

## Etiology of obesity: two “key issues” and other emerging factors

Lluís Serra-Majem and Inmaculada Bautista-Castaño

Department of Clinical Sciences. University of Las Palmas de Gran Canaria. Las Palmas de Gran Canaria. Spain. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERObn). Instituto de Salud Carlos III (ISCIII). Madrid. Spain.

### Abstract

The current obesity epidemic is known to have coincided with profound societal changes involving both physical activity levels and food consumption patterns as well as demographic and cultural changes affecting the conduct of human beings in various ways.

On the other hand, obesity is a complex and multifactorial chronic disease that usually becomes manifest in childhood and adolescence. Its origin is a genetic and environmental interchange, of which environmental or behavioral factors play the most important role, stemming from an imbalance between energy intake and expenditure. Still and all, it is rather simplistic to assume that obesity is only due to excessive consumption and/or deficient physical activity levels. Currently, various lines of investigation have been initiated that evaluate the determinants of obesity, of which nutrigenomics and gut microbiota deserve special attention.

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Key words: *Obesity. Dietary factors. Physical activity. Sedentary behaviors. Gut microbiota.*

### ETIOLOGÍA DE LA OBESIDAD: LOS “DOS GRANDES” Y OTROS FACTORES EMERGENTES

#### Resumen

Se sabe que la epidemia actual de obesidad ha coincidido con un profundo cambio de hábitos de la población, tanto a nivel de actividad física como de patrones alimentarios y que los cambios demográficos y culturales han afectado el comportamiento de los seres humanos en múltiples vías.

Por otra parte, a obesidad es una enfermedad crónica, compleja y multifactorial, que suele iniciarse en la infancia y la adolescencia, y que tiene su origen en una interacción genética y ambiental, siendo más importante la parte ambiental o conductual, que se establece por un desequilibrio entre la ingesta y el gasto energético. Sin embargo, es muy simplista pensar que la obesidad sólo se debe a un consumo excesivo y/o a una actividad física deficiente. En la actualidad hay abiertas diversas vías de investigación en cuanto a los factores causantes de la obesidad, mereciendo especial atención dentro de los mismos la nutrigenómica y la microbiótica.

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Palabras clave: *Obesidad. Factores dietéticos. Actividad física. Comportamientos sedentarios. Microflora intestinal.*

### Abbreviations

IOTF: International Obesity Task Force.  
WHO: World Health Organization.  
BMI: Body Mass Index.  
WC: Waist Circumference.  
PA: Physical Activity.

### Introduction

Obesity is a chronic disease of multifactorial origin that involves genetic as well as environmental determinants. It's characterised by altered body composition

having an increased adipose component. In the majority of cases, this augmented level of adipose tissue deposits is accompanied by greater body weight and an increased risk of comorbidities that affect the life expectancy and quality.

Evidence points out that a large percentage of obesity cases involve a clear environmental component linked to sedentary lifestyles and dietary habits that lead to positive energy balance and, as a result, the gradual accumulation of fatty tissue. As for current knowledge on the genetic factors implied in obesity, the principal problem is in the majority of cases it deals with a polygenic pathology. Moreover there is an incomplete understanding of its physiopathology which makes it complex to discern the role of distinct polymorphisms and their interaction with environmental factors.

When applying the analysis of body composition, cases of obesity are defined when percentages of adipose tissue are above 33% in women and over 25% in men. There is increasing emphasis on the distribu-

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**Correspondence:** Lluís Serra-Majem, MD, PhD.  
Department of Clinical Sciences.  
University of Las Palmas de Gran Canaria.  
PO Box 550.  
35080 Las Palmas de Gran Canaria. Spain.  
E-mail: lserra@dcc.ulpgc.es

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tion of abdominal fat and its role in augmenting cardiovascular risk.

The International Obesity Task Force (IOTF) and the World Health Organization (WHO) have declared obesity as the epidemic of the 21st century due to the dimensions acquired within the last few decades, its impact on morbi-mortality, quality of life and related healthcare costs. WHO recognizes the impact obesity has on the development of the most prevalent chronic diseases in our society: type 2 diabetes, cardiovascular diseases, musculoskeletal pathologies and an increasing number of certain cancers.

Increased body volume also provokes the onset of disorders related to body image, self-esteem and social interactions. It generates important direct and indirect economic costs as well as significant increases in social and health services (medical visits, absenteeism, loss of autonomy, special needs, etc). Another obesity-related issue is that once established, it's associated with a large degree of therapeutic failures and the tendency towards relapse, thus making prevention a fundamental pillar in combating obesity.

As such, it is of vital importance to evaluate the current state of obesity determinants-physical activity (PA), dietary intake, environmental and sociocultural factors —so as to establish adequate platforms for its prevention.

### Mortality associated with obesity

Diverse epidemiological studies describe a direct relationship between Body Mass Index (BMI) and mortality. The majority of evaluations have demonstrated a J shaped curve in this association. Most studies coincide in cases of increased mortality with BMIs of at least 30. These individuals show a 50% to 100% higher risk of all cause mortality. It's worth noting the result of McGee's study conducted in 2005.<sup>1</sup> "The Diverse Populations Collaboration" is a meta-analysis of 26 studies conducted in diverse countries that evaluated the relationship between mortality for all causes, coronary disease, cardiovascular disease and cancer and persons with overweight and obesity as compared to normal weight individuals. The analysis included 388,622 subjects with a follow up period varying from 3 to 36 years, and the number of mortalities registered was 60,374. Table I shows the relative risk between obese subjects (BMI  $\geq 30$  kg/m<sup>2</sup>) and normal weight persons (BMI 18,5-25 kg/m<sup>2</sup>).

