anses
French agency for food, environmental and occupational health & safety

Assessment of the risks related to dietary weight-loss practices

Collective expert report

November 2010 Scientific publication

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The "Evaluation of the risks related to dietary weight-loss practices" Working Group

Expert Committee on "Human Nutrition"

November 2010

This report was prepared by the "Evaluation of the risks related to dietary weight-loss practices" Working Group and validated by the Expert Committee (CES) on "Human Nutrition". Given the subject's complexity and the diversity of stakeholders involved, ANSES wished to submit this report for broad consultation among the scientific and medical community, in order to incorporate, where appropriate, further feedback and scientific contributions.

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1. REVIEW OF THE REQUEST

On Thursday 2 April 2009, the French Food Safety Agency received a request from the Directorate General of Health for an assessment of the risks related to dietary weight-loss practices.

2. BACKGROUND

Today in France, the collective social representation of the body makes thinness, or even underweight, a model of beauty. Faced with such demand, weight-loss practices have grown considerably, largely without medical supervision, and sometimes leading to serious abuses: the quest for thinness can result in behavioural eating disorders, especially among vulnerable people and adolescents.
This solicited request falls within the scope of the overall issue of "body image" addressed by the PNNS 2 (2006-2010) and within the framework of development for professionals of obesity management recommendations coordinated by the High Authority for Health. A voluntary collective charter focusing on advertising, fashion and the appearance of the body, as well as protection of people working in the modelling industry, was signed by the Minister of Health, Youth, Sports and Associations and some of the stakeholders concerned, on 9 April 2008. This charter will be followed by concrete proposals.

In pursuing this work, it seems essential to assess the risks associated with following special diets and taking medication or food supplements in order to lose weight. These practices are often recommended or followed without any scientific basis and undertaken indiscriminately.

The objective is to conduct an assessment of the risks related to dietary weight-loss practices, i.e. to evaluate the risks that may, on the basis of a collective, adversarial scientific expert appraisal, be associated with characteristics specific to the different diets studied, during their different phases, regardless of the individual situation of the person following the diet. This is therefore not a benefit-risk assessment based on each individual's specific situation, nor a position on whether or not to follow a diet (i.e. whether or not it is necessary), as this concept is subjective and depends on physiological, pathological, psychological and social characteristics that this assessment cannot take into account. The risks will be assessed within the broad categories of diets for which relevant scientific data are available.
This work is intended to provide a scientific basis for measures that may be proposed by the authorities in the forthcoming PNNS 3, in a context of a sharp increase in dietary weight-loss practices related to the increasing prevalence of overweight and obese in the population, as well as a societal trend towards seeking thinness, which is accentuated by the scale of the marketing activities that promote these various diets. The aim is thus to provide, through a transparent process, objective benchmarks in order to identify more effectively the potential negative consequences of such practices and enable the authorities to develop a better policy of prevention in the forthcoming PNNS 3.

This report will not address restrictions following surgical procedures, nor weight-loss methods not involving a change of diet such as coaching, hypnosis, etc. Similarly, diets based on lifestyles, philosophies or life principles not aiming primarily at weight loss will not be assessed: these include the Okinawa diet (based on the lifestyle of inhabitants of the Japanese island), the macrobiotic diet, the blood group diet and the Mediterranean diet. In addition, diets that focus on changing the way food is consumed have not been considered: for example Fletcherism (chewing food until it becomes liquid in the mouth), the Forking diet (only food that can be consumed with a fork) or the "prehistoric" diet (eating raw food that has not been cooked or processed).

The risk assessment will not include those risks related to the consumption of food supplements claiming weight-loss effects - given their diverse composition (ingredients) and conditions of use (target populations, dose) - despite them being part of the normal diet. A specific risk assessment of these products in due course seems all the more necessary in view of the potential impact of the changing European regulatory context with respect to nutrition and health claims.

3. METHOD OF EXPERT APPRAISAL

The collective expert appraisal was conducted by the "Assessment of the risks related to dietary weight-loss practices" Working Group and validated by the Expert Committee (CES) on "Human Nutrition" which met on 30 September 2010.

4. DISCUSSION

The arguments put forth by the French Agency for Food, Environmental and Occupational Health & Safety are based on the expert report of the "Assessment of the risks related to dietary weight-loss practices" Working Group, which was validated by the Expert Committee (CES) on "Human Nutrition", and whose elements are presented below:

PREAMBLE

For the record, in adults, there is an international consensus on the use of the Body Mass Index (BMI) as a criterion for measuring obesity. The international classification defines obesity in women and in men up to the age of 65 as a BMI equal to or greater than 30 kg/m². Above a BMI of 30 the term obesity is used, whereas morbid obesity is used for a BMI of over 40. A BMI of between 25 and 29.9 corresponds to overweight. Moreover, in adults, abdominal adiposity is associated with metabolic and vascular complications. Waist circumference is the simplest anthropometric index for estimating the extent of abdominal fat deposits. A waist circumference of over 90 cm in women and over 100 cm in men characterises abdominal obesity (WHO World Health Organization 1997). In the elderly there is no consensual definition of obesity.

Table 1: Classification of adults according to BMI

CLASSIFICATION	BMI (kg/m²);	Associated risk of morbidity
Underweight	< 18.5	Low (but increased risk of other clinical problems)
Normal range	18.5 - 24.9	Average
Overweight	25.0 - 29.9	Increased
Obesity	≥ 30.0	
Class I (moderate or common)	30.0 - 34.9	Moderate
Class II (severe obesity)	35.0 - 39.9	High
Class III (morbid obesity)	≥ 40.0	Very high

The definitions of different levels of bodyweight (Annex 3 and 4) in children are as follows:

- underweight (or thinness): BMI < 3rd percentile of French references
- normal weight: 3rd-97th percentile of French references
- overweight (including obesity): ≥ 97th percentile of French references
  or ≥ IOTF-25 threshold of international references
- obesity: ≥ IOTF-30 threshold of international references

In France, overweight and obesity, which affect respectively 31.9% and 14.5% of subjects over 18 years[1], are a real public health problem due to the number of metabolic dysfunctions that may accompany them, and the pathological risks incurred.

The INCA 2 study (AFSSA 2009), conducted in 2006-07 among a representative sample of the population living in mainland France (1455 children aged 3-17 years and 2624 adults aged 18-79 years), aimed primarily to measure as precisely as possible the population's food consumption and nutrient intakes.

Other variables were nevertheless collected in this study, including data on people following weight-loss diets. Thus, according to this study, 23.6% of adults declared that they were following or had followed a weight-loss diet in the year preceding the survey (Annex 6). Regardless of age, dieting was consistently found more frequently in the female population. Forty percent of women considered themselves "too fat" and 60% would like to weigh less. In addition, 44% of men would also like to

[1] ObÉpi-Roche 2009. National epidemiological survey on overweight and obesity.

weigh less. Fifteen percent of 'thin' women (BMI <22) followed a diet during the survey or had followed one during the year preceding the survey. Among adolescents aged 11 to 14 years, 30% considered themselves too fat and 47% would like to weigh less (AFSSA 2009).

These data reflect an increasingly widespread social phenomenon which makes thinness, or even underweight, a model of beauty. Thus, the collectively-developed tyranny of body image - which is not simply a self-centred individual construct, but a social fact - constantly pressures the individual into accepting canons of aesthetics and social norms regarding body size, and reflects the concerns of an era more than the product of one's self-image. This explains that the idea of diet is pervasive in society and requires health professionals to deal with the emergence of the cult of thinness. This social phenomenon has thus contributed to the development of a varied arsenal of therapeutic strategies for dealing with obesity, and an abundance of nutritional practices to reduce body weight. However, weight-loss diets, sometimes unjustified, whether or not followed under medical supervision, are not without psycho-behavioural or organic risks, that may be systemic or limited to specific organs or tissues.

4.1. Methodology followed by the working group

The assessment of the risks related to weight-loss diets was conducted in several stages:

- identification and characterisation of weight-loss diets to determine their impact on nutritional intake, particularly with regard to the risks of inadequate intakes;
- analysis of the available literature to identify the biological and metabolic consequences of weight-loss diets; this analysis included the identification of nutritional imbalances (macronutrients) and deficiencies in vitamin and mineral intakes;
- analysis of the available literature to identify the pathophysiological and psycho-behavioural consequences of weight-loss diets.

Special attention was paid to specific categories of the population such as children, adolescents, pregnant women and nursing mothers, the elderly, athletes and individuals engaging in intense physical activity.

4.1.1.Identification of the major diet types

Whether they are known as weight-loss, slimming or elimination diets, many diets are now available to cause loss of weight through modification of food intake. These diets can be differentiated according to their macronutrient composition, whether in terms of quality or quantity. Different diets propose excluding one or more categories of foods, maintaining a single category of foods or even totally excluding certain foods. The list of diets given is not intended to be exhaustive, as fashions change quickly and each summer sees the emergence of new variants. The diets were selected on the basis of their French popularity, i.e. those most frequently mentioned on the Internet or corresponding to the best-selling books in stores or on the Internet. They are given as examples, since other diets named differently but with similar characteristics will have similar effects. The details of the diets and menus have been drawn from books whenever possible (except for the Lemon Detox, Cabbage Soup and Mayo Diets, which were out of stock with the publisher). As mentioned previously, only diets specifically addressing weight loss were assessed.
Accordingly, dietetic products for very low-calorie diets defined in the Ministerial Order of 20 July 1997[2,3] and in that of 4 May 1998[4] were not assessed in the context of this solicited request.
Moreover, these products, often sold in the form of protein sachets, have different psychological consequences for the consumer. Indeed, it is feared that they may be more destructuring than diets based on foods in their classic form, as they may aggravate the loss of dietary references and disconnect the act of eating from its emotional and social determinants. However, intakes of macronutrients and thus their physiological and iatrogenic effects may be comparable to those of the weight-loss diets examined in this report, if the energy levels involved are identical. Thus, a specific assessment of these products in due course seems necessary and inevitable.

4.1.2. Bibliographic scope for associating hazards/risks with each major diet type

[2] Ministerial Order of 20 July 1997 (Official Journal of 18-09-1997, Rectif. of 13-10-1997) Title I Chapter V
[3] Codex Standard 203-1995
[4] Ministerial Order of 4 May 1998 amending the Ministerial Order of 20 July 1997 implementing the Decree of 24 July 1975 on dietetic and diet products.

The methodology adopted involved collectively defining all the keywords related to the potential hazards of dietary weight-loss practices (the table of keywords is provided in the Annex). The literature search was conducted on conventional literature search websites (e.g. pubmed.gov). Following an initial search, some irrelevant keywords were removed, either because they yielded no references, or they returned a lot of irrelevant references, such as those relating to pre- and post-operative diets. Each expert received a list of references corresponding to his/her area of expertise. He/she then selected the articles relating to the subject of the solicited request. Additional literature searches were performed by the members of the working group during the analysis.

The selected studies were either studies conducted in animals, primarily to determine the medium- or long-term effects of changes in the proportions of macronutrients, particularly protein intake, or studies in humans. Relatively few of the human studies were conducted to investigate the deleterious effects of changes in food intake; the main objective of most was to identify the positive effects of these diets.

4.2. Psychological aspects of human eating behaviour

Like all living things, humans must eat to live. An omnivorous mammal, "it must overcome a dual nutritional challenge:

- ensure energy intake intermittently, while expenditure is continuous;
- avoid toxic substances and maintain a balanced diet by choosing, from a wide variety of foods, those whose combination will cover the basic needs."

The needs of the omnivorous human mammal are not only nutritional. Human survival is also dependent on belonging to a social group whose specific eating culture, 'table manners', all form part of the rules for living together in a given group (Pouillon 1972).

Human eating behaviour, which can be defined as "an integrated series of behaviours, triggered by internal or external stimuli, and contributing to the achievement of a goal," serves this vital dual necessity. But it cannot be reduced to its purely behavioural, acted, immediately observable dimension, which is only the very small, visible part of the adaptive iceberg that is the human eating function. This function has gradually become more complex throughout evolution and is party to the process of humanisation, which is constantly changing. The human eating function fulfils a triple purpose:

- energetic and nutritional, ensuring survival and health at the biological level;
- hedonic, contributing to individual psychological balance through affects and emotions;
- symbolic, of a relational and cultural nature, a constituent of membership of the human community.

"The harmonious conjunction (i.e. the integration of the messages determining them) of these three registers, interdependent and interactive, is vital to the smooth operation of the eating function, which is as essential to the survival of the individual as to the construction and development of his personality." (Guy-Grand et al. 2000)
The least that can be said is that human eating behaviour, inherently multifactorial and heterogeneous, is a vital adaptive function that is particularly complex to observe, understand and describe.

Food intake is controlled by an infinitely complex and sophisticated, yet poorly understood, physiological regulation system which ensures weight stability and coverage of energy and nutrient requirements in terms of the micronutrients needed for health. "In a healthy subject, weight and energy reserves (body fat) are relatively constant - fluctuating from 1 to 2% on a weekly basis - around a 'reference value'." Laplace describes the "extraordinary machinery entirely devoted to the control of [the] food intake by redundant systems with great finesse." Controlled by the brain, their "central integrator", "four partners (level of energy intake, metabolic energy use, level of fat reserves and functional digestive capacity) [ensure] the regulation of energy balance and body mass" (Laplace 2008).

On a psychological and behavioural level, eating behaviour must also meet the oral hedonic requirements vital to the subject's instinctive, emotional and affective stability, and must facilitate the subject's successful socialisation through conviviality and adherence to cultural values transmitted by eating traditions.
"The term "pathology of eating behaviour" refers to when eating habits:

- differ significantly from the attitudes usually adopted by most individuals placed in the same nutritional and sociocultural environment;
- induce adverse consequences for health of a somatic (obesity, malnutrition, undernutrition) or psychological (social exclusion, a feeling of abnormality, depression) nature."

According to Le Barzic, this definition is not without ambiguity. It may designate as 'normal' cognitive restraint behaviour whose pathogenic effects are known (Le Barzic 2001) but which is nevertheless becoming standard behaviour among most consumers by virtue of the fight against obesity. It risks only accepting as 'normal' the eating behaviour of a subject of normal weight (between 20 and 25 kg/m^2 according to the WHO), who sits down at the table to eat at regular times, three times a day, who does not snack between meals and who follows the recommendations in terms of energy, macronutrients and micronutrients, while satisfying his hedonic needs through conviviality guaranteeing his proper social integration. This same definition can lead to the spontaneous eating behaviour of an obese subject being designated as 'abnormal' solely because of his obesity. How does an obese subject, with a happy family life, comfortable in society, whose weight has been stable for years and who has never suffered from the slightest binge eating disorder or compulsive snacking behaviour, manage to get their eating behaviour accepted as normal? It has been shown that certain behaviours observed among the obese were the consequence and not the cause of obesity (Stunkard et al. 1992). Should these behaviours be considered as normal or pathological? All tastes and appetites are merely part of human nature! Is it appropriate to establish a statistical average at the population level as a normal value for individual nutrient requirements? Will its systematic individual application not induce a risk of imbalance in subjects whose idiosyncrasies place their needs at the extremes of the normal probability curve?

Medical semiology of eating behaviour, which emphasises the function's behavioural logic and nutritional aspects, is particularly revealing about the subjectivity of the concept of normality. "As the standard for a normal eating behaviour has not yet been scientifically established [*editor's note: if indeed it even can be one day*], 'normality' can be determined by noting the absence of disorders, [and] an individual's chances of getting his eating behaviour accepted as normal diminish as the science of eating disorders progresses." (Le Barzic et al. 1998). The influence of American criteriology (Diagnostic and Statistical Manual of Mental Disorders), weighs on this standardised design of eating behaviour (American Psychiatric Association 1983, 1989, 1996).
The individual clinical approach can be adapted to the infinite variety of capacities for adjustment, unique to the countless situations encountered by human consumers.

The psychoanalyst Jean Bergeret considered psychodynamic *normality* to be "a state of happy functional adequacy" in a given individual "who indulges in a rather flexible interaction between their instinctive needs, [...] on both a personal and social level, while taking reality fully into account" (Bergeret 1974). Transposed to eating behaviour, this definition leads us to consider as *normal* a behaviour that fulfils its triple mission and satisfies equitably each of a given individual's specific energy, psychological and social requirements, in a given environment, without any of them being incompatible with the satisfaction of the others. According to the WHO's definition of health (2003): "Health is a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity."

Disease occurs when the harmonious adjustment of this complex, subtle and evolving adaptive system is prevented by one or more external or internal factors. Inappropriate medicalisation may be a pathogenic factor for eating behaviour; by imposing nutritional standards without consideration of individual tastes and appetites, it risks bypassing the metabolic regulation signals, hunger and satiety, and facilitating the onset of behavioural eating disorders (Le Barzic 2000).

The best may be the enemy of the good. The blind application of food standards without regard for singular diversity can lead to worse evils than those it claims to treat. This is why diagnosis and dietary 'prescriptions' should be restricted to clinicians who are specialised, experienced and aware of the complexity of the phenomena involved.

4.3. Impact of the different diets on nutrient intakes

4.3.1. General principles of the various diets studied

A search on the Internet (blogs, websites selling books online, etc.) revealed the wide variety of weight-loss diets, which varies with fashions and times of the year. This diversity explains why the establishment of an exhaustive list of weight-loss diets is not possible. Thus, the chosen diets[5] were selected on the basis of their apparent popularity, i.e. those most frequently mentioned on the Internet or corresponding to the best-selling books in stores or on the Internet. These diets are as follows (in alphabetical order):

- The Atkins Diet: This consists of four phases. The first lasts at least two weeks, during which sources of carbohydrates (sugar, sweetened products, starches, legumes, fruits, milk, yogurt, etc.) should be avoided and carbohydrate intake should not exceed 20 g per day. The second phase gradually reintroduces foods containing carbohydrates, such as fruits, cereals and dairy products. This phase continues until only 2 to 4 kg must be lost to attain the target weight. The third, or stabilisation phase, enables carbohydrate intake to be increased by 10 g daily. When the desired weight has been stable for four weeks, the subject can go to the final phase. This lasts a lifetime and the amount of carbohydrates depends on each individual and on the level of physical activity (Atkins 2002; Freedman et al. 2001).

- The Cabbage Soup Diet: this consists in drinking a bowl of soup at every meal for seven days. Added to this is fruit (day 1), vegetables (day 2), fruits and vegetables (day 3), bananas and skim milk (day 4), beef and tomatoes (day 5), veal or beef and vegetables (day 6), brown rice, unsweetened fruit juice and vegetables (day 7)[6].

- The Chrononutrition Diet (Dr Delabos): its principle is "to align food consumption with the body's biological clock". Breakfast should be high in fat but contain no sugar, lunch should be rich in protein, the snack should include fruit and dark chocolate, and dinner should be "light". This diet requires that the order of meals not be reversed, there be no eating "at inopportune moments", the share of "plant foods" in dishes not be increased, and that hunger be satisfied with "animal foods" but never with "plant foods", etc. (Delabos 2005).

- The Dr Cohen Diet proposed in the book "*Maigrir, le grand mensonge*" [Slimming, the Big Lie]: the first phase, "the booster effect diet", aims to achieve rapid weight loss (5 kg in 15 days) through a diet low in "sugars[7]" (less than 40 g/day). This step should not be followed for more than one month. The second phase is the "balanced diet": according to the author, its calorie level should be between 1200 and 1500 kcal and requires strict monitoring of food intake while maintaining a normal social life. The third step is the consolidation phase, during which it is recommended that one of the two main meals follows the menus from the second phase (Cohen 2009).
During these phases, the author explains that if any weight is regained or if weight loss levels off, the diet proposed in Phase 1 may be resumed for a few days.

- The Dukan Diet proposed in the book *"Je ne sais pas maigrir"* [I Don't Know How to Lose Weight]: Phase 1 of the diet or the "attack phase" (diet of 'pure' proteins) lasts for 5 days. The "cruise phase" (diet of 'alternative' proteins) consists of alternating days of eating exclusively protein then protein associated with vegetables, for an average duration of one week per kilogram lost. The phase of consolidation of the weight obtained (lasting 10 days for each kg lost) includes the protein foods consumed during the "attack phase", the vegetables consumed during the "cruise phase", plus a serving of fruit per day (except for bananas, grapes and cherries), two slices of wholemeal bread per day, 40 g of ripened cheese, 2 tablespoons of oat bran, and a 25 minute walk. Each week it is possible to consume two servings of starch, some leg of lamb, roast pork and two banquet meals, while reserving one day for eating protein foods. The final stabilisation phase must include one fixed day per week for eating foods from the "attack phase" (Thursdays, for life) and the 3 tablespoons of oat bran per day. It is also recommended to use the stairs rather than the lift (Dukan 2010).

[5] Not an exhaustive list
[6] http://www.regimesmaigrir.com/regimes/soupe-aux-choux.php
[7] Digestible carbohydrates with low and high molecular weights (sugar and starch in particular)

- The Dr Fricker Diet proposed in the book *"Maigrir vite et bien"* [Lose Weight Quickly and Well]: it consists of an initial phase of weight loss (between 3 and 8 weeks) during which proteins play an important part. This phase is based on meat, fish, dairy products, fruit and at least 400 grams of 'low-carbohydrate' vegetables. They are accompanied by a "small amount" of fat. This phase is based on three meals a day. Alleged weight loss during this period is between 1 and 1.5 kg per week for women, and between 1.5 and 2.5 kg for men. The second phase of the diet allows the consumption of cereal products and some starchy foods amounting to 100 to 150 g cooked weight per day and a 50 to 60 g piece of bread. Readjusting the body, for at least two weeks, to larger servings of food, is recommended. The last step of the diet allows unlimited consumption of foods rich in 'complex carbohydrates'. References to stabilise the weight attained are also given (Fricker 2010).

- The Lemon Detox Diet: this is not strictly speaking a diet as it corresponds more to a fast. It consists of a drink composed primarily of lemon juice and maple and palm syrup. The lemon is meant to act "like an internal detergent to dissolve excess fat". This diet must be followed for between 5 and 7 days for beginners and for 10 days for more experienced dieters[8].

- The Mayo Diet: this lasts 14 days during which fats, sugars, starches, pulses and dairy products are prohibited[9].

- The Montignac Diet proposed in the book *"Je mange donc je maigris !"* [Eat yourself slim!]: Phase 1 of the diet must last at least two months and involves never combining 'bad' carbohydrates (e.g. white bread) with fats (e.g. meat) in the same meal. Carbohydrate-fat components (e.g. chocolate, avocado), potatoes, white rice and white pasta must all be avoided, and only unrefined flour and bread should be eaten. Phase 2 of the diet aims to maintain the 'new weight balance'. It incorporates the principles of Phase 1 (i.e. not combining fats and carbohydrates, not eating sugar, drinking as little as possible while eating, etc.) (Montignac1991).

- The Ornish Diet: This vegetarian diet is very low in fat. The consumption of meat, fish, and sauces containing avocados, olives and butter, etc. should be avoided. Unlimited consumption of vegetables and fruit is permitted. It is also recommended to eat several small meals rather than three meals per day[10].

- The Scarsdale Diet (Dr Tarnower): this lasts 14 days during which alcohol and fat are excluded. Weight loss is estimated by the author at 0.5 kg/d and up to 9 kg or more in two weeks (Tarnower et al. 1979).

- The Sonoma Diet (Dr Guttersen): Phase 1 lasts 10 days, during which products made from refined flour and refined sugar, sweetener-based confectionery, fruit, wine and potatoes are excluded to reduce habituation to sugar. Quantities are specified as a percentage of the size of the plate. Phase 2, to be followed until the desired weight is reached, includes fruit, a wider choice of vegetables and low-fat natural yogurt. Sugar-free confectionery is permitted, and a glass of wine per day (Guttersen 2007).

- The South Beach Diet (Dr Agatston): Phase 1 of this diet lasts two weeks, during which bread, rice, pasta, potatoes, pies, croissant-like pastries and all fruit are excluded. During Phase 2, to be followed until the desired weight is reached, these foods are allowed again. Phase 3, which is to be adopted on a permanent basis, is no longer regarded by the author as a diet but as a lifestyle (Agatston 2004).

[8] http://www.regimesmaigrir.com/regimes/citron-detox.php
[9] http://www.mesregimes.com/regime_mayo.htm
[10] http://www.regimesmaigrir.com/regimes/ornish.php

- The WeightWatchers Diet: this focuses on motivation and peer support provided to members at weekly meetings. It works according to a set number of points depending on the person's height, weight, age and sex. This unit, called a "ProPoint", is based on measurement of the energy remaining available in the body once the food has been processed[11]. Thus, each food is evaluated in terms of "ProPoint" units. This "ProPoint budget" should be used according to a number of daily recommendations: eat at least 200 g of fruit and 300 g of vegetables, consume two to three dairy products a day, drink 1.5 L of fluids (at least 1 L of water), consume 2 teaspoons of vegetable fat, take carbohydrates with at least two meals, eat protein with at least one meal and engage in physical activity for at least 30 minutes (Freedman et al. 2001).

- The Zone Diet (Dr Sears): This diet distinguishes men from women and considers that weight gain is dependent on insulin levels. Thus, 'dangerous' foods such as pasta, rice, cereals, bread, dried fruit, fruit juice, etc. must be "removed from the kitchen". According to the author, the distribution of macronutrients as a function of total energy intake (TEI) should be as follows: 40% carbohydrate, 30% fat and 30% protein (Sears 2000).

Key points

- **Changing food intake in order to lose weight may involve several mechanisms such as the amount of energy and the macronutrient composition (e.g. high in proteins, low in carbohydrates).**
- **Some diets focus on the total exclusion of some foods or food categories.**
- **For some weight-loss diets, the duration varies according to the individuals and the amount of weight they wish to lose.**
- **It is not possible to establish from the data for how long and at what frequency an individual will follow a diet, which can mitigate or exacerbate the consequences on health.**

[11] Extract from the hearing with the WeightWatchers France team, and the website http://www.weightwatchers.fr

4.3.2. Characterisation of the diets

The objective is to be able to classify the diets by quantifying intakes (energy, macronutrients, vitamins and minerals) and comparing them to requirements.
By definition, the estimated average requirements (EAR) apply to individuals, whereas the [French] population reference intakes (ANC - *apports nutritionnels conseillés*) relate to population groups, in both cases ones in good health. The nutritional requirement is the amount of nutrients needed for the proper functioning of the body. The ANC for a given nutrient is defined as the EAR plus two standard deviations of 15% each, such that it covers the needs of virtually the whole population (97.5%)[12].

For each diet, the accompanying book was consulted to determine the dietary recommendations (proposed menus) related to the diet. When there was no accompanying book (i.e. for the Cabbage Soup, Lemon Detox and Mayo diets), the recommendations were obtained from the Internet by visiting discussion forums devoted to the various weight-loss diets. Lastly, some diets were relatively complex to model. For instance, some cannot easily be transposed to French eating habits (e.g. the American Atkins Diet). Moreover, some diets do not offer typical days (for example, WeightWatchers, which offers a daily credit of points). Thus, the nutritional intakes allocated to these diets were drawn from a publication (Freedman et al. 2001).

For certain weight-loss diets, several typical days are proposed for any given phase. In this case, the menu for one of them was chosen, preferably the typical menu with the most quantitative data.

For each typical day, the dietary recommendations for the diets studied were recorded for each of that day's meals: the type of foods, portion sizes and, where applicable, recipes. When portion sizes were not specified, average data from the INCA2 study were applied. Similarly, some diets introduce a notion of flexibility, by allowing unlimited consumption of certain foods. This theoretical variability is difficult to take into account and model, since it varies with individuals. For the particular case of the Cabbage Soup Diet, for the foods eaten in addition to the soup, quantities were approximated from the photo manual used to estimate portions for the Su.Vi.Max study. The maximum portion size was chosen, since these foods accompany a single bowl of soup.
The amount of sodium added during cooking or during food preparation was taken into account only when its use was specifically mentioned in the books.
Data on the nutritional composition of the foods listed above were extracted from the Ciqual database[13]. The list of elements and components selected for analysis is as follows: energy, fats, proteins, carbohydrates, fibre, iron, calcium, magnesium, potassium, selenium, sodium, vitamin B9, vitamin D, vitamin C and finally vitamin E.

Comparing consumption data with nutritional composition data enabled nutrient intakes to be calculated, the results of which are detailed in the following pages.

For each diet, a typical day for each successive phase was analysed separately. For example, Dr Cohen recommends a first diet phase, called the "booster", followed by a second phase, known as "balanced". In the analyses performed, the first of these phases has been named Cohen1 and the second Cohen2.

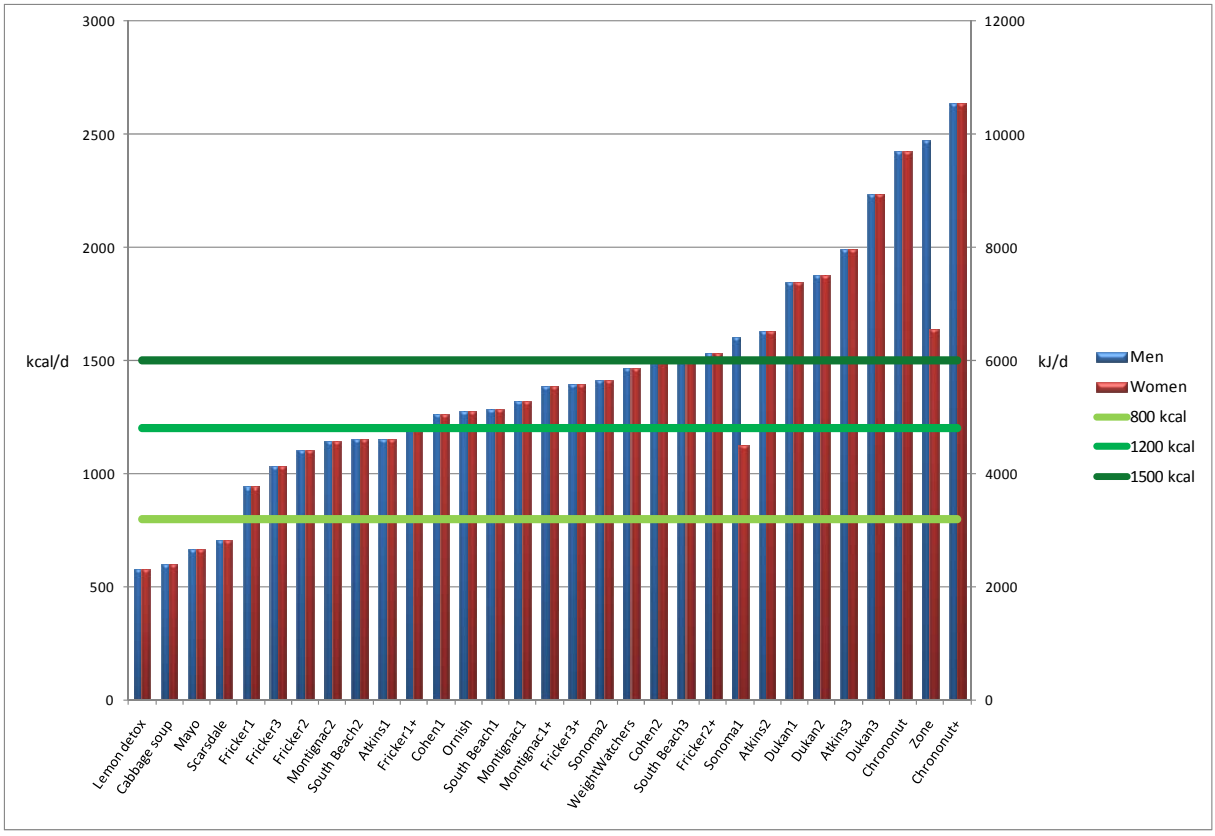
Moreover, for some diets, a basic menu is proposed, which can be supplemented with additional food taken during the meal or as separate snacks. In this case, nutrient intakes were calculated first for the basic menu (e.g. Fricker1 in the legends, for the first phase of the Dr Fricker Diet) and secondly for this menu supplemented by the optional food intake (e.g. Fricker1**+** for this first phase, with the foods proposed in addition).
For most diets, the food recommendations are identical for men and women. However, the recommendations for the Zone and Sonoma diets differ according to sex (alternative snacks for the Sonoma Diet, or different menus for the Zone Diet). The energy and nutrient intakes therefore vary by sex only for these two diets.

The overall results for each component are detailed and discussed in the following pages. These results are presented independently for each phase of the weight-loss diets.

[12] The estimated average requirements result from values acquired from an experimental group consisting of a limited number of individuals and corresponding to average individual requirements.
[13] ANSES (2010). Ciqual databank of the nutritional composition of foods, consulted in August 2010

4.3.3.Impacts on energy and macronutrient intake

Figure 1: Energy intake according to diet and gender (kcal/d and kJ/d).



The energy intakes associated with the different diets and diet phases studied range from 574 to 2600 kcal/d (2.4 to 11 MJ/d), given that the ANC is respectively 1800 and 2200 kcal in women and men, for normal physical activity.

More specifically, the Lemon Detox, Cabbage Soup, Mayo and Scarsdale diets provide less than 800 kcal per day. In contrast, the Chrononutrition, Chrononutrition+, Dukan3 and Zone diets (for men) correspond to higher energy intake at 2000 kcal.

Energy intakes for the phases of the Fricker1, Fricker2, Fricker3, Montignac2 and South Beach2 diets, and the Atkins1 and Sonoma1 diets for women are below 1200 kcal. The phases of the Fricker1+ and Fricker3+, Cohen1, Ornish, South Beach1, Montignac1, Montignac1+, Sonoma2, and WeightWatchers diets provide an energy intake that lies between 1200 and 1500 kcal.

Macronutrient intakes are shown in grams per day and as a percentage of total energy intake.

Figure 2: Protein intake according to diet (g/d).

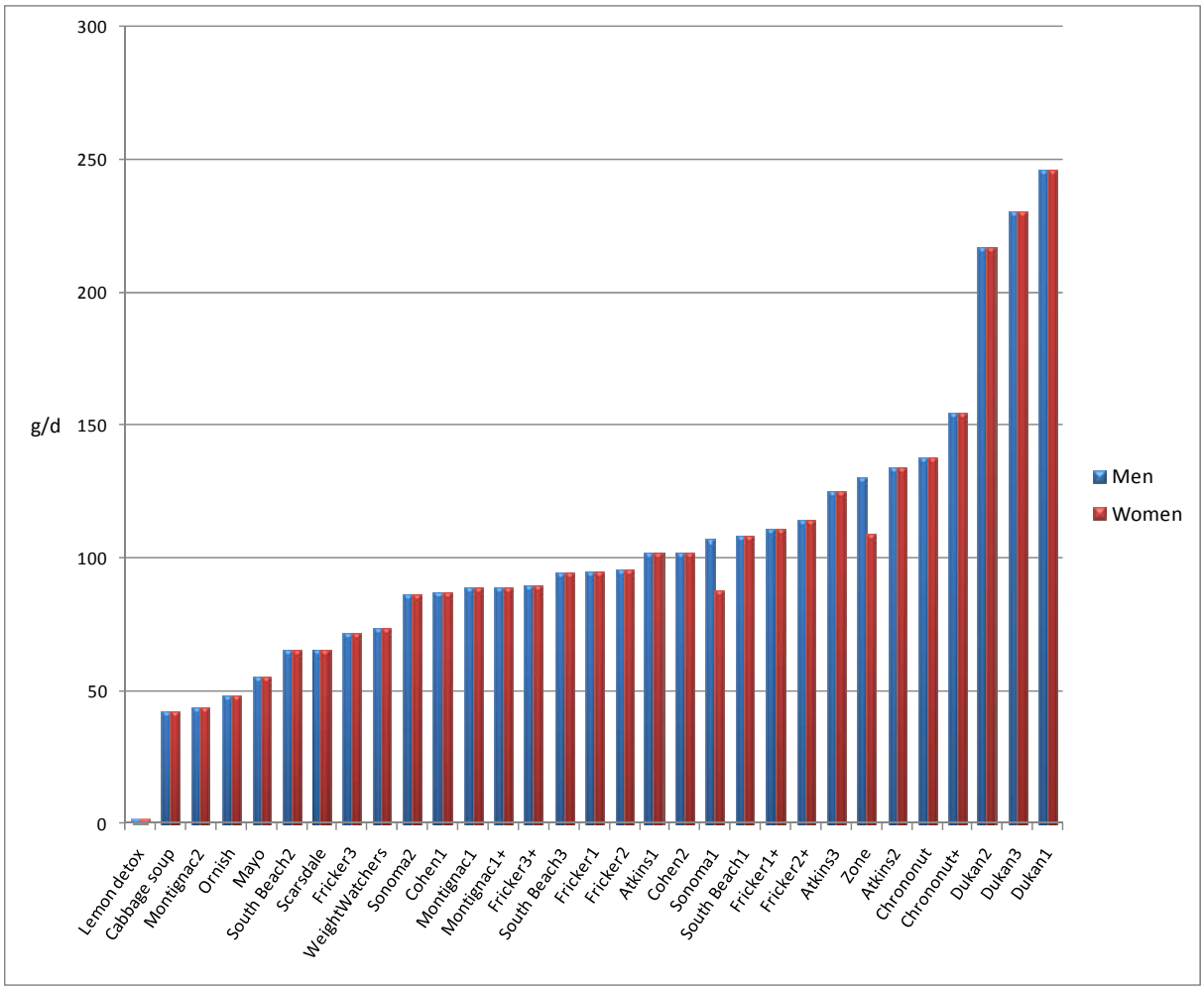
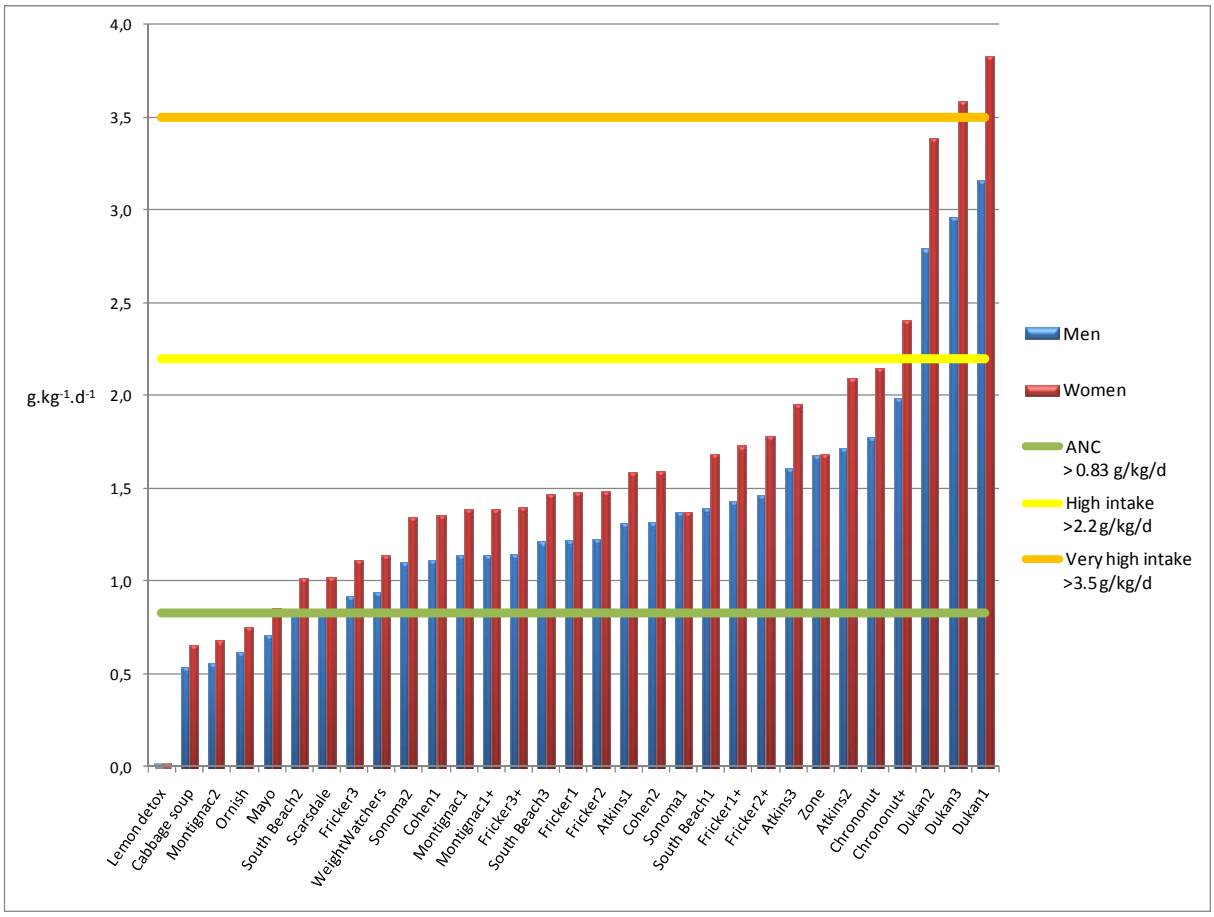
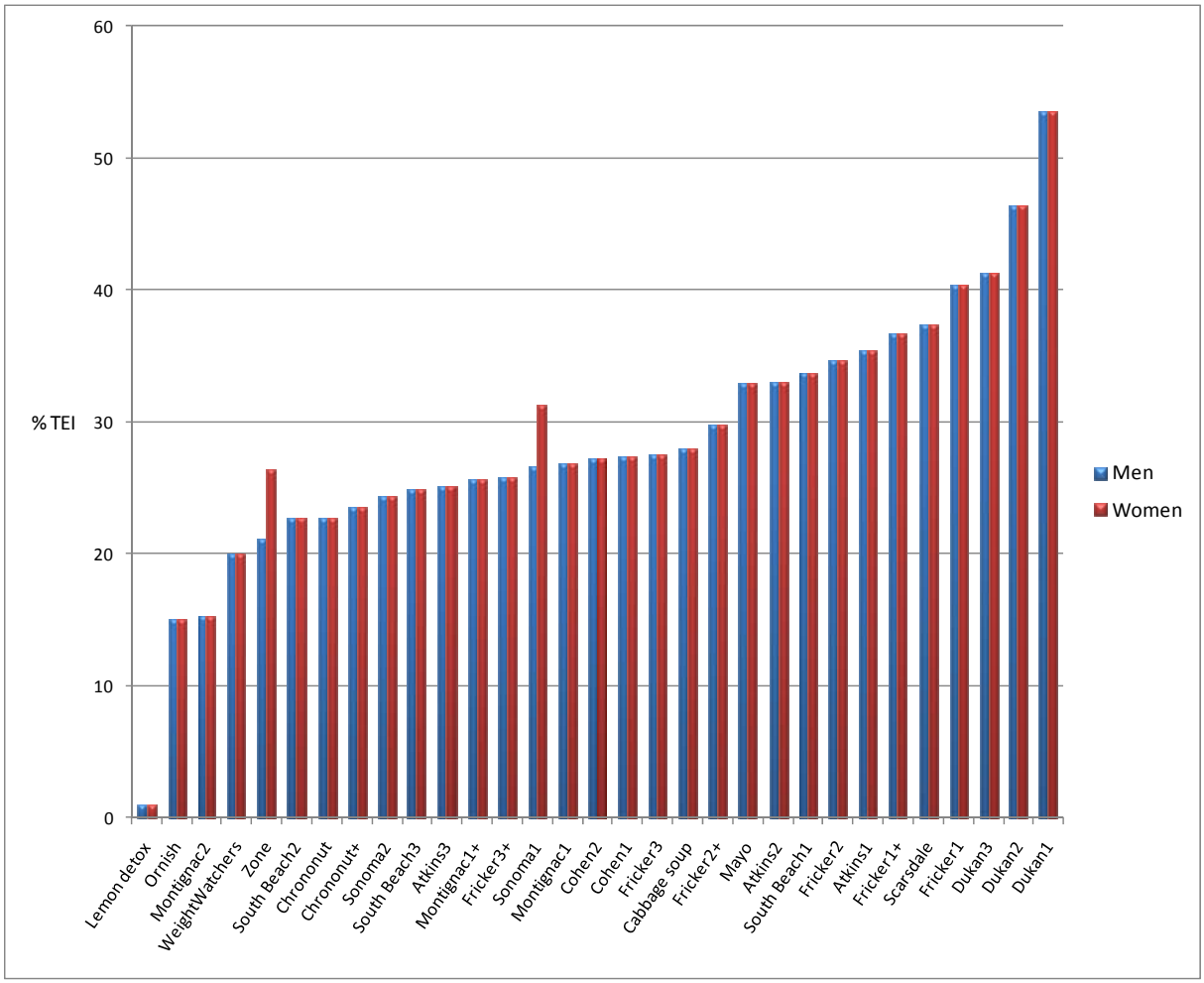


Figure 3: Protein intake according to diet (g.kg of body weight^{-1}.d^{-1})



Given the average weight of adult men and women according to the INCA 2 study, for more than 80% of the diets and diet phases, protein intake in g per kg of body weight per day was observed to be above the ANC, which is 0.83 g/kg/d. Intakes are sometimes two to three times higher than the ANC. In particular, it was noted that for the Dukan1, Dukan2 and Dukan3 diets, protein intake is high (over 2.2 g/kg/d) or even very high for Dukan1 and Dukan3 in women (over 3.5 g/kg/d) (AFSSA 2007).

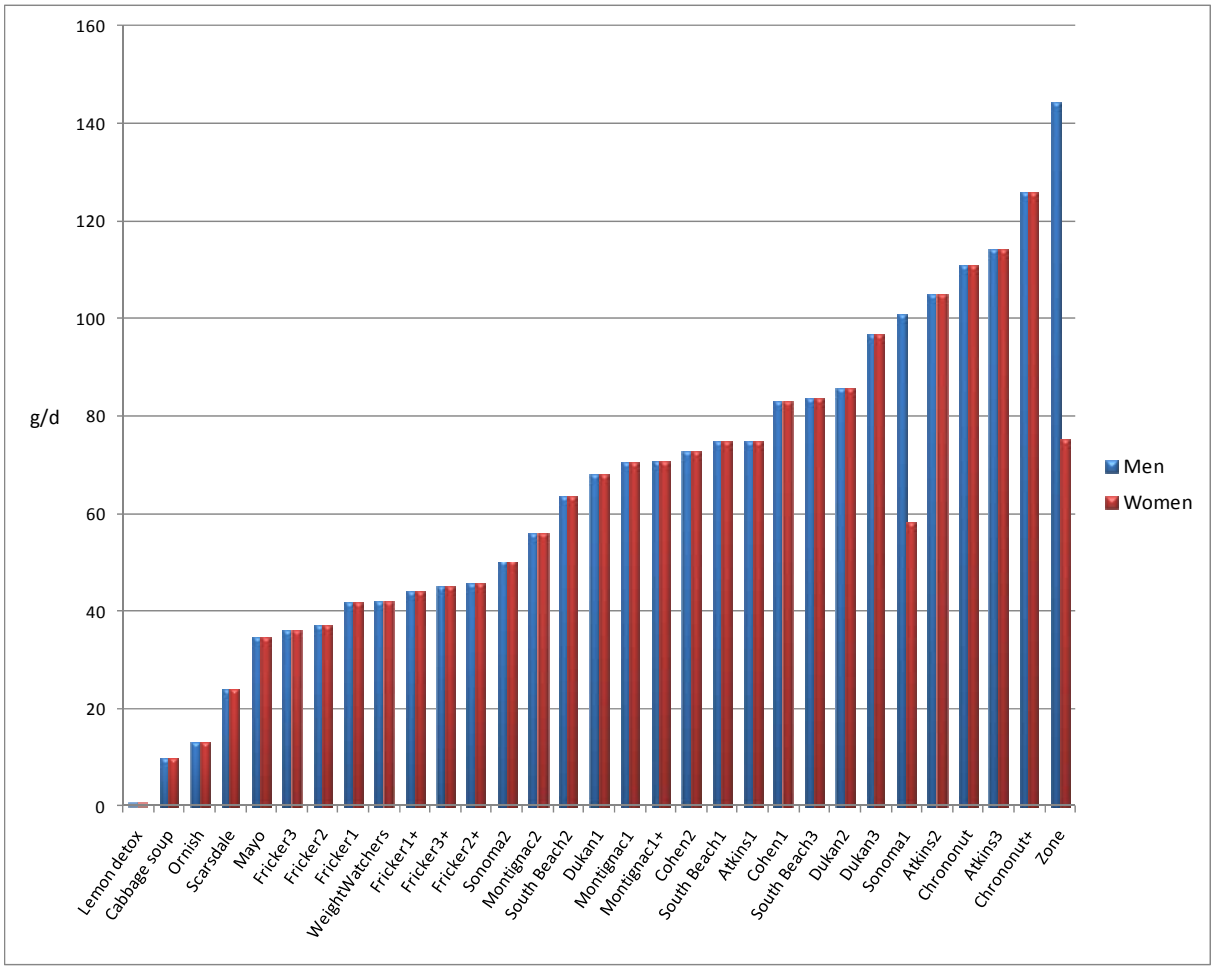
Figure 4: Contribution of protein to total energy intake according to diet (% total energy intake)



The contribution of protein to total energy intake varies between 1 (the Lemon Detox Diet, which is almost devoid of protein) and over 50% of total energy intake (the Dukan1 diet).

