



Artículo especial

Physical activity, hydration and health

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Abstract

Since the beginning of mankind, man has sought ways to promote and preserve health as well as to prevent disease. Hydration, physical activity and exercise are key factors for enhancing human health. However, either a little dose of them or an excess can be harmful for health maintenance at any age. Water is an essential nutrient for human body and a major key to survival has been to prevent dehydration. However, there is still a general controversy regarding the necessary amount to drink water or other beverages to properly get an adequate level of hydration. In addition, up to now the tools used to measure hydration are controversial. To this end, there are several important groups of variables to take into account such as water balance, hydration biomarkers and total body water. A combination of methods will be the most preferred tool to find out any risk or situation of dehydration at any age range.

On the other hand, physical activity and exercise are being demonstrated to promote health, avoiding or reducing health problems, vascular and inflammatory diseases and helping weight management. Therefore, physical activity is also being used as a pill within a therapy to promote health and reduce risk diseases, but as in the case of drugs, dose, intensity, frequency, duration and precautions have to be evaluated and taken into account in order to get the maximum effectiveness and success of a treatment. On the other hand, sedentariness is the opposite concept to physical activity that has been recently recognized as an important factor of lifestyle involved in the obesogenic environment and consequently in the risk of the non-communicable diseases.

In view of the literature consulted and taking into account the expertise of the authors, in this review a Decalogue of global recommendations is included to achieve an adequate hydration and physical activity status to avoid overweight/obesity consequences.

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Key words: Physical Activity. Hydration. Health. Prevention. Decalogue of Recommendations.

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ACTIVIDAD FÍSICA, HIDRATACIÓN Y SALUD

Resumen

Desde los comienzos del género humano, el hombre ha buscado el modo de promover y preservar la salud, así como prevenir la enfermedad.

La hidratación, la actividad física y el ejercicio son factores clave para mejorar la salud. Sin embargo, estos factores en dosis excesivamente bajas o en exceso pueden ser perjudiciales para el mantenimiento de la salud a cualquier edad. El agua es un nutriente esencial para el organismo y un factor clave para la supervivencia y la prevención de la deshidratación. Sin embargo, hay todavía una controversia general en cuanto a la cantidad necesaria de ingesta de agua u otros líquidos con objeto de conseguir un nivel adecuado de hidratación. Además, hasta la fecha no hay consenso sobre las herramientas a utilizar para medir la hidratación. Con este fin, hay varios grupos importantes de variables a tener en cuenta, como el equilibrio de agua, biomarcadores de hidratación y el agua total corporal. Se prefiere en general una combinación de métodos para evaluar riesgo de situaciones de deshidratación en cualquier franja etaria.

Por otro lado, se ha demostrado que la actividad física y el ejercicio promueven la salud, evitando o reduciendo la susceptibilidad a enfermedades de tipo vascular o inflamatorio, así como para ayudar en el manejo del peso. Por todo ello, la actividad física está siendo utilizada también a modo de “píldora” en terapias para promover la salud y reducir el riesgo de enfermedad. Como en el caso de los medicamentos, hay que evaluar la dosis, intensidad, frecuencia, duración y tener en cuenta las precauciones necesarias para conseguir la máxima eficacia y el mayor éxito del tratamiento. Por el contrario, el sedentarismo es el concepto opuesto a la actividad física y se ha reconocido recientemente como un factor importante de estilo de vida implicado en el ámbito obesogénico y en consecuencia en el riesgo de las enfermedades no transmisibles.

Teniendo en cuenta la bibliografía consultada y la experiencia de los autores, en esta revisión se concluye con unas recomendaciones a modo de decálogo dirigido a la población general para conseguir un estatus de hidratación y actividad física adecuados con el fin de evitar las consecuencias del sobrepeso y la obesidad.

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Palabras clave: Actividad Física, Hidratación, Salud, Prevención, Decálogo de Recomendaciones

Introduction

This article is the result of the presentation and discussion of 10 lectures at the I Symposium on Physical Activity, Hydration and Health, that was held at the Royal and Illustrious Official College of Pharmaceutics from Sevilla, Spain with the collaboration of Coca-Cola Iberia, on the 7th November, 2013.

All the authors expressed freely their ideas and studies according to their expertise and knowledge. Discussions were held among all of them and the audience.

The Symposium included both the opening and closing lectures, with the respective following titles and speakers:

Health maintenance through exercise, by Pedro Manonelles

Physical activity and immunity: practical applications, by Eduardo Ortega.

Two round tables were included, as follows:

1. “What do we know and what can be improved in healthy subjects? The following lectures were selected (in order of appearance at the scientific programme):

- *Composition of beverages for sportspeople* by Nieves Palacios,
- *Evaluation of hydration* by Julia Wärnberg,

- *Prescription of physical exercise for health* by José Antonio Casajús,
- *Exercise as medicine* by Margarita Pérez.

2. “Preventing through physical activity and hydration” included the following lectures:

- *Relationship between physical activity levels and childhood obesity* by Susana Aznar
- *Myths and realities of the loss weight programmes* by Pedro J. Benito
- *Physical activity, sedentariness and inflammation in adolescence* by David Martínez-Gómez
- *Physical exercise and hydration: not too little, not too much* by Francisco B. Ortega.

The coordination of the scientific programme and the discussion of the presentations were led by Ascensión Marcos.

It is well known that since the beginning of mankind, man has sought ways to preserve health and prevent disease. Hydration, physical activity and exercise are key factors for enhancing human health (fig. 1). However, either a little dose of them or an excess can be harmful for people at any age.

Therefore, the aim of this event was to discuss about how these two apparently independent entities such as hydration and physical activity/exercise, have an impor-

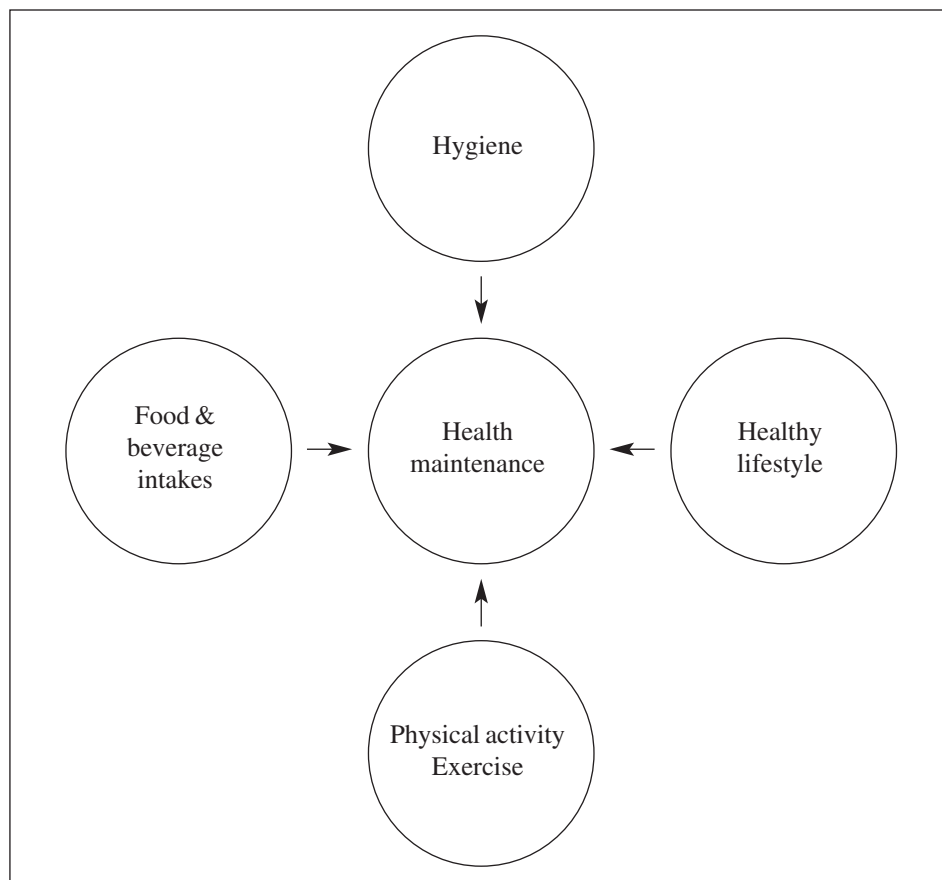


Fig. 1.—Key factors involved in enhancing human health.

tant role both separately and interacting between both of them in the maintenance and improvement of health. Recent findings were discussed and recommendations for appropriate behaviour related to hydration and physical activity have been offered in this overview.

Hydration

Water is an essential nutrient^{1,2} for human body and a major key to survival has been to prevent dehydration. However, there is still a general controversy regarding the necessary amount to drink water or other beverages to properly get an adequate level of hydration and also the best way of measuring hydration in humans in order to know to what extent an individual can be at risk of dehydration and how to prevent any situation of dehydration at any age range.

Measurement of hydration

In clinical nutrition and field studies, commonly used assessment methods of hydration are: estimates of water balance (thirst rating, total water intake and output or body weight changes), hydration markers (plasma or urine osmolarity) and total body water (TBW) measurements by bioelectrical impedance or isotope dilution.

Water balance

Thirst rating

For the majority of healthy population, fluid balance is maintained via thirst, a feedback-controlled variable, acutely regulated by central and peripheral mechanisms. However, voluntary drinking is also a behaviour influenced by other environmental, social, and psychological cues. Indeed, thirst perception is typically assessed by subjective ratings using either categorical or visual analogue scales. Therefore, factors and conditions (e.g., age, disease, temperature) that influence thirst should be also recognized, taking into account that humans may drink also for other reasons, particularly for hedonic ones. For example, during cold exposure, thirst is significantly blunted independently of hydration status or activity³.

Water intake and output

Water balance can be estimated by the assessment of both water intake (input) and water losses (output) during a period of time.

