



Food and Health


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Executive Summary

SCENARIO

This study has been based on a number of fundamental **logical and conceptual premises** which are: the growing importance of prevention within the overall health policies of countries; increased awareness of the impact of lifestyles and diet, in particular, on individual health; the difficulty in implementing suitable prevention policies and the search for best practices in this area.

Within the context of these baseline considerations, our study concentrates on the issue of **prevention**, examining in particular the area of **diet** - which constitutes its specific area of examination - and it offers **concrete proposals for the future** in the form of the recommendations presented below.

In terms of human health, starting in the second half of the 20th century, we witnessed a gradual change in the eating-health pattern of human beings that could be called an actual "diet and health" shift. **Four main phenomena** characterized the change over the last 50 years: **scientific-medical progress; increase in average life expectancy; gradual transformation in diseases; a significant change in diet and lifestyle** towards a reduction in physical activity and an increase in the average amount of calories intaken.

The role of diet is increasingly key in the prevention of some diseases, such as chronic diseases, that have registered a significant increase within the population on a global level in recent decades.

Noncommunicable diseases, such as cardiovascular disease, diabetes and cancer, are today the main risk to human health, as well as an enormous social-economic burden for the community as a whole.

These diseases are responsible for the majority of deaths and each year cause nearly **35 million deaths**. This corresponds to **60% of all deaths on a global level and 80% of those in low- and medium-income countries**. Major studies have shown that approximately **80% of the cases tied to these diseases could be prevented by eliminating a number of risk factors, such as consumption of tobacco, unhealthy diet, physical inactivity and excessive alcohol consumption**. Contrarily, without suitable prevention, their impact on world health could increase by 17% over the next ten years.

Focusing the analysis on the dietary factor, it can be

seen that **in almost all countries in the world there is an exponential growth in the phenomenon of obesity**. This trend is so pronounced that it has led the *European Association for the Study Of Diabetes* (EASD) to recognize the prevention and **treatment of obesity as "the most important public health problem throughout the world"**. More than 65% of Americans are obese or overweight and the number of cases of overweight youth has tripled from 1970 to the present.

What emerges strongly from the numerous leading medical-scientific studies published, is that poor dietary habits are one of the most important factors in the increased risk of cardiovascular disease. Regarding this, the World Health Organization has indicated that in 2005 there were approximately **17.5 million deaths due to cardiovascular disease** throughout the world, a number equal to **30% of all deaths**. Of these, 7.6 million were due to cardiac problems and 5.7 million to stroke.

Forecasts indicate that by **2015, the number of deaths caused by cardiovascular disease on a global level will rise to 20 million individuals**, confirming itself as the no. 1 cause of death in the world.

Translated into monetary terms, the sums involved are astounding. Most recent forecasts of the **total cost of cardiovascular disease in the United States** indicate an impact of **473.3 billion dollars** for the year 2009. This amount includes both direct healthcare costs (hospital services, drugs, home care, etc.), as well as indirect costs calculated as a loss of work productivity caused by the disease or premature death of patients. In **Europe**, the overall economic impact of cardiovascular disease for the year 2006 was approximately **192 billion euros**; this corresponds to an **average per capita cost of 391 euros**.

In terms of diabetes, another disease significantly influenced by dietary habits, for people between 20 and 79 years of age, in 2007 it was estimated that the **worldwide incidence of this disease was around 6.0%**, equal to **approx. 246 million people**, with an increase of approx. 27% from 2003 (when it was estimated that 194 million people were affected by the disease). Each year around the globe, **more than 7 million new cases of diabetes are reported** (one every 5 seconds). **Estimates up to the year 2025** indicate a significant increase in incidence, reaching **7.1% of the world population to involve 380 million people**, for an increase of 54.5% compared with 2007.

As in the case of cardiovascular disease, the treatment costs for diabetes are very high and, according to estimates of the International Diabetes Federation, in 2007 they were around **232 billion dollars on a worldwide level**, increasing up to **300 billion dollars by 2025**.

From the studies analyzed, it was seen that, once again, improper diet is a factor in the increase of the risk of cancer. According to World Health Organization data, in 2007 there were **7.9 million deaths** in the world **due to tumors**; of these, three-quarters were in medium-to-low income countries. Estimates for the future indicate a **growth** worldwide in **deaths caused by tumors** up to a level of **9 million in 2015** and **11.4 million in 2030**, the net majority of which will be in medium-to-low income countries.

According to estimates by the US National Institutes of Health, in 2008, the **economic impact of cancer** was over **228 billion dollars**, including both healthcare costs and productivity loss of those ill. In terms of **Europe (EU-25)**, in 2002 cancer was responsible for a loss of **almost 10 million years**, equivalent to approx. 16.7% of the total life years lost by European citizens due to illness¹. In 2004, **direct cancer-related health-care costs alone in Europe** were estimated by the European Society for Medical Oncology to be **56.6 billion euros**.

The extent of the social-economic impact attributable to cardiovascular disease, diabetes and cancer is so significant that an in-depth study must be undertaken on the role played by the various dietary and behavioral choices (physical activity being the most important) in the risk of main chronic diseases.

In particular, the **main evidence from the international scientific literature on the relationship between diet and cardiovascular disease, diabetes and cancer** was examined and **evaluated**, underscoring the connections between the **consumption** of a wide range of **macro- and micronutrients** and the **risk of the onset of these diseases**.

The subsequent phase of the analysis process was the translation of this complex and quite technical evidence into dietary and behavioral recommendations, that can be comprehended even by a non-specialist reader.

From the studies performed it was then possible to formulate in-depth and comprehensible **nutritional and dietary recommendations** that **represent a synthetic and tangible tool** for the overall **prevention of chronic disease** and the attainment of **good health** on a general scale. On the basis of the analysis results, the recommendations for adopting a correct lifestyle and healthy eating habits are: engage in



regular physical activity, on average 30 to 60 minutes per day for most days of the week; **avoid becoming overweight/obese** both in the short-term as well as the long-term; **avoid excessive consumption of alcoholic beverages**, which means not more than one glass per day for women and two glasses per day for men; **do not smoke**; eat a **balanced diet**, in which the overall caloric intake is regulated and which includes the right mix of macro- and micronutrients; **increase** (up to approx. 400 grams per day) **intake of fruit and vegetables** which is equivalent to 4-5 servings; **prefer complex carbohydrates sources** and **increase the consumption of whole grains** (e.g., bread, pasta and breadsticks made with whole grain flour); **increase intake of legumes**; **consume 2-3 servings of fish per week**; favor the use of **vegetal condiments** (vegetable oils) over condiments with high animal-fat content (butter, lard); **limit intake of food with high fat content** (e.g., hot dogs, sauces, creams, dairy products, cured meats) preferring “low-fat” products (such as low-fat yogurt and skim milk); **limit intake of fried foods**; **limit consumption of meat and poultry to a maximum of 3-4 portions per week**; **limit use of added salt** over that normally contained in foods to not more than 5-6 g, equal approx. to a half teaspoon; **limit intake of foods/beverages with high sugar content** (e.g., baked goods and soft drinks); **avoid use of daily dietary supplements**.

Adopting behaviors in line with these recommendations seems capable of significantly preventing on a broad scale the risk of cardiovascular disease, diabetes and cancer.

After having identified the main dietary-related recommendations in the prevention of chronic disease, the diets most commonly-followed throughout the world were analyzed, the goal being to verify to what extent the findings and recommendations of published medical-scientific studies are adhered to.

Three wide-reaching gastronomic traditions were identified, each with its own characteristics: the Mediterranean model, the North American model and the Asian model (which includes a number of major subsets of tradition and culture, including Japanese, Vietnamese and Chinese).

The results of the analysis showed that, thanks to its strict similarity with the recommendations made on a scientific level, **the Mediterranean model is one of the most effective in terms of well-being and prevention of chronic disease**.

On the basis of these results, with the goal of measuring the extent to which a diet adheres - or diverges - from the Mediterranean diet, researchers and nutritionists have

developed a number of **Mediterranean adequacy indices** showing that, from the 1950s to the present, **throughout the Mediterranean area, including Italy**, there has been a **gradual abandonment of this diet in favor of less healthy dietary habits**.

If diet and life style constitute a fundamental part of effective preventive strategies in the onset of major chronic diseases, it seemed useful to attempt to **quantify the spin-offs** from the practical adoption of such strategies, not only in medical, but also in economic-financial terms.

Towards this purpose, a simulation model to analyze the **benefits of increasing resources destined for prevention in terms of reduced public health expenditure** was developed.

The **results of the simulation runs conducted showed that a 1% increase in the ratio of prevention expenditure to public health expenditure was correlated to a 3% reduction in the percentage of expenditure destined to treatment and rehabilitation services**.

For Italy in specific, the **net positive impact by the year 2050 of this increase was estimated at approx. 17 billion euros**, equal to a reduction of 0.6% in the ratio of public health expenditure to GDP.

Finally, as an example, from analysis of leading medical-scientific studies, it was seen that in Europe, adoption of a low-sodium (salt) diet alone **would avoid the 7% increase in coronary death risk**, equivalent to **3.4 billion euros per year of costs saved**, and **10% stroke risk**, equivalent to **3.8 billion euros per year of costs saved**.

In total, **reducing salt in the diet** (one of the factors tied to high blood pressure), **the benefits for European healthcare systems would be around 7.2 billion euros each year**.

To conclude, the analysis and simulation work carried out on the issue between prevention and diet, highlighted the existence of what we believe to be four areas for priority action: **promote healthy eating styles** on the basis of leading scientific studies; **improve available scientific knowledge** pointing out potentially interesting areas to be deeply analyzed through integrated and interdisciplinary research; **adopt social-healthcare policies aimed at spreading healthy dietary behavior**; **improve communication processes to adopt lifestyles and dietary behavior in line with available scientific knowledge**, with the aim to develop an educational path for the new generations.

NOTE EXECUTIVE SUMMARY

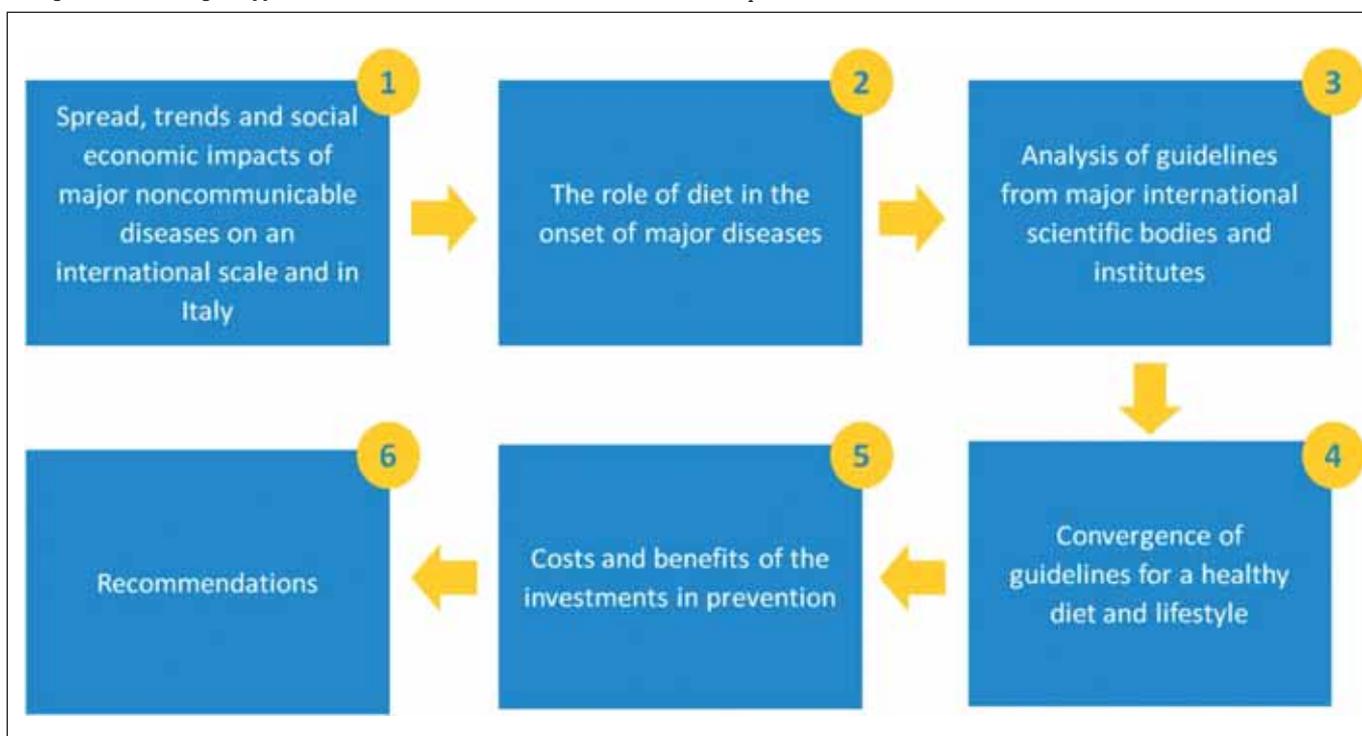
1. *To evaluate the social-economic impact of tumors see Chapter 1.*

Introduction

The role of diet seems increasingly key in the prevention of some diseases, like chronic ones, that have registered a significant increase in the population on a global level in recent decades.

The method of analysis adopted by the Barilla Center for Food & Nutrition, and in line with its mission, starts from this basic consideration to analyze in detail the impact of various diet-related factors on human health. The schema below (Figure 1) summarizes the approach followed.

Figure 1. Methodological approach



In light of the goal set, the main trends on a worldwide and Italian level were analyzed in relation to obesity and three groups of pathologies whose onset appear largely “tied” to diet, specifically cardiovascular disease, diabetes/metabolic syndrome and cancer. For these pathologies, the most recent scientific data available regarding their spread, mortality and social-economic impact were examined.

This analysis, concentrated in the first chapter of this report, clearly evidences the **growing incidence of these diseases** on an international level and brings a basic question to the fore

in a very compelling way: in what way is it possible to check the spread of chronic diseases that now also affect even the youngest age groups? Medical sources tell us that 80% of the cases connected to these diseases could be prevented by eliminating a number of risk factors. The most important among these are poor eating habits and lack of physical activity.

Analyzing in detail the role played by a range of dietary and behavioral choices (physical activity *in primis*) in the prevention of the most significant chronic diseases was the first logical step resulting from these observations. In particular, in Chapter 2, the main evidence from the international scientific

literature on the relationship between diet and cardiovascular disease, diabetes and cancer were examined, underscoring the connections between the consumption of a wide range of **macro- and micronutrients** and the risk of the onset of these diseases.

Translating this complex and quite technical evidence into dietary and behavioral recommendations that can be comprehended even by a non-specialist reader marked the subsequent phase in the analysis process. To do this in a rigorous and scientific manner, the third chapter provides

analysis of the guidelines of the most prestigious international scientific bodies and institutes in the area of proper diet and life styles for the prevention of chronic disease.

On the basis of the comparison between the various dietary and behavioral recommendations proposed on an international scale, a summary highlighting the points of similarity between the prevention approaches for individual chronic diseases was prepared. This made it possible to identify a **convergence of nutritional and dietary recommendations across-the-board** which - through the close interrelationship between dietary choices and life styles adopted - can represent a synthetic and tangible tool for overall prevention of chronic disease and attainment of good health on a general scale.