Recently Katherine M. Flegal, of the National Center for Health Statistics in Hyattsville and collaborators published a meta-analysis studying the relationship between obesity and mortality. 97 studies were retained for analysis, providing a combined sample size of more than 2.88 million individuals. They concluded that relative to normal weight, both obesity (all grades) and grades 2 and 3 obesity were associated with significantly higher all-cause mortality. Grade 1 obesity overall was

**Tabla I**  
*Relative risk of mortality for all causes and for diverse causes in obese versus normal weight individuals (McGee D and the Diverse Populations Collaboration)<sup>1</sup>*

Cause of death	Relative Risk of Mortality (Odds ratios and 95% confidence intervals)			
	All causes	Coronary disease	Cardiovascular disease	Cancer
Obese women as compared to normal weight women	1.27 (1.18-1.37)	1.62 (1.45-1.80)	1.52 (1.38-1.69)	1.10 (1.00-1.21)
Obese men as compared to normal weight women	1.20 (1.19-1.28)	1.50 (1.36-1.67)	1.45 (1.32-1.59)	1.05 (0.97-1.13)

not associated with higher mortality, and overweight was associated with significantly lower all-cause mortality. The use of predefined standard BMI groupings facilitated between-study comparisons.<sup>2</sup> However the methodology of this meta-analysis has raised considerable controversy in the scientific community due to identified errors dealing with the age of the populations included and in the time that passed between their inclusion in the cohort until accounting of mortality for previously existing causes of death, and as such, making it obligatory to interpret the results with caution. Nevertheless, it demonstrates that the role obesity plays in overall mortality is variable, and most likely to a considerable degree, from one country to another. Moreover variability is also secular with the passing of time within the same country, essentially for the same causes of obesity (diet and PA), which can vary from one part of the world to another as time elapses. Obesity's role can also be variable due to the weakness of using BMI as a predictor of mortality.

### Factors associated with obesity

A series of sociodemographic and lifestyle factors have been related to excess body weight.

#### 1. Sociodemographic factors

##### Age and gender

In almost all studies conducted in adults residing in Spain the prevalence of obesity is higher in the male subgroup and increases as age advances. These differences in distribution according to age and sex have also been documented in Spain by the ENRICA study,<sup>3</sup> the ENKID<sup>4</sup> and in the National Health Study. Weight indexes and obesity prevalence increase with age in both men and women, reaching a maximum at around 60 years of age.

## Cultural level

In the majority of epidemiological studies on obesity, an inverse relationship has been observed between cultural level and obesity prevalence, so that at lower educational levels, the prevalence of obesity is more elevated. In children and adolescents, and according to the Enkid study, this was particularly important in girls and for the cultural level of the mother.

## Socioeconomic level

The influence of socioeconomic factors is different in developing as compared to more economically advanced countries. In the latter case, generally speaking, obesity prevalence is greater in the most socioeconomically disadvantaged groups. Contrariwise in less developed countries this problem most frequently affects the most well-off socioeconomic groups, particularly those who have incorporated western lifestyles.

## Geographic distribution

Geographic differences have been observed in obesity prevalence for distinct Spanish regions, with the

highest rates seen in the Autonomous Communities located in the Southeastern part of the country, the Canary Islands as well as in the Northwestern region. Figure 1 shows data from the ENRICA study,<sup>3</sup> which illustrates the age-adjusted prevalence of obesity in general as well as central obesity by Autonomous Community.

## 2. Lifestyle related factors

### Sedentary habits

Obesity is more frequent in sedentary persons as compared to those that regularly practice PA. It's been observed that individuals who dedicate more time to sedentary activities and don't regularly do sports more frequently have problems with excess body weight.

### Diet

Greater risk of obesity has been estimated for persons having low fruit and vegetable consumption and a high fat intake, especially in saturated fatty acids. In certain countries, habitual alcohol consumption has

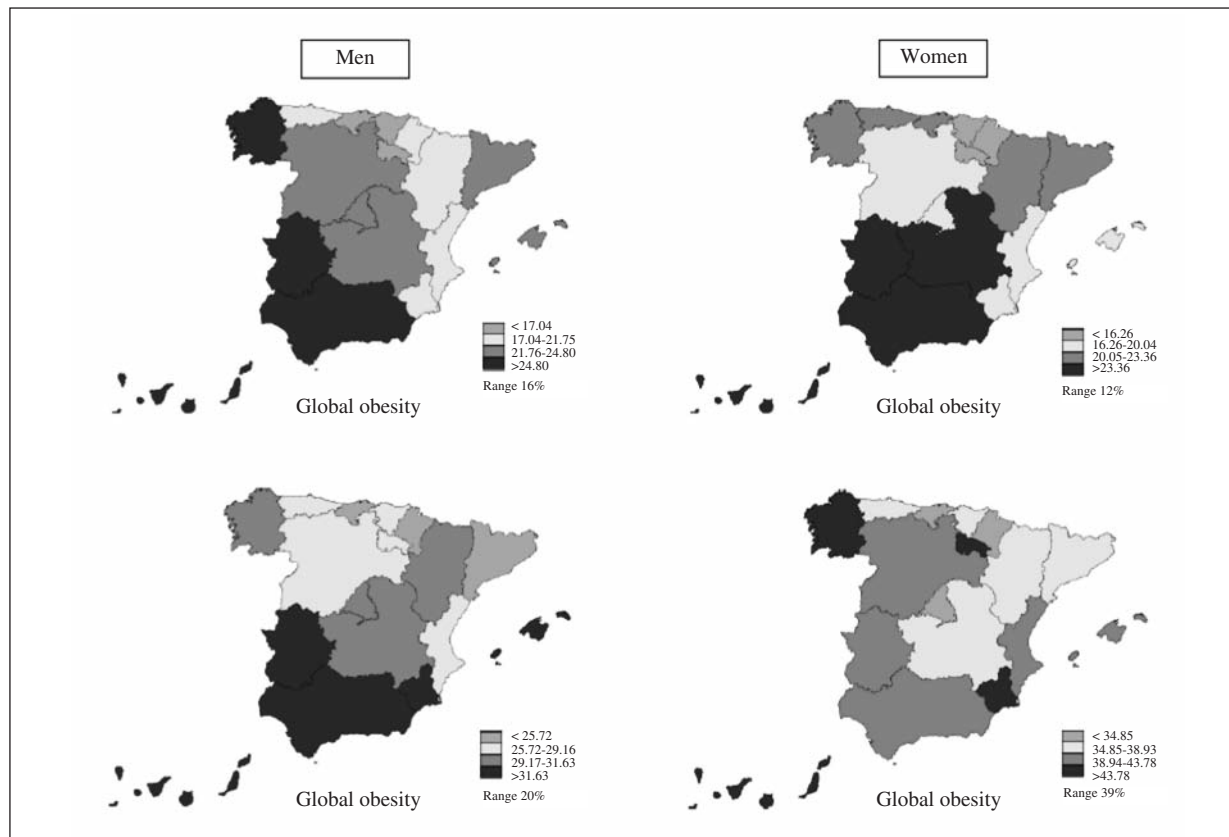


Fig. 1.—Age-adjusted prevalence of general and central obesity by Autonomous Community. ENRICA Study.<sup>3</sup> Source: Gutiérrez-Fisac et al, 2012.<sup>3</sup>