Virtually all the diet phases include protein intakes of more than 20% of TEI.

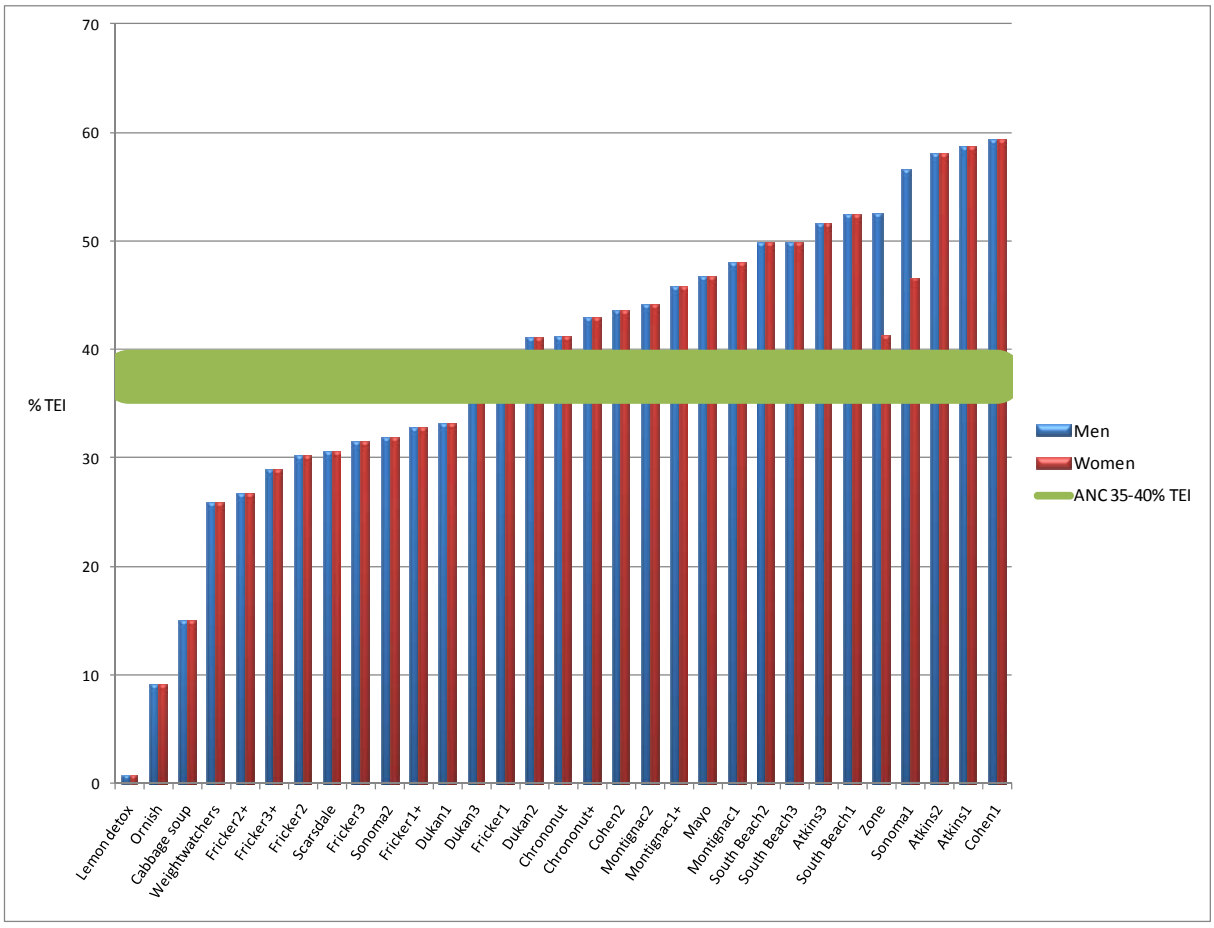
Figure 5: Contribution of lipids according to diet (g/d)



The amount of lipids in the various diets and diet phases studied differs, ranging from 1 to 144 g of fat per day.

Thus, several phases of the weight-loss diets studied proposed lipids intakes above 90 g/d (upper range of the ANCs, or 40% of energy intake calculated for a daily food intake of 2000 kcal).

Figure 6: Contribution of lipids to total energy intake according to diet (% TEI)

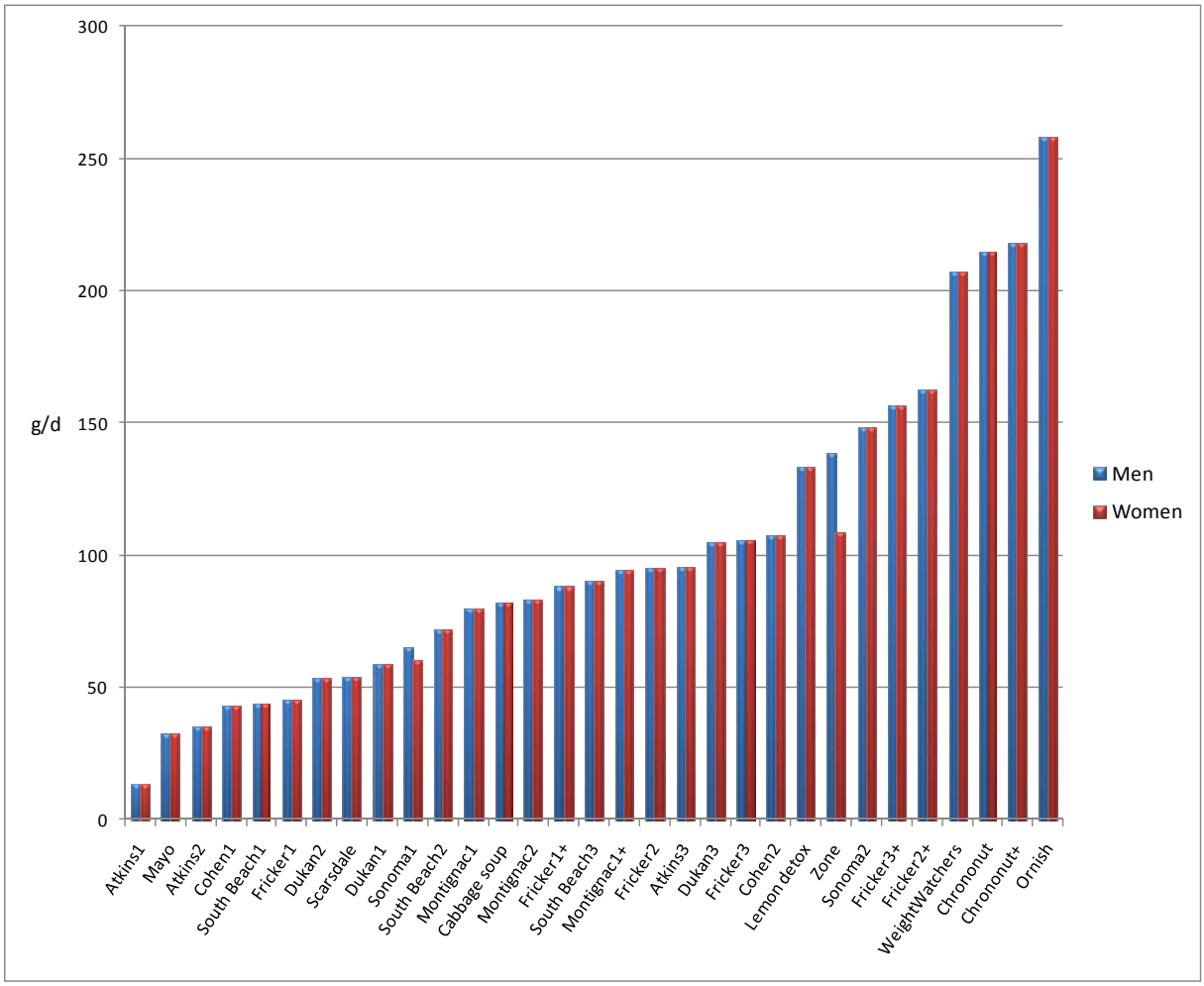


For the different diets and diet phases studied, the contribution of fat to total energy intake is between 1 (Lemon Detox diet, which is almost devoid of fat) and nearly 60% (Cohen1, Atkins1 and Atkins2).

More than half of the diet phases studied provide fat intakes higher than the ANC (35-40% of energy intake) and 40% have lipids intakes below the ANC.

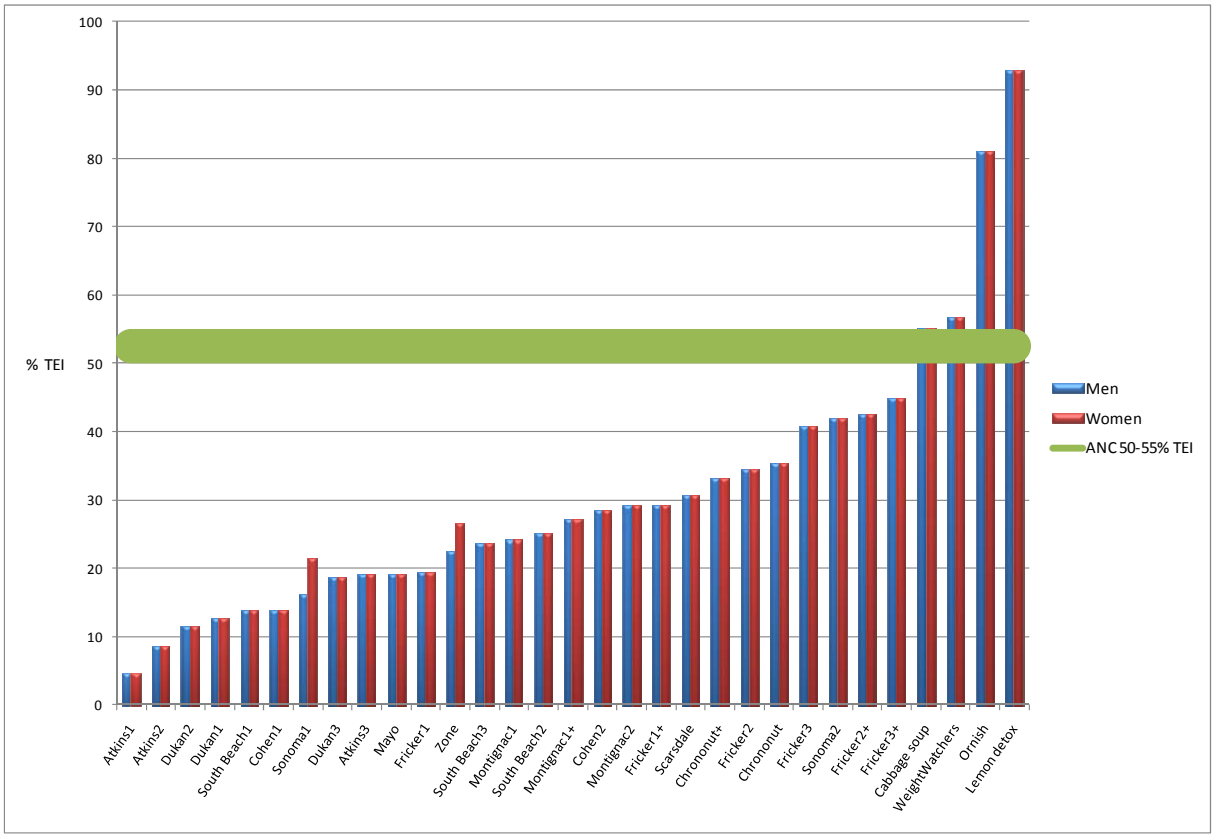
These relative values should be compared with absolute values (grams).

Figure 7: Carbohydrate intake according to diet (g/d).



The different diets and diet phases studied provide highly variable quantities of carbohydrates: between 13 g/d for Atkins1 and 258 g/d for the Ornish Diet.

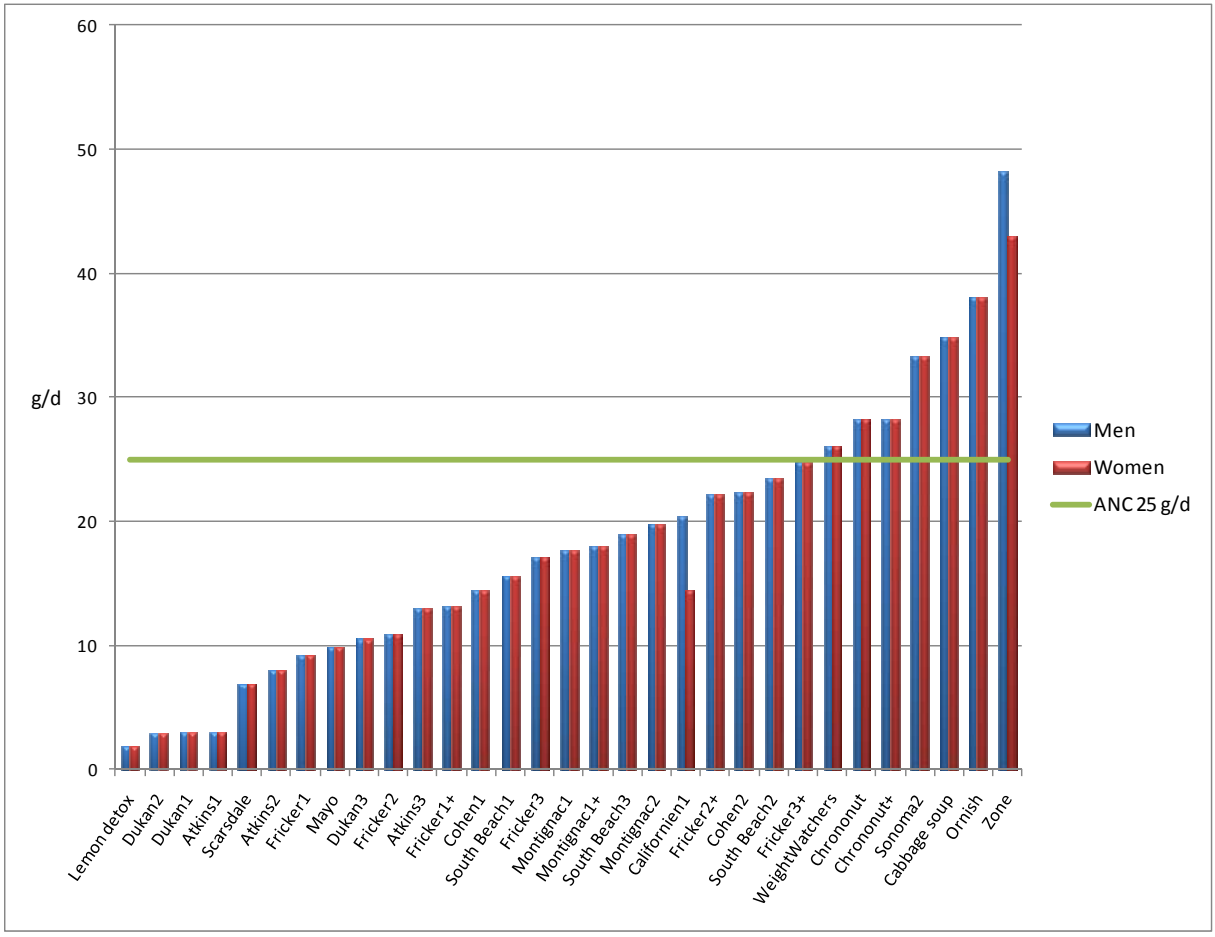
Figure 8: Contribution of carbohydrates to total energy intake according to diet (% TEI)



For the different diets and diet phases, the contribution of carbohydrates to total energy intake ranges from 5 to more than 90%.

Virtually all of the diet phases studied provide carbohydrate intakes below the ANC (50-55% of energy intake).

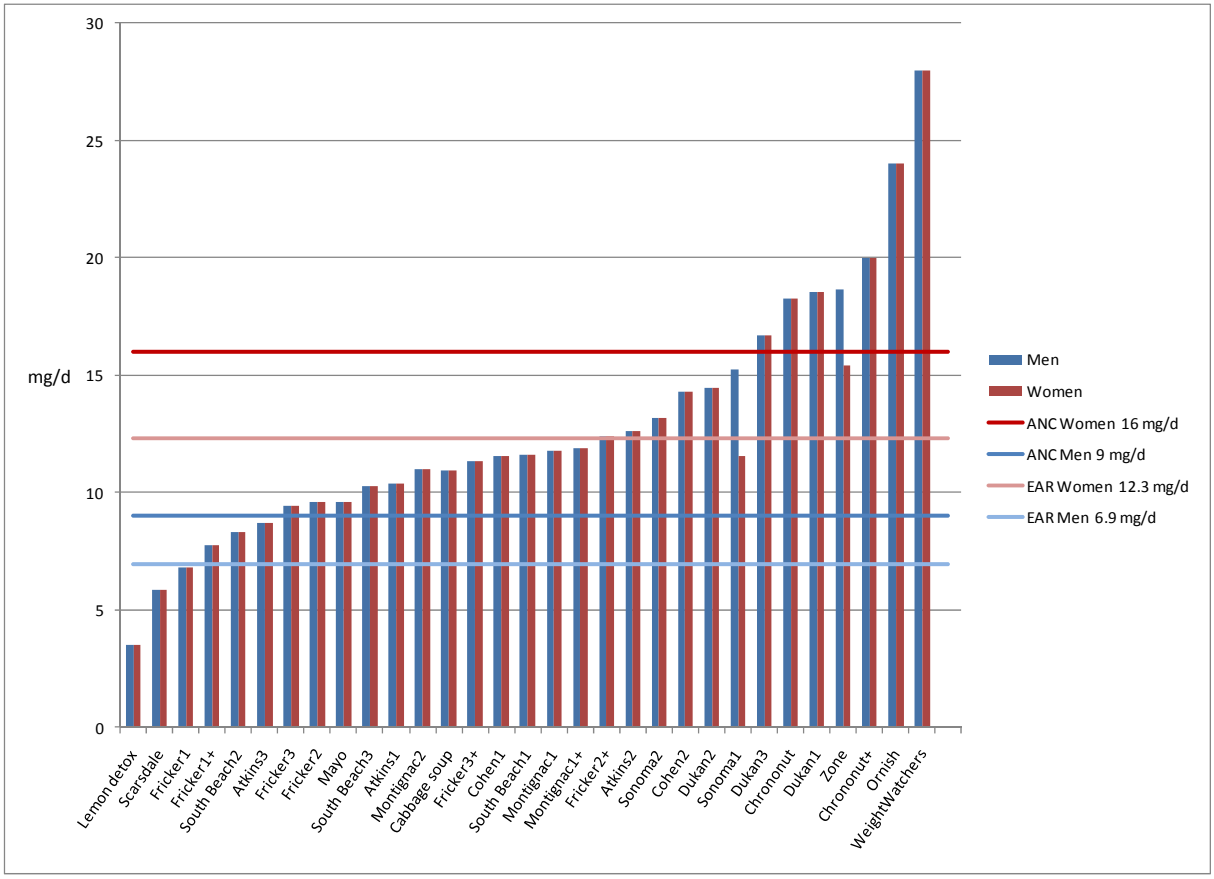
Figure 9: Fibre intake according to diet (g/d)



Fibre intakes from the diets and diet phases studied ranged from 2 to 59 g/d.
In 74% of the diets and diet phases, fibre intake is lower than the ANC (25 g/d), sometimes almost ten times lower (for the Lemon Detox, Atkins1, Dukan1 and Dukan2 diets).
Only a few diets rich in fruit and vegetables follow the recommendations for fibre intake.

4.3.4.Impacts on micronutrient intake

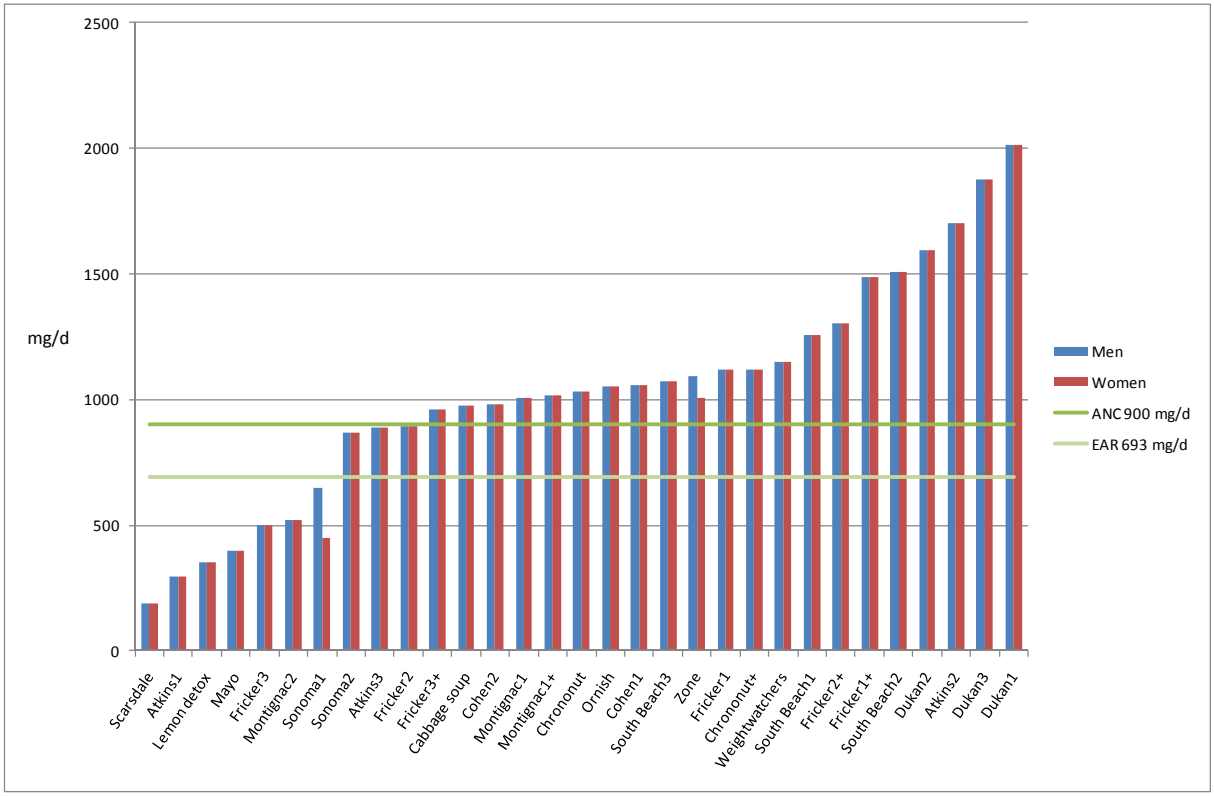
Figure 10: Iron intake according to diet (mg/d)



The EAR for iron for adults is not met by the Lemon Detox and Scarsdale diets.
Furthermore, for women, the EAR is not met by the South Beach, Cabbage Soup or Mayo diets, nor by the different phases of the Fricker Diet except for Fricker2+, nor by the diet phases Atkins1, Atkins3, Montignac1, Montignac1+, Montignac2 and Cohen1.

The ANCs for iron for adults are not met by the Lemon Detox or Scarsdale diets, nor by the diet phases Fricker1, Fricker1+, South Beach2 and Atkins3.
For women, the ANCs for iron are not met by 80% of the diets or diet phases phases studied.

Figure 11: Calcium intake according to diet (mg/d)



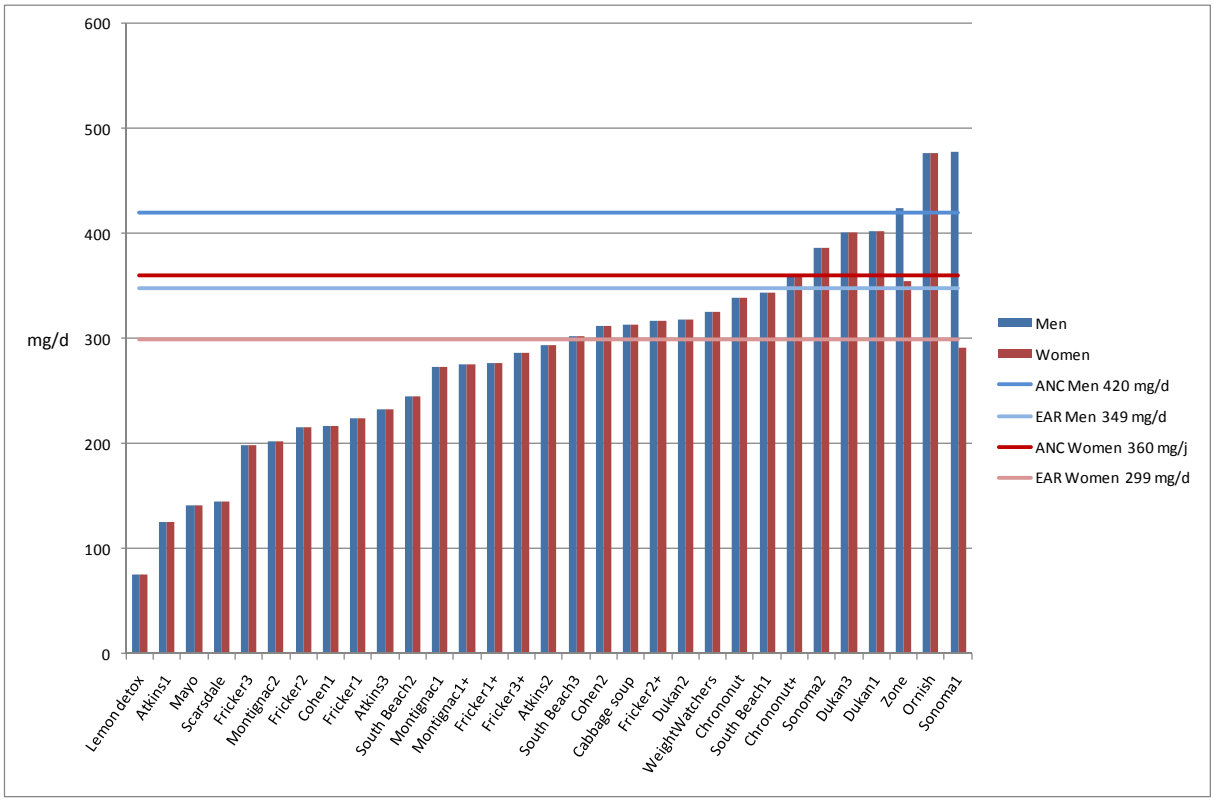
Calcium intakes from the diets studied range from 190 to over 2000 mg/d.

The EAR for calcium for adults is not met by the Scarsdale, Lemon Detox or Mayo diets, nor the diet phases Atkins1, Fricker3, Montignac2 and Sonoma1.

The ANCs for calcium for adults are not met by the diet phases Sonoma2, Atkins3 and Fricker2.

Calcium intakes from the diet phases Dukan1 and Dukan3 are double the ANCs.

Figure 12: Magnesium intake according to diet (mg/d)

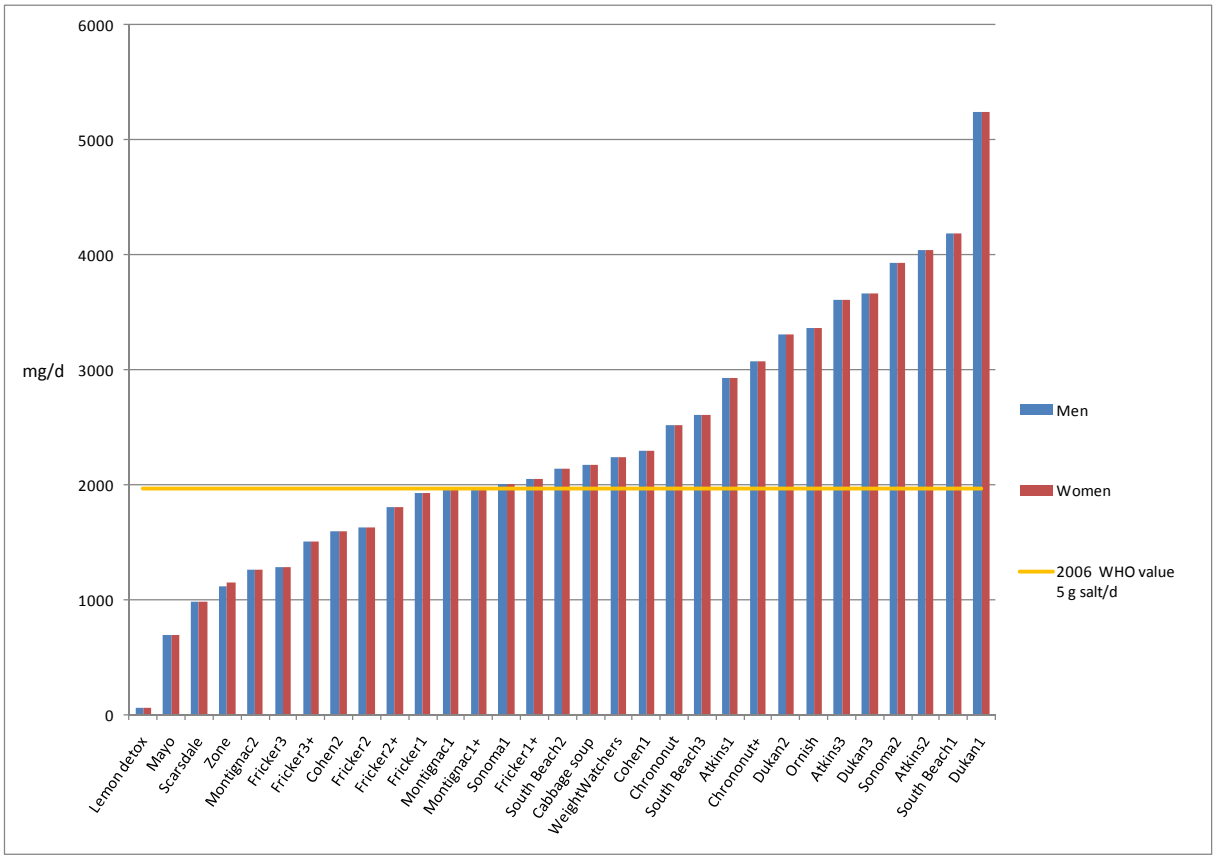


The diets and diet phases studied provide from 75 to nearly 500 mg of magnesium per day.

Fifty percent of the diet phases studied and designed for women have magnesium intakes below the EAR, and even more so for men, for whom the EAR is higher.

Magnesium intakes are higher than the ANC in a minority of diets or diet phases: Zone, Ornish and Sonoma1 for men, plus the diet phases Sonoma2, Dukan1 and Dukan3 for women.

Figure 13: Sodium intake according to diet (mg/d)



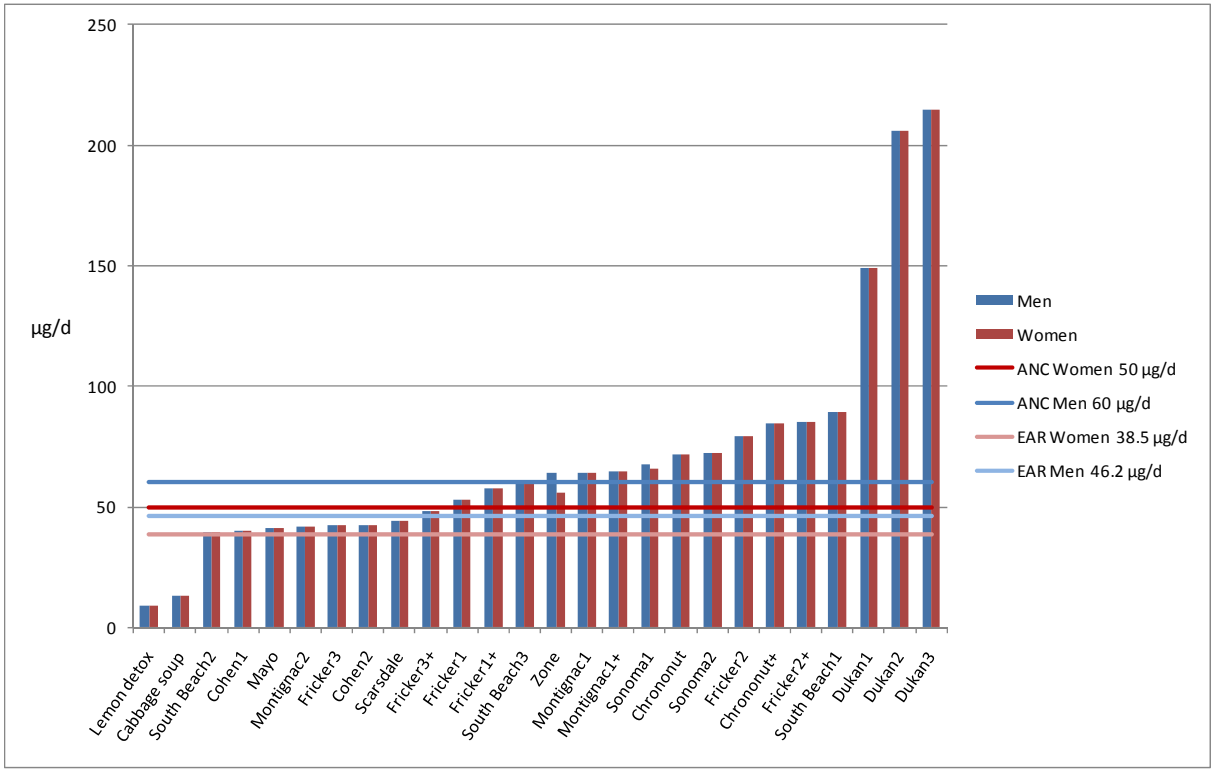
The diets or diet phases studied provide from 63 to over 5000 mg of sodium per day.

Intakes are above the limit recommended by the WHO (5 g of salt per day, or about 2000 mg of sodium) (WHO 2007), in the following diets and diet phases: Ornish, WeightWatchers, Cabbage Soup, Dukan1, Dukan2, Dukan3, South Beach1, South Beach2, South Beach3, Atkins1, Atkins2, Atkins3, Sonoma1, Sonoma2, Chrononutrition, Chrononutrition+, Cohen1 and Fricker1+.

In particular, the Dukan1 diet provides more than twice the limit recommended by the WHO.

Given the reference value of 8 g/d defined for the French population and not to be exceeded (AFSSA 2002), the Ornish diets and the diet phases Dukan1, Dukan2, Dukan3, South Beach1, Atkins2, Atkins3, Sonoma2 all provide an intake over this limit.

Figure 14: Selenium intake according to diet (µg/d)

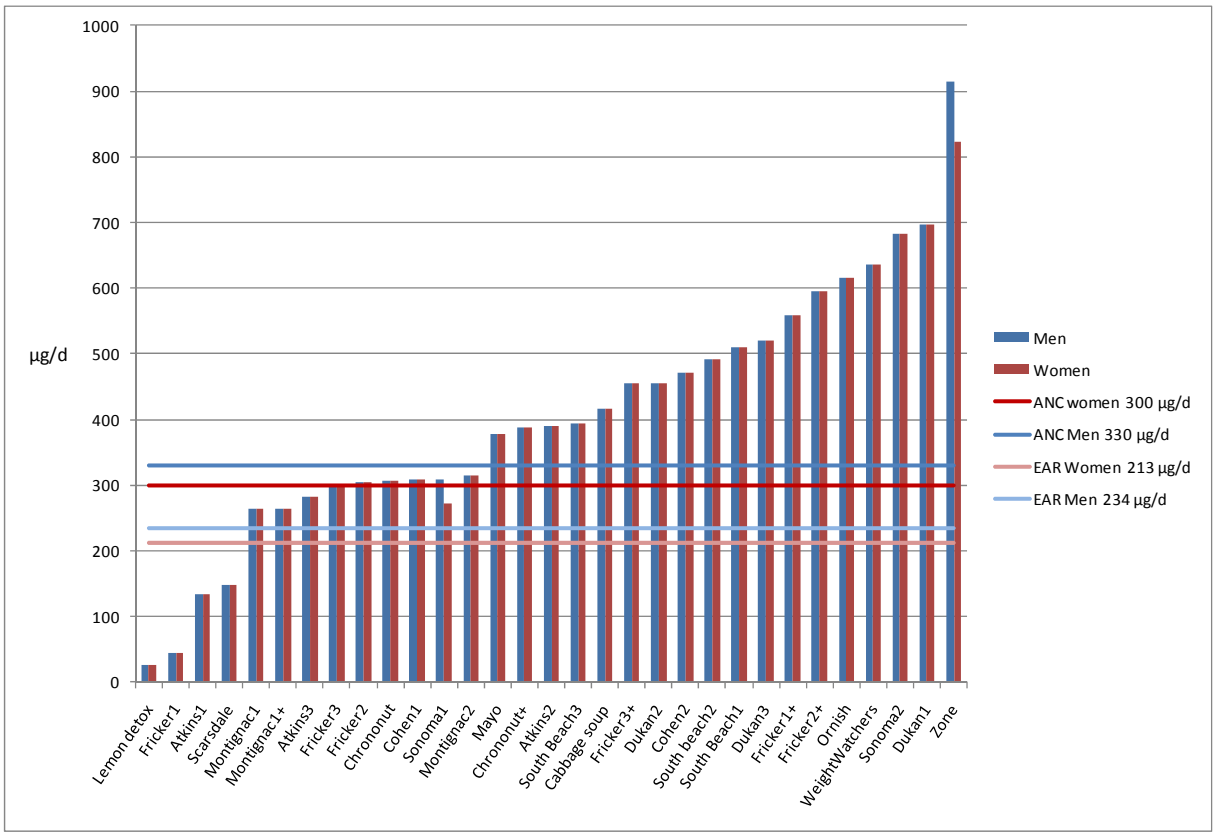


The diets or diet phases studied provide from 9 to more than 200 µg of selenium per day.

The EAR for selenium for adults is not met by the Lemon Detox and Cabbage Soup diets. Furthermore, the EAR for men is not met by the Mayo and Scarsdale diets, nor by the diet phases South Beach2, Cohen1, Cohen2, Montignac2 and Fricker3.

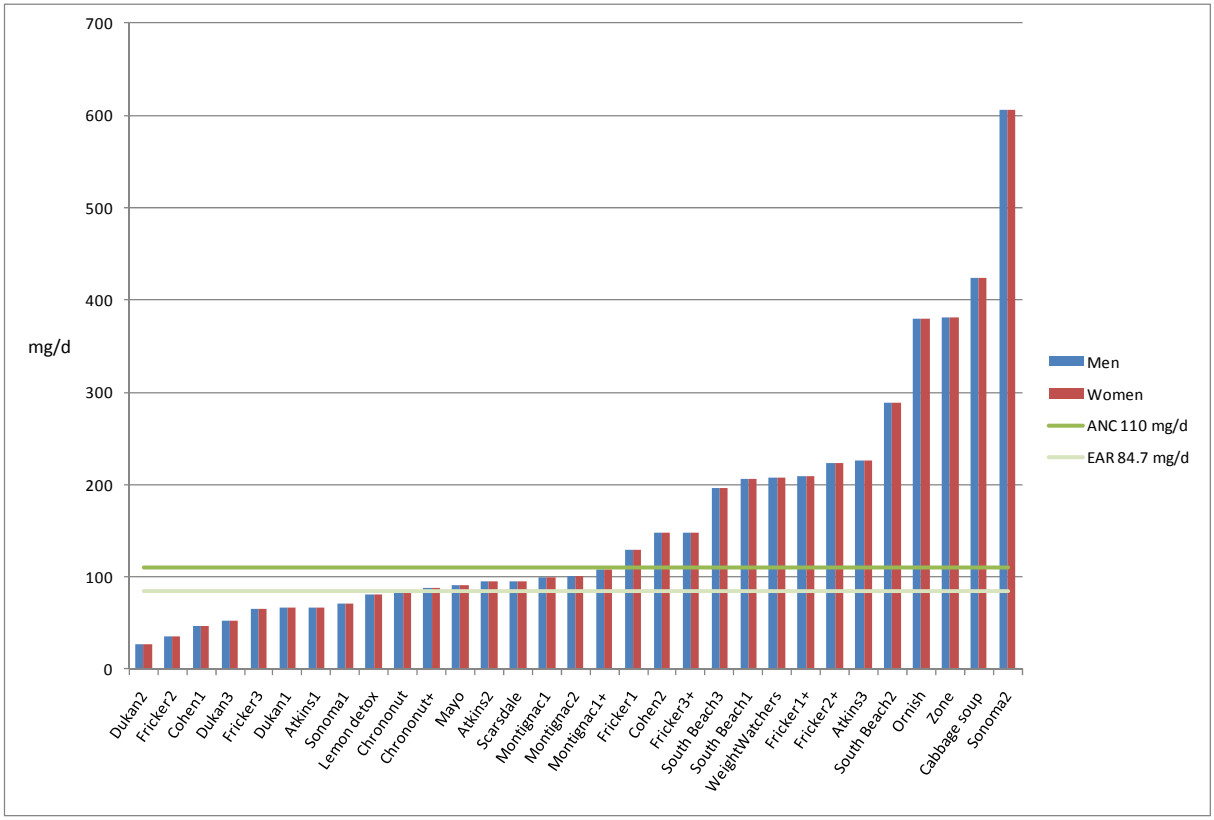
In addition, the ANCs for men are only reached in 45% of the diet phases. In women, the ANC is not reached for 29% of the diet phases.

Figure 15: Vitamin B9 intake according to diet (µg/d)



Vitamin B9 intake does not meet the EAR for an adult for the following diets and diet phases: Lemon Detox, Scarsdale, Fricker1 and Atkins1.
In addition, the ANCs for men are only reached by 42% of the diet phases. For women, the ANC is not reached by 29% of the diet phases.

Figure 16: Vitamin C intake according to diet (mg/d)

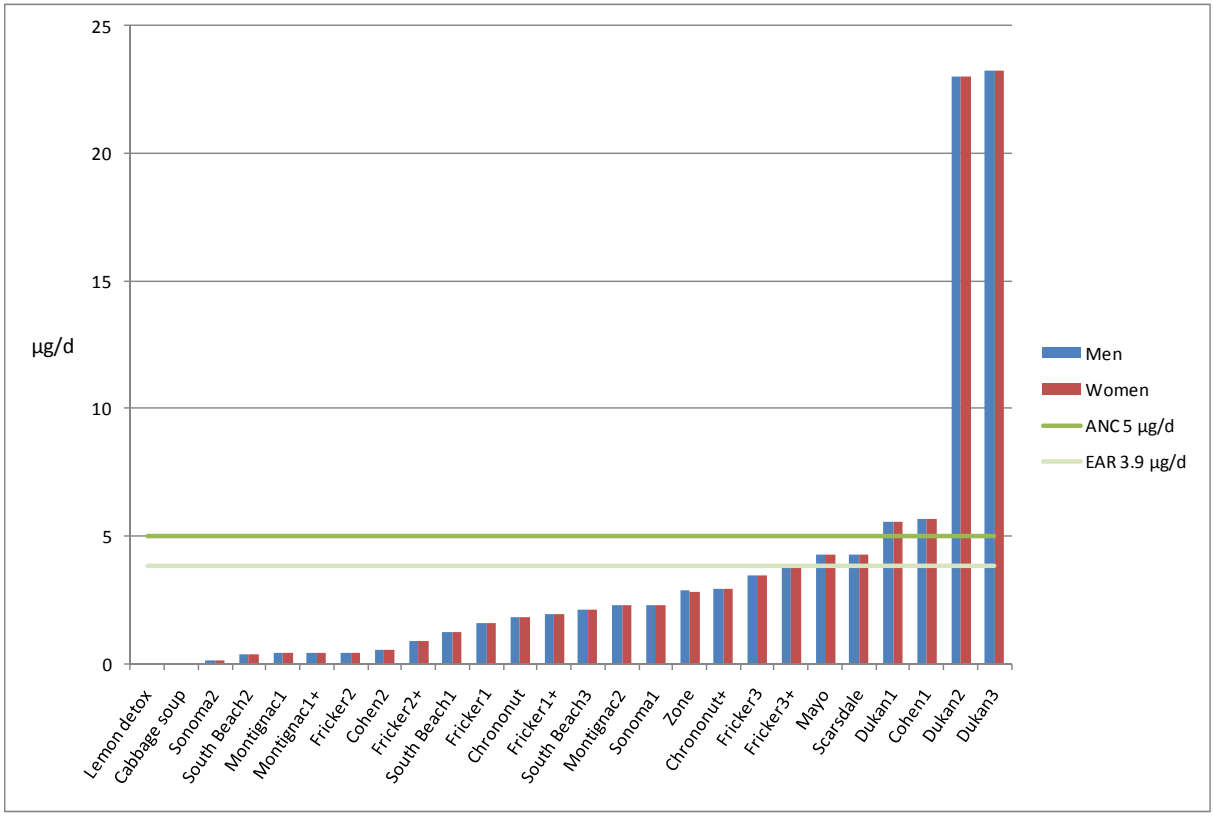


The vitamin C intake provided by the Lemon Detox diet and by the diet phases Dukan1, Dukan2, Dukan3, Fricker1, Fricker3, Cohen1, Atkins1, Sonoma1 does not meet the EAR for adults.

Intakes do not reach the ANC for 55% of the diets or diet phases studied.

In the particular case of the Sonoma2 diet phase, vitamin C intake for the considered day is high due to the high consumption of certain vegetables.

