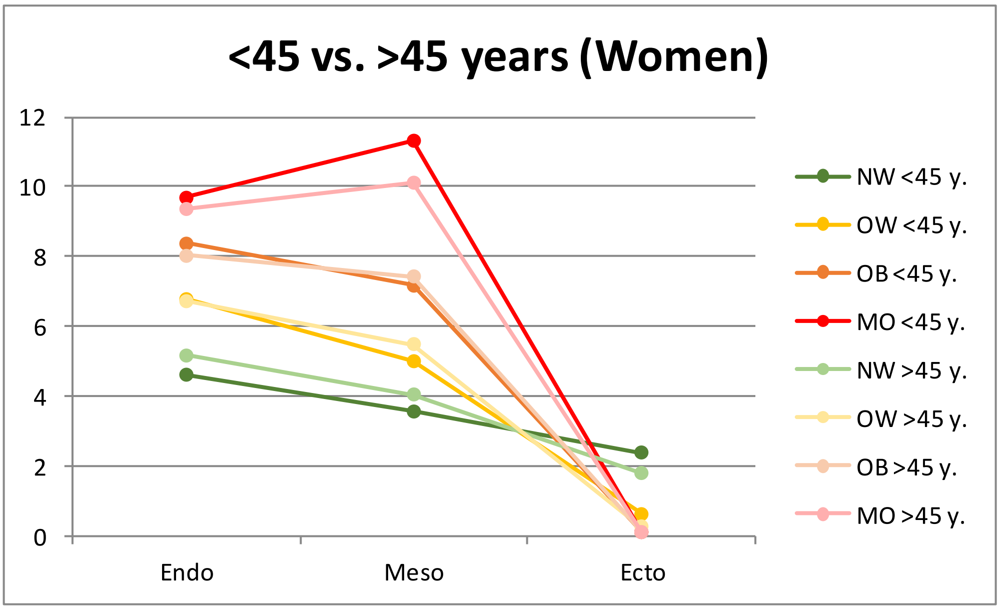
Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure A.4.2. Comprogram representing the three somatotype components means for men and women in the older group.



Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure A.4.3. Comprogram representing the three somatotype components means for younger and older men.



Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity; MO: morbid obesity.

Figure A.4.4. Comprogram representing the three somatotype components means for younger and older women.

Table A.4.6. SDD between somatoplots of consecutive nutritional categories.

SDD	NW vs. OW	OW vs. OB	OB vs. MO
Men < 45 y.	**5.83**	**5.96**	**5.32**
Men >45 y.	**4.52**	**4.61**	**4.44**
Women <45 y.	**7.25**	**4.89**	**5.66**
Women >45 y.	**6.06**	**3.74**	**4.54**

NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity
Significant SDD at $p<0.05$ are shown in bold

Table A.4.7. Differences in mean somatotype components between the three groups based on nutritional category in the group of **"men; no sport"**.

	NW		OW		OB		Estatistic		Sig.
Endomorphy	3.047	**a**	4.79	**b**	6.688	**c**	F	37.453	**1.7E-11**
Mesomorphy	4.129	**a**	5.662	**b**	7.649	**c**	F	59.449	**3.8E-15**
Ectomorphy	2.639	**a**	0.811	**b**	0.142	**c**	F	114.662	**7.0E-22**

a, b, c: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.8. Differences in mean somatotype components between the three groups based on nutritional category in the group of **"men; sport"**.

	NW		OW		OB		Estatistic		Sig.
Endomorphy	3.206	**a**	4.357	**b**	6.171	**c**	F	33.924	**3.0E-11**
Mesomorphy	4.723	**a**	5.369	**b**	6.694	**c**	F	30.881	**1.5E-10**
Ectomorphy	2.313	**a**	1.158	**b**	0.229	**c**	F	107.341	**7.3E-23**

a, b, c: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.9. Differences in mean somatotype components between the three groups based on nutritional category in the group of **"men; rugby"**.

	NW		OW		OB		Estatistic		Sig.
Endomorphy	2.776	**a**	3.958	**b**	4.96	**c**	F	10.319	**3.9E-04**
Mesomorphy	4.673	**a**	5.86	**b**	7.554	**c**	F	22.686	**1.0E-06**
Ectomorphy	2.545	**a**	1.058	**b**	0.285	**c**	F	46.411	**6.6E-10**

a, b, c: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.10. Differences in mean somatotype components between the three groups based on nutritional category in the group of **"women; no sport"**.

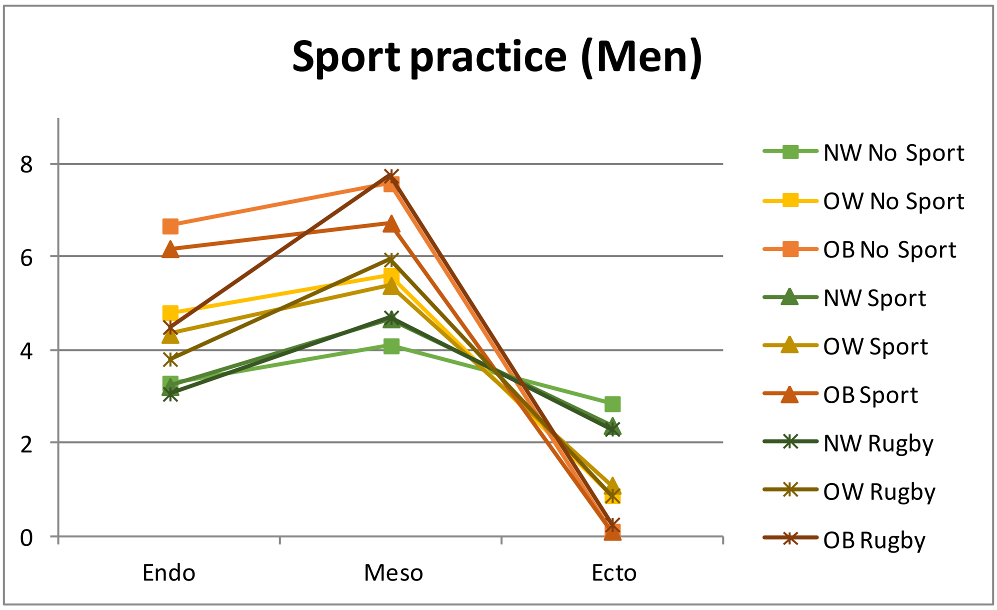
	NW		OW		OB		Estatistic		Sig.
Endomorphy	5.14	**a**	7.029	**b**	8.23	**c**	F	68.519	**8.1E-21**
Mesomorphy	3.848	**a**	5.243	**b**	7.325	**c**	F	93.483	**1.5E-25**
Ectomorphy	1.884	**a**	0.381	**b**	0.13	**b**	F	142.632	**1.0E-33**

a, b, c: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.