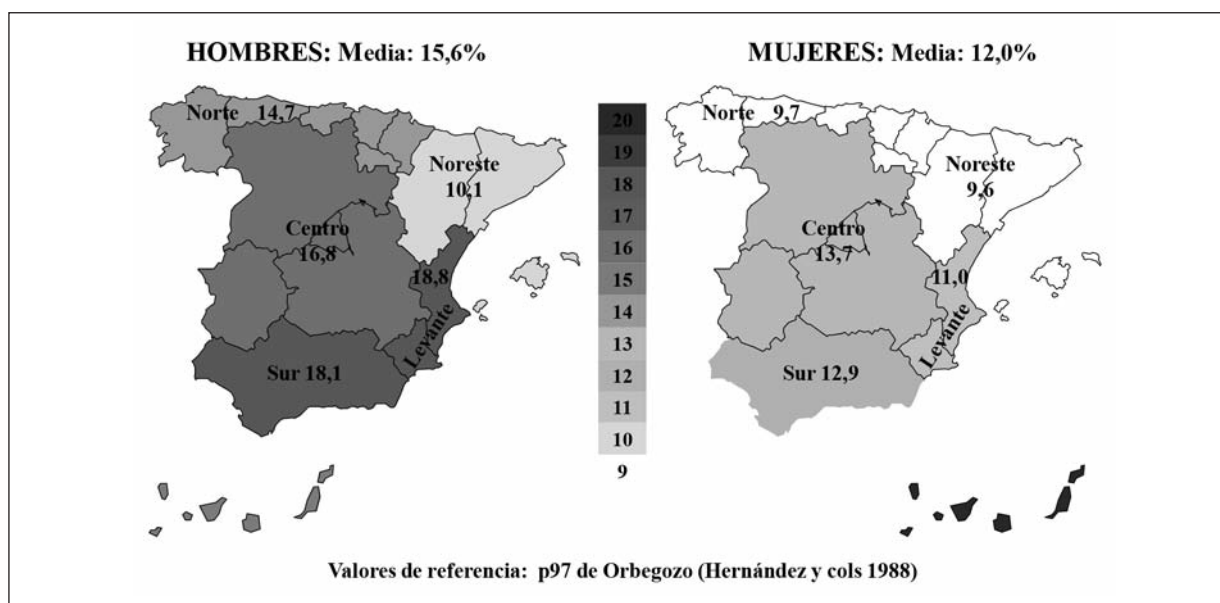


Fig. 2.—Prevalence of obesity in Spanish children and youth, by gender and geographical area. EnKid Study (1998-2000).<sup>4</sup> Source: Serra Majem et al, 2003.<sup>4</sup>

also been associated with excess weight, as well as sugared beverages.

#### Smoking cessation

Increased BMI has also been associated with persons who have quit smoking. The analysis of results from a subsample of the NHANES III Study demonstrated an average weight gain caused by smoking cessation of 4.4 kg in males and 5 kg in females who had stopped smoking within the last 10 years.<sup>5</sup>

#### Number of children (parity)

Women who had given birth to a greater number of children were more frequently obese. In general, women tend to increase their usual weight by a certain number of kilograms two years post partum as compared to nulliparous women of the same habitat and age group. In the DORICA study<sup>6</sup> this positive association between parity and excess body weight was also observed.

#### Etiology of childhood obesity

Multiple studies have shown that obesity in children and adolescents increases the risk of obesity in the future. Its onset in childhood and beyond is clearly predictive for being obese as an adult, even more than other factors such as birthweight and lifestyle variables, and being independent of whether or not parents are obese. Based on data from the EnKid study,<sup>4</sup> conducted in the Spanish population aged 2 to 24 years, the prevalence of obesity in Spanish children and youth (2-

24 years old) was estimated to be 13.9%, applying the 97th percentile cutoff based on anthropometric tables published by Hernández et al. The prevalence of overweight and obesity combined (excess body weight) was 26.3% and 12.4% for only obesity. Obesity prevalence was higher in males (15.6%) than in females (12%) and the same trend was observed for overweight. Stratified by age, obesity was highest in the youngest age group (6-13 years old).

#### Lifecycle stages with increased risk for developing obesity

The prenatal period is one of the three critical moments in the development of childhood obesity in conjunction with the period of adiposity rebound and adolescence. Research analyzing the exposure to hunger during pregnancy or at an early age as well as children of diabetic mothers suggest that excessive or low nutrient intakes during the prenatal and perinatal period play a role in the appearance of obesity in other life stages. In a study conducted at the end of World War II in northern Holland, where food supplies were controlled by Germany from October 1944 to May 1945, the effect that hunger produced on infants born during this period could be observed. In children whose mothers suffered from hunger during the last trimester of pregnancy, at the age of 18 years obesity prevalence was lower. However, an increase in obesity rates were observed in children whose mothers had markedly low intakes during the first two trimesters of pregnancy. It therefore appears that it is in the last trimester of pregnancy and thus of fetal life, when adipocyte replication occurs and adipose tissue increases.



It has been shown that elevated birth weight increases the risk of obesity in later life and that low weight, head circumference and weight for length at birth, accompanied by rapid weight increases in the first years of life, predispose to adults developing more often certain diseases such as obesity, type 2 diabetes, hypertension, hyperlipidemias, metabolic syndrome, coronary disease and arteriosclerosis.