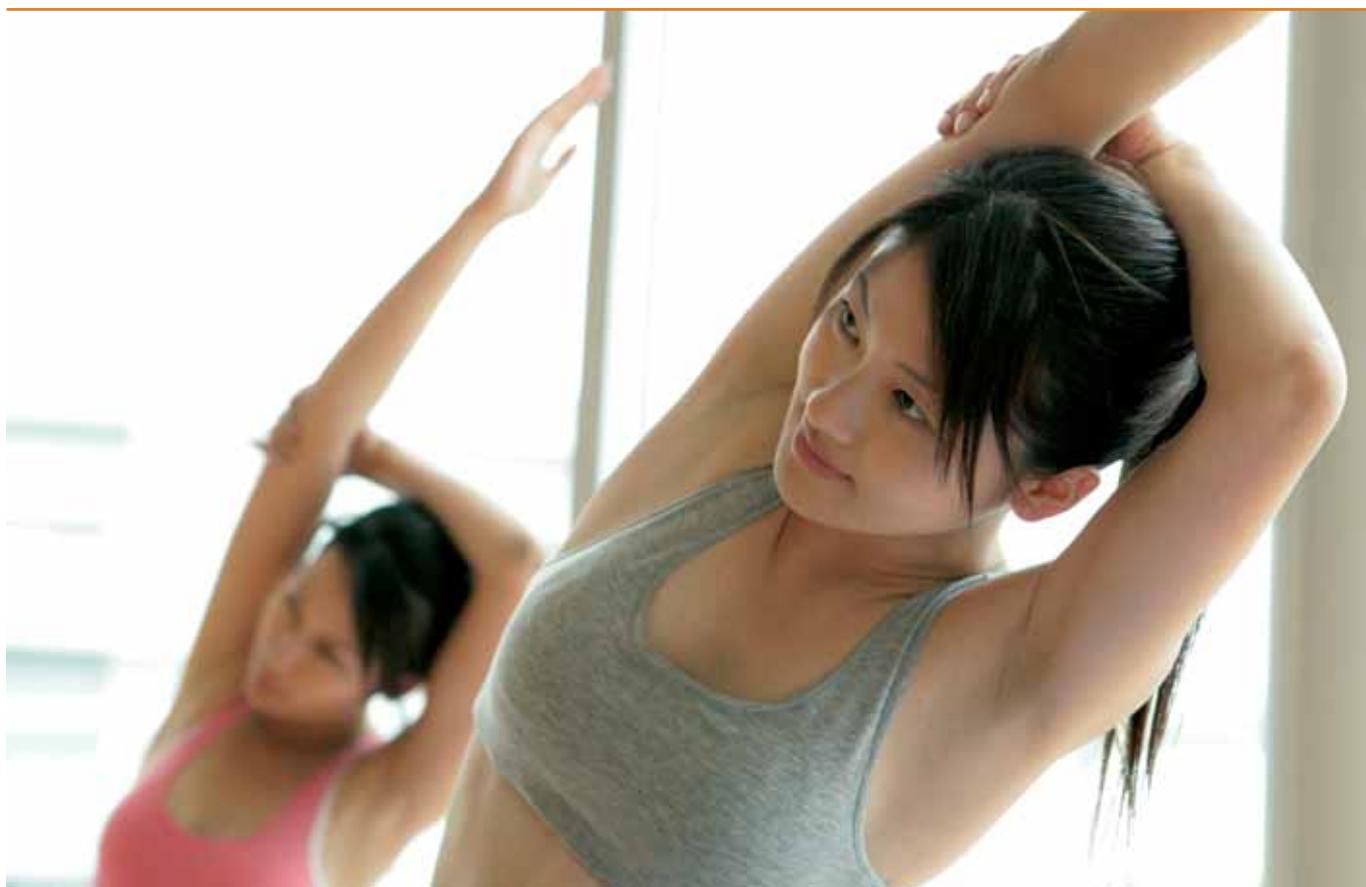
On the basis of these last considerations, Chapter 4 offers an analysis of the **adherence to the most widespread dietary regimens** to the principles identified for an healthy diet.

If diet and life style appear able to constitute a fundamental part of effective preventive strategies in the onset of major chronic diseases, it seemed useful to attempt to **quantify the spin-offs** from the practical adoption of such strategies, not only in medical, but also in economic-financial terms. This task of analysis and forecasting was done not only in general terms, but also in relation to the specific Italian situation. For this purpose, a simulation model was developed and this model,

together with the results generated by it, form the content of the fifth chapter.

Finally, on the basis of the data emerged, a number of very practical and concrete **recommendations** were developed which are aimed at all those directly or indirectly involved in promoting the growing spread and adoption of dietary approaches that aid individual well-being.

These observations and recommendations form the sixth and last chapter of this report that embodies, contemporaneously, a goal, certainty and hope. The goal of synthesizing all aspects which link diet to prevention through a wide-ranging, rigorous and scientific analysis; they are elements which are strictly tied to each other but are almost never considered together in those aspects in which they interrelate and intersect. The certainty of having brought together around the realization of this project some of the most skilled, experienced and highly-esteemed professionals in the field of medicine and prevention on a national and international level. There is no doubt but that the members of the Scientific Advisory Board of the Barilla Center for Food & Nutrition represent one of the greatest elements of value added in this study. The hope of being able to provide a concrete contribution to improving knowledge and definition of prevention policies and individual behaviors aimed at a tangible improvement in conditions of life and health in people, both today and tomorrow.



Part A: scenario

1. SPREAD, TRENDS AND ECONOMIC/SOCIAL IMPACT OF MAJOR NONCOMMUNICABLE DISEASES ON AN INTERNATIONAL SCALE AND IN ITALY

Noncommunicable diseases, especially cardiovascular disease, cancer, diabetes and chronic respiratory ailments, are today the main risk to human health on a worldwide basis, as well as an enormous social-economic burden for the community as a whole.

These four diseases are responsible for the majority of deaths and each year cause around **35 million deaths, 60% on a global level and 80% in low- and medium-income countries**¹.

It is estimated that **80% of the cases tied to these diseases could be prevented by eliminating a number of risk factors, such as consumption of tobacco, unhealthy diet, physical inactivity and excessive alcohol consumption**. Contrarily, without suitable prevention, their impact on world health could increase by 17% over the next ten years.

This chapter will present the most recent published data available regarding the spread, mortality rates and social-economic impact of the three groups of **diseases apparently most closely tied to diet**:

- cardiovascular disease;
- diabetes and metabolic syndrome;
- tumors.

It will be even analyzed what has become one of the most serious we have to face nowadays: the global spread of obesity.

1.1 Obesity and overweight

Almost all countries around the world are experiencing an exponential growth in the phenomenon of obesity and overweight² that has lead the European Association for the Study Of Diabetes (EASD) to recognize the prevention and treatment of obesity as *"the most important public health problem throughout the world"*.

Despite the fact that overweight and obesity can be found on an international level, there are some differences in the dynamic and seriousness of their diffusion in various geographical areas. Specifically, while in developing countries these problems are common, above all, in middle-aged adults and those with medium-high income, in high-income countries,

obesity and overweight are no longer common primarily in middle-aged adults and are pathologies increasingly found in young people and children, thus creating a serious situation and one that continues to worsen.

Although, as has been said, the United States is not an isolated case, it certainly represents the paradigmatic case of the trend in the spread of obesity and overweight. **More than 65% of all Americans are obese or overweight** and approximately 31% of the adult population (more than 61 million people) would seem to fall within the definition of obesity [an individual is defined as obese if his or her body mass index (BMI) exceeds 30]. The NIH (National Institutes of Health) further maintains that 4.7% of the adult population in America meets the criteria for what is defined "extreme obesity" (with a BMI over 40)³.

The seriousness of the spread of overweight and obesity into the younger age bracket of the population is seen (to quote, once again, an alarming American statistic) **in the tripling of cases of overweight in young people from 1970 to the present day**. According to a recent study by the Trust for America's Health and the Robert Wood Johnson Foundation, almost **one third of American children and adolescents are overweight or obese**⁴. Specifically, according to the NIH, 16% of children between 6 and 19 years of age are currently overweight, while a further 15% are in dangerous risk of becoming so.

The level of overweight at a young age is of fundamental importance for the probability of serious problems and diseases as an adult. In particular, type 2 diabetes – once considered to be a disease of elderly adults – is now increasingly being seen in children and young people.

Medical-scientific research (as will be seen in more detail later in this report) has found a significant correlation between obesity and the onset of certain pathologies such as type 2 diabetes, cardiovascular disease and cancer. Among the consequences of obesity are, in fact, some of the main risk factors for these diseases, such as arterial hypertension (linked to all cardiovascular disease) and insulin resistance (key in diabetes).

In addition to being relevant in terms of the overall state of health of the population, **overweight and obesity also appear to be problems that have a significant negative effect in economic terms**. In reference to the United States, for example, the WHO⁵ estimates that, in 1995, the direct cost of obesity

represented approx. 7% of all health costs in the United States, close to 70 billion dollars.

The factors behind the origin of overweight and obesity are many. For some of these, no type of preventive or other initiatives are possible because they are genetic in nature. For others, on the other hand, preventive and informational initiatives aimed at correcting certain trends in life style and dietary habits of the population on a global level are possible. The dramatic nature of the empirical data available on these pathologies and the serious consequences faced by those affected by them certainly merit serious reflection at the very least.

1.2 Cardiovascular disease

Diseases of the cardiovascular system⁶ are the **no. 1 cause of death in all developed countries**; these pathologies are often disabling and their spread is destined to grow because of the continued rise in life expectancy.

The main proven **risk factors** are tied above all to **improper lifestyles**: tobacco smoking, reduced physical activity, high cholesterol levels, blood pressure, type 2 diabetes and abdominal obesity, are partly due to improper diet (the presence of two or more factors multiplies the risk of ischaemic heart disease and cardiovascular incidents).

Data from the World Health Organization⁷ indicate that in 2005, worldwide, there were **17.5 million deaths due to cardiovascular disease, 30% of total deaths**. Of these, 7.6 million were due to cardiac pathologies and 5.7 million to stroke.

While previously cardiovascular pathologies were considered diseases that affected only industrialized nations, **today 80% of deaths occur in developing or emerging countries**.

By 2015 it is calculated that the number of deaths caused by cardiovascular disease on a global level will rise to **20 million individuals**, becoming the no. 1 cause of death in the world.

In the **United States**, in the 2006, it was estimated that **80 million people were affected by one or more cardiovascular pathologies**. Deaths for the year 2005 indicate, however, that over **864 thousand people died (35.3% of the total, i.e., one out of every 2.8 deaths) because of cardiovascular disease**, with coronary pathologies being the primary cause of death overall, registering 445,000 deaths. In the United States, the number of deaths caused by cardiovascular disease is much higher than the sum of deaths due to cancer (559,000), accidents (117,000) and HIV/AIDS (12,000)⁸.

Despite the fact that the number of deaths is still very high, there has been a decrease compared with previous years. Specifically, between 1995 and 2005 there was a drop of 9.6% in the overall number of deaths, while the standardized death

rate⁹ decreased by 26.4%. For the near future, on the other hand, estimates derived from a report on demographic changes and cardiovascular disease over the period 1950-2050 indicate that deaths due to cardiovascular disease in the US is destined to increase **between the years 2000 and 2030¹⁰**. This analysis suggests that a concerted preventive effort **must concentrate on the initial period of this century**.

In the **European continent**, on the other hand, cardiovascular pathologies are responsible for **4.3 million deaths each year (2 million within the European Union)¹¹**. Coronary pathologies represent the disease responsible for the largest number of deaths (1.9 million deaths in all Europe and more than 741,000 in member states of the European Union).

Over the last 30 years, mortality rates for these pathologies (please refer to the figure below) have decreased in the Western and Northern European countries, but they have increased rapidly in some countries in central and eastern Europe. For example, mortality rates from coronary disease for men under the age of 65 dropped between the years 1994-2004 by 37% in Finland and 42% in the United Kingdom, while it increased by 57% in Albania and 19% in the Ukraine.

Figure 2. Standardized mortality rate for coronary disease in Europe, men under 65 years of age, most recent year available



Source: The European House-Ambrosetti re-elaboration of data from "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009

In **Italy**, the prevalence of cerebral and cardiovascular disease is estimated by the Osservatorio Epidemiologico Cardiovascolare. The most recent data is given in the table below.

Figure 3. Age-adjusted (35-74 years of age) prevalence of cerebral and cardiovascular disease in Italy (% of population), 2002

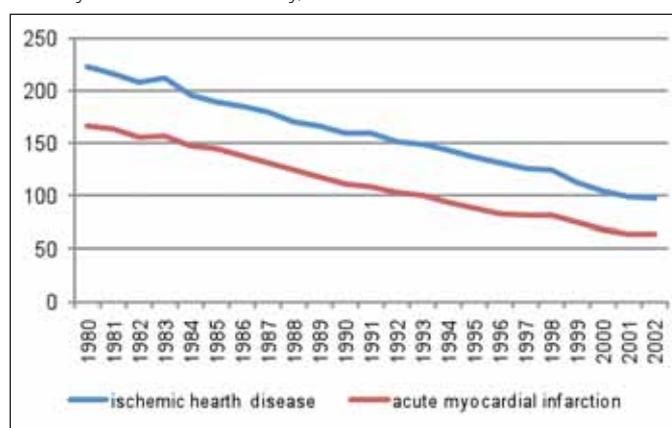
	Men	Women
Stroke	1.5	0.4
Ictus	1.1	0.8
Atrial fibrillation	0.8	0.7
Angina pectoris	3.3	3.9
Intermittent claudication	1.9	2.5
Transitory ischemic attack (TIA)	0.8	0.6
Left ventricular hypertrophy	2.6	1

Source: The European House-Ambrosetti re-elaboration of data from the Osservatorio Epidemiologico Cardiovascolare, <http://www.cuore.iss.it/indicatori/prevalenza.asp>

In terms of deaths, cardiovascular disease continues to be the primary cause of death in Italy, even if from mid '70s the death rate is slowing diminishing.

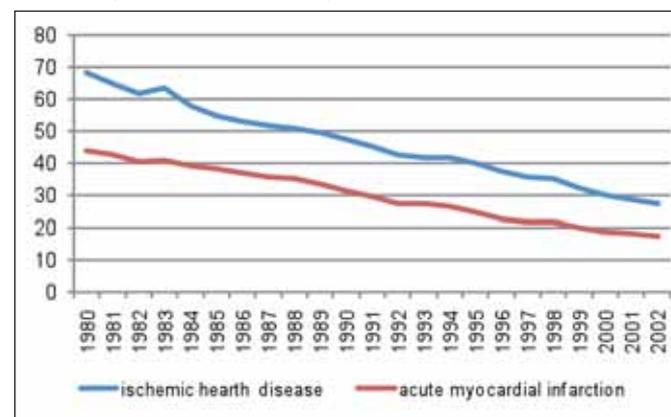
The following figures (broken down by sex) show the trend of the mortality for ischemic heart disease and for the acute myocardial infarction from 1980 to 2002 in Italy.

Figure 4. Men's mortality for 100,000 for ischemic heart disease and for the acute myocardial infarction in Italy, 1980-2002



Source: The European House-Ambrosetti re-elaboration of ISS latest available data. Mortality Rates are age-standardized (35-74 years) with the direct method. The European population as been used as the reference one.

Figure 5. Women's mortality for 100,000 for ischemic heart disease and for the acute myocardial infarction in Italy, 1980-2002



Source: The European House-Ambrosetti re-elaboration of ISS data

Considering the potential years of life lost¹², each year cardiovascular disease deprives 300,000 years of life from people under 65, 240,000 in men and 68,000 in women¹³.

From this standpoint, the possible effect of the increase in brain strokes seems critical. In Italy, individuals who suffer strokes and survive with residual disability are 913,000, many of whom are over 65 years of age (the estimated frequency of strokes in the over-65 population is 7.4% for men and 5.9% for women)¹⁴.

Finally, even data pertaining to cardiac decompensation, a chronic syndrome that involves a high level of disability and numerous hospitalizations each year, are quite alarming. There are approximately 1 million cases in Italy (of which 300,000 in patients over 60) and hospital stays are 200,000 each year (cardiac decompensation is the second most common reason for hospitalization, following childbirth, and its DRG¹⁵ is the most expensive).

The health and social significance of the above data is even greater if it is considered that the majority of the cases are largely preventable (at least 50%, according to available estimates¹⁶). Many of the risk factors in cardiovascular disease are modifiable (i.e., they can be eradicated or at least reduced by modifying the habits and lifestyle of the individual)¹⁷ and when there is more than one, its effect is not additive, but multiplicative or synergic in determining disease risk.

1.2.1 Economic and social impacts of cardiovascular disease

On average, treatment of cardiovascular disease involves quite high health care costs, due, in particular, to hospitalization of patients in acute phases of the disease, drug costs and rehabilitation and home care.

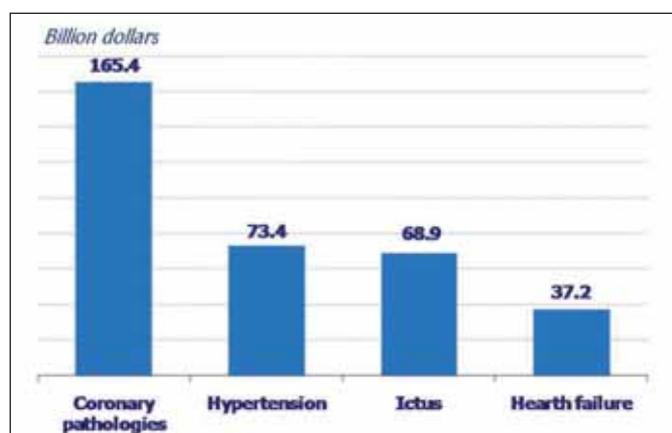
Moreover, this type of diseases generally cause a chronic condition for the patient and represent one of the main causes of long-term illness and the interruption of work activities.