Table A.4.11. Differences in mean somatotype components between the three groups based on nutritional category in the group of **"women; sport"**.

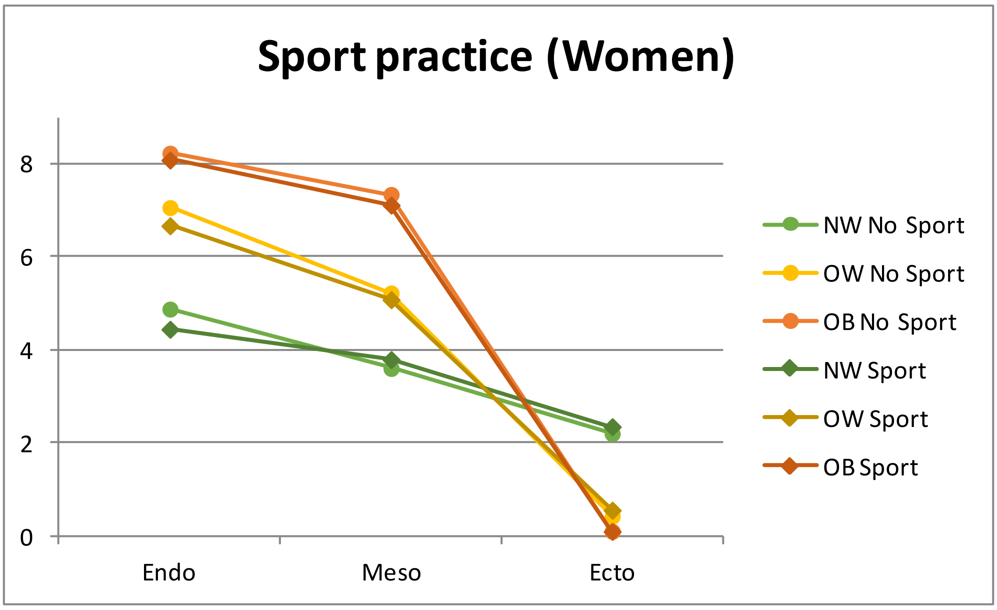
	NW		OW		OB		Estatistic		Sig.
Endomorphy	4.722	**a**	6.631	**b**	8.066	**c**	F	51.779	**2.9E-15**
Mesomorphy	4.072	**a**	5.045	**b**	7.017	**c**	F	48.388	**1.5E-14**
Ectomorphy	1.987	**a**	0.577	**b**	0.193	**b**	F	66.203	**5.5E-18**

a, b, c: there are significant differences between values with different bold letters.
NW: normal weight; OW: Overweight; OB: obesity; MO: morbid obesity.



Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity.

Figure A.4.5. Comprogram representing the three somatotype components means for sport and non-sport men.



Endo: endomorphy; Meso: mesomorphy; Ecto: ectomorphy; NW: normal weight; OW: overweight; OB: obesity.

Figure A.4.6. Comprogram representing the three somatotype components means for sport and non-sport women.

Appendix II

U-Mann Whitney *p= 1.80E-05*

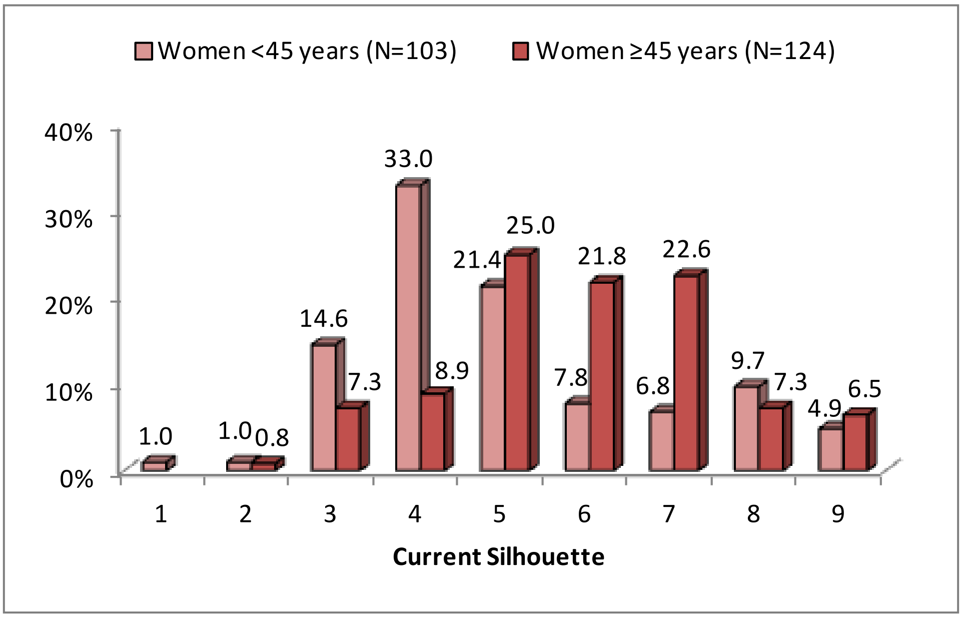


Figure A.5.1. Percentage of women with less than 45 years and with 45 years or more who chose each of the silhouettes as the best representing their current body image.