Figure 17: Vitamin D intake according to diet (µg/d)

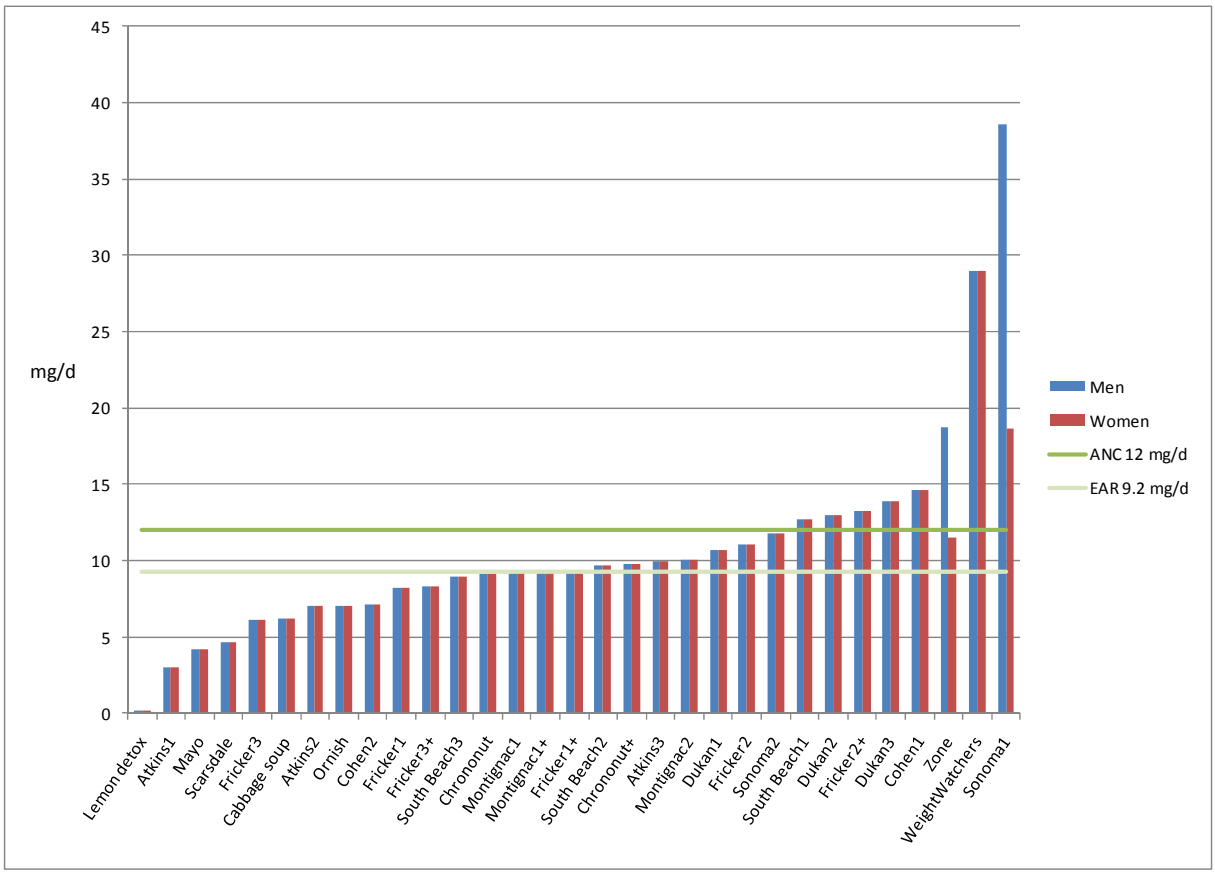


The EAR for vitamin D is not met in most diets (77%).

For 87% of the diets or diet phases, vitamin D intakes are below the ANCs.

In the particular case of the diet phases Dukan2 and Dukan3, vitamin D intake on the considered days is high, due to the presence of large quantities of oily fish.

Figure 18: Vitamin E intake according to diet (mg/d)



The EAR for vitamin E is not met in the Lemon Detox, Mayo, Scarsdale, Cabbage Soup and Ornish diets, nor in the diet phases Atkins1, Atkins2, Fricker1, Fricker3, Fricker3+, Cohen2 and South Beach3.
The EAR is therefore not met in 35% of the diets or diet phases.

The ANCs for vitamin E are reached in only 26% of the diets or diet phases.

Tables 2 and 3 provide a summary, respectively for women and men, of the dietary intakes from the various diets. The dietary intake values indicated for the different diets are compared with those from the INCA2 study, the French population reference intakes (ANC), the EARs and for sodium only, the recommended intake from the WHO (WHO 2007).

Table 2: Dietary intake provided by each weight-loss diet, for women[14]

	Energy (kcal/d)	Energy (kJ/d)	Lipids (g/d)	Lipids %TEI	Proteins (g/d)	Proteins %TEI	Carbohydrates (g/d)	Carbohydrates %TEI	Fibres (g/d)	Iron (mg/d)	Calcium (mg/d)	Magnesium (mg/d)	Potassium (mg/d)	Selenium (µg/d)	Sodium (mg/d)	Vitamin B9 (µg/d)	Vitamin C (mg/d)	Vitamin D (µg/d)	Vitamin E (mg/d)
Atkins1	1152		75	59	102	35	13	5	3	10.4	294	126	1734		2934	135	67.0		3
Atkins2	1627		105	58	134	33	35	9	8	12.6	1701	294	2562		4046	391	95.0		7
Atkins3	1990		114	52	125	25	95	19	13	8.7	889	233	3339		3604	282	226.0		10
Sonoma1	1127	4718	58	47	88	31	60	21	14	11.5	451	292	1957	66	2011	271	70.5	2.3	19
Sonoma2	1415	5954	50	32	86	24	148	42	33	13.2	869	386	3987	72	3932	683	605.5	0.1	12
Chrononut	2419	10141	111	41	138	23	214	35	28	18.3	1034	339	3834	72	2524	308	85.0	1.8	9
Chrononut+	2638	11051	126	43	155	23	218	33	28	20.0	1121	360	4124	85	3073	388	88.3	2.9	10
Cohen1	1261	5255	83	59	87	27	43	14	14	11.5	1057	217	1741	40	2299	309	46.7	5.7	15
Cohen2	1504	6303	73	44	102	27	107	28	22	14.3	980	312	3764	42	1598	471	147.3	0.5	7
Lemon detox	574	2405	1	1	1	1	133	93	2	3.5	353	75	788	9	63	26	81.6	0.0	0
Dukan1	1844	7751	68	33	246	53	58	13	3	18.6	2013	403	4178	149	5243	696	66.8	5.6	11
Dukan2	1873	7855	86	41	217	46	53	11	3	14.5	1596	318	3612	206	3306	456	26.3	23.0	13
Dukan3	2233	9370	97	39	230	41	104	19	10	16.7	1874	401	4054	215	3663	519	53.0	23.2	14
Fricker1	940	3945	42	40	95	40	45	19	9	6.8	1118	224	2254	53	1935	44	129.7	1.6	8
Fricker1+	1207	5078	44	33	111	37	88	29	13	7.8	1484	276	3168	58	2056	559	209.2	2.0	9
Fricker2	1101	4633	37	30	95	35	95	34	11	9.6	896	216	2664	79	1633	305	35.8	0.4	11
Fricker2+	1531	6450	45	27	114	30	163	42	22	12.4	1305	317	4175	85	1811	595	223.2	0.9	13
Fricker3	1035	4349	36	31	71	28	105	41	17	9.5	498	199	2256	42	1288	299	65.6	3.5	6
Fricker3+	1392	5859	45	29	90	26	157	45	25	11.3	958	286	3614	49	1508	455	147.9	3.8	8
Mayo	668	2792	35	47	55	33	32	19	10	9.6	397	141	1638	41	691	377	91.5	4.3	4
South Beach1	1287	5379	75	52	108	34	44	14	16	11.6	1254	344	3643	89	4184	509	206.8	1.2	13
South Beach2	1150	4834	64	50	65	23	72	25	23	8.3	1507	246	2496	40	2140	492	288.8	0.4	10
South Beach3	1515	6335	84	50	94	25	90	24	19	10.3	1071	302	3200	60	2613	394	196.5	2.1	9
Montignac1	1317	5507	70	48	89	27	80	24	18	11.8	1008	273	3417	64	1963	264	100.2	0.4	9
Montignac1+	1383	5788	70	46	89	26	94	27	18	11.9	1014	275	3455	64	1967	264	108.2	0.4	9
Montignac2	1143	4770	56	44	44	15	83	29	20	11.0	521	202	2734	42	1263	315	100.4	2.3	10
Ornish	1273		13	9	48	15	258	81	38	24.0	1053	477	4026		3358	615	380.0		7
Scarsdale	700	2943	24	31	65	37	54	31	7	5.9	190	145	1961	44	984	148	95.3	4.3	5
Cabbage soup	594	2513	10	15	42	28	82	55	35	11.0	976	313	3484	13	2169	416	423.4	0.0	6
Weightwatchers	1462		42	26	73	20	207	57	26	28.0	1147	325	3773		2243	636	207.0		29
Zone	1637	6856	75	41	108	26	108	27	43	15.4	1007	355	4255	56	1151	822	381.1	2.8	11
Inca2	1855	7754	80	39	74	16	199	43	16	11.5	850	262	2681	48	2533	268	94.3	2.4	11
ANC									25	16.0	900	360		50.0		300	110.0	5.0	12.0
BNM										12.3	693	299		38.5		213	84.7	3.9	9.2
2006 WHO value															1967				

Notes:
- Fibre: cells shaded in red correspond to intakes below the ANC.
- Iron, calcium, magnesium, selenium, vitamins B9, D, E and C: cells shaded in red correspond to intakes below the EAR. Cells shaded in yellow correspond to intakes above the ANC.
- Sodium: cells whose values are in red correspond to intakes above the value recommended by the WHO (5 g/d).

[14] For the Atkins, Ornish and WeightWatchers diets, the dietary intake values come from the publication by Freedman et al., which does not specify vitamin D, selenium and energy intakes in kJ.

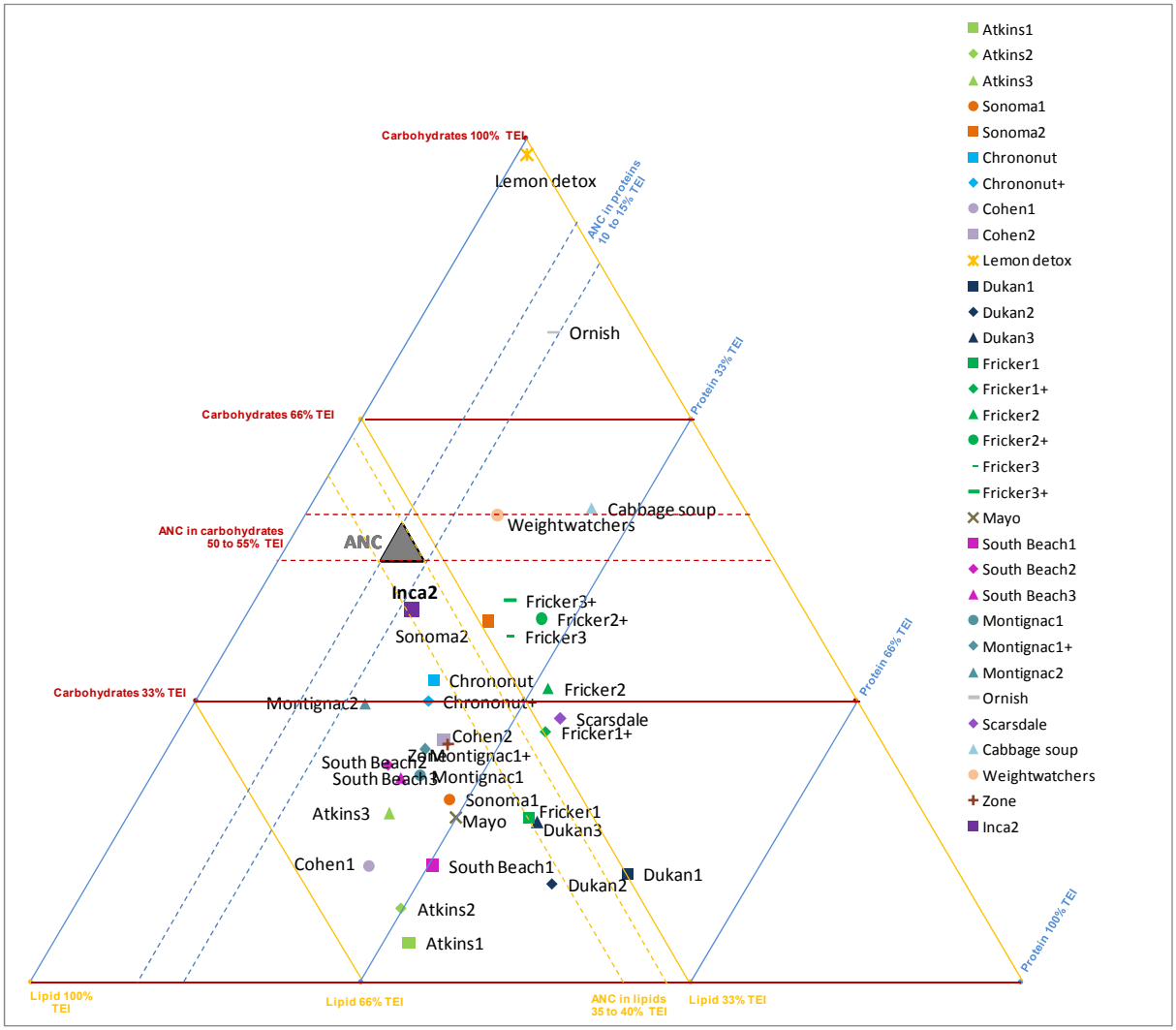
Table 3: Dietary intake provided by each weight-loss diet, for men[15]

	Energy (kcal/d)	Energy (kJ/d)	Lipids (g/d)	Lipids %TEI	Proteins (g/d)	Proteins %TEI	Carbohydrates (g/d)	Carbohydrates %TEI	Fibres (g/d)	Iron (mg/d)	Calcium (mg/d)	Magnesium (mg/d)	Potassium (mg/d)	Selenium (µg/d)	Sodium (mg/d)	Vitamin B9 (µg/d)	Vitamin C (mg/d)	Vitamin D (µg/d)	Vitamin E (mg/d)
Atkins1	1152		75	59	102	35	13	5	3	10.4	294	126	1734		2934	135	67.0		3.0
Atkins2	1627		105	58	134	33	35	9	8	12.6	1701	294	2562		4046	391	95.0		7.0
Atkins3	1990		114	52	125	25	95	19	13	8.7	889	233	3339		3604	282	226.0		10.0
Sonoma1	1602	6681	101	57	107	27	65	16	20	15.2	650	478	2645	67.7	2012	310	70.7	2.3	38.6
Sonoma2	1415	5954	50	32	86	24	148	42	33	13.2	869	386	3987	72.5	3932	683	605.5	0.1	11.8
Chrononut	2419	10141	111	41	138	23	214	35	28	18.3	1034	339	3834	72.0	2524	308	85.0	1.8	9.1
Chrononut+	2638	11051	126	43	155	23	218	33	28	20.0	1121	360	4124	84.6	3073	388	88.3	2.9	9.8
Cohen1	1261	5255	83	59	87	27	43	14	14	11.5	1057	217	1741	40.1	2299	309	46.7	5.7	14.7
Cohen2	1504	6303	73	44	102	27	107	28	22	14.3	980	312	3764	42.3	1598	471	147.3	0.5	7.1
Lemon detox	574	2405	1	1	1	1	133	93	2	3.5	353	75	788	9.0	63	26	81.6	0.0	0.2
Dukan1	1844	7751	68	33	246	53	58	13	3	18.6	2013	403	4178	148.8	5243	696	66.8	5.6	10.7
Dukan2	1873	7855	86	41	217	46	53	11	3	14.5	1596	318	3612	205.7	3306	456	26.3	23.0	13.0
Dukan3	2233	9370	97	39	230	41	104	19	10	16.7	1874	401	4054	214.9	3663	519	53.0	23.2	13.9
Fricker1	940	3945	42	40	95	40	45	19	9	6.8	1118	224	2254	52.8	1935	44	129.7	1.6	8.2
Fricker1+	1207	5078	44	33	111	37	88	29	13	7.8	1484	276	3168	57.5	2056	559	209.2	2.0	9.4
Fricker2	1101	4633	37	30	95	35	95	34	11	9.6	896	216	2664	79.4	1633	305	35.8	0.4	11.1
Fricker2+	1531	6450	45	27	114	30	163	42	22	12.4	1305	317	4175	85.1	1811	595	223.2	0.9	13.3
Fricker3	1035	4349	36	31	71	28	105	41	17	9.5	498	199	2256	42.3	1288	299	65.6	3.5	6.1
Fricker3+	1392	5859	45	29	90	26	157	45	25	11.3	958	286	3614	48.5	1508	455	147.9	3.8	8.3
Mayo	668	2792	35	47	55	33	32	19	10	9.6	397	141	1638	41.3	691	377	91.5	4.3	4.2
South Beach1	1287	5379	75	52	108	34	44	14	16	11.6	1254	344	3643	89.5	4184	509	206.8	1.2	12.7
South Beach2	1150	4834	64	50	65	23	72	25	23	8.3	1507	246	2496	39.6	2140	492	288.8	0.4	9.7
South Beach3	1515	6335	84	50	94	25	90	24	19	10.3	1071	302	3200	59.8	2613	394	196.5	2.1	8.9
Montignac1	1317	5507	70	48	89	27	80	24	18	11.8	1008	273	3417	64.2	1963	264	100.2	0.4	9.3
Montignac1+	1383	5788	70	46	89	26	94	27	18	11.9	1014	275	3455	64.4	1967	264	108.2	0.4	9.3
Montignac2	1143	4770	56	44	44	15	83	29	20	11.0	521	202	2734	41.7	1263	315	100.4	2.3	10.0
Ornish	1273		13	9	48	15	258	81	38	24.0	1053	477	4026		3358	615	380.0		7.0
Scarsdale	700	2943	24	31	65	37	54	31	7	5.9	190	145	1961	44.0	984	148	95.3	4.3	4.7
Cabbage soup	594	2513	10	15	42	28	82	55	35	11.0	976	313	3484	12.8	2169	416	423.4	0.0	6.2
Weightwatchers	1462		42	26	73	20	207	57	26	28.0	1147	325	3773		2243	636	207.0		29.0
Zone	2471	10316	144	53	130	21	139	22	48	18.7	1093	424	4901	64.1	1118	915	435.8	2.9	18.7
Inca2	2500	10450	100	36	100	16	262	42	19	14.9	984	325	3287	58.8	3447	307	91.3	2.7	11.9
ANC									25	9.0	900	420		60.0		330	110.0	5.0	12.0
BNM										6.9	693	349		46.2		234	84.7	3.9	9.2
2006 WHO value															1967				

Notes:
- Fibre: cells shaded in red correspond to intakes below the ANC.
- Iron, calcium, magnesium, selenium, vitamins B9, D, E and C: cells shaded in red correspond to intakes below the EAR. Cells shaded in yellow correspond to intakes above the ANC.
- Sodium: cells whose values are in red correspond to intakes above the WHO-recommended value (5 g/d).

[15] For the Atkins, Ornish and WeightWatchers diets, the dietary intake values come from the publication by Freedman et al., which does not specify vitamin D, selenium and energy intakes in kJ.

Figure 19: Ternary diagram of the contributions of carbohydrates, lipids and proteins to total energy intake for women



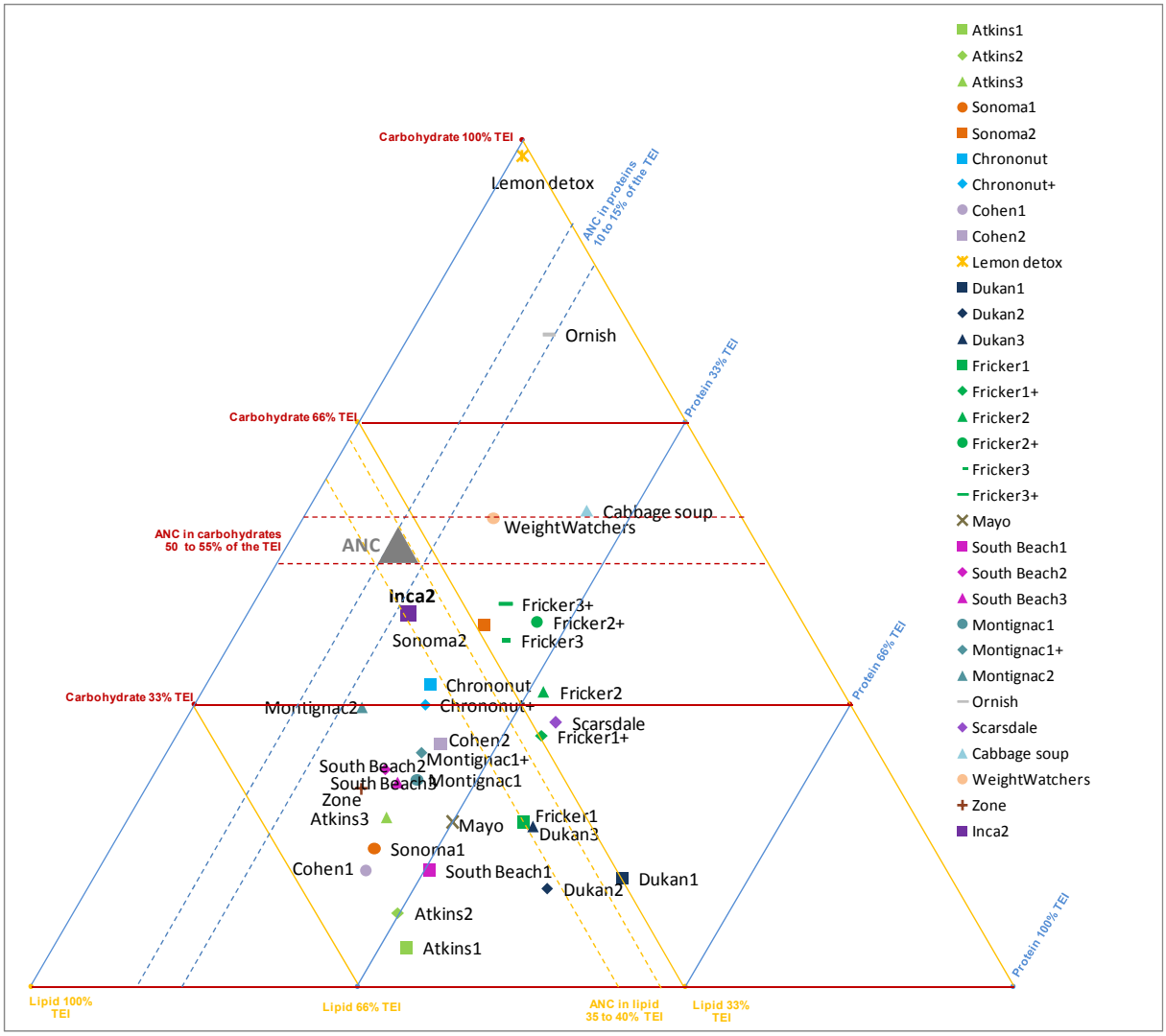
The similarities or differences between the diets studied, as well as their positioning relative to each other can be viewed as a ternary diagram (Figures 19 and 20). The principle is to represent graphically in an equilateral triangle the contributions to total energy intake of carbohydrates, fats and proteins. At any point in the triangle, the sum of the three variables is equal to 100%[16]. The yellow, red and blue straight lines indicate respectively for fats, carbohydrates and proteins, areas of the triangle corresponding to increasing contributions of these components to total energy intake.

For example, it can be observed that for the energy intake from the Scarsdale diet, just over 30% comes from carbohydrates, 30% from fats and nearly 40% from proteins. When projected onto the triangle, diets with similar contributions of macronutrients to total energy intake appear close to each other.

Interpretation of this diagram should be combined with an analysis of intakes in absolute values as it does not illustrate either energy intakes (hence macronutrients in absolute value) nor micronutrient intakes of the diet and diet phases analysed. Regardless of the energy intake, the diets furthest away from the ANC area are the least nutritionally balanced. However, those diets closer to the grey-shaded ANC triangle should not *a priori* be considered as the most balanced without considering their energy and micronutrient intakes (see Tables 2 and 3).

[16] This amount is reduced mathematically to one hundred in cases where alcohol (the Zone and Montignac diets) or organic acids also contribute to energy intake.

Figure 20: Ternary diagram of the contributions of carbohydrates, fats and proteins to total energy intake for men



For demonstration purposes and on the basis of the above results, a typology of diets using the ANCs and total energy intake is proposed below.

Table 4: Classification of diets

Diet types	High-protein >27%[1] of TEI	High-carbohydrate > 55% of TEI	High-fat >40% of TEI
Extremely low calorie *(<800 kcal)*	Mayo Scarsdale	Lemon Detox Cabbage Soup	
Very low calorie *(800 -1200 kcal)*	Atkins1 Sonoma1 women Fricker1, 2 and 3		Atkins1 Sonoma1 women South Beach2 Montignac2
Low calorie *(1200-1500 kcal)*	Cohen1 Fricker1+ and 3+ South Beach1	Ornish WeightWatchers	Cohen1 South Beach1 Montignac1 and 1+
Not low calorie *(>1500 kcal)*	Atkins2 Cohen2 Dukan1, 2 and 3 Fricker2+		Atkins2 and 3 Sonoma1 men Chrononutrition Chrononutrition+ Cohen2 Dukan2 South Beach3 Zone

[1] AFSSA (2007) Protein intake: consumption, quality, requirements and recommendations.

Key points

- **Energy intakes associated with the diets or diet phases studied ranged from 574 to 2600 kcal/d (ANC being 1800-2200 kcal/d respectively for women and men engaging in normal physical activity).**

Regarding macronutrients:

- **Protein intake is above the ANC for more than 80% of the diet phases. For some, intakes are two to three times higher than the ANCs;**
- **More than half of the diet phases studied have fat intakes above the ANC, whereas 40% are lower;**
- **Virtually all of the diets or diet phases studied have carbohydrate intakes below the ANC;**
- **Seventy-four percent of the diet phases result in fibre intakes lower than the ANC, sometimes almost ten times lower. Only 26% of the diets or diet phases studied follow the recommendations for fibre intake.**

Regarding micronutrients:

- **For women, the EAR for iron is not met by 61% of the diets or diet phases studied;**
- **The EAR for calcium for adults is not met by 23% of the diet phases. In contrast, two of the diet phases studied correspond to intakes that are double the ANC;**
- **Half of the diets studied and designed for women correspond to magnesium intakes below the EAR. Seventy-seven percent of the diets or diet phases proposed to men fail to meet the EAR (which is higher than for women);**
- **Sodium intakes are above the limit recommended by the WHO (5 g of salt per day, or about 2000 mg of sodium) for 58% of the diet phases, and in one case they correspond to more than double the recommendation;**
- **For vitamin C, 26% of the diet phases do not cover the EAR. In particular, one of the diets studied is below the EAR in every one of its phases;**
- **The EAR for vitamin D is not met by the majority of the diet phases (77%);**
- **The EAR for vitamin E is not met by 35% of the diet phases.**

However, this analysis should not provide a basis for individual nutritional advice in connection with the different diets considered, as the consumption data from the INCA 2 or Su.Vi.Max studies (used for the nutritional characterisation of the diets or diet phases where the quantities were not specified by the author) do not reflect inter-individual variability.

4.3.5. Nutritional data from the INCA 2 study

The INCA 2 study was conducted in 2006-07 among a representative sample of the population living in mainland France: it consisted of 1455 children aged 3-17 years and 2624 adults aged 18-79 years (AFSSA 2009). Pregnant women (n=28) were excluded from the analyses that follow.
The main objective of this cross-sectional study was to measure as precisely as possible the food consumption and nutrient intakes of the population. Other variables were nevertheless also collected, including data on people following weight-loss diets.

Information on consumption (food and beverages) was collected at the individual level using a 7-day food diary. This was then compared with nutrient composition data from the CIQUAL base to estimate dietary intakes (Ireland et al. 2008).
A questionnaire, based on face-to-face interviews, collected various information on the interviewee's socioeconomic status (education level, socio-professional category, etc.), level of physical activity, and other lifestyle aspects. A self-administered questionnaire included additional questions on dietary habits, health status, as well as weight-loss diets.
Weight and height were also measured.

In this study, men claiming to be on a diet, during the survey or in the year preceding the interview, reported lower intakes of starchy foods (such as rice and pulses), partly associated with a lower consumer rate. They were also distinguished from others by lower consumption of sweetened products.
Women claiming to be on a diet also reported lower consumption of sweetened products (the lower consumer rate partly explains this result), but the reverse was true for pastries and cakes. They were conspicuous mostly by their lower consumption of bread and higher consumption of ultra-fresh dairy products.
However, these data do not reflect the application of specific weight-loss diets, but rather a non-analytical observation of what people do, regardless of any specific prescription or application of a particular diet.

4.4. Assessment of the nutritional and pathophysiological risks

The assessment of the health risks related to following weight-loss diets should be based primarily on firstly identifying the hazards related to this practice and secondly estimating human exposure. With regard to identification of the nature of the hazards, the literature search revealed many adverse health effects. Regarding estimation of human exposure to these adverse effects, the bibliography varies widely depending on the nature of the hazards identified. Indeed, many studies more specifically address the benefits of following weight-loss diets rather than their inherent risks. It was therefore not possible to accomplish a comprehensive risk assessment. It was however possible, despite the disparate exposure data, to propose a characterisation of these risks.

In addition, very few data in the literature specifically concern the examples of weight-loss diets described in this report. Thus, the comparison between the adverse effects listed and the weight-loss diets can only be made on the basis of the general principles of these diets, namely their characteristic level of energy intake and macronutrient distribution.

4.4.1. Nutritional imbalance and deficiencies in vitamins and minerals

a. Macronutrient nutritional imbalances

The risks associated with carbohydrate deficiency are described later in this report, in connection with the existence of metabolic pathways that can compensate for the absence of glucose or sources of glucose in the diet.
The risk of lipids deficiency relates primarily to essential fatty acids as they are not synthesised by the body, or are only synthesised under certain conditions, despite being necessary for proper functioning.

In the context of the Western diet, a fat intake below 30% of energy intake leads to a significant reduction in the intake of essential polyunsaturated fatty acids, particularly docosahexaenoic acid (DHA) (AFSSA 2010).
A deficiency in protein and essential amino acids leads inevitably to loss of muscle mass (or lean body mass) that can be dramatic in obese and/or elderly subjects. This loss of lean body mass is not specific to low-calorie diets as it is associated with all weight loss. Indeed, all diets, of any kind, cause the loss of lean body mass that can be attenuated when the diet includes a minimum protein intake and is combined with physical exercise. Thus, a meta-analysis has shown, on the basis of 87 clinical studies conducted over short periods, that protein intake greater than 1.05 g/kg of body weight is associated with better retention of lean body mass during dieting than when protein intake is less than 1.05 g/kg (Krieger et al. 2006).
The review of Weinheimer et al. (2010) discusses the problems of loss of lean body mass during very low-calorie diets in overweight or obese subjects over 50 years old or elderly (Weinheimer et al. 2010). It confirms the systematic loss of lean body mass during low-calorie diets that is nevertheless attenuated by engaging in physical exercise. Thus, according to their analysis, 81% of subjects subjected to energy restriction and 39% of those who also engaged in physical exercise lost more than 15% of their weight as lean body mass. The authors concluded that in these subjects a modest weight loss associated with physical exercise reduces the risk of significant loss of muscle mass. The share of weight loss corresponding to lean body mass varies according to the type of weight-loss diet and the physical activity. The review by Chaston et al. showed a loss of lean body mass (as a percentage of weight loss) of 14%, 23% and 22% in subjects following respectively a low-calorie diet, very low-calorie diet and very low-calorie diet with physical activity (Chaston et al. 2007).

b. Nutritional imbalances and metabolic adaptations

This section presents the general principles of how the metabolism adapts to deficiencies or excesses in several macronutrients induced by fasting and/or different types of diets.

- *Metabolic adaptation to an energy deficiency*

Weight-loss diets generally tend to deprive the body so that it draws on its reserves of body fat. The vast majority of energy reserves are in fact formed by the triglycerides found in white adipose tissue (Table 3). However, this is not the most immediately available energy reserve.

In the short term, fasting mobilises the glycogen in the liver, whose reserves are exhausted after 24 hours of fasting. During this phase, proteins are mobilised for gluconeogenesis, supplying glucose primarily to the brain, where it is rapidly oxidised (until 2-3 days of total fasting). Blood glucose and insulin levels decrease slightly, while glucagon secretion increases. These changes reduce the use of glucose by tissues such as skeletal muscle, which can then use fatty acids. Pyruvate dehydrogenase (PDH) activity is lessened in insulin-sensitive tissue which reduces the irreversible removal of glucose. Then lipolysis is stimulated in adipose tissue as is glucose production in the liver via gluconeogenesis. At this stage, gluconeogenesis occurs at the expense of muscle protein. This phase can last from 3 to 4 days (Frayn et al. 2003).

After about a week of fasting, blood glucose and insulin levels continue to decline while proteins begin to be spared as an energy source. This decrease in protein mobilisation is reflected by a gradual decrease in urinary nitrogen excretion. The cellular mechanism underlying protein sparing has not yet been fully elucidated (Frayn et al. 2003). The resulting increase in lipolysis leads to an increased release of nonesterified fatty acids (NEFAs) and glycerol from adipose tissue. Since glycerol is a precursor for gluconeogenesis, the metabolic use of amino acids is reduced. Oxidation of NEFAs in the liver is stimulated by the high glucagon/insulin ratio and ketone bodies are found in high concentrations in the circulation. While the brain cannot use NEFAs, it can use the derived water-soluble ketone bodies. Accordingly, under these ketosis conditions, glucose consumption is decreased in the cortex and cerebellum (LaManna et al. 2009).

If fasting is prolonged for 2 to 3 weeks, the concentration of ketone bodies stabilises at around 7-9 mmol/L (for comparison, it is at 0.2 mmol/L after an overnight fast) and they largely replace glucose as an energy substrate for the brain (about two thirds of the brain's energy needs). Consequently, the use of proteins for gluconeogenesis is further diminished. Because of the inactivation of PDH (due to low concentrations of insulin), the glucose used by tissues other than in the brain is only partially

metabolised to pyruvate and lactate which can be recycled in the liver by gluconeogenesis. Thus, for example, red blood cells, which have an absolute need for glucose, do not deplete the body's reserves of glucose. High concentrations of NEFAs and ketone bodies may be responsible for metabolic acidosis (low blood pH), but this is partly corrected by the production of ammonia from the metabolism of glutamine in the kidneys.

Table 5: Energy reserves in a 70 kg subject (adapted from Frayn et al. 2003)

Macronutrients	Energy substrates	Tissue	Weight (kg)	Equivalence in energy (MJ)	Daily consumption (g)	Daily consumption in % of reserves
Fats	Triglycerides	White adipose tissue	12-18	550	100	0.7
Carbohydrates	Glycogen	Liver, muscle	0.5	8.5	300	60
	Glucose	Circulating fluids				
Proteins	Proteins	Muscles	12	200	100	0.8

In conclusion, strong adaptation mechanisms are established to provide the body with glucose essential to the brain, while maintaining the minimum amount of proteins essential to life.

- *Metabolic adaptation to a carbohydrate deficiency*

The body's adaptation to a sub-clinical carbohydrate deficiency is well known. It has been explored particularly in the case of overnight fasting, and fasting lasting 24 hours or several days. Concerning low-carbohydrate weight-loss diets, they are considered ketogenic when carbohydrate intake is lower than 20% of energy intake. The definition proposed by Westman et al. (2007) is:

- a diet "low in carbohydrates" provides 50 to 150 g of carbohydrate per day, which does not induce the presence of ketones in the urine, for most people;
- a diet "low (or very low) in carbohydrates" and ketogenic provides less than 50 g or even less than 20 g of carbohydrates per day.

Table 6: Energy substrates during a low-carbohydrate and ketogenic diet (Westman et al. 2007)

Fatty acids (≈70% of caloric intake)
- Dietary fats
- Lipolysis
  - Adipose tissue

Ketone bodies (≈20% of caloric intake)
- Dietary fats and proteins
- Lipolysis and ketogenesis
  - Fat reserves

Glucose (≈10% of caloric intake)
- Gluconeogenesis
  - Dietary proteins and fats (glycerol)
- Glycogenolysis

When a weight-loss diet is followed, and to a greater degree during prolonged fasting, metabolic adaptations occur to maintain stable minimum blood sugar levels and preserve muscle protein reserves. Thus, carbohydrate reserves (glycogen) are depleted rapidly by first mobilising liver glycogen reserves (which disappear within 24 hours of fasting) and then muscle glycogen reserves which disappear within a few days. Muscle glycogen does not directly provide glucose (due to the absence of glucose-6 phosphatase), but lactate and pyruvate from muscle glycolysis fuel liver glycogenesis (the Cori cycle). Muscle glycogenolysis may thus indirectly contribute to maintaining blood glucose levels.

During overnight fasting, constant blood glucose levels are maintained by the hepatic production of glucose (2.0-2.5 $mg.kg^{-1}.min^{-1}$, for a 70 kg man). Seventy-five percent of this glucose comes from glycogenolysis and 25% from hepatic gluconeogenesis. It is used primarily by the brain, kidneys, blood cells (non-insulin-dependent tissues) and muscles (Table 5). Thus, in this phase of fasting, only 25% of peripheral glucose use is regulated by insulin (primarily muscle and white adipose tissue).

Table 7: Consumption of glucose by the body (Riou et al. 1994)

Tissue	g/24 h at rest duration of fast 12h 8d 40d			g/h maximum effort
Brain	120	45	22	5
Muscle	30	5	5	300
Kidney	30	5	5	1.6
Blood	34	34	34	1.5
Total	*214*	*89*	*66*	*308*

After overnight fasting (post-absorptive period), glycogenolysis peaks until liver glycogen reserves are depleted.

Gluconeogenesis, which started at the beginning of fasting, peaks after 48 h of fasting. It decreases after 10 to 20 days of total fasting (in macronutrients) due to the decrease in gluconeogenic substrates, particularly amino acids. Despite this decrease, blood glucose remains constant due to changes in the peripheral use of glucose, which decreases through at least three mechanisms:

- fall in insulin levels (occurring very early on in fasting) which results in decreased synthesis of insulin-dependent glucose transporters (GLUT 4) and thus the ability to use glucose and white adipose tissue;
- preferential use of ketone bodies as energy substrates for the brain instead of glucose;
- peripheral insulin resistance secondary to the increase in plasma concentrations of NEFAs and ketone bodies.

Weight-loss diets, based on low energy intakes in general, and low or very low carbohydrate intakes in particular, have implications that are logically related to the fasting situations mentioned above. There have however been few clinical studies in humans to specifically examine metabolic changes in the individual as a result of partial carbohydrate deficiencies. In their review, Westman et al. (2007) mentioned the origin of energy substrates during a low-carbohydrate and ketogenic diet (see Table 4).

Carbohydrate restriction in overweight or obese subjects alters hepatic metabolism by increasing gluconeogenesis and ketosis. The Browning et al. (2008) study concluded that hepatic gluconeogenesis is modified by increasing the use of lactate and amino acids, but not glycerol (Browning et al. 2008). This change is associated with a reorganisation of hepatic energy metabolism suggesting hepatic β-oxidation.
An earlier study in healthy subjects indicated that under isocaloric conditions, the carbohydrate content (high or very low level) of a diet followed for 11 days altered the rate of glucose production primarily by modulating glycogenolysis. In contrast, the low carbohydrate intake diet (compared to the high-carbohydrate diet) increased gluconeogenesis only very slightly in the post-absorptive phase (Bisschop et al. 2000).

In 2005, Erlanson-Albertsson et al. concluded from a literature review of clinical studies that a diet low in carbohydrates would lead to weight loss (after 3 to 6 months), due to loss of appetite explained by the high protein content of the diet, the ketogenic nature of the diet and lastly by the lack of sugars (sucrose and fructose) that stimulate hunger (Erlanson-Albertsson et al. 2005).

- *Metabolic adaptation to a lipid deficiency*

After overnight fasting (post-absorptive state), about 60% of non-protein energy is supplied by the oxidation of carbohydrates, and 40% by that of fats. White adipose tissue, in which energy is stored as triglycerides, releases its energy in the form of NEFAs and glycerol, the latter being a substrate for gluconeogenesis.
The production of ketone bodies (acetoacetate and β-hydroxybutyrate) by the liver depends mainly on the regulation of intrahepatic oxidation of NEFAs.
During fasting, ketogenesis increases for 4 to 5 days, with the increase in ketogenic flux being considerable, and provides energy intake first to the brain but also to the muscles, digestive tract and kidneys. If fasting persists, the concentration of ketone bodies continues to increase due to a drop in

their peripheral use, while their production remains constant. The massive increase in ketogenesis during fasting is accompanied by metabolic acidosis, which is usually compensated for.
The rise in ketone bodies may be one of the mechanisms that prevent muscle proteolysis from being fully activated and that may allow the nitrogen balance to be maintained close to 0 during prolonged fasting, whereas it is clearly negative at the beginning of fasting.

Table 8: Concentration and flow of energy substrates during fasting (Riou et al. 1994)

Substrates		Fasting period 12h	48h	10d	20d	40d
Glucose	[C] mmols.L^{-1}	4.5	3.5	3	3	3
	Flow mmols.kg^{-1}.min^{-1}	14	10	8.5	8.5	8.5
NEFA	[C] mmols.L^{-1}	0.4	1	1.3	1.5	1.5
	Flow mmols.kg^{-1}.min^{-1}	6	12	-	-	-
Ketone bodies	[C] mmols.L^{-1}	0.1	2	5	6	7
	Flow µmols.kg^{-1}.min^{-1}	2-3	10	10	10	10
Insulin	[C] mU.l^{-1}	10	6	3	3	3

- *Metabolic adaptation to a protein deficiency*

A protein deficiency can be encountered when practising total fasting but also in situations of 'balanced' energy restriction affecting all sources of nutrients.

During fasting, the body's protein reserves are mobilised mainly from the muscle. Proteolysis releases the 20 constituent amino acids of proteins, but due to their intramuscular metabolism, 80% of the amino acids released are alanine and glutamine. Much of the alanine produced is derived from the transamination of pyruvate, from which this amino acid is derived. These amino acids are used by the liver (gluconeogenesis) and the digestive tract; their concentration does not therefore increase in peripheral tissues, unlike that of the branched-chain amino acids (leucine, isoleucine and valine), due to a decrease in their peripheral use.
From 15 days of fasting, proteolysis decreases by a mechanism that has not yet been fully elucidated.

In conclusion, the body is adapted to deal with famine situations lasting several weeks. It is thus able to mobilise its glycogen reserves, part of its protein reserves and a very large proportion of its lipids contained in adipose tissue. It should be borne in mind that weight loss does not only occur at the expense of body fat reserves and that the loss of lean body mass rapidly causes the subject to weaken through loss of muscle mass.

Key points

- **Weight loss does not only occur at the expense of body fat reserves: the loss of lean body mass rapidly causes the subject to weaken through loss of muscle mass.**

c. Nutritional deficiencies and deficiencies in vitamins and minerals

Few studies have evaluated the potential adverse effects of weight-loss diets on intakes of vitamins and minerals (Gardner et al. 2010). The available data concern, for the most part, the consequences of possible insufficient calcium intake related to certain diets and their impact on bone mineralisation. Other studies have analysed the impact of diets on magnesium, iron and group B vitamin intakes.

- *Calcium intake and bone mineralisation (see 4.4.2 a)*

Weight-loss diets cause a decrease in bone mineral density, with an average 1-2% reduction in bone mineral density for a weight loss of 10% (Shapses et al. 2006). This effect appears more severe in non-obese individuals and in women from pre-menopause (48 years old). It seems to be more pronounced in cases of significant weight loss (≥ 14%) over a short period (3 months), compared to weight loss over a longer period (Shapses et al. 2006). The possible protective effect of engaging in

physical exercise was assessed in women after menopause, but this only seems to have a partial effect on the prevention of bone loss, with the effect only being detectable at a few bone sites.

The factors discussed as being responsible for bone loss include the declining production of oestrogen, IGF-1 and leptin, and increased production of cortisol. The lower calcium intake associated with diets low in dairy products is another explanation offered. This insufficient calcium intake is compounded by the intestine's reduced capacity to absorb calcium, as has been demonstrated in post-menopausal women placed on moderate energy restriction, of around 1000-1200 kcal/d (Cifuentes et al. 2004). This reduction may be related to a failure of the kidneys to produce the biologically active form of vitamin D due to a clinical deficiency in calcium arising from insufficient IGF-1 levels. However, this hypothesis needs to be verified. Interestingly, the situation is different in younger women, because for them, weight loss does not result in significant loss of bone mineral (Riedt et al. 2007; Shapses et al. 2001), nor in a reduced capacity of the intestine to absorb calcium (Riedt et al. 2007).
To compensate for the insufficient calcium intake and absorption in post-menopausal women, several intervention studies have assessed the effect of calcium supplements on the bone metabolism of these women during energy restriction. Two randomised studies evaluated the effect of calcium supplementation (1 g/day) on bone mineral density in post-menopausal obese women placed on energy restriction (Jensen et al. 2001; Ricci et al. 1998). In both studies, a loss of bone mineral (bone density or bone mineral content of the whole body) was observed after 3 or 6 months of energy restriction in the supplemented groups, as well as in the non-supplemented groups, but with lower loss of lumbar mineral content in the supplemented groups (Jensen et al. 2001). In addition, the calcium supplements (2 g/d of calcium carbonate or 0.75 to 1 g/d of elemental calcium) did not influence weight loss, nor changes in markers of bone and calcium metabolism (parathyroid hormone, alkaline phosphatases) during 3 months of moderate energy restriction (500-750 mg/d calcium intake) in overweight or obese women (Holecki et al. 2008; Wagner et al. 2007). Thus, calcium intake does not appear to play a key role in the loss of bone mineral observed in post-menopausal women practising energy restriction.

However, studies do suggest that the intake of milk proteins prevents or reduces bone loss during dieting. The type of diet should thus be taken into account. A randomised study showed bone loss at 12 months (4 months of weight loss) in obese women (Thorpe et al. 2008). These women had received a normal-carbohydrate diet (about 55% of energy from carbohydrates, 0.8 g/kg/d of protein and 766 mg/day of calcium, i.e. two servings of dairy products per day). This bone loss was not observed in women receiving a diet rich in milk proteins providing 1.4 g/kg/d of protein, or about 30% of energy intake and 1140 mg/d of calcium (three servings of dairy products/day). This is corroborated by the results of another randomised study which showed lower bone loss relative to weight loss, in women with a high-protein diet and adequate calcium intake, compared to those receiving a high-carbohydrate diet (Skov et al. 2002).
Indeed, it has been shown that a diet rich in protein but relatively low in calcium (777 mg/day) followed for 2 months is unable to reduce the increase in bone turnover markers (urinary D-pyridinoline and osteocalcin) observed in obese women, suggesting increased bone resorption, compared to control women receiving a diet rich in carbohydrates and providing 594 mg/d of calcium (Noakes et al. 2005). However, the elevation of these markers was lower in 25 obese adults receiving a diet rich in milk proteins (2400 mg/day of calcium) for 3 months (+ 1 month of maintenance), compared with 25 obese control subjects fed a diet rich in non-milk proteins providing 500 mg/day of calcium (Bowen et al. 2004).

- *Vitamins and other minerals*

Very few intervention studies have assessed the effects of weight-loss diets on vitamins and minerals other than calcium. Only four before/after intervention studies comparing two diet types for 3-8 weeks were found. They concern the effects of various diet types on the intakes or blood concentrations of some micronutrients, mainly folates, vitamins B6 and B12, and iron.
While we can assume that insufficient intake of foods rich in vitamin D can reduce the reserves of this vitamin, it must be borne in mind that more than half of these reserves are provided by the cutaneous production of this vitamin when the skin is exposed to sunlight. In fact, vitamin D status has not been assessed in regard to weight-loss diets, and the intervention studies that have assessed the effects of calcium supplements have been conducted in women receiving vitamin D supplements.

As expected, diets emphasising cereals, fruits and vegetables (diets low in saturated fat and high in carbohydrates) increase the intake and blood concentration of folates (Keogh et al. 2008; Meksawan et al. 2004; Noakes et al. 2005), in contrast to high-fat diets (Keogh et al. 2008; Meksawan et al. 2004). Similarly, diets rich in protein or fat increase the serum values of vitamin B12, whereas diets high in carbohydrates hardly increase or even decrease these values (Keogh et al. 2008; Noakes et al. 2005). Furthermore, the measurement of the activation of pyrophosphates suggests an improvement in vitamin B6 status in subjects subjected to energy restriction with diets low in fats but rich in carbohydrates or protein (Noakes et al. 2005).
Finally, while very low-calorie diets (including 2 weeks at 300 kcal/d) affect iron status, with decreased serum iron, transferrin saturation and higher TFRs (Beguin et al. 1997), other diets do not seem to influence iron status, such as those low in fats but rich in carbohydrates or proteins (Noakes et al. 2005).

To conclude, the limited data published on this subject do not allow the micronutrient status to be assessed, despite the intake deficiencies demonstrated by the analysis of the diets (see 4.3.3). However weight loss, if it is significant and rapid, can cause bone loss in women approaching menopause or after menopause. This bone loss, amounting to about 1% for 10% of weight loss, can cause problems when diets are followed repeatedly over several years. Some intervention studies suggest that diets rich in protein and calcium pose a lower risk than diets rich in carbohydrates or even diets rich in protein only (Bowen et al. 2004; Thorpe et al. 2008).