These pathologies significantly modify the **quality of life** of patients and often lead to a **decrease in work productivity** and the ability of the patient and other members of the family to generate income.

In the following chapters will be presented the results of a number of recent studies undertaken on an international level that highlight the high financial burden and major social impact of cardiovascular diseases.

The most recent estimates of the total cost of cardiovascular disease in the **United States** indicate an impact of **473.3 billion dollars** for the year 2009¹⁸. This amount includes both direct health costs (hospital services¹⁹, drugs, home care, etc.), as well as indirect costs calculated as a loss of work productivity caused by the disease or premature death of patients. The figure below shows the economic impact of major cardiovascular pathologies.

Figure 6. Total economic impact of major cardiovascular pathologies in the United States, 2009



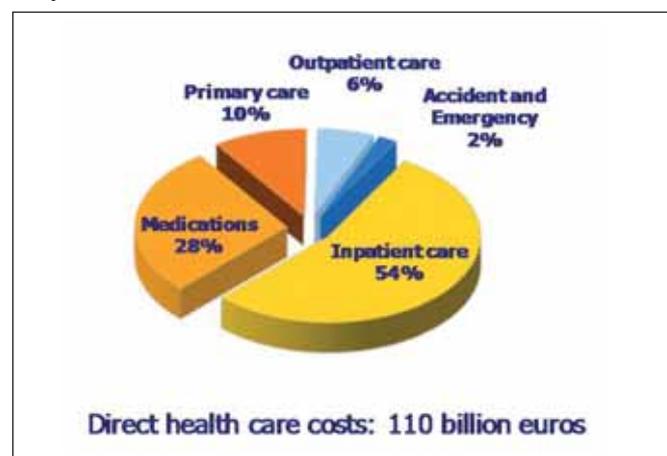
Source: The European House-Ambrosetti re-elaboration of data from "Heart Disease and Stroke Statistics - 2009 Update", The American Heart Association Statistics Committee and Stroke Statistics Subcommittee, *Circulation*, 2008

The spread of cardiovascular disease not only has significant economic and social repercussions for developed countries, but also developing ones, such as **China**. According to recent estimates by the World Health Organization²⁰, in ten years, the cumulative impact of heart disease, strokes and diabetes (between 2006 and 2015) in China will amount to a national loss of **558 billion dollars**.

In 2006, the overall economic impact of cardiovascular disease in Europe was approximately **192 billion euros**²¹; this corresponds to an **average per capita cost of 391 euros**. More specifically, costs for **heart disease amount to 49 billion euros per year** (about one-quarter of the total) and those related to **stroke to 38 billion euros** (approx. one-fifth of the total). 57% of the total economic impact is due to **direct health costs**, with **43% for indirect costs** due to productivity loss and other non-health related costs.

In particular, **health costs** totaled just under **110 billion euros**, which is equal to **10% of overall health expenditure**. The figure below provides a breakdown of these costs.

Figure 7. Breakdown of direct health costs for cardiovascular disease in Europe, 2006

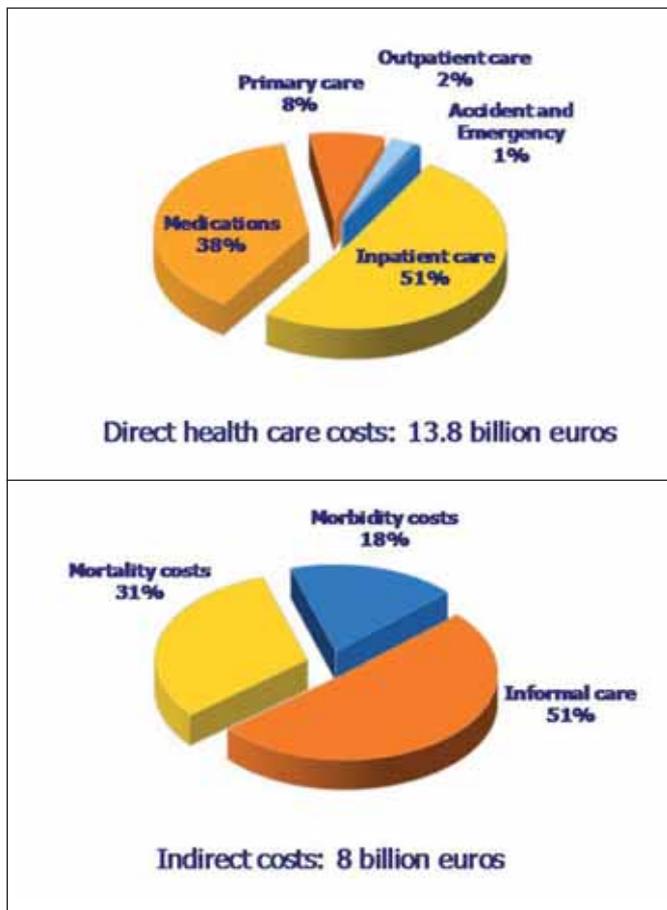


Source: The European House-Ambrosetti re-elaboration of data from "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009

Average per capita health costs for cardiovascular disease in Europe is **223 euros**, but there are **significant differences between individual countries expenditure**. For example, in Germany, expenditure is **413 euros**, in the UK **313 euros**, in Italy **235 euros**, in France **207 euros** and in Spain **130 euros**.

Total costs for cardiovascular disease in Italy were calculated to be approx. **21.8 billion euros** for 2006²². Of these, **63%** (totaling **13.8 billion euros**) involved **direct costs borne by the health care system**, which include in particular hospital care and drug costs. **37%** of the total economic impact of cardiovascular disease is instead attributable to **indirect costs of productivity loss in workforce-age patients** due to the illness (morbidity costs of **1.4 billion euros**) and death (mortality costs of **2.6 billion euros**), as well as **other unofficial costs for patient care**²³ (**4 billion euros**), for a total of approx. **8 billion euros**.

Figure 8. Breakdown of direct and indirect health costs for cardiovascular disease in Italy, 2006



Source: The European House-Ambrosetti re-elaboration of data from "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009

In terms of individual diseases, coronary pathologies alone amount to 4.8 billion euros (21.9%) and strokes 4.5 billion euros (20.8%).

To understand the extent of the economic impact of cardiovascular disease on public health care expenditure, we can observe how expenditure for **hospitalization for cardiac insufficiency** is the no. 1 medical expenditure for hospital resources; over 60% of those hospitalized are elderly (hospitalization rates for the over-65 is 1,469 per 100,000 inhabitants)²⁴.

To conclude, re-elaborating data provided by ISTAT surveys of families, the number of **individuals affected by cardiovascular disability** can be estimated at **4.4 per thousand**. These estimates have an inevitable impact on social security expenditures for disability pensions which, according to INPS data, indicate cardiovascular disease as the most-frequent cause (31.2%)²⁵.

1.3 Diabetes and metabolic syndrome

Diabetes is one of the most common chronic pathologies throughout the world, especially in highly-industrialized countries and is one of the most significant and costly social diseases of our day, especially because it is chronic and tends to create complications over the long-term. Specifically, complications related to this disease cause cardiovascular and kidney ailments, as well as vision problems and it is estimated that diabetes reduces average life expectancy in patients between 5 and 7 years.

Using the year 2007 as a point of reference, among people between 20 and 79 years of age, it is estimated that the prevalence²⁶ of this disease worldwide is 5.9%²⁷, which is 246 million patients with an increase of approx. 27% over 2003 (when it was estimated that 194 million people were affected by this disease). Each year around the globe more than 7 million new cases of diabetes are reported (one every 5 seconds)²⁸.

Estimates up to the year 2025 indicate a significant increase in prevalence, reaching 7.1% of the population involving 380 million people throughout the world, with an increase of 54.5% compared with 2007.

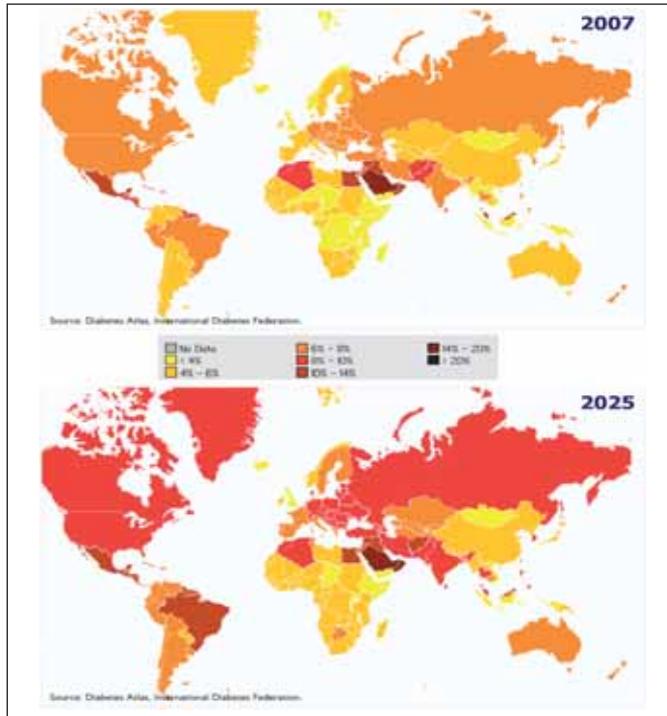
The prevalence of diabetes will grow both in industrialized as well as **developing countries**. In **China**, for example, it is estimated that in 2007 the number of people suffering from diabetes was approx. 39.8 million, 4.3% of the population; in 2025, this number is expected to rise to just under 60 million (5.6% of the population), with an increase of 50% in the number of cases. An even more alarming growth trend is expected in **India**, where from the current 40.8 million sufferers (6.2% of the population), this level is expected to increase by 2025 to 69.8 million (7.6% of the population).

In addition, although diabetes is a pathology that appears in later years, it is expected that there will be a **gradual increase in the spread of this disease among relatively young individuals**.

The causes behind this pathology, that has been defined as a true epidemic, and are to be found in four basic factors:

- an aging population;
- the proliferation of poor eating habits;
- the growth in the number of **overweight/obese people**, especially among teenagers and young adults;
- increasingly sedentary lifestyles.

Figure 9. Estimated prevalence of diabetes in the 20-79 age bracket, 2007 and 2025

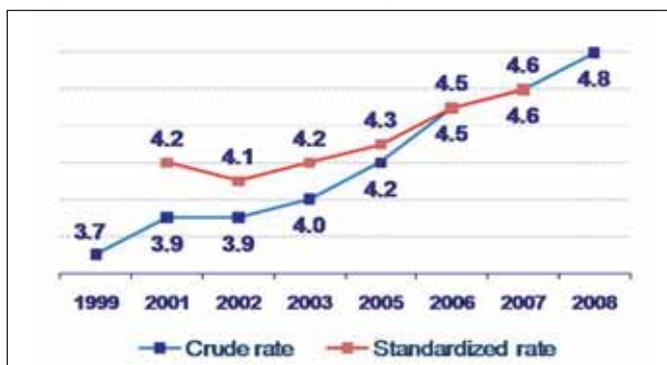


Source: The European House-Ambrosetti re-elaboration of data from the International Diabetes Federation 2009

The International Diabetes Federation estimates that in 2007, 3.8 million deaths were attributable to diabetes, including death due to cardiovascular complications caused by diabetes (deterioration in the lipid profile, high blood pressure, etc.). This is equal to 6% of deaths worldwide, a level similar to that of HIV/AIDS.

With regard to Italy, ISTAT, for the 2008, has estimated a prevalence for diabetes of 4.8% of the population²⁹ (with a higher percentage in women, 5.2%, compared to men, 4.4%). On the basis of this data, the number of people in Italy with diabetes should be approximately 2.8 million.

Figure 10. Trend in diabetes prevalence in Italy (% of total population), 1999-2008



Sources: The European House-Ambrosetti re-elaboration of data from Progetto IGEA, "Il diabete fatti e numeri - Dai di prevalenza a livello nazionale", ISTAT-ISS

Diabetes prevalence over the last ten years has shown a **constant growth trend** also in Italy: the crude rate has increased to 4.8% in 2008 from the 3.7% registered in 1999, while the standardized rate has increased to 4.6% in 2007 from the 4.2% registered in 2001.

Its prevalence is lower in the North (3.9%), compared with Central (5.3%) and South Italy (5.8%). Irrespective of the geographical area, the prevalence increases with age, arriving at 14.3 for people between 64 and 75 years of age, and 18.8% in people over 75.

Metabolic syndrome

The metabolic syndrome is a pathological condition that has become increasingly common in the populations of more industrialized countries and is characterized by the simultaneous presence in one patient of **different metabolic disorders** that are correlated to each other³⁰. It is a condition that **significantly increases the risk of type 2 diabetes, cardiovascular disease and stroke**³¹.

Currently in Europe, the prevalence of this disease in **adults over 20 years of age** is the 24% of individuals, while in those over 50, it is 30%³². Other estimates suggest that already today, **young people** affected by metabolic syndrome in Europe are 550,000³³.

The causes for mass spread of this syndrome can be found, above all, in the **rapid increase in overweight levels and visceral obesity** (i.e. accumulation of abdominal fat), in increasingly young age groups, and in insulin-resistance. These two factors, which interact in a complex manner, also contribute to causing other risk factors that comprise the syndrome.

To combat the syndrome, which risks generating highly-significant negative effects on health and on the healthcare and social system costs in advanced countries (including Italy), what are required above all **are behavior-based measures** aimed to lose weight, such as increase in physical activity and changes in **eating habits**.

1.3.1 Economic and social impact of diabetes

The many studies carried out internationally to estimate the economic costs connected with diabetes indicate that the impact level is very high.

For example, the International Diabetes Federation estimates that in 2007, 232 billion dollars have been spent worldwide in the treatment and prevention of diabetes and its related complications. These costs will increase at least to 302 billion dollars in 2025.

A recent study by the American Diabetes Association³⁴ placed the cost of diabetes for the United States in 2007 at 174 billion dollars, an amount that includes 116 billion for direct medical expenses and 58 billion calculated as lost productivity of patients and family members involved in their caring.

On average, American diabetic patients have medical costs of 11,400 dollars per year, of which **6,650 dollars attributable directly to diabetes**.

A study³⁵ carried out at the European level, estimated that the average annual **direct health care costs** associated to this disease (hospitalization, out-patient costs, drugs, etc.) amount to **2,834 euros per patient**. The majority of these costs (55%) are due to hospitalization for serious and chronic complications.

With regard to Italy, hospitalizations linked to diabetes and its complications (stroke, myocardial heart attack, kidney insufficiency, amputation of lower limbs) are estimated to be over 75,000. On the basis of these data, an economic impact analysis of **diabetes in Italy** done in 2000 (CODE-2, a study performed on a sampling of 1,263 patients) estimated the annual average cost of a type 2 diabetes patient to be **3,135 euros**.

Using the estimated number of 2.8 million diabetic patients in Italy, we obtain the figure of **8.8 billion euros** per year as the total cost of this disease for the country.

It is interesting to highlight how the **cost of health care** provided for a diabetic patient **increases 3- to 4-fold** if there are only cardio-cerebral-vascular complications or only micro-vascular complications (affecting the kidneys, retina and peripheral nervous system), and **5-fold** if both types of complications are present.

In conclusion, it should be stressed that all the analyses mentioned underestimate the total impact of diabetes in that they omit a certain level of **social costs** that are difficult to quantify and are connected with the pain, suffering and, more generally, the **worsening of the quality of life** of patients and their family members, the care provided by unpaid caregivers (family members themselves, volunteers, etc.), the costs associated with failure to diagnose or late diagnosis of the disease, etc.

1.4 Tumors

Tumors, the second cause of death both in Europe and Italy, are **pathologies that continue to rise**. Because they are a disease which generally affects people later on in years, the lengthening of average life span is an important factor in their growing spread. With reference to 2007, 12 million new cases of tumors in the world was estimated³⁶.