U-Mann Whitney *p=0.020*

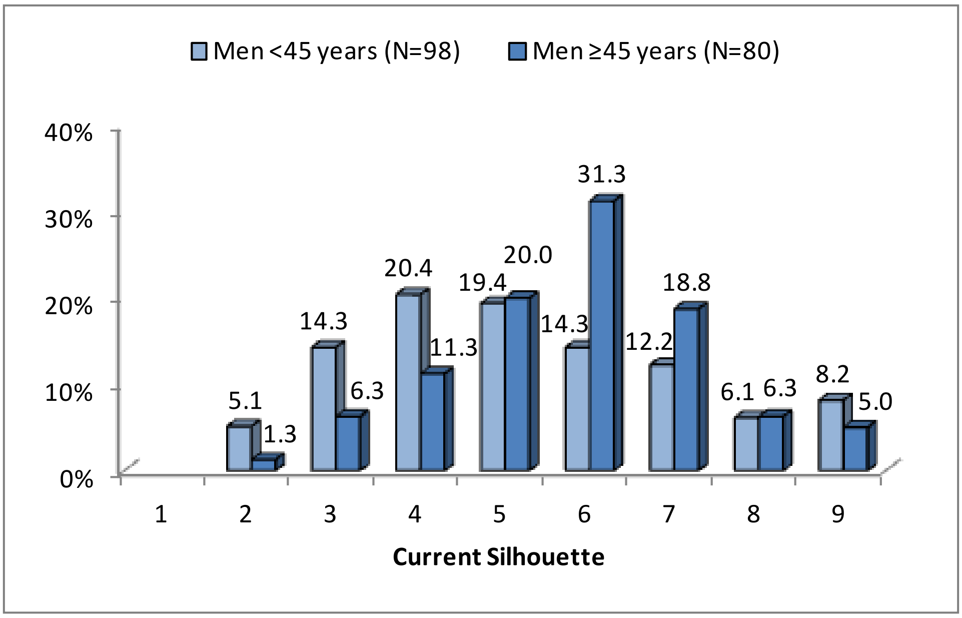


Figure A.5.2. Percentage of men with less than 45 years and with 45 years or more who chose each of the silhouettes as the best representing their current body image.

U-Mann Whitney *p=0.235*

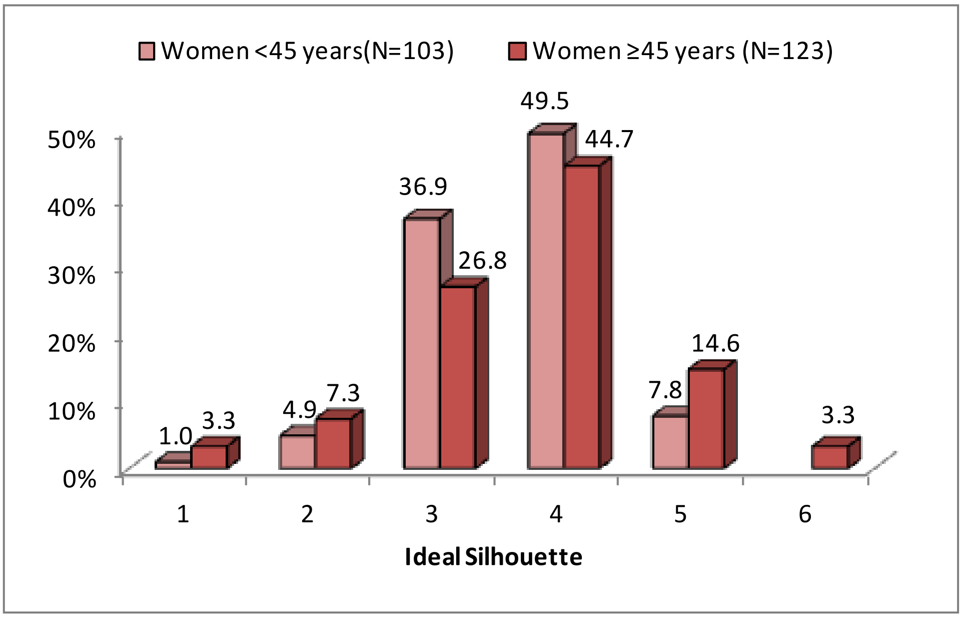


Figure A.5.3. Percentage of women with less than 45 years and with 45 years or more who chose each of the silhouettes as their ideal body image.

U-Mann Whitney *p=0.829*

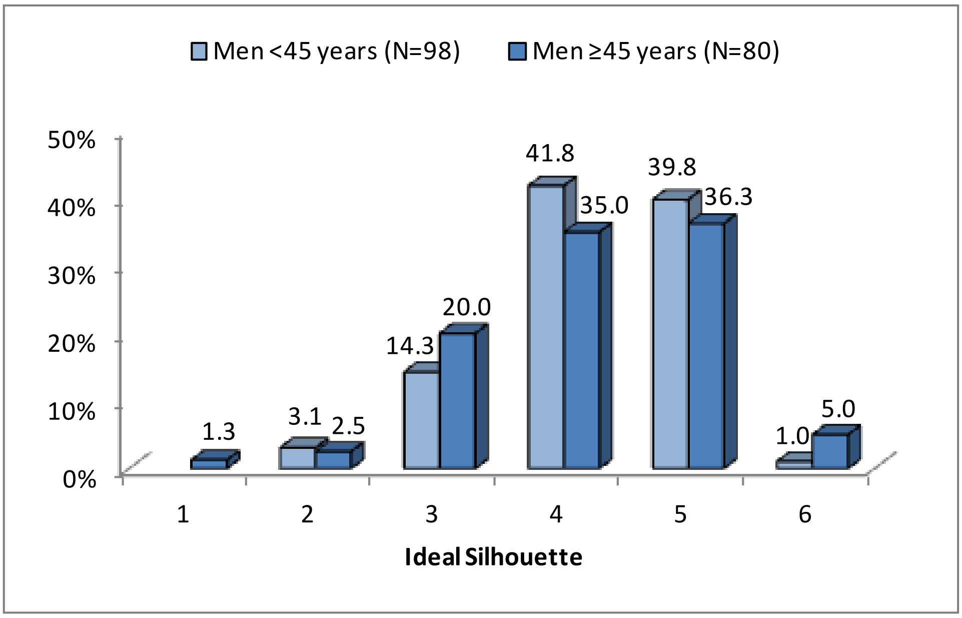


Figure A.5.4. Percentage of men with less than 45 years and with 45 years or more who chose each of the silhouettes as their ideal body image.