Children born to mothers who smoked during pregnancy and lactation have an increased risk of obesity and type 2 diabetes. The prevalence of obesity in children whose mothers are diabetic is significantly higher than children of the same age born to non or pre-diabetic mothers, independently of the mother being obese at the time of birth.

Moreover, evidence has also shown the importance of nutrition in the first year of life and its relationship to overweight and obesity in later years. Numerous cross-sectional and cohort studies have confirmed that breastfed children present with lower risk for both overweight and obesity.

A second period of time when obesity becomes manifest is around 5 to 7 years old, otherwise known as adiposity rebound. An inverse relationship exists between the age of adiposity rebound and the risk of increased BMI as well as for obesity occurring in childhood and adulthood. Rebound at an early age (<5 years) significantly increases posterior obesity risk as compared to children who have adiposity rebound at a later age (>6 years). Adiposity rebound increasingly occurring at earlier ages could be another factor to keep in mind in rising obesity prevalence.

On the other hand puberty is a period with a tendency towards obesity onset, particularly in females. In this type of pubertal obesity age of menarche is usually earlier than non obese adolescents. Some studies have shown that girls with early menarche (<11 years) are twice as likely to become obese adults compared to those that mature at a later age (>14 years). Moreover, females having earlier menarche appear to present with obesity in adolescence that tends to continue on through adulthood. As such, 70% of obese adolescent males normalize their body weight at a later stage as compared to only 20% in obese adolescent females.

### *Genetic and Family Factors*

Family and genetic factors play an important role in the development of obesity. Through the mechanism of thrifty genes, humans have evolved developing the ability to deposit fat and thus utilize it during periods of energy deficit. This ability for depositing fat has possibly turned into a detriment for developed societies in which overabundance and easy access to foods are the norm.

It should always be kept in mind that a strong interaction exists between genetics and the environment. This is because susceptibility towards obesity is mainly determined by genetic factors, but the environment conditions genotype expression. Currently numerous

obesity-related chromosomes have been discovered and research is focussing on locating the specific genes involved in the development of this disease.

On the other hand, the role that the family context plays in the development of childhood obesity has been recognized in numerous occasions as being a critical factor. Having one or both parents being overweight constitutes a determinant for developing childhood obesity, increasing the risk of their child becoming obese. This may be a result of genetic and environmental factors that can affect the development of obesity in childhood. For children aged 5 and under, the BMI of their parents is more representative than the children's actual weights for predicting the development of obesity in the future. Moreover, data obtained from the Framingham study suggest that in reference to childhood obesity, this is not only associated to parental restrictive dieting but also to their uninhibited eating behavior. As such, restrictive and uninhibited parental dietary habits constitute two potentially modifiable factors that may greatly influence the early eating experiences of their offspring.

### *Nutritional factors<sup>7</sup>*

#### Calorie intake

Diverse studies have evaluated whether obese children had higher calorie intakes than non-obese counterparts. In a review conducted by the authors of the present paper, contradictory results were obtained.<sup>7</sup> Therefore, it remains unclear as to whether obese children consume more calories than non-obese children, making it necessary for further research on this topic. Such studies should analyze the caloric density of the diet in relation to childhood obesity, taking into account important confounding factors of which PA, stage of maturity, basal metabolic rate and parental obesity stand out. Duration of meals has also an impact on caloric intake.

#### Macronutrient composition

Studies have investigated the possible association between the proportion of energy provided by macronutrients in the diet (proteins, fats and carbohydrates) and the presence of childhood obesity. Only two studies analyzing protein intake and obesity were identified and as such no significant conclusions could be made. With respect to fats and carbohydrates, some studies didn't find any association with greater or lesser intakes and childhood obesity, including its development over time. However, after reviewing published studies, it was observed that a large percentage of them had found that in general, obese as compared to non-obese children consumed a higher percentage of energy coming from fats, and in some cases at the expense of a reduced percentage from carbohydrate intake. Studies that eva-

lated changes in fat consumption and their relationship to changes in BMI in children concluded that an increase in the percentage of fat intake was associated with higher BMIs.

Analyzing the possible reasons that could explain the role of greater fat consumption on the development of childhood obesity, it is worth noting that proportions of fats and carbohydrates in the diet tend to be inversely related. As such, decreasing fat in the diet is usually accompanied by an increase in carbohydrate intake and vice versa. On the other hand, diets high in carbohydrates with low to moderate fat content tend to be low in calories. Moreover, numerous studies have shown that fats have a powerful capacity to destabilize control mechanisms for body weight due to their high energy density. Compared to proteins and carbohydrates, fats provide a greater amount of energy per gram. However, fats are easily stored; in conditions of excess calories, fats are store stored at an energy cost of 3%, in contrast to 28% for carbohydrates and 24% for proteins. Fats are also highly palatable and don't appear to possess homeostatic auto regulation that controls the consumption and oxidation of these substances. Furthermore, the satiating effect is relatively small (in reference to proteins and carbohydrates) compared to the quantity ingested. All the aforementioned reasons could help to explain the possible function fats have in the development of childhood obesity.

#### Calorie distribution throughout the day

One of the most frequent alterations in the dietary habits of adolescents consists of irregular eating patterns. The studies reviewed that analyzed this variable seem to indicate that childhood obesity is associated with a lower frequency of breakfast consumption. Obese children and adolescents have less desirable breakfast habits than non-obese counterparts. This leads to the question of whether breakfast has bearing on the adequacy of the total diet. Does the possibility exist that an inadequate breakfast contributes to making further inadequate (nutritionally speaking) choices the rest of the day, and in the long term, to increasing obesity risk? Information is scarce on the role of dinner and of its omission on excess body weight.

#### *Physical activity*<sup>7</sup>

A variety of studies conducted in children and youth show that PA is inversely related to excess body weight. Sedentary activities such as watching television, videos or playing videogames, etc are conducive to becoming overweight. However, other authors after adjusting for basal expenditure, conclude that obese children expend more energy during PA than non obese children, and some studies show distinct results when stratifying by gender.