Key points

- **The limited data published on this topic do not allow a formal assessment to be made of the micronutritional status regarding vitamins and minerals, other than calcium, despite the inadequate intakes demonstrated by the analysis of the weight-loss diets, and the diets observed during short-term studies.**
- **Very low-calorie diets (including 2 weeks at 300 kcal/d) affect iron status.**
- **Weight-loss diets cause a decrease in bone mineral mass, with an average 1-2% reduction in bone mineral density for a weight loss of 10%.**
- **Weight loss, if it is significant and rapid, can promote bone loss in women approaching menopause or after menopause, and in non-obese individuals. This effect may be more pronounced in cases of significant weight loss (≥ 14%) over a short period (3 months).**
- **The available data suggest that engaging in physical exercise only prevents bone loss incompletely.**
- **Calcium deficiency is only one factor of bone loss observed in menopausal women subjected to energy restriction.**

4.4.2.Pathophysiological consequences

a. Bone risks (see 4.4.1 c)

The existence of a relationship between weight, body composition and bone mass has been demonstrated repeatedly (Kirchengast et al. 2002; Reid 2008; Reid 2010; Rosen et al. 2006). Morbid obesity, often associated with diabetes, is indeed considered a risk factor, due to the inflammatory processes it generates (Greco et al. 2010). In contrast, overweight is also considered as protective with regard to the process of osteopenia (Zhao et al. 2007), while a low BMI is a risk factor for osteoporosis (Galusca et al. 2008).

- *Nutritional foundations for optimal bone health*

The concept of nutritional prevention of osteoporosis is based on conventional recommendations in terms of calcium and vitamin D. It also incorporates the complexity of our diet and therefore the other food categories as purveyors of osteoprotective nutrients (Coxam et al. 2008). Pragmatically, a balanced and varied diet, introduced at an early age, in its entirety, will optimise bone mass.

The requirements for optimal bone health are therefore as follows:

- adequate status in components such as proteins (development of the organic matrix) and calcium (mineralisation of collagen framework), which must also be bioavailable, hence the need for vitamin D to potentiate its intestinal absorption;
- respect of the major nutrient balances. This means limiting high-protein diets and sodium overload, which in extreme situations may cause metabolic acidosis resulting in a urinary calcium leak. The calcium balance, and consequently age-related osteopenia, depends not only on intakes but also losses, and are usually not controlled by mineral supplementation alone. It is also recommended to combine alkalising foods (fruits and vegetables) to compensate for any metabolic acidosis generated by a diet high in salt and animal protein products;
- intake of protective nutrients/micronutrients.

Thus, any food that does not take these principles into account may be deleterious to the skeleton.

- *Epidemiological foundations for the relationship between bone mass and body weight*

The analysis of the literature reveals that, at any age, bone mass is partly dependent on body weight. Thus, a low weight or any weight loss, even only a small degree, can exacerbate the osteopenia process at menopause or related to age (1% change in bone mass for 5-6 kg of weight loss) (Hui et al. 2002; Macdonald et al. 2005; Nguyen et al. 1998; Pouilles et al. 1995; Shapses et al. 2006) and increase the risk of fractures (Ensrud et al. 2003). The same is true in the elderly, regardless of sex (Ensrud et al. 2005; Knoke et al. 2003). In contrast, weight gain is protective (Cummings et al. 1995; Hui et al. 2002; Pouilles et al. 1995).

Fluctuations in body weight (whether or not intentional) are therefore considered as predictors of bone mass. Consequently the history of weight change is an important parameter to consider in the management of bone mass.

- *Weight-loss diets and bone mass*

✓ *Energy restriction*

In a literature review, the authors concluded that there was a bone loss of 1 to 2% (at different sites), for a weight reduction of 10% (Shapses et al. 2006). What is important for healthcare professionals to consider is that weight loss (from a loss of 5%) and the "yoyo" effect exacerbate the risk of fractures (Langlois et al. 2001; Margolis et al. 2000; Meyer et al. 1998).

Effect of age and physiological status

Bone-related complications observed following food restriction vary depending on the population considered (Shapses et al. 2006). Thus the decrease in bone mineral density (BMD) and bone mineral content (BMC) ranges from 0 to 2.5% and 3 to 4%, respectively. In addition, the response depends on the bone site considered, i.e. demineralisation of between 1 and 13%.

In menopausal women, a weight reduction of 4-13% was associated with bone loss of about 1 to 4% (Avenell et al. 1994; Riedt et al. 2005; Salamone et al. 1999). Before menopause, the effects on bone were lower (BMD and BMC decreased by 0.5% and 1.8%, respectively) (Ramsdale et al. 1994; Van Loan et al. 1998), or even nonexistent (Hinton et al. 2010; Riedt et al. 2005; Shapses et al. 2001).

In men, a weight reduction of 7% resulted in bone loss of 1% (Pritchard et al. 1996). This data is also entirely consistent with the results of epidemiological studies conducted in men (Ensrud et al. 2005).

However, in children and adolescents, the consequences of weight-loss practices do not seem to modulate bone mass (Paakkunainen et al. 2002). This study is corroborated by that of Stettler et al. who measured, in obese adolescents subjected to a low-calorie diet (1200-1500 Kcal/d), an increase in vertebral BMC and a reduction in the appendicular bones (Stettler et al. 2008). However, this effect disappears after adjusting for size.

Effect of initial weight

Nguyen et al. measured higher osteopenia (> 1%) in cases of weight loss in subjects with normal initial weight, compared to that observed in overweight or obese individuals (Nguyen et al. 1998).

Effect of intensity of weight loss

The impact on bone depends on the intensity of weight reduction. Therefore if weight loss is equivalent to or greater than 14%, and over a short period (3-4 months), the resulting osteopenia process is significant (Van Loan et al. 1998), whereas lower weight loss affects the skeleton to a lesser degree (Ramsdale et al. 1994), or not at all (Riedt et al. 2005; Shapses et al. 2001).

✓ *Low-fat diets*

Fatty acids, precursors of prostaglandin synthesis, can also modulate intestinal absorption of minerals or oxidant and inflammatory status and, therefore, play an important role in bone physiology. Fats in the diet are therefore to be considered in the nutritional management of bone mass.

As part of a clinical investigation designed to induce low amplitude weight loss (-3.2 ±4.7 kg) in premenopausal women, Salamone et al. reduced fat intake and recommended engaging in physical activity (Salamone et al. 1999). They observed an annual decline in bone mineral density in the hip, twice as fast in the intervention group compared with control volunteers, while the change was not significant for the lumbar region, probably due to physical exercise. Avenell et al. also led a study in overweight or normal weight menopausal women, involving a low-fat diet (1200 kcal/d, 20% of energy) high in fibre (28 g/d) with daily calcium intake of 330 mg (Avenell et al. 1994). Following the diet resulted in weight loss (2.8 kg after 6 months) and an exacerbation of the osteopenia process (assessed by bone densitometry), typical in this population category. As part of a similar strategy adopted by overweight men, Pritchard et al. demonstrated that the observed reduction in bone mineral content correlates with the loss of body fat (Pritchard et al. 1996).

In summary, the practice of energy restriction based on a reduced fat intake is deleterious to bone mass.

✓ *High-protein diets*

Clinical studies investigating the impact of proteins on bone mass are sometimes contradictory and have aroused a controversy that remains unresolved. According to an initial series of claims advanced, proteins play a fundamental role, with inadequate intakes being detrimental to the functioning of the somatotropic axis (growth hormone and IGF-1). In contrast, according to a second series of arguments, excess protein can upset the mineral balance, since the level of consumption is a major factor determining calcium leak (Coxam et al. 2008).

Unfortunately, there is only minimal literature on the skeletal impact of high-protein weight-loss diets.

As part of a randomised cross-over study, increased bone resorption was observed in menopausal women receiving a high-protein diet (90 g/d and 180 mmol of NaCl/d) compared with control subjects (70 g/d of protein and 65 mmol of NaCl/d), where taking hormone replacement therapy prevented the increase in osteoclast markers (Harrington et al. 2004). However, it is likely that the deleterious effect results from the combination of a high-protein, high-salt diet and not solely from protein overload. Moreover, Skov et al. did not observe exacerbated demineralisation due to weight loss in obese and overweight women following a high-protein weight-loss diet (102.5 g/d, fat 76.9 g/d) compared to the group on a normal protein diet (85.7 g/d, fat 99 g/d) (Skov et al. 2002). Conversely, a high-protein diet (30% of energy) including the consumption of three dairy products, while generating higher urinary calcium excretion, was able to mitigate the reduction in bone mineral density caused by weight loss, compared to a normal carbohydrate diet (55% of energy) with consumption of only two dairy products (6276 kJ/d in women and 7113 kJ/d in men) (Thorpe et al. 2008). The observed effect persisted during the stabilisation phase.

Similarly, investigations on animal models have not highlighted the significant effect of a diet rich in protein (Mardon et al. 2008; Pye et al. 2009).

It is therefore premature to draw any conclusions as to the bone-related complications resulting from following high-protein diets, beyond the weight loss effects.

- *Conceptual foundations for the interactions between body weight and bone mass*

Various processes have been elicited to explain the positive relationship between body weight and bone mass, such as mechanical stimulation related to the weight load, hormonal systemic mechanisms (insulin, growth hormone, IGF-1, etc.), the relationship between adipose and bone tissue which constitutes a homeostatic feedback system involving adipokines.

In conclusion, it is clear that following weight-loss diets is detrimental to the integrity of bone mass (due to the impact on bone mass and the fracture risk). The loss of body fat is the primary determining factor of their impact on bone mass, but it is likely that both compartments (body fat and lean mass) contribute to the skeleton's integrity (Reid 2008). The intensity of bone-related complications depends on the population concerned (in terms of age and gender), initial weight, and conditions of weight loss (speed and degree). Multiple mechanisms have been elicited to explain such bone-related complications.

Key points

- **Following weight-loss diets is detrimental to the integrity of bone mass (impact on bone mass and thus presumably on fracture risk).**
- **Low weight or any weight loss, even a small degree, can exacerbate age-related or menopausal osteopenia (1% variation in bone mass for 5-6 kg of weight lost).**
- **Fluctuations in body weight (whether intentional or not) are considered as predictors of bone mass. Therefore the history of weight change is an important parameter to consider in the management of bone mass.**
- **The practice of energy restriction based on reduced fat intake is harmful to bone mass.**
- **High-protein diets and sodium overload, in extreme cases, can cause metabolic acidosis resulting in urinary calcium leak.**
- **However there is still a lack of data to assert that following high-protein weight-loss diets exacerbates the deleterious effect of weight loss on bone mass. This deleterious effect may result from the combination of a high protein and high-salt diet.**
- **The intensity of bone-related complications depends on the population concerned (in terms of age and gender), initial weight, and conditions of weight loss (speed and degree).**

b. Kidney, liver and digestive risks

The value of the studies presented lies in determining whether the ingestion of high amounts of protein is deleterious to the liver and kidney, two organs which are very heavily involved in the management of excess protein.

- *Effects on the kidney and renal function*

The potentially deleterious effect of high intakes of protein on renal function has often been advanced as an argument for limiting the use of high-protein diets.

In animals, it is acknowledged that following a high-protein diet increases the size of the kidney (Jean et al. 2001; Morens et al. 2001) but this increase is transient and does not persist beyond three months of diet (Lacroix et al. 2004). On a model of obese young pigs, a diet with 34% protein administered over two weeks did not cause hyperplasia (Schoknecht et al. 1993). In rats, chronic *ad libitum* consumption of a diet high in protein (50% of energy) for 6 months (period corresponding to a quarter of the animals' life) did not lead to alterations in renal tissue (Lacroix et al. 2004). The transient increase in kidney size may be related to the increased glomerular filtration rate, which effectively increases the elimination of nitrogenous wastes, including urea. This increase in glomerular filtration rate has been observed in rats (Burtin et al. 1994), rabbits (Benabe et al. 1992) and also humans

(Skov et al. 1999). This last study is one of the few in humans to address the effect of a long-term high-protein diet on renal function. Sixty-five overweight or obese subjects followed for 6 months a diet providing 12% or 25% of energy from protein and 30% from fats without energy restriction. Kidney size and glomerular filtration rate had indeed increased, but without any deleterious effect, such as signs of kidney failure, being detected.
Conversely, protein restriction has a detrimental effect on renal function. Rats exposed *in utero* to a diet of 9% protein had impaired renal development and fewer nephrons compared with rats fed a diet of 18% (Nwagwu et al. 2000).

In patients with renal failure, a drastic restriction of protein intake (0.28 g/kg/d) compared with a moderate restriction (0.58 g/kg/d) multiplied twofold the risk of mortality after a renal failure episode (Menon et al. 2009). In other cases, there are not, to our knowledge, any clinical data on the effects of such diets (mainly fruit and/or vegetable based diets) on renal function.
Concerning the effect of energy restriction, it has also been shown in humans that fasting increases diuresis and natriuresis in the first week (Sigler 1975). In hypertensive obese subjects, energy restriction for 4 days produced the same effects, probably by increasing the biological activity of atrial natriuretic peptide (ANP) (Dessi-Fulgheri et al. 1999). However, no adverse effects were associated with this observation.

Ultimately, energy restriction itself does not seem to have deleterious effects on renal function. A high protein intake increases the glomerular filtration rate but does not cause alterations to kidney tissue or kidney failure. Thus, regarding low-calorie high-protein diets, as energy restriction has the effect of moderating the daily amount of protein ingested, there is no proven risk to renal function (provided that the candidate for slimming has no previously declared kidney disease). For example, for a 1200 kcal diet, a 15% protein intake represents 45 g of protein, i.e. an intake of 0.75 g/kg/d for a 60 kg person, and 0.56 g/kg/d for an 80 kg person. This value is below the safety intake level (0.83 g/kg/d). Raising the percentage of protein to 30% then represents an intake of 90 g of protein, i.e. an intake of 1.5 g/kg/d for a 60 kg person (which is close to the spontaneous consumption of protein in Western countries (AFSSA 2007)), and 1.1 g/kg/d for an 80 kg person. It is therefore difficult with energy restriction to exceed the maximum level considered satisfactory, estimated at an intake of 2.2 g/kg/d (AFSSA 2007). A clinical case of renal failure was reported in a patient with glomerulonephritis - but not renal failure - and who, within the framework of a bodybuilding exercise programme, consumed an amount estimated at 2.6 g/kg/d of protein (Combe et al. 1993). However, there do not seem to be any other similar clinical cases found in the literature.
While it is rare for these limits to be exceeded, they can be observed in certain population groups, such as bodybuilders, or when the diet is not based on energy restriction, such as non-low-calorie high-protein diets (see Table 2). The latter case involves protein intake beyond which there is a risk of saturation of the liver's ability to synthesise urea, which can cause an undesirable increase in plasma levels of amino acids and ammonium ion (AFSSA 2007).

- *Effects on the liver and liver function*

The liver is largely involved in protein and energy homeostasis, particularly in the management of excess proteins and carbohydrates. Weight-loss diets are often rich in protein and/or fats (ketogenic diets), rarely in carbohydrates. The question therefore arises of the safety of high levels of these two macronutrients. However, it must be borne in mind that energy restriction has the effect of reducing the intake of macronutrients, and a high contribution of a macronutrient to energy intake is not generally reflected by an excess of this macronutrient in terms of daily amount ingested.
In mice, a ketogenic diet *ad libitum* increased hepatic triglycerides and circulating free fatty acids (Kennedy et al. 2007). A study in rabbits showed the occurrence of hepatic steatosis following a 24-week ketogenic diet (Birkner et al. 2005).
Nevertheless, most studies concerned with the effect of energy restriction are consistent with improved liver function (Patel et al. 2009; York et al. 2009). Thus, in 41 obese individuals subjected for 8 weeks to a low-calorie diet providing mainly proteins and carbohydrates, a decrease in hepatic steatosis was noted (Andersen et al. 1991). In 33 obese individuals subjected for 6 weeks to a high-protein low-calorie diet (800 kcal maximum), liver size and hepatic triglycerides were reduced (Lewis et al. 2006), while no adverse effects were noted.
In rats exposed for 6 months to a diet of 50% protein, without energy restriction, there was no alteration to liver tissue (Lacroix et al. 2004). Instead, the rats fed the normal diet exhibited hepatic triglyceride inclusions from 3 months of the diet, unlike the rats subjected to the high-protein diet,

explained by the fact that the rat's normal diet is rich in carbohydrates and that postprandial lipogenesis is inhibited in rats consuming the high-protein diet (Stepien et al. 2010).
However, some authors noted transient disturbances of liver function related to the weight loss. Friis et al. reported that rapid weight loss (an average of 13 kg over the first 2 weeks) results in a transient increase in bilirubin, transaminases, lactate dehydrogenase (LDH) and alkaline phosphatase (Friis et al. 1987). These markers of liver function stabilised after 4 weeks of diet, whereas subjects had continued to lose 10 kg on average over the final 2 weeks. Furthermore, Andersen et al. reported that 24% of patients developed mild inflammation or mild portal fibrosis after weight loss of 34 kg over 10 weeks (Andersen et al. 1991). They attributed this phenomenon to rapid weight loss, associated with excessive energy restriction, generating the massive mobilisation of intrahepatic lipids. The authors noted that previous studies have also reported the onset of inflammation and liver and portal fibrosis following bariatric surgery (gastric bypass, gastroplasty) or fasting.

Furthermore, energy restriction appears to increase the risk of gallstones. Thus, Hoy et al. verified the presence of gallstones before and after a low-calorie diet of 800 kcal, followed for 10 weeks (Hoy et al. 1994). Two out of 53 patients developed gallstones after following the diet. These two patients had attained the highest rate of weight loss (25 kg over 10 weeks compared to an average weight loss of 10 kg). The authors explained this phenomenon by bile stasis due to the deprivation of dietary fats. Indeed, in the best case, fat intake was 25% of energy intake, a daily amount of 22 g. This stasis disrupts the solubilisation of biliary cholesterol and promotes the formation of calculus. These authors cite previous studies which found a higher prevalence of patients with gallstones after more severe energy restriction (around 500 kcal).

In conclusion, significant energy restriction, of the kind that may be practiced in very low calorie diets, can cause moderate inflammation and liver and portal fibrosis as well as gallstones. The high protein content often associated with weight-loss diets poses no proven risk to liver function. However, the available studies preclude reaching a conclusion on the safety of ketogenic diets for liver function.

- *Effect on the gastrointestinal tract*

Several reviews mention that various side effects of gastrointestinal origin can occur with diets rich in fat and low in carbohydrates: halitosis, thirst, diarrhoea, constipation and nausea or vomiting (Clifton et al. 2008; Freedman et al. 2001). However, these side effects remain minor and limited to the first week of dieting, even for very restrictive carbohydrate diets (20 g/d) such as those used to treat epilepsy that is unresponsive to any other treatment (Carrette et al. 2008; Kang et al. 2004). Constipation is well described for diets low in fibre, these diets may eventually lead to other complications such as haemorrhoids and/or diverticulosis, if continued for a prolonged period. A significant fibre intake (pure or enriched extracts) should, in most cases, remedy constipation problems related to these diets.
Diets high in carbohydrates and low in fats can cause flatulence (Barnard et al. 1992).

To our knowledge, there are no epidemiological studies on the risk of colon cancer associated with long-term and/or repeated weight-loss diets. However, many weight-loss diets, particularly those with a low intake of complex carbohydrates, are low in fibre. According to the 2007 report of the WCRF/AICR, foods containing dietary fibre probably protect against colorectal cancer (World Cancer Research Fund / American Institute for Cancer Research 2007). Thus, diets low in complex carbohydrates and fibre are a risk factor for colorectal cancer, if followed over the long term. Indeed, there was a clear dose-response relationship on the basis of the 14 cohort studies analysed in the report, although the report's authors do not exclude the existence of "confounding factors" that may be linked to other food fractions than dietary fibre.

Key points

- **The data suggest that diets with very low calorie intake cause moderate inflammation and liver and portal fibrosis as well as gallstones.**
- **High-protein non low-calorie diets lead to intakes that exceed the adequate intake threshold (2.2 g/kg/d). Consequently, a renal assessment is needed in patients at risk of kidney disease, before commencing any diet.**
- **Certain weight-loss diets, especially low-carbohydrate diets, are often associated with digestive disorders, usually transient. They mainly include constipation, related in particular to lower consumption of fibre.**

c. Cardiovascular risks

Overweight and obesity are not always associated with increased cardiovascular risk (morbidity, mortality): it is the case with overweight (BMI of 25 - 29.9 kg/m^2) and moderate gynoid obesity, overweight and moderate obesity in the elderly, overweight and moderate or average obesity in subjects with satisfactory physical ability without other risk factors (Lecerf 2008). Following the accepted nutritional guidelines for the prevention of cardiovascular diseases, prevention of coronary recurrence, reduction of hypertension, and regression of atherosclerosis, is usually beneficial in coronary patients (Imamura et al. 2009; Kris-Etherton 2009). Losing weight usually improves cardiovascular risk factors, insulin resistance, blood pressure, plasma lipids, factors involved in atherosclerosis (Graffagnino et al. 2006; Tsigos et al. 2008). But there is no evidence that intentional weight loss in healthy subjects reduces cardiovascular mortality (Simonsen et al. 2008); in thin women, weight loss observed in a longitudinal study was associated with an increased cardiovascular risk (Harris et al. 1993). Regarding weight-loss diets, what are their effects on cardiovascular risk factors and on cardiovascular risk itself? Are they always beneficial? Are there any negative effects? Can we separate them from their effect on weight?

- *Very low calorie diets (VLCDs)*

The effects of extremely low calorie diets (400-800 calories) were the subject of a review of the early literature by Wadden in 1993. They lead to a weight loss of 20 kg in 12 to 16 weeks but are followed by weight regain in the first two years, total after five years, identical to methods combining a conventional diet (1200 Kcal) and behavioural therapy (Torgerson et al. 1999; Wadden 1993).
Benefits to cardiovascular risk factors are established in the short term (1 year) but they have not undergone long-term evaluation, probably because of the weight regain.
In the short term VLCDs reduce oxidative stress in diabetics (Skrha et al. 2005); risk factors (blood pressure, plasma lipids) improve in obese women (Pekkarinen et al. 1998) and in obese diabetic subjects (Uusitupa et al. 1990), with a genetic component in the degree of this improvement (Hainer et al. 2000).
A review of the early literature reported a significant number of sudden deaths with VLCDs based on poor quality (in terms of biological value) liquid proteins, some of these deaths had occurred in patients with no previous medical history (Apfelbaum et al. 1987). The poor quality of the protein diet, its excessive duration, and an initial weight that was not dramatically high were risk factors. The cause of death appears to be the occurrence of arrhythmias, and can occur during re-feeding which would cause a sudden increase in cardiac blood volume in failing cardiac muscle.
It seems that today these incidents are less frequent, firstly because these diets are used less apart from their short-term benefit in some cases of insulin-resistant diabetes, secondly because the protein quality has been improved (Krempf 2009). They have been partly replaced by alternative Protein Sparing Modified Fast (PSMF) formulas, where caloric intake is between 600 and 800 Kcal, with a low intake of carbohydrates and fats and micronutrient supplementation.
The total fast, close in spirit and letter to the VLCDs, with fluid intake alone, is not a diet since it is a way of "not eating". Such exclusion of food is dangerous and harmful, and has no value in terms of weight as it alters lean body mass profoundly and carries a high risk of hypokalaemia and sudden death in the event of prolonged use. It should be formally prohibited for weight loss.
These diets (particularly those proposing a fast for a week), if they are actually combined with physical activity, can lead to risks of vagal or hypoglycemic episodes which may be exacerbated by dehydration in the event of severe food restriction.

- *Very low-carbohydrate diets*

These diets, whose prototype is the Atkins diet which was launched in 1972, are sometimes known by the abbreviation HPLC (high fat, high protein, low carbohydrate) (Atkins 1972).
This very popular type of diet results in rapid and significant weight loss. Two cases of cardiovascular death, one by cardiovascular disease, the other by sudden death due to arrhythmia, have been described (Stern et al. 2004; Stevens et al. 2002). A third observation was reported with the development of symptomatic coronary artery disease in a subject initially free of cardiovascular disease (Barnett et al. 2009).
LDL cholesterol (LDL-C) increases by an average of 10% (2-70%), but an increase in oxidative stress related to the formation of methylglyoxal as a result of ketosis has also been noted (Beisswenger et al.

2005) as well as the occurrence of arrhythmias (Best et al. 2000; Larosa et al. 1980; Stevens et al. 2002).
Two recent large prospective studies conducted in Greece and Sweden reported an increase in total and cardiovascular mortality in subjects with low spontaneous carbohydrate intake (Lagiou et al. 2007; Trichopoulou et al. 2007). Another prospective study did not show an increased coronary risk (Halton et al. 2006). But more recently, an American study of nurses and healthcare professionals showed, during 26 years of follow-up in 130,000 subjects, that a diet low in carbohydrates and high in animal-based protein and fats was associated with an increased risk of cardiovascular and all-cause mortality compared with a diet low in carbohydrates and high in vegetable-based protein and fats (Fung et al. 2010). However, this was an observational study and it is difficult to extrapolate these results to those that could ensue from following such a diet to lose weight. The mechanisms involved appear to be related to increased classical risk factors. The increase in LDL-C is irregular (1/3 of cases) (Astrup et al. 2004). Studies conducted on the short term (4-12 weeks) (Noakes et al. 2006; Sharman et al. 2002; Volek et al. 2003; Wood et al. 2006) have shown that this type of diet (6 to 13% carbohydrate) does indeed cause an increase in total cholesterol and LDL-C, but also an increase in LDL size (presumably beneficial) and in HDL cholesterol (HDL-C, also presumably beneficial). Fasting and postprandial triglycerides decrease in all studies, as well as blood glucose levels, fasting and postprandial insulin levels, and insulin resistance including in diabetic obese subjects (Boden et al. 2005). According to the studies, the inflammatory markers CRP and TNFα decrease, as well as blood pressure. The kind of proteins and fats can have different effects on the lipid profile. Thus an "Eco-Atkins" diet based on proteins and fats of plant origin resulted in a greater drop in LDL-C in the short term (4 weeks) than a diet rich in carbohydrates (58% carbohydrate) with identical weight loss (-5 kg) (Jenkins et al. 2009).
A meta-analysis of six-month studies (Nordmann et al. 2006), comparing “Low-Fat” diets confirmed greater weight loss at 6 months (but not at 12 months) (Foster et al. 2003) and more favourable changes in triglycerides and HDL-C, less favourable in total cholesterol and LDL-C, including at one year (Samaha et al. 2007; Stern et al. 2004). Over the medium term, at one year (Brinkworth et al. 2009) a very low-carbohydrate diet (4%), compared to a normal-fat diet (30%) also led to reduced triglycerides and increased HDL-C and LDL-C in subjects with abdominal obesity and a metabolic syndrome risk factor.
One hypothesis put forward for the possible deleterious cardiovascular effect of HPLC diets in the long term comes from studies in mice. Foo et al. showed that an HPLC diet leads to the development of twice as many atherosclerotic plaques despite weight loss (Foo et al. 2009). In these mice, free or nonesterified fatty acids (NEFAs) were twice as high as in control mice. Hernandez et al. recently demonstrated that a high-fat diet (rich in saturated fatty acids and low in carbohydrates) increases circulating free fatty acids during fasting and for 24 hours, which is correlated to the increase in LDL-C (Hernandez et al. 2010). However, in humans the NEFAs released from adipocytes (Jouven et al. 2001; Marfella et al. 2001) can promote arrhythmias and activate inflammation pathways (Smith 2009); in animals this type of diet reduces circulating endothelial progenitor cells (which are normally involved in maintaining vascular reactivity by improving endothelial function and repair of the vessel wall) which would be a factor for atherosclerosis (Sacks et al. 2009).
Thus recently Bradley et al. enrolled 24 overweight or obese subjects (BMI 33.6 ± 3.7 kg/m²) in a randomised eight-week trial comparing a low-fat (20%) high-carbohydrate (60%) diet and a high-fat (60%) low-carbohydrate (20%) diet with an identical energy deficit of 500 kcal (Bradley et al. 2009). Weight loss was identical, as was the reduction in insulin sensitivity. However, in the low-carbohydrate diet group, the systemic arterial stiffness index increased, which could have an adverse effect on vascular risk. Another recent study showed that a low-carbohydrate diet leads to a decrease in endothelial dependent vasodilation compared with a low-fat diet, despite similar weight loss in the short term (Miller et al. 2009).
In the long term, the safety of Atkins-style HPLC diets has not been established (Foreyt et al. 2009; Lara-Castro et al. 2004). Firstly, ketogenic diets prescribed for other indications may lead to arrhythmia (Bank et al. 2008; Best et al. 2000). Secondly, a high fat intake of saturated fatty acids can increase insulin resistance despite weight loss (49). Finally, cases of death by hyperosmolar coma have been reported (Samaha et al. 2007; Stern et al. 2004); as have cases of metabolic acidosis or even ketoacidosis with low-carbohydrate diets (Chen et al. 2006; Shah et al. 2006; Steffen et al. 2006).
When these diets are combined with physical activity, they can cause headaches or even migraines.
Some of these diets (primarily high-protein diets, see Figure 13) provide an excess of salt (sodium), which is a major factor in increasing blood pressure and a risk factor for cardiovascular diseases (stroke, ischemic heart disease) (AFSSA 2002; Strazzullo et al. 2009; WHO 2007).

Due to insufficient consumption of cereals, fruits and vegetables, etc., these diets may be deficient in fibre and antioxidant micronutrients (vitamin E, vitamin C, etc.). It is widely established in the literature that this is, through changes in lipid and carbohydrate metabolism and through a lack of defence systems against oxidative stress, a risk factor for atherosclerotic thrombosis. When diets are followed over the long term, this point must be taken into consideration (Anderson et al. 2009; Dauchet et al. 2005; Ignarro et al. 2007).

- *Low-fat and very low-fat diets*

Very low-fat diets provide around 10-12% of energy intake as fat, whereas that of low-fat diets is between 15 and 30% fat. Consequently, they are necessarily high in carbohydrates, both relatively and absolutely.

In terms of weight, all studies are consistent in indicating that weight loss is initially less (at 3-6 months) then identical at one year, with a statistically identical secondary weight regain; weight loss depends mainly on the calorie level and subject's commitment to the diet (see section on the risk of weight regain (d))
The effects of very low-fat (6.8%) (Ornish et al. 1990) or moderately low-fat (< 20% to 27%) diets on the regression of atherosclerosis have been shown (Gould 1994; Quinn et al. 1994; Schuler et al. 1992; Watts et al. 1992).
However, the negative effects on the lipid profile and particularly on triglycerides have been known for 50 years (Ahrens et al. 1961). Isolated observations have subsequently reported this (Siguel et al. 1996). Early work has shown that in the absence of weight loss, a low-fat diet leads to both higher triglyceride and lower HDL-C levels (Schaefer et al. 1995).
The triglyceride/HDL-C ratio is increasingly considered a relevant and predictive marker of coronary risk (Cordero et al. 2009; Hadaegh et al. 2009). It may also be a marker of insulin resistance.
Numerous studies have refined the metabolic consequences of a low-fat diet (Dreon et al. 1998; Dreon et al. 1999; Knopp 2000; Krauss et al. 2006; Lefevre et al. 2005).
It is known that the LDL phenotype B (small dense LDLs) is atherogenic (St-Pierre et al. 2001) partly due to the greater oxidisability of LDLs. Dreon et al. clearly showed that with a low-fat diet (24%), LDL size decreases and is inversely correlated to the intake of saturated fatty acids, probably due to the activity of hepatic lipase (Dreon et al. 1998). The decrease in LDL size is correlated to higher triglyceride levels (Dreon et al. 1999). The more fat intake increases (and carbohydrate intake decreases), the more the frequency of LDL phenotype B decreases. One third of phenotype A subjects (large LDLs) under a high-fat diet (46%) converted to phenotype B under a low-fat diet (24%). Among the remaining phenotype A subjects, regardless of the diet type (24 or 46%), when following a very low-fat diet (10%) two thirds maintained the phenotype A and one third converted to phenotype B (Dreon et al. 1999). However, not all low-fat diets, according to their composition, would lead to the promotion of small, dense LDLs (Kenney et al. 1999).
Lefevre et al. showed that in healthy men of normal weight, a low-fat diet (24% or 28% fats) followed for 6 weeks compared to a normal-fat diet (37%) results in a reduction in LDL-C, but higher triglyceride levels and lower HDL-C (Lefevre et al. 2005). The decrease in LDL-C was even lower and the increase in the total cholesterol/HDL-C ratio was even greater if the subjects had insulin resistance.
For stable weights, Krauss et al. showed that a low-fat diet (30%) causes a more atherogenic lipid profile (small LDLs, increased triglycerides and apolipoprotein B, decreased HDL-C) than a moderately high-fat diet (46%) (Krauss et al. 2006). This deleterious effect was correlated to carbohydrate intake, although it was lower after weight loss than before (Krauss et al. 2006).
In the medium term, at one year, a comparison of diets with varying levels of fat intake, with identical weight loss of 3 kg, showed that in the "low fat" group, triglycerides increased by 39% (Knopp et al. 1997).
Carbohydrate-induced hypertriglyceridemia has long been known and has been widely studied (Parks et al. 2000). In the medium term, it has been clearly shown that this effect appears only when fats in the diet fall below 25%, for an equal caloric intake, and it is compensated for at a weight loss of over 4 kg (Kasim-Karakas et al. 1997). In addition, it has been shown that an elevation in triglycerides was not observed when the increase in carbohydrates (and therefore the reduction in fats) was gradual (Ullmann et al. 1991). In addition, the response differs according to the initial level of triglycerides: thus a moderately high-fat (40%) diet is more favourable to triglycerides than a moderately low-fat (29%) diet in subjects with initial levels of triglycerides lower than 4.5 mmol/L (Jacobs et al. 2004).

The response for HDL-C also varies depending on its initial level. With a low-fat diet (24 or 28%) in "normal-fat" subjects having initially normal HDL-C levels, the LDL-C/HDL-C ratio was unchanged whereas it decreased in subjects with initially low HDL-C levels (Asztalos et al. 2000).
However, the mechanism involved in the decrease of HDL-C during a low-fat diet is not the same as that which explains the spontaneously low rate of HDL-C with this diet, and thus does not have the same meaning in terms of cardiovascular risk (Brinton et al. 1990).
It is therefore necessary to measure the impact of these diet types on the cardiovascular risk itself.

In a longitudinal observational study, 235 menopausal women were followed for 3 years, and 2243 coronary segments were analysed by angiography (Mozaffarian et al. 2004). Women with the lowest intakes of fats (and saturated fatty acids), and consequently the highest intakes of carbohydrates, had a greater progression of their atherosclerosis.
The aim of the Women's Health Initiative (WHI) was to reduce mortality through a reduction in fat intake and weight (combined with an increased consumption of fruit and vegetables) (Howard et al. 2006). 48,385 women aged 62.3 years on average, moderately overweight (BMI 29.1 ± 5.9 kg/m²), were randomised into two groups and followed for 8.1 years. In the active group, fat intake was reduced by 8.2%, from 37.8% to 28.8% due to a decrease in intake of all fatty acid families. After a year, the average maximum weight loss was 2.2 kg, then the weight returned to the initial level and that of the control group, regardless of age, ethnicity and initial weight. Over a period of 8 years, not only was there no observed reduction in the incidence of coronary events (HR 0.97 CI 0.90-1.06), strokes (HR 1.02 CI 0.90-1.15) and cardiovascular disease (HR 0.98 CI 0.92-1.05), but among those with a history of cardiovascular disease (3.4% of the population group), a significant increase in cardiovascular events of 26% (HR 1.26 CI 1.03-1.54) was observed. It is interesting to note that Howard et al. showed that at 6 years, with a 7.8% reduction in fats and a 7.6% increase in carbohydrates, no significant difference was observed in plasma lipids (LDL-C, triglycerides, HDL-C), except in the group of Caucasian women with diabetes in whom triglyceride levels increased significantly (Howard et al. 2010).
There are however insufficient studies to determine whether any sustainable weight loss with a low-fat diet would still be beneficial despite a lipid profile that seems less favourable.

- *Inflammation*

In overweight, the existence of low-grade inflammation is well established. It results in an increase in acute-phase proteins of inflammation (ultra-sensitive CRP, pro-inflammatory cytokines, etc.). Weight loss improves the low-grade inflammation observed in overweight but the effects differ greatly according to the diets: it has been determined that a very low-carbohydrate diet (12%/fats 59%) reduced markers of inflammation further than a low-fat diet (24%/carbohydrates 56%) (Forsythe et al. 2008), although the reverse was observed in a short-term study (Miller et al. 2009).
Similarly, the effects of weight loss on endothelium-dependent vasorelaxation are not unambiguous and depend on the diet type. A low-carbohydrate diet (high in saturated fatty acids) does not alter markers of endothelial function compared with an isocaloric low-fat diet (low in saturated fatty acids). (Keogh et al. 2008).

- *Weight fluctuation, metabolic syndrome and cardiovascular risk*

Several studies support an increased cardiovascular risk in obese subjects with weight fluctuation (Dulloo et al. 2006; Montani et al. 2006) due to an independent deleterious effect on cardiovascular risk factors (Folsom et al. 1996; French et al. 1997; Hamm et al. 1989; Iribarren et al. 1995; Lissner et al. 1991; Peters et al. 1995). This weight fluctuation is mainly related to the practice of successive weight-loss diets with subsequent weight regain.
However, other studies have shown that the weight itself had a more negative impact than the weight fluctuations (Dyer et al. 2000; Lissner et al. 1990; Wannamethee et al. 2002). The contradictions could be due to difficulties in defining the weight fluctuation, for which there is no consensus. This deleterious effect could lead to an increased occurrence of metabolic syndrome, a cardiovascular risk factor.
In the Su.Vi.Max study, weight fluctuation was considered on the basis of the RMSE (Root Mean Square Error) method from four measurements during the seven-year follow-up of 3553 subjects by classifying them according to four levels: no weight fluctuation and three tertiles of weight fluctuation (Vergnaud et al. 2008). Subjects in the highest tertile of weight fluctuation had an odds ratio (OR) of 2.06 (CI 1.20 to 3.52) for the risk of metabolic syndrome compared with the first tertile, independent of

confounding variables and the relative change in weight. This confirms data from another study conducted in Japan, which highlighted an increased risk of metabolic syndrome with weight fluctuation (Zhang et al. 2005). In the Su.Vi.Max study, an identical association with weight fluctuation was demonstrated for several components of metabolic syndrome (blood pressure, low HDL-C and waist size), but a high weight gain was also associated with an increased risk of metabolic syndrome (Vergnaud et al. 2008).

- *Comparisons of different diets*

Numerous studies have compared the effects of diets on weight or on cardiovascular risk factors. In the short term (3 months), low-carbohydrate diets lead to greater weight loss than low-fat diets, but at 6-12 months weight loss is identical and related to the energy deficit and commitment to the diet (Morgan et al. 2009; Nordmann et al. 2006; Sacks et al. 2009; Truby et al. 2006).
In terms of cardiovascular risk factors, as indicated above, in the short and medium term, low-carbohydrate diets lead to an increase in LDL-C, especially if the proportion of saturated fatty acids is high, associated with increased LDL size (Morgan et al. 2009). The quality of the fats and the kind of protein may alter these changes (Jenkins et al. 2009). Losing weight through a normal-fat (35%) weight-loss diet (1500 kcal/d for women and 1800 kcal/d for men) has a more favourable effect on glycemic control than the low-fat diet (below 30%) (Shai et al. 2008).

Low-fat diets lead to increased triglyceride and HDL-C levels compared to low-carbohydrate diets (Yancy et al. 2004); a high glycemic index may reduce this effect (McMillan-Price et al. 2006). But it is difficult to judge the contribution of the effect to weight loss and that of the type of diet on the cardiovascular risk itself in the absence of specific studies. Only the WHI study allows for an approach as the diet did not result in weight loss or cardiovascular benefit.
Finally, no studies have been conducted over the long-term to analyse the effect of different diet types on cardiovascular risk: it is possible that this is made difficult by the fact that not only is weight loss rarely sustainable, but it is often followed by weight regain or even gain (Jeffery et al. 2002; Korkeila et al. 1999).

The resumption of physical activity in a subject who has been sedentary for several years and who has one or more vascular risk factors (see the French Cardiology Society recommendations on the instructions for conducting a cardiovascular stress test) can have adverse cardiovascular consequences (Franklin 2005). Indeed, in the amateur athlete, the combined practice of physical activity and a weight-loss diet is accompanied in the short-term by the risk of faintness (hypoglycemic, vagal, and/or exacerbated by dehydration) if food restriction is significant.

It can therefore be concluded that dieting may have adverse cardiovascular and metabolic effects. This is the case with very low-calorie ketogenic diets that may lead to accidents with sudden death from arrhythmia. The safety of very low-carbohydrate diets has not been established from a cardiovascular point of view insofar as they can increase LDL-C, when the fats are mainly composed of saturated fatty acids. Very low-fat diets are harmful because they cause an atherogenic lipid profile: thus some clinical and/or epidemiological studies suggest an increased cardiovascular risk particularly in the event of metabolic syndrome and/or a history of cardiovascular disease. In addition to the lipid abnormalities, other adverse changes may occur with a low-fat or low-carbohydrate diet to markers of inflammation, endothelium-dependent vasorelaxation. Finally, weight fluctuation could be a cardiovascular risk factor through the increased risk of metabolic syndrome.
However, there are no studies enabling the long-term impact of these adverse effects to be assessed, compared to the potential benefits of weight loss, partly due to the weight regain observed in most cases in the medium and long term.

Key points

- **Very low-calorie diets may acutely induce accidents with sudden death from cardiac arrhythmia.**
- **The safety of very low-carbohydrate (high-fat) diets has not been established from a cardiovascular point of view. In this context, a high intake of saturated fatty acids can increase insulin resistance despite weight loss.**
- **Very low-fat diets are harmful because they cause an atherogenic lipid profile, particularly in cases of metabolic syndrome.**

- **Weight fluctuation could be a cardiovascular and metabolic syndrome risk factor.**
- **In amateur athletes, the combined practice of physical activity and weight-loss diets is accompanied in the short term by:**
  - **a risk of stroke, mainly during the resumption of physical activity in a subject who has been sedentary for several years and who has one or more vascular risk factors;**
  - **a risk of faintness (hypoglycemic, vagal, and/or exacerbated by dehydration) if food restriction is very significant.**

d. Risks associated with weight loss

- *Risk associated with the release of persistent organic pollutants during weight loss*

In recent years, many studies have focused on persistent organic pollutants (POPs). POPs are harmful chemicals (pesticides, industrial chemicals and by-products or contaminants) that constitute a threat to the environment and health.
As POPs are fat-soluble, they accumulate in body lipids, mainly in adipose tissue and the liver (Dewailly et al. 1999). Several studies have shown a relationship between plasma concentrations of organochlorines and adiposity (Jung et al. 1997; Pelletier et al. 2002). In addition, a correlation was demonstrated between concentrations of polychlorinated biphenyls (PCBs) in plasma and in femoral and abdominal adipose tissue (Pelletier et al. 2003). This relationship between obesity and circulating POPs has not been confirmed for all pollutants, thus showing a great disparity in the level of accumulation of POPs (Dirinck et al. 2010) leading to no relationship (Hue et al. 2006), or even a negative relationship (Dirinck et al. 2010) being established between the BMI and plasma levels of PCBs. A similar study showed that the degree of obesity may be a determining factor in this relationship since the concentration of POPs was higher in overweight patients, whereas it was lower in obese subjects (Agudo et al. 2009). A possible explanation is that, for an equal amount of POPs assimilated by the body, the greater the adiposity, the lower their concentrations in adipose tissue.
For this reason, various studies have examined the impact of weight loss on POP concentrations in plasma and adipose tissue. There is consensus on the effects of weight loss. Many studies clearly show that weight loss is accompanied by an increase in the concentration of POPs in plasma (Chevrier et al. 2000; Hue et al. 2006; Imbeault et al. 2002a; Imbeault et al. 2001; Lim et al. 2010; Pelletier et al. 2002). In extreme cases of morbid obesity, a combination of bariatric surgery and a weight-loss diet has led to weight loss ranging from -12 to -46%, accompanied by an increase of from 18.8 to 338.2% in the plasma concentration of PCBs, thus revealing a strong association between weight loss and plasma concentration of PCBs (Hue et al. 2006). Therefore, even moderate weight loss leads to an increase in POPs in plasma and adipose tissue. It seems that this release of POPs by adipose tissue is the result of increased lipolytic activity in these tissues (Imbeault et al. 2001). The main health hazards of POPs include disruptions of the endocrine, reproductive and immune systems, metabolic dysfunctions, developmental disorders and cancers (Pelletier et al. 2003). Increases in POPs following weight loss are associated with a reduction in the use of fatty acids by the muscle (Imbeault et al. 2002b), in the resting metabolic rate (Pelletier et al. 2002), in the immune system (Tremblay et al. 2000) as well as with the development of metabolic syndrome (Lee et al. 2007). Consequently, weight loss leads to an increased release of POPs, which, due to their effects on energy balance, could contribute to weight regain.

- *Risk of weight regain*

The main problem with weight-loss diets is the high rate of weight regain after the initial loss: using as a criterion for successful slimming a weight loss greater than or equal to 10% of initial weight and maintaining this loss over one year, only 20% of overweight people lose weight successfully in the long term (Wing et al. 2005). Weight regain increases in subsequent years, regardless of the previous rate of weight loss (Anderson et al. 2001).

✓ *Dietary factors*

The vast majority of studies focusing on weight stabilisation after weight loss have assessed the subjects' dietary habits and lifestyle during the stabilisation phase, as compared to the number of kilograms regained. Most diets are followed for a relatively short duration, usually less than six months or a year; then each subject establishes their own strategy, which can certainly be influenced by the

initial weight-loss diet, but also by the subject's former habits, tastes and lifestyle. Weight regain is common, with only 20% of overweight people maintaining their weight loss (Wing et al. 2005) and various studies have sought to identify the factors likely to favour long-term success or failure (Anderson et al. 2001). Thus, authors have suggested the role of such factors as the energy density of the daily food intake (Rolls et al. 2005), the energy distribution of protein, carbohydrates and fats (Clifton et al. 2008; Harris et al. 1994; Lejeune et al. 2005; Leser et al. 2002; McAuley et al. 2006; Shick et al. 1998) and the regular eating rhythm over the week (Wing et al. 2005), and over the day when breakfast is taken (Elfhag et al. 2005; Wing et al. 2005).

The study by Sacks and colleagues provides additional information due to its randomised prospective character, right from the initial weight-loss diet (Sacks et al. 2009). This study compared, after randomisation, four isocaloric diets with varying levels of protein, carbohydrates and fats.
At six months and at two years, the mean weight loss was the same for all four diets. This reveals two important concepts:

- in accordance with what one might expect from the laws of thermodynamics and the physiology of the individual's energy balance, overall caloric intake is a major factor in a diet's effects on weight;
- adapting the diet to the patient's tastes and habits is important to ensure their long-term commitment. Indeed, in the study by Sacks and colleagues, the subjects who were monitored regularly to facilitate this commitment had, at two years, lost significantly more weight than the group average (9 kg compared with 4 kg).

Unlike young adults (Prentice et al. 1992), successive weight loss and regain in elderly people, after the age of 65, leads to a loss of lean body mass and a gain in body fat (Lee et al. 2010).

Lastly, a sustainable change in lifestyle, based on a varied, balanced diet with a caloric intake corresponding to needs, is a key factor in weight stability.

✓ *Role of physical activity*

In this section, the term physical activity falls within international recommendations for physical activity for health. Indeed, it helps to reduce the loss of muscle mass associated with a low-calorie diet and limit weight regain after dieting.
The impact of regular physical activity can occur at different times:

- physical activity during energy restriction (CR): physical activity alone does not induce significant weight loss (Jakicic 2009). When combined with CR, it induces little further weight loss compared with CR alone (Jakicic 2009) but it does help to maintain muscle mass;
- physical activity after CR during the weight stabilisation phase: physical activity is one of the most, if not the most powerful predictors of maintaining weight loss after CR (Blair 1993; Jakicic et al. 2009; Jakicic et al. 2008; Mekary et al. 2010; Wu et al. 2009).