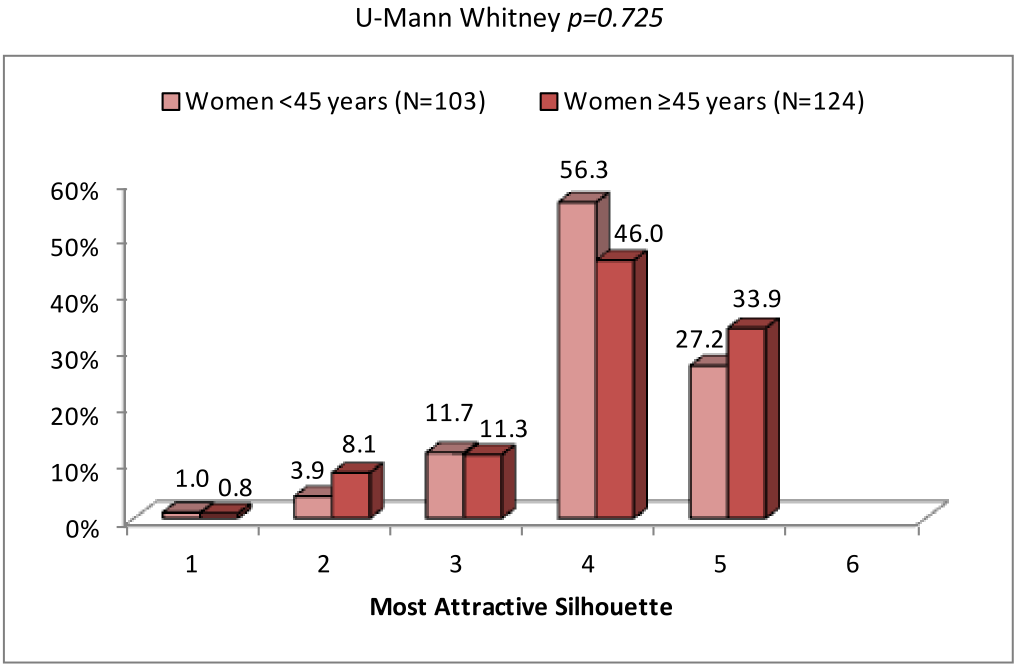


Figure A.5.5. Percentage of women with less than 45 years and with 45 years or more who chose each of the silhouettes as the ideal body image for the opposite sex.

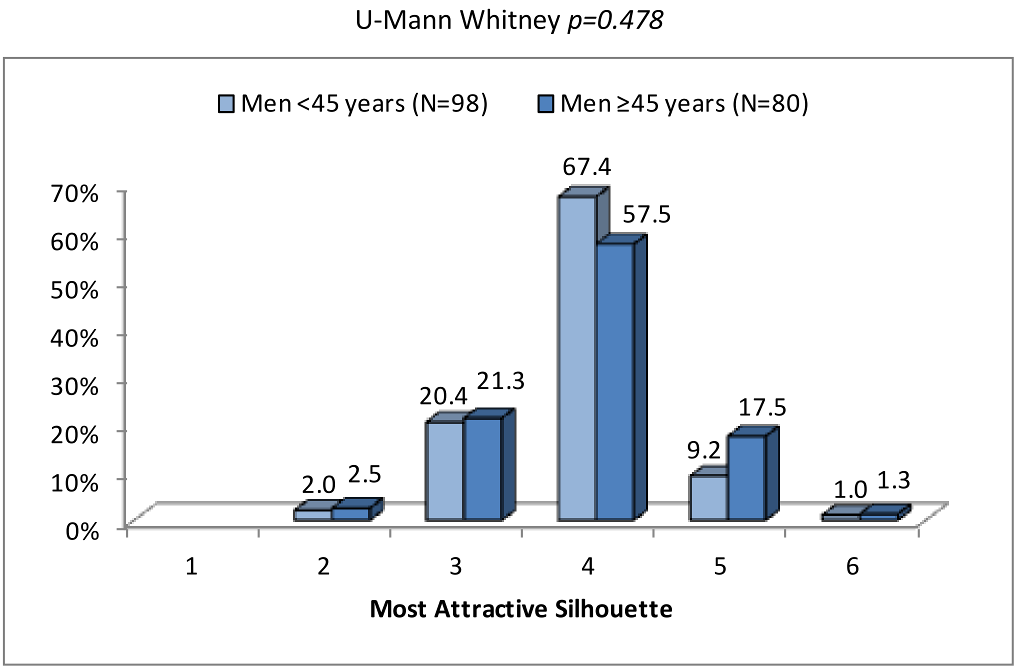


Figure A.5.6. Percentage of men with less than 45 years and with 45 years or more who chose each of the silhouettes as the ideal body image for the opposite sex.

U-Mann Whitney *p=0.001*

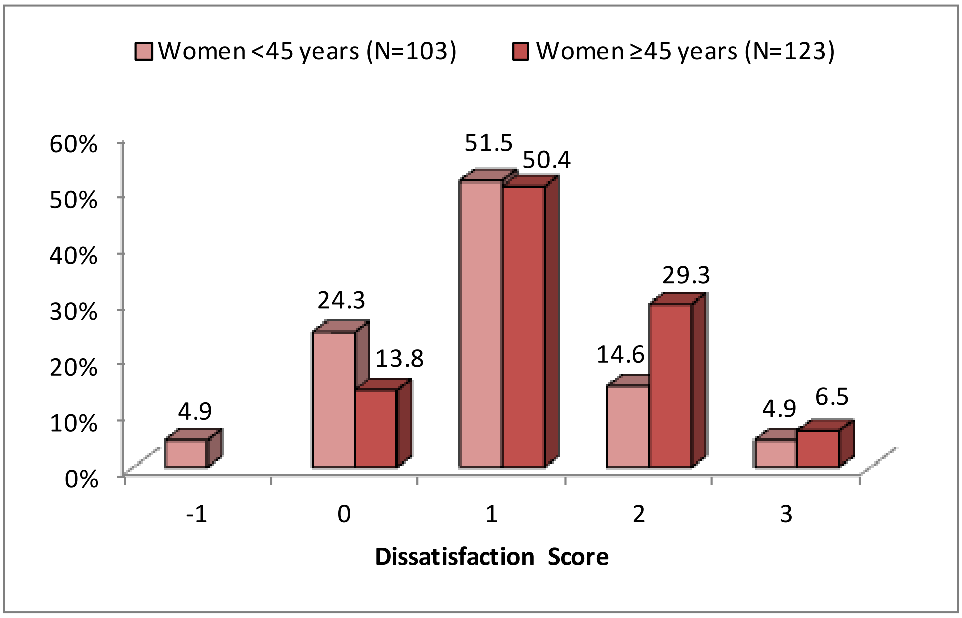


Figure A.5.7. Percentage of women with less than 45 years and with 45 years or more in each dissatisfaction score.