As such, in boys a greater level of PA corresponds with higher levels of BMI, whereas in girls, PA is inversely related with body fat. Other studies failed to find associations between anthropometric measurements and PA, after adjusting for lean muscle mass. With respect to longitudinal studies evaluating PA and childhood obesity, some authors concluded that PA did not predict the onset of obesity over time, whereas other associated increased PA in obese children with a greater reduction in BMI.

After reviewing studies addressing this issue, it's possible to suggest that PA plays an important role in maintaining normal weight in children and adolescents and that physical inactivity contributes to maintaining obesity. It's well known that PA in these age groups has decreased in the recent past and that perhaps part of this decline is attributable to fewer chances for realizing physical exercise in daily activities, such as walking to school (due to the use of school transport services) and due to increased television viewing, which has displaced PA in youth. In this respect, it seems that watching television implies not only reducing time available for PA but also increasing calorie intake, as it's frequently accompanied by consuming calorie dense nutrient poor foods. Such consumption is sometimes induced by the large quantity of announcements featuring these types of foods that are shown when children's programmes are emitted. Increasing the opportunity to spontaneously play games may be one of the requirements for children to increase their levels of PA. In this way reducing the time that children dedicate to watching television offers the opportunity for spending more time on PA as well as diminishing the response to food advertisements.

#### *Sleeping patterns*

Recent epidemiological studies suggest that short sleep duration may be associated with the development of obesity from childhood to adulthood, and that sleep duration was also inversely associated with BMI and waist circumference (WC) after being controlled for potentially confounding variables.<sup>8</sup> Intervention programs aiming for improving sleeping habits among childhood and adolescents need to consider such potential association of lifestyle variables with sleep duration.

#### **Factors associated with the etiology of obesity in adults**

It's common knowledge that the current obesity epidemic has coincided with profound societal changes affecting PA levels as well as dietary habits, and that demographic and cultural changes have affected human conduct in a variety of ways. Moreover, obesity is a complex and multifactorial chronic disease whose onset usually occurs during childhood or adolescence. Its origin is an interaction between genetics and environ-

ment, of which the latter (environmental or behavioral factors) predominates as conduct is what establishes the imbalance between intake and energy expenditure. However it would be very simplistic to think that obesity is only due to excess consumption and/or inadequate PA. Currently, various lines of investigation evaluate emerging determinants of obesity, of which nutrigenomics and gut microbiota deserve special attention.

#### *Dietary factors associated with the prevention of obesity*

Dietary habits comprise an essential determinant for health, although their exact contribution in health promotion and disease prevention is difficult to quantify. In the last few decades there has been a significant increase in the amount of scientific evidence that supports a series of associations between diverse dietary factors and chronic diseases, particularly cardiovascular disease, cancer, diabetes, obesity and osteoporosis.

On the other hand, few human rights have been violated so frequently and to such a scale as those that address the right to food and nutrition. According to FAO (Food and Agricultural Organization of the United Nations) estimate, approximately 923 million people worldwide don't have access to sufficient quantities of adequate foods so as to meet their basic nutrition requirements, and this constitutes an unacceptable assault against basic human rights.

The nutrition transition phenomenon also stands out, which occurs in less developed countries and requires them to deal with deficiency diseases in conjunction with the onset of chronic diseases such as obesity, resulting from the rapid incorporation of western dietary habits, among other factors. In general we can state that humans have inadequate dietary habits for three reasons: because they don't know how to, they can't achieve it or they don't want to. Confronting these three obstacles requires different actions:

- *Don't know how*: Nutrition education to provide the right information at the right time
- *Can't do it*: Facilitate economic access, geographic and seasonal availability, eliminating barriers in terms of price, distance or climate. It won't be possible to eliminate certain cultural barriers (religious, etc.)
- *Don't want to*: Health education with the focus of achieving behavior modification, strengthening it, keeping in mind pre-existing motivations, attitudes, influences and beliefs of the population. Resorting to food enrichment and/or nutrient supplementation is an option.

#### Food and nutrition in the etiopathogenesis of diseases

The evidence associating diet with the onset of given diseases has exponentially increased over the last

decade. Although findings have at times been contradictory, improved knowledge of the physiopathology of given diseases along with better designed epidemiological studies have facilitated increasing knowledge of a relationship that is still wrought with gaps in its understanding. Apart from obesity, pathologies with the strongest evidence for diet related factors are: cardiovascular disease, cancer, type 2 diabetes mellitus, osteoporosis, dental caries, anemia deficiencies, immunological disorders, cataracts, neural tube defects and Cognitive decline.

#### Mediterranean diet and health<sup>9</sup>

The Mediterranean diet is perhaps the healthiest food model in the world, which has been corroborated by numerous nutrition epidemiological and experimental studies which demonstrate that Mediterranean countries have lower morbidity rates for chronic diseases and longer life expectancy.

The traditional Mediterranean diet is characterized by an abundance of plant food such as bread, pasta, vegetables, legumes, fruits and nuts; the use of olive oil as the main source of fat; moderate consumption of fish, seafood, poultry, dairy products and eggs; consumption in small quantities of red meat and; consumption of wine and champagne (cava) usually accompanying meals.

In the last few years scientific evidence has been accumulating regarding the health benefits of the Mediterranean diet. Currently in Spain, two key projects are being conducted. One is the SUN Project<sup>10-12</sup> (Seguimiento Universidad Navarra), a cohort study conducted by the University of Navarra (initiated in 1999 and with a current total of more than 20,000 participants) and the second is the intervention study Predimed (Prevention with the Mediterranean diet).<sup>13-15</sup> Both studies will continue to provide conclusive data on the benefits of this diet which has already demonstrated favorable effects on cardiovascular morbidity, cognitive decline, certain cancers and obesity prevention, among others.

#### Diet and obesity

Recently the scientific associations, FESNAD (Spanish Federation of Nutrition, Food and Dietetic Associations) and SEEDO (Spanish Association for the Study of Obesity), have published a Consensus Document, about the role of the diet in the prevention of overweight and obesity in adults<sup>16</sup>.