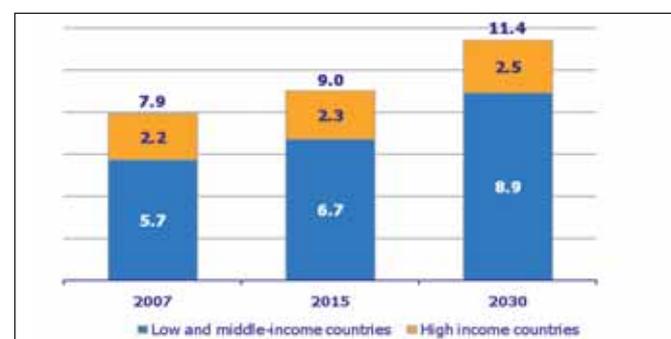
In addition to demographic considerations, the frequency of this disease is generally higher in developed countries, but it is only in the most advanced and wealthy societies, where major resources are committed to the health of the population, that the possibility exists to reduce its risk and prolong life expectancy of people who contract the disease. Today, in fact, in the most economically-advance countries, over 50% of those diagnosed with a tumor are able to return to their normal lives.

On the contrary, in middle-to-low income countries, the risk of death from tumors is much higher. According to World Health Organization data, in 2007 there were **7.9 million deaths** in the world due to tumors³⁷; of these, three-quarters were in medium-to-low income countries. One death out of eight throughout the world is due to cancer and this pathology causes more deaths than AIDS, tuberculosis and malaria combined.

The types of tumors that cause the greatest number of deaths on a global level are lung tumors (1.3 million deaths per year), stomach tumors (803,000 deaths per year), colon-rectal tumors (639,000 deaths per years), liver tumors (610,000 deaths per year) and breast tumors (519,000 deaths per year).

Estimates for the future indicate a worldwide growth in deaths caused by tumors up to a level of **9 million in 2015** and **11.4 million in 2030**, the net majority of which will be in medium-to-low income countries.

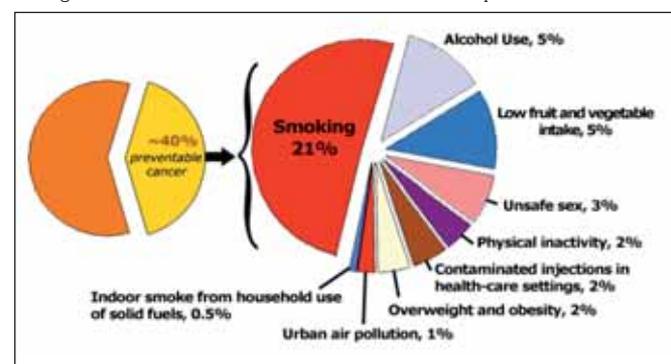
Figure 11. Future estimates of number of tumor deaths in the world, 2007, 2015, 2030



Source: The European House-Ambrosetti re-elaboration of data from the World Health Organization, 2009

It is also estimated that approx. **40% of tumor deaths could be prevented by working on risk factors** of this pathology that can be modified. First on the list is **smoking**, which is the most significant risk (21%), **alcohol abuse** (5%) and **low consumption of fruit and vegetables** (5%).

Figure 12. Risk factors that can be modified in tumor prevention

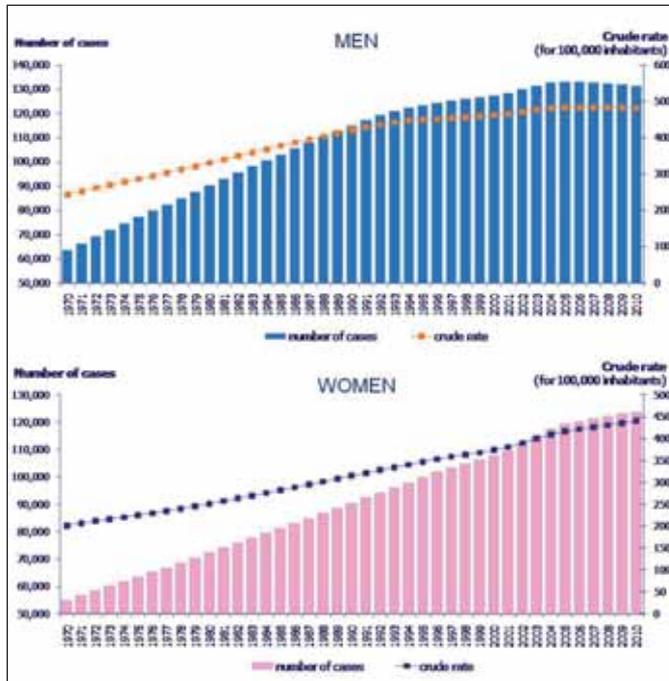


Source: Danaei G, Vander Hoorn S, Lopez A.D, Murray C.J, Ezzati M, "Causes of cancer in the world: comparative assessment of nine behavioural and environmental risk factors", The Lancet, 2005

In Italy, in the 2008, over 250,000 new cases of tumor were forecast, with approx. 125,000 deaths. The overall number of people affected by this disease (prevalence), including those that have been cured, new cases and those under treatment is 1,840,000 individuals.

As can be seen in the figures below, referred to all kind of malignant tumors in men and women, the incidence³⁸ of tumors from the 1970s to the present is in constant increase (although a turnaround in the tendency starting in 2005 can be noted for men), this is largely due to the aging of the population and lengthening of average life expectancy, but also due to the exposure to known, and unknown, risk factors, carcinogens such as cigarette smoke, and the spread of pollutants in the atmosphere.

Figure 13. Trend of tumor incidence in Italy, 1970-2008



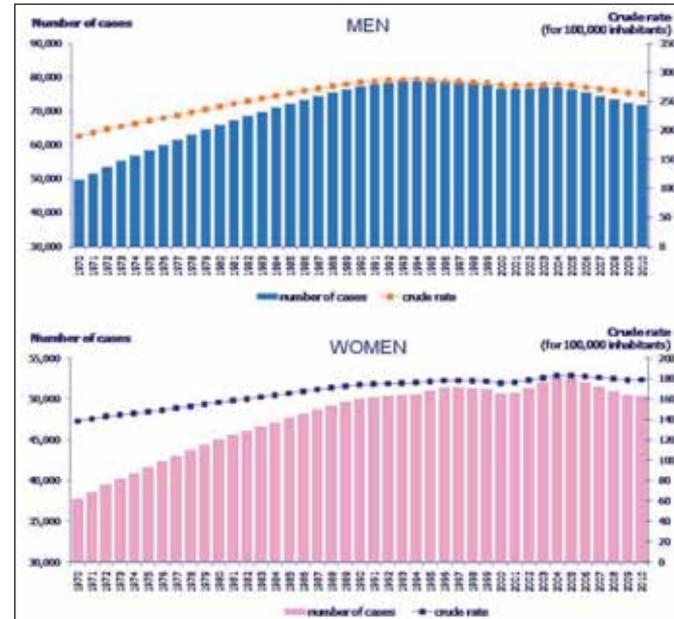
Source: The European House-Ambrosetti re-elaboration, taken from Micheli A., Francisci S., Baili P., De Angelis R., Current cancer profiles of the Italian Regions, Tumori 93(4), 2007

It is estimated that by the end of this decade, there will be almost 2 million people who have been diagnosed with cancer during their lives; of these 400,000 will be those who have received the diagnosis less than two years before, on which the most intense medical treatment is required, and 700,000 who have been ill for over 10 years and are potentially cured or who suffer from physical, psychological or social after affects of treatment. These totals are destined to rise over the coming decades³⁹.

In terms of number of deaths, in the figure below can be seen that in Italy - as in a number of countries in the European Union - mortality from tumors (expressed as crude death rate), after having risen constantly and reached its peak in the early

1990s for men and more recently for women, has shown a slight decrease in recent years.

Figure 14. Trend of tumor deaths in Italy, 1970-2008

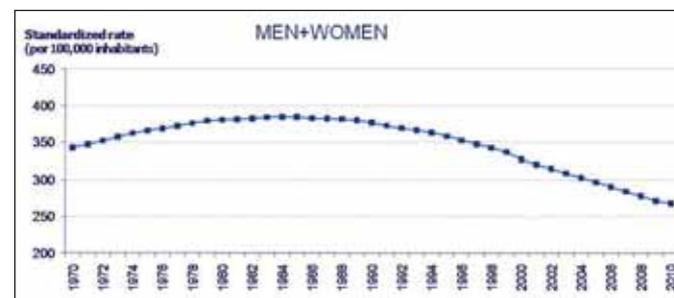


Source: The European House-Ambrosetti re-elaboration, taken from Micheli A., Francisci S., Baili P., De Angelis R., Current cancer profiles of the Italian Regions, Tumori 93(4), 2007

Taking into consideration the standardized mortality rate, which eliminates the effect caused by the different age structure of the population for the period under consideration, and which expresses the risk of death, the slowdown in deaths due to tumors is even clearer. Having reached its peak in the mid-1980s (385/100,000 inhabitants), the death rate declined to 277/100,000 inhabitants in 2008 and is expected to further decline in the near future.

This tendency is the result of the improvement in patient survival rates which, in Italy, has reached an average of 53.5% for survival 5 years after diagnosis (47% and 60% respectively for men and women).

Figure 15. Trend in standardized mortality rate for tumors in Italy, 1970-2008



Source: The European House-Ambrosetti re-elaboration, taken from Micheli A., Francisci S., Baili P., De Angelis R., Current cancer profiles of the Italian Regions, Tumori 93(4), 2007

The decrease seen in tumor deaths is due to **multiple factors**, including:

- early diagnosis through organized or spontaneous screening (breast, cervix-uterus, colon-rectal, etc.);
- new drugs and treatment advances;
- spread of new surgical procedures;
- increased attention to personal health;
- improvement in technologies and dietary habits and variety of diet (e.g., improved food conservation, greater availability of fruit and vegetables and fresh products throughout the year, etc.);
- across-the-board reduction in consumption of tobacco and alcohol.

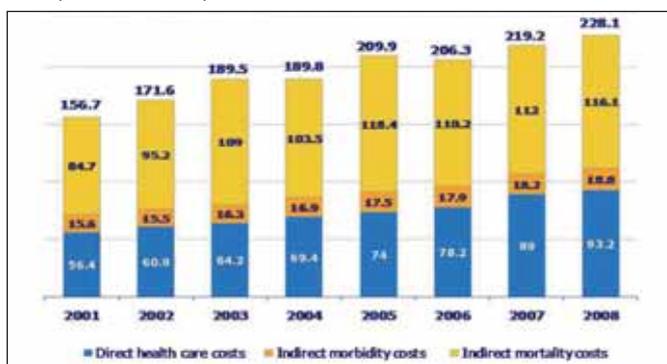
1.4.1 Economic and social impact of tumors

The economic impact of cancer is very high and can be measured through evaluation of **direct health care costs** (treatments, hospitalization, rehabilitation, etc.) and **indirect costs**, tied to reduced productivity for work days lost because of the disease (indirect morbidity costs) and premature death (indirect mortality costs).

The unavailability of comparable data makes it impossible to estimate cancer's global economic impact. Nonetheless, the studies and statistics gathered in a number of countries makes it possible to comprehend the enormous economic impact of this pathology.

For example, in the United States, the National Institutes of Health estimates the economic impact of cancer in 2008 to be over **228.1 billion dollars per year**, including both health care expenditure and patient productivity loss⁴⁰. In particular, direct health care costs amount to 93.2 billion dollars, with indirect morbidity costs 18.8 billion and indirect mortality costs 116.1 billion. As can be seen in the figure below, in recent years total economic costs **have risen constantly**, in particular the direct health care costs components (in 1963 they amounted for 1.3 billion dollars, in 1980 it was up to 13 billion dollars, in 1990 27.5 billion dollars, in 2000 55 billion, finally reaching 93 billion in 2008).

Figure 16. Trend in the economic impact of cancer in the United States, 2001-2008 (billions of dollars)



Source: The European House-Ambrosetti re-elaboration of data from the American Cancer Society (Cancer Facts&Figures 2009 and previous years)

In terms of Europe (EU-25), in 2002 cancer was responsible for **16.7% of healthy life years lost by European citizens⁴¹, totaling almost 10 million years** (compared with the 12.5% registered in the United States and Canada). Direct health care costs related to cancer in Europe (19 countries) were estimated at **56.6 billion euros** in 2004⁴².

In France, the economic impact of tumors related to only direct costs, was calculated at 7.5 billion euros in 2004, equal to 5.3% of the entire French health care⁴³ expenditure. Figures referred to 1999 indicate that hospitalization costs for tumors reached 6 billion euros, 16-18% of which was for chemotherapy⁴⁴.

In the United Kingdom, direct costs were estimated at 5.6 billion euros in 2004, 5% of total health care expenditures⁴⁵. According to another study which calculated the costs of anti-tumor treatments in 2000-2001 covered by the National Health Service, the economic impact was approx. 3 billion euros, 10.6% of public health expenditure⁴⁶.

Sale of cancer-fighting drugs rose in Sweden, from 37.3 billion dollars in 2000 to 118.7 billion dollars in 2004⁴⁷.

For **Italy**, it is estimated that direct health care costs were **6.7 billion euros in 2004, 6.6% of overall health care expenditure**.

Finally, assistance to cancer patients in the terminal phase of the disease has an **extremely significant physical, psychological, social and economic impact on family members**. According to the ISDOC (*Italian Survey of the Dying Of Cancer⁴⁸*) study carried out in Italy, each year, in approximately **40,000 Italian families**, a member of the family must **reduce work hours or leave his/her job to care for a family member**.

According to results of a recent survey performed at the Policlinico Umberto I in Rome⁴⁹, commitment to caring for a cancer patient by a family member often involves **severe repercussions for the latter's work**:

- 72% of family members caring for a cancer patient say that it had severe repercussions on their working life. Of these, 38% suffer losses due to the drop in earnings for the hospitalization period of between 700 and 1,000 euros, while 25% complain of even higher losses, over 1,200 euros;
- 13% are forced to ask for a leave of absence;
- 22% must quit their jobs.

2. THE ROLE OF DIET IN THE ONSET OF MAJOR DISEASES

The World Health Organization (WHO) defines **health** “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”, while defines **healthy living** as “a way of living aimed at reducing the risk of illness and premature death⁵⁰. Not all diseases can be avoided (such as heart attacks and cancer), but in many cases attentive prevention can postpone or reduce the risk of onset.

As it will be discussed in the following paragraphs, diet is a highly relevant component in defining a healthy lifestyle and improper eating habits can be a prime risk factor in the onset of major noncommunicable disease.

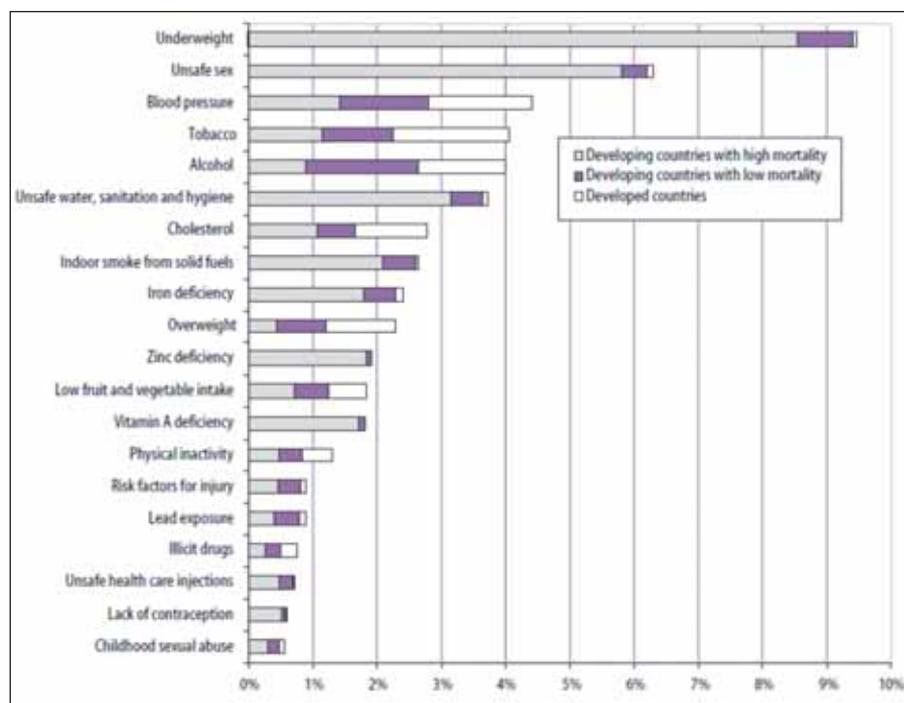
2.1 Risk factors, lifestyles and eating habits

2.1.1 Risk factors

Each year the World Health Organization (WHO) publishes the “*World Health Report*”, a report on the state of health worldwide. In 2002, the report focused on the issue of “health risks” which examined the main risk factors to human health⁵¹.