In a review of the literature dating from 1997 and relating to a meta-analysis of studies over the previous 25 years on three types of intervention (energy restriction (CR) alone, exercise alone (EX), or energy restriction and exercise combined (CR+EX)) (Miller et al. 1997), the authors showed that the percentage of weight loss maintained at one year was twice as high in the CR+EX group than in the CR group. While the average duration of the intervention was short (15 weeks), it nevertheless demonstrated that maintaining weight loss (an identical loss in both cases) at one year was significantly higher in the CR+EX group than for the CR group.

Other meta-analyses have since been published which confirm these results, but these meta-analyses related to observational studies with no randomisation between the types of intervention. This was not the case with the meta-analysis by Wu et al. which included only randomised controlled studies comparing the two intervention types (CR versus CR+EX) on weight loss for a minimum of 6 months in obese or overweight subjects (Wu et al. 2009). The results of these studies show a significant effect on weight loss at one year of the CR+EX combination, with a significant difference between the CR and CR+EX groups at the end of the monitoring period. Of the studies included in the meta-analysis, seven lasted for a period of 2 years or more and yielded the same results. One of these studies attained a 5.6% decrease in BMI after 6 years, suggesting that substantial long-term weight loss is possible with the CR+EX combination (Pan et al. 1997).

The Jakicic et al. study illustrates these data. The work focused on 201 overweight or obese women subjected to an intervention combining CR+EX with a total follow-up of 24 months (including 18 months of monthly monitoring) (Jakicic et al. 2008). At 24 months, the women who had maintained a weight loss corresponding to at least 10% of their original weight were the ones who had maintained the physical activity started at the beginning of the intervention. This activity lasted for at least 300 minutes per week (1500 kcal of energy expenditure per week, corresponding to a 60-minute walk at a good pace five times a week).
Thus, the intervention type combining CR+EX induced greater weight loss and long-term maintenance of weight loss than following a diet alone. Nevertheless, it should be noted that both types of interventions (CR and CR+EX) were associated with partial weight regain.

Moreover, with regard to eating behaviour in humans, many studies show that regular physical activity reduces appetite, at least in men, while the effect in women was more variable (Hagobian et al. 2010).

Thus, it is clear that physical activity plays an important role in obtaining weight stabilisation after energy restriction. There is a high degree of scientific evidence on this preventive effect of physical activity in inhibiting weight regain after dieting (INSERM collective expertise 2008).

- *Mechanisms of weight regain*

  ✓ *Physiology*

To reduce weight (and thus excess body fat) a negative energy balance (energy intake < energy expenditure) needs to be induced. This is the principle of energy restriction. Conversely, to maintain a stable weight, an energy balance must be obtained (energy intake = energy expenditure). However, it has been clearly shown that the energy intakes that allow weight loss to be maintained after dieting (including diets that induce a moderate weight loss of 10% of initial weight) are lower than those which allowed a stable weight to be maintained before weight loss (Dulloo et al. 2006; Rosenbaum et al. 2003). This implies that the food intake after one or more cycles of food restriction have to be less than the food intake prior to these restriction phases, even for the same body mass.

The return to the initial weight is accompanied by a preferential regain of body fat, whether energy restriction occurred in subjects of normal weight or obese subjects (Dulloo et al. 2006). This means that the physiological processes involved in maintaining energy reserves primarily favour a return to pre-diet body fat, often with a muscle mass that does not return spontaneously to the pre-diet level. In other words, there is a disproportionate regaining of body fat versus lean body mass during refeeding (Dulloo et al. 2006). These elements were first identified in studies of subjects having suffered from severe energy restrictions (wars, famines, etc.). They were then confirmed by the work of Weyer et al. which followed subjects of both sexes who had lost 15% of their initial weight when subjected to moderate energy restriction for two years (Weyer et al. 2000). Although their weight returned to the initial weight six months after the end of energy restriction, the regained weight was almost exclusively body fat. This phenomenon of preferential regain of body fat relative to muscle mass has also been described in adult patients after massive weight loss (undernutrition due to poverty, anorexia nervosa, chronic diseases with hypermetabolism).
The mechanisms involved in this process of weight regain after energy restriction are becoming clearer. The primary one is a fall in 24-hour energy expenditure, owing to a decrease in thermogenesis (and mainly the basal metabolic rate).

  ✓ *Role of striated skeletal muscle*

Decrease in basal metabolic rate by reducing lean body mass

The factor that determines the level of basal metabolism is the amount of lean body mass (muscle mass and visceral mass). This is true in subjects before and after weight loss (Thompson et al. 1997).

A decrease in muscle mass induces a reduction in basal metabolism. This means that to maintain an energy deficit, it is necessary either to reduce food intake or increase energy expenditure. Regular physical activity is sometimes the only way, or the only reasonable way, to increase energy expenditure for a subject who, as a result of following multiple diets with multiple cycles of weight loss

and weight regain, has experienced a decrease in basal metabolism of as much as 800 kcal/d (Dulloo et al. 1997; Leibel, et al. 1995).

In a given subject, the energy cost of the functioning of a kilo of lean body mass varies from one study to another. Thus, depending on the factors taken into account (energy cost of muscle protein synthesis and turnover, muscle energy metabolism, energy cost of the visceral mass, etc.), it ranges between 10 kcal/day/kg of lean body mass (Wolfe 2006) and 40 to 50 kcal/day/kg of lean body mass (Goldsmith et al. 2010). Based on these data, it seems reasonable to select an intermediate value of 20 kcal/day/kg of muscle mass. Thus, a loss of 3 kg of muscle mass corresponds to a decrease in the basal metabolic rate of 60 kcal/day, which over a period of 150 days leads to a difference in energy expenditure of 9000 kcal, assuming a stable food intake. This difference of 9000 kcal will be stored by the body as a kilo of body fat.

In sedentary subjects, basal metabolism accounts for nearly 80% of the 24-hour energy expenditure (the remaining 20% is distributed as follows: 10% in dietary thermogenesis and 10% in energy expenditure related to everyday physical activity). However, it has clearly been shown that even a well balanced diet is associated with loss of muscle mass (Dixon et al. 2007; van Aggel-Leijssen et al. 2001). For example, loss of muscle mass was 2 kg in obese subjects who lost 14 kg in 12 weeks. The phenomenon is accentuated with massive weight loss. The decrease in lean body mass (including muscle mass) therefore induces a decrease in basal metabolism.

Even if this decrease in muscle mass is taken into account, the decrease in 24-hour energy expenditure is still 300 to 400 kcal greater than that calculated from changes in body composition (Dulloo et al. 2006; Goldsmith et al. 2010; Leibel et al. 1995).

Increased metabolic efficiency

Another mechanism involved is that of better muscular efficiency (Goldsmith et al. 2010) demonstrated with low-intensity muscular work, i.e. intensities corresponding to everyday physical activities (10 W). Thus, after weight loss (10% of initial weight), muscular efficiency[17] increases, which means that energy expenditure during low-intensity physical activity is lower after weight loss. This improvement in muscular efficiency during low-intensity work is explained by biochemical, histological and molecular changes in skeletal muscle (Dulloo et al. 2006; Goldsmith et al. 2010).

✓ *Role of the biology of adipose tissue and its changes after energy restriction*

The main objective of energy restriction is to reduce body weight by reducing body fat while attempting to maintain lean body mass. The decrease in body fat is obtained through a reduction in adipocyte size without a significant change to their numbers. The main difficulty is maintaining this weight loss after a return to an unrestricted diet.

The mechanisms explaining the increased lipolysis during the energy restriction phase and the nature of the mechanisms likely to counter this process are still poorly understood (Galitzky et al. 2009). It has been demonstrated that expression of adipose triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL) is lower in hyperinsulinemic and insulin-resistant obese subjects. Thus, it is easy to see the link between the lipolytic capacity limitation and the risk factor for weight regain following energy restriction in these individuals (Jocken et al. 2007). It seems that the response of agents involved in the lipolytic pathways to energy restriction depends on the magnitude and duration of the restriction phase, the adipose tissue considered and the population considered (Galitzky et al. 2009).

It was recently reported that subjects who regained weight after an active intervention phase of weight loss over a period of six months had an increase in their subcutaneous adipose mass rather than their visceral mass (Lien et al. 2009).

The development of transcriptome analysis of adipose tissue is leading to initial identification of the relevant predictive markers of weight regain. Specifically, the gene expression profile of subcutaneous adipose tissue could be an interesting tool to develop, as it seems to reflect the molecular adaptations

[17] Muscular efficiency is measured on a cycle ergometer by calculating the following ratio: generated power (watt) / energy expenditure by indirect calorimetry (ml oxygen consumed / kg body weight).

to different changes in diet. It has been demonstrated that energy restriction, rather than the diet's lipid and carbohydrate composition, has an impact on gene expression in adipose tissue (Viguerie et al. 2005). The vast majority of genes regulated by energy restriction are involved in energy, lipid and carbohydrate metabolism. They include genes involved in *de novo* lipogenesis and storage of triglycerides, such as lipoprotein lipase (Capel et al. 2008). These same authors also noted that the diet's fat composition has an influence on the expression of genes such as FABP4, involved in intracellular transport of fatty acids in adipocytes. Increased expression of this gene was observed with a moderate fat intake (40%). Taken together, these data may partly explain changes in the blood lipid profile of subjects studied, such as triglyceridemia and a lower rate of VLDL-cholesterol in individuals with a moderate fat intake as compared to those receiving a low intake (20%).

Moreover, the link between transcriptome of the subcutaneous adipose tissue and an individual's ability to maintain his body weight has been revealed. Some authors even suggest that it will be possible to predict the level of weight loss due to a low-energy diet low in fats by using the gene expression profile of subcutaneous adipose tissue, before the nutritional intervention (Mutch 2007).
Another study compared differences in gene expression profiles of subcutaneous adipose tissue in subjects who successfully maintained their weight loss and in others (Marquez-Quinones et al. 2010). The authors demonstrated that these differences were mainly due to variations in weight rather than the macronutrient composition of diets. Thus, it was observed that the expression of genes involved in cell growth and proliferation processes, and cell function and maintenance, was greater in subjects who regained weight compared to the other individuals. In contrast, the expression of genes involved in mitochondrial oxidative phosphorylation was activated in individuals who maintained their weight loss. The authors stated that while the genes involved in inflammation and cell proliferation processes were activated in subjects who failed to maintain their weight loss, expression of genes encoding proteins associated with mitochondrial function was diminished. While it has not yet been clearly established whether the inhibition of mitochondrial genes observed in patients regaining weight is a cause or consequence of weight gain, these results demonstrate a link between mitochondrial dysfunction and the phenomenon of weight regain following cessation of dietary restriction. They are supported by a recent review which has provided further insight into the role of mitochondrial functions during adipogenesis and in mature adipocytes (De Pauw et al. 2009). In preadipocytes, mitochondrial dysfunction induced by different factors (hypoxia or deficient mitochondrial respiration due to inhibitors of oxidative phosphorylation) leads to impaired lipid metabolism and/or oxidation of lipids, proteins and mitochondrial DNA. This results in an accumulation of triglycerides in the cytosol of preadipocytes, through a decrease in β-oxidation of fatty acids and increased lipogenesis. Conversely, in mature adipocytes, mitochondrial dysfunction induced by factors such as aging, obesity or type 2 diabetes leads to decreased ATP production, the development of insulin resistance, apoptosis, or a decrease in triglyceride levels through stimulation of lipolysis and a decrease in lipogenesis.

Besides these metabolic aspects (lipolysis and lipogenesis), adipose tissue produces numerous molecules involved in metabolism, food intake, insulin secretion, immunity and inflammation ((Lafontan 2005) cited in (Galitzky et al. 2009)).
During periods of weight loss, decreased insulin and leptin levels, together with many other nutritional, neural and endocrine signals (decreased free triiodothyronine (T3) and activity of the sympathetic nervous system, and increased activity of the parasympathetic system), sends an "energy deficit" signal to the brain's energy metabolism control centres: the result is a fall in energy expenditure and a decrease in satiety (Cottone et al. 2009; Kelesidis et al. 2010; Leibel et al. 1995; MacLean et al. 2009; Rosenbaum et al. 2000).

It has been demonstrated in humans that a decrease in leptinemia increases the feeling of hunger. Specifically, the decrease in fasting leptinemia during four days of energy restriction was associated with an increased feeling of hunger as perceived by the subject. Moreover, this association became more pronounced at the end of the energy restriction period. These results suggest that leptin plays a key role in compensating the energy deficit caused by energy restriction, through the expression of the feeling of hunger (Mars et al. 2006). Thus, subjects subjected to energy restriction spontaneously seek to compensate this decrease in energy intake when they are in a situation of unlimited food consumption. However, no correlation was found between the size of the decrease in leptinemia and that of energy compensation (Mars et al. 2005). These observations confirm what has been shown on an experimental basis: treatment with leptin can compensate for the decrease induced by energy restriction and thus inhibit behavioural and metabolic adaptations such as increased hunger (Rosenbaum et al. 2005; Thorburn et al. 2000).

Moreover, a relationship has been shown between leptinemia before energy restriction and the degree of weight loss and the propensity to regain it. Thus, plasma concentrations of leptin before a weight-loss diet are positively correlated to weight loss in overweight men. This effect was not observed in overweight women (Ramel et al. 2010). In addition, subjects with higher plasma leptin and lower ghrelin levels, before a period of energy restriction, are more likely to regain the weight lost (Crujeiras et al. 2010).

Key points

- **Weight loss leads to an increased release of persistent organic pollutants which cause disruption to the endocrine, reproductive and immune systems, and metabolic dysfunction, which may contribute to weight regain, developmental disorders and cancers.**
- **Weight regain affects 80% of subjects at one year and increases in the long term.**
- **The overall caloric intake (and not the variable macronutrient content) is a major factor in a diet's effects on weight. Adapting the diet to the patient's tastes and habits is important to ensure their long-term commitment.**
- **The main stabilising factor is undertaking physical activity from the beginning of energyrestriction and maintaining it after this period of restriction ends.**
- **Energy intakes that allow weight loss to be maintained after dieting are lower than those which allowed a stable weight to be maintained before weight loss, a situation which promotes weight regain.**
- **The return to the initial weight is accompanied by a preferential regain of body fat.**
- **The loss of muscle mass plays a major role in reducing the energy expenditure (mainly basal metabolic rate) observed after energy restriction, which underlines the importance of limiting losses of muscle mass during energy restriction through exercise.**
- **During periods of weight loss, decreased leptinemia, together with many other nutritional, neural and endocrine signals, sends an "energy deficit" signal to the brain, which results in an increased feeling of hunger.**

4.4.3. Psychological and behavioural consequences of weight-loss diets

a. Current status of the literature

The harmful effects of weight-loss diets on behaviour and the psyche have rarely been documented in the international literature. Aware of the physical risks associated with obesity since the 1960s, the international medical community has been primarily concerned with warning of the dangers of overweight to physical and mental health (Metropolitan Life Insurance Co 1960). It has focused mainly on demonstrating the health and psychological benefits of weight loss and, therefore, on promoting restrictive diets rather than exploring the associated pitfalls and even dangers.

Considered in the light of clinical experience, this over-abundance of literature would itself benefit from a serious weight-loss diet to eliminate all the scientifically rigorous studies whose methodological variables are unrelated to the clinical reality of obesity. Even if "in a healthy subject, weight and energy reserves (body fat) are relatively constant - fluctuating from 1 to 2% on a weekly basis - around a 'reference value'", weight is not a fixed and constant variable. It can vary over time according to existential events and especially weight-loss diets, which may have been medically prescribed. A given weight as an absolute value does not mean the same thing according to whether it refers to a subject's 'reference value', or whether it deviates by plus or minus x kilos. This makes the kinetics of the curve a key element in the analysis of clinical obesity. In addition, the distribution of body fat (android or gynoid obesity) and body composition (lean mass and body fat) are important elements of diagnosis and prognosis (Allison et al. 1991). However, virtually all studies only refer to the absolute value of weight at the time of the study without taking into account either the kinetics of the curve or the morphological type of obesity.

In terms of weight loss, disillusionment often follows the initial success and hope of the initial dieting period. Results need to be evaluated in the long term. The period of six months to a year, frequently chosen by medical researchers because it is relevant to common diseases, is a very short term with

regard to weight. The period of two years, often proposed as the long term, is clinically the medium term. Indeed, it is usually in this one-to-two-year period that the weight curve is inverted, even after 'successful' weight loss, attained under good conditions, including after bariatric surgery (Sjöström et al. 2004). Regarding obesity, assessing the long-term prognosis requires longer durations. This reality, which is obvious to a seasoned clinician, seems overlooked by the vast majority of studies.

In 1996, Field et al. indicated that the filter of memory - highly subjective and irrational - risked impairing the objectivity of self-observation. Weight and diet data collected by declarative surveys should therefore be interpreted with caution, regardless of the weight of the individuals (Field et al. 1996). This explains a phenomenon regularly reported in clinical monitoring: the difference between the weight curve established at the first consultation with the doctor and that obtained after one or more assessment interviews with the clinical psychologist (who reconstructs step by step the history of events simultaneous to the weight history).

Finally, all studies now refer to the official definition of obesity and the classification of body types developed by the WHO in 1997 (WHO World Health Organization 1997) in an understandable concern for the harmonisation of international research. The ambiguity of this definition and the difficulty of applying it at the individual level, as well as the thresholds for weight categories that the medical community often adopts blindly, have already been reported (Le Barzic 2010).

A critical review of the literature on parental influences on eating behaviour and children's weight highlights how much the very purpose of research often reflects the causal link presupposed by the authors (Ventura et al. 2008). All the studies which - sometimes to the point of caricature - make no attempt to look beyond the stereotypical view held up as scientific truth ("fat people are *too fat* because they *eat too much")* in order to resolve the phenomenon must be rejected. The other studies can be highly instructive without necessarily meeting all the ideal criteria, as long as the statistics are interpreted in the light of a rigorous clinical approach, avoiding blindly and systematically applying collective values to individuals.

b. Psychological consequences of weight-loss diets

Although the risk of depression triggered by dieting and/or weight loss is often mentioned in clinics, data from the literature are relatively rare and contradictory: dieting leads to depression in some subjects (Keys et al. 1950), and alleviates it in others (Wing et al. 1984). In reality, the direction of mood change varies according to methodological parameters: the method for assessing depression (O'Neil et al. 1992; Smoller et al. 1987), the presence or absence of depression prior to the diet, its intensity, whether or not it is related to weight issues, or the time between the diet and the assessment (Ogden 1995).

In the short term, undertaking a weight-loss diet always has a positive effect. Experiencing the 'mental trigger' that provides the strength and willpower to 'control' one's own weight and diet in order to 'take care of oneself' obviously affects mood, self-esteem, and confidence in oneself and in the future. The improved mood rewards entry into the diet even before weight loss commences and is further accentuated when the effort begins to pay dividends. In the short term, all patients proclaim that slimming "boosts your spirits", which is confirmed by all studies. However, in the long or even medium term, the disillusionment is often bitter.

The study by Bacon et al. confirms and demonstrates this reality (Bacon et al. 2005). It compared changes over two years in biological and psychological variables in obese, middle-aged women, all chronic dieters, and who were divided into two treatment groups with comparable methods (24 weekly group sessions) but different objectives. One group was conventionally focused on weight loss (DIET), the other on the improvement of health conditions without seeking weight loss (HAES - health at every size). A year later, both groups showed psychological improvement. A trend towards improved self-esteem was seen in both groups. The reduction in depression scores, statistically significant in both groups, was greater in the DIET group. Improved self-image, common to both, was significant only in the HAES group, the only one in which body dissatisfaction decreased. An assessment at two years showed that the improvement had continued, even increasing, in the HAES group, whereas it had regressed in the DIET group, in which self-esteem attained a score that was worse than at the beginning of the study.

This study contradicts the notion of 6-month results that proponents of weight-loss diets typically refer to. It also shows that the psychological improvements that could be attributed to weight loss are related to patient enrolment in a therapeutic scheme that allows them to talk about their difficulties to an audience presumed capable of empathetic listening. This study also indicates that the most dramatically positive short-term results may be the most damaging in the medium and long term.

The psychological consequences of dieting may be more serious due to unintentional stigmatisation by the medical profession, especially of children. In a book recounting her personal experience, Anne Zamberlan described the extent of the irreversible psychological damage that resulted from her designation as obese by the school physician who had summoned her parents to urge them to treat her, or in other words "to make her lose weight" (Zamberlan 1991). Aware of the possible adverse effects of medical management of obesity in children, due first to the stigmatising effect of the child being designated as obese, and second to the potentially disruptive interference of the doctor in the relationship between the child and its parents (who are key players in the prevention and treatment of weight problems), Golan and Crow conducted an experimental form of care involving only the parents of obese children aged from 7 to 8 (Golan et al. 2004a). Seven years after the study began (Golan et al. 2004b), the superiority of the results of this method ("parents only" group) over those of traditional care in which the child is the designated patient ("child only" group) was overwhelming: 60% of children were no longer obese in the first group, compared with 31% in the second group. Moreover, there were no eating disorders among the patients (now teenagers at this stage of the study) in the "parents only" group compared with 6.6% in the "child only" group. In everyday practice, while the child's presence is not indispensable at consultations, the care of a young obese child is inconceivable without the parents. Practitioners need to bear in mind the importance of preserving the parent-child relationship.

It has been demonstrated that parental concerns about the weight of their children and their efforts to restrict their food intake have a negative psychological impact on self-esteem and physical and intellectual self-confidence in girls from the age of 5 years (Davison et al. 2001), regardless of their weight status. At the end of their study, Kirsten Davison and Leann Birch warned against the counterproductive effects of dietary restriction of children by parents who are not aware of the risks of cognitive restraint, and they underlined the potential consequences of this early negativity of self-image on the harmony of future emotional development. They also showed that girls that were most dissatisfied with their bodies and concerned about their weight at 5 years old were, regardless of their weight, the most likely to adopt food restriction attitudes, or even to follow restrictive diets at 9 years of age (Davison et al. 2003). Thus, under the pretext of preventing obesity, young girls are likely to be driven to anorexia nervosa, especially in the upper classes of the population where thinness is a particularly valued sign of distinction (Bourdieu 1979). There is every reason to believe that the generalisation of preventive discourse on overweight intensifies the pressure to be thin, an aggravating circumstance deplored by child psychiatrists, leading potentially to the earlier onset of this serious disease, which can be fatal in young people (Mouren-Simeoni et al. 1993).

c. Behavioural consequences of weight-loss diets

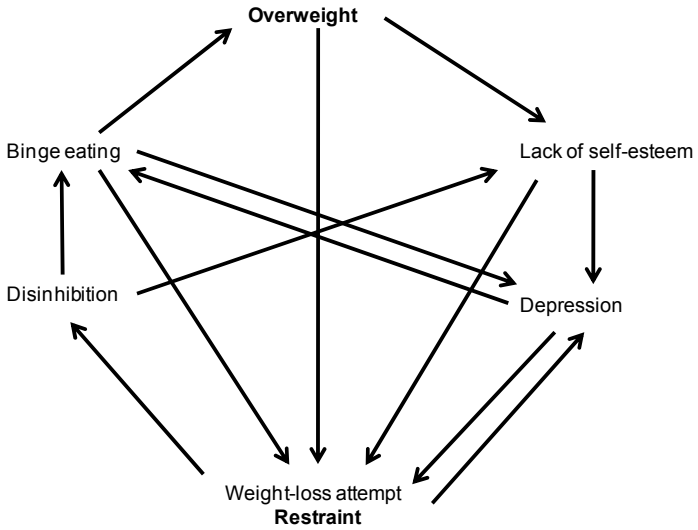
Logically, the practice of weight-loss diets mostly affects eating behaviour. Its most common and best known complication is the syndrome of cognitive restraint, discovered in 1975 (Herman et al. 1975), then described in 1980 by Herman and Polivy and defined as "an attempt - successful or not - to reduce one's daily food intake to reach a weight below one's spontaneous weight and to maintain it" (Herman et al. 1980). This fundamentally psychological phenomenon leads to characteristic eating behaviour that was first identified in obese subjects and considered to be the cause of obesity, until it was discovered that this behaviour was also seen in individuals on a diet, regardless of their weight. "When an individual decides to lose weight, he ceases to select his food according to the pleasure it will give him and determines his choices from what he knows (or thinks he knows) about the dietary properties of various foods. He adopts an inward disposition with respect to food, in which he replaces pleasure with reason, by forcing himself to focus on cognitive information - external and unfamiliar to him - to the detriment of his own physiological sensations - internal and personal - when choosing his food" (Le Barzic 2001). The sole intention of *eating less to weigh less* creates the state of cognitive restraint which "results in chronic hypophagia, possibly interspersed with more or less regular and consistent bouts of hyperphagia when disinhibition thwarts the will to control. Thus it may paradoxically lead to eating more and 'worse' than if one had not tried to eat 'well' and less in order to weigh less." It has been shown that cognitive restraint paradoxically accentuates nutritional

imbalances by increasing the proportion of fats and proteins at the expense of carbohydrates (Lluch et al. 2000). It is a risk factor for triggering or exacerbating behavioural eating disorders (Patton et al. 1999). Indeed, how can we believe that the disinhibiting effect of cognitive restraint is unconnected to the greater frequency of Binge Eating Disorder (American Psychiatric Association 1983, 1989, 1996) in the obese (Basdevant et al. 1995)? Yet the impact of cognitive restraint on behavioural eating disorders is variously accepted by the scientific community, who are often more inclined to look for causes within (Niemeier et al. 2007) "subjects at risk" (de Zwaan et al. 1994), or even to attribute responsibility to the “media and the images they impose", than to reconsider its own weight standards and dietary recommendations (Romon 2000).
In the study by Bacon et al., subjects responded to the Stunkard-Messick Eating Questionnaire on dietary restraint (Stunkard et al. 1992) at each stage of the study (Bacon et al. 2005). Initially, scores on cognitive restraint, hunger and disinhibition were completely identical in both groups. In the HAES group, the three scores became significantly lower than the initial score at six months, then at one and two years. In the DIET group, the restraint score increased from the sixth month and then remained consistently higher than the initial score, whereas the hunger and disinhibition scores decreased at six months and then rose again steadily at one and two years towards the initial score. The same deterioration following the initial apparent improvement in eating behaviour was observed as for the psychological symptoms in the DIET group that was pursuing the goal of weight loss, while the overall improvement still persisted after two years in the HAES group which was not seeking to lose weight. The cognitive restraint score was the only one that changed from the outset, from as early as six months, in opposing directions in the two groups; this is a compelling argument that demonstrates the influence of cognitive restraint on the other variables studied.
Longitudinal studies are particularly demonstrative of the influence of parents’ nutritional education methods on the development of eating behaviour in children. We mentioned above how dietary restriction at age 5 can induce body dissatisfaction in young girls that can lead them to follow diets at the age of 9, a phenomenon which can itself cause behavioural eating disorders. Early food restriction in 5 year old girls by their mothers leads them to develop, in the years that follow, regardless of their starting weight, the ability to eat beyond their hunger (Birch et al. 2003), an eating behaviour which itself is related to an increase in BMI (Fisher et al. 2002).

To improve readability, the psychological and behavioural aspects have been addressed separately. This division is completely artificial and does not correspond to clinical reality. As with body image and eating behaviour, all these phenomena constantly interact and are closely intertwined; they are all subject to the influence of their environment, food availability and prevailing social values. The long-term psychological, physiological, behavioural and weight-related repercussions of engaging in chronic food control are not without consequences. By focusing on cognitive information, external to the subject, to the detriment of recognition of the internal state, cognitive restraint tends to short-circuit the physiological signals of hunger and satiety. Dieters’ inability to follow the ideal weight-loss diet to obtain the ideal figure constitutes a repeated failure for which they always hold themselves responsible without ever questioning prevailing standards concerning weight and diet (Polivy et al. 1999). This sense of failure undermines their self-esteem and self-confidence, and may trigger or exacerbate behavioural eating disorders and overweight, which then further exacerbate a lack of self-esteem, etc.

Le Barzic offers a diagram illustrating the web of weight-related, psychological and behavioural registers, in a vicious cycle that could lead individuals wishing to undertake weight-loss diets into a spiral of failure in the longer term.

Figure 1: Vicious cycle of weight (Le Barzic 2004b)



d. Remarks on the principle of dieting

All diets, from the most scientifically developed to the most fanciful, are based more or less openly on the same principle: to provide an eating framework that reduces the quantity of calories ingested to a level lower than the calories expended. Eat less to weigh less, the principle is logical, simple and effective. Who among us has not seen the two or three kilos gained during the holidays disappear by cutting out bread and/or butter, and/or cheese, and/or cakes, etc. for a week or two?

In the short term, all diets lead to weight loss. They help with slimming more or less rapidly, more or less 'effectively', with more or less effort, but this does not mean that they are all of equal merit. The most spectacular weight-loss results in the short term are often the most devastating in the long term. Some short-term weight loss may be obtained at the cost of nutritional imbalances whose long-term deleterious effects may be more lasting than the weight loss itself. There are therefore 'good' and 'bad' diets. The 'good' diets achieve weight loss while preserving a nutritional balance. It can be useful to compare the respective dietary intakes of the different diets, as distinguishing between them would allow the public to be informed of the dangers of the poorest ones. However, even if such a study were conducted with the utmost rigour, how can the resulting theoretical data be applied to everyday practice? Irrespective of how scientifically balanced it is, no diet is followed indefinitely, nor rigorously. How do we know whether or not any 'deviations from the diet', inevitable and forgotten the instant they are committed, can compensate for any theoretical sub-clinical deficiencies of one diet or another? What dieting period is required to cause a sub-clinical or clinical deficiency? Is this period the same for everyone, or, under strictly identical dieting conditions, does it vary depending on the dieter? The number of unknown factors is such that it is illusory to imagine that one day that they could all be controlled.

The long-term ineffectiveness of weight-loss diets is now widely established and their potentially aggravating effects on weight are accepted by clinicians and have been demonstrated by research (see below). From a systemic perspective (Onnis 1989), a problem without a solution is often a problem that has been incorrectly formulated. The principle of the weight-loss diet makes sense, it impresses with its mathematical simplicity that everyone can grasp. It follows from the assumption that there is a simple, direct and linear relationship between bodyweight and calorie intake. While the existence of this relationship is not disputed, it is clear that it is neither simple, nor direct, nor linear, nor constant. Individuals' bodies - and thus bodyweights - and their diets are complex objects that obey the circular logic of existential phenomena, not the linear-causal logic of medicine. Might not dieting prove to be the "simple, direct and false solution" that "exists for every complex problem?" (Skrabanek et al. 1992) A linear medical response applied inappropriately to existential phenomena governed by circularity as is partly illustrated in Figure 1?

An initial error of logic results in a cascade of denial about the reality of the phenomena involved: denial of the complexity of the metabolism that subtly modulates the energy efficiency of food calories differently depending on the individual (Bouchard et al. 1990), of the efficient complexity of the regulatory system that works to ensure weight stability and, finally, "the formidable unconscious power

that rules the body and the appetite" because food is reduced to its nutritional and quantitative aspect alone (Le Barzic 2004a).

The problem does not lie in one or other of the diet's characteristics, but in its very principle. This is a radical change of perspective, a "change 2" (Watzlawick et al. 1975) as defined by systemic therapists, which is opposed to the "change 1", which "appears to be based on common sense", but helps to maintain the system's dysfunction.

The principle of the diet is based on the standardised modelling of bodyweights and appetites. It gives patients the illusion that they can - or must - meet the bodyweight standards advocated by the WHO, or those promoted by fashion magazines. In the short term, the predetermined diet simplifies the task of the practitioner and saves time. By providing a food guide certified as healthy by the medical establishment, it reassures patients intimidated by the general cacophony surrounding diets. In the long term it ensures that everyone fails.

We are obliged to abandon the 'diet solution' if we agree to accept that the possibilities for weight loss are both limited and variable among individuals, and that only a fundamental change in eating behaviour will enable a sustainable balance of nutrients, and not the reverse. Individual clinical consultations should put statistical standards and nutrition knowledge into perspective, and adjust them to each individual case. This practice requires that nutritionists be available over the long term, first to take the time to carefully assess the patient's weight history in relation to his environment (family, society), then to guide him towards the far-reaching, existential readjustments that will allow his eating behaviour to be sustainably modified and/or restored. It requires experienced clinicians with in-depth specialisation. In these circumstances, patient and practitioner can in some cases share the long-term satisfaction of a sustainable outcome.

Ultimately, the diet 'solution' often aggravates the weight 'problem'. The desire to lose weight is justified by apparently reasonable aesthetic and health arguments. However, the body types promoted by fashion or recommended by health institutions are not for everyone. The relationship between bodyweight and caloric intake is neither simple nor straightforward. In the short term, eating less causes weight loss but this rarely leads to long-term slimness. More importantly, following weight-loss diets is often counterproductive. By disconnecting the act of eating from its unconscious affective and symbolic determinants, reducing it to its solely nutritional objective, it disrupts the psychodynamic economy of the dieter and may lead to psychological and behavioural disturbances. The psychic energy invested in the effort of cognitive control of intakes has a negative effect on mood and self-esteem. The systematic circumvention of internal signals regulating food intake (hunger, appetite, satiety) causes the deregulation of the "extraordinary machinery devoted to the control of food intake" (Laplace 2008) and paves the way for behavioural eating disorders, which risk turning subjectively or objectively determined overweight into more or less morbid obesity. Health professionals, parents, and educational and political leaders should be warned of the pathogenic risks of this seemingly simple and logical solution.

Key points

- **By focusing on cognitive information, external to the subject, to the detriment of recognition of the internal state, cognitive restraint tends to short-circuit the physiological signals of hunger and satiety.**
- **Prospective dieters are often unaware of the negative psychological and behavioural consequences.**
- **Depression and loss of self-esteem are common psychological consequences of repeated failures in dieting.**
- **With regard to behaviour, cognitive restraint and the resulting disruption of eating behaviour very often exacerbate the weight problem.**

4.4.4. Specific risks related to particular population groups

a. Pregnant women and nursing mothers

- *During pregnancy*

During pregnancy, a range of mechanisms are put in motion to meet the needs in energy, proteins, vitamins and trace elements related to the growth of the foetus and changes to the mother's own body. The gradual increase in the mother's appetite and therefore food intake contributes directly to meeting these needs, while her metabolism adapts in readiness for a range of nutrients and an increase in intestinal absorption. These transformations allow women in good health to carry a normal pregnancy to term while building up the reserves necessary for lactation. These changes are reflected in a gradual increase in weight during the course of the pregnancy.
For a woman of normal weight, the mean weight gain in the absence of any oedema is about 12 kg. During the first half of pregnancy it is in the region of 4 to 5 kg, most of which directly concerns the mother in the form of lipid reserve and increased volume of the bloodstream. The mother gains more weight towards the end of the pregnancy (1 to 2 kg per month), mainly benefiting the foetus and the placenta.
Overweight is a risk factor for both mother and foetus and can lead to gestational diabetes, risk of thromboembolism and hypertension. It increases the likelihood of premature births and caesarean deliveries. An overweight condition at the start of pregnancy therefore justifies more moderate weight gain than the average, but never less than 7 kg and always under medical supervision to ensure that intake remains above 1500 kcal/day (Institute of Medicine 2009).
Conversely, the results of animal and human epidemiology studies have shown that restrictive weight-loss practices during pregnancy in women who are slim or of normal weight can influence foetal development and have consequences for the child's health later on in adult life.

- ✓ *Studies in animals*

There are many animal studies investigating maternal restriction of proteins or energy. It was shown that restricted protein intake in rats during gestation was responsible in the offspring for delayed sexual maturity and reduced fertility (Zambrano et al. 2005), glycaemic regulation disorders (Zambrano et al. 2006) and anomalies in the replication of pancreatic β cells, likely to favour the later onset of Type 2 diabetes (Petrik et al. 1999). Other studies showed that offspring can suffer impaired muscle structure and function (Toscano et al. 2008), anomalies of trabecular volume and bone growth (Ashton et al. 2007; Fetoui et al. 2008; Mehta et al. 2002) and disorders of the metabolism of cerebral tissue (Gallagher et al. 2005).
The effects of energy restriction was also studied in gestating rats. It was found that the offspring suffered modifications to obesity hormones (a rise in resistin, a fall in adiponectine) causing a predisposition to insulin resistance (Hietaniemi et al. 2009), and blood pressure anomalies that increase with age (Ozaki et al. 2001). In marmoset monkeys, energy restriction during gestation led to an increase in the number of abortions and premature births, preceded by a reduction in urinary excretion of cortisol and maternal estradiol (Tardif et al. 2004; Tardif et al. 2005).
Lastly, one study evaluated the effects of a high-protein diet in gestating rats which showed a reduction in energy expenditure and an increase in body fat in the offspring (Daenzer et al. 2002).

- ✓ *Human data*

There is a shortage of data on the effects of weight-loss diets in pregnant women. Of course, most women know that weight-gain is physiological and beneficial, and interrupt any diet when they learn that they are pregnant. However, a North American study carried out involving 8000 pregnant women showed that 8% of them attempted to lose weight and that these attempts were associated with obesity, and also with other risk behaviour: alcohol consumption and psychological distress (Cohen et al. 2009).
It is possible to study the effects of food restriction during pregnancy *via* studies carried out on pregnant women suffering from anorexia nervosa (Bulik et al. 1999; Franko et al. 2001; Stewart et al. 1987; Treasure et al. 1988; Waugh et al. 1999). These studies agree in reporting lower birth weights than in the general population, with slower foetal growth during the 3rd trimester of pregnancy (Treasure et al. 1988). Others showed a high incidence of miscarriages, premature births (Bulik et al. 1999) and caesarean deliveries (Bulik et al. 1999; Franko et al. 2001; Waugh et al. 1999). An increase in the incidence of gestational diabetes and caesarean deliveries was also reported in women having observed the periodic Ramadan fast during their pregnancy (Mirghani et al. 2006).
Studies by D.J. Barker showed the significance of the antenatal nutritional status of the foetus for later health. Indeed, children born with a low birth weight, and who were victims of foetal malnutrition, have greater risk in adulthood of heart failure, hypertension and/or Type 2 diabetes. The risk differs depending on the period of the pregnancy during which the undernutrition occurred. Undernutrition has the greatest impact on foetal growth during the 3rd trimester, a period of rapid foetal growth. These

observations led D.J. Barker to propose the hypothesis of the foetus undergoing "reprogramming" by malnutrition-adaption phenomena, which becomes imprinted in the epigenetic code and definitively modifies the metabolism, with insulin-resistance leading eventually to such complications as hypertension, Type 2 diabetes and coronary disorders (Barker et al. 1993; Godfrey et al. 2000; Martyn et al. 1998).
Proof that food restriction during pregnancy affects foetal development and, later, the health in adulthood of the individuals born from these pregnancies was provided by studies carried out on adults born to mothers that had been exposed to the famine conditions prevailing in Amsterdam in the winter of 1944-45. Ravelli et al. and de Rooij et al. showed that prenatal exposure to famine, especially during the 2nd half of pregnancy, was associated 50 years later with glucose tolerance disorders, related to insulin-resistance that varied positively with low birth weight and with the individuals concerned having become obese adults (de Rooij et al. 2006; Ravelli et al. 1998). A study of the same population by R.C. Painter and colleagues revealed a higher frequency of coronary disorders, dyslipidemias and obesity in individuals who had suffered prenatal exposure to famine at the start of pregnancy, and higher frequency of glucose regulation disorders in individuals exposed to famine at the end of pregnancy (Painter et al. 2005).
More directly, carotid intima-media thickness (IMT) was measured in 216 children aged 9 whose mothers had participated in a nutritional study during their pregnancy. After adjustment for gender, blood pressure and weight, IMT was higher in children whose mothers had had the lowest caloric or protein intakes (lowest quartile of the distribution) at the beginning or end of pregnancy, causing increased susceptibility to atherosclerosis in these children (Gale et al. 2006).
All these data show that antenatal nutritional deficiencies have important consequences for later health, particularly when food restriction occurs during the second part or last trimester of the pregnancy, the period of fastest foetal growth.

- *During lactation*

Milk production has an energy cost for the mother, compensated for by an increase in caloric intake and, if necessary, the mobilisation of body fat. The WHO has calculated that in women producing 750 ml of milk per day, this cost represents an increase in needs of 630 kcal/day (WHO 1985). Insofar as these increased needs are covered by the mobilisation of body fat accumulated during the pregnancy, studies have estimated that (for a mean weight loss of 800 g/month) lactation requires an increase to the diet of about 450 kcal per day (Butte et al. 1998). A restrictive weight-loss diet during this period can therefore cause maternal deficiencies.
However, the nutritional value of milk is relatively independent of maternal nutritional status. Even in conditions of significant protein deficiency, there is no change to the essential micronutrients (FAO 1995). Concentrations of calcium, iron, zinc and copper in milk are stable irrespective of the maternal mineral status (Domellof et al. 2004). However, the concentration of other nutrients such as iodine and certain vitamins (particularly water-soluble vitamins), and the quality of fatty acids (particularly levels of LC n-3 PUFAs) remain influenced by the mother's diet. In general, it is the quantity rather than the quality of milk production that is affected by malnutrition in terms of proteins and calories and which can therefore influence the growth and development of the child (FAO 1995).
This was confirmed by animal studies carried out on the offspring of lactating rats administered diets restricted in proteins and calories, which showed delayed growth, delayed puberty and glucose regulation disorders (da Silva Faria et al. 2004; Zambrano et al. 2006; Zambrano et al. 2005). Furthermore, difficulties in providing and maintaining lactation were reported in women suffering from anorexia nervosa (Bulik et al. 1999; Treasure et al. 1988; Waugh et al. 1999).

Overall, maternal food restriction during lactation can have harmful consequences for both the child and the mother. Post-partum reduction of excess weight therefore requires recording the mother's weight before the start of pregnancy, monitoring it as appropriate during the pregnancy and, after birth, returning to an active lifestyle, and not undertaking a restrictive diet (Lederman 2001).

Key points

- **Few data are currently available on the effect of weight-loss diets in pregnant women.**
- **Energy restriction (anorexia, famine, etc.) during pregnancy leads to slower foetal growth in the 3rd trimester of the pregnancy and lower birth-weights than in the general population, as well as a high prevalence of miscarriages, premature births and caesarean deliveries.**

- **Antenatal nutritional deficiencies have significant consequences on the later health of the individual, especially when energy restriction occurs in the second part or final trimester of the pregnancy.**
- **Consequently, there should be no energy restriction during pregnancy without medical supervision.**
- **The level of milk production is affected by protein-energy malnutrition and can therefore affect the growth and development of the child.**
- **Although the quality of maternal milk is relatively unchanged, the concentration in nutrients such as iodine and certain vitamins (particularly water-soluble ones), and the quality of fatty acids (especially levels of LC n-3 PUFAs) are nonetheless influenced by the maternal diet.**

b. Children/adolescents (growth and puberty)

It is by no means exceptional for children and adolescents to follow weight-loss diets, especially girls. The INCA2 study showed that 28% of girls aged 14-17 and 22% of those aged 11-14 were following a diet or had followed one during the previous year (AFSSA 2009). In the same age ranges, almost 30% of the girls considered themselves to be overweight and 67% wished that they weighed less. These figures were lower for the boys (AFSSA 2009). In a Dutch study carried out on schoolchildren aged 13 to 15, 13% of the girls and 5% of the boys stated that they were following a diet at the time of the survey (Brugman et al. 1997).

If such eating disorders as anorexia are excluded, restrictive practices of this nature can be found in this age group in different situations. It may be a case of unsuitable medical prescriptions in the context of supervised treatment for overweight or dyslipidemia, contrary to expert opinion which recommends maintaining a balanced diet in these situations, adapted to the needs of the age group (ANAES 2004; Lebars et al. 2010; Tounian et al. 2004). More frequently, it can be a case of self-medication in adolescent girls influenced by what they read or hear from their entourage, or even from obsessive, rigid parents (Francis et al. 2005; Pugliese et al. 1983). It can also be the result of voluntary restriction in young athletes, gymnasts or dancers, who are subject to very strict weight requirements (Golomer et al. 1991).

In addition to the risks described in other sections (see the sections on micronutrients, bone health, etc.), energy restriction and nutritional imbalances have specific consequences in children and adolescents, in particular on growth and pubertal development.
Adaptation to the caloric deficiency characteristic of a restrictive diet results in a relative reduction in energy expenditure and, in particular, a reduction followed by an interruption of the expenditure related to growth. The energy cost of growth includes the quantity of energy deposited in the tissues and therefore varies with body composition and consequently gender. It also includes the energy expenditure related to synthesis and protein synthesis in particular. It is therefore especially high during the period of rapid growth characteristic of puberty. Growth in children also requires a positive nitrogen balance. Protein restriction associated with energy restriction is therefore an additional factor in slowing growth (Goulet et al. 1993).
The consequences of energy restriction on pubertal development were also confirmed by animal studies carried out on young female rats (Arts et al. 1992).

There have been few clinical studies on the effects of weight-loss diets on children. One retrospective study concerning 14 children aged 9 to 17, five of whom were girls, showed that voluntary restriction in protein and calories, motivated by a fear of becoming overweight, induced slower growth in stature for 11 of them and delayed puberty in 7 of the 14 (Pugliese et al. 1983). A randomised prospective study carried out on 94 obese children aged 11 to 13 showed that energy restriction of 30% was associated with faster weight loss than for the non-restricted control group, but also with slower growth in stature, greater loss of lean body mass and slower pubertal development (Amador et al. 1990). Conversely, a high-protein and moderately low-calorie diet under medical supervision was shown to be well tolerated and more efficient in terms of a reduction in BMI and its duration than a low-fat diet in a controlled study involving 46 severely obese adolescents aged 12 to 18 (Krebs et al. 2010). Furthermore, various mild or clinical deficiencies in vitamins and minerals were described in children subjected to restrictive diets (Kirby et al. 2009). In addition, even under appropriate medical supervision, the psychological disadvantages of diets in obese children, and particularly the consequences of cognitive restraint, have often been emphasised (Le Barzic et al. 2001). Even though weight-loss practices in children

and adolescents are not without physical or psychological risk, it can nonetheless be useful to try and help an obese child lose weight, by re-establishing eating habits appropriate to the needs of the child's age and the family's lifestyle. An intervention study carried out on a cohort of 341 obese children aged 5 to 16 not using a restrictive diet but a balanced nutritional approach adapted to the age group, together with a programme of physical activity, thus revealed a correlation between the reduction in BMI and an improvement in insulin sensitivity (Reinehr et al.).
Certain specific situations confirm the risks involved in nutritional restriction in children and adolescents.
For example, young dancers in ballet schools are subjected to rigorous morphological criteria in terms of BMI. This leads many of them to follow various diets, often extremely restrictive, sometimes from the age of 11, either voluntarily or under parental influence. This results very frequently in primary or secondary amenorrhoea (constant when body fat is less than 13% of body weight), as well as tendinitis, bone demineralisation and clinical iron deficiency [personal communication[18]].
Another specific situation is that of adolescent girls suffering from anorexia nervosa. These girls, who force themselves to accept major overall food restriction, suffer a range of complications that can even lead to death: bradycardia, low blood pressure, erythrocyanosis of the extremities, hypothyroidism, blood disorders, bone mineralisation disorders, or hydroelectrolytical disorders dominated by hypophosphataemia and hypokalemia, which can be responsible for cardiac arrhythmia (Alvin et al. 1993; Swenne 2008).

Taken together, all these data demonstrate the risks to children of following restrictive nutritional diets. Although it may be desirable to try and help obese children lose weight, such efforts should involve changes to the child's lifestyle combining varied food intake, adapted to the needs of the age group, with regular physical activity. Restrictive diets should only be prescribed at this age under exceptional circumstances, exclusively in specific situations such as certain cases of morbid obesity, and always under close medical supervision.