The conclusions obtained were classified according to several evidence levels. Subsequently, in agreement with these evidence levels, different degrees of recommendations were established. These recommendations could be potentially useful to design food guides as part of strategies to prevent overweight and obesity. The major weakness of the Document was that most of the evidence was set from studies not conducted in Spain.

The main conclusions and recommendations of the study were:

*Dietary factors associated with a lower BMI:*

- Diets with higher content of complex carbohydrates (approximately  $\geq 50\%$  of the total energy intake) are associated to a lower BMI in healthy adults.
- A high dietary fibre intake in the context of a diet rich in food of vegetable origin is associated to a better control of body weight in healthy adults.
- A high intake of fruit and vegetables is associated with a lower long-term body weight increase in adults.
- A high intake of whole grains is associated with a lower BMI.
- Even though inconsistent results exist, the studies so far performed suggest a possible role of the “Mediterranean” diet in the prevention of overweight and obesity.
- The existing evidence suggests that greater adherence to the “Mediterranean” diet might prevent increases in WC.
- Vegetarian diets are associated, in healthy adults, to a lower BMI.

*Dietary factors associated with a higher BMI:*

- Dietary patterns of high energy density may lead to body weight increase in adults.
- Some evidence suggests a certain level of association between high ethanol intake and weight gain.
- Frequent intake of sugared beverages is associated with a higher BMI - A high intake of meat and processed meat products might increase weight gain and WC.
- Offering larger portions conditions an increase of the individual’s caloric intake.
- The absence of supermarkets with fruit and vegetable availability, or their location at greater distances—in particular from neighborhoods with low socioeconomic levels—are conditioning factors for a higher population mean BMI.
- The habitual intake of “fast food” (over once a week) might contribute to increased energy intake and to weight gain and obesity.

*Dietary factors not associated with BMI:*

- Fat intake, after adjusting for total energy intake, is not associated to weight gain in healthy adults.
- The intake of olive oil does not seem to be associated with significant body weight gain risk in healthy adults.
- The addition of nuts to the usual diet is not associated with body weight gain.

Moreover, Mozzafarian et al, in 2011,<sup>17</sup> performed prospective investigations involving three separate cohorts that included 120,877 U.S. women and men, who were free of chronic diseases and not obese at baseline, with follow-up periods from 1986 to 2006, 1991 to 2003, and 1986 to 2006. The relationships between changes in lifestyle factors and weight change were evaluated at 4-year intervals, with multivariable adjustments made for age, baseline BMI for each period, and all lifestyle factors simultaneously.

Within each 4-year period, participants gained an average of 3.35 lb (5th to 95th percentile,  $-4.1$  to  $12.4$ ). On the basis of increased daily servings of individual dietary components, 4-year weight change was most strongly associated with the intake of potato chips (1.69 lb), potatoes (1.28 lb), sugar-sweetened beverages (1.00 lb), unprocessed red meats (0.95 lb), and processed meats (0.93 lb) and was inversely associated with the intake of vegetables ( $-0.22$  lb), whole grains ( $-0.37$  lb), fruits ( $-0.49$  lb), nuts ( $-0.57$  lb), and yogurt ( $-0.82$  lb).

Other lifestyle factors were also independently associated with weight change ( $P < 0.001$ ), including PA ( $-1.76$  lb across quintiles); alcohol use (0.41 lb per drink per day), smoking (new quitters, 5.17 lb; former smokers, 0.14 lb), sleep (more weight gain with  $< 6$  or  $> 8$  hours of sleep), and television watching (0.31 lb per hour per day). Non similar studies have been published in Spain and other European countries.

Based on the previous studies, it can be deduced that a need exists to identify those foods whose consumption significantly contributes to the onset of obesity in each country, given that calories obtained from the diet have different distributions according to the food habits of each region. Such information is critical for more effectively targeting and implementing effective prevention policies.

### **Physical activity and prevention of obesity**

In order to understand the importance of PA in the onset and/or prevention of obesity, the relationship between intake, energy expenditure and body fat deposit. Following this, the association between the deficit of PA and illness will be analyzed and then the prevalence of sedentary lifestyles and different means of promoting PA at the individual and population level will be presented.

*Interrelationships between energy intake, energy expenditure and body fat stores*

Obesity is the result of a small and prolonged state of positive energy balance, where total energy intake exceeds total energy expenditure. As Hill pointed out in 2012,<sup>18</sup> understanding the interrelationship between energy intake, energy expenditure and body fat stores



can help us to develop strategies that lead to reducing obesity. The objective of obesity treatment is to reverse this balance and the goal of obesity prevention is to ensure that this balance doesn't become positive.

The messages aimed at the population shouldn't be divided into messages about the importance of eating well in order to prevent obesity and separate messages about the importance of doing PA for the same purpose. Both should go together, as both are components of the same equation, whose result is the deposition of body fat when the equation is positive, loss of body fat when it's negative and maintenance of fat stores when they are balanced. In fact, when referring to weight control, Hill claims that our body functions in a different way when a high level of PA is realized than when at lower levels. The figure 3 illustrates this point.

The idea that energy balance is best regulated at high (but not excessive) levels of have been initiated that PA was first proposed by Mayer and colleagues in the 1950s.<sup>19</sup> They observed that energy intake was better matched to energy expenditure when people were physically active. A healthy body weight is maintained with a high level of PA and a high energy intake. This would be the well-regulated zone in which energy intake and energy expenditure are very sensitive to changes in the other. At low levels of PA, substantial food restriction is needed to maintain a healthy body weight. This would be the unregulated zone in which energy intake and expenditure are only weakly sensitive to changes in each other.

The decline in daily activity that came from industrialization, mechanized transportation, urbanization, and other aspects of technology created the largest decline in activity and created the right conditions under which an increase in food access, availability, and decreased cost could have a major impact on body weight. In effect, the decline in the daily energy expenditure necessary for subsistence prevalent over a century ago was the

“permissive” factor that allowed the effect of the changing food environment to become apparent. Furthermore, as PA levels declined, body weight increased, which would have increased total energy expenditure as a result of increases in RMR (resting metabolic rate) and the energy cost of movement. It is not surprising that total energy expenditure has not changed because becoming obese is a way to increase energy expenditure in a sedentary population.