For the WHO, by risk is meant “probability that involves negative consequences for health or a factor that increases that probability”. The 2002 report provides an analysis of the vast number of negative factors that are the cause of premature

Figure 17: Worldwide distribution of deaths caused by main risk factors compared with total world DALYs (Disability-Adjusted Life Years)⁵³



Source: World Health Organization, “The World Health Report 2002 - Reducing risks, Promoting Healthy Life”

death of millions of people. The study, conducted on a global scale, identified **ten major health risks** in the world:

- underweight and malnutrition;
- unsafe sex;
- high blood pressure;
- tobacco consumption;
- alcohol consumption;
- unsafe water, sanitation and hygiene;
- high cholesterol;
- indoor smoke from solid fuels;
- iron deficiency;
- overweight.

These factors, if taken together, are responsible for more than one third of all deaths worldwide, a total of approx. 19 million deaths each year (deaths worldwide amount to approx. 56 million⁵²) (Figure 17).

On a global level, these risk factors are the cause of a greater or lesser number of deaths depending on the country involved. The figure above, which provides a worldwide breakdown of deaths caused by risk factors compared with total DALYs (an index of the number of life years in good health lost), shows, first of all, that a limited number of factors are the cause of a very high number of premature deaths and responsible for a significant amount of diseases. Also bearing in mind the division between developing and developed countries, a clear-cut distinction can be made between the key risk factors. Specifically, the **first three risk factors** broken down by geographical area, would appear to be:

- in developing countries with high mortality rates: malnutrition, unsafe sex, unsafe water, lack of adequate sanitation and hygiene;
- in developing countries with low mortality rates: alcohol consumption, high blood pressure and tobacco consumption;
- in developed countries: tobacco consumption, high blood pressure and alcohol consumption.

To generalize, it can be said that in poor countries, the greatest risk is from underweight and malnutrition, while in high-income countries it is from excess food and incorrect lifestyles.

As data gathered by the WHO shows, underweight at birth is the primary cause of death in developing countries. While tobacco, alcohol, high blood pressure, high cholesterol and obesity (or a combination of these factors) are the main cause of disease in the most industrialized countries (estimated to be at least one-third for countries in North America and Europe⁵⁴).

Specifically, tobacco, hypertension and high cholesterol (or a combination of these factors) are the origin of more than three-quarters of cardiovascular disease, the no. 1 cause of death in the world⁵⁵.

In terms of the number of deaths caused by these risk factors, the WHO report estimates that, in the world, each year:

- **high blood pressure** is the cause of 7 million deaths;
- **tobacco consumption** is the cause of 5 million deaths;
- **high cholesterol** is the cause of 4 million deaths;
- **obesity** is the cause of 3 million deaths.

Specifically, while in developing countries there are approx. 170 million individuals (mainly children) who are underweight, in developed countries there are approximately one billion overweight people. It is estimated that in Western Europe and the United States, approximately half a million people die each year for diseases tied to obesity.

In its forecasts for the year 2020, the WHO highlights a significant increase in the number of deaths, especially in developed countries. In fact, the risk factors expected to be the primary cause of death will be tobacco consumption (with 9 million estimated deaths in 2020) and obesity (5 million deaths in 2020).

2.1.2 Lifestyles

According to the most recent report, *World Health Statistics 2008*, published by the World Health Organization, noncommunicable diseases (such as high blood pressure, diabetes, cancer, cardiovascular disease, etc.) are increasingly becoming the most important cause of death in the world, surpassing infectious disease (e.g., HIV, diarrhea, tuberculosis, malaria, etc.)⁵⁶. Although the latter are still widely diffuse in developing countries because of the poor sanitary and hygienic conditions, in the rest of the world there is an increase in the number of people who die due to diseases that are closely lifestyle-related⁵⁷. It is estimated that this type of disease affects at least 35 million people each year, equal to 60% of all deaths worldwide⁵⁸.

Cancer, cardiovascular disease and diabetes share several risk factors, i.e., they are among the primary noncommunicable diseases whose epidemiology were extensively covered in Chapter 1:

- **Tobacco consumption:** it is estimated that this is the cause of death of over 4.2 million people each year⁵⁹, with forecasts for 2025 of over 3 million deaths in industrialized countries and 7 million people in developing countries. Tobacco contains 4,000 chemical agents, many of which have negative effects on virtually all organs and a full 60 compounds in a cigarette are recognized as being cancerogenous⁶⁰. Among diseases, tobacco causes or contributes to the onset of cancer in the mouth, throat and lungs, damages to the skin, psoriasis, cardiac disease, gastric ulcers, wrinkles, osteoporosis, cataracts, diabetes, Alzheimer's, leukemia, sexual dysfunction, infertility and gum disease;

- **Poor eating habits:** nutrition is fundamental to health. The role played by poor diet has been widely noted in many diseases. It is estimated that, annually, 2.7 million deaths can be attributed to low consumption of fruit and vegetables⁶¹. In fact, it has been proven that certain vitamins and nutritional substances should be an integral part of diet to safeguard health to the extent possible. At the same time, it has been shown that there are some foods which have a harmful effect on the body's physical state, such as salt abuse, sugar and fat. Moreover, an excessive energy intake can lead to overweight and obesity which can favour the onset of metabolic anomalies that induce diabetes, cardiovascular diseases and cancer;

- **Physical inactivity:** it is estimated that 1.9 million deaths each year can be linked to physical inactivity⁶². There are manifold scientific evidences that demonstrates how regular physical activity promotes healthy living with noteworthy benefits for overall individual health. Among the positive aspects is the possibility of reducing the risk of developing cardiac disease, cancer and diabetes by up to 50%. The importance of engaging in regular physical activity is also confirmed by national health programs. In the United States, for example, the "*Healthy People 2010*" program indicates physical activity as one of the main goals for the country. Through its "*Public Health Programme (2003-2008)*", the European Union proposes projects to support and promote physical activity. In Italy, the National Health Plan 2003-2005 stressed the importance to health of physical activity and the subsequent plan (National Health Plan 2006-2008) took on the issue of a sedentary lifestyle, especially from the point of view of the causes of diabetes.

The evidence of the importance of a correct lifestyle is confirmed by numerous scientific studies⁶³. In particular, a recent study performed in Iran has shown how changes in lifestyle, especially diet and amount of physical activity, improve the health of the entire community⁶⁴. Specifically, the population under examination was subjected to a 4-year program during which time a number of initiatives (food education, promotion of physical activity, reinforcement of anti-smoking laws, etc.) were implemented. These initiatives made it possible to effect noteworthy changes in the lifestyles of people in terms of diet, physical activity and smoking. While at the start of the study only 14% of participants followed a proper diet, after four years, the percentage rose to 30%. The amount of time dedicated to physical activity increased from 81 to 181 minutes a week. However, there was only a slight reduction in tobacco consumption (from 14.8% to 13.9%) because of its addictive nature and the limited length of time of the study.

2.1.3 Eating habits

Among the components of healthy living, eating habits play an especially important role.

The relationship between diet and health has been known to man since prehistoric times. In fact, history shows that man learned early to recognize the effect of different foods on his

body and, as a result, through criteria of choice and selection of the foods hunted or gathered, to avoid harmful and toxic foods. Man's attention to health and prevention has continued to increase over time, in particular with the introduction of techniques for cooking and preserving food (drying, salting and smoking) which made it possible for foods to be exposed for extended periods of time in complete safety.

In light of this, the meanings of the terms **diet** and **nutrition** are clear. The former indicates **selective consumption of foodstuffs in a conscious manner**, while the second refers to an **independent process of assimilating, transforming and metabolizing food**.

The role of diet as a preventive factor of major diseases is also recognized scientifically by many scientific studies which have examined the relationship between diet and cancer, cardiovascular disease and diabetes.

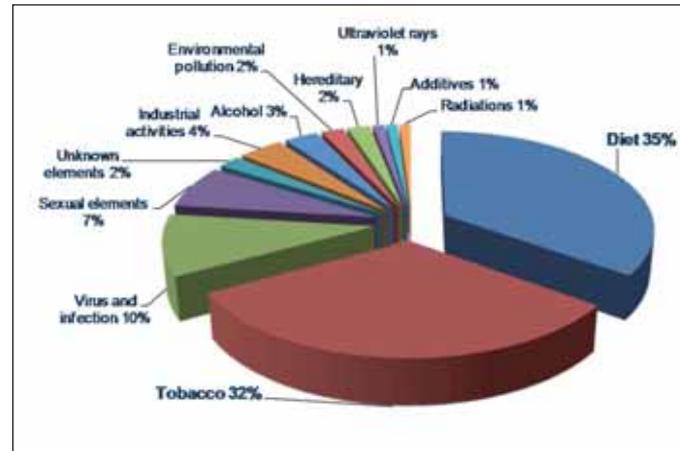
Diet and cancer

At the start of this millennium, for the first time, deaths from cancer began to decrease⁶⁵. The merit for this epochal shift goes to prevention, seen as individual lifestyle capable of directly affecting the formation of tumors and their curability. This is demonstrated clearly by the causes at the root of tumor formation. Studies performed, especially those of Doll and Peto, have shown that approx. 30-35% of the responsibility for cancer can be attributed to diet-related factors and 30-32% to tobacco consumption⁶⁶. Despite what is normally thought, only 2-4% of tumors are caused by what we breathe (i.e., air pollution) (Figure 18).

Additional and more recent studies have confirmed the key role of diet in human health, demonstrating that there is a close relationship between diet and cancer rates throughout the world.

An illustrative example of this is found in scientific studies that highlighted the existence of a direct relationship between the consumption of red meat and the onset of colorectal

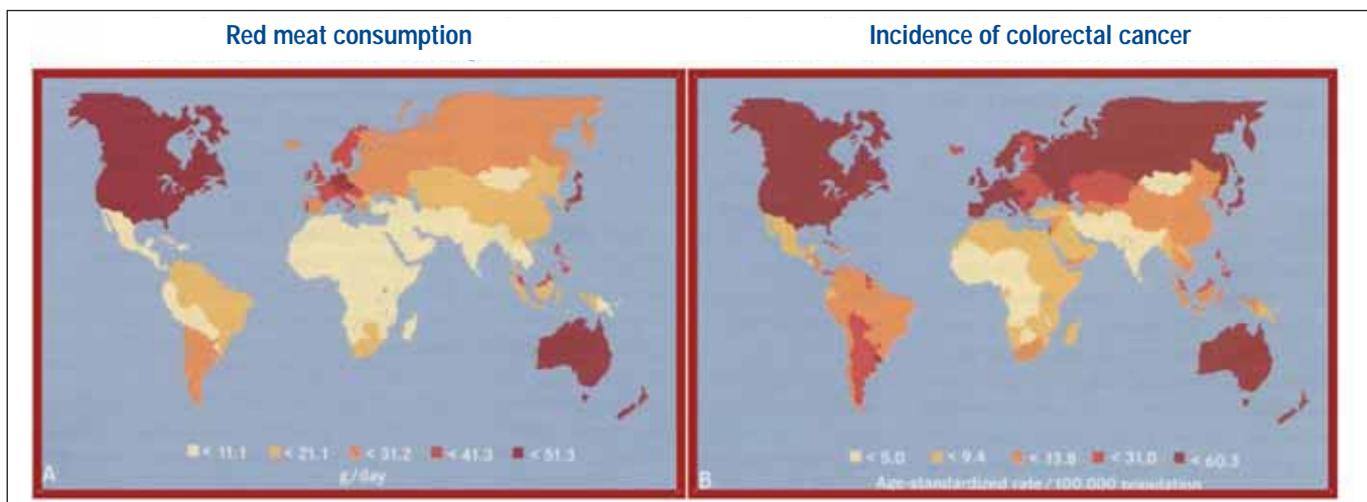
Figure 18: Estimated overall risk for human neoplasms



Source: The European House-Ambrosetti re-elaboration of data from Doll and Peto, 1980

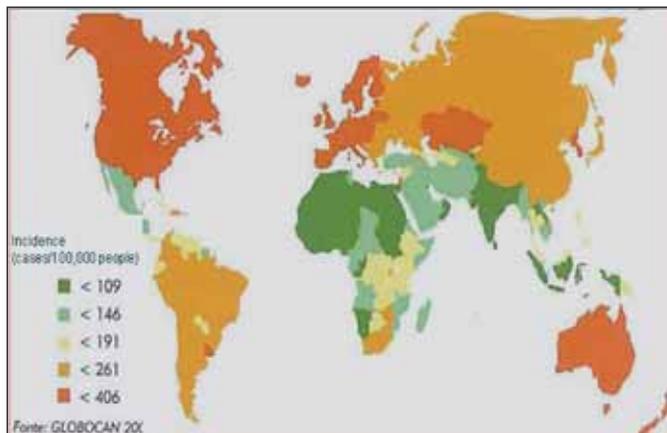
cancer. Case histories indicate that these tumors are twenty times more frequent in the countries of North America and Europe, compared with countries in Africa and Asia. The difference is so marked that it gives rise to the hypothesis that the typical Western diet, characterized by a higher percentage of fats and consumption of red meat, could favour the onset of this neoplasia. In reality, comparing the global distribution of meat consumption and the incidence of colorectal cancer, demonstrates that there is a perfect complementarity between the two distributions. There are also many studies that observed people who have emigrated from a poor to a rich country who, after just a few decades, are affected by tumors that are not common in their home countries, but that are frequent in the new country of residence. A concrete example of this is what has happened to Asian women who have moved to the United States and are affected by breast cancer with an higher incidence rate with respect to the one observed in their country of origin (Figure 19).

Figure 19: Worldwide distribution of red meat consumption and incidence of colorectal cancer



As can be seen quite clearly in the figure below, there is a strong presence of cancer in more highly-developed, high-income countries (North America, Australia and Western Europe), compared with poorer countries (Africa, Central America and parts of Asia). This confirms what was stated previously: diet and lifestyle are the principal causes of tumor insurgence.

Figure 20: Distribution of the incidence of cancer worldwide



Source: Globocan, 2002

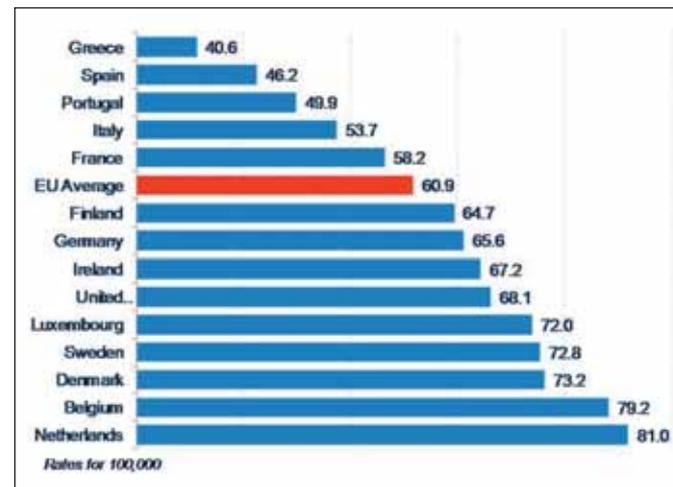
In particular, the diet adopted in rich countries would favour the development of cancer. This diet is distinguished by unbalanced consumption of animal fats and meat without any valid nutritional reason for this.

A diet oriented to an excessive meat consumption means, not only an increase in the risk of contracting cancer, but also a strong negative impact on the environment. If we consider that approximately six billion people and four billion animals live on the Earth, it is clear why most of the grains produced are used in livestock raising with consequent effects on climate change (animal husbandry is one of the main causes of the greenhouse effect) and water consumption (it is estimated that each kilogram of beef requires 15,500 liters of water⁶⁷). For a more detailed discussion of this, please refer to the "Water Management" and "Climate Change, Agriculture and Food" position papers published by the Barilla Center for Food & Nutrition in 2009.