Key points

- **Weight-loss diets in children and adolescents are not without physical and psychological dangers.**
- **Energy restriction, whether or not it is associated with protein restriction, leads to slower growth and pubertal development.**
- **Alongside these risks there is the danger of primary or secondary amenorrhea, as well as tendinitis, bone demineralisation and clinical iron deficiency, particularly in young female athletes.**

c. The elderly

In obese or overweight elderly people, as with young people, energy restriction for the purpose of weight-loss can bring well-known benefits for the cardiac function, reduce the risk of developing Type 2 diabetes and the circulating markers of chronic inflammation (Holloszy et al. 2007; Miller et al. 2008). However, the few existing studies concerning the elderly suggest several particular features compared with younger subjects:
- the negative influence of overweight (25-29.9 kg/m^2) on mortality is less clear (Janssen et al. 2007), as is the association between BMI and cardiovascular risk (Miller et al. 2008);
- the association between weight-loss and lower values for four markers of metabolic syndrome (waist, hypertension, HDL cholesterol and glycaemia), and conversely, their positive association with weight gain, seems to be less certain over the age of 50 (Bot et al. 2010);
- a recent meta-analysis suggested that, with average reductions of 3 kg, weight-loss diets may have less effect on weight and no effect on HDL-cholesterol, LDL-cholesterol and triglycerides, after the age of 60 (Witham et al. 2010).

Weight-loss diets may have another beneficial effect on the elderly. Animal studies suggest that energy restriction may increase longevity and slow the ageing process. This remains unproven in humans, however (Bengmark 2006), and the impact of weight-loss in obese subjects on the markers associated with ageing has only been studied in young adults (Holloszy et al. 2007). Furthermore, one study suggested the opposite effect after observing a shortening of leukocyte telomeres, associated

[18] Extract from the interview with Mathieu Jouys, from the Dance School of the *Opéra National de Paris*.

with an increased risk of morbidity and mortality, in women who had tried several times to lose weight, examined before and after menopause (Kiefer et al. 2008).
However, the negative impact of weight loss on bone mineralisation and bone metabolism markers is much better documented in women after menopause than in younger women (see 4.4.2. a.). These diets, if accompanied by a magnesium deficiency (average intake of 101 mg/day), can also aggravate the risk of cardiac arrhythmia, and even of atrial fibrillation, in post-menopausal women (Nielsen et al. 2007).
Furthermore, the negative impact of weight loss seems to be more pronounced in the elderly as regards the risk of certain cancers, the development of pressure ulcers, and above all loss of muscle mass. Restrictive diets in subjects over the age of 75 multiplied by 3.6 the probability of having a low Mini Nutritional Assessment (MNA) that is to say of being at risk of undernutrition (Molato et al. 2009).

Low-fat diets (18-22% of caloric intake), and in particular diets deficient in linoleic acid, were associated with a higher incidence of relapse in colorectal tumours (Nakamura et al. 2010). However, energy restriction with weight loss does not seem to aggravate the decrease in immunity associated with ageing (McFarlin et al. 2006).

Malnutrition is frequently observed in the elderly. It is the result of multiple factors associating, among others, reduced appetite, physical or neuropsychological eating difficulties, illness, and medication that reduces appetite or increases faecal losses. The resulting malnutrition aggravates the development of bedsores and delays their recovery. This risk needs to be taken into account when considering weight-loss diets for elderly obese patients.

Increasing age is generally accompanied by weight-loss related to a loss of both body fat and lean body mass. Weight-loss diets accelerate muscle wasting in elderly obese patients and should therefore be limited in these subjects, especially those with sarcopenic obesity with low lean body mass (Miller et al. 2008). A study of women aged between 50 and 70 showed that nutritional restriction in the region of 2800 kcal per week led to an average weight loss of 10.8 kg, of which 32% was lean body mass (Bopp et al. 2008). This loss is even greater when protein intake is low and concerns both total lean mass and limb lean mass (Bopp et al. 2008).

Key points

- **If weight-loss diets are accompanied by a magnesium deficiency (mean intake of 101 mg/day), they can aggravate the risk of cardiac arrhythmia and atrial fibrillation in postmenopausal women.**
- **The data suggest that the negative impact of weight-loss on older people is greater concerning the risk of relapse for colorectal tumours, the development of bedsores and especially the loss of muscle mass and skeletal mineralisation. The malnutrition that is frequently observed in the elderly, which aggravates the development of bedsores and delays their recovery, must be taken into account.**
- **Low-fat diets (18-22% of caloric intake), and in particular diets deficient in linoleic acid, were associated with a higher incidence of relapse for colorectal tumours.**
- **Food restriction for the purpose of weight-loss in elderly obese subjects accelerates muscle wasting.**

d. Male athletes

- *Nutritional factors*

The most frequently-mentioned risk concerns dysfunction of the gonadotropic axis, although this is not very widely observed in men. Several authors have reported a reduction in plasma concentrations of testosterone with the regular practice of muscle exercise requiring stamina but not with resistance training (Duclos 2001; Duclos et al. 1996). Plasma concentrations of testosterone observed were found to be below the lower limit of what is considered normal. This reduction in testosterone concerns total testosterone and free testosterone, while SHBG (Sex Hormone-Binding Globulin) levels were no different to those found in sedentary subjects (Duclos 2001). No reduction in testosterone levels was observed if nutritional intake was adapted to energy expenditure. Nutritional intake therefore plays an important role in the etiology of this moderate hypotestosteronemia observed as a response to training.

At the quantitative level, it is possible to increase training loads drastically without inducing any reduction in testosterone levels if food intake compensates for this increase and if there is no loss of weight and therefore of body fat (Hall et al. 1999).

At the quantitative level, a reduction in resting testosterone levels was reported in subjects for whom lipids made up 20% of their food intake compared with subjects for whom lipids made up 40% of their food intake (Hamalainen et al. 1984). These results were also confirmed in subjects that had undergone resistance training: at rest, when not taking exercise, their plasma concentration of testosterone was significantly correlated with the percentage of lipids in their diet (Volek et al. 1997). More precisely, diets with different lipid contents modified the composition of the testicular plasma membrane, leading to modifications of the response of the Leydig cells and stimulation of hypophyseal gonadotropins (Luteinising hormone) thus influencing the synthesis of testosterone (Sebokova et al. 1990). The protein content of the diet also played an important role. In resting subjects or subjects who had undergone resistance training, a low-protein diet (10% of total energy) was associated with higher levels of testosterone when compared with a diet higher in protein (44% of total energy) (Volek et al. 1997).

Overall, the data suggest that qualitative modifications to the diet are implicated in the physiology of the reduction in testosterone levels associated with intense physical and athletic activity.

- *Consequences of reduced testosterone levels in subjects undergoing endurance training*

  ✓ *Concerning fertility*

In a study of 20 marathon runners and 10 sedentary adults, the results of a spermogram for each individual was compared with their plasma concentration of testosterone, and no correlation was found between testosterone levels and sperm count (Ayers et al. 1985). However, according to De Souza et al., it would seem that there is a training load (running more than 100 km a week - amateur athletes) beyond which spermogram anomalies may be observed (reduced spermatozoid mobility and an increase in the number of immature cells). Nevertheless, these alterations are considered to be subclinical as they have few consequences on fertility (De Souza et al. 1994).

✓ *Concerning muscle damage and bone metabolism*

It would seem that there is no long-term harmful effect of a moderate reduction in testosterone levels on the frequency of muscle damage in athletes. However, concerning bone metabolism, the question remains open, particularly in "non-weight-bearing sports", i.e. sports in which there is no mechanical constraints applied to the skeleton (e.g. cycling and swimming). Indeed several studies reported a high incidence of osteopenia and even of osteoporosis in cyclists but not in distance runners (for identical BMIs, body composition and nutritional intake). This effect may be explained by the absence of mechanical constraints applied to the skeleton during cycling (Rector et al. 2007). Given the role of testosterone in bone mineralisation, the issue of the long-term effect of a moderate reduction in testosterone levels on bone density in high-performance athletes practising "weight-bearing" sports remains open and unanswered at this time.

Key points

- **The data suggest that qualitative modifications to the diet are implicated in the physiology of the reduction in testosterone levels associated with intense physical and sporting activity.**
- **Restricted fat intake can have consequences on the plasma concentration of testosterone.**
- **If nutritional intake is adapted to energy expenditure, no reduction in testosterone levels is observed.**

e. Female athletes

The literature search shows that beginning intense training and regular participation in intense training can lead to anomalies in ovarian function ranging from luteal insufficiency to anovulation and then, in extreme cases, to amenorrhea. Although the mechanisms underlying these cycle disorders are not yet

clearly defined, the energy imbalance between caloric intake and energy expenditure is the most likely hypothesis (for a review, see (Duclos et al. 2005))

- *Nutritional factors*

Laughlin and Yen (1997) compared three groups of women: sedentary women with regular cycles, athletes with regular cycles, and amenorrheic athletes (Laughlin et al. 1997). They had similar age, weight, height and BMI. However, despite the high energy costs of physical activity in the two groups of women athletes (an extra 1000 kcal of energy expenditure per day related to sporting activity), the daily food intake was identical in quantity for the athletic and sedentary groups. There was therefore a chronic energy deficit in both groups of athletes because there was a difference of 700 to 1000 kcal per day between the 24-hour energy expenditure and the caloric intake. In addition to this overall nutritional deficit relative to energy expenditure, the amenorrheic women athletes had a qualitative deficit in fat intake (12 to 15% of the daily food intake). These results show that nutritional factors (an overall nutritional deficit relative to energy expenditure and a qualitative deficit in fat intake) were implicated in anomalies of the gonadotropic axis and, more specifically, disorders in the pulsatile secretion of hypothalamic GnRH in female athletes.

- *Relationship between energy deficiency and ovarian cycle disorders*

The relationship between energy deficit and disorders of the ovarian cycle can be explained, at least partly, by a drop in leptin production by the adipocytes. Leptin secretion is proportional to the mass of adipose tissue. Leptin receptors are located, among other places, in the hypothalamus and the ovaries.

The frequency of cycle disorders varies with the type of sport. Regarding amenorrhea, it is more frequent in endurance sports (30.9%), in so-called 'aesthetic' sports (figure skating and gymnastics) (34.5%) and in weight-category sports (23.5%) (Torstveit et al. 2005), i.e. in sports that may be grouped together as "weight-bearing sports", in which mechanical constraints imposed by weight are a limiting factor for performance.
The frequency of amenorrhea is lower in "non-weight-bearing" sports such as swimming and cycling (about 12%, which also corresponds to the incidence found in the population as a whole) (Torstveit et al. 2005). These differences suggest that amenorrhea is more frequent in female athletes who subject themselves to diets designed to maintain a low level of body fat, in sports where keeping control of one's body composition is a factor for success. This hypothesis is confirmed by the meta-analysis undertaken by Redman et al. which showed that body fat is significantly lower in female athletes with amenorrhea: the mean percentage of body fat in athletes with regular cycles is 17.9 ± 0.7% vs 15.7 ± 0.6% in athletes with amenorrhea ($p<0.05$ for the two groups) (Redman et al. 2005).
Conversely, in what are known as technical sports (golf, diving, curling, horse-riding, shooting) or ball sports, which can be considered as requiring intermittent effort (volleyball, basketball) the frequency of cycle disorders was no higher in the athletes practising intense sporting activity (up to 12 or 18 hours of training per week) than in the sedentary women (Torstveit et al. 2005).

Female athletes could serve as a model in which leptin acts as a metabolic signal for the gonadotropic axis. In a 24-hour period the mean plasma concentration of leptin in the athletes, irrespective of their ovarian status (regular or irregular cycles) was only one third the level found in the sedentary women. This 24-hour average was inversely correlated with body fat. There was also a diurnal rhythm for the leptin with an approximate increase of 50% between the nadir (at 9am) and the peak of concentration (at 1am). This diurnal rhythm was found in the sedentary women and the female athletes with regular cycles but was totally suppressed in the female athletes with amenorrhea (Hilton et al. 2000).

Recent data have shown that in women with hypothalamic amenorrhea (including athletes), separate administration of leptin for three months at doses calculated to obtain plasma concentrations similar to those of women with normal weight and body fat, improve the reproductive functions (increase in plasma concentration of LH and the frequency of pulses of LH, appearance of ovulatory cycles). Leptin, which is a marker of an adequate level of energy reserves, appears to be necessary for the reproductive function and for normal neuroendocrine function (Welt et al. 2004).

Numerous findings obtained from either animals (Williams et al. 2001) or humans (De Souza et al. 1998; Hilton et al. 2000) confirm the role of the energy deficit in ovarian function disorders induced by

muscle exercise, with the gravity of the cycle disorder forming a continuum which is parallel to the degree of energy deficit. In female athletes with ovulatory cycles, 24-hour energy expenditure was well balanced by the food intake for the same 24 hours, while in women presenting a short luteal phase there was often a transient and moderate energy deficit. Anovulation in athletes was associated rather with alternation between periods of balanced food intake and periods of food restriction. Lastly, oligomenorrhea, and to an even greater extent amenorrhea, were due to a chronic energy deficit (Laughlin et al. 1997). Conversely, if energy intake and expenditure were balanced (with the exception of training loads exceeding the individual's capacity for adaptation), the amount of training (up to 17 hours a week) did not induce cycle disorders (Torstveit et al. 2005).

Overall, these results underline the relationship between the adipocytes, nutritional status and the integrity of the gonadotropic axis in women and the fact that there is a real continuum between the severity of the energy deficit, the severity of the cycle disorders and the extent of the body's metabolic, hormonal and energy adjustments.

- *Consequences of menstrual cycle disorders in female athletes*

Menstrual cycle disorders in female athletes have proven consequences on fertility, bone density and the endothelial function.

✓ *Fertility*

The short-term consequences of amenorrhea in female athletes concern fertility. Unfortunately, there are no exploitable epidemiological data on sufficiently large populations of non-amenorrheic female athletes to conclude that there is any reduction in fertility.

✓ *Disorders of the endothelial function*

Because they cease to produce oestrogen, amenorrheic female athletes suffer from (Rickenlund et al. 2005):

- disorders of the endothelial function: inflammatory endothelial activation;
- an atherogenic lipid profile: significant increase in total cholesterol, LDL cholesterol, apo B and lipoprotein A, compared to sedentary women with regular cycles.

These same anomalies are found in oligomenorrheic female athletes, in a less pronounced way than in amenhorreic female athletes but more pronounced than in female athletes with regular cycles. The long-term consequences on cardiovascular risk are unknown.

✓ *Osteopenia and osteoporosis*

Amenorrhea in female athletes is accompanied by a clinical deficiency of oestrogen leading to bone loss that is identical to that observed in menopausal women. The main bone loss occurs during the first years following the onset of amenorrhea. It is necessary to diagnose and treat the condition as early as possible. It has been shown that amenorrheic female athletes lose their bone mass particularly in the first years following the onset of amenorrhea (an average of 4% per year in the lumbar region) although less bone loss is reported later.
If amenorrhea occurs at puberty (primary amenorrhea), bone loss occurs before bone mass has attained its peak. Such adolescents enter adult life with what could be an irreversible deficit of bone mass and an increased risk of bone compression fractures throughout their lives (Gibson et al. 2000; Tomten et al. 1998). Neither high calcium intake nor physical activity will be sufficient to compensate for the lack of bone accretion at the end of adolescence.
Cycle disorders such as oligomenorrhea or anovulation also have consequences on bone status. Several studies have shown that there is a relationship between the severity of cycle disorders and bone mineral density (Gibson, Harries, Mitchell, Godfrey, Lunt, & Reeve 2000; Tomten, Falch, Birkeland, Hemmersbach, & Hostmark 1998) and that a return to regular cycles after several years of menstrual irregularity does not lead to the complete restoration of bone density (Tomten, Falch, Birkeland, Hemmersbach, & Hostmark 1998) even in the cortical bone in women pursuing a load-bearing physical activity.

Key points

- **A clear link has been established between energy deficits and cycle disorders.**
- **Amenorrhea is more common in female athletes following diets designed to maintain low body fat in sports where controlling one's body composition is a factor for success.**
- **There is a real continuum between the severity of the energy deficit, the severity of the cycle disorders and the degree of the body's metabolic, hormonal and energy adjustments.**
- **Amenhorreic female athletes also have an atherogenic lipid profile (significant increase in total cholesterol and LDL cholesterol). However, the long-term consequences on cardiovascular risk are unknown.**
- **Amenorrhea in female athletes is accompanied by a clinical oestrogen deficiency, inducing bone loss identical to that observed in menopausal women.**
- **There is a relationship between the severity of cycle disorders and bone mineral density. A return to regular cycles after several years of menstrual irregularity does not lead to the complete restoration of bone density.**
- **Cycle disorders, which indicate changes in ovarian function, are related to low energy availability and not exercise stress.**

4.5. Summary

In a context in which slimness, or even underweight, is held to be a model of beauty and the quest for thinness is growing within the population, it became essential to conduct an assessment of the risks related to dietary weight-loss practices.

Initially, the nutritional analysis of weight-loss diets consisted in characterising them according to their intakes in energy, protein, carbohydrate, lipid, vitamins and minerals. This made it possible both to classify the different diet phases according to their caloric intake (not low-calorie, low-calorie, very low-calorie and extremely low-calorie) and to establish the protein, carbohydrate and lipid contributions to TEI.

- *Concerning the general principles of the different weight-loss diets studied*

Altering food intake in order to lose weight may involve several mechanisms, such as modifying the amount of energy ingested or the macronutrient composition of food (e.g. high in protein, low in carbohydrate).
Some weight-loss diets focus on the total exclusion of certain foods or food categories and their duration varies according to the individuals and the amount of weight they wish to lose.
It is not possible to establish from the data for how long and at what frequency an individual will follow a diet, which can mitigate or exacerbate the consequences on health.

- *Concerning energy intake and protein, lipid and carbohydrate in the different diets*

The energy intakes associated with the diets or diet phases studied range from 574 to 2600 kcal/d (with the ANC being 1800 and 2200 kcal/d in women and men respectively, for normal physical activity).

Protein intake is greater than the ANC for more than 80% of the diets or diet phases. Intake for some is two to three times higher than the ANCs.

More than half of the diets or diet phases studied provide fat intake higher than the ANC, whereas 40% are below.

Virtually all the diets or diet phases studied propose carbohydrate intake below the ANC.

In 74% of the diet phases, intakes of fibre are lower than the ANC, sometimes almost ten times lower. Only 26% of the diets or diet phases studied follow the recommendations for fibre intake.

- *Concerning vitamin and mineral intakes of the various diets*

For women, the EAR for iron is not met by 61% of the diets or diet phases studied.

The EAR for calcium for adults is not met by 23% of the diets or diet phases. In contrast, two of the diet phases studied include intakes that are double the ANC.

Half of the diets studied that were designed for women correspond to magnesium intakes below the EAR. Seventy-seven percent of the diets or diet phases designed for men fail to meet the EAR (which is higher than for women).

Sodium intake is above the limit recommended by the WHO (5 g of salt per day, or about 2000 mg of sodium) for 58% of the diets or diet phases, and in one case it corresponds to more than double the recommendation.

For vitamin C, 26% of the diets or diet phases do not meet the EAR. In particular, one of the diets studied is below the EAR in every one of its phases.

The EAR for vitamin D is not met by the majority (77%) of the diets or diet phases.

The EAR for vitamin E is not met by 35% of the diets or diet phases.

The proposed classification, as well as the insufficient intakes, should be compared with literature data on the pathophysiological consequences related to dietary weight-loss practices.

Subsequently, an analysis of the scientific literature highlighted the physiological and psychological risks, for both the general population and specific population groups (pregnant women and nursing mothers, children and adolescents, the elderly, athletes, etc.). The main risks highlighted in this report are as follows:

General population

- *Concerning the status in vitamins and minerals*

The limited data published on the medium and long term do not enable the status in vitamins and minerals to be assessed, apart from calcium, despite the insufficient intakes demonstrated by the analysis of the weight-loss diets and the intakes observed in short-term studies.
Very low-calorie diets (including 2 weeks at 300 kcal/d) affect iron status.

- *Concerning bone mass*

Weight-loss diets are deleterious to the integrity of bone mass (due to the impact on bone mass and the fracture risk) as they cause a decrease in bone mineral mass, with an average 1-2% reduction in bone mineral density for a weight loss of 10%. Weight loss, if it is significant and rapid, can promote bone loss in women approaching or after menopause, and in non-obese individuals. This effect may be more pronounced in cases of significant weight loss (> 14%) over a short period (3 months). Moreover, a low weight or any weight loss, even only a small degree, can exacerbate menopausal or age-related osteopenia (1% change in bone mass for 5-6 kg of weight loss).

It has also been clearly established that fluctuations in body weight (whether or not intentional) are considered as predictors of bone mass. Consequently, the history of weight change is an important parameter to consider in the management of bone mass. Furthermore, the available data suggest that engaging in physical exercise seems to have only a partial effect on the prevention of bone loss.

A diet's protein, lipid and carbohydrate composition seems to have an impact on the deleterious effects observed on bone health. Practising energy restriction based on a reduction of lipid intake is harmful to bone mass. There is still however a lack of data from which to assert that following high-protein weight-loss diets exacerbates the deleterious effect of weight loss on bone mass. This deleterious effect may result from the combination of a high-protein and high-salt diet.

In addition, calcium deficiency is only one factor in the bone loss observed in menopausal women subjected to energy restriction.

In general, the intensity of bone-related complications depends on the population concerned (in terms of age and gender), initial weight, and conditions of weight loss (speed and degree).

- *Concerning energy metabolism*

Weight loss leads to an increased release of POPs which cause disruption to the endocrine, reproductive and immune systems, and metabolic dysfunction, which may contribute to weight regain, developmental disorders and cancers.
Decreased leptinemia, together with many other nutritional, neural and endocrine signals, sends an "energy deficit" signal to the brain, which results in a sensation of increased hunger.

The overall caloric intake (and not the variable macronutrient intake) is a major factor in a diet's effects on weight. Adapting the diet to the patient's tastes and habits is important to ensure their long-term commitment to the diet.

Irrespective of the individual or the diet considered, it has been clearly established that all weight-loss diets, regardless of protein intake, result in a loss of lean body mass (around 15% of the total mass lost during the diet) which can only be mitigated by concomitantly engaging in physical activity. Weight regain affects 80% of subjects after one year and increases over time. Thus the main stabilising factor is undertaking physical activity from the start of energy restriction and maintaining it after this period of restriction ends.

The energy intakes that allow weight loss to be maintained after dieting (including diets that induce a moderate weight loss corresponding to 10% of initial weight) are lower than those which allowed a stable weight to be maintained before weight loss, a situation which promotes weight regain. Moreover, the return to the initial weight is accompanied by a preferential regain of body fat mass.

Ultimately, the loss of muscle mass plays a major role in reducing energy expenditure (mainly basal metabolic rate) observed after energy restriction, which underlines the importance of maintaining muscle mass during energy restriction.

- *Concerning the cardiovascular system*

Very low-calorie diets may acutely induce accidents with sudden death from cardiac arrhythmia.

The safety of very low-carbohydrate (high-fat) diets has not been established from a cardiovascular point of view. In this context, a high intake in saturated fatty acids can increase insulin resistance despite weight loss.
Very low-fat diets, generally high-carbohydrate, are harmful because they cause an atherogenic lipid profile, particularly in cases of metabolic syndrome.

Weight fluctuation may be a cardiovascular and metabolic syndrome risk factor.

In amateur athletes, the combined practice of physical activity and weight-loss diets is accompanied in the short term by:
- Cardiovascular risks, mainly during the resumption of physical activity in a subject who has been sedentary for several years and who has one or more vascular risk factors;
- A risk of hypoglycaemic or vagal episodes (which may be exacerbated by dehydration) if food restriction is very significant.

- *Concerning the liver, kidney and gastrointestinal tract*

The data suggest that diets with very low calorie intake cause moderate inflammations and fibroses on the liver and the portal vein as well as gallstones.

High-protein non-low-calorie diets lead to intakes that exceed the adequate intake threshold (2.2 g/kg/d). Consequently, a renal assessment is needed in patients at risk of kidney disease before commencing any diet.

Certain weight-loss diets, especially low-carbohydrate diets, are often associated with digestive disorders, usually transient. They mainly include constipation, related in particular to lower consumption of fibre.

- *Psychological aspects*

Prospective dieters are often unaware of the negative psychological and behavioural consequences of dieting.
Depression and loss of self-esteem are common psychological consequences of repeated failures in dieting.

With regard to behaviour, cognitive restraint and the resulting disruption of eating behaviour very often exacerbate the weight problem.

Specific population groups

- ✓ *Concerning pregnant women and nursing mothers*

Few data on the effect of weight-loss diets on pregnant women are currently available. Nevertheless, it has been revealed that energy restriction during pregnancy leads to slower foetal growth (3rd trimester), birth weights lower than in the general population and a higher prevalence of miscarriages, premature births and births by caesarean section.

Antenatal nutritional deficiencies have a significant impact on an individual's subsequent health, especially when the dietary restriction occurs during the second part or last trimester of pregnancy. No energy restriction should be undertaken during pregnancy without medical supervision.

The level of milk production is affected by protein-energy malnutrition and may have repercussions on the child's growth and development. Although the quality of breast milk is relatively stable, the concentration of nutrients such as iodine and certain water-soluble vitamins, the quality of fatty acids, especially long-chain omega-3 polyunsaturated fatty acids, are strongly influenced by the mother's diet.

- ✓ *Concerning children and adolescents*

With children and adolescents, following weight-loss diets is not without risk, whether somatic or psychological. Accordingly, energy restriction with or without protein restriction leads to slower growth and pubertal development.

These risks are accompanied by risks of primary or secondary amenorrhoea, as well as tendinitis, bone mineral loss and clinical iron deficiency, especially among young female athletes.

- ✓ *Concerning the elderly*

If it is accompanied by a magnesium deficiency, dieting may increase the risk of cardiac arrhythmia and atrial fibrillation in women after menopause.

The negative impact of weight loss is more pronounced in the elderly with regard to the risk of some cancers, the development of pressure ulcers, and especially the loss of muscle mass and skeletal mineralisation.

Diets low in fat (18-22% of energy intake), and especially linoleic acid-deficient diets, have been associated with a higher incidence of colorectal tumour relapse.

When elderly obese subjects engage in food restriction in order to lose weight, this accelerates muscle wasting.

- ✓ *Concerning male athletes*

The data suggest that qualitative changes to the diet are involved in the physiology of the decline in testosterone levels associated with intense physical and sporting activity. Lipid restriction may affect the plasma concentration of testosterone.
If nutritional intake is adapted to energy expenditure, no reduction in testosterone levels is observed.

- ✓ *Concerning female athletes*

A relationship between the energy deficit and menstrual cycle disorders has been clearly established. There is a real continuum between the severity of the energy deficit, the severity of the cycle disorders and the extent of the body's metabolic, hormonal and energy adjustments.
Amenorrhoea is more common in female athletes following diets to maintain low body fat mass in sports where controlling the body's composition is a factor for success.
Amenhorreic female athletes also have an atherogenic lipid profile (significant increase in total cholesterol and LDL cholesterol).
The long-term consequences on cardiovascular risk are unknown.
Amenorrhea in female athletes is accompanied by a clinical oestrogen deficiency which induces bone loss similar to that observed in menopausal women.
There is a relationship between the severity of cycle disorders and bone mineral density. A return to regular cycles after several years of menstrual irregularity does not lead to the complete restoration of bone density.
Menstrual cycle disorders, which are evidence of changes in ovarian function, are related to low availability and not exercise stress.

Limitations to these data

It is worth recalling that this argumentation as a whole has several limitations:

- *In terms of the diets selected:* the list of weight-loss diets presented in this interim report is not exhaustive. Those selected appear most frequently when searching on the Internet or correspond to the bestselling books in stores and on the Internet.

- *In terms of individual practice:* for a given diet, there are as many interpretations of the recommendations as there are individuals. In addition, there are no data with which to ascertain the actual duration, or the frequency at which individuals follow diets. The risks associated with consecutive or even simultaneous practice of different diets were not taken into account.

- *In terms of the nutritional analysis of the diets:* for each phase and each typical day, the food consumption recommended by the diets studied was recorded for that day's different meals. When portion sizes were not specified, average data from the INCA2 study were applied. This approximation, while it does not represent the reality of consumption, particularly that described as "unlimited", is the most effective way of estimating the French population's nutrient intakes related to these diets. In addition, characterisation of nutritional intake was limited to data on the nutritional composition of foods available from the Ciqual databank[19].

- *In terms of the available scientific literature*: many studies address the benefits of dietary weight-loss practices rather than the risks. The vast majority of these studies focus on obese subjects and the available data have been extrapolated to the general population. Furthermore, the heterogeneity of the population groups studied, the nature of the risks assessed and the type and nature of energy restriction practiced all constitute factors limiting the extent of the analysis. While it is clear that the main risks involve bone health, weight regain and behavioural disorders, the safety of the diets with respect to other risks has not been established, especially since the level of evidence is not always satisfactory.

[19] ANSES (2010). Ciqual databank of the nutritional composition of foods, consulted in August 2010

5. GENERAL CONCLUSION

Today, the collectively-developed tyranny of body image - which is not simply a self-centred individual construct but a social fact - constantly pressures the individual into accepting aesthetic canons and social norms regarding the body. Moreover, overweight and obesity, which affect respectively 31.9% and 14.5% of subjects over 18 years of age in France, are a real public health problem, due to the number of metabolic dysfunctions that may accompany them and the pathological risks incurred. One of the consequences of these two phenomena is the development of a varied arsenal of strategies, including nutritional practices, which are often applied without medical justification (in the absence of overweight or obesity) or medical supervision, in order to reduce body weight.
As a reminder, the data from the INCA2 study show that over 30% of women with a 'normal' BMI, to which can be added 15% of 'thin' women (BMI <22), followed a weight-loss diet during the survey or had followed one during the year preceding the survey.

This work enabled an assessment to be conducted on the risks related to dietary weight-loss practices, on the basis of a collective, adversarial scientific expert appraisal, taking into account the specific characteristics of the different diets studied, regardless of the individual situation of the person following the diet. It did not therefore involve a benefit-risk assessment based on each individual's specific situation, nor a position on whether or not anyone should follow a diet, nor on the choices to be made.

Foodstuffs such as food supplements claiming weight-loss effects and dietetic products for low-calorie diets have not been assessed in the context of this report, given their diverse composition and conditions of use. However, an assessment of the effects of their use seems necessary in due course.

Following weight-loss diets is not a trivial matter. Indeed, the risk of the onset of harmful effects on health of varying severity cannot, under any circumstances, be neglected.

This work enabled the clinical, biological, behavioural and psychological risks related to dietary weight-loss practices to be demonstrated, based on the scientific literature.
The characterisation of several examples of weight-loss diets has shown that they can lead to nutritional imbalances and inappropriate intakes (insufficiency and excess), especially with regard to vitamins and minerals. However, the consumption data used in the nutritional characterisation of the diets or diet phases, especially when the quantities were not specified by the author, do not reflect inter-individual variability. For this reason in particular, it was not possible to extract information enabling these diets to be ranked in terms of the risks that may be related to their practice.

In addition, the literature emphasises that following these diets may result in somatic disturbances, mainly relating to bone and muscle, as well as psychological disturbances (including behavioural eating disorders), and profound changes to energy metabolism and the physiological regulation of eating behaviour. Such modifications often cause a vicious cycle of weight regainin the more or less long term which may be even greater than the original weight. In this context, physical activity should be considered as an essential criterion for weight stabilisation.

In addition, there are potentially further specific risks associated with particular physiological situations, including growth disturbances (foetuses, children, adolescents), the risk of malnutrition (especially among the elderly), and hormonal disorders (athletes).

The following recommendations may be issued at the conclusion of this assessment:

- to the population groups affected

- Seeking to lose weight without formal medical indication bears risks, especially when it involves unbalanced eating with limited variety. Undertaking a weight-loss programme therefore requires specialised medical supervision.

- This supervision must be adapted to the patient's weight status (BMI, waist circumference):
  - in the absence of overweight: weight-loss diets are risk practices, whether or not they are recommended by doctors. The public should therefore be warned of the adverse short-, medium- or long-term consequences of following these diets, especially since they are

unbalanced, associated with severe behavioural eating disorders, and may eventually lead to possible irreversible weight gain.
  - the management of obesity, overweight, or significant weight gain requires an accurate diagnosis of the causes, an analysis of the context and an estimate of the consequences: the indication whether or not to lose weight should be questioned and the objectives and the means to be implemented should be defined. These are not limited merely to management of the diet; they should aim for an appropriate and cautious reduction in weight, planned in good time (in order to address the causal factors) and then stabilised by the appropriate means, while taking care to maintain physical and psychological health in the medium and long term.

- Changes in eating habits should be combined with the introduction, maintenance, or even increase of regular physical activity.

- Obesity is a multifactorial chronic disease and its management requires an interdisciplinary approach (doctor specialising in nutrition, endocrinologist, dietician, psychologist, etc.).

- with regard to *assessment and research*

- The analysis of the potential risks related to dietary weight-loss practices should be supplemented by:
  - an assessment of dietetic products intended for very low-calorie diets (meal replacements such as "protein mixes"),
  - an assessment of the consumption of food supplements claiming weight-loss effects.

- Several types of studies and research needed for the risk assessment could be considered by acquiring data on:
  - the benefits, risks and changes to health status and weight in the medium (2 years) and long term (10 years), by analysing nutritional intakes and status (vitamins and minerals, fatty acids, etc.) in subjects with or without overweight, following weight-loss diets, with or without medical supervision; such work should take into account the different types of diets and population groups;
  - the key biological, psycho-behavioural and social determinants of weight gain and regain.

Key words:
WEIGHT-LOSS DIET, LOW-FAT, LOW-CALORIE, HIGH-PROTEIN, LOW-CARBOHYDRATE, PHYSICAL ACTIVITY.

6. ANNEXES

Annex 1. Composition of the working group and people interviewed

EXPERT ADVISORS TO ANSES

Dr. Jean-Michel LECERF (Institut Pasteur) – *Endocrinology, metabolism of lipids – Chairman of the Working Group*

Dr. Martine CHAMP (INRA) – *Metabolism of carbohydrates*
Dr. Véronique COXAM (INRA) – *Micronutrients, bones*
Marie-Dominique DANIEL-LAMAZIERE (Bordeaux University Hospital Centre) – *Dietician*
Pr. Martine DUCLOS (Auvergne University Hospital Centre) – *Physical activity*
Dr. Jacques FRICKER (AP-HP, Bichat) – *Private practitioner and also Hospital consultant in the Nutrition/Obesity Department*
Dr. Michèle GARABEDIAN (AP-HP, Saint-Vincent de Paul) – *Micronutrients, growth*
Dr. Claire GAUDICHON (UMR INRA-AgroParisTech) – Protein m*etabolism and high-protein diets*
Pr. Jean-Philippe GIRARDET (AP-HP, Trousseau) – *Nutrition of children and pregnant women*
Michelle LE BARZIC (AP-HP, Hôtel Dieu) – *Psychology and eating behaviour*

The Working Group was deliberately made up of experts from a variety of disciplines, as agreed with the CES on "Human Nutrition". The choice of experts took into account knowledge of nutrition applied in teaching, clinical and general practice.

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Scientific contributions and coordination
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Dr. Esther KALONJI (UENRN)
Pr. Irène MARGARITIS (UENRN)
Perrine NADAUD, M.Sc. (UENRN)
Dr. Sandrine WETZLER (UENRN)

Specific scientific contributions
Dr. Florie FILLOL (ANSES)
Dr. Sandrine LIORET (ANSES)

RAPPORTEURS

Sylvie BENKEMOUN (Allegro Fortissimo)
Dr. Pascal CRENN (*Assistance Publique - Hôpitaux de Paris* Raymond Poincaré)
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PEOPLE INTERVIEWED BY THE WORKING GROUP

Jean-Loup ALLAIN (Alliance 7 – food producers' association)
Philippe La DROITTE (Alliance 7)
Brigitte LELIEVRE (Alliance 7)
Olivier ANDRAULT (UFC-Que Choisir – national consumer association)
Claire GARNIER (UFC-Que Choisir)
Dr. Dominique BAELDE (DGCCRF)
Mathieu JOUYS (Dance school of the *Opéra National de Paris*)
Marie-Laure VEYRIES (AFSSAPS)

PEOPLE INTERVIEWED BY ANSES

Dr. Jean-Michel COHEN (GP, Paris)
Dr. Pierre DUKAN (GP, Paris)
Muriel CHABANOIS-MARREAU (WeightWatchers)
Corrine POLLIER (WeightWatchers)

[20] ***Centre d'information sur la qualité des aliments*** **(French Information Centre on Food Quality)**
[21] *Unité d'évaluation sur la nutrition and les risques nutritionnels* (Unit for Assessment of Nutrition and Nutritional Risks)

Annex 2. Glossary

ANC (*apport nutritionnel conseillé* - Population Reference Intake)
The ANC is the average nutritional requirement measured for a group of individuals, plus two standard deviations representing inter-individual variability, designed to cover the requirements of the majority (97.5%) of the population. The reference intake therefore relates to a population group.

Athlete
In this report, an athlete is considered to be an individual practising a physical or sporting activity of high intensity and/or for long periods.

Clinical deficiency
The term clinical deficiency is used to describe conditions where a deficiency is associated with obvious clinical manifestations.

Diet
A 'diet' is a specific dietary practice. It can therefore correspond to a type or style of food consumption practised by an individual or a social group. It is often part of a lifestyle choice. In common language, a 'diet' is often taken to mean restriction. It can be spontaneous or imposed (whether prescribed medically or not). In this case, a distinction can be made between 'balanced diets' and 'exclusion diets'.

Energy balance
The concept of energy balance, which involves comparing energy input provided by food with energy expenditure related to body functions and the various activities carried out, is a simple way of understanding weight variations capable of leading to overweight or obesity.

Estimated Average Requirement (EAR)
The estimated average requirements result from values acquired from an experimental group consisting of a limited number of individuals and corresponding to average individual requirements. It therefore relates to the individual.

Health risk assessment
Health risk assessment is a method developed to define the effects on the health of an individual or a population group of exposure to hazardous substances (chemicals, materials, etc.) or situations. The health risk assessment process is normally broken down into 4 stages:

1. *Identification of the hazard* describes the biological disorders or pathologies liable to occur as a result of the substance or situation considered; it also describes the degree of likelihood of a causal relationship between the situation or practice considered and the onset of these disorders and pathologies (the 'weight of evidence').
2. *The 'dose-response' relationship* (also known as 'risk of exposure') gives a mathematical description of the association between a 'dose' of exposure and the observed response (the observation of an effect on health, i.e. the existence of risk) over a given period.
3. *The significance of excessive health risk* depends not only on the 'hazard' (as defined above), but also on the level of exposure and its duration (intensity of the exposure) and also its frequency. It is necessary to establish these parameters as a part of the process of assessing the exposure.
4. *The risk is then characterised* using the results of the preceding stages in order to describe the type and extent of the excess risk expected, bearing in mind the conditions of exposure to the element or the situation identified within a population group, considered in all its diversity. Characterisation also includes a discussion of the uncertainties associated with the risk assessment.

Insufficient intake
At an individual level, insufficient intake describes an intake below the Estimated Average Requirement for the nutrient considered.

Lean body mass
Lean body mass consists of water (about 72.5%) and solids (minerals and organic compounds). It consists mostly of muscle tissue and is mainly responsible for the energy needs of basal metabolism.

Nutritional requirements
The requirements in terms of a given nutrient or in terms of energy are defined as the amount of nutrient or energy necessary for the maintenance and the metabolic and physiological functions of an individual in good health (homeostasis), comprising the requirements for physical activity and thermoregulation, and the additional requirements that may be necessary during certain periods of life such as growth, gestation and lactation.

Physical and sporting activity
The WHO defines this as “any bodily movement produced by skeletal muscle that requires energy expenditure”. Physical and athletic activities form a continuum from at least moderate activity up to regular high-intensity activity (such as high-performance athletes).

Safety limit
The safety limit is the total chronic daily level of intake for a nutrient (from all sources) considered to be without risk of harm to human health. It is a scientific estimate based on a risk assessment. These limits apply to the entire population, including sensitive individuals, except where one or more population groups are more susceptible to one or more harmful effects of a nutrient. It should be remembered that safety limits are not recommended intake levels.

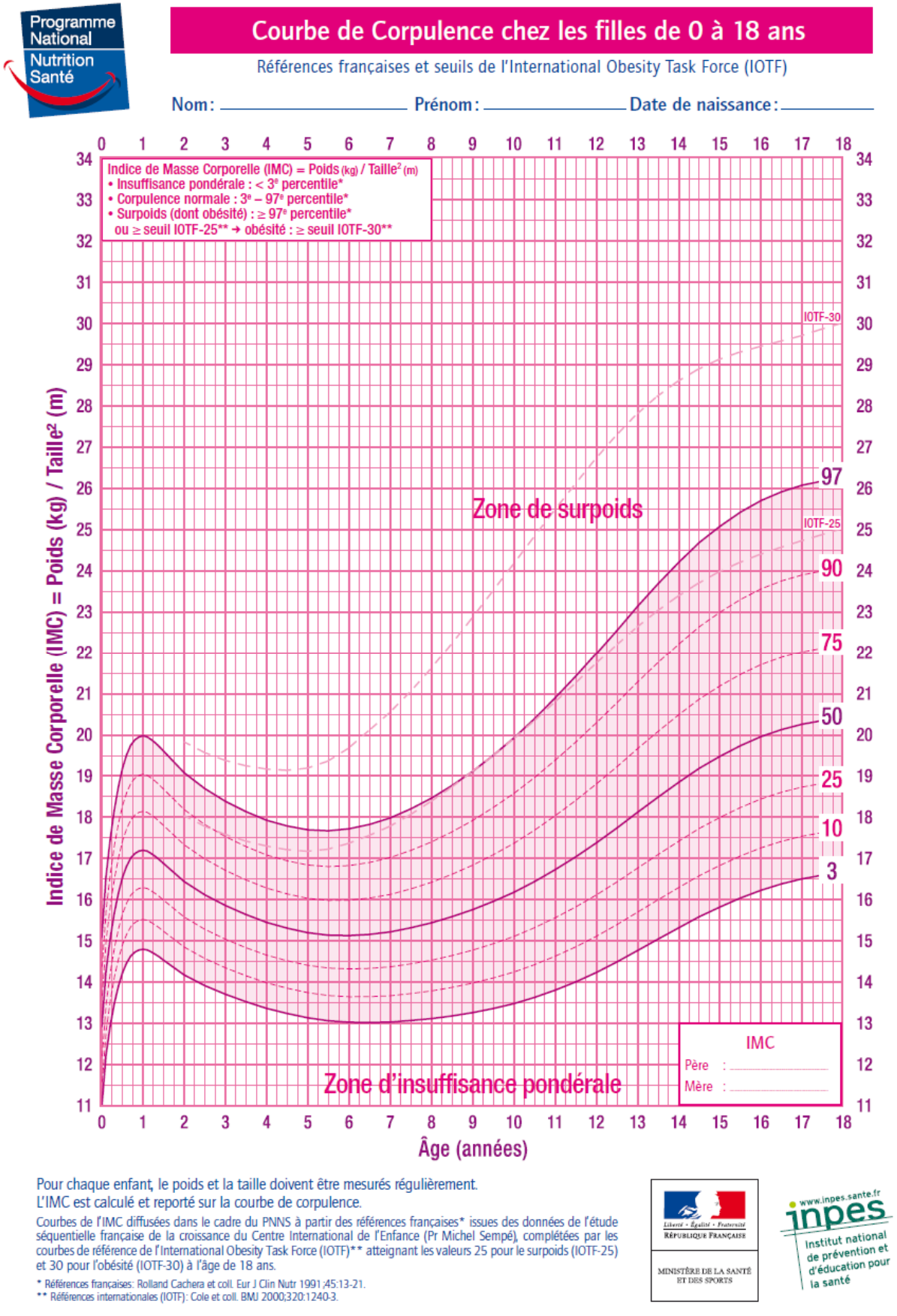
Sub-clinical deficiency
The term sub-clinical deficiency is used to describe conditions that can be objectively characterised biologically with validated markers. Sub-clinical deficiency conditions are not associated with specific clinical manifestations, but these situations can lead to morbidity or affect the quality of health.

Weight-loss diet
The principle behind weight-loss diets is to establish an energy deficit (relative to the requirements of the individual) by reducing food intake and thus losing weight.