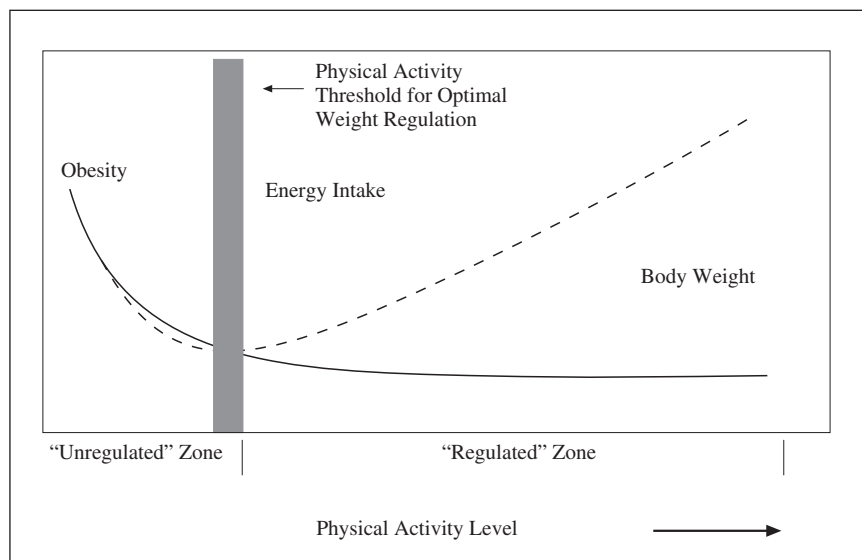
From an energy balance point of view, we are likely to be more successful in preventing excessive weight gain than in treating obesity. The reason is that the energy balance system shows stronger opposition to weight loss than to weight gain. Although large behavior changes are needed to produce and maintain reductions in body weight, small behavior changes may be sufficient to prevent excessive weight gain.

The concept of energy balance combined with an understanding of how the body achieves balance may be a useful framework for developing strategies to reduce obesity rates.

#### *Prevalence of physical activity and sedentary habits*

The population increasingly adopts sedentary lifestyles, which of late have been caused by progressive urbanization, the type of urban planning and transport that determine city living as well as new technologies, passive recreation, new work styles, etc. In addition, over the last 40 years, numerous epidemiological studies have demonstrated that being physically inactive leads to important negative health effects.

On a positive note, the promotion of PA provides a great opportunity for obesity prevention. According to WHO, every year at least 1.9 million people die as a result of physical inactivity. In contrast 30 minutes of regular PA 5 days a week reduces the risk of various



*Fig. 3.—Illustration of the hypothesis that energy balance may be easier to achieve at high energy throughput (ie, high energy expenditure). Shown is the concept of a threshold for PA above which people are in the regulated zone of energy balance and below which they are in the unregulated zone. In the regulated zone, energy intake is pulled along to meet high energy needs, and energy intake and expenditure are very sensitive to changes in each other. At low energy throughput, energy intake and expenditure are only weakly sensitive to changes in each other, and maintaining a healthy body weight requires sustained food restriction. Developed based on Mayer et al<sup>19</sup>. Source: Hill JO et al<sup>18</sup>.*

chronic diseases, making PA a modifiable risk factor for the most common non infectious diseases.

In relation to carrying out PA, it's been observed that although PA in leisure time has remained stable in the last 50 years, technological advances have led to a reduction in energy utilized in household chores, at the worksite and in transport. Moreover, sedentary conduct such as watching television has drastically increased, which translates into an overall decrease in PA. Various sociodemographic groups are especially inclined to being physically inactive, including women, adults from low socioeconomic levels as well as the elderly, people with financial problems and those living alone.

- In *Europe* the Eurobarometer survey conducted in 2009 showed a situation of sedentary lifestyles. The majority of Europeans (60%), don't do any sports (39%) or only rarely do so (21%). As

seen in figure 4, Spain has a high ranking of sedentarism as 42% of Spanish citizens never do any kind of sport.

- In *Spain*, the National Health Survey of 2006 showed that 59.6% of the sample exercised in their free time, with a higher percentage in men than in women (63.1% vs 56.3%, respectively).

#### *Relationship between physical activity and health*

Analytical epidemiological studies have been increasing the evidence base not only for the protective effect of PA against diverse pathologies, but also that being physically fit reduces the risk of all-cause mortality, independently of the presence of other risk factors and also considerably improves quality of life. In addition, even when increases in the level of PA are only