In recent years, **nutrigenomics** - the science which studies the diet and dietary components more suitable to the genomic structure of each individual in order to prevent the onset of diseases - allowed to recognize which dietary choices influence the most the risk of disease in individuals with different genetic profiles. On this regard, there are some foods that increase the risk of cancer, but there are also foods - like **fruit and vegetables** - that **reduce the risk**.

In fact, countries which follow the Mediterranean diet - characterized by high consumption of fruit, vegetables, cereals, olive oil and fish - such as Greece, Spain, Portugal, Italy and France, have a lower incidence of breast cancer.

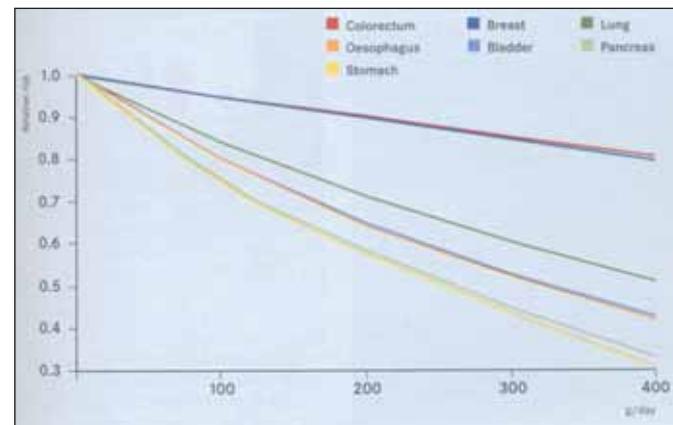
Figure 21: Estimated incidence of breast cancer in countries of the European Union in 1990



Source: The European House-Ambrosetti re-elaboration of data from Black et al., 1997

Numerous scientific studies have shown a positive correlation between daily consumption of fruit and vegetables and the reduced risk of contracting cancer. Among these, the results of the analysis presented below are of particular scientific importance. They show that an increase in the amount of fruit and vegetables consumed (expressed in grams per day) coincides with a proportional reduction in the risk of contracting cancer (expressed by the relative risk factor).

Figure 22: Consumption of fruit and vegetables (grams per day) and related reduction in the risk of contracting tumors



Source: WHO, "World Cancer Report", Edited by Stewart B. W., Kleihves P., IARC Press, 2003

To conclude, there is a close connection between diet and prevention of cancer. Further confirmation of this is provided in the table below which summarizes scientific studies conducted on this subject. As can be seen, for consumption of **vegetables**, at least 80% of the studies examined showed a reduction of 59% in the risk of cancer. While for **fruit**, 64% of studies examined showed a risk reduction of 36%.

Figure 23: Epidemiologic studies of the relationship between consumption of fruit and vegetables and developing cancer

Food studies	Registered risk reduction	Total number of studies	% of studies that indicate risk reduction
Vegetables	59	74	80
Fruits	36	56	64
Raw vegetables	40	46	87
Cruciferas (broccoli, cabbage etc.)	38	55	69
Vegetables of the <i>Allium</i> family (garlic, onion, etc.)	27	35	77
Green leaves vegetables	68	88	77
Carrots	59	73	81
Tomatoes	36	51	71
Citrus fruits	27	41	66

Source: World Cancer Research Fund and American Institute for Cancer Research, 1997

Diet and cardiovascular disease

The relationship between lifestyle and proper diet and lower incidence of cardiovascular disease, has been shown with clear scientific proof in the “North Karelia Project” study conducted starting in 1972 among residents of that province in Finland⁶⁸.

The goal of this project, which was instituted in response to an excessive number of heart attack deaths recorded in North Karelia, was to reduce that number through the implementation of initiatives aimed at modifying the habits and behavior of residents and businesses in the communities studied.

This study revealed the close connection between the onset of cardiovascular disease and improper lifestyle (unbalanced diet, smoking, physical inactivity and alcohol consumption) and demonstrated that it is possible to take action that reduces the number of heart attacks.

The measures taken involved significant changes in the healthcare system and Finnish agriculture and business sectors. For example, the food industry collaborated through a project that promoted a low-fat and low-salt diet. Dietary habits were modified through involvement of the schools and local media in order to promote a context of correct eating behavior.

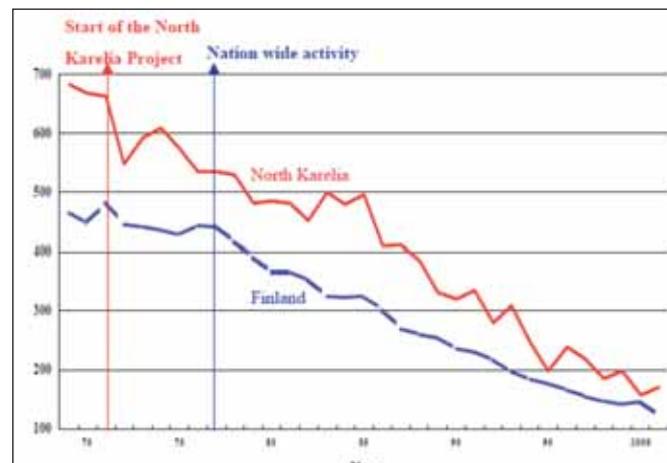
The results show that these initiatives were fully effective. While in 1972 nearly 90% of the population spread their bread with butter, in 1992 only 15% continued to do so. Consumption of fruit and vegetables increased from 20 kg per person in 1972 to 50 kg in 1992.

After 25 years of the study, this approach remains valid. The overall mortality rate for men decreased by 49%, while death by cardiovascular disease and heart attacks decreased by 68% and 73% respectively. Finally, the change in behavior and lifestyles made it possible to reduce risk factors in general, allowing for positive effects in cholesterol and blood pressure levels.

The “North Karelia Project” (subsequently extended to a national level) represents an extraordinary example of the

efficacy of measures and approaches aimed at improving the health of the population through promotion of a correct lifestyle and diet.

Figure 24: Heart attack deaths in North Karelia and Finland for men between 35 and 64 from 1969 to 2001 (in thousands of persons)



Source: World Health Organization

Diet and diabetes

The nutritional approach is recognized unanimously as the basic tool for preventing the onset of diabetes, treating diabetes and preventing and/or mitigating the development and seriousness of the diseases/complications directly correlated to diabetes itself.

There are two basic types of diabetes, type 1 (also known as “juvenile diabetes”) and type 2 (“adult-onset diabetes”). These two diseases are profoundly different in terms of origin, seriousness and treatment.

In general terms, diabetes is connected to insulin-deficiency (type 1 diabetes) or insulin-resistant (type 2 diabetes). Insulin is a substance produced by the “Islets of Langerhans” located in the pancreas and has a fundamental role in proper absorption by cells in the human body of glucose, an essential element in their correct functioning. Insulin is characterized by “basal”, continuous and independent production through food consumption, and a “post-prandial” production, i.e., subsequent to the individual, specific consumption of food. Improper functioning of the osmotic mechanism of glucose absorption leads, on one side, to a lack of glucose internal to the cells, and on the other, to its accumulation in the blood (marked by a high glycemia level).

In the case of type 1 diabetes, production in the human organism (for genetic reasons) of antibodies destructive to the pancreatic cells responsible for the production of insulin (beta cells), leads to *insulin-deficiency*, in other words a severe insulin deficiency which is followed by a severe hypoglycaemia associated with other metabolic perturbation. The nature of this serious pathology makes it impossible to identify dietary behaviour and life styles that can prevent its onset; all that can be done is implement a treatment that can combat it (basically direct assumption of insulin by the patient and a diet able to combat the negative effects and degeneration of the disease).

Type 2 diabetes is an *insulin-resistant* form, in other words, the incapacity of the body's cells to respond adequately to the insulin released in normal (or slightly reduce) doses by the pancreas. With equal levels of glucose present in the blood, more insulin is required to correctly activate glucose transport. In this case, the factors that can cause incorrect glucose transport may be environmental and connected to life style, and only partially hereditary. For this reason, prevention and treatment tied to diet and life style can be implemented which will diminish type 2 diabetes risk and contain the seriousness of its side effects.

Economic and social development causes a change in lifestyles and diet and, as a result, an increase in the number of individuals affected by diabetes and obesity. One cause of the onset of these diseases can be identified in particular in the excessive caloric intake of the population. For example, in Italy, in the early 1980s, the average daily caloric intake was approx. 3,500 calories, while today it is 3,700 calories with a daily energy requirement that continues to decrease. These trends are seen in virtually all countries, especially in industrialized ones, where there is a rise in the number of diabetics due to obesity and overweight.

The relationship between **diabetes** and **diet** has been demonstrated by several studies⁶⁹ that have identified, as one of the causes of diabetes, a diet that is unbalanced from a caloric standpoint, i.e., one that is rich in fats and sugars and, at the same time, low in vitamins, minerals and other micronutrients. In addition, this is connected with another current tendency towards a more sedentary lifestyle with low energy requirements due to modern-day types of work, transportation and urbanization.

The World Health Organization estimates that this dietary imbalance will be the cause of a worldwide increase in the number of people with diabetes. Forecasts indicate an **increase of 50% in deaths from diabetes** throughout the world over the next 10 years.

To reduce this risk, the population should modify its diet by introducing into its habitual diet foods and nutrients that are beneficial for health, as has been shown scientifically. Specifically, daily caloric intake should be balanced, maintaining equilibrium between calories and the amount of energy expended. Some epidemiological studies have shown that the increase in caloric intake is due to the inclusion in the diet of calorie-rich foods with high levels of fats and sugars, especially snack foods and sugared drinks.

Scientific data suggests that, to reduce the number of people with diabetes, action must be taken involving individual behavior and habits⁷⁰. This means working on cultural and social changes that encourage the population to increase consumption of fruit and vegetables and increase physical activity, while at the same time reducing the caloric imbalance⁷¹. In addition, specifically in terms of diabetes, the FAO suggests that greater amounts of carbohydrates and fiber (grains and

legumes) be introduced into the diet because of their capacity for glycemic control and ability to reduce the risk to develop this pathology⁷².

2.2 Results of Major International Studies

In terms of health, starting in the second half of the 20th century, we witnessed a gradual change in the eating-health pattern of human beings that could be called an actual "diet and health" shift. Four main phenomena characterized the change over the last 50 years:

- scientific-medical progress;
- increase in average life expectancy;
- gradual transformation of diseases;
- a significant change in diet and lifestyle towards a reduction in physical activity and an increase in the daily intake of calories.

Despite some differences between developed and developing countries, this situation of change continues to accelerate and, as a counter-trend, there is a constant reduction in infections, underweight and malnutrition as factors in death and disability⁷³. Especially for developing countries, the phase of "dietary transition", together with the probable increase in cardiovascular disease (as occurred in developed countries), could create concerted economic tension as a result of the discrepancy between available resources and those resources required for creating an efficient public health system.

A summary report that is especially useful on the question of diet/prevention is the recent contribution from the WHO, "*Diet, nutrition and the prevention of chronic diseases*": When useful, reference will also be made to the scientific findings and summarized dietary information given in that international-level report.

2.2.1 Major findings in international studies about the relation between diet and cardiovascular disease

On an international level, cardiovascular disease represents a very significant share of chronic and noncommunicable diseases. From a number of international scientific studies and publications of the World Health Organization (WHO), it can also be seen that there is a "**lag time**" in the appearance of cardiovascular disease compared with the risk factors an individual manifests.

This "lag time" implies that current mortality rates represent, and are a consequence of, dietary habits and behavior that pre-date the appearance of the disease.

From studies conducted by leading scientific bodies, it emerges that the reduction of the risk of contracting cardiovascular disease occurs through an higher consumption of fruit and vegetables, and through the consumption of eicosapentaenoic acid and docosahexaenoic acid (especially present in fish), foods with high linoleic acid⁷⁴ and potassium levels, as well as proper physical activity (at least 30 minutes per day) and low alcohol consumption.

At a lower level of statistical significance, scientific studies indicate that the consumption of linoleic acid⁷⁵, oleic acid⁷⁶, non-starch polysaccharides⁷⁷ and folate⁷⁸, would reduce the risk of the onset of cardiovascular disease.

Contrarily, the factors which significantly increase the risk of contracting cardiovascular disease are elevated consumption of saturated fatty acids, sodium, alcohol and overweight.

Fatty acids and high-cholesterol diet

Numerous studies have shown how cholesterol in the blood and tissues is a factor that can increase the risk of cardiovascular disease. Cholesterol originates from two sources: the diet of an individual or a population, and the endogenous synthesis. A diet rich in fats, dairy products and meat significantly contributes to a rise in plasma cholesterol.

The relationship between cardiovascular problems and diets with **high concentration of fats** has been widely researched and examined in scientific studies which implemented the various analyses of observational, clinical and metabolic studies performed on different ranges of human populations⁷⁹ and in animal experiments.

What emerges from the evidence is that saturated fatty acids increase both the total amount of cholesterol and the quantity of LDL cholesterol, commonly known as "bad" cholesterol, since the lipoproteins of LDL transport cholesterol from the liver and deposit it on the walls of the arteries, thus promoting formation of arteriosclerotic plaque. Other studies have shown that not all saturated fatty acids produce the same negative effects for human health and the cardiovascular system⁸⁰.

Among the factors that increase the risk of the onset of cardiovascular disease, myristic acid⁸¹ and palmitic acid⁸² are those that have the greatest effect and are found in large quantities in meat and dairy products (cheese, milk, butter, cream, tropical oils). Stearic acid, on the other hand, has not been shown to raise blood cholesterol levels.

One of the most effective solutions to reducing the risk of coronary disease is to replace saturated fatty acids with unsaturated fatty acids (monounsaturated and polyunsaturated), such as, for example, oleic acid. Numerous studies and clinical tests have demonstrated that substitution of saturated fatty acids and trans fatty acids with polyunsaturated vegetable oils significantly lowers the risk of heart disease⁸³.

The same studies have shown the existence of a relationship between diets containing high quantities of trans fatty acids⁸⁴, coronary disease and arteriosclerosis. Trans fatty acids are more dangerous for the cardiovascular system and are especially formed during the hydrogenation process used, for example, for manufacturing margarine.

To summarize, trans fatty acids are generated by three main sources:

- hydrogenation or formation of a liquid oil into a solid fat;
- high-temperature treatments (frying);
- bacterial activity of the digestive system of ruminants which generates the only natural trans fatty acids that are present in milk and milk products.

A 1990 study by Mensink showed that trans fats raise the level of LDL cholesterol, while reducing HDL cholesterol, thus worsening cardiovascular risk⁸⁵. Many other subsequent studies confirmed these findings. In particular, two studies⁸⁶ compared trans fats with saturated fats and concluded that the former represented a higher risk factor for cardiovascular disease. In 2002, the National Academy of Sciences⁸⁷ (NAS) further confirmed the theory that trans fats are much worse than saturated fats for the risk of cardiovascular disease and they recommended that they be eliminated from the diet of every individual⁸⁸.

Epidemiologic studies have also confirmed the relationship between cardiovascular risk and trans fats. Both the study by Willett⁸⁹, based on a well-known data base of the Nurses Health Study which examined over 85,000 women, and that by Ascherio⁹⁰ reached the same conclusions: a 27% increase in the risk of contracting cardiovascular disease and approx. 30,000 deaths each year in the US connected with a trans fat-rich diet. A subsequent study by Koletzko⁹¹ confirmed these findings, estimating deaths to be between 25,000 and 30,000 individuals in the US. These results calculated in reference to the US are also confirmed in studies performed in other contexts by Oomen⁹² and Willett⁹³.

On the basis of the clear and evident correlations in scientific studies between the amount of trans fatty acids and cardiovascular disease risk, the concentration of these fatty acids in foods has been the **object of regulation and restrictive legislation** on an international level. This legislation has set the maximum concentration of trans fatty acids for each foodstuff and has developed long-term plans aimed at totaling eliminating trans fatty acids in the food industry⁹⁴.

Eicosapentaenoic acid and docosahexaenoic acid⁹⁵ which are found in fish, alpha-linolenic acid which is found in nuts, some oils and green vegetables, represent the polyunsaturated fats that are most important in reducing the risk of cardiovascular disease. The beneficial effects of polyunsaturated fats also involve arterial pressure, cardiac functioning, endothelial function and vascular reactivity⁹⁶.