U-Mann Whitney *p=0.002*

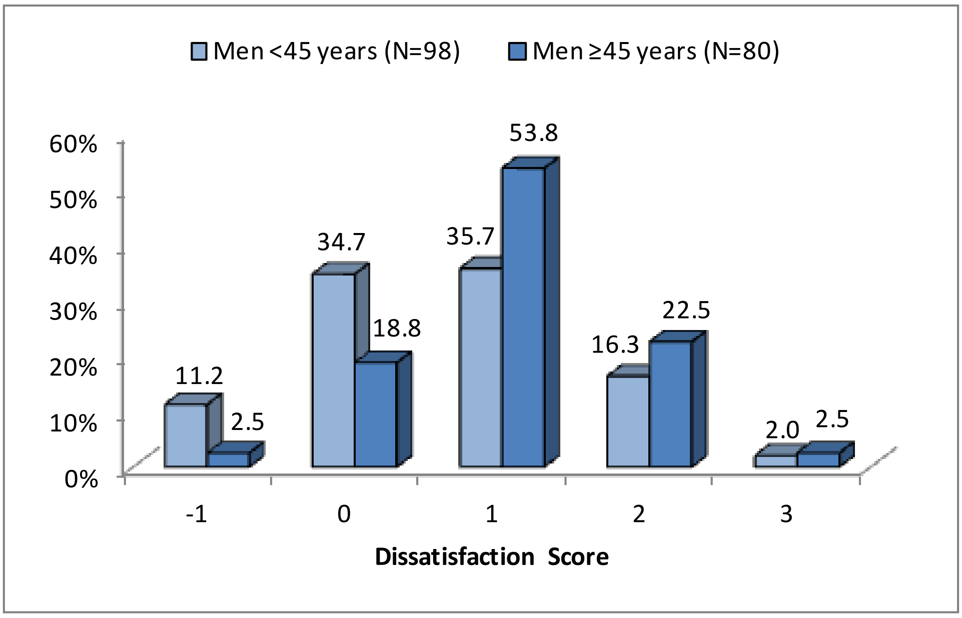


Figure A.5.8. Percentage of men with less than 45 years and with 45 years or more in each dissatisfaction score.

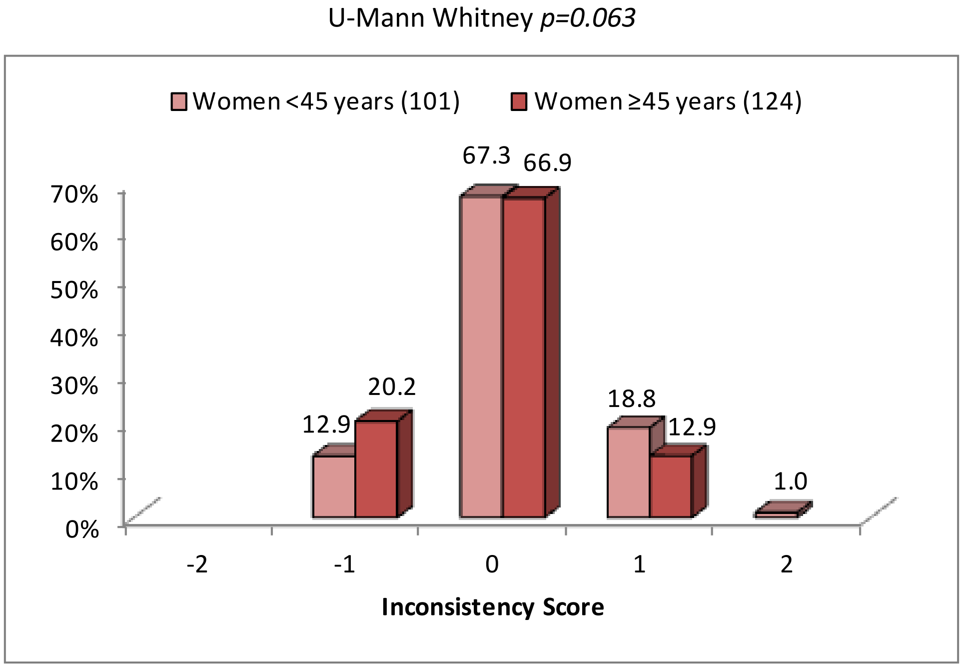


Figure A.5.9. Percentage of women with less than 45 years and with 45 years or more in each inconsistency score.

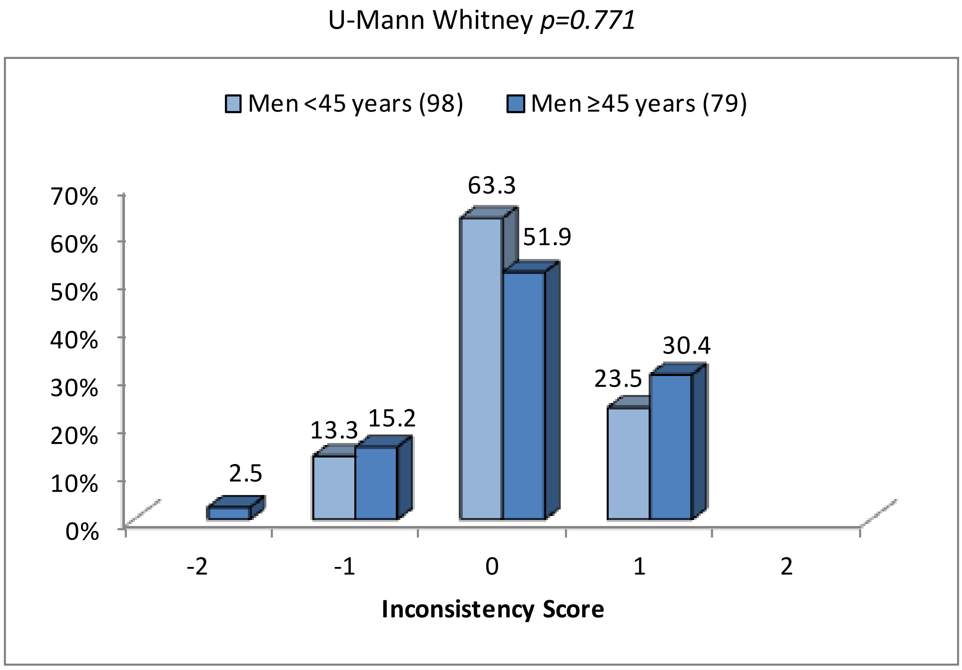


Figure A.5.10. Percentage of men with less than 45 years and with 45 years or more in each inconsistency score.

Table A.5.1. Percentage of individuals, BMI and percentage of obesity in each silhouette representing the current silhouette perceived by the individuals.