Total water input includes total water intake (from beverages, and food) and to a small extent also from oxidation of macronutrients (metabolic water). Estima-

tions of water intake from food and beverages are typically assessed by using dietary records or recalls, and total water derived from food composition data bases. Fruits and vegetables are generally the largest relative sources of water from solid foods, besides soups, infusions and juices, after pure water and beverage consumption, but proportions vary largely according to dietary patterns and climate conditions. In this regard, sodium replacement should be taken into account especially in those zones where temperatures are high during at least half a year and hydration care may become more important than in cold places; this is the reason why sport drinks emerge as interesting options as hydration-producer. The habit of drinking water is more complex than the habit of food consumption and measurement of pure water consumption is fairly new in focus in dietary research and still adequate validation of dietary assessment methods of water intake is needed⁴.

On the other hand, water output includes the losses in urine and stool as well as the insensible losses from respiration and non-sweating perspiration. 24h urine volume is used to measure water output or water retention or clearance by the kidneys in hydration studies.

Body weight changes are a sensitive, accurate and easily measured indicator of water balance when measured regularly and under standard conditions. Acute losses in body weight are almost always due to changes in total body water.

Hydration biomarkers

Plasma osmolarity and urine indices

Water balance regulation is very precise, and a loss of 1% body water is usually compensated within 24 h. Changes in plasma osmolarity (P_{osm}) trigger these homeostatic mechanisms. When P_{osm} is normal or increased, kidneys are conserving water. As the P_{osm} rises, the urine osmolarity should also rise as an expected physiological response to dehydration. In this context, plasma and urine osmolarity as well as urine specific gravity are the most widely used biomarkers of hydration⁵. Urine indices are best measured in morning urine or 24 h urine, while P_{osm} is usually measured in a single morning venous sample.

In clinical nutrition, however, dehydration may be confounded with hyperglycemia (diabetes mellitus) and high protein diets as these conditions increase osmolarity despite adequate hydration status. Population values for P_{osm} or urine osmolarity cannot be used to estimate human water requirements (i.e., on the basis of dehydration), because the healthy body's neuroendocrine mechanisms maintain P_{osm} within normal limits, even when total water intake varies greatly⁶. On individual level, when laboratory analysis is not available or when a quick estimate of hydration is necessary, morning urine colour can be used as an indicator of hydration with reasonable accuracy.

Total body water (TBW)

Bioelectrical impedance analysis (BIA)

BIA measures the impedance or resistance to a small electrical current as it travels through the body's water pool. It is a commonly used method to quantitatively estimate body composition and is based on a two-compartment body composition model, namely body fat mass (FM) and fat-free mass (FFM) and assuming that 73% of the body's FFM is water for TBW estimation. Single-frequency BIA (SF-BIA) is most commonly used for assessing TBW and FFM but cannot distinguish TBW into its intracellular and extracellular compartments. Bioimpedance spectroscopy (BIS) or multi-frequency BIA allows for the differentiation of TBW into intracellular and extracellular water compartments^{7,8}. Specific prediction equations may be developed against dilution techniques, e.g. the TBW equation model developed for Spanish children which incorporated height (cm)²/Reactance and weight: TBW (kg) = 0.495 × height (cm)²/Reactance + weight (kg) × 0.107 + 6.08 (R² = 0.91; SEE = 2.0 kg)⁹.

Dilution and tracer techniques

Dilution techniques are considered the golden standard of the qualitative measurement of FM, FFM and TBW (again, assuming that water in the FFM is constant at about 73%). To this end, a known dose of isotop-labelled water (2H, 18O or 3H) is ingested and allowed to equilibrate within the body water (4–5 h) and urine is collected for later spectrophotometry determinations. The tracer sodium bromide (NaBr) can be used for the measurement of extracellular water space. Administration of these tracers and collection of samples are easy but these methods are expensive and impractical for large-scale studies.

In summary, at the population level one standard method has not been still accepted to adequately assess the hydration status; therefore, a combination of methods is preferred. When body water intake and output are in balance, TBW and P_{osm} provide objective measurements of volume and concentration. TBW may be assessed by BIA or dilution techniques. At an individual level, maintaining a constant morning body weight, adequate fluid intake, a pale yellow urine colour, and controlled normal urine volume will assist healthy individuals to achieve euhydration¹⁰.

Interactions between hydration and exercise

The importance of hyponatremia

Childhood and elderly people are groups of population with a high risk of dehydration¹¹. Specially, the risks and consequences of dehydration while exercising are well-known. This is the case of hyponatremia that has been de-

finied as plasma sodium concentration below 135 mmol/L, which may cause a pathological situation and might occur when doing exercise and unfortunately it is very common in endurance events. Hyponatremia becomes more frequent as the duration of the exercise increases, specially, in ultra-endurance exercise (events lasting longer than 6 hours). As an example, during the London Marathon in 2006, the incidence of hyponatremia was 12.5%¹². Indeed, it is the first cause of severe disease in ultra-endurance events, such as the popular Ironman¹³. Therefore, in ultra-endurance events (more than 6 hours, but often lasting 10 and 20 hours, such as Ironman) the amount of beverage intake containing carbohydrates and sodium should be smaller, around 0.5 L per hour of event, being the amount of liquid intake per hour smaller as the duration of the sport activity increases in order to avoid any renal or metabolic disfunction.

Recent data support that 95% of the variance in the decrease in sodium concentration (that can lead to hyponatremia) after exercise is explained by increases in body weight as a consequence of over drinking^{14,15}. These findings may have important implications for guiding athletes participating in ultra-endurance sports (fig. 2).

In addition, since many of the effects of the exercise on the inflammatory cells are mediated by changes in the systemic concentrations of stress hormones and proteins, such as glucocorticoids, catecholamines, and 72 kDa heat shock proteins¹⁶, an optimal hydration during sport performance must be important in order to avoid potential hemoconcentration of these “stress mediators”.

Beverages for sportspeople

According to Spanish law¹⁷, beverages for sportspeople are considered among food preparations for dietary and/or special regimes, under the heading on foods adapted to intense muscular wear.

These beverages have a specific composition aimed to achieve rapid absorption of water and electrolytes and to prevent fatigue. In addition, they have specific requirements¹⁸.

Therefore, the main aims of these beverages are as follows:

1. To provide carbohydrates to maintain an appropriate concentration of glucose in blood and to delay the exhaustion of glycogen deposits.
2. The replacement of electrolytes, particularly of sodium.
3. Hydric replacement to avoid dehydration.

These beverages usually have a particular nice overall perception of flavour, so it is reasonable to bear in mind that they will be more easily consumed than water on its own.

In February, 2001, the European Commission's Health and Consumer Protection, through the Scientific

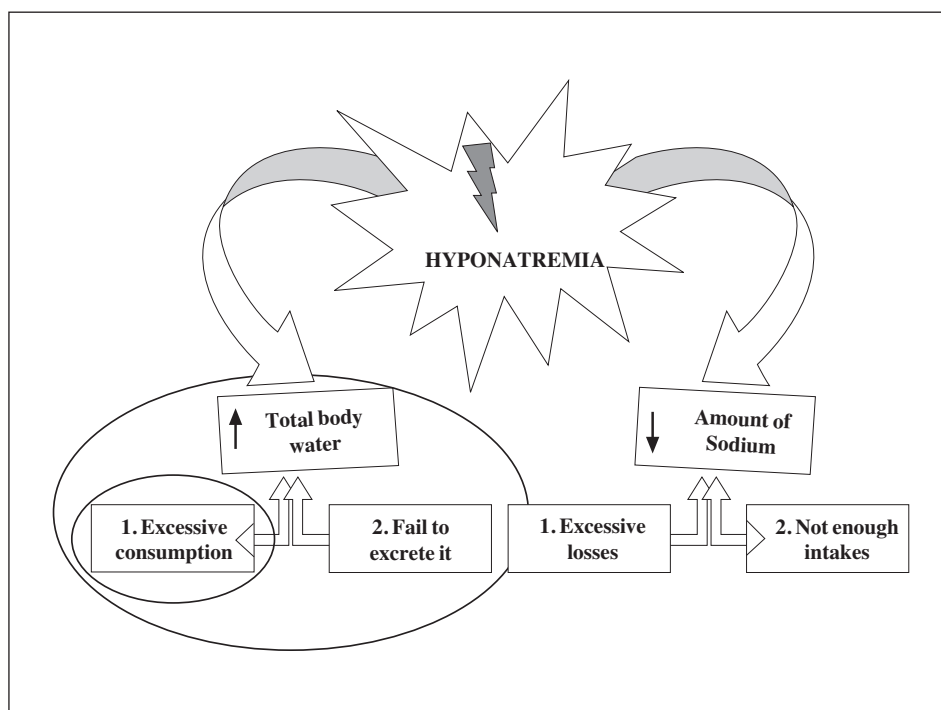


Fig. 2.—Summary of the main factors that might cause hyponatremia during exercise.

Committee on Food, drew up a report on the composition of food and beverages intended to meet the expenditure of great muscular effort, especially among sportsmen and women. This report points out that specially adapted foods and liquids help solve specific problems in order to achieve an optimum nutritional balance. These beneficial effects are not confined only to sportspeople, who take regular and intensive muscular exercise, but also people who, in their jobs, make major exertions in adverse conditions, and people who during their leisure time do physical exercise and training. It indicates that the sports beverage should supply carbohydrates as a fundamental source of energy and should be efficient in maintaining optimum hydration or in rehydrating recommending the following margins in the composition of the beverages to drink while doing sport:

- Not less than 80 kcal per litre (L) and not less than 350 kcal/L.
- At least 75% of the calories should come from carbohydrates with a high glycemic index (glucose, sucrose, maltodextrins).
- Not less than 460 mg/L of sodium (46 mg per 100 mL/20 mmol/L) and not more than 1,150 mg/L of sodium (115 mg per 100 mL /50 mmol/L).
- Osmolality between 200-330 mOsm/kg of water.