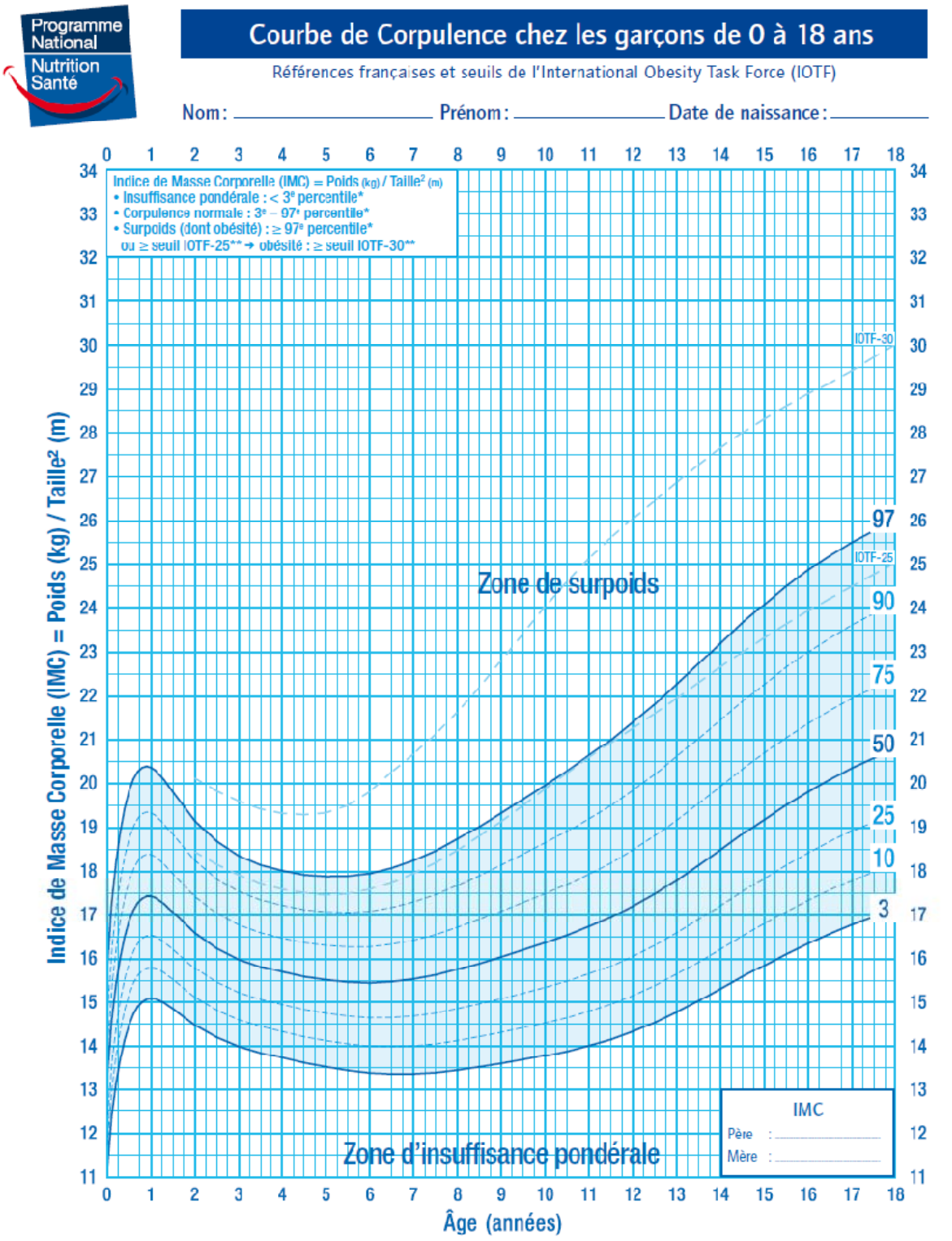
Annex 3: Acronyms and abbreviations

ANC: *Apport nutritionnel conseillé* [see PRI]
ATGL: Adipose Triglyceride Lipase
BMC: Bone Mineral Content
BMD: Bone Mineral Density
BMI: Body Mass Index
CES: *Comité d'experts specialisé* (ANSES Expert Committee)
CIQUAL: *Centre d'information sur la qualité des aliments* (French Information Centre on Food Quality)
DHA: Docosahexaenoic Acid
EAR: Estimated Average Requirement
HDL: High Density Lipoprotein
HSL: Hormone-Sensitive Lipase
IGF: Insulin-like Gross Factor
IOTF: International Obesity Task Force
LDH: Lactate dehydrogenase
LDL: Low Density Lipoprotein
LH: Luteinising Hormone
NEFA: Nonesterified Fatty Acid
PCB: Polychlorinated Biphenyl
PDH: Pyruvate dehydrogenase
PNNS: *Programme national nutrition santé* (French National Health and Nutrition Programme)
POP: Persistent Organic Pollutant
PRI: Population Reference Intake
SHBG: Sex Hormone-Binding Globulin
VLDL: Very Low Density Lipoprotein
WHO: World Health Organization

Annex 4. Bodyweight curve for girls aged 0 to 18 (French references)



Annex 5: Bodyweight curve for boys aged 0 to 18 (French references)



Annex 6. Keywords used for the literature search and assignment depending on the field of expertise of the members of the Working Group

Table 1: Keywords for literature search

	Keywords
Diets	Dietary practice; weight loss; weight management; regimen; diet restriction; weight reducing diet; low fat; low carbohydrate; low carb; restricted carbohydrate; energy restriction; low calorie diet; low glycaemic index; fast; very low calorie diet; atkins; protein diet; carbohydrate free; mayo; scarsdale; weight watcher; montignac; the zone; ornish; herbalife; ketogenic diet; calorie-restricted diet; strategy for controlling weight; popular diet;. (or)
Risk	risk; deficiency; vitamin deficiency; minerals deficiency; essential fatty acid deficiency; energy deficiency; micronutrient deficiency; macronutrient deficiency; protein deficiency, calcium deficiency; calcium loss; magnesium deficiency; iron deficiency, potassium deficiency; mineral toxicity; folate deficiency; nitrogen balance; osteoporosis; bone mass; fracture; bone; muscle; sarcopenia; lean body mass; muscular strength; cardiovascular risk; cardiovascular disease, coronary heart disease; HDL-cholesterol; LDL-cholesterol; small and dense LDL; oxidative stress; low grade acidosis; inflammation; metabolic stress; pro-inflammatory; hyperuricemia; triglycerides; hypertriglyceridemia; gall bladder; urinary lithiasis; renal lithiasis; liver; hepatic steatosis; renal disease; anorexia nervosa; bulimia; binge eating; night eating syndrome; craving; cognitive restriction; puberty; thyroid disorder; insulin resistance; menstrual cycle; hormonal disturbance; amenorrhea; menarche; birth weight; fetal growth; intra uterine growth; pregnancy; hypotension; hypothalamic effect; hypophyse; weight regain; long term weight loss; weight stabilisation; yo-yo syndrome; diarrhoea; nausea; constipation; headache; pancreatitis; gastritis; immunity; lymphopenia; muscle cramps; skin rash; sudden death; depression; mood disorder; distress; growth disorder; sleep disorder; insomnia; cognitive performance; breastfeeding; sga; iodine deficiency/status; sport; exercise.
Population	elderly; children; pregnancy; adolescent; foetus; athlete; adult; infant;

Table 2: Expert appraisal work assigned to members of the Working Group

Expert	Field of risk and population categories
Michèle GARABEDIAN	risk; deficiency; vitamin deficiency; minerals deficiency; micronutrient deficiency; calcium deficiency; calcium loss; magnesium deficiency; iron deficiency, iodine deficiency/status; thyroid disorder; potassium deficiency; mineral toxicity; folate deficiency; pancreatitis; gastritis; immunity; lymphopenia;
Véronique COXAM	osteoporosis; bone mass; fracture; bone; muscle; sarcopenia; lean body mass; muscular strength; muscle cramps;
Jacques FRICKER	weight regain; long term weight loss; weight stabilisation; yo-yo syndrome;
Martine CHAMP	risk; deficiency; essential fatty acid deficiency; energy deficiency; macronutrient deficiency; protein deficiency, nitrogen balance; macronutrient balance, diarrhoea; nausea; constipation, headache; muscle cramps; skin rash;
Jean-Michel LECERF	cardiovascular risk; insulin resistance; sudden death, cardiovascular disease, coronary heart disease; HDL-cholesterol; small and dense LDL; oxidative stress; low grade acidosis; inflammation; metabolic stress; pro-inflammatory; hyperuricemia; triglycerides; hypertriglyceridemia; hypotension;
Jean Philippe GIRARDET	puberty; menstrual cycle; hormonal disturbance; amenorrhea; menarche; birth weight; foetal growth; intra-uterine growth; growth disorder; pregnancy; breastfeeding; sga; hypothalamic effect; hypophyse;
Claire GAUDICHON	gall bladder; urinary lithiasis; renal lithiasis; liver; hepatic steatosis; renal disease;
Michèle LE BARZIC	anorexia nervosa; bulimia; binge eating; night eating syndrome; craving; cognitive restriction; depression; mood disorder; distress; sleep disorder; insomnia; cognitive performance;
Marie-Dominique DANIEL-LAMAZIERE	Dietary practice; weight loss; weight management; regimen; diet restriction; weight reducing diet; low fat; low carbohydrate; low carb; restricted carbohydrate; energy restriction; low calorie diet; low glycaemic index; fast; very low calorie diet; atkins; protein diet; carbohydrate free; mayo; Scarsdale; weight watcher; montignac; the zone; ornish; herbalife; ketogenic diet; calorie-restricted diet; strategy for controlling weight; popular diet.

Annex 7. Daily nutritional intake (INCA2) and nutritional reference values for vitamins and minerals

	Total daily nutritional intake (INCA2)		Nutritional reference values	
	Average intake	95th percentile	ANC[22]	Safety limit (EFSA, 2006)
Retinol (µg)	704.5	2389	800/600	3000
Vitamin D (µg)	2.56	5.46	5	50
Vitamin E (mg)	11.63	22.06	12	300
Vitamin K (µg)			45	
Vitamin B_1 (mg)	1.23	1.96	1.3/1.1	
Vitamin B_2 (mg)	1.87	2.94	1.6/1.5	
Vitamin B_3 (mg)	19.29	30.96	14/11	(a) 900, (b) 10
Vitamin B_5 (mg)	5.63	8.53	5	
Vitamin B_6 (mg)	1.74	2.76	1.8/1.5	25
Vitamin B_8 (µg)			50	
Vitamin B_9 (µg)	289.4	466.1	330/300	1000
Vitamin B_{12} (µg)	5.81	14.54	2.4	
Vitamin C (mg)	92.8	194.6	110	
Beta-carotene (mg)	3332.9	7307.2		
Calcium (mg)	913.1	1487.5	900	2500
Magnesium (mg)	291.7	457.8	420/360	
Iron (mg)	13.12	21.22	9/16	
Copper (mg)	1.46	2.78	2/1.5	5
Iodine (µg)	119.5	187.4	150	600
Zinc (mg)	10.69	17.28	12/10	25
Manganese (mg)	2.92	5.11		
Sodium (mg)	2967.4	4872.1		
Potassium (mg)	2979.7	4416.5		
Selenium (µg)	53.7	87.3	60/50	300
Chrome (µg)			65/55	
Molybdenum (µg)				600
Fluorine (mg)			2.5/2	7
Chlorine (mg)				
Phosphorus (mg)	1265.3	1915.3	750	

(

a) nicotinamide, (b) nicotinic acid

[22] Where ANC values are different, they are given first for men and then for women.

Annex 8. Data from the INCA2 study

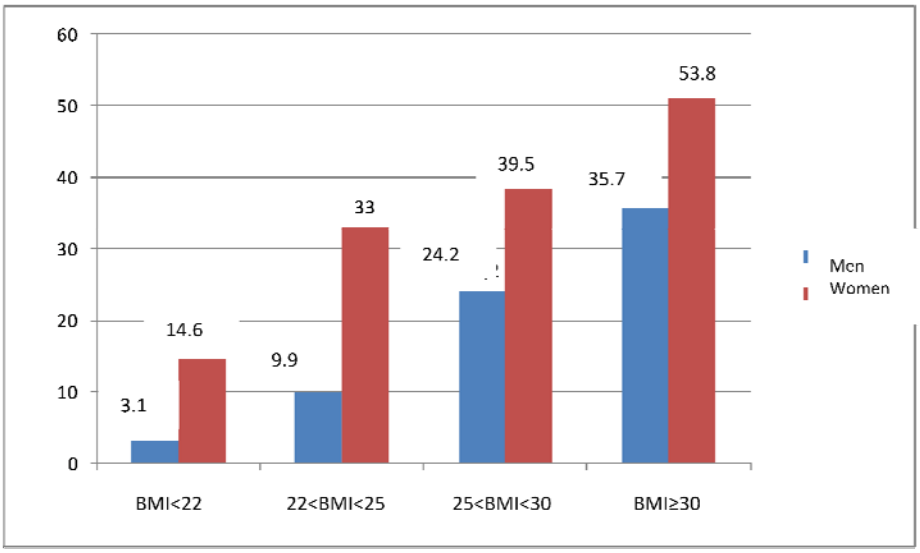
Table 1. Perception of own weight, wishes, and previous history of weight fluctuation, by gender and age (N=2587).

Variable	Age	Men	Women	Overall	*P (gender)*
Opinion of own weight. Considers himself/herself to be:					
Of normal weight, % (CI95%)	18-34	61.4 (55.2-67.6)	51.7 (46.3-57.1)	56.4 (52.2-60.5)	
Too fat, % (CI95%)		27.4 (21.8-33.1)	36.5 (30.9-42.2)	32.1 (28.1-36.2)	
Too thin, % (CI95%)		9.5 (6.4-12.7)	4.2 (2.0-6.3)	6.8 (5.0-8.6)	
Does not know, % (CI95%)		1.6 (0-3.4)	7.6 (4.0-11.2)	4.7 (2.6-6.8)	*0.0001*
Of normal weight, % (CI95%)	35-54	57.7 (52.8-62.6)	48.6 (44.2-53.0)	52.7 (49.4-56.1)	
Too fat, % (CI95%)		36.9 (32.3-41.5)	42.7 (38.2-47.2)	40.1 (36.8-43.3)	
Too thin, % (CI95%)		3.2 (1.4-5.0)	2.2 (1.3-3.0)	2.7 (1.7-3.6)	
Does not know, % (CI95%)		2.2 (1.0-3.3)	6.5 (4.5-8.5)	4.5 (3.3-5.7)	*0.0002*
Of normal weight, % (CI95%)	55-79	57.9 (52.6-63.2)	44.7 (39.7-49.7)	51.8 (48.5-55.1)	
Too fat, % (CI95%)		37.0 (32.1-41.9)	47.4 (42.3-52.4)	41.8 (38.7-44.9)	
Too thin, % (CI95%)		2.0 (0.7-3.4)	1.4 (0.1-2.8)	1.8 (0.8-2.7)	
Does not know, % (CI95%)		3.1 (1.0-5.1)	6.5 (3.8-9.3)	4.7 (3.1-6.3)	*0.004*
Of normal weight, % (CI95%)	Overall	58.9 (55.5-62.2)	48.4 (45.7-51.1)	53.5 (51.4-55.7)	
Too fat, % (CI95%)		34.1 (31.0-37.3)	42.2 (39.4-45.0)	38.2 (36.1-40.4)	
Too thin, % (CI95%)		4.7 (3.5-5.9)	2.6 (1.8-3.4)	3.6 (2.9-4.3)	
Does not know, % (CI95%)		2.3 (1.3-3.3)	6.9 (5.3-8.4)	4.6 (3.7-5.6)	*<0.0001*
P (age)		*<0.0001*	*0.06*	*<0.0001*	
Wishes for own weight. Would like to weigh:					
More, % (CI95%)	18-34	17.3 (12.8-21.8)	7.4 (4.0-10.9)	12.2 (9.5-15.0)	
Less, % (CI95%)		37.7 (31.8-43.6)	56.9 (51.6-62.2)	47.6 (43.7-51.5)	
Same as now, %% (CI95%)		41.1 (35.4-46.7)	32.4 (27.4-37.3)	36.6 (33.0-40.2)	
Does not know, % (CI95%)		4.0 (1.7-6.3)	3.3 (1.4-5.2)	3.6 (2.2-5.1)	*<0.0001*
More, % (CI95%)	35-54	5.0 (2.9-7.0)	2.7 (1.7-3.6)	3.7 (2.6-4.8)	
Less, % (CI95%)		45.5 (40.4-50.7)	61.0 (56.7-65.3)	54.0 (50.4-57.5)	
Same as now, % (CI95%)		46.7 (41.5-51.8)	33.1 (28.9-37.3)	39.3 (35.9-42.6)	
Does not know, % (CI95%)		2.8 (1.8-3.8)	3.3 (1.9-4.7)	3.1 (2.2-3.9)	*<0.0001*
More, % (CI95%)	55-79	1.9 (0.5-3.2)	2.5 (0.8-4.3)	2.2 (1.1-3.2)	
Less, % (CI95%)		46.2 (40.7-51.7)	62.0 (56.6-67.3)	53.5 (49.7-57.2)	
Same as now, % (CI95%)		48.2 (42.7-53.7)	32.1 (27.1-37.3)	40.8 (37.2-44.3)	
Does not know, % (CI95%)		3.7 (1.5-5.9)	3.5 (1.6-5.3)	3.6 (2.1-5.1)	*0.0005*
More, % (CI95%)	Overall	7.5 (5.9-9.1)	4.1 (2.9-5.3)	5.8 (4.8-6.7)	
Less, % (CI95%)		43.5 (40.1-46.8)	60.0 (57.2-62.8)	51.9 (49.6-54.2)	
Same as now, % (CI95%)		45.6 (42.0-49.1)	32.6 (29.8-35.3)	38.9 (36.7-41.1)	
Does not know, % (CI95%)		3.5 (2.3-4.6)	3.3 (2.4-4.3)	3.4 (2.7-4.1)	*<0.0001*
P (age)		*<0.0001*	*0.01*	*<0.0001*	
History of weight loss followed by regain of at least 10 kg					

Variable	Age	Men	Women	Overall	*P (gender)*
Never, % (CI95%)	18-34	57.8 (51.0-64.6)	59.4 (54.1-64.8)	58.7 (54.3-63.1)	
Once, % (CI95%)		13.4 (9.6-17.1)	12.6 (9.3-15.9)	13.0 (10.4-15.5)	
Twice or more, % (CI95%)		5.9 (2.9-8.8)	6.4 (3.1-9.8)	6.2 (3.9-8.5)	
No answer or DNK, % (CI95%)		23.0 (16.4-29.5)	21.5 (16.9-26.1)	22.2 (18.0-26.4)	*0.95*
Never, % (CI95%)	35-54	61.6 (56.5-66.8)	54.1 (49.7-58.6)	57.6 (54.0-61.1)	
Once, % (CI95%)		18.6 (14.8-22.4)	21.8 (18.0-25.6)	20.3 (17.8-22.9)	
Twice or more, % (CI95%)		9.4 (6.5-12.2)	14.6 (11.2-18.0)	12.2 (9.9-14.5)	
No answer or DNK, % (CI95%)		10.4 (7.3-13.4)	9.5 (6.4-12.5)	9.9 (7.6-12.2)	*0.05*
Never, % (CI95%)	55-79	61.0 (55.0-66.9)	53.7 (48.6-58.9)	57.6 (53.6-61.7)	
Once, % (CI95%)		11.8 (8.4-15.3)	14.0 (10.1-17.9)	12.8 (10.1-15.6)	
Twice or more, % (CI95%)		11.2 (7.7-14.7)	21.2 (17.2-25.2)	15.8 (13.1-18.6)	
No answer or DNK, % (CI95%)		16.0 (11.8-20.3)	11.0 (7.9-14.1)	13.7 (11.0-16.4)	*0.001*
Never, % (CI95%)	Overall	60.3 (56.5-64.0)	55.6 (52.8-58.5)	57.9 (55.5-60.3)	
Once, % (CI95%)		14.7 (12.7-16.6)	16.7 (14.6-18.9)	15.7 (14.3-17.1)	
Twice or more, % (CI95%)		9.0 (7.1-10.9)	14.0 (12.0-16.1)	11.6 (10.1-13.0)	
No answer or DNK, % (CI95%)		16.1 (13.3-18.9)	13.6 (11.6-15.6)	14.8 (13.0-16.6)	*0.0006*
P (age)		*0.0003*	*<0.0001*	*<0.0001*	

Irrespective of age, women said they considered themselves “too fat” more often than men; overall, this perception concerned more than 40% of women, and increased with age. Inversely, with the exception of young men (aged 18-35), very few adults considered themselves too thin (<5%).
Subjects wishing to weigh less were proportionately more numerous than those who declared that they were too fat: 44% and 60% for men and women respectively. These rates change with age in the same way as the variable of weight perception.
More than a quarter of the population declared that they had lost and regained 10 kg at least once in their lives, which is a considerable proportion. It should be noted, furthermore, that this question elicited a relatively high proportion of non-responses: 15%.

Figure 1. Proportion of subjects following or having followed a diet in the past year as a function of their weight status (legend: BMI<22 kg/m^2; 22≤BMI<25; 25≤BMI<30; BMI≥30).



This graph illustrates the positive relationship between dieting and bodyweight (P<0.0001 in both men and women). It also shows that almost 15% of 'thin' women (BMI<22 kg/m^2) were either on a diet during the survey or had followed one during the previous year. It should be noted that as only diets declared during the week of the survey were taken into account, this rate is only 3.3% (1.3-5.2). It is therefore possible that some women may have become slim because of their diet or had realised that they did not need to diet.

Table 2. Nutritional intake for adults 18-79 years old depending on whether they were dieting or not dieting. Analyses stratified by gender and adjusted for age.

		MEN			WOMEN		
Nutrient	Diet	Average adjusted for age	SEM	*P*	Average adjusted for age	SEM	*P*
Energy intake	No	2289.7	26.1		1734.5	18.3	
	Yes	2168.4	44.1	*0.02*	1668.7	23.7	*0.03*
Total carbohydrates, g/d	No	241.2	3.3		187.3	2.3	
	Yes	218.9	5.8	*0.001*	175.8	3.0	*0.004*
Simple carbohydrates, g/d	No	93.6	1.9		83.5	1.3	
	Yes	82	3.1	*0.002*	79.8	1.8	*0.1*
Complex carbohydrates, g/d	No	140.7	2.0		99.5	1.5	
	Yes	130.3	4.1	*0.03*	92	1.8	*0.002*
Fats, g/d	No	91.7	1.2		74.1	0.9	
	Yes	89.6	1.9	*0.37*	71.5	1.2	*0.09*
Proteins, g/d	No	93	1.0		69.7	0.7	
	Yes	90.1	2.0	*0.19*	70	1.0	*0.78*
Calcium, mg/d	No	905.2	15.0		795.6	10.0	
	Yes	924.7	33.2	*0.58*	818.8	17.0	*0.25*
Iron, mg/d	No	13.7	0.2		10.6	0.1	
	Yes	13.5	0.5	*0.62*	10.9	0.3	*0.35*
Magnesium, mg/d	No	297.8	3.8		242.8	2.7	
	Yes	294.6	9.0	*0.7*	252.0	6.7	*0.2*
Potassium, mg/d	No	3006.7	33.4		2523.5	26.5	
	Yes	2951.6	79.3	*0.51*	2538	43.3	*0.77*
Folate, µg/d	No	281.3	3.9		247.8	3.4	
	Yes	276.6	7.1	*0.57*	254.8	4.9	*0.21*
Vitamin C, mg/d	No	83.5	1.9		86.8	2.1	
	Yes	85.7	4.3	*0.64*	88.7	2.6	*0.56*
Vitamin D, µg/d	No	2.6	0.08		2.3	0.1	
	Yes	2.5	0.2	*0.6*	2.3	0.1	*0.88*
Vitamin E, mg/d	No	10.7	0.2		10.3	0.2	
	Yes	11.2	0.5	*0.36*	9.9	0.3	*0.21*

Adults following diets have lower intakes of energy, total carbohydrates and complex carbohydrates than others. Furthermore, dieting men also declared lower intake of simple carbohydrates. No significant difference was observed for the vitamins and minerals studied.

Annex 9: Tables summarising the studies

Table 1: Impact of weight-loss diets on bone health - studies on humans

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Observation studies						
May *et al* 1994	942 men and women aged 65-75	Age ≥ 65	Cross-sectional study: relationship between BMD, age and weight	-DEXA: BMD of femur (femoral neck, trochanter, Ward's triangle) and lumbar region (L2-L4)	Reduction in BMD at equivalent rates in men and women, positive correlation with weight	Maintaining weight during aging could partly mitigate age-related bone loss
Pouillès *et al* 1995	44 menopausal women (6 months to 5 years before the study)	Normal weight (BMI 20-25) 3 densitometric measurements at 6-monthly intervals	Longitudinal study: observation of relationship between weight variations and rate of bone loss	-DEXA: BMD of lumbar region (L2-L4) and right femoral neck	Significant correlation (p<0.05) between weight variations and change to vertebral and femoral BMD which persists after adjustment for physical characteristics	Weight changes can influence the process of osteopenia in menopausal women
Cummings *et al* 1995	9516 women aged ≥65	Caucasian No hip fractures	Prospective study on cohort	-DEXA: BMD of calcaneus bone and proximal femur -Examination of weight and weight variations from the age of 25 -Occurrence of fractures	-Risk of hip fracture is doubled if there is a history of maternal hip fracture -Risk is reduced if weight gain after the age of 25 -Low BMD of the calcaneus bone = independent risk factor	Although the individual effect of each is moderate, numerous factors can increase the risk of hip fracture: sedentary lifestyle, sedatives, caffeine, smoking, impaired vision

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Langlois *et al* 1996	3683 women aged ≥67		Prospective study on cohort	Weight at age 50	-Risk of hip fracture is highest in women with low BMI at age 50 -In the thinnest women, a weight loss of 5-10% is associated with an increase in risk -Increased weight ≥10% after age 50 seems to provide protection	Weight history is determining factor in risk of hip fracture
NGuyen *et al* 1998	827 women from the DOES* study	Aged ≥ 60	Prospective study over 2.7 years	-DEXA: BMD of femoral neck	Rate of loss of BMD increases with age, and at a higher rate in sedentary women It is higher in thin women and women losing weight	Age, basal BMD, weight, weight variation, and physical activity are predictors of bone loss
Langlois *et al* 2001	2180 American women from the NHEFS* cohort Aged 50-74	Risk of fracture	Observation over 22 years	-Fractures of the femoral neck	Weight loss ≥ 10% relative to maximum weight is a significant indicator of the risk of fracture in middle-aged or older women	The history of weight change must be taken into account by health professionals
Hui *et al* 2002	130 non-Hispanic pre-menopausal women Aged 31-50	Uterus and ovaries intact	Observation of BMC, BMD and sex hormones at least three times over 1-9 years	-DEXA: body composition, BMC, BMD lumbar region (L2-L4), proximal femur (neck, hips) -Serum: SHBG, LH, FSH, E1, E2, E1 sulphate, progesterone, T, androstenedione, DHEA, DHEA-S	Reduction in BMD in the femoral neck ≈ 0.4%/year, particularly if the level of E2 is low Weight gain associated with lower bone loss	Early detection of suboptimal rates of sex hormones could allow preventive measures to be taken against bone loss, particularly in women losing a lot of weight

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Sirola *et al* 2003	940 Finnish women from the OSTPRE* cohort Aged 48-59	Peri-menopause or post-menopause (with or without HRT)	Observation over 3.8-5.9 years	-DEXA: BMD of the femur (neck, greater trochanter, Ward's triangle) and lumbar region (L2-L4)	Transition at menopause, HRT and weight loss are the major determinants for bone loss (femoral neck and lumbar region)	HRT seems effective in preventing bone loss related to weight loss
Ensrud *et al* 2003	6785 elderly women	Aged ≥ 65, Caucasian, able-bodied and not having had hip surgery	Prospective study of a cohort	4 examinations of weight and the incidence of fractures of the femoral neck every ≈ 5.7 years DEXA: 2 measurements of hip BMD	Higher rate of bone loss in women losing weight (- 0.92%/year, $p< 0.001$), independently of BMI or the intention of losing weight, with risk of fracture 1.8 times higher	Weight loss in elderly women increases the risk of fracture (even if weight loss is intentional in overweight women)
Knocke & Barrett-Connor 2003	469 American men and 745 American women from the Rancho Bernardo* cohort Aged 71 (50-92) Followed over 4 years	Men (aged 54-87): physical exercise (80%), Ca supplement (17%) BMI =26.2 Menopausal women (aged 50-92): physical exercise (73%), Ca supplement (44%) BMI =24.2 HRT = 42%	Observation study (Rancho Bernardo* cohort) Influence of weight loss on BMD, followed over 4 years	-DEXA: BMD of femoral neck	Bone loss in both sexes is 0.5% per year It is 1% in 29% of men and 28% of women. After 4 years this loss doubles the risk of osteoporosis One volunteer out of five loses 1% of body weight per year. These subjects have twice the risk of loss of bone mass	In the elderly, weight loss has a harmful effect on bones
Ensrud *et al* 2005	1342 elderly men (aged ≥ 70) from the MrOS* study	BMD measurements technically adequate at basal state and at 2nd examination	Prospective longitudinal study over 1.8 ± 0.4 years: observation of relationship between weight variations and BMD	-DEXA: body composition, BMC, BMD Hips	Weight loss is associated with bone loss independently of adiposity Variation in BMD/year of +0.1% if weight gain, -0.3% if weight is stable and -1.4% if weight loss	Weight loss, whether intentional or not, leads to bone loss in the hips in elderly men, including in the obese, independently of BMI

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Macdonald *et al* 2005	1064 Scottish women Aged 48.0 ± 1.5 (45-54)	Premenopause or early postmenopause (with or without TSH)	Observation over 5-7 years	-DEXA: BMD of proximal femur (neck, greater trochanter, Ward's triangle) and lumbar region (L2-L4)	Significant relationship between weight variations and BMD (p< 0.003) in pre-, peri- and especially post-menopausal women, except with HRT	Low body weight or weight loss at menopause (without HRT) can aggravate bone loss
Nguyen *et al* 2007	1059 women and 644 men from the DOES* study Aged 70 ± 6	Aged ≥ 60 At least 3 measurements of BMD on inclusion	Observation over 9-14 years	-Mortality -Fractures unrelated to major trauma -DEXA: BMD of femoral neck ≈ every two years	Low basal BMD is an independent predictor of mortality only in women In men and women, rate of BMD loss, weight fluctuations and low basal BMD are also significant predictors of mortality (all causes), independent of age and concomitant diseases	High rate of BMD loss, weight loss and weight variations = independent predictors of mortality after age 60
Forsmo *et al* 2009	1421 woman from the First Nord-Trondelag Health Study	Aged 45 – 60	Longitudinal study over 4.6 years	-Weight changes -DEXA: forearm	-Weight loss over the 15.5 years of the study has a negative effect on bone loss (even if this occurred before the two DEXA measurements)	-Weight loss in middle-aged women is associated with a lasting negative effect on the skeleton (including on non-load-bearing bones)

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Energy restriction						
Nishizawa *et al* 1992	8 very obese women (BMI = 42.7 ± 1.1) Aged 34.3 ± 1.2	Obesity index ≈ 200 BMI = 42.7 ± 1.1 Study of calcium homeostasis	Intervention = gradual lowering of caloric intake (1440-1200-880 Kcal/d), then very low-calorie diet (VLCD, 420 Kcal/d, 800 mg/d Ca and P) 4 weeks	-Total and regional BMC, fat and lean body mass (DPA) -Serum: Ca, P, calcitonin, PTH (RIA), TRAP (Kind-King method), bone Gla protein (BGP, RIA) -Urine: Ca/creatinine, P	Weight loss ≈ 9 kg (especially body fat) Increase in BMC for the head with reduction for the legs (p<0.05) Reduction in P in urine Significant rise in PTH and BGP activities with reduction in TRAP	The treatment of obesity by VLCD alters homeostasis of Ca, resulting in regional variations in BMC Body weight seems to be the main regulator of BMC in the regions concerned (legs)
Compston *et al* 1992	8 women Aged 37-60 22.8 ≤ BMI ≤ 43.2	2 measurements of BMD: 10 days beforehand, during a very low-calorie diet (11 weeks of VLCD), then 23 and 57 weeks later	Intervention: VLCD (405 kcal/d) for 10 weeks	-DEXA: BMC and BMD of entire body	Weight loss ≈ 15.6 kg accompanied by a significant decrease in BMD (p<0.005) Gradual weight regain up to basal values 10 months after stopping the diet and parallel recovery of BMD	Weight loss induced by VLCD is associated with rapid bone loss, with consecutive weight regain accompanied by an increase in BMD
Jensen *et al* 1994	51 obese patients Aged 19-70 67.4-132.4 kg BMI 27-45		Intervention: low-calorie diet, 15 weeks: 2 weeks at 1.9 and 2.4 MJ/d (men and women), then 4.2 and 4.7 MJ/d 800 mg Ca and P, 200 IU Vit D	-BMC of entire body, body composition (DPA)	Significant bone loss after 15 weeks (p<0.0001), the same for body fat Good correlation between the two parameters	Bone loss seems to be a process of physiological normalisation accompanying weight loss in the obese

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Ricci *et al* 1998	Post-menopausal obese women		Intervention: diet moderately restricted in calories, supplemented with Ca (1g/d) or placebo, 6 months	-DEXA: BMD entire body -Serum: OC, PTH, IGF, SHBG, 25(OH)D	Weight loss ≈ 10% and rise in SHBG in both groups (p<0.001) Ca supplement reduces PTH, OC and Dpd significantly (p<0.05)	Ca 1g/d normalises the activity of the Ca-PTH axis and the rate of bone turnover in menopausal women during voluntary energy restriction
Van Loan *et al* 1998	14 moderately overweight women Aged 25-42	Weight-loss programme over 15 weeks 39-54% body fat	Study in 3 phases: -Baseline = 3 weeks of stabilisation (studying energy needs, 5 km of walking per day) -Intervention over 15 weeks (50% reduction in energy intake) -Weight maintained for 3 weeks	-Lean body mass and % body fat (TOBEC = total body electrical conductivity) -DEXA: BMC, BMD, bone surface, body composition	Loss of weight and body fat during the restriction (-17 and -25%, (p<0.0001)) Significant reduction in BMD, but not in BMC nor in bone surface	Variation of BMC and bone surface in opposite directions, resulting in a drop in BMD = artefact (influence of body composition on this type of measurement)
Ryan *et al* 1998	41 menopausal women in good health Aged 52-72	Menopausal for at least 2 years, without either medication or HRT Stable weight and not having participated in a regular exercise programme in the previous 6 months	Intervention = energyrestriction of 250-350 kcal/d to induce weight loss of 0.25-0.5 kg/week (WL) (30% lipids), with or without aerobics (WL+AEx), 6 months	-DEXA: body composition, BMC, BMD femur (neck, greater trochanter, Ward's triangle) and lumbar region (L2-L4)	Weight loss associated with a significant reduction in femoral BMD in WL group, but not in WL+AEx	It seems that practising aerobics during weight-loss programmes can reduce the risk of bone loss in menopausal women not following HRT

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Gossain *et al* 1999	11 obese, Caucasian women Aged 22-78 BMI ≥ 29	Intention to lose weight	Intervention over 1 year: VLCD for 12 weeks (protein supplement, 800 kcal/d), then 6 weeks of normal meals (800 kcal/d), then 6 weeks of customised meals (1000 kcal/d), then 24 weeks of customised meals for weight maintenance Ca intake maintained at 1g/d	-DEXA: BMD of entire body, hips and lumbar region -Urine: OH-Proline (HPLC), Ca, PO_4, bALP	Significant weight loss after 6 months, maintained over 12 months Significant reduction (p<0.05) of total BMD at 12 months (after 6 months for the hip)	Modest reduction in BMD = direct consequence of weight loss
Vestergaard *et al* 2000	20 obese women 33 ≤ BMI ≤ 45 Aged 21-48	18 < age < 50 Length of study: 8 weeks	Double-blind study = VLCD 740 kcal/d, 4 weeks, followed by 1200 kcal/d, 4 weeks, with control of intake of Ca and vitD 2 groups: placebo or Growth Hormone (GH) treatment	-DEXA: body composition, BMC, BMD entire body and lumbar region (L2-L4) -Serum: IGF-1 (TR-IFMA), PINP and PIIINP, OC (RIA), BAP (precipitation/lectin) -Urine: DPD (chemiluminescence)	Weight loss of 5.5% accompanied by a reduction in BMC proportionate to the reduction in bone surface Treatment by GH increases the markers for bone turnover, without modifying BMC	Since 89% of changes observed for BMC can be explained by variations in bone surface without alteration of the circulating markers, the reduction observed in BMC is no doubt an artefact
Zanker & Swaine 2000	8 men Aged 25 ± 6	Men trained for physical endurance Test: running on treadmill (60 mn)	Intervention 3 days of diet during 3 periods of testing = subjected or not to energy restriction (50% of needs)	-Serum: PINP (ELISA), OC, IGF-1 (RIA) -Urine: Dpd, NTx (ELISA)	Reduction in serum PINP (-15%, p= 0.008) and IGF-1 (-17%, p= 0.007) in response to exercise, only in the case of simultaneous energy restriction Good correlation between IGF1 and PINP	In long-distance runners, repeated training periods do not affect bone remodelling, except in the case of simultaneous energy restriction

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Jensen *et al* 2001	62 obese women BMI 25.2-51.6	No HRT Motivation to lose weight	Randomised intervention: 3 months ≤ 4.2 MJ/d (800 mg Ca and P, 200 IU Vit D) With or without Ca supplement 1g/d, then 3 months without prescription	-DEXA: body composition, BMC entire body, lumbar and femoral regions -Serum: 25(OH)D, $1,25(OH)_2D$, OC (ELISA), PTH (RIA) -Urine: Ca, creatinine, pyridinoline and DPD (HPLC, fluorescence detection)	Significant reduction in total and lumbar BMC in the group not supplemented in Ca Reduction in PTH in the supplemented group	Moderate weight loss is accompanied by generalised bone loss which can be partially inhibited by high levels of Ca intake Ca should be supplemented beyond recommended levels during weight loss diets
Shapses *et al* 2001	38 pre-menopausal obese women Age = 42.1 ± 6.2 BMI = 35.0 ± 3.9	Weight stable for at least 3 months	Double-blind randomised study: low-calorie diet supplemented in Ca (1g/d Ca-citrate) or not, over 6 months	-DEXA: body composition, BMC and BMD of entire body, and lumbar region -Serum: 25(OH)D, PTH, SHBG (RIA) -Urine: pyridinoline and DPD (HPLC)	Energy restriction induces weight loss ≥ 7%, with no effect on bone parameters Supplementation in Ca tends to raise lumbar BMD by 1.7% (p=0.05)	Unlike results obtained on menopausal women, low intake of Ca during moderate weight loss does not lead to bone loss
Ricci *et al* 2001	27 menopausal women Aged 55.9 ± 7.9 BMI 33.0 ± 3.8	Menopausal for at least 3 years, without HRT 28 ≤ BMI ≤ 39 Weight stable for at least 3 months	Intervention over 6 months, 2 groups: -Reduction in food intake according to a weight loss programme (WL), -Controls: normal food intake (WM)	-DEXA: body composition, BMC and BMD of entire body -Serum: OC, 25(OH)D, leptin, estrone, PTH, SHBG (RIA) -Urine: pyridinoline and DPD (HPLC, fluorescence detection), Ca	Weight loss ≈ 10%, body fat ≈ 18%, total BMD 1.2% in WL group (p<0.001 *vs* basal) Rate of bone turnover increased in WL group (p<0.05 vs WM) Increase in SHBG (p<0.001 *vs* basal) and PTH in WL, with reduction in estrone rates	In obese menopausal women, moderate energy restriction increases bone turnover, which could be partially regulated by serum estrone and PTH

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Paakkunaien *et al* 2002	139 Finnish children from the STRIP* intervention project Aged 6.5-9		Cross-sectional study of a 6-year randomised intervention: nutritional advice designed to reduce the fat content to 30% of caloric intake, in comparison with a normal diet	-Measurement of the properties of the calcaneus bone using ultrasound	No modification to Ca intake related to the diet No modification to bone health	Cross-sectional study with a single measurement of bone health
Bowen *et al* 2004	50 overweight adults Aged 20-65	27 ≤ BMI ≤ 40	Study of a randomised intervention =12 weeks energy restriction (5.5 MJ/d), then 4 weeks of isocaloric intake 2 groups following protein-rich diets (34% of energy): DP = dairy proteins + 2400 mg/d Ca MP = mixed proteins + 500 mg/d Ca	-DEXA: BMD entire body -Serum: OC (immunometric assay) -Urine: 24h DPD and Pyr (HPLC), Ca	Energy restriction induces weight loss of 10% (p<0.01) and a decrease in urinary excretion of Ca (p<0.01), irrespective of diet DPD and OC higher with MP (p=0.008 and p=0.001, *vs* DP) No modification of BMD	Weight loss is the major determining factor for the increase in bone resorption, with high-protein diets causing a reduction in urinary excretion of Ca Ca intake in high-protein diets seems to protect against weight-loss-related bone loss

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Daly *et al* 2005	36 sedentary overweight diabetes patients Aged 60-80	Established Type II Diabetes treated nutritionally and/or medicinally 27 ≤ BMI ≤ 40	Randomised study over 1 year, intervention in 2 phases: 1) = 2 groups subjected to a moderate weight-loss diet for 6 months, with or without gymnastics training 2) = 6 months training at home, without intake requirements for both groups	-Serum: HbA_{1c}, SHBG, insulin, testosterone, estradiol, IGF-1 (RIA), albumin, ALP, creatinine, Ca, P -Urine: 24h Ca -DEXA: BMC and BMD entire body, femur (neck) and lumbar region (L2-L4), bone surface, lean and fat body mass	Phase 1: reduction in both weight and body fat in both groups (p<0.01), with increase in lean mass only with exercise (p<0.05) BMC and BMD of entire body not affected in subjects who underwent training, but reduced in the absence of exercise (p<0.05) Phase 2: increase in weight and body fat in both groups with no significant effect on lean body mass or bone	In overweight Type II diabetics, a moderate weight-loss diet can be combined with a gradual increase in the intensity of sports training, in order to optimise the effects on body composition with no negative effect on bone health
Hinton *et al* 2006	6 men and 13 women (BMI > 27) Aged 18-44	Class I obesity 6-week programme of energy restriction	Intervention over 6 weeks: energy restriction of 3140kJ/d + exercise (aerobics 1675 kJ/d) to obtain weight loss of 5%	- Body composition (skinfold measured at 3 points) -Serum: RANKL, OC, OPG, bALP, CTX, IGF-1, leptin, cortisol (ELISA)	Weight loss of 5%, reduction in BMI, % of body fat and serum leptin (p<0.05) Significant rise of serum OC and bALP, without modification of resorption markers	The practice of aerobics favourably influences bone remodelling during a weight-loss diet

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Villareal *et al* 2006	18 men and 30 women aged 57 ± 3, non-obese (BMI = 27± 2) Without HRT for the women	Menopausal women (3 to 20 years of menopause) - Controls (good health practices) - Energy restriction (16% for the first 3 months, 20% the following months) - Physical exercise (inducing equivalent caloric deficiency) Comparison of these two weight loss strategies for bone mass BMD measured at 1, 3, 6, 9 and 12 months and bone markers at 1, 6 and 12 months	Intervention, 3 groups - Controls in good health (n =10 receiving 162 mg/d of Ca and 400 IU Vit D) Randomised study over 1 year with energy restriction of 16% for 3 months, then 20% for 9 months (CR, n=19) and/or physical exercise (EX, n=19)	-DEXA: BMD of entire body, lumbar region (L2-L4) and femoral neck -Serum: BALP, OC and CTX1 by ELISA Estradiol and leptin by RIA -Physical activity by questionnaire (Stanford)	The treatment induces a reduction in body weight of 8 to 10% in both groups (about 7kg); no variation among controls. Energy restriction leads to a 2% reduction in BMD at the femoral neck and lumbar region due to increased bone turnover (increase in CTX1). Body weight is correlated with BMD Physical exercise did not modify the BMD but increased bone turnover	Physical exercise could be an alternative in the event of energy restriction to preserve BMD

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Riedt *et al* 2007	44 overweight premenopausal women (BMI = 27.7 ± 2.1) Aged 38 ± 6.4	Weight stable for at least 3 months	Intervention = restriction in energy intake (WL) with normal (1g/d) or high (1.8g/d) Ca intake Randomised double-blind study, over 6 months	-DEXA: BMC, BMD femur (neck, greater trochanter, Ward's triangle), radius and lumbar region -Serum: OC, 25(OH)D, $1,25(OH)_2D$, estradiol, estrone, cortisol (RIA), NTx (ELISA) -Urine: 24h Ca, creatinine, pyridinoline and DPD (HPLC, fluorescence detection) - Absorption of Ca (^{44}Ca detected by ICP-MS)	Initial weight reduced by ≈ 7 kg with no significant effect on BMD, bone turnover or the Ca-PTH axis, irrespective of the level of Ca ingested	In overweight premenopausal women, weight loss does not lead to bone loss if the level of Ca ingested is sufficient
Wagner *et al* 2007	58 women aged 19 to 53 (36 ± 2.2 for the controls), -Obese (BMI from 26 to 41) -Controls (BMI = 32.4 ± 1.5)	Pre-menopausal, energy restriction (500 kcal), Ca intake (750 mg/d) and physical exercise (3 times/week) Treatment over 12 weeks	Intervention Randomised study with supplementation in Ca (800mg/d) in capsule form (calcium lactate or calcium phosphate) or semi-skimmed milk 4 groups -Control: n=13 (750mg/d) -Calcium lactate: n=12 -Calcium phosphate: n=16 -Semi-skimmed milk: n=17	-Body composition by bioelectrical impedance analysis -Urine: BALP and peptide alpha 1 in urinary collagen by ELISA Urinary creatinine by colorimetry	Ca intake in controls is 788mg/d and about 1600mg/d in the 3 other groups Weight loss is similar in all groups (5kg) The % of fat is significantly reduced but less with milk Increase in BALP Calcium lactate, however, causes an increase in resorption marker	In obese premenopausal women, supplementation in Ca does not exacerbate loss of body weight or body fat Only Ca in lactate form induces a reduction in a resorption marker, a beneficial effect in the context of a weight-loss programme

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Lucey *et al* 2008	276 overweight young adults (BMI 27.5-32.5) Aged 20-40	Weight stable for at least 3 months	Intervention over 8 weeks (30% restriction of calorie intake) with or without seafood produce 4 groups (control, cod, salmon, fish oil, i.e. different levels of n-3)	-Serum: OC, bALP, CTx, 25(OH)D, PTH (ELISA) -Urine: NTx (ELISA)	Weight loss > 5kg in all 4 groups Increase in urinary NTx and CTx and decrease in OC (p<0.05), irrespective of the diet Rise in serum 25(OH)D associated with an increase in salmon consumption	Energy restriction of 30% has negative effect on bone turnover biomarkers in overweight young adults
Redman *et al* 2008	46 overweight young adults		Randomised study of 4 groups: control, 25% energy restriction with or without exercise, low-calorie diet (890 kcal/d), 6 months	-DEXA: body composition, total and right hip BMC and , BMD -Serum: CTx, NTx, OC, bALP	Weight loss > 10% in the 3 restricted groups without repercussion on BMD, but increase in serum CTx The low-calorie diet leads to the highest rise in CTx levels (74% vs the controls) and NTx Reduction in bALP only if 25% energy restriction	6 months of moderate energy restriction, with or without exercise, with Ca intake preserved, induces significant modifications in body composition without significant effect on bone health in young adults
Villareal *et al* 2008	27 obese elderly adults (men and women) Aged 70 ± 5	Aged ≥ 65 BMI ≥ 30 Sedentary Weight stable (± 2kg/year)	Randomised clinical study over 1 year 2 groups: -Control without intervention, -Low calorie diet (500-750 kcal/d) + exercise in order to lose ≥ 1.5 kg/week	-DEXA: body composition, BMC, BMD Lumbar region (L2-L4), proximal femur and entire body (basal measurement, 6 and 12 months) -Serum: CTX, OC, BAP (ELISA), estradiol, leptin, IGF-1, cortisol, 25(OH)D, $1,25(OH)_2D$ (RIA), PTH (chemiluminescence)	Weight loss in the treated group (-10 ± 2%, p<0.001), with a significant reduction in BMD, leptin, E2 and a rise in circulating levels of OC, CTX (p<0.05)	Weight loss following a diet in obese elderly adults increases bone turnover and induces a reduction in BMD; there is no effect from exercise

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Stettler *et al* 2008	62 obese adolescents subjected to an intensive diet 66 overweight adolescents as controls Aged 9-17	32 ≤ BMI ≤ 44 Treatment with sibutramine for 6 months, then placebo for 6 months	Observation study on bone accretion in obese adolescents subjected to a diet (1200-1500 kcal/d) for 12 months	-DEXA: body composition, bone surface, BMC entire body, BMD lumbar region (L1-L4), hip	Basal BMC higher in the obese group Weight loss accompanied by an increase in vertebral BMC and reduction in BMC in limbs (but no effect on total BMC after adjustment for height) Correlation between BMC and change in lean body mass	Obese adolescents have a BMC higher than normal Unlike in adults, the BMC continues to increase during weight loss
McTiernan *et al* 2009	48,835 menopausal women Aged 50-79	Women's Health Initiative (WHI) Dietary Modification Trial	Randomised intervention ≈ 8 years Reduction in fats to 20% of caloric intake, fruit and vegetables ≥ 5 times/d, cereals ≥ 6 times/d (for 40% of the women, the remaining 60% continuing with their normal diet)	-DEXA: BMD entire body, hips and lumber region (L2-L4)	Number of falls ≥ 2 significantly reduced in the intervention group (p<0.01), reduction in BMD at the hips (p=0.003) without any increase in the risk of fracture over the following 8 years	A low-fat diet rich in vegetable produce moderately reduces the risk of multiple falls It causes a slight reduction in BMD, without modifying the risk of fractures
Rector *et al* 2009	36 overweight or Class I obese premenopausal women (BMI 25.0-29.9 or 30-34.9) Aged 18-35	Weight stable for at least the last three months (variation < 3%) Sedentary (structured activity < 60 min/week)	Weight-loss programme of 5% in 6 weeks 3 groups: energy restriction only (1000-1200 kcal/d), with or without weight-bearing exercise	-Serum OC, CTX, BAP, IGF-1, fT3, cortisol, leptin (ELISA) 25(OH)D (RIA), iPTH (chemiluminescence)	Weight loss ≈ 5% in all 3 groups, accompanied by an increase in serum OC and CTX (p<0.05), with no variation of BAP No effect resulting from the exercise	Weight loss is associated with an increase in bone remodelling, irrespective of the intervention programme in terms of physical exercise