Silhouette	Age group	%		BMI (kg/m^2)[&]			Obesity (%)[&&]		
		Men	**Women**	**Men**	**Women**	**P[$]**	**Men**	**Women**	**P[$]**
1	**<45 y**	-	1.0	-	17		-	0	
	≥45 y	-	-	-	-		-	-	
	P[$$]								
2	**<45 y**	5.1	1.0	20.2	17.8		0	0	
	≥45 y	1.3	0.8	22.9	17.4		0	0	
	P[$$]								
3	**<45 y**	14.3	14.6	22.5	19.7	**	0	0	
	≥45 y	6.3	7.3	23.3	21.8		0	0	
	P[$$]								
4	**<45 y**	20.4	33.0	23.5	22.3	*	0	0	
	≥45 y	11.3	8.9	25.7	23.4		11.1	0	
	P[$$]			*					
5	**<45 y**	19.4	21.4	24.8	25.8		0	13.6	
	≥45 y	20.0	25.0	28.4	29.5		25	41.9	
	P[$$]			**	**		*	*	
6	**<45 y**	14.3	7.8	28.7	30.5		35.7	62.5	
	≥45 y	31.3	21.8	30.7	33.4	*	45.8	77.8	*
	P[$$]			*					
7	**<45 y**	12.2	6.8	37.4	42.2		91.7	100	
	≥45 y	18.8	22.6	34.2	37.4		80	96.4	
	P[$$]				*				
8	**<45 y**	6.1	9.7	42.4	44.8		100	100	
	≥45 y	6.3	7.3	37.6	41.6		100	100	
	P[$$]								
9	**<45 y**	8.2	4.9	50.9	51.6		100	100	
	≥45 y	5.0	6.5	40.9	48.3		100	100	
	P[$$]			*					

[&]Mann-Whitney U test was used to obtain the p-values in the comparisons between BMI values.
[&&] Chi-square test was used to obtain the p-values in the comparisons between obesity percentages.
[$]p-values for comparisons between men and women
[$$]p-values for comparisons between individuals with <45 years and individuals with ≥45 years.

Table A.5.2. Percentage of individuals, BMI and percentage of obesity in each silhouette representing the ideal silhouette chosen by the individuals.

Silhouette	Age group	%		BMI (kg/m^2)[&]			Obesity (%)[&&]		
		Men	Women	Men	Women	P[$]	Men	Women	P[$]
1	<45 y	-	1	-	50.4		-	100	
	≥45 y	1.3	3.3	34.8	33.8		100	100	
	P[$$]								
2	<45 y	3.1	4.9	22.3	20.6		0	0	
	≥45 y	2.5	7.3	34.1	33.3		50	66.7	
	P[$$]				*			*	
3	<45 y	14.3	36.9	24.3	23.8		7.1	8.1	
	≥45 y	20	26.8	28.7	29.9		37.5	45.5	
	P[$$]			*	***			***	
4	<45 y	41.8	49.5	27.3	30		17.1	38	*
	≥45 y	35	44.7	29.1	31.6	*	29.6	56.4	*
	P[$$]			**					
5	<45 y	39.8	7.8	33.6	39.6		53.8	87.5	
	≥45 y	36.3	14.6	33.3	39.5	**	69	94.4	*
	P[$$]								
6	<45 y	1	-	31.2	-		100	-	
	≥45 y	5	3.3	28.4	48.8	*	25	100	*
	P[$$]								

[&]Mann-Whitney U test was used to obtain the p-values in the comparisons between BMI values.
[&&] Chi-square test was used to obtain the p-values in the comparisons between obesity percentages.
[$]p-values for comparisons between men and women
[$$]p-values for comparisons between individuals with <45 years and individuals with ≥45 years.

Table A.5.3. Percentage of individuals, BMI and percentage of obesity in each silhouette representing the most attractive silhouette for the opposite sex chosen by the individuals.

Silhouette	Age group	%		BMI (kg/m^2)$^{\&}$			Obesity (%)$^{\&\&}$		
		Men	Women	Men	Women	P$^{\$}$	Men	Women	P$^{\$}$
1	<45 y	-	1	-	50.4		-	100	
	≥45 y	-	0.8	-	20.1		-		
	P$^{\$\$}$								
2	<45 y	2	3.9	23.2	21.8		0	0	
	≥45 y	2.5	8.1	31.6	29.6		100	50	
	P$^{\$\$}$						*		
3	<45 y	20.4	11.7	25	23.2		10	8.3	
	≥45 y	21.3	11.3	30.2	31.9		43.8	64.3	
	P$^{\$\$}$			**	**		*	**	
4	<45 y	67.3	56.3	28.9	26.7	**	28.8	23.2	
	≥45 y	57.5	46	30.6	33.2		43.5	63.2	*
	P$^{\$\$}$			**	***			***	
5	<45 y	9.2	27.2	39.9	33.7		88.9	53.6	
	≥45 y	17.5	33.9	31.2	34.3		50	66.7	
	P$^{\$\$}$			*					
6	<45 y	1	-	58.2	-		100	-	
	≥45 y	1.3	-	35.3	-		100	-	
	P$^{\$\$}$								

$^{\&}$Mann-Whitney U test was used to obtain the p-values in the comparisons between BMI values.
$^{\&\&}$ Chi-square test was used to obtain the p-values in the comparisons between obesity percentages.
$^{\$}$p-values for comparisons between men and women
$^{\$\$}$p-values for comparisons between individuals with <45 years and individuals with ≥45 years.

Table A.5.4. Percentage of individuals, BMI and percentage of obesity in each dissatisfaction score.

Dissatisfaction score	Age group	%		BMI (kg/m^2)[&]			Obesity (%)[&&]		
		Men	Women	Men	Women	P[$]	Men	Women	P[$]
3	<45 y	2	4.9	60	49.1		100	100	
	≥45 y	2.5	6.5	42.6	39.8		100	100	
	P[$$]								
2	<45 y	16.3	14.6	43.7	43.6		100	93.3	
	≥45 y	22.5	29.3	35.7	38.6		83.3	94.4	
	P[$$]			**	*				
1	<45 y	35.7	51.5	28.9	26.2	**	31.4	21.2	
	≥45 y	53.8	50.4	30.3	32		45.2	56.5	
	P[$$]			*	***			***	
0	<45 y	34.7	24.3	23.7	21.3	***	2.9	0	
	≥45 y	18.8	13.8	25.5	22.1	**	6.7	0	
	P[$$]			**					
-1	<45 y	11.2	4.9	21.2	17.2	**	0	0	
	≥45 y	2.5	-	21.6	-		0	-	
	P[$$]								

[&]Mann-Whitney U test was used to obtain the p-values in the comparisons between BMI values.
[&&] Chi-square test was used to obtain the p-values in the comparisons between obesity percentages.
[$]p-values for comparisons between men and women
[$$]p-values for comparisons between individuals with <45 years and individuals with ≥45 years.