Other components of replacement beverages

Antioxidants

The ingestion of antioxidants to minimize the damage caused by reactive species generated in the electron

transport chain has produced different results when assessing an increase in performance, so their presence in beverages for sportsmen and women is not essential¹⁹.

Proteins

The ideal protein concentrate to be added to a beverage for sportspeople would be whey protein from milk. Another alternative is just to provide serum lactoproteins, i.e. milk serum deprived from lactose, which can be useful in people with lactase deficit^{20,21}.

General recommendations

A consensus was reported in view of the needs to get proper beverages for sportspeople, including the definition of the composition and guidelines to healthy liquid replacements²².

1. Hydration should be optimized as much as possible.
2. Beverages for sportsmen or women used during training sessions or in competitions should be ranged between 80-350 kcal/1000 mL, of which at least 75%, simple carbohydrates, e.g. glucose.
3. Beverages for sportsmen or women used during training sessions and in competitions should be ranged between 20-50 mmol/L (460-1,150 mg/L) of sodium ion content according to the heat, intensity and duration of the exertion. The osmolality of such beverages should be ranged between 200-330 mOsm/L of water, and should

not under any circumstances exceed 400 mOsm/L of water.

4. Replacement beverages used after training or competitions should have a calorie content of 300-350 kcal/1000 mL, of which at least 75% should come from a mix of high glycemic load carbohydrates such as glucose, sucrose, maltodextrins and fructose.
5. Beverages for sportsmen used for immediate post-exertion should have sodium ion content in the range of 40-50 mmol/L (920-1,150 mg/L). Likewise, they should provide potassium ion in the range of 2-6 mmol/L. The osmolality of those beverages should be comprised 200-330 mOsm/L of water, not exceeding 400 mOsm/L.

Physical activity/exercise

Not in vain Hippocrates mentioned his famous sentence (IV B.C): *“Eating alone will not keep a man well; he must also take exercise. For food and exercise... work together to produce health”*.

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting expenditure (>1.5 METs), as walking to and from work, taking the stairs instead of elevators and escalators, gardening, and doing household chores²³. Exercise, however, is a type of physical activity that requires planned, structured, and repetitive bodily movement with the intent of improving or maintaining physical fitness level. Exercise can be accomplished through activities such as cycling, dancing, walking, swimming, yoga, working out at the gym, or running, just to name a few. Regular exercise, depending upon the kind, improves aerobic fitness, muscular strength, and flexibility^{24,25}.

In the XXI century the practice of regular physical activity/exercise has been associated with both a healthier and a longer life, being recognized as one of the most powerful health tools for preventing disease and improving the quality of life in developed countries. Indeed, frequent and regular physical exercise boosts the immune system, and can be beneficial in detecting, preventing and managing the “diseases of affluence”, such as hyperlipidaemia, hypertension, type 2 diabetes, obesity, arthritis, dyslipidaemia, depression, chronic obstructive pulmonary disease, nicotine addiction, affective disorders, cancer, osteoporosis, and age-related declines in muscular strength²⁶⁻²⁸.

The main outcome of regular physical activity, achieving moderate-to-high peak cardiorespiratory fitness (> 8 METs) may reduce the risk of cardiovascular events and all-cause mortality²⁹⁻³¹. Those moderate-to-vigorous physical activity (MVPA) (≥ 450 min/wk) values that are clearly above the minimum international recommendations of 150 min/wk of MVPA³² are associated with longer life expectancy³³.

Indeed, regular exercise is probably the lifestyle intervention with the most profound up-regulating effect on hundreds of genes involved in tissue maintenance and homeostasis, implying a complex cross talk between muscles and other tissues³⁰, which has been selected for optimizing aerobic metabolism to conserve energy in an environment of food scarcity^{31,34} resulting in numerous beneficial adaptations and the benefits of exercise on metabolic, psychological and physiological health (table I).

Table I
Benefits of regular physical activity on metabolic, psychological and physiological health

Effects on performance / fitness	<ul style="list-style-type: none"> • Improved endurance • Improved strength • Improved balance • Improved flexibility
Reduction of cardiovascular risk factors	<ul style="list-style-type: none"> • Sedentary lifestyle • Fibrinogen • Insulin sensitivity
Reduction of social misbehaviours	<ul style="list-style-type: none"> • Violence, smoking, consumption of alcohol, drugs and unhealthy diets (especially in children and young people)
Prevention of chronic diseases	<ul style="list-style-type: none"> • Obesity / overweight • Hypertension • Ischemic cardiopathy • Stroke • Hypercholesterolemia • Type 2 diabetes • Osteoporosis • Musculoskeletal disorders • Lumbar pain • Cancer: colon, breast, prostate
Prevention of psychological, psychiatric and behavioural disorders	<ul style="list-style-type: none"> • Stress • Increased psychological balance • Improved cognitive function • Anxiety • Depression • Self-confidence • Self-esteem • Attenuation of CV and neuroendocrine responses to mental stress • Reduction of some type A behaviours
Aging	<ul style="list-style-type: none"> • Prevention of muscle loss • Prevention of bone loss • Reduction of functional limitation • Reduction of falls • Reduction of fractures
Reduction of mortality	<ul style="list-style-type: none"> • Global • Cardiovascular

However, it is important to highlight that nowadays we are facing with a paradox: technology development and certain social behaviours have caused increased physical inactivity rates that have altered the configuration of the human biological machine; when we forget our biological evolutionary process we become hypoactive, sedentary, the contrary to what our evolution has been developed over thousands of years. The result is decoupling numerous biological functions involving loss of health and rise of the so-called “diseases of civilization”. Both physical inactivity and sitting behaviour in contemporary obesogenic environments initiate a situation of maladaptation that may lead to chronic diseases, and therefore it has become one of the most important health problems across all over the world.

Sedentary behaviour refers to activities that do not increase energy expenditure substantially above the resting level (1-1.5 METs) and includes activities such as sitting, lying down, and watching television, and other types of screen-based entertainment³⁵. Hundreds of thousands of people die each year as a result of developing diseases highly related to inactivity. The direct economic costs as consequence of inadequate physical activity behaviours are huge²⁹.

Unfortunately, there are no reliable estimates of the economic costs, advantages and savings that may produce weight loss programmes based not only on dietary restrictions, but especially on promotion of physical activity and the avoidance of sedentariness. Only few data are known regarding some specific diseases, but certainly very far from reality, since the investment in all kinds of slimming products is much higher than the official pharmaceutical costs.

The EEUU is the country where the most health care resources are associated with obesity and the estimated amount is around 5.5 to 9.4% of their health expendi-

ture (more than 100,000 million dollars). In other countries, such as Canada, Switzerland, New Zealand, Australia, France and Portugal, obesity has been reported to cause between 2 and 3.5% of health expenditures. In Spain, the cost of obesity could reach 7% of health expenditure of the Spanish National Health System, although these figures are still controversial³⁶. Indeed, due to the fact that the figures in Spain are surprising, being more than 2500 million euros a year only spent in public health on healthy problems related to overweight and obesity, rationalizing resources is crucial³⁷.

Nevertheless, before interventions can be properly designed and their findings correctly interpreted, it is important to understand how physical activity levels can be changed across different periods of life.

Physician prescription

The US Office of Disease Prevention and Health Promotion³⁸ pointed out that at that time over 8000 articles reported the benefits of exercise. According to this report, two important conclusions must be drawn:

- Important health benefits can be obtained by performing 30 minutes of moderate physical activity on most, if not all, days of the week.
- Additional health benefits result from greater amounts of physical activity.

Evidence supports the inverse relationship between physical activity intensity and premature mortality, cardiovascular diseases, stroke, type 2 diabetes, metabolic syndrome, colon cancer, breast cancer or depression, vigorous physical activity being more effective (around 30-40%) than moderate physical activity levels (fig. 3).

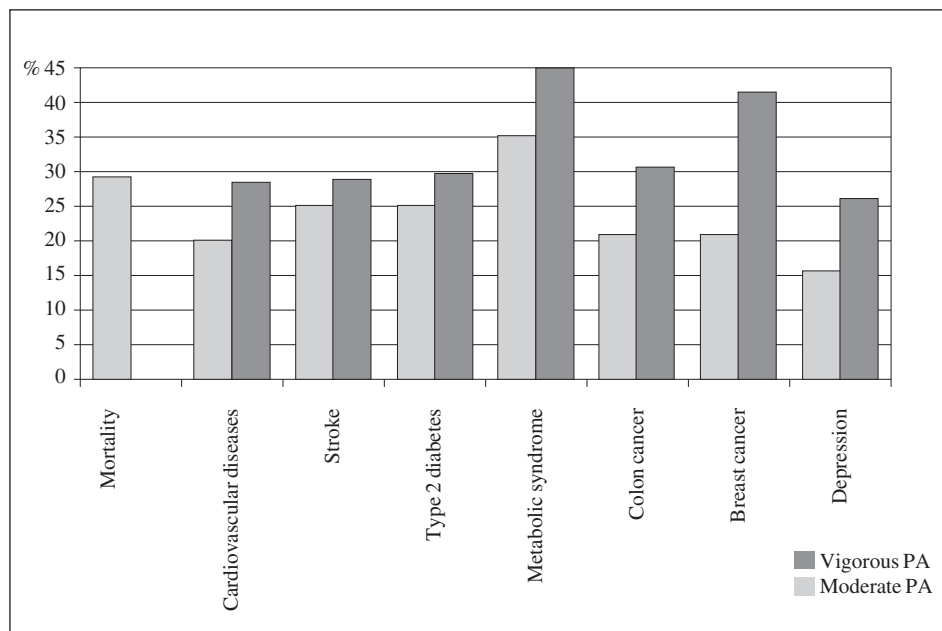


Fig. 3.—The inverse relationship (around 30-40%) between physical activity and premature mortality, cardiovascular diseases, stroke, type 2 diabetes, metabolic syndrome, colon and breast cancers, or depression.