The majority of findings from epidemiological studies performed on polyunsaturated fats (n-3) were concentrated on analyzing fish consumption in different populations. In particular, fish oil was used in studies conducted by the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)⁹⁷. Results showed that after 3-1/2 years of administering fish oil (in pharmaceutical grade) which is rich in n-3 fatty acid, there was a 20% reduction in mortality rates, a reduction of 30% in deaths caused by cardiovascular disease and a 45% reduction in sudden deaths.

In terms of fish, many, but not all studies performed showed that regular consumption of fish is associated with a lower risk of contracting cardiovascular disease. Systematic analysis of available studies, undertaken by Marchmann⁹⁸, showed that discrepancies in findings could be the result of the type of sample and population analyzed, and that consumption of fish only benefits in a significant way those individuals at high cardiovascular disease risk. The same study also estimated that an increase in 40-60 grams per day of fish (2-3 portions per week) could bring about a reduction of 50% in deaths from cardiovascular disease in high-risk individuals.

Burr⁹⁹, analyzing individuals who had already had a heart attack, noted a reduction in deaths following a second heart attack in individuals who had received advice to eat fish at least twice a week. Zhang¹⁰⁰, in a study of 36 countries, indicate that consumption of fish reduces the risk of death generally and therefore also that tied to the onset of cardiovascular disease.

Studies by Hu¹⁰¹ and Ascherio¹⁰² showed a reverse relationship between consumption of alpha-linolenic acid and cardiovascular disease.

Non-starch polysaccharides and dietary fiber

Dietary fiber is the edible part of the plant that is resistant to digestion (it is not affected by digestive enzymes), is not absorbed by the human small intestine, but is absorbed by the large intestine where it undergoes complete or partial fermentation thanks to the resident microflora.

Belonging to this category are cellulose, gums, algae polysaccharides, pectins, hemicellulose, arabinogalactans, arabinoxylans and the β -glucans which are also defined as non-starch polysaccharides.

The studies by Anderson¹⁰³ show that **dietary fibers help to reduce the concentration of low-density lipoproteins (LDL)**, known as "bad" cholesterol. Other studies carried out in different countries by Truswell¹⁰⁴ and Rimm¹⁰⁵ showed that a fiber-rich diet and whole-grains reduce the risk of cardiovascular disease.

Among high fiber food, fruit and vegetables play a special role. More specifically, studies by Ness¹⁰⁶, Liu¹⁰⁷, Joshipura¹⁰⁸ and Gilman¹⁰⁹ have shown that there is a very strong protective relationship between the consumption of fruit and vegetables and the risk of cardiovascular disease and stroke.

The effects produced by increasing daily intake of fruits and vegetables, combined with a reduction of fats in the diet, was analyzed by the US Department of Health in its study entitled "Dietary Approaches to Stop Hypertension".

The results show how this diet has greater beneficial effects in terms of reducing blood pressure¹¹⁰.

Antioxidants, folates and flavonoids

Theoretically, antioxidants (glutathione, vitamin C and vitamin E) could protect against cardiovascular disease. Scientific evidence about this is contradictory and there are no

certain results regarding the fact that antioxidants reduce the risk of cardiovascular disease.

The International Task Force for Prevention of Coronary Heart Disease¹¹¹ has performed a wide-ranging study with the goal of analyzing the relationship between vitamin E supplements and cardiovascular disease. Their findings did not indicate any relationship between assuming vitamin E supplements and death from cardiovascular disease, heart attack and stroke¹¹². In addition, results from the same study indicate that there are no significant benefits tied to the assumption of vitamin E, vitamin C and beta carotene supplements by individuals at high risk of cardiovascular disease¹¹³.

A number of observational studies have indicated that carotenoids have a protective role in cardiovascular disease, while, on the contrary, other meta-analysis studies, conducted by Egger¹¹⁴, have shown an increase in risk of death for cardiovascular disease following assumption of carotenoid supplements.

The relationship between folates and cardiovascular disease has also been widely analyzed in scientific studies through the effect on homocysteine, which can be an independent risk factor for cardiovascular disease and stroke. Folic acid is used in the methylation of homocysteine in methionine. Low concentrations of folate in the blood have been associated with high levels of homocysteine. Brouwner¹¹⁵ has shown that folate supplements have reduced homocysteine levels. Nonetheless, despite the numerous studies that have been conducted¹¹⁶, the scientific community has yet to reach adequate consensus about the relationship between homocysteine and cardiovascular disease. Data from the Nurses' Health Study¹¹⁷ showed that folate and vitamin B6, taken as part of a normal diet or as a supplement, provide protection against coronary arteries diseases¹¹⁸.

A meta-analysis study conducted by Wald and published recently showed that a folate-rich diet would reduce the risk of cerebral ischemia by 16% and stroke by 24%¹¹⁹.

Finally, with reference to flavonoids which are secondary metabolite polyphenol compounds of plants that are mainly water-soluble and present in vegetables, tea, onions and apples, the results of studies by Keli¹²⁰ e Hertog¹²¹ indicated that there is an inverse relationship between flavonoid-rich diets and cardiovascular disease.

Sodium and potassium

High blood pressure is one of the factors that most significantly increases the risk of cardiovascular disease and stroke. Among the numerous factors tied to high blood pressure, sodium is the one that has been studied the most through epidemiologic studies and experimental models on animals¹²².

The results of these studies have clearly demonstrated that sodium (salt) is directly correlated to blood pressure.

More specifically, a number of observational studies have shown that a difference of 100 millimoles in the daily intake of sodium results, on average, in a difference in systolic pressure of 5 mmHg for people between 15 and 19 years of age, and 10 mmHg for people between 60 and 69¹²³.

Moreover it has been estimated that an average daily reduction of 50 millimoles of sodium would result in a reduction of 50% in the number of people who are involved in antihypertensive treatments and a reduction of 22% in the number of stroke deaths and of 16% in the number of cardiovascular disease deaths, respectively.

A study conducted on 24 hour urine samples (which is an extremely reliable method for estimating the dietary sodium intake), showed a positive relationship between the risk of acute coronary events and sodium¹²⁴. This relationship is even greater in overweight individuals.

More specifically, Cutler¹²⁵ and Midgley¹²⁶ investigated the effects tied to a reduction in daily salt consumption and blood pressure levels in hypertensive individuals. Results showed that a reduction of 70-80 millimoles of sodium results in a reduction in systolic pressure in hypertensive individuals of approx. 5 mmHg and in normotensive individuals of approx. 2 mmHg. Two studies have been done on this, one in China by Tian¹²⁷ and one in Portugal by Forte¹²⁸, which showed significant reduction in blood pressure in the populations involved in the studies.

Sacks¹²⁹ also showed that hyposodic diets do not have any particular side effects on human health and are, therefore, sustainable, effective and safe.

In terms of potassium, what emerges from the meta-analysis study by Whelton¹³⁰ is that, on the average, supplementary doses of potassium help to reduce systolic blood pressure by approx. 2 mmHg in normotensive individuals and approx. 4 mmHg in hypertensive individuals.

Moreover, Ascherio¹³¹ and Khaw¹³² have shown that there is an inverse correlation between potassium assumption and stroke risk. These studies underscore that even if potassium has been shown to have positive effects on blood pressure and cardiovascular disease, there is no scientific evidence which demonstrates that assumption of potassium supplements will reduce blood pressure significantly, in the long term.

However, a study performed in the long term, has demonstrated that oral sodium supplements are associated to a significant reduction of antihypertensive therapy in hypertensive individuals (Siani A., "Increasing the dietary potassium intake reduces the need for antihypertensive medication", *Intern Med.* 1991 Nov 15; 115(10): 753-9).

Generally, daily consumption of fruit and vegetables assures an adequate amount of potassium for the body.

Other types of nutrients and foods

Various epidemiologic studies performed by Kris-Etherton¹³³ and Hu¹³⁴ showed that frequent consumption of nuts (walnuts, peanuts, almonds, etc.) is linked to a reduction in cardiovascular disease. Studies conducted on this question analyzed the effects of nuts as a food group, combining walnuts, almonds, peanuts, etc. This food group is both high in unsaturated fats with a low concentration of saturated fats. It should be borne in mind that, given its high caloric count, the inclusion of this food group should be balanced in terms of the individual's overall caloric requirements.

For soy, the studies carried out by Crouse¹³⁵ indicated that consumption of soy has beneficial effects of the level of fats in the blood¹³⁶. Analysis of 38 clinical studies revealed that, on average, consumption of 47 grams of soy per day results in a reduction of 9% in overall cholesterol and a reduction of 13% in LDL cholesterol in individuals who do not suffer from cardiovascular disease¹³⁷. Soy is rich in isoflavonoids which are similar to estrogens in structure and function. Various experiments on animals have suggested that intake of isoflavonoids can provide protection against cardiovascular disease, but confirmed, reliable data on their efficacy for man are not yet available.

In terms of alcohol and coffee consumption, a meta-analysis study by Rimm¹³⁸ provides findings that suggest that low/moderate consumption of alcohol reduces cardiovascular disease risk. The same study indicates that consumption of beer, wine and spirits is associated with a reduction in coronary disease risk. By contrast, other studies have found that excessive alcohol consumption is tied to an increase in other cardiovascular disease (arterial hypertension).

Finally, boiled, unfiltered coffee (which increases cholesterol because the coffee beans contain terpenoid fats) is a factor that raises cardiovascular disease risk. The amount of terpenoids in the cup will depend on how it is made and is zero for filtered coffee, while the levels of concentration are high in unfiltered coffee that is still widely drunk today in Greece, Turkey and the Middle East. Tverdal¹³⁹ has noted that consumption of unfiltered coffee significantly increases the risk of coronary disease. A study conducted in Finland by Pietinen¹⁴⁰ revealed that switching from unfiltered to filtered coffee made a significant contribution to reducing cholesterol levels in the population.

In light of the findings of the studies analyzed, the table below summarizes their results in terms of the connection between diet and prevention of cardiovascular disease.

Figure 25. Summary of major findings on life styles and diet factors and the risk of developing cardiovascular disease

Evidence	Decreased risk	Increased risk	No relationship
Convincing	Regular physical activity	Myristic acids	Vitamina E supplements
	Linoleic acid	Palmitic acids	
	Fish and fish oils (EPA e DHA)*	Trans fatty acids	
	Fruit and Vegetables	High sodium intake	
	Potassium	Overweight	
	Low to moderate alcohol intake (for coronary heart disease)	High alcohol intake (for stroke)	
Probable	Alfa-linolenic acid	Dietary cholesterol	Stearic acid
	Oleic acid	Unfiltered boiled coffee	
	Dietary fiber		
	Wholegrain cereals		
	Nuts (unsalted)		
	Folate		
Possible	Flavonoids	Fats rich in lauric acid	
	Soy products	Beta-carotene supplements	
		Sugar	
Insufficiente	Calcium	Iron	
	Magnesium		
	Vitamin C		

(*) EPA – Eicosapentaenoic acid, DHA – Docosahexaenoic acid

Source: The European House-Ambrosetti re-elaboration of WHO, "Diet, Nutrition and the Prevention of Chronic Disease, 2003

2.2.2 Major findings in international studies about the relation between diet and diabetes

The relationship between diet and treatment/prevention of diabetes has been analyzed by numerous studies which considered the effects and consequences of the consumption of the main macro- and micronutrients on the onset of diabetes and its course. A useful point of departure for the building of the tie between diet and diabetes are the studies conducted by the main diabetes associations worldwide¹⁴¹, aimed at identifying a number of dietary guidelines in the prevention and treatment of diabetes.

Body weight and physical activity

Heredity seems to have a significant role in the onset of type 2 diabetes, nonetheless, according to all major scientific associations, the current observed increment in the incidence of this disease is strongly linked to life style changes in the world population. These changes are generally characterized by overall dietary increase in caloric intake and reduction in regular physical activity.

Numerous studies have demonstrated the positive potential of a moderate reduction in body weight in terms of reducing the risk of type 2 diabetes and improving the glycemic control in individuals affected by this pathology.

A modest drop in body weight seems to be able to improve insulin sensitivity (therefore reduce the level of insulin-resistance in individuals at-risk) as well as glucose tolerance, and reduce levels of plasma lipids and blood pressure (see Eriksson et al., 1991¹⁴²; Goldstein et al., 1992¹⁴³; Brage et al., 2004¹⁴⁴; St-Onge et al., 2004¹⁴⁵).

In numerous clinical trials (e.g., Tuomilehto et al., 2002¹⁴⁶ and Knowler et al. 2002¹⁴⁷), in addition, a modest reduction in body weight has been shown effective in slowing the progress of glucose intolerance in type 2 diabetes in individuals at-risk.

Of special importance in the prevention of type 2 diabetes and improvement of a number of risk factors associated with it, would seem to be control of abdominal adiposity. Numerous studies (among others, those conducted by Colditz et al., 1990¹⁴⁸; Després et al., 2001¹⁴⁹; Chan et al., 1994¹⁵⁰ and Boyko et al., 2000¹⁵¹) have demonstrated how the latter represents a more determining factor compared with general body mass in the risk of type 2 diabetes since it is also strictly correlated to insulin-resistance, the key element in diabetes, as shown by JP Després. (2001)¹⁵².

Since overweight and obesity have numerous negative effects on factors tied to the onset of diabetes (primarily on insulin-resistance), programs aimed at changing life styles - in the direction of reducing body weight (by about 5-7%) and to increasing physical activity - seem to have a positive impact on the probability of contracting type 2 diabetes, as also suggested in a recent study by Franz et al. (2002)¹⁵³.

Particularly wide-ranging and recent studies confirm this hypothesis. The results obtained by the Finnish Diabetes Prevention study in Finland (Tuomilehto et al., 2001¹⁵⁴) and the Diabetes Prevention Program in the United States (Knowler et al., 2002¹⁵⁵), as well as the evidence gathered by, among others, Hu et al. (2001)¹⁵⁶, Pan et al. (1997)¹⁵⁷ and Ramachandran et al. (2006)¹⁵⁸, confirm that a reduction of 5-7% in body weight, combined with regular physical activity of 2-1/2 hours per week and diet strategy that calls for a reduction in fats and calorie intake, is capable of noticeable reducing (~60%) type 2 diabetes risk.

In particular, physical activity (which not only aids in weight loss and independently of it) seems to have positive direct effects on type 2 diabetes risk, as shown in studies by Manson et al. (1992)¹⁵⁹, Kriska et al. (1993)¹⁶⁰ e Helmrigh et al. (1991)¹⁶¹ and is able to have a positive impact on insulin sensitivity and glucose levels in the blood (see McAuley et al., 2002¹⁶²).

While generally all international scientific associations underscore the importance of adopting good dietary practices that are tailored and specific to each individual on the basis of a range of parameters (age, overall state of health, dietary habits, cultural traditions, etc.) entering into analysis of long-term effects of different diets on the possibility of reducing body weight, it must be stated immediately that further analysis of diets available to-date

is necessary in order to reach an approach that is shared and unequivocal (as noted by Klein et al., 2004¹⁶³).

From the standpoint of prevention, although it is traditionally believed that a diet oriented towards reducing fat content is the most appropriate, it should be noted that recent analysis (Foster et al., 2003¹⁶⁴ and Stern et al., 2004¹⁶⁵) has highlighted - although without adequate long-term substantiation - the significant weight-loss potential of short-term low-carbohydrate diets.

In any case, it seems generally acknowledged that a very low-calorie diet is capable of bringing about significant weight loss and positive results in terms of glycemia and lipidemia¹⁶⁶. Nonetheless, numerous studies have noted how such low-calorie diets are not able, on their own, of producing long-term positive effects in terms of weight reduction and diabetes risk prevention. Therefore, these diets should be considered as part of a structured, long-term program of optimum weight maintenance (see Ryan et al., 2003¹⁶⁷) which, in addition to dietary guidelines, also includes regular physical activity and, in some cases, use of special weight-maintenance strategies (including, for example, the "exchange diet"¹⁶⁸).

In conclusion, it is important to note that weight-loss in overweight individuals also has collateral benefits on the risk and/or seriousness of diseases most closely correlated with diabetes, such as high blood pressure and dyslipidemia, as noted by, among others, Van Gaal et al. (1988)¹⁶⁹, Lean et al. (1995)¹⁷⁰, the Scottish Intercollegiate Guidelines Network-SIGN (2003)¹⁷¹ and the WHO (2003)¹⁷².

Macronutrients

Taking a more detailed look at the relationship between diet and diabetes, it is immediately clear that there are some macronutrients which are particularly important in diabetes prevention.

Carbohydrates (sugars, starches, fiber), fats and protein must be part (in differentiated amounts and ways) of a diet unanimously defined as "balanced".