Table A.5.5. Percentage of individuals, BMI and Percentage of obesity in each inconsistency score.

Inconsistency score	Age group	% Men	% Women	BMI (kg/m^2)[&] Men	BMI (kg/m^2)[&] Women	P[$]	Obesity (%)[&&] Men	Obesity (%)[&&] Women	P[$]
-2	**<45 y**	-	-	-	-		-	-	
	≥45 y	2.5	-	36.4	-		100	-	
	P[$$]								
-1	**<45 y**	13.3	12.9	29.8	35.1		30.8	61.5	
	≥45 y	15.2	20.2	29.5	35.8	**	41.7	84	**
	P[$$]								
0	**<45 y**	63.3	67.3	30	27.5	**	37.1	25	
	≥45 y	51.9	66.9	31.8	33		61	63.9	
	P[$$]			**	***		*	***	
1	**<45 y**	23.5	18.8	26.9	26.7		13	26.3	
	≥45 y	30.4	12.9	29	28.8		20.8	25	
	P[$$]			**					
2	**<45 y**	-	1	-	23.5		-	0	
	≥45 y	-	-	-	-		-	-	
	P[$$]								

[&]Mann-Whitney U test was used to obtain the p-values in the comparisons between BMI values.
[&&] Chi-square test was used to obtain the p-values in the comparisons between obesity percentages.
[$]p-values for comparisons between men and women
[$$]p-values for comparisons between individuals with <45 years and individuals with ≥45 years.

Appendix III

Table A.6.1. Descriptive statistics for "Obesity in family" by sex and age group.

Obesity in family	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
No	49	20.4	61	19.7	43	27.9	50	30.0	27.1	7.5	25.6	7.7	28.3	4.0	28.0	5.9
Grade 1	35	40.0	50	34.0	33	60.6	84	58.3	30.9	10.3	29.6	9.4	32.7	5.9	32.5	8.0
Grade 2	16	6.3	17	11.8	10	30.0	6	50.0	24.5	3.1	25.0	5.5	28.3	5.4	28.4	4.1

N: number of individuals; %: percentage; m: mean; SD: standard deviation.
No: there are not familiars with obesity; Grade 1: first degree relatives with obesity; Grade 2: second degree relatives with obesity.

Table A.6.2. Descriptive statistics for "Obesity related diseases" by sex and age group.

Obesity related diseases	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
No	95	23.2	120	21.7	39	33.3	88	35.2	27.3	7.3	26.4	7.6	28.5	4.0	29.0	7.4
Yes	5	60.0	10	50.0	47	46.8	53	69.8	40.2	16.9	34.3	12.5	31.3	6.0	34.0	6.8

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.3. Descriptive statistics for "Perceived physical condition" by sex and age group.

Perceived physical condition	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Good	55	10.9	62	16.1	35	28.6	49	32.7	25.9	6.4	24.6	5.9	28.0	4.3	28.3	6.0
Regular	29	31.0	37	10.8	32	37.5	49	40.8	27.1	5.6	25.4	6.6	29.8	5.1	29.0	5.7
Bad	17	64.7	31	54.8	19	68.4	43	74.4	37.5	12.1	33.6	10.7	34.0	5.6	35.8	8.7

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.4. Descriptive statistics for "Physical activity" by sex and age group.

Physical activity	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Nothing	37	35.1	69	31.9	40	55.0	79	62.0	30.7	11.2	27.9	8.8	32.2	6.0	33.1	8.4
Walk	4	75.0	8	25.0	23	30.4	28	32.1	33.0	3.8	31.4	13.0	28.5	3.9	28.3	5.2
Regular	59	16.9	52	11.5	23	26.1	34	29.4	26.2	5.8	24.7	5.6	27.7	3.9	27.7	5.2

N: number of individuals; %: percentage; m: mean; SD: standard deviation
Nothing: the subject do not practice any sport; Walk: the subject walk as sport and not as a daily activity; Regular: the subject practice a regulated sport.

Table A.6.5. Descriptive statistics for "Since how long (Physical activity)" by sex and age group.

Since how long (PA)	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Nothing	37	35.1	69	31.9	40	55.0	79	62.0	30.7	11.2	27.9	8.8	32.2	6.0	33.1	8.4
<1 years	7	14.3	9	44.4	1	0.0	8	75.0	24.9	3.4	30.3	10.9	24.2	-	33.8	6.5
1-2 years	6	66.7	16	18.8	7	42.9	10	20.0	36.0	11.4	27.2	9.1	29.3	4.4	27.6	5.0
3-6 years	13	15.4	11	0.0	7	42.9	12	16.7	25.2	4.4	23.5	2.9	29.7	4.0	25.4	3.5
>6 years	38	15.8	23	4.3	30	23.3	29	24.1	25.9	4.2	23.8	4.5	27.6	3.8	27.4	4.6

N: number of individuals; %: percentage; m: mean; SD: standard deviation.
PA: physical activity (regulated sport); Nothing: the subject do not practice any sport.

Table A.6.6. Descriptive statistics for "Work intensity" by sex and age group.

Labor intensity	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Light	55	23.6	71	26.8	51	31.4	67	46.3	27.1	7.6	27.2	8.3	29.1	5.6	30.3	7.1
Strong	46	28.3	59	20.3	34	52.9	70	47.1	29.2	9.3	26.7	8.4	31.3	5.0	30.9	7.7

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.7. Descriptive statistics for "Sleep quality" by sex and age group.

Sleep quality	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Good	68	16.2	84	17.9	55	36.4	63	36.5	26.9	7.9	25.4	6.2	29.4	4.2	29.5	7.9
Regular	19	36.8	33	30.3	24	58.3	46	54.3	28.3	7.2	28.9	10.6	32.2	7.1	31.2	6.6
Bad	13	53.8	13	46.2	6	16.7	32	62.5	33.4	11.2	32.2	10.6	26.8	5.3	33.1	7.8

N: number of individuals; %: percentage; m: mean; SD: standard deviation

Table A.6.8. Descriptive statistics for "Place of the mean meal" by sex and age group.