The way to perform physical activity has consequences and should be prescribed but it is recommended in moderate or moderate-to-vigorous intensity levels for overall health maintenance, since strenuous exercise, especially in training sportspeople, can lead to risks and harms in some occasions (fig. 4)³⁹.

It is important to highlight that physicians also need more training in how to make best use of a powerful therapy, such as the physical activity. Physicians can successfully encourage activity by giving patients a written exercise prescription along with printed advice on how to design a safe and enjoyable routine²⁶.

For physicians, the prescription pad is a familiar and easy way to transmit the recommendations to maintain or recover health. Similarly, the exercise prescription directs patients to initiate, maintain or increase their physical activity levels. Unfortunately at the end of the XX century primary care physicians, family doctors, etc. were limited to recommend exercise only in certain clinical situations without specifying the type of physical activity performed and no guarantee adhering to it. The academic subject “exercise prescription” is unknown in undergraduate studies and the physician must update as a postgraduate. Thus, the initiative “Exercise is Medicine”^{7,40} promoted by the American College of Sports Medicine could help physicians and other health professionals to understand the exercise prescription process. The performance of prescription requires a multidisciplinary team that will need to have an expert on physical activity. The success of prescription depends on the ability of the health team to prepare and develop a specific exercise prescription for each subject⁴¹. In this context, the concept of a *polypill* is receiving growing attention to prevent cardiovascular disease. Indeed, compared with drugs, exercise is available at low cost and relatively free of adverse effects⁴².

The components of a prescription for medicaments include the name of the medication, strength, route and frequency of administration, as well as duration and precautions related to doses. The components of an exercise prescription follow a similar format, defining type of exercise, intensity, frequency, duration, precautions and progression of the doses. The prescription of exercise for sedentary people should begin with at a minimal effective “dose”, focusing first on the preliminary aspects of the regular exercise programme. From this “small dose” of exercise, the patient, with the professional encouragement and guidance should hopefully progress to the final optimal dose (table II).

Physical activity and sedentariness inadequacy in early ages

Due to the limitations of self-reported methods to assess physical activity in young people of different ages, the information available on this regard has been very limited.

The European Youth Heart Study (EYHS) is a school-based, cross-sectional study designed to examine the interactions between personal, environmental, and lifestyle influences on the risk factor for future cardiovascular diseases in several European countries. Within the EYHS, in the assessment of physical activity in a 6 to 10 year-follow up conducted in Sweden and Estonia, a decline in MVPA (overall change = 30 min/d) was observed together with an increase in sedentary time (overall change = 2 h 45 min/d) from childhood to adolescence⁴³. These authors observed that MVPA decreased from childhood to adolescence (-1 to -2.5min/d per year of follow-up, P = 0.01 and < 0.001, for girls and boys, respectively) and also from adolescence to young adulthood (-0.8 to -2.2 min/d per

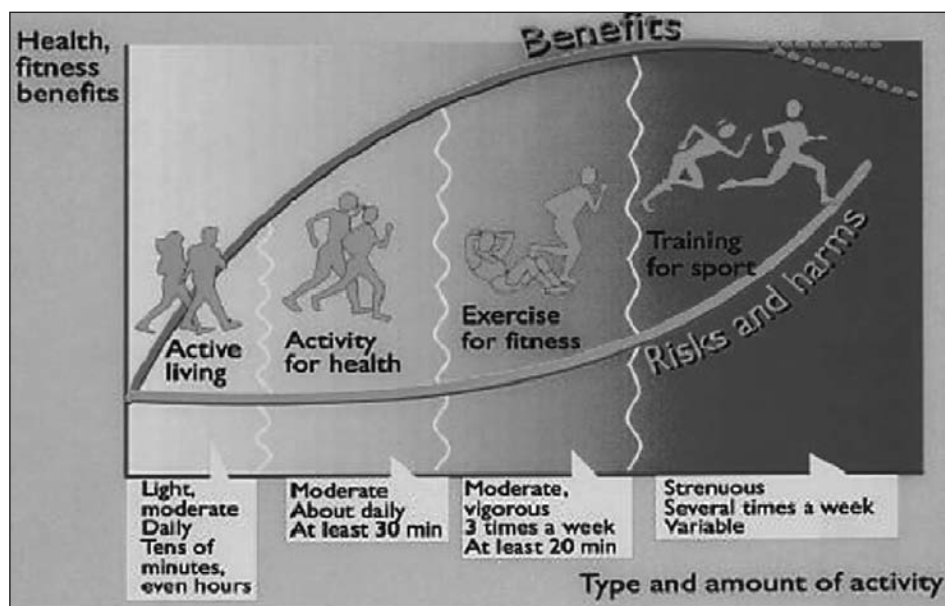


Fig. 4.—Different physical activity and exercise levels can promote health fitness benefits or the opposite, risk and harms.

Table II
A comparison between several factors involved for medication and exercise prescriptions

Medication Prescription

Drug	Acetaminophen with codeine
Strength	300 mg / 30 mg, Tablet
Route	By mouth
Frequency	1 tablet every 8 h
Duration	1 week
Precautions	Avoid drinking alcohol

Exercise prescription

Type of exercise	Walk
Intensity	4-6 km-h-1 RPE 3-5
Frequency	Three days a week. Target 5/w
Duration	Forever
Precautions	Sprain in the right ankle two months ago
Progression	Start at 4 km-h-1. Increase gradually every 4 weeks

year, $P = 0.02$ and < 0.001 for girls and boys, respectively). Sedentary time increased from childhood to adolescence (+15 and +20 min/d per year, for girls and boys, respectively, $P < 0.001$), with no substantial change from adolescence to young adulthood. The magnitude of the change observed in sedentary time was 3-6 times higher than the change observed in MVPA. Overall, these results support that MVPA declined 30min/d while sedentary time increased 2 h 45 min/d

from childhood to adolescence. These findings are of concern and might increase the risk of developing obesity and other chronic diseases later in life. In addition, these findings suggest that if a long-term intervention conducted in individuals of this age obtains no change in physical activity or sedentary time, it would actually be a very successful intervention, since the observed trend above reported has substantially modified⁴³.

Recent cross-sectional studies have reported positive associations between physical activity and obesity prevention as well as with cardiovascular risk factors in European children⁴⁴⁻⁴⁶. The majority of Spanish adults and children do not engage in enough physical activity to achieve beneficial effects for health⁴⁷. There is a need for objective and accurate assessment of the proportion of children meeting the recommendation for healthy levels of physical activity. Current health-related physical activity recommendations for children and adolescents have been established in at least 60 minutes of MVPA for 5 days a week^{48,49} and they were updated later³². Assessing the patterns of physical activity both between days (during weekdays and weekend days) and within days is of interest to improve our understanding of the variation in physical activity in Spanish children and to provide more efficient intervention programmes to prevent obesity. Therefore, some studies have been aimed to find out the patterns of physical activity in children and to compare them between overweight/obese and non-overweight/obese children⁵⁰ and also to assess the association be-

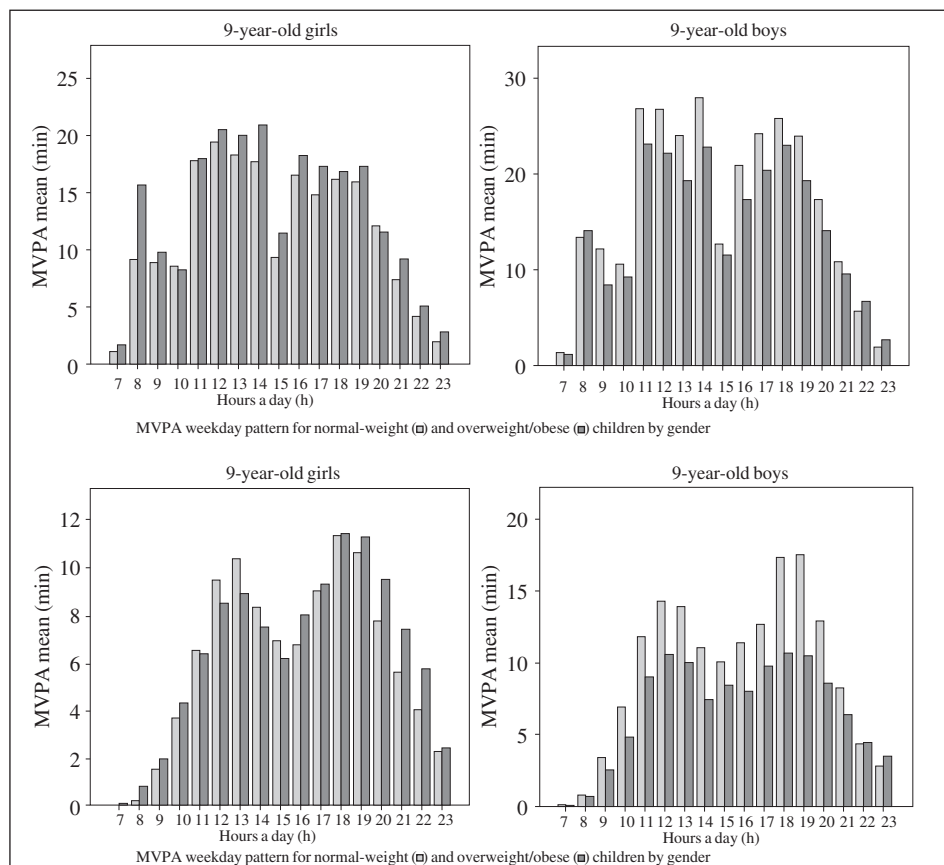


Fig. 5.—MVPA weekday and weekend day patterns in non-overweight/obese and overweight/obese 8-10 yr-old children. The EYHS study.

tween current physical activity guidelines and obesity in children⁵¹ (fig. 5). As an example, one of the studies performed in Spain was a part of the EYHS and involved a total of 439 children (233 girls, 216 boys) aged 8-10 y, with the main outcomes as follows: a) children's MVPA levels are more closely associated to gender than to obesity status, b) children tend to be more active during school periods, however they achieved a low amount of MVPA and c) 60 minutes of MVPA is inversely associated with overweight and obesity risk; however, vigorous physical activity (VPA) is a more important component and it should be specifically included into the children physical activity recommendations⁵⁰⁻⁵².