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Hinton *et al* 2010	113 obese adults Aged 19-50 BMI 30-40	Obese and sedentary Programme restricting food intake Programme of moderate exercise	Randomised clinical study: 12 weeks of a diet moderately restricted in calories (1200 kcal/d) with the goal of losing 10% of initial weight, then separation into 2 groups: with ≤ 1 dairy product/day or ≥ 3 (recommended quantity), stabilisation of weight at 24 weeks	-DEXA: total BMC and BMD -Plasma: glucose, insulin, Ca, 25(OH)D, $1,25(OH)_2D$, PTH (measured in an independent laboratory)	Weight loss leads to significantly higher total BMC in the women, and in BMD in the men, with reduced PTH in both cases No difference between the 2 groups during the stabilisation phase, but reduction in total BMC and BMD in the men	Moderate weight loss does not lead to bone loss, even though the recommended Ca intake is <1g The number of dairy products consumed in the stabilisation phase does not influence BMC
Low-fat diets						
Salamone *et al* 1999	236 pre-menopausal women Aged 44-50	White, no HRT	Randomised intervention study: reduction in intake in fats and increase in physical activity in order to induce moderate weight loss or avoid gaining weight over 18 months	-DEXA: BMD of lumbar region (L1-L4), hip (femoral neck, trochanter and inter-trochanteric region) -Serum: OC (chemiluminescence) Urine NTx (ELISA)	Weight loss after 18 months of intervention (-3.2 ± 4.7 kg, $p<0.001$) Annual reduction in BMD twice as rapid in the intervention group as in the control group concerning hips ($p<0.015$), but not significant for lumbar region	Modification of eating practices with a view to losing weight leads to a faster reduction in BMD than if weight remained stable An increase in physical activity attenuates this effect on the lumbar region, but not at the hips
Avenell *et al* 1994	16 overweight menopausal women 46 controls of normal weight, chosen for their age and their age at menopause	Menopause ≥ 4 years BMI > 27	Case study Intervention on the overweight women = low-fat diet (1200 kcal/d, 20% of energy) and rich in fibres (28 g/d), 330 mg/d of Ca, 6 months, in order to lose 20% of the excess weight, with return to starting weight after 6 months	-DEXA: BMD of lumbar region (L2-L4) and femoral neck	Weight loss of 2.8 kg after 6 months Reduction in vertebral BMD faster in the treated grouped ($p<0.05$), NS for femoral neck Bone loss not reversed by weight regain 6 months later	Repeated cycles of weight-loss diets rich in fibres followed by weight regain can increase the risk of vertebral osteoporosis

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Pritchard *et al* 1996	66 overweight men Aged 43.4 ± 5.7 years BMI 29.0 ± 2.6	Overweight (110-130%, BMI 26-35)	Randomised intervention study over 12 months 3 groups: -Control – weight maintenance, -Low-fat diet (20-22% of energy intake), -Aerobic exercise	-DEXA: body composition, bone surface, BMC, BMD entire body and lumbar region (L2-L4)	Weight loss of 6.4 kg in the diet group, accompanied by reduced BMC and BMD (1.4 and 1.5%) Loss of 2.6 kg in the exercise group with no modification to bone parameters	The variations in BMC are correlated with the loss of body fat in both intervention groups
High-protein diets						
Thorpe *et al* 2008	130 overweight, middle-aged American adults (including 59 men) Aged 30-65	BMI > 26 Weight < 140 kg	Randomised multicentre study over 12 months 2 groups: high-protein diet (30% of energy intake) + 3 dairy products/day, or high-carbohydrate diet (55%) + 2 dairy products, 4 months then maintaining the weight attained for 8 months 6276 Kj/d for the women 7113 Kj/d for the men	-DEXA: BMD for entire body, lumbar region (L1-L4), hips -Urine: 24h Ca	Weight loss in both groups, with strongest reduction in BMD with the high-carbohydrate diet (p<0.01) Intake and urinary excretion of Ca higher with the high-protein diet	A protein-rich diet + 3 dairy products reduces energy intake and attenuates bone loss related to weight loss and during the 8 months of stabilisation

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Skov *et al* 2002	65 women aged 18 to 56 with BMI of 25 to 29.9 or BMI>30 (obese)	Overweight or obese women aged between 18 and 56 The subjects retained their lifestyle habits during the study (physical exercise, smoking, etc.)	Intervention study 3 groups -High-protein diet (102.5g/d, fat=76.9g/d, n=25) -Low-protein diet (70.5g/d, fat=72.9, n=25) -Controls (85.7g/d, fat=99g/d, n=15) over 6 months	-DEXA: BMI, lumbar BMC and BMD	In the high-protein group, weight loss was 8.9kg with a reduction in BMC of 4% In the low-protein group, weight loss was 5.1kg and BMC dropped by 3%	A high-protein diet does not exacerbate the demineralisation induced by weight loss
Harrington *et al* 2004 (EJCN)	18 menopausal women aged from 49 to 60 (54.5) Stratification on the basis of HRT	Menopausal women, menopausal for 1 to 10 years, in 2 groups HRT (n=8) no HRT (n=10)	Randomised crossover study with a calciuric diet: High-protein (90g/d) and high-sodium diet (180mmol/d) or a diet with a moderate protein intake (70g/d) and low in sodium (65 mmol/d) over 1 month	-Serum: OC, BALP, NTX and PTH by ELISA, 25(OH)D and $1,25(OH)_2D$ by HPLC Ca, Na and K by AAS Urinary nitrogen by Kjeldah -Urine: urinary creatinine by colorimetry	The hypercalciuric diet increased urinary excretion of Na, nitrogen and Ca in both groups (HRT and no-HRT) It increased the level of NTX in the no-HRT group but not in the HRT group	A hypercalciuric diet increases bone resorption in menopausal women not taking HRT, with no observed effect on volunteers taking HRT
Harrington *et al* 2004 (BJN)	24 menopausal women aged 50 to 67 with BMI = 23	Post-menopausal women (from 1 to 12 years) Stratification into 2 groups on the VDR genotype: *f*+VDR and *f*-VDR Ca intake of 800mg/d	Randomised crossover study with a calciuric diet: High-protein (90g/d) and high-sodium diet (180mmol/d) or a diet with a moderate protein intake (70g/d) and low in sodium (65 mmol/d) over 1 month Followed for 1 and 2 months	-Serum: OC, BALP, NTX and PTH by ELISA, 25(OH)D and $1,25(OH)_2D$ by HPLC Ca, Na and K by AAS Urinary nitrogen by Kjeldah -Urine: urinary creatinine by colorimetry	The hypercalciuric diet increased urinary excretion of Na, nitrogen and K, Ca and NTX (25.6%) compared with the base diet, with no effect on levels of PTH, OC, BALP, 25(OH)D and $1,25(OH)_2D$ in *f*+VDR No effect observed in the *f*-VDR group	In menopausal women, the VDR genotype can modulate the impact of a hypercalciuric diet on bone resorption,

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Various diets						
Chao *et al* 2000	67 American women from the TONE* cohort Aged 65.9 ± 5 Obese (BMI>27.3 (30.9 ± 2.9))	Post-menopause, with or without HRT, with or without diuretics, after withdrawal of an anti-hypertensive drug	Intervention (TONE) Randomised study over 1 year with restricted sodium intake and weight loss (physical exercise) Monitored at 6 and 12 months	-DEXA: BMD of entire body, BMD of lumbar region (L2-L4) and BMD of femoral neck Serum: OC by RIA BALP and NTX by ELISA -Urinary creatinine by colorimetry	Weight loss of 19% after 6 months and 24% after 12 months, associated with a reduction in entire body BMD and an increase in OC with the control measurements as covariable	In elderly, obese menopausal women, weight loss is harmful for bone mass. It must be accompanied with recommendations for reducing bone loss (physical exercise, etc.)
Carter *et al* 2006	22 women 8 men Aged ≈ 40 (15 subjects, 15 controls)	BMI > 26	Intervention 3 months, low-carbohydrate test diet (20 g/d the first month and 40 g/d the second and third months)	-Serum: BSAP (EIA) Urine NTx (chemiluminescence)	Significant weight loss (p= 0.0008) induced by the low-carbohydrate diet No significant effect on bone turnover markers	Low-carbohydrate diets are suspected of altering bone health in animals, but no effect was noted in this study
Bergqvist *et al* 2008	25 prepubescent epileptic children (9 boys and 16 girls) Aged 7.3 ± 1.9	Untreatable Epilepsy Steroid medication stopped 3 months before the study	Randomised longitudinal study in 2 phases over 15 months: 3 months of ketogenic diet (high-fat and low-carbohydrate) adapted to maintain growth, followed by 12 months of energy restriction (maintaining the weight achieved)	-Serum: 25(OH)D, $1,25(OH)_2D$, PTH (RIA), Ca, P, Mg -DEXA: BMC of entire body and lumbar region (L1-L4) Calculation of z scores (age, height) to correct the effects of growth	Suboptimal growth, serum 25(OH)D and bone status on inclusion (also Ca and Vit D intake) Gradual reduction in total and lumbar BMC during the study, despite supplementation in Ca and Vit D	A ketogenic diet (fats/(carb+prot)= 4) reduces the predisposition to attacks in cases untreatable by anti-epileptics (20-30% of cases), but with harmful effects, particularly on bones

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Surgical interventions						
Guney *et al* 2003	16 patients (14 women and 2 men) suffering from morbid obesity undergoing a vertical gastroplasty (VGB) 65 medically treated cases of obesity	BMI ≥ 40	Study of surgical (VBG) or nutritional intervention (LCD, 1200 kcal/d) Observation before and 12 months after the start of the treatment	-DEXA: bone surface, BMC, BMD of lumbar region (L2-L4), hip (femoral neck, trochanter, inter-trochanter region, Ward's triangle) -Serum: E2, testosterone (RIA), OC, BAP, PTH (ELISA), -Urine: DPD (ELISA)	Greater weight loss with VGB, accompanied by bone loss in the hip (p<0.05) No variation in calcium excretion nor in PTH for either treatment, but a rise in the markers of bone turnover	Weight loss induces bone loss, in either treatment Bone loss is independent of the method of weight loss
Pereira *et al* 2007	39 premenopausal women (11 non-obese, 12 obese, 16 obese having undergone bariatric surgery)	Bariatric surgery carried out at least 3 months before the study BMI ≤ 30 for the non-obese and ≥ 40 for the obese	Prospective study, monitored every 3 months, for a year	-DEXA: BMD of lumbar region (L2-L4), femoral neck, distal forearm -Serum: Ca, Mg, P, PTH (chemiluminescence), IGF-1, OC, 25(OH)D (RIA), BAP -Urine: DPD (EIA)	Significant reduction in IGF-1 for the operated cases, and reduction in BMD in lumbar region, femoral neck and forearm	The weight loss induced by bariatric surgery leads to bone loss, associated with a drop in IGF-1, including for non-weight-bearing bones
Fleisher *et al* 2008	23 obese adults having undergone bariatric surgery (RYGB) Aged 20-64	Morbid obesity (BMI = 47 ± 1)	Prospective longitudinal study before (baseline) and 3, 6 and 12 months after RYGB Supplements in Ca-citrate/vitD (1500 mg/600 IU for those aged 19-50 and 1800mg/800 IU after 50)	-DEXA: BMD of lumbar region (L1-L4), hip, femoral neck, forearm -Serum: 25(OH)D, $1,25(OH)_2D$, PTH (RIA), OC, Ca -Urine: NTx	Loss of 45 ± 2 kg 1 year after the operation (p<0.001), early rise in PTH (p<0,001) and reduction in urinary excretion of Ca (p<0.01), despite doubling the intake Reduction in BMD (p<0.005), with an increase in the OC and NTx markers (p<0.01)	Malabsorption of Ca and Vit D apparent after bariatric surgery, despite an increase in intake Reduction in BMD at the hips strongly associated with weight loss

Authors	Subjects	Conditions	Protocol	Markers	Results	Observations
Balsa *et al* 2009	63 women who had undergone a biliopancreatic diversion (BPD), 49 of whom suffered from hyperparathyroidism 34 controls with morbid obesity	BPD carried out at least 2 years before the study	Prospective study Supplements of Ca in the form of calcifediol (2g/6160 IU for those operated)	DEXA: BMD of lumbar region (L1-L4), hip -Serum: 25(OH)D, $1,25(OH)_2D$ (ELISA), PTH, OC and β-CTx (electrochemiluminescence)	BPD increases the circulating levels of PTH, OC and β-CTx Negative correlation between levels of OC and β-CTx and lumbar BMD (p=0.002 and p=0.02)	Chronic hyperparathyroidism and weight loss determine the rate of bone turnover and the reduction in BMD in patients having undergone a BPD
Tsiftsis *et al* 2009	52 premenopausal women treated for morbid obesity by long-limb biliopancreatic diversion (BPD-LL)	Randomised in 2 groups	Randomised intervention: high-protein diet enriched in Ca 2 groups -Supplementation in Fe (80 mg), Ca (100 mg) and Vit D (200 IU) -Ditto + 2 g Ca	-DEXA: BMC, BMD of lumbar region (L1-L4) -Serum: 25(OH)D (immuno-luminometry), PTH, OC, PINP, PIIINP (RIA), CTx (chemiluminescence)	Loss ≈ 55 kg, 1 year after the operation, with a significant increase in bone turnover markers and reduction in BMD in both groups, irrespective of calcium intake and levels of PTH	No hyperparathyroidism consecutive to malabsorption of Ca and Vit D => bone loss related to weight loss Bone loss corresponds to an adaptation to the reduction in load-bearing and not to malabsorption or hyperparathyroidism

**OSTPRE = prospective Kuopio Osteoporosis Risk Factor and Prevention Study cohort*
NHEFS = Epidemiologic Follow-up Study of the first National Health and Nutrition Examination Survey
STRIP = Special Turku Coronary Risk Factor Intervention Project for Children
MrOS = Osteoporotic Fractures in Men Study
DOES = Dubbo Osteoporosis Epidemiology Study

Table 2: Impact of weight-loss diets on bone health - studies in animals

Authors	Model	Protocol	Markers	Results	Observations
Low-calorie diets					
Talbott *et al* 2001	Female Sprague-Dawley rats aged 4 months (n=12) or 12 months (n=16) receiving 0.52% of Ca Diet with energy restriction for 9 weeks	4 groups -40% energy restriction diet (ER group) *vs* control *ad libitum* diet, at 4 and 12 months The ER group received 0.86% of Ca	BMD by DEXA PYD, DPD Hydroxyproline and proteoglycans by HPLC Insulin and estradiol by RIA Biomechanical properties by 3-point INSTRON test Ca by AAS	Energy restriction reduces bodyweight by 15%, and reduces femoral BMD by 32% in all groups Energy restriction reduces BMD in the tibia and the humerus, as well as biomechanical properties in rats aged 12 months, and levels of insulin and leptin	A energy restriction of 40% reduces bone mass and skeletal biomechanical properties
Lane *et al* 2001	Female macaque monkeys Aged 7-27 (n=40) in peri- or post-menopause receiving 12.2g/kg of ingested diet of Ca and 3.5 IU/d of Vit D	Cross-sectional study - Energy restriction diet (ER, n=19) at 30% *vs* control diet (CONT, n=21) over 6 years The ER group received 1.3 vs 1.8 g/d of Ca for the CONT group and 364 vs 491 IU/d of Vit D	BMD and BMC by DEXA DPD by HPLC OC, PTH, 25(OH)D, estradiol, progesterone, FSH, LH by RIA Ca and creatinine by colorimetry	Energy restriction reduces bodyweight by about 15% and reduces body fat mass by 45%, without modifying BMD, BMC and bone metabolism parameters Good correlation (P<0.04) between bodyweight and BMC Energy restriction does not modify the parameters of hormonal status (estradiol, progesterone, FSH, LH)	Energy restriction of 30% does not modify bone or hormonal parameters, whether in peri- or post-menopause

Talbott *et al* 1998	Female Sprague-Dawley rats aged 3 months (n=22) or 10 months (n=44) receiving 0.52% Ca and 0.35% of P (Ca/P=1.5) Diet with energy restriction and supplementation in Ca over 9 weeks	4 groups - Energy restriction diet (ER) of 40% *vs* control diet supplemented or not in Ca -Control (CNTL =0.52%Ca, 68% E) -Control deficient in Ca (CR =0.10% Ca, 68% E) -Restriction E (ER=0.86% Ca, 46% E) -Restriction E + deficient in Ca (CER =0.17%, Ca, 46% E) BMD measured at start and at sacrifice (9 weeks)	BMD by DEXA OC by RIA Urinary excretion of H3-tetracycline (resorption)	Energy restriction reduces bodyweight by 5 to 21%, and increases bone formation by 10 to 20% (OC) in all groups of the same age -In rats aged 3 months, BMD increases in all groups; at sacrifice, it is reduced in the CR group *vs* CNTL -In rats aged 10 months, reduced BMD at sacrifice in CR, ER and CER *vs* CNTL	Irrespective of age (3-10 months), Ca or energy restriction (40%) increases bone turnover Only a restriction of Ca reduces total BMD In rats aged 10 months, only energy restriction has a negative effect on BMD

Hawkins *et al* 2010	Female Sprague-Dawley rats aged 2 months rendered obese (47% fat) or not (16% fat) up to 6 months receiving 0.50% Ca and 0.30% P (Ca/P = 1.66) Energy restriction diet for 10 weeks	Calorie restricted diet (ER, n=18) of 40% *vs* control AIN-93 diet (CTL, n=18) *ad libitum* 4 groups -Non-obese, control (lean CTL) -Obese, control (obese CTL) -Non-obese, ER 40% (lean ER) -Obese, ER 40% (obese ER) Measured at 0 and after 10 weeks	BMD by DEXA and CT PTH, 25(OH)D, Estradiol by RIA PYD, DPD by HPLC Hydroxyproline and proteoglycans by ELISA	Energy restriction reduces bodyweight by about 28% in the obese vs 22% in the non-obese. Associated with an increase in 25(OH)D and a reduction in BMD in the proximal femur and femoral neck and in trabecular volume Energy restriction reduces estradiol levels in non-obese rats The level of PTH diminishes between 0 and 10 weeks in the CTL group (lean and obese)	Energy restriction of 40% reduces bone density in non-obese rats This effect could be due to the low levels of estradiol and 25(OH) observed
Bielohuby *et al* 2010	Growing rats aged 1 month, rendered obese (66% or 99.4% fat) or not (9% fat) for 1 month receiving 0.60 to 1% Ca and 0.4 to 1% P (Ca/P = 1.05 to 1.6) Restricted carbohydrate diet	Restricted carbohydrate diet (LC) at 1% *vs* control diet (58%) 3 groups -Control (CH = 9% Fat, 33% Prot, 58% Carb) -Control restricted in carbohydrates (LC-HF1 = 66% Fat, 33% Prot, 1% Carb) - Control restricted in carbohydrates (LC-HF1 = 94.5% Fat, 42% Prot, 1.3% Carb)	BMD by pQCT and CT Biomechanical properties by 3-point ZWICK test Leptin, IGF1, NTX and CTX by ELISA Runx2, osterix and C/EBPbeta by RT-qPCR in bone marrow cells Adipocytes in bone marrow by microscopy	In obese rats, carbohydrate restriction increases visceral and bone marrow fat levels by increasing leptinemia and reducing the level of IGF1 It reduces the size of the body by reducing the BMD of the tibia, without modifying the biomechanical properties It reduces the NTX without modifying the CTX It reduces the osteoblastogenesis transcription factors by 80%	In obese rats, carbohydrate restriction slows longitudinal growth and reduces BMD by reducing the level of IGF1, which could be due to the low level of differentiation of the mesenchymal cells

Douchi *et al* 1996	Female rats aged 2 months Restricted diet with oestrogen treatment for 1 month followed by 4 and 5 months *ad libitum*	4 groups -D= Control, without OVX - C= Ovariectomy - B= Restricted diet + oestrogens - A= Restricted diet	Vaginal smears BMD	15 days after the start of the restriction, the rats are in diestrus and return to a normal cycle 4 days after the start of ad libitum At 3 months, the restricted diet (groups A and B) leads to a reduction in bodyweight and BMD compared to the other groups At 20 months, BMD remains lower than for the controls At 16 and 20 months, the OVX rats still have a BMD lower than the controls	Weight loss has a stronger effect on BMD than that induced by a clinical deficiency in oestrogen
High-protein diets					
Mardon *et al* 2008	Male Wistar rats aged 2 months receiving 0.25% Ca and 0.2% P (Ca/P = 1.25) Diet with a variable level of wheat proteins for 7, 15 and 19 months	4 groups (n=30) - Isoprotein diet (NP = 13%) - High-protein diet (HP = 26%) - Isoprotein diet, supplemented with potassium citrate (NPKcitr = 13%+3.6%) - High-protein diet, supplemented with 3.6% of potassium citrate (HPKcitr =26%+3.6%) The animals are sacrificed at 9, 16 and 21 months	BMD by DEXA OC, DPD, IGF1 by ELISA, RIA Urinary Ca, Mg by AAS Citraturia by ion-exchange chromatography	HP diet induces metabolic acidosis (hypercalcuria, hypermagnesuria and hypercitraturia) The supplementation in potassium citrate inhibits this effect BMD, bone metabolism markers and IGF1 level are not modified, irrespective of the diets At 21 months, the Ca retained is reduced in the HP group	The high level of protein in the diet induces acidosis, but preserves the skeleton by providing an adapted amount of calcium

Pye *et al* 2009	Adult female Sprague-Dawley rats receiving 0.50% Ca and 0.30% P (Ca/P = 1.66) Diet with variable levels of protein (1/3 plant origin and 2/3 animal origin) for 4, 8, 12 and 17 months	2 groups (n=80) - Normal protein-level diet (NP = 15%) - High-protein diet (HP = 35%) The animals are sacrificed at 4, 8, 12 and 17 months	BMD by DEXA and CT OC, CTX, IGF1 leptin and adiponectin by ELISA Biomechanical properties by 3-point INSTRON test Ca and P by Nova analyser	- HP diet induces a reduction in bodyweight, abdominal fat and an increase in lean body mass associated with an increase in levels of leptin and adiponectin - HP diet leads to a relative increase in BMC of the femur, tibia and vertebrae BMD, micro-architecture, biomechanical properties, bone metabolism markers and the IGF1 level are not modified, irrespective of the diet	The high level ofprotein in the induces a reduction in body fat, without modifying bone mass or bone biomechanical properties
Funaba *et al* 1990	Male Wistar rats aged 50 days receiving 0.47 to 0.6% Ca - Diet with variable protein levels (casein and lactoglobulin) for 21 days	2 groups (n=20) - Isoprotein diet (NP = 18% casein) -High protein diet (HP = 38%, casein 18% and lactoglobulin 20%) The animals are sacrificed at 4 and 21 days after IM implantation of bone powder Implant removed and samples taken of urine and blood	The bone powder was prepared from the femur and tibia of adult rats Bone Ca by AAS Ca, P, urea, plasmatic proteins, urinary sulphates, ALP activity and acid phosphatase in the implants by colorimetry Implants embedded in paraffin wax for histology	- HP diet at 14 days induces the presence of cartilage in the implants without calcification - HP diet at 21 days induces an increase in urinary excretion of Ca and sulphates associated with a reduction in calcaemia No significant difference for the Ca content of the implants or in activity of ALP and acid phosphatase	The high level of proteins induces a delay in bone formation that could be due to the restricted level of Ca used during calcification (Ca content of the implants is identical in both groups)

Protein restriction (gestation)					
Fetoui *et al* 2008	Gestating Wistar rats Restricted protein diet from 14th day of gestation until 14th day after birth	Low-protein diet (PR, n=25) at 7% *vs* commercial diet (SICO, Tunisia) control at 20% (CR, n=25) The animals are sacrificed 14 days after birth (mothers and new-borns)	BMC by colorimetry Ca and P by AAS ALP and ACP by colorimetry Amino acids by HPLC fT3 and fT4 by RIA	In the 14-day-old pups, the protein restriction reduces bodyweight by 47%, skeletal growth by 11%, levels of protein, aa, albumin, levels of fT3 and fT4 and the level of ALP by 19%, while increasing the level of ACP by 33% Positive correlation ($p<0.01$) observed between bone mass and the levels of fT3, fT4, ALP, and proteins	Protein restriction of 7% in female rats at the end of gestation and for 14 days after birth induces, in the young, a negative effect on bone and its metabolism. Correlation (negative) with thyroid status
Mehta *et al* 2002	Gestating Wistar rats Restricted protein diet throughout gestation	Low protein diet (PR, n=4) restricted to 9% *vs* commercial diet (control at 18% (CR, n=5) The new-born pups receiving a control diet are sacrificed at 22 months (PR, n=23) and 19.5 months (CR, n=31) post natal	BMD, BMC and % of fat by DEXA Bone embedded in paraffin	In gestating rats, protein restriction reduces weight gain from day 15 to day 22 of gestation, even though the quantity ingested tends to be higher This restriction leads to a reduction in bone surface, femoral diameter and BMC, without modifying the BMD of the pups at 20 months (size and weight as co-variables) In addition, it induces an increase in the width of cartilage	A protein restriction of 9% in gestating rats reduces BMC and induces programming of the growth of bone and cartilage during development

Table 3: Impact of weight-loss diets on kidney/liver/biliary functions – animal studies

Authors	Journal, Year	Model	Protocol	Results	Search for harmful effects
Nwagwu *et al*	British J Nutr, 2000	Young rats	150 rats exposed *in utero* (16 females) to protein restriction (9% vs 18% of proteins)	Renal development of offspring altered progressively (from 12 weeks) Reduction in the number of nephrons	Search for the harmful effect of malnutrition on renal function (no energy restriction)
Schoknecht *et al*	Proc Soc Exp Biol Med, 1993	Young obese pigs, 6 weeks	12 pigs, diet with 17% or 34% protein, 15 days	Size of kidneys, protein levels increased No effect on cellularity (no hyperplasia)	Yes None observed after 15 days of diet
Boon *et al*	Histochem Cell Bio, 1999	Rats	Diet with 0, 20 and 60% protein for 10 days	Increase in capacity of liver to detoxify ammonia	Unspecified Mechanistic study
Lacroix *et al*	Am J Physiol, 2004	Rats	Diets at 14% or 50% protein for 6 months	No harmful effect (in histological terms) on the liver or kidneys. Transient increase in kidney size (15 days)	Yes None observed in 6 months of diet (no energy restriction)
Benabe *et al*	Am J Physiol, 1992	Rabbits	Diets at 16% or 40% protein for 3 weeks	Increase in glomerular filtration rate	No Mechanistic study
Birkner *et al*	J Physiol Pharmacol, 2005	Rabbits	Atkins diet	Fatty liver disease	Yes

Table 4: Impact of weight-loss diets on kidney/liver/biliary functions – Clinical cases

Authors	Journal, Year	Number of patients	Symptoms/Disease	Cause	
Stevens *et al*	Ann Intern Med, 2005	2 men, aged 27-30	1 Fatigue, jaundice 2 + vomiting, fever Reversible	Consumption of Hydroxycut 9 tablets/day	
Tarantino *et al*	World J Gastroenterol, 2009	1 obese woman, aged 22	Jaundice, itching, stomach ache, nausea, vomiting, dark urine, mild fever Operation Reversible symptoms	Herbal therapy for losing weight (*Lycopodium serratum* and *Chelidonium maius*)	
Adachi *et al*	Ann Intern Med, 2003	12 Japanese patients	Fatigue, nausea, diarrhoea, loss of appetite Abnormal liver profiles	*Chaso* or *Onshido* (2 plants used for weight loss) Contain n-nitroso-fenfluramine	
Dara *et al*	World J Gastroenterol, 2008	2 women, aged 33-40	Abdominal cramps, diarrhoea, nausea, vomiting, fatigue Abnormal liver profile + jaundice, dark urine, itching Reversible symptoms	Hydroxycut	Agents suspected: *Garcina Cambodgia, Camellia Sinensis*
Combe and Apparicio	The Lancet, 1993	1 man, aged 21, with a history of glomerulonephritis	Renal failure	Body building with protein intake of 2.6 g/kg/day	

Table 5: Impact of weight-loss diets on kidney/liver/biliary functions – Clinical studies

Authors	Journal, Year	Number of patients	Symptoms/Diseases	Cause	
Tiikainen *et al*,	Diabetes, 2003	27 obese women	High-calorie diet, to lose 8% of bodyweight over 3 to 6 months. Fat/Carb./Prot.: 30/50/20	Reduction in hepatic lipids	No
Hoy *et al*	Am J Clin Nutr, 1994	73 obese subjects	Pre-adjustment to 1200 kcal for 2 weeks. Then 800 kcal for 10 weeks, with either a 45/30/25 or 35/50/15 diet (Fat/Carb./Prot.)	Out of 53 patients investigated for gallstones before and after the diet, 2 had gallstones.	Yes. 3 previous studies, with lower caloric intake, reported levels observed of 13 to 17%. Stagnation of bile
Friis *et al*	J Clin gastroenterol, 1987	46 obese subjects (37 women, 9 men)	VLCD (420 kcal), 6 weeks	Transient disturbance of liver functions (LDH, SOGT, SGPT, bilirubin) No functional consequences	Yes
Palmer and Schaffner	Gastroenterol, 1990	39 obese subjects	VLCD (600-800 kcal)	Weight loss of 10% associated with a correction of anomalies in liver functions	No
Andersen *et al*	J Hepatol, 1991	41 obese subjects (35 women, 6 men)	VLDC then gastroplasty. Liver biopsies	Reduction in steatosis but liver fibrosis (12% of the patients) and periportal inflammation (24%)	Yes
Lewis *et al*	Obesity Surgery, 2006	33 obese subjects	Optifast for 6 weeks, 800 kcal maximum (Low fat, low carb)	Reduction in liver size and triglycerides No harmful effect mentioned	No

Menon *et al*,	Am J Kidney Dis, 2009	255 subjects suffering from liver failure	Diets at 0.28 or 0.58 g/kg/d of protein Monitored for 3 years, on average	No effect on kidney failure but increase in mortality after kidney failure (HR x 2) in low-protein diet	No (positive effect sought)
Chagnac *et al*,	J Am Soc Nephrol, 2003	8 obese subjects	Bariatric surgery	Improvement of kidney function (reduction in glomerular hyperfiltration)	No
Dessi-Fulgheri		8 obese subjects with high blood pressure	2 weeks with isocaloric diet, 4 days low-calorie diet	Increase in diuresis and natriuresis, but no harmful effect suggested	No
Skov *et al*,	Int J Relat Metab Disord, 1999	65 overweight or obese subjects	Diets ad lib, HP (30%) or NP (12%) for 6 months	Increase in TFG and kidney size, with no harmful effect	Oui

Table 6: Impact of weight-loss diets during pregnancy – studies on humans

Author - Journal	Type of study	Size and type of cohort	Type of diet	Results	Observations
Cohen JH Prev Chronic Dis 2009	Questionnaire – BRFSS database	8036 pregnant women aged 18-44 over 8 years	Slimming practice unspecified	8.1% of the women interviewed have followed a weight-loss diet	Association with age>35 years, BMI>30, alcohol consumption and mental disorders
Treasure JL BMJ 1988	Longitudinal cohort study	6 pregnant women with anorexia nervosa	Low overall food intake	Reduction in abdominal diameter of foetus during 3rd trimester; Low birth-weight	
Stewart DE Am J Obstet Gynecol 1987	Retrospective cohort study	23 pregnancies in 15 women with anorexia or bulimia nervosa	Low overall food intake	Lower birth-weight in mothers showing symptoms at time of conception than in those in remission	

Bulik CM J Clin Psychiatry 1999	Randomised prospective study	66 women with anorexia nervosa and 98 women as controls	Low overall food intake	Significant increase in the number of miscarriages, premature births and caesarean deliveries in the anorexia group; Birth-weight of children significantly lower in the anorexia group.	No difference between active or remission anorexics
Waugh E Int j Eat Disord	Questionnaire and interview. Controlled non-randomised study	Cohort (size not given) of women with anorexia nervosa	Low overall food intake	Lower birth-weight in children with anorexic mothers vs children in control group	Study concentrating on post-natal development of children born to anorexic mothers and not on the pregnancies themselves
Franko DL Am J psychiatry 2001	Longitudinal cohort study. Questionnaire and interviews	49 pregnancies resulting in live births in women with anorexia nervosa, taken from a cohort of 246 anorexic women participating in a longitudinal study	Low overall food intake	Greater increase in the number of births by caesarean delivery in women with 'active' anorexia during their pregnancy	No mention is made of any possible pregnancies not reaching term in the cohort studied
Mirghani HM Am J Perinatol 2006	Retrospective case-control study	168 pregnant women having fasted for Ramadan 156 control pregnant women of similar age, parity and age of foetus	Daytime fasting for one month	In the group having fasted: higher incidence of diabetes and caesarean deliveries. Birth-weight identical for both groups	

Table 7: Impact of weight-loss diets during gestation – animal studies

Author – Journal	Model	Protocol	Marker	Results
Zambrano E J Physiol 2005	Female Wistar rats (n=70)	- 30 gestating rat (13 controls, 17 prot. restriction. [10% casein]) - 40 lactating rats (20 controls, 10 prot. restriction)	In the male offspring: birth-weight, weight of testes, semen analysis, fertility	Delayed sexual maturity and late fertility in restricted group
Zambrano E J Physiol 2006	Female Wistar rats (n=70)	- 30 gestating rats (13 controls, 17 prot. restriction [10% casein]) - 40 lactating rats (20 controls, 10 prot. restriction)	In the offspring: glycaemia, insulinemia, cholesterol, triglycerides, leptin	Increase in fatty tissue, cholesterol, triglycerides, insulin resistance greater if restriction during gestation followed by new diet during lactation
Petrik J Endocrinology 1999	Female Wistar rats	2 groups of gestating rats: protein restriction (8% prot.), control (20% prot.)	In the offspring: mass of pancreatic β cells, insulin secretion	Alteration of the replication of β cells in foetus and new-born pups, of insulin secretion and pancreatic expression of IGF2.
Toscano AE Nutrtion 2008	Female Wistar rats	22 gestating rats - 11 controls (17% protein) - 11 restricted in protein (7.8%)	In the male offspring: histochemical analysis and contractile properties at 25 and 90 days	Maternal protein restriction induces an alteration of the contractile and elastic properties of the skeletal muscles as well as structural anomalies (proportion fibres1/fibres2)
Ashton N AJP Regul Integr Comp Physiol 2006	Female Wistar rats	2 groups of 30 gestating rats: LP group: protein restriction (9% prot.), control group (18% prot.)	In the offspring at 4 weeks: femoral morphology, renal clearance, total body calcium, renal calcium transporters, renal Na/K ATPase activity, PTH.	In the LP group: reduction in trabecular bone mass, increase in renal excretion of calcium and sodium, reduction in glomerular filtration and calcaemia
Gallagher EAL J Physiol 2005	Wistar rats	36 gestating rats - 22 controls (18% protein): LP group - 14 restricted in protein (9%)	In the offspring at Day21 of embryonic life and Day1 post natal: oxygen consumption of a homogenate of cerebral tissue	Reduction in VO_2 Max in the LP group interpreted as a developmental adaptive response to maternal restriction

Mehta G Calcif Tissue Int 2002	Gestating Wistar rats Restricted protein diet throughout gestation	Restricted protein diet (PR, n=4) 9% vs commercial diet, control at 18% (CR, n=5) The new-born pups receiving a control diet were sacrificed at 22 months (PR, n=23) and at 19.5 months (CR, n=31) after birth	BMD, BMC and % fat by DEXA Bone embedded in paraffin	A protein restriction of 9% in rats during gestation reduces the BMC and causes programming of bone and cartilage growth during development
Fetoui H J Anim Physiol Anim Nutr 2008	Gestating Wistar rats Restricted protein diet from 14th day of gestation to 14th day after birth	Restricted protein diet (PR, n=25) 7% vs commercial diet (SICO, Tunisia), control at 20% (CR, n=25) The animals are sacrificed 14 days after birth (mothers and new-born pups)	BMC by colorimetry Ca and P by AAS ALP and ACP by colorimetry Amino acids by HPLC fT3 and fT4 by RIA	Protein restricted to 7% in rats during the end of gestation and for 14 days after birth induces a negative effect on bone and its metabolism in the new-born pups. There is correlation (negative) with thyroid status
Hietnemi H Peptides 2009	Sprague-Dawley rats	3 groups of gestating rats - control (n=2) fed *ad libitum* - 2 groups restricted in calories to 75% (n=3) or 50% (n= 3) in group C	In the offspring at one month after birth: triglycerides, cholesterol, insulin, adiponectin, leptin, ghrelin, plasma resistin	Increased cholesterol and resistin, reduced adiponectin in the restricted groups
Ozaki T J Physiol 2001	Wistar rats	2 groups of gestating female rats - one control group, fed normally (C) - one restricted group receiving 70% of C intake from start of gestation	In the offspring: weight at Day0 and Day20, TA from Day60 and sensitivity to vasoconstrictor drugs	In the offspring, maternal restriction induces cardiovascular anomalies that increase with age and are more pronounced in males.

Tardif SD Brit J Nutr 2004	Female Marmoset monkeys	20 pregnancies followed to term with viable offspring: - 5 fed *ad libitum* - 8 with energy restriction (75%) from mid-pregnancy - 7 with energy restriction (75%) at the end of pregnancy	Maternal weight gain, foetal growth, progress of pregnancy	Maternal restriction did not induce delayed intrauterine growth, despite the absence of maternal weight gain. Increase in the number of aborted pregnancies in the group with restrictions at mid-pregnancy
Tardif SD 2005 J Clin Endocr Metab	Marmoset monkeys	6 females, each having had 2 pregnancies: - one fed *ad libitum* - the other with energy restriction (75%) at mid-pregnancy	Urinary cortisol, chorionic gonadotropin, and estradiol	No pregnancy subjected to energy restriction went to term (abortion 11 to 47 days after the start of energy restriction) The abortions were preceded by a drop in urinary hormones
Daenzer M J Nutr 2002	Wistar rats	2 groups of gestating rats, subjected to: -either (HP group) a high-protein diet (40% prot); - or (NP group) an isoprotein diet (20% prot) Male offspring randomised for lactation by a mother who is from either the HP or NP group	Male offspring: at Day60: energy expenditure by indirect calorimetry, VO_2, respiratory quotient then measurement of body composition by studying the carcass	Prenatal exposure to an HP diet leads to an increase in body fat and a decrease in energy expenditure Simple exposure to an HP diet has no effect

Da Silva Faria t J Nutr Biochemistry 2004	Female Wistar rats	9 female rats randomised into 3 groups at parturition: - C group: normal feeding - RP group: restricted protein diet (8% prot.) - RE group: restricted calorie diet 6 rat pups assigned to each lactating female rat	Female offspring: Linear growth, age at puberty (vaginal opening), weight of uterus and ovaries after sacrifice	In the RP and RE groups: slower growth delayed vaginal opening lower weight of uterus and ovaries
Del Rosario Ayala M Brit J Nutr 2006	Sprague-Dawley rats	20 female rats randomised into 2 groups for the duration of gestation and lactation: - C group (n=10): normal feeding with casein as source of protein - R group (n=10): restricted-calorie (85% of C) and iso-protein diet but with gluten as source of protein 6 rat pups assigned to each lactating female	In the lactating rats: weight, energy expenditure, measurement of arteriovenous difference in 3-hydroxybutyrate, glucose, lactate and triacylglycerol across the mammary glands	In the R group, a drop in energy expenditure was observed and the use of ketones as substrates as adaptive mechanisms to cover the energy cost of milk production. In the R group, there was a reduction in the weight of the females and their offspring from Day9 of lactation.

Table 8: Impact of weight-loss diets – studies in children and adolescents

Author – Journal	Type of study	Size and type of cohort	Type of diet	Results	Observations
Brugman E. Int J Obesity 1997	Questionnaire on dietary practices, duration and type	159 schoolchildren aged 13 to 15	-	13% of the girls and 5% of the boys declared that they were following a diet at the time of the study: more meals missed, less snacking, sweet beverages and bread	No difference in weight or days missed from school with the children not declaring a diet
Pugliese MT N Engl J Med 1983	Retrospective cohort study	14 children (5 girls) aged 9 to 17 with delayed growth and/or puberty through malnutrition related to voluntary restriction	Protein and energy restriction	14 weight deficits < 5th percentile 14 slowed growth in stature (11 <5th percentile) 7 delayed puberty	No symptoms of anorexia nervosa; Restriction related to “fear of obesity” Recovery of growth after provision of nutritional advice
Amador M Exp Clin Endocrinol 1990	Randomised prospective study	94 obese children, Tanner’s “stage 2” (10.6-12.9 years) - control group (C): energy restriction to 30% of needs - studied group (E): no restrictions	Energy restriction of 30%	At 6 months, for group C: - greater weight loss - slower development of puberty - growth in stature less rapid and greater loss of lean body mass - greater number of subjects abandoning the study	Greater efficacy of an isocaloric diet But study limited in time

Krebs NF J Pediatr 2010	Randomised prospective study	46 obese children (aged 12-18) (PpT>175%) - HPLC group (n=24): high-protein diet (32% of energy intake) low-carbohydrate (11% of energy intake) - LF group (n=22): low-fat diet (29% of energy intake)	High-protein diet restricted in carbohydrates *versus* Low-fat diet	Significant drop in BMI z-score at 12 and 36 weeks in both groups, faster and more marked in HPLC group. Good tolerance in both groups in terms of body composition (lean mass), BMD, lipid profile, glucose tolerance (HOMA)	Greater efficacy of the HPLC diet (even though it was slightly more low-calorie than the LF diet) but no effect on protection of lean body mass. Greater reduction in triglycerides with HPLC
Reinehr T Pediatric Diabetes 2009	Prospective intervention study	341 obese children (aged 5-16, BMI z-score =+2.47) -315 with normal birth weight - 26 who were small for gestational age (SGA: birth weight < 10th percentile)	Nutrition adjusted for age + physical activity Tracked for 1 year.	In multiple linear regression analysis, the improvement in insulin resistance (HOMA) was associated with: - reduction in the BMI z-score BMI for 10% - SGA status at birth for an extra 4%	The caloric intakes are not specified. Protein and fat intakes, probably high-energy, correspond to the needs of the age-group
Alvin P Arch Fr Pédiatr 1993	Retrospective cohort study	99 children and adolescents with anorexia nervosa	Overall nutritional restriction	Weight loss of 35% was associated with bradycardia, low blood pressure, hydroelectrolytic disorders and ECG anomalies 1 death	

Table 9: Impact of weight-loss diets on the onset of puberty – studies on animals

Author –-Journal	Model	Protocol	Marker	Results
Arts CJM Acta Endocrinologica 1992	Female Fisher rats	45 immature young rats randomised into 3 groups: - G1: *ad libitum* high-fibre diet (bran) - G2: *ad libitum* low-fibre diet - G3: energy restriction, low-fibre diet	- Weight change - onset of puberty (rupture of vaginal membrane). - mammary development and cellular proliferation of mammary tissue	- Least weight gain in G3 - onset of puberty delayed in G3 - mammary development delayed in G3, to a lesser extent in G1 (G1 had lower spontaneous calorie consumption than G2) - least mammary cellular proliferation in G3

Table 10: Stabilisation – studies on humans

Reference	Population	Diets and results
(Wing et al. 2005)	Based on data taken from the National Weight Control Registry, it was observed that, contrary to received wisdom, about 20% of overweight people manage to lose weight successfully in the long term, i.e. they lose at least 10% of their initial weight and maintain this for at least a year. Group of subjects having lost an average of 33 kg, and having maintained this for more than 5 years: - Regular and intense physical activity, - Low-calorie and low-fat eating, - Eating breakfast, - Little difference between weekdays and weekends - Regular weighing.	
(Anderson et al. 2001)	A meta-study of weight stabilisation after initial loss, covering 29 studies carried out in the USA, each having followed its subjects for at least two years. A total of 1080 subjects were followed for 5 years.	Overall, individuals stabilising their weight after initial weight loss maintained this for: - 67% - one year, - 44% - two years, - 32% - three years, - 28% - four years, - 21% - five years. - There was no difference between men and women. - The stabilisation rate was higher after a very low calorie diet (lower than or equal to 800 kcal/day) than after a moderately low-calorie diet (29.4% stabilisation rate compared to 17.8%). - Six studies examined the effect of physical exercise: the subjects with a high level of physical activity were twice as likely to stabilise their weight than sedentary subjects (53.8% compared to 27.20%).
(Rolls et al. 2005)	200 overweight or obese subjects, followed for a year and subjected to a low-calorie diet	*Two groups, each taking an isocaloric supplement but with different caloric densities:* - *High: snack* - *Low: broth* Weight loss 50% higher in the group with the lower density supplement.
(Clifton et al. 2008)	9 moderately obese women BMI = 32.8 kg/m^2	*12 weeks of intensive weight loss, then 64 weeks of stabilisation in two groups:* - *HP[1]:34% of caloric intake in the form of proteins,* - *HC[2]: 64% of caloric intake in the form of carbohydrates.* Protein intake correlated with stabilisation, and, at 6 months, total weight loss = 6.5 ± 7.5 in the highest protein intake tertile, compared with 3.4 ± 4.4 in the other two.
(Lejeune et al. 2005)	113 overweight women BMI = 29.5 kg/m^2	*4 weeks of high protein diet, then 6 months of stabilisation diet.* *Two groups were formed: one took 30g of proteins in addition to the diet, the other did not.* No difference during the weight-loss phase, but during the stabilisation phase, the high-protein group regained less weight than the other (0.8 kg vs 3 kg), with a gain of lean body mass in the first and of body fat (and lean body mass) in the second.
(Ochner et al. 2007)	103 people subjected to a low-calorie diet for 22 weeks, then followed at 6 months and 18 months after the weight-loss phase	Caloric intake inversely correlated with weight regain.

Reference	Population	Diets and results
(Harris et al. 1994)	75 women and 82 men followed for 18 months	Reduction in BMI correlated with: - Rise in physical activity, - Drop in fat intake, - Rise in vegetable intake, - Drop in intake of sweetened foods and hot dogs.
(Shick et al. 1998)	355 women and 83 men, both overweight and obese	After weight loss of at least 13.6 kg in 1 year and successful stabilisation for 5 years. The nutritional survey found low-calorie and low-fat eating habits (24% fats).
(Leser et al. 2002)	37 overweight and obese women	*After a VLCD, evaluation at 3 years.* Two factors predictive of stabilisation: - moderate fat intake - increase in physical activity
(McAuley et al. 2006)	93 overweight women with insulin resistance	*3 diets over 12 months:* - *HC (and enriched in fibres)* - *HF*[3] - *HP* At 6 months, better results on metabolic syndrome with HF and HP, but at 1 year, an increase in body fat, waist measurement and insulin resistance with the HF diet, whereas there was an improvement in the HC and especially HP diets.
(Elfhag et al. 2005)	Meta-analysis on the predictors of stabilisation	Stabilisation for 6 months or more is associated with: - initial weight loss, - physical activity, - regular eating practices, including breakfast.
(Sacks et al. 2009)	811 obese and overweight women and men	Randomisation into 4 diets: - HC-LF[4] - HP-LF - HF - HF-HP No difference concerning weight loss after 2 years.
(Lavery et al. 1993)	509 people having participated in a weight-loss programme	*Declarative*. Factors favouring long-term maintenance: - initial weight loss, - frequency of weighing, - increased physical activity - no “compulsive eating”.
(Field et al. 2001)	47,515 young or middle-aged women	*Weight tracking by declaration for 6 years.* The women who lost most weight in the first 2 years regained more in the following 4 years, but overall, at the end of the 6 years, they had lost more than those who had lost only a few kilos in the first 2 years. Physical activity greater than 5h per week associated with lower weight regain.

Reference	Population	Diets and results
(Astrup et al. 2000)	Meta-analysis comparing weight regain after a traditional low-calorie diet and after a very low-calorie diet	Higher initial weight loss was followed by a higher rate of long-term stabilisation. Higher rate of stabilisation if there was an increase in physical activity during the stabilisation phase, irrespective of the initial diet.
(Greenberg et al. 2009)	322 moderately obese subjects. BMI = 31 kg/m^2	*3 diets:* - *Low fat* - *Mediterranean* - *Low carbohydrates* Primary criterion for success at 2 years: number of kilos lost at 6 months. Physical activity associated with a reduction in energy intake.
(Lee et al. 2010)	147 elderly people of both sexes having lost and then regained at least 3% of their weight in the 2 previous years, compared with individuals of the same age, gender and race whose weight had remained stable over the same period. Male “weight cyclers” had lower lean body mass than individuals whose weight remained stable.	

1. HP = High-protein diet
2. HC = High-calorie diet
3. HF = High-fat diet
4. LF = Low-fat diet

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