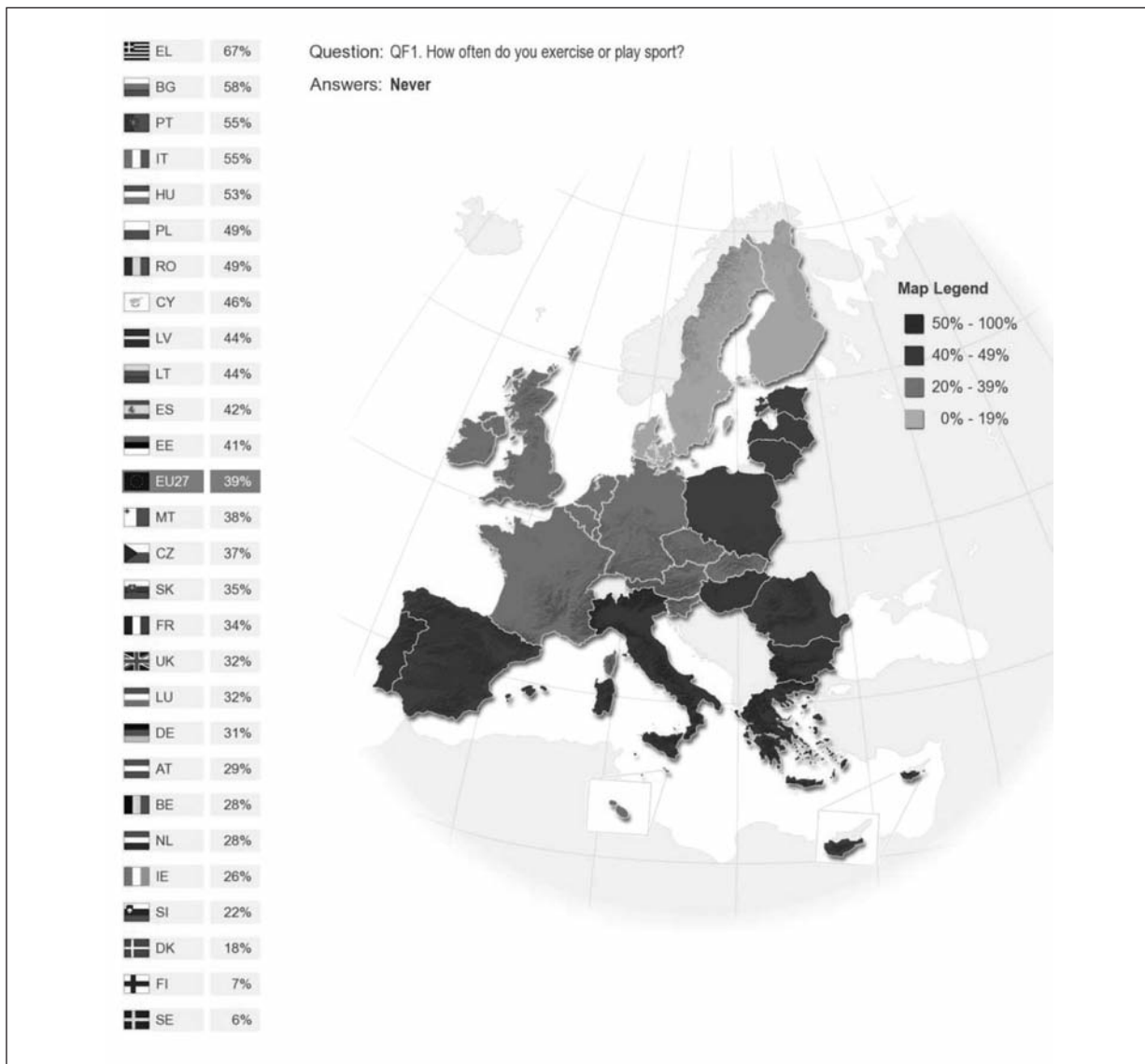


Fig. 4.—Percentage of population that never exercises or play sports in European Union countries. Eurobarometer 2009.

moderate, they confer significant health benefits. Moreover, there is large sector of the population that can benefit from this possibility and thus, considerably increases the potential impact of interventions.

Apart from all-cause mortality and obesity, the main pathologies and processes in which preventive potential exists for adopting a more physically active lifestyle are: Hypertension, Type 2 diabetes mellitus, musculoskeletal diseases, mental health disorders and ischemic heart disease. Although less solid, evidence also exists for a protective effect against the incidence of certain cancers and gallstones.<sup>20-24</sup>

The WHO has designed a global strategy on nutrition, PA and health, which was adopted by the 57th World Health Assembly on 22 May 2004.

In Spain, in order to combat childhood obesity the NAOS (Strategy for Nutrition, Physical Activity and Obesity Prevention) Strategy was established. Apart from striving to improve dietary habits, it also aims to foment the practice of PA, especially during childhood.<sup>25,26</sup> Different Autonomous Communities in Spain have also initiated plans and strategies for fighting against obesity, which include the promotion of PA and healthy eating habits such as the PASEA programme in Galicia, DELTA in the Canary Islands or PAAS in Catalonia.

### Gut microbiota and the development of obesity

The human gut harbors a highly diverse microbial ecosystem of approximately 400 different species, which is characterized by high interindividual variability. The intestinal microbiota has recently been suggested to contribute to the development of obesity and the metabolic syndrome. Transplantation of gut microbiota from obese mice to nonobese, germ-free mice resulted in transfer of metabolic syndrome-associated features from the donor to the recipient. Proposed mechanisms for the role of gut microbiota include the provision of additional energy by the conversion of dietary fibre to short-chain fatty acids, effects on gut-hormone production, and increased intestinal permeability causing elevated systemic levels of lipopolysaccharides (LPS). This metabolic endotoxemia is suggested to contribute to low-grade inflammation, a characteristic trait of obesity and the metabolic syndrome. Finally, activation of the endocannabinoid system by LPS and/or high-fat diets is discussed as another causal factor. In conclusion, there is ample evidence for a role of gut microbiota in the development of obesity in rodents. However, the magnitude of its contribution to human obesity is still unknown.<sup>27</sup>

A recently published review has shown that the fact that gut microbiota can be modulated through dietary components highlights the importance of studying how fatty acids, carbohydrates, micronutrients, prebiotics, and probiotics can influence gut microbiota composition and the management of obesity. It is also crucial to

study the effect of dietary patterns such as the Mediterranean Diet. Gut microbiota seems to be an important and promising target in the prevention and treatment of obesity and its related metabolic disturbances in future studies and in clinical practice.<sup>28</sup>

### Final considerations

Obesity is currently a global public health problem. Obesity in early life increases the risk of long-term energy imbalance, adult obesity and its comorbidities-type 2 diabetes and cardiovascular disease. Since infancy and childhood are critical periods for the adoption of food preferences and PA, prevention strategies must intervene in these early periods to promote healthy habits and reduce risk behaviors.<sup>29,30</sup>

We are witnessing a series of unprecedented scientific, environmental and behavioral changes in the human species, which have brought us many new, and until now unknown, issues that impact upon our health. The obesity epidemic constitutes one of them. Only a global and wide-ranging vision of factors involved in this epidemic will provide us with the necessary tools to introduce adequate and effective preventive measures. Such a vision should address: the idiosyncrasy of distinct populations, their past and present dietary habits, their capacities and attitudes towards PA, their knowledge of nutrition, the interaction between genetics and environment, and a profound knowledge of factors associated with weight gain. Finally, it is essential that interventions include a community based approach combined with a high risk group strategy.

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