These results emphasize the relevance of physical activity in children to prevent obesity. This outcome showed the need to focus on VPA opportunities and these efforts should be carried out particularly outside school time (afternoon-evening time).

Sedentariness: on the threshold of inflammatory processes

The New England Journal of Medicine 2008 has pointed out the importance of skeletal-muscle homeostasis⁵³. Skeletal-muscle fibres can produce several hundred secreted factors, including proteins, growth factors, cytokines, with such secretory capacity increasing during muscle contractions, myogenesis or after exercise training. Several studies conducted have considered the potential impact of sarcopenia on metabolic function, chronic disease, and mortality⁵⁴. Acutely, i.e. in response to a single bout of exercise, a pro-inflammatory response is generated (increase in circulating number and function of leukocytes and in systemic concentrations of pro-inflammatory cytokines and chemokines), whose damaging potential is limited by simultaneous activation of anti-inflammatory mechanisms^{16,55}. Conversely, repeated exercise training results in significant reduction of the systemic inflammatory state⁵⁶. The overall health effects of exercise are therefore induced by the correct balance between these apparently opposed pro- and anti-inflammatory effects⁵⁷. The physiological relevance of pro- and anti-inflammatory effects of exercise will be also depending on the inflammatory status of people performing exercise, especially in individuals with low-grade inflammatory diseases⁵⁸⁻⁶⁰.

Cardiovascular diseases (CVD) are the principal causes of death in developed countries⁶¹. It is well documented that the genesis of CVD occurs in early ages⁶²⁻⁶⁴, although the clinical symptoms are not clearly observed until adulthood⁶⁵. The trigger of CVD is the atherosclerosis, which involves an inflammatory process during the atherogenesis with a continued and substantial increase of inflammatory cytokines and acute-phase reactant levels within the arterial wall^{65,66}. Since CVD risk factors usually track from childhood to adulthood⁶⁷, a healthy lifestyle beginning in early ages is the focus of public health strategies.

Sedentary lifestyle has officially been recognized as a major risk factor for CVD, being responsible for 6% of the major CVD mortality, which makes inactivity comparable to well-known risk factors such as smoking and obesity⁶⁸. Information on the detrimental effect of sedentariness (mainly sitting) on health is relatively new, but there is compelling evidence for its key role on CVD mortality, regardless of physical activity³⁵. Since both physical activity and sedentary behaviours have been identified as crucial risk factors for CVD mortality, public health interventions to (i) increase physical activity and (ii) decrease sedentary behaviour in children and adolescents might have the potential to provide health protection against future CVD.

To date, there are a few studies that examined whether regular physical activity influences the inflammatory process in children and adolescents. The main findings in such studies suggest that the total amount and intensity of physical activity (i.e. light, moderate and vigorous intensities) are not directly associated with inflammatory markers in youth, but it would have a crucial indirect role through increasing cardiorespiratory fitness and decreasing body fat^{63,64,69,70}. The majority of Spanish adults and children do not engage in enough physical activity to be beneficial for health⁴⁷. Regarding the influence of sedentary behaviour on inflammation in these ages, nowadays there is limited evidence to draw any conclusion. Overall, some studies that used accelerometers for assessing sedentary time found null associations with inflammatory biomarkers in youth^{71,72}. Also, there is some evidence that high levels of television viewing might have an indirect role on the inflammatory process in youth because this behaviour is associated with unhealthy dietary patterns⁷¹. Further longitudinal or clinical trials will provide insights into the role of physical activity and sedentary behaviour on inflammation in young people.

The interrelationship between physical activity and the immune system

It is well known that, together with skeletal muscle, metabolic and cardiovascular systems, physical activity also strongly modulates the immune system⁷³⁻⁷⁵. As a consequence, people who perform some type of sport regularly have been associated with less susceptibility to infection compared with sedentary people. However, while regular moderate exercise is very likely to be associated with decreased susceptibility to infection, intense exercise has been associated with symptoms of transient immunodepression, leading to increased susceptibility to infection, especially in high competition athletes^{74,76-78}. Thus, as on the other physiological systems, the effects of exercise on the immune system also depend on the frequency, intensity, and duration. Nevertheless, there has been an excessive generalization of the idea that, while moderate exercise is beneficial, intense exercise is harmful for the immune system. This general finding cannot be extended to the

innate/inflammatory response mediated by phagocytes, which can be stimulated even after intense sessions of exercise. The reduction of the functional capacity of lymphocytes in situations of excessive intense exercise can induce a temporary immunosuppression that allows microorganisms time to evade immunological recognition and become established, giving rise to infections in athletes. Innate immune defences may play an important role in the defence against infection of sportspeople, probably preventing the entry and maintenance of the antigen in situations where the adaptive immune response is depressed⁷⁴. Indeed, the stimulation of the innate/inflammatory responses during strenuous physical activity might counterbalance the decreased lymphocyte activity, and this may be regarded as an adaptation of this response to exercise-stress situations, in which stress hormones and mediators are involved (fig. 6)⁷⁹.

It is also necessary to take into account that while innate and/or inflammatory responses are crucial in host defence for healthy people, uncontrolled inflammatory reactions may be responsible for the initiation and progression of autoimmune and inflammatory diseases. Thus, many of the benefits induced by exercise have been proposed to be mediated by the induction of an anti-inflammatory response^{58,80}. However, it is not formally proven whether an induced anti-inflammatory effect of exercise in healthy people, with an optimal inflammatory regulation could be beneficial for an optimal regulation of homeostasis. Then, the potential anti-inflammatory effects of exercise would be positive only for those people with unhealthy high inflammatory status⁵⁸. In addition, while cellular oxidative stress is dangerous for most of the cells, this process is necessary for phagocytes in order to destroy pathogens, and phagocytic cells also need a good balance between oxidative and anti-oxidative mechanisms. From an im-

munophysiological perspective, anti-oxidant and anti-inflammatory supplements make sense especially when one physical activity induces excessive oxidative/inflammatory response⁸¹.

In this context, physical exercise has been found to improve the overall health of people suffering from certain autoimmune diseases such as the case of children with cystic fibrosis, who often have to be hospitalized because of acute exacerbation of their immune system exhibiting respiratory symptoms. Therefore, this is a powerful prognostic factor since aerobic fitness is associated with lower risk of hospitalization in children with cystic fibrosis, given that physical exercise can reduce the decline in VO₂ peak that occurs in these patients⁸².

Physical activity/exercise as a therapy

Cardiovascular diseases

Exercise training has been shown to exert a restoring/improving effect on endothelial function⁸³, which is shown to be a risk factor for CVD. Longitudinal studies have shown that increased levels of physical activity reduce thrombosis-related cardiovascular events⁸⁴.

Diabetes

A meta-analysis has demonstrated that exercise training is associated with an overall 0.67% decline in glycosylated hemoglobin levels. This reduction, derived from the exercise, is similar to that reached by treatment of oral antidiabetic drugs⁸⁵.

A more recent meta-analysis of randomized control trials has shown a significant decrease in triglycerides

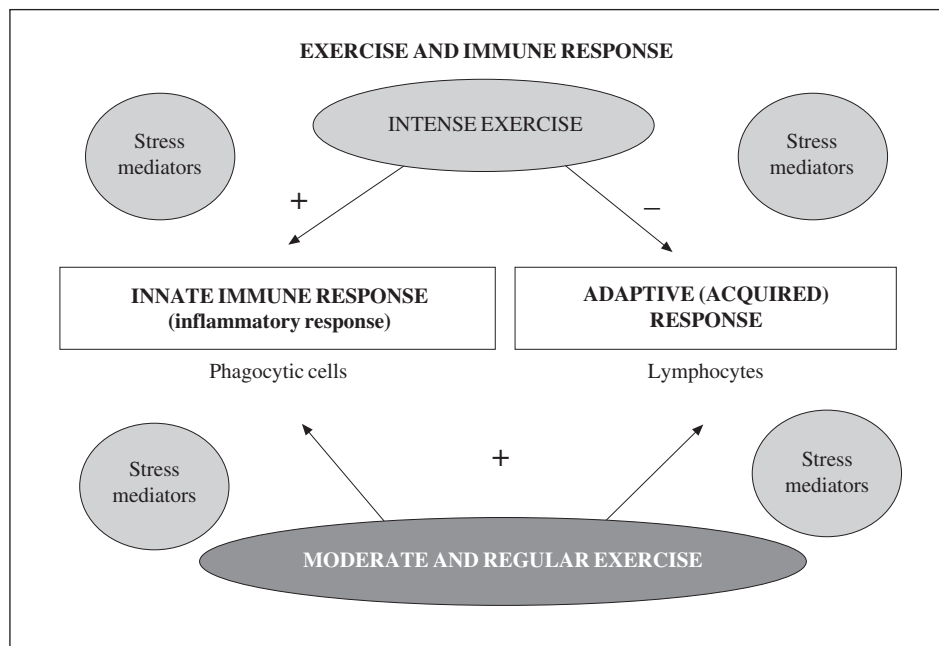


Fig. 6.—The stimulation of the innate/inflammatory responses during strenuous physical activity/exercise might counterbalance the decreased lymphocyte activity as an adaptation of this response to exercise-stress situations, in which stress mediators are involved.

after exercise interventions but no effects were found on total cholesterol, high-density lipoprotein cholesterol or low-density lipoprotein cholesterol. A meta-analysis was recently conducted on both the efficacy and tolerability of *polypills*⁸⁶ in 2,218 subjects (fig. 7). The authors concluded that the *polypills* can reduce blood pressure and lipids in comparison with a placebo group and the differences found in both groups about the tolerability of *polypills* were moderate. Therefore, further studies are necessary to elucidate the status of *polypills* in primary care and prevention strategies.