Place of the mean meal	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Home	52	30.8	71	29.6	45	53.3	110	56.4	30.0	10.2	28.2	9.1	31.0	5.0	32.2	7.5
Tupperware	13	23.1	28	17.9	5	40.0	6	16.7	27.5	6.8	25.9	8.0	30.4	7.2	27.1	8.5
Restaurant	9	55.6	6	16.7	17	41.2	8	25.0	30.1	4.8	25.0	8.9	30.8	6.3	27.7	7.7
C. dining room	27	7.4	23	17.4	19	10.5	17	17.6	24.0	3.4	25.1	6.0	26.8	3.7	25.2	3.8

N: number of individuals; %: percentage; m: mean; SD: standard deviation.
C: company (place of work).

Table A.6.9. Descriptive statistics for "Number of eating episodes" by sex and age group.

Number of eating episodes	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
3 times	32	34.4	38	21.1	44	36.4	38	47.4	28.6	6.0	27.0	8.0	29.6	5.1	30.6	9.3
4 times	36	13.9	44	25.0	24	25.0	39	53.8	26.2	8.0	27.1	8.8	29.0	4.3	31.8	7.6
5 times	22	18.2	43	23.3	17	76.5	51	43.1	26.7	7.2	26.4	7.3	32.9	6.5	30.1	6.1
6 times	7	57.1	4	25.0	0	0.0	10	50.0	34.4	11.5	24.8	6.4	0.0	0.0	29.7	5.7
1 or 2 times	4	50.0	1	100.0	1	0.0	3	66.7	37.3	18.3	54.8	-	22.9	-	37.7	11.4

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.10. Descriptive statistics for "Smoking" by sex and age group.

Smoking	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
No	36	17.5	64	15.6	23	30.4	69	50.7	26.1	7.1	25.3	7.4	28.7	4.3	30.9	6.6
Yes	38	39.5	66	31.8	63	44.4	72	45.8	31.3	9.5	28.6	8.9	30.5	5.7	30.8	8.4

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.11. Descriptive statistics for "Alcohol" by sex and age group.

Alcohol	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
No	20	45.0	37	40.5	15	53.3	71	53.5	32.6	11.0	29.1	8.5	30.2	6.0	32.6	8.2
Yes	79	20.3	93	17.2	68	36.8	68	42.6	27.0	7.4	26.1	8.1	29.8	5.3	29.1	6.5

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.12. Descriptive statistics for "Alcohol frequency" by sex and age group.

Alcohol frequency	Obesity								BMI							
	<45 years				≥45 years				<45 years				≥45 years			
	Men		Women		Men		Women		Men		Women		Men		Women	
	N	%	N	%	N	%	N	%	m	SD	m	SD	m	SD	m	SD
Never	20	45.0	37	40.5	15	53.3	71	53.5	32.6	11.0	29.1	8.5	30.2	6.0	32.6	8.2
Occasionally	22	27.3	43	14.0	6	16.7	17	41.2	29.0	9.4	25.7	8.4	27.3	6.2	29.7	5.6
Weekends	39	15.4	40	20.0	13	23.1	21	33.3	25.2	4.5	26.5	8.7	27.5	3.4	27.9	5.3
Some days	8	25.0	7	28.6	15	26.7	9	55.6	26.2	5.0	27.1	4.0	29.7	4.2	30.0	6.0
Every days	10	20.0	3	0.0	34	50.0	21	47.6	30.1	11.7	24.3	3.8	31.2	5.9	29.5	8.4

N: number of individuals; %: percentage; m: mean; SD: standard deviation.

Table A.6.13. Descriptive statistics for "Time walking" by sex and age group.

Nutritional category	Time walking (min/day)											
	<45 years						≥45 years					
	Men			Women			Men			Women		
	N	m	SD	N	m	SD	N	m	SD	N	m	SD
No OB	74	44.9	29.9	97	59.4	44.5	49	48.9	34.1	71	54.2	35.5
OB	25	52.2	32.1	29	55.9	45.6	32	83.6	69.6	67	59.0	46.8

N: number of individuals; m: mean; SD: standard deviation.
No OB: no obesity (BMI <30 kg/m^2); OB: obesity (BMI ≥30 kg/m^2).

Table A.6.14. Descriptive statistics for "Time spend on television" by sex and age group.

Nutritional category	Time spend on television (h/week)											
	<45 years						≥45 years					
	Men			Women			Men			Women		
	N	m	SD	N	m	SD	N	m	SD	N	m	SD
No OB	75	14.4	8.1	99	12.0	8.9	50	17.0	10.4	73	14.4	10.3
OB	26	15.7	11.2	30	21.5	15.8	35	18.9	10.5	66	23.8	15.3

N: number of individuals; m: mean; SD: standard deviation.
No OB: no obesity (BMI <30 kg/m^2); OB: obesity (BMI ≥30 kg/m^2).

Table A.6.15. Descriptive statistics for "Sleep duration" by sex and age group.

Nutritional category	Sleep duration (h/day)											
	<45 years						≥45 years					
	Men			Women			Men			Women		
	N	m	SD	N	m	SD	N	m	SD	N	m	SD
No OB	75	7.0	1.0	99	7.2	1.0	50	6.9	1.2	73	6.8	1.2
OB	26	6.9	1.2	31	6.8	1.6	35	7.4	1.1	68	7.0	1.4

N: number of individuals; m: mean; SD: standard deviation.
No OB: no obesity (BMI <30 kg/m²); OB: obesity (BMI ≥30 kg/m²).

Table A.6.16. Descriptive statistics for "Main meal duration" by sex and age group.

Nutritional category	Main meal duration (min)											
	<45 years						≥45 years					
	Men			Women			Men			Women		
	N	m	SD	N	m	SD	N	m	SD	N	m	SD
No OB	75	24.3	10.4	99	25.3	13.5	51	28.5	12.0	72	23.4	10.8
OB	24	19.0	9.5	31	22.7	14.2	32	27.3	14.4	66	20.3	11.4

N: number of individuals; m: mean; SD: standard deviation.
No OB: no obesity (BMI <30 kg/m²); OB: obesity (BMI ≥30 kg/m²).

Table A.6.17. Descriptive statistics for "Smoked cigarettes" by sex and age group.

Nutritional category	Smoked cigarettes (cigarettes/day)											
	<45 years						≥45 years					
	Men			Women			Men			Women		
	N	m	SD	N	m	SD	N	m	SD	N	m	SD
No OB	23	11.0	10.2	45	11.6	9.3	33	18.4	12.8	38	14.9	8.5
OB	15	23.6	14.9	21	14.3	10.1	28	28.8	15.7	30	20.6	13.8

N: number of individuals; m: mean; SD: standard deviation.
No OB: no obesity (BMI <30 kg/m²); OB: obesity (BMI ≥30 kg/m²).