Obesity

With the aim of losing weight there are more and more alternative programmes and therapies that include different types of exercise along with dietary

food products, specific diets, besides of surgical methods, certain drugs and finally “miracle” type products.

However, it is important to highlight that thousands of these supposed miracle products and exercises very frequently show up in developed countries, claiming any number of healthy advantages, although there is always a lack of scientific precision. Facing to the difficulties found to lose weight the consumers still wonder about the reasons and about the short period of success if any. In this scene, the consumer should be helped by health professionals to dispel any doubt about what may be valid or under which circumstances these alternatives can be applied.

The most agreed explanation is the multifactorial component of overweight/obesity, such it can be seen at the following website: <http://www.shiftn.com/obesity/Full-Map.html> where many factors are involved, such as: energy balance, individual, social or collective

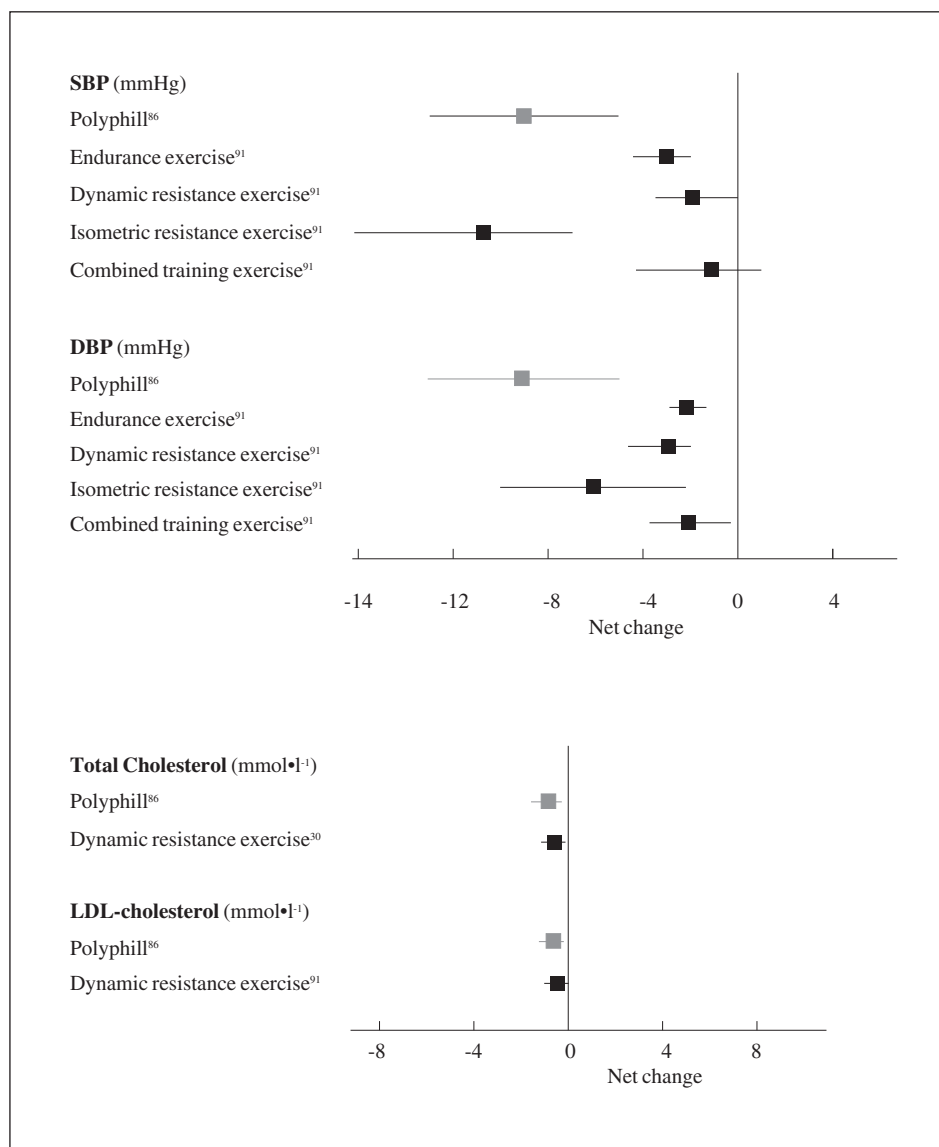


Fig. 7.—Comparison on the effects of the polypill vs. exercise interventions on outcomes related to CDV risk using data from meta-analyses⁸².

psychological factors, individual and social factors of physical activity, energy consumption, access to food products, individual or collective physiological factors (genetic, epigenetic, etc.). This is the reason why those interventions available to combine a large group of factors are more sensible to achieve success.

Certainly, in the area of physical activity it is necessary to further fight for achieving successful goals by avoiding myths such as the use of abdominal exercise⁸⁷ or vibration platforms⁸⁸ to lose weight. Even the apparently best classic cardiovascular exercise has been evaluated and discredited in an interesting meta-analysis showing that isolated cardiovascular exercise only causes an average weight loss of 1.7 kg in 12 months⁸⁹.

Aging

Moreover, regarding aging, physical activity has been shown as a protective agent of healthy mental and organic improvement, leading to an enhanced autonomy situation and thus, contributes to attenuate aging autonomic dysfunction and to the reduction of morbidity and mortality^{81,90}.

Final remarks

Hydration status and physical activity/exercise are very important concepts to work on to tackle inadequate nutritional situations and promote well-being. Further research studies are necessary regarding the measurement of the hydration status and the binomial physical activity/sedentariness as well as the doses of water intake supplied both by foods and beverages and the ideal proportion of physical activity/sedentariness to achieve the healthiest status by reducing disease risks.

In view of all the opinions expressed by the speakers according to their knowledge, there was a consensus about a guideline as a Decalogue with several advices related both to hydration and physical activity/exercise to achieve an adequate health status.

Decalogue: global recommendations to achieve an adequate hydration and physical activity status to avoid overweight/obesity consequences

Hydration

1. For the general population, intake of 2-2.5 litres (L)/day of fluids, including water, infusions, natural juices, soups and beverages, all of them in moderation and variety.
2. For sportspeople, intake of adequate amounts of liquids according to the training periods or during competitions (80-350 kcal/1,000 mL, of which at least 75%, simple carbohydrates, e.g. glucose), after training or competitions (300-

350 kcal/1,000 mL, of which at least 75% should come from a mix of high glycemic load carbohydrates such as glucose, sucrose, maltodextrins and fructose).

3. In order to avoid hyponatremia, sportspeople should drink beverages with appropriate amounts of sodium (460-1,150 mg/L) between 0.6-1.2 L/hour in long-term sport activities.

Food consumption

4. The dietary daily intake has to be balanced: 55-60% of total carbohydrates from which 5-10% should be simple carbohydrates; 30-35% fats as long as 10% are monounsaturated fatty acids, especially supplied by olive oil, 10% saturated fatty acids and 10% polyunsaturated fatty acids; and 10-12% protein, providing a high variety of different foods but in moderate amounts (less is more).
5. Consumption of 20-30 g/day fibre (including legumes, natural cereals and 3 portions/day of each vegetables and fruits)
6. An appropriate food behaviour consisting of 4-6 meals during the day (breakfast, mid-day snack, lunch, afternoon snack, dinner, after dinner snack) in adequate amounts and at the appropriate times.

Physical activity, exercise and sedentary behaviours

7. 420 minutes of moderate to vigorous physical activity per week for children and adolescents, and at least 3 days per week of vigorous-intensity physical activity
8. 150 minutes of moderate physical activity per week or 75 minutes at vigorous intensity for adults. Every minute of physical activity really does count and intensity plays an important role for health.
9. Sitting breaks every 30 minutes to avoid the negative consequences for health associated with prolonged sedentary behaviours.

Global remark

10. Globally, each person should find his/her own energy balance to achieve a healthy and well-being status through the establishment of an adequate nutritional, hydration and physical activity/inactivity status.

References

1. Serra-Majem L, Riobó Serván P, Belmonte Cortés S, Anadón Navarro A, Aranceta Bartrina J, Franco Vargas E, García-Closas

- R, Gómez-Candela C, Herrero Sancho E, La Vecchia C, López Díaz-Ufano ML, Varela-Moreiras G, Vázquez Castro J, Ribas-Barba L, Alcaraz-Cebrián F, García-Luna PP, González-Gomis M, González-Gross M, Granado de la Orden S, López-Sobaler AM, Moreno Villares JM, Ortega Anta RM, Pérez-Rodrigo C, Polanco Allué I, Urriale de Andrés R. Chinchón Declaration; Decalogue on low- and no-calorie sweeteners (LNCS). *Nutr Hosp* 2014; 29: 719-34.
2. Serra-Majem LI, Gil A on behalf of Palou A, Adan A, Anadón A, Marcos A, Murray B, Gómez-Candela C, Pérez-Rodrigo C, Maffei C, Ramón D, Benton D, Alonso-Aperte E, Martínez de Victoria E, O'Neal E, Varela-Moreiras G, Braun H, Polanco I, Araneta J, González-Alonso J, del Coso-Garrigós J, Kaiser KA, Kenney WL, Sardinha LB, Díaz-Rubio M, González-Gross M, Kapskefalou M, Nissensohn M, Millard-Stafford M, Sawka MN, Palacios N, Hébel P, Riobó P, Urriale R, Wirth R, Mora-Rodríguez R, Maughan RJ, Ortega RM, Gellert R, Shirreffs S, Partearroyo T. Conclusions of the I International and III National Hydration Congress Madrid, Spain 3rd and 4th December, 2013. *Rev Esp Nutr Comunitaria* 2014; 20 (Supl. 1): 2-12.
 3. Millard-Stafford M, Wendland DM, O'Dea NK, Norman TL. Thirst and hydration status in everyday life. *Nutr Rev* 2012; 70: S147-51.
 4. Popkin BM, D'Anci KE, Rosenberg IH. Water, hydration, and health. *Nutr Rev* 2010; 68: 439-58.
 5. Cheuvront SN, Ely BR, Kenefick RW, Sawka MN. Biological variation and diagnostic accuracy of dehydration assessment markers. *Am J Clin Nutr* 2010; 92: 565-73.
 6. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA); Scientific Opinion on Dietary reference values for water. *EFSA J* 2010; 8: 1459.
 7. Heymsfield SB, Wang Z, Visser M, Gallagher D. Techniques used in the measurement of body composition: an overview with emphasis on bioelectrical impedance analysis. *Am J Clin Nutr* 1996; 64: S478-84.
 8. Alvero-Cruz JR, Correas Gómez L, Ronconi M, Fernández Vázquez R, Porta Manzanido J. La bioimpedancia eléctrica como método de estimación de la composición corporal: Normas prácticas de utilización. *Rev And Med Deporte* 2011; 4: 167-74.
 9. Alvero-Cruz JR, Carnero EA, Barrera J, Quiterio A, Sardinha LB. A prediction Equation for total body water in Spanish Children. *Med Sci Sports Exerc* 2008; 40: S274.
 10. Armstrong LE. Assessing hydration status: the elusive gold standard. *J Am Coll Nutr* 2007; 26: S575-84.
 11. Jequier E, Constant F. Water as an essential nutrient: the physiological basis of hydration. *Eur J Clin Nutr* 2010; 64: 115-23.
 12. Kipps C, Sharma S, Pedoe DT. The incidence of exercise-associated hyponatraemia in the London marathon. *Br J Sports Med* 2011; 45: 14-9.
 13. Ortega FB, Ruiz JR, Castillo MJ, Gutierrez A. Hyponatremia in ultraendurance exercises. Effects on health and performance. *Arch Latinoam Nutr* 2004; 54: 155-64.
 14. Baker LB, Lang JA, Kenney WL. Quantitative analysis of serum sodium concentration after prolonged running in the heat. *J Appl Physiol* (1985) 2008; 105: 91-9.
 15. Noakes TD. Changes in body mass alone explain almost all of the variance in the serum sodium concentrations during prolonged exercise. Has commercial influence impeded scientific endeavour? *Br J Sports Med* 2011; 45: 475-7.
 16. Giraldo E, García JJ, Hinchado MD, Ortega E. Exercise intensity-dependent changes in the inflammatory response in sedentary women: Role of neuroendocrine parameters in the neutrophil phagocytic process and the pro-/anti-inflammatory cytokine balance. *Neuroimmunomodulation* 2009; 14: 237-44.
 17. Royal Decree 2885/1976 of 16 October and modified as 1444/2000 of 31 July. Spanish National Bulletin 183, 1st August 2000.
 18. Report of the Scientific Committee on Food on composition and specification of food intended to meet the expenditure of intense muscular effort, especially for sportsmen. Access 20/03/2006. URL: http://europa.eu.int/comm/food/fs/sc/out64_in.pdf
 19. Morillas-Ruiz J, Zafrilla P, Almar M, Cuevas MJ, Lopez FJ, Abellan P, Villegas JA, Gonzalez-Gallego J. The effects of an antioxidant-supplemented beverage on exercise-induced oxidative stress: results from a placebo-controlled double-blind study in cyclists. *Eur J Appl Physiol* 2005; 95: 543-9.
 20. Blomstrand E, Saltin B. BCAA intake affects protein metabolism in muscle after but not during exercise in humans. *Am J Physiol Endocrinol Metab* 2001; 281: 365-74.
 21. Tipton KD, Elliott TA, Cree MG, Wolf SE, Sanford AP, Wolfe RR. Ingestion of casein and whey proteins result in muscle anabolism after resistance exercise. *Med Sci Sports Exerc* 2004; 36: 2073-81.
 22. Palacios N, Bonafonte L, Manonelles P, Manuz B, Villegas JA. Consensus on drinks for the sportsman. Composition and guidelines of replacement of liquids. Document of consensus of the Spanish Federation of Sports Medicine. *Arch Med Deporte* 2008; 25: 245-58.
 23. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; 100: 126-31.
 24. Lee IM, Paffenbarger RS Jr., Hennekens CH. Physical activity, physical fitness and longevity. *Aging (Milano)* 1997; 9: 2-11.
 25. Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *New Eng J Med* 1986; 314: 605-13.
 26. Elrick H. Exercise is medicine. *Phys Sportsmed* 1996; 24: 72-6.
 27. Burnham JM. Exercise is medicine: health benefits of regular physical activity. *J La State Med Soc* 1998; 150: 319-23.
 28. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000; 343: 16-22.
 29. Blair SN. Physical inactivity: the biggest public health problem of the 21st century. *Br J Sports Med* 2009; 43: 1-2.
 30. Timmons JA, Knudsen S, Rankinen T, Koch LG, Sarzynski M, Jensen T, Keller P, Scheele C, Vollaard NB, Nielsen S, Akerström T, MacDougall OA, Jansson E, Greenhaff PL, Tarnopolsky MA, van Loon LJ, Pedersen BK, Sundberg CJ, Wahlestedt C, Britton SL, Bouchard C. Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* (1985) 2010; 108: 1487-96.
 31. Booth FW, Laye MJ, Lees SJ, Rector RS, Thyfault JP. Reduced physical activity and risk of chronic disease: the biology behind the consequences. *Eur J Appl Physiol* 2008; 102: 381-90.
 32. World Health Organization. Global Recommendations on Physical Activity For Health. Geneva, Switzerland: WHO Press, 2010.
 33. Moore SC, Patel AV, Matthews CE, Berrington de Gonzalez A, Park Y, Katki HA, Linet MS, Weiderpass E, Visvanathan K, Helzlsouer KJ, Thun M, Gapstur SM, Hartge P, Lee IM. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. *PLoS Med* 2012; 9: e1001335.
 34. Booth FW, Lees SJ. Fundamental questions about genes, inactivity, and chronic diseases. *Physiol Genomics* 2007; 28: 146-157.
 35. Owen N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010; 38: 105-13.
 36. Oliva J, González L, Labeaga JM, Álvarez Dardet C. Salud pública, economía y obesidad: el bueno, el feo y el malo. *Gaceta Sanitaria* 2008; 22: 507-10.
 37. Sánchez RV, Lopez-Alemany JM. Los costes de la obesidad alcanzan el 7% del gasto sanitario. *Rev Esp Econ Salud* 2002; 3: 41-2.
 38. U.S. Department of Health and Human Services; Physical Activity Guidelines Advisory Committee. Physical activity guidelines for Americans. 2008. <http://www.health.gov/PAGuidelines/>. Accessed 5 February 2010.
 39. World Health Organization. WHO/NMH/NPH/PAH/03.2 Health and Development Through Physical Activity and Sport. World Health Organization Noncommunicable Diseases and Mental Health Noncommunicable Disease Prevention and Health Promotion. 2003. http://whqlibdoc.who.int/hq/2003/WHO_NMH_NPH_PAH_03.2.pdf
 40. Jonas S, Phillips E. *ACSM' Exercise is Medicine. A Clinician's Guide to Exercise Prescription*. 2009, Philadelphia: Walkers Kluwer.

41. Matute-Llorente A, Vicente Rodríguez G, Casajús JA. Bases generales de la prescripción de ejercicio físico. Ejercicio físico como prescripción terapéutica, in *Ejercicio físico y salud en poblaciones especiales*. EXERNET. (Casajús JA, Vicente Rodríguez G, eds.) 2011, Consejo Superior de Deportes: Madrid.
42. Fiuzza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the Real Polypill. *Physiology (Bethesda)* 2013; 28: 330-58.
43. Ortega FB, Konstabel K, Pasquali E, Ruiz JR, Hurtig-Wennlof A, Maestu J, Löf M, Harro J, Bellocco R, Labayen I, Veidebaum T, Sjöström M. Objectively Measured Physical Activity and Sedentary Time during Childhood, Adolescence and Young Adulthood: A Cohort Study. *PLoS One* 2013; 8: e60871.
44. Ekelund U, Sardinha LB, Anderssen SA, Harro M, Franks PW, Brage S, Cooper AR, Andersen LB, Riddoch C, Froberg K. Associations between objectively assessed physical activity and indicators of body fatness in 9- to 10-y-old European children: a population based study from 4 distinct regions in Europe (the European Youth Heart Study). *Am J Clin Nutr* 2004; 80: 584-90.
45. Ortega FB, Ruiz JR, Sjöström M. Physical activity, overweight and central adiposity in Swedish children and adolescents: the European Youth Heart Study. *Int J Behav Nutr Phys Act* 2007; 4: 61.
46. Ruiz JR, Ortega FB. Physical activity and cardiovascular disease risk factors in children and adolescents. *Curr Cardiovasc Risk Rep* 2009; 3: 281-7.
47. Aznar S, Naylor PJ, Silva P, Pérez M, Angulo T, Laguna M, Lara MT, López-Chicharro J. Patterns of physical activity in Spanish children: a descriptive pilot study. *Child Care Health Dev* 2011; 37: 322-8.
48. Biddle S, Cavill N, Sallis JF. Policy framework for young people and health-enhancing physical activity. In: Biddle S, Sallis JF, Cavill N, editors. *Young and Active? Young People and Health-Enhancing Physical Activity: Evidence and Implications*. London, England: Health Education Authority; 1998.
49. Cavill N, Biddle S, Sallis JF. Health Enhancing Physical Activity for Young People: Statement of the United Kingdom Expert Consensus Conference. *Pediatr Exerc Sci* 2001; 13: 12.
50. Laguna M, Ruiz JR, Gallardo C, García-Pastor T, Lara MT, Aznar S. Obesity and physical activity patterns in children and adolescents. *J Paediatr Child Health* 2013; 49: 942-9.
51. Laguna M, Ruiz JR, Lara MT, Aznar S. Recommended levels of physical activity to avoid adiposity in Spanish children. *Pediatr Obes* 2013; 8: 62-9.
52. Martínez-Gómez D, Ruiz JR, Ortega FB, Casajús JA, Veiga OL, Widhalm K, Manios Y, Béghin L, González-Gross M, Kafatos A, España-Romero V, Molnar D, Moreno LA, Marcos A, Castiello MJ, Sjöström M; on behalf of the HELENA study group. Recommended levels and intensities of physical activity to avoid low cardiorespiratory fitness in European adolescents. The HELENA Study. *Am J Human Biol* 2010; 22: 750-6.
53. Laurie J Goodyear The exercise pill- too good to be true? *N Engl J Med* 2008; 359: 1842-4.
54. Karakelides H, Nair KS. Sarcopenia of aging and its metabolic impact. *Curr Top Dev Biol* 2005; 68: 123-48.
55. Ploeger HE, Takken T, de Greef MH, Timmons BW. The effects of acute and chronic exercise on inflammatory markers in children and adults with a chronic inflammatory disease: a systematic review. *Exerc Immunol Rev* 2009; 15: 6-41.
56. Nemet D, Oh Y, Kim H-S, Hill MA, Cooper DM. The effect of intense exercise on inflammatory cytokines and growth mediators in adolescent boys. *Pediatrics* 2002; 110: 681-9.
57. Cooper DM, Nemet D and Galassetti P. Exercise, stress, and inflammation in the growing child: from the bench to the playground. *Curr Opin Pediatr* 2004; 16: 286-92.
58. Ortega E, García JJ, Bote ME, Martín-Cordero L, Escalante Y, Saavedra JM, Northoff H, Giraldo E. Exercise in fibromyalgia and related inflammatory disorders: known effects and unknown chances. *Exerc Immunol Rev* 2009; 15: 42-65.
59. Martín-Cordero L, García JJ, Hinchado MD, Ortega E. The interleukin-6 and noradrenaline mediated inflammation-stress feedback mechanism is dysregulated in metabolic syndrome: Effect of exercise. *Cardiovasc Diabetol* 2011; 10: 42.
60. Bote ME, García JJ, Hinchado MD, Ortega E. Fibromyalgia: Anti-inflammatory and stress responses after acute moderate exercise. *PlosOne* 2013; 8: e74524.
61. World Health Organization. The top 10 causes of death. Media Centre. <http://who.int/mediacentre/factsheets/fs310/en/index2.html>
62. Wärnberg J, Nova E, Moreno LA, Romeo J, Mesana MI, Ruiz RJ, Ortega FB, Sjöström M, Bueno M, Marcos A, and the AVENA study group. Inflammatory proteins are related with total and abdominal adiposity in a healthy adolescent population. The AVENA study. *Am J Clin Nutr* 2006; 84: 505-12.
63. Martínez-Gómez D, Eisenmann JC, Wärnberg J, Gomez-Martínez S, Veses A, Veiga OL, Marcos A; AFINOS Study Group. Associations of physical activity, cardiorespiratory fitness and fatness with low-grade inflammation in adolescents: the AFINOS Study. *Int J Obes (Lond)* 2010; 34: 1501-7.
64. Martínez-Gómez D, Eisenmann JC, Healy GN, Gomez-Martínez S, Diaz LE, Dunstan DW, Veiga OL, Marcos A; AFINOS Study Group. Sedentary behaviors and emerging cardiometabolic biomarkers in adolescents. *J Pediatr* 2012; 160: 104-10.
65. Insull W Jr. The pathology of atherosclerosis: plaque development and plaque responses to medical treatment. *Am J Med* 2009; 122: S3-14.
66. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 2005; 352: 1685-95.
67. Camhi SM, Katzmarzyk PT. Tracking of cardiometabolic risk factor clustering from childhood to adulthood. *Int J Pediatr Obes* 2010; 5: 122-9.
68. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT; Lancet Physical Activity Series Working Group. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012; 380: 219-29.
69. Thomas NE, Williams DR. Inflammatory factors, physical activity, and physical fitness in young people. *Scand J Med Sci Sports* 2008; 18: 543-56.
70. Carson V, Ridgers ND, Howard BJ, Winkler EA, Healy GN, Owen N, Dunstan DW, Salmon J. Light-Intensity Physical Activity and Cardiometabolic Biomarkers in US Adolescents. *PLoS One* 2013; 8: e71417.
71. Martínez-Gómez D, Gomez-Martínez S, Ruiz JR, Diaz LE, Ortega FB, Widhalm K, Cuenca-García M, Manios Y, De Vriendt T, Molnar D, Huybrechts I, Breidenassel C, Gottrand F, Plada M, Moreno S, Ferrari M, Moreno LA, Sjöström M, Marcos A; HELENA Study Group. Objectively-measured and self-reported physical activity and fitness in relation to inflammatory markers in European adolescents: the HELENA Study. *Atherosclerosis* 2012; 221: 260-7.
72. Carson V, Janssen I. Volume, patterns, and types of sedentary behavior and cardio-metabolic health in children and adolescents: a cross-sectional study. *BMC Public Health* 2011; 11: 274.
73. Barriga C, Pedrera MI, Maynar M, Maynar J, Ortega E. Effect of submaximal physical exercise performed by sedentary men and women on some parameters of the immune system. *Rev Esp Fisiol* 1993; 49: 79-85.
74. Ortega-Rincon E. Physiology and Biochemistry: Influence of exercise on phagocytosis. *Int J Sport Med* 1994; 15: 172-4.
75. Ruiz JR, Ortega FB, Wärnberg J, Moreno LA, Carrero JJ, González-Gross M, Marcos A, Gutiérrez A, Sjöström M. Inflammatory proteins and muscle strength in adolescents; The AVENA Study. *Arch Pediatr Adolesc Med* 2008; 162: 462-8.
76. Ortega E, Barriga C, De la Fuente M. Study of the phagocytic process in neutrophils from elite sportswomen. *Eur J Appl Physiol* 1993; 66: 37-42.
77. Wärnberg J, Cunningham KM, Romeo J, Marcos A. Physical activity, exercise and low-grade systemic inflammation. *Proc Nutr Soc* 2010; 69: 400-6.
78. Romeo J, Wärnberg J, Pozo T, Marcos A. Physical activity, immunity and infection. *Proc Nutr Soc* 2010; 69: 390-9.
79. Ortega E. Neuroendocrine mediators in the modulation of phagocytosis by exercise: physiological implications. *Exerc Immunol Rev* 2003; 9: 70-94.
80. Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol* 2005; 98: 1154-62.

81. De la Fuente M, Cruces J, Hernández O, Ortega E. Strategies to improve the functions and redox state of the immune system in aged subjects. *Curr Pharm Des* 2011; 19: 3966-93.
82. Pérez M, Groeneveld IF, Santana-Sosa E, Fiuza-Luces C, Gonzalez-Saiz L, Villa-Asensi JR, López-Mojares LM, Rubio M, Lucia A. Aerobic fitness is associated with lower risk of hospitalization in children with cystic fibrosis. *Pediatric Pulmonol* 2013 Sep 9. doi: 10.1002/ppul.22878. [Epub ahead of print].
83. DeSouza CA, Shapiro LF, Clevenger CM, Dinunno FA, Monahan KD, Tanaka H, Seals DR. Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation* 2000; 102: 1351-7.
84. Laufs U, Werner N, Link A, Endres M, Wassmann S, Jurgens K, Miche E, Bohm M, Nickenig G. Physical training increases endothelial progenitor cells, inhibits neointima formation, and enhances angiogenesis. *Circulation* 2004; 109: 220-6.
85. Li TL, Gleeson M. The effects of carbohydrate supplementation during the second of two prolonged cycling bouts on immunoenocrine responses. *Eur J Appl Physiol* 2005; 95: 391-9.
86. Elley CR, Gupta AK, Webster R, Selak V, Jun M, Patel A, Rodgers A, Thom S. The efficacy and tolerability of 'polypills': meta-analysis of randomized controlled trials. *PLoS One* 2012; 7: e52145.
87. Vispute SS, Smith JD, LeCheminant JD, Hurley KS. The effect of abdominal exercise on abdominal fat. *J Strength Cond Res* 2011; 25: 2559-64.
88. Vissers D, Verrijken A, Mertens I, Van Gils C, Van de Sompel A, Truijen S, Van Gaal L. Effect of long-term whole body vibration training on visceral adipose tissue: a preliminary report. *Obes Facts* 2010; 3: 93-100.
89. Thorogood A, Mottillo S, Shimony A, Filion KB, Joseph L, Genest J, Pilote L, Poirier P, Schiffrin EL, Eisenberg MJ. Isolated aerobic exercise and weight loss: a systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2011; 124: 747-55.
90. Joyner MJ, Green DJ. Exercise protects the cardiovascular system: effects beyond traditional risk factors. *J Physiol* 2009; 587: 5551-8.
91. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and metaanalysis. *J Am Heart Assoc* 2013; 2: e004473.