Carbohydrates

Post-prandial concentration of glucose in the blood is a key element, both in individuals with diabetes as well as in those at risk. Both the quantity and quality/source of the carbohydrates consumed have a primary relevance.

The set of variables that influence the effect of foods containing carbohydrates on glucose blood levels are several: from the specific type of food consumed to the type of starch (amylose or amylopectin), type of sugar (glucose, fructose, saccharose, lactose), the extent the food was processed and the way it was prepared.

Numerous studies have stressed the general importance of the overall amount of carbohydrates consumed, rather than their type or source¹⁷³.

However, in order to measure the post-prandial effect of consuming a constant amount of different types of foods containing carbohydrates, the so-called "glycemic index" was also developed (see Jenkins et al., 1981¹⁷⁴). Briefly stated, this is a measure of the increase in glucose levels in the blood for two hours following consumption of a constant amount of a given food (normally a portion equivalent to 50 grams of carbohydrates) compared with the effect generated by a "reference" food (normally glucose or white bread).

The fact that, as noted above, not only the quantity of carbohydrates but also the glycemic index of each food consumed during a meal impact on the glycemic response, led to the identification of a new marker of the hyperglycemic ability of food, a mixed meal or a diet: the "Glycemic Load" (GL). This index is calculated as the product of the quantity of carbohydrates a food has and its glycemic index (see Willet et al., 2002¹⁷⁵). It guarantees an enhanced comparability between different quantities of different foods and allows to measure the glycemic load of a meal or a diet, by easily adding the glycemic load of all foods consumed.

A number of studies have indicated that diets characterized overall by a low glycemic index¹⁷⁶ are able to reduce type 2 diabetes risk, as well as the glycemic level in already-diabetic individuals (see Frost et al., 1994¹⁷⁷; Brand et al., 1991¹⁷⁸; Fontvieille et al., 1992¹⁷⁹ and Wolever et al., 1992¹⁸⁰). A recent study by Jenkins et al. (2008)¹⁸¹ noted that, in diabetic patients, a diet characterized by a low glycemic index is able to significantly reduce the level of glycated hemoglobin (HbA_{1c}). Nonetheless, other analyses on this issue have not confirmed the existence of a similar effect (see Liese et al., 2005¹⁸² and Sheard et al., 2004¹⁸³); as a result, a scientifically-proven and unequivocal relationship between a low glycemic index and risk/course of diabetes cannot be identified. These discrepancies would appear due, in part, to high-level variability in the glycemic response on the basis of intake of different types of carbohydrate-rich foods (Wylie-Rosett et al., 2004¹⁸⁴) and the equally as significant personal response of each individual to administration of carbohydrates. In general, as also noted by EASD, the glycemic index would appear a useful tool for initial classification of foods; however, it appears to only have real value if utilized with "comparable" foods and in conjunction with analysis of many other characteristics pertaining to the foods themselves. Among these are the caloric content and overall composition of the various macronutrients contained in them (see Buyken et al., 2001¹⁸⁵ and Riccardi et al., 2003¹⁸⁶). In fact, foods with a low glycemic index can also be rich in saturated fats and simple sugars. Therefore, the glycemic index, if utilized alone, can prove to be a misleading and incomplete indicator.

As briefly mentioned earlier, in terms of the relationship between overall amount of carbohydrates present in the diet and diabetes risk factors, there is not sufficient scientific proof about potential long-term benefits deriving from the adoption of diets with very low carbohydrate content. In fact, these diets

have not been shown to be effective in terms of long-term weight loss and on the development of diabetes¹⁸⁷.

A particularly wide-ranging meta-analysis (Garg et al., 1998¹⁸⁸) compared (in this case in patients already affected by type 2 diabetes) high-carbohydrate diets with diets with high monounsaturated fat content and low carbohydrate content, in relation to the observable effect in terms of lipids and glycemia. Findings did not indicate significant differences in glycemic control between the two types of diets since none of the studies analyzed identified significant difference in the drop in glycated hemoglobin between the two diets.

More specifically in terms of certain types of carbohydrates, it can be seen that a number of studies have underscored the positive effect on health of consumption of fibers which are found in many foods, including, in particular, legumes, certain types of grains (especially whole-grains) and certain types of fruit and vegetables¹⁸⁹.

A number of studies (in particular analysis by Salmeron et al., 1997¹⁹⁰ and the study by Meyer et al., 2000¹⁹¹) demonstrated the protective potential of fiber in the diet for type 2 diabetes, irrespective of age of the individuals analyzed, body mass index and level of physical activity. In numerous studies (see Mann J., 2001¹⁹²) high fiber consumption was linked to the observation of a reduction in glucose and insulin levels in the blood in individuals with reduced glucose tolerance and type 2 diabetes patients.

In addition, some studies (Tuomilehto et al., 2002¹⁹³; Knowler et al., 2002¹⁹⁴) demonstrated that diets with higher intake of whole grains, fruit and vegetable (fiber-rich foods) are able to reduce the risk of developing type 2 diabetes in individuals with low glucose tolerance.

Consumption of fiber-rich foods also seems to favor the reduction and/or containment of the body mass index in both diabetic and healthy individuals (Appleby et al., 1998¹⁹⁵ and Toeller et al., 2001¹⁹⁶) and increase insulin sensitivity in non-diabetic individuals (McKeown et al., 2004¹⁹⁷).

While generally the positive aspects of dietary fiber in diabetes prevention would seem clear, the question regarding the connection between certain types of fiber and diabetes prevention is still unresolved. While some studies indicate that soluble fibers are the main source of benefits in diabetes prevention (Mann et al., 2001¹⁸⁹ and 1984¹⁹⁹; Simpson et al., 1981²⁰⁰; Chandalia et al., 2000²⁰¹), other studies have indicated that the main principal effect is found in insoluble forms of grain fiber (Salmeron et al., 1997²⁰²). Naturally, these differences do not change the sign of the relationship between dietary fiber and diabetes risk.

On the basis of studies conducted during the 1980s, it would seem evident that there is a positive effect on glycemic control of high-carbohydrate and -fiber diets (more than 50 grams per day, of which at least 50% water-soluble), compared with

diets with low-carbohydrate and -fiber content (see Lousely et al., 1984²⁰³). During the same period, other studies have shown the existence of an hyperglycemic effect on glycemia levels of high-carbohydrate/low-fiber diets if compared with low-carbohydrate diets (Simpson et al., 1979²⁰⁴; Simpson et al., 1982²⁰⁵ and Perrotti et al., 1984²⁰⁶).

Taking into consideration both these analyses, the fundamental role of fiber in the improvement of the glycemic control in diabetic patients would seem evident (see Mann J., 1984²⁰⁷ and 2001²⁰⁸).

In samplings of diabetes patients, a number of studies are interesting from the standpoint of general dietary guidelines (these include Sargeant et al., 2001²⁰⁹; Riccardi et al., 1984²¹⁰; Simpson et al., 1981²¹¹; Chandalia et al., 2000²¹²) which analyzed the effects of a fiber-rich diet on lipid and plasma lipoprotein concentrations. In many cases, a reduction in overall cholesterol and LDL cholesterol was recorded.

Finally, it is interesting to note how, in non-diabetic individuals, intake of fiber-rich foods can be beneficial, also in terms of anomalies of the glycemic and lipid metabolism associated with cardiovascular risk. In particular, numerous studies (Rimm et al., 1996²¹³; Bazzano et al., 2003²¹⁴; Wu et al., 2003²¹⁵; Pereira et al., 2004²¹⁶) have noted the existence of an inverse and significant relationship between dietary fiber and the onset/seriousness of cardiovascular disease.

Another group of carbohydrates that has a specific role in the risk of developing diabetes is that of sugars.

In addition, numerous clinical studies have shown how quantities of saccharose in a diet do not cause an increase in the glycemic levels, compared with similar quantities of starches. This means that no direct relationships were detected between intake of saccharose and diabetes risk. Clearly there is an indirect relationship seen in overweight and obesity, conditions that can be facilitated by excessive intake of sugars.

From a comparison of high-sugar diets and diets rich in starches - for individuals who do not suffer from diabetes and those affected by metabolic syndrome²¹⁷ - it would seem to emerge that the former are capable of provoking hypertriglyceridemia (among sugars, a more hyperglycemic effect is attributed to fructose). It was also found - for individuals with metabolic syndrome - that a starch-rich and partially fiber-rich diet is capable of reducing body weight, compared with diets with high sugar content (see Poppitt et al., 2002²¹⁸).

Some studies (including Raben et al., 2002²¹⁹) found that the habitual consumption of sugared beverages, compared with beverages with sweeteners, can cause an increase in calorie levels, body weight, fat mass and level of plasmatic lipids, while suggesting that there is a correlation between consumption of sugared beverages and principal risk factors for diabetes and some main cardiovascular diseases connected to it.

In terms of fructose, available studies have shown that it aids the containment of the post-prandial glycemic response when consumed instead of saccharose or starch within the diet. However, in terms of glycemia, the benefits would seem to be counterbalanced by a negative effect on the plasmatic triglycerides in the blood (Franz et al., 2002²²⁰ and Bantle et al., 2000²²¹). In any case, scientific evidences are referred to fructose added to food and beverages: intake of fructose in quantities found naturally in fruit and vegetables does not appear negative to individuals with diabetes or those at risk.

The connection between other types of sugars (low-calorie sugars, non-nutritive sugars) and diabetes remain little studied. While in relation to alcohol sugars some studies have demonstrated a reduction in post-prandial glycemic response higher than that observable following intake of saccharose and glucose, there are, in fact, no clear results on the relationships between non-nutritive sugars and diabetes (see Raben et al., 2002²²²).

In conclusion, there appears to be sufficient scientific evidence to support a general observation: there must be a sufficient amount of carbohydrates (especially whole grains and fiber) in the diet of each individual. In addition, numerous studies have noted that carbohydrates found in wholegrains and the fiber and carbohydrates found in fruit, vegetables and skim milk don't have to be reduces by individuals with type 2 diabetes or at risk from it as they don't increase the risk of diabetes or of cardiovascular diseases (see Meyer et al., 2000²²³; Schulze et al., 2004²²⁴; Stevens et al., 2002²²⁵; Liese et al., 2003²²⁶).

According to Joshipura et al. (2001)²²⁷ and Sargeant et al. (2001)²²⁸ Regular intake of vegetables, legumes, fruit and whole-grain products would seem capable of guaranteeing the body the correct amount of fiber and micronutrients, promoting control of lipoprotein abnormalities²²⁹, increasing the sense of satiety and, therefore, contributing to reducing the risk of type 2 diabetes.

Fats

It is generally accepted that the quantity and quality of fatty acids consumed has an especially significant influence on numerous diabetes risk factors (and diseases connected to it, particularly cardiovascular).

Many studies (including Mayer et al., 1993²³⁰ and Lovejoy et al., 1992²³¹) have indicated, in particular, how a high daily caloric intake based on consumption of fats (indicatively over 30-35%) is a major risk to weight gain, changes in insulin sensitivity and significant increase in LDL cholesterol values in the blood.

Observational studies have indicated the existence of a significant relation between intake of high levels of fats and high probability for development of glucose intolerance as well

as conversion from intolerance to actual type 2 diabetes (see Feskens et al., 1995²³² and Marshall et al., 1994²³³).

While there are some general relationships between dietary intake of fatty acids and diabetes, there exist numerous major differences within the fatty acid family between saturated fatty acids, unsaturated fatty acids (monounsaturates, polyunsaturates and trans) and dietary cholesterol in their relationship to diabetes risk factors, both before and after its onset.

Numerous studies have shown that increased intake of saturated fatty acids is associated with a higher risk of glucose intolerance and observation of higher fasting insulin and glucose levels (see Feskens et al., 1995²³⁴; Bo et al., 2001²³⁵; Feskens et al., 1990²³⁶ and Parker et al., 1993²³⁷).

Analyzing both individuals who do not suffer from diabetes as well as diabetes sufferers, recent studies (Peréz-Jimenez et al., 2001²³⁸; Summers et al., 2002²³⁹; Thomsen et al., 1999²⁴⁰; Thomsen et al., 2003²⁴¹; Vessby et al., 2001²⁴²) have shown that replacing saturated fatty acids by unsaturated fatty acids within the diet can generate significant benefits for insulin sensitivity and post-prandial lipid levels. This substitution could also improve glucose tolerance (see Uusitupa et al., 1994²⁴³ and di Vessby et al., 1980²⁴⁴).

Folsom et al. (1996)²⁴⁵, Vessby et al. (1994)²⁴⁶ and Vessby et al. (1994)²⁴⁷ have found that increased intake of saturated fatty acids is associated to a higher risk of type 2 diabetes. Salmeron et al. (2001)²⁴⁸ and Meyer et al. (2001)²⁴⁹ have shown that reduction in type 2 diabetes risk can be correlated, above all, to an increase in intake of vegetal unsaturated fatty acids.

Shifting dietary intake of fats from saturated to monounsaturated fats appears especially positive on the influence of diabetes risk factors. Both for individuals with reduced glucose tolerance and healthy individuals, this substitution has positive impact on the level and composition of plasma lipidemia and insulin sensitivity (Katan et al., 1995²⁵⁰; Howell et al., 1997²⁵¹; Mensink et al., 2003²⁵²; Vessby et al., 1980²⁵³; Vessby et al., 2001²⁵⁴).

While maintaining constant the body weight of individuals analyzed and their overall caloric intake, some metabolic studies have shown how diets with a low saturated fatty acid component and high level of carbohydrates or cis-type monounsaturated fatty acids can reduce the level of LDL cholesterol in the blood (Franz et al., 2002²⁵⁵ and Garg et al., 1994²⁵⁶; Katan et al., 1995²⁵⁷; Howell et al., 1997²⁵⁸; Mensink et al., 2003²⁵⁹), including in diabetic patients (Heine et al., 1989²⁶⁰).

Nonetheless, it should be noted that numerous studies (see Storm et al., 1997²⁶¹) have shown in a significant way that stearic acid also does not cause an increase in cholesterol, as do other saturated fatty acids (lauric, myristic and palmitic). In

addition, among these, myristic and palmitic acids seem able to generate a greater increase in cholesterol in the blood (total and LDL), compared with lauric acid, both for diabetic and healthy individuals (Cox et al., 1995²⁶²).

Comparative analysis of high-carbohydrate diets (~55% of total calories) and diets with a high level of monounsaturated fatty acids showed that, compared with the latter, the former can lead to a relatively higher level of post-prandial glucose, insulin and triglycerides in the blood. In addition, partial substitution of carbohydrates within the diet with monounsaturated fatty acids have a positive effect on concentrations of plasma lipids (Garg A., 1998²⁶³) and blood pressure levels (Rasmussen et al., 1993²⁶⁴ Thomsen et al., 1995²⁶⁵).

Nonetheless, other studies have not confirmed the existence of a significant difference in the metabolic effect of diet rich in monounsaturated fats or, respectively, in complex carbohydrates (Pérez-Jimenez et al., 2001²⁶⁶; Thomsen et al., 1999²⁶⁷; Bonanome et al., 1991²⁶⁸; Luscombe et al., 1999²⁶⁹; Rodrigues-Villar et al., 2000²⁷⁰).

In addition, substitution of carbohydrates by fats could facilitate an increase in body weight, above all due to the potential increase in calorie intake, while following a low-fat diet containing foods rich in fiber and carbohydrates with low glycemic index seems capable of promoting weight loss and metabolic control both in diabetic and metabolic syndrome patients (Toeller et al., 2001²⁷¹; Poppitt et al., 2002²⁷²).

Finally, numerous studies have indicated a positive connection between vegetal polyunsaturated fats in the diet (with high n-6-type linoleic fatty acid content) and reduction in type 2 diabetes risk (Feskens et al., 2001²⁷³; Hu et al., 2002²⁷⁴; Marshall et al., 2002²⁷⁵; Salmeron et al., 2001²⁷⁶ and Meyer et al., 2001²⁷⁷).

However, in terms of intake of linoleic acid, it should be remembered that a practical consideration that is widely accepted (although no specific findings exist to support it) is that this acid should not be consumed excessively within the diet (no more than 10% of daily caloric intake) as a precautionary measure due to the potential increased risk of lipid peroxidation (Mann et al., 2000²⁷⁸).

In relation to long-chain n-3 polyunsaturated fatty acids (α-linoleic) some studies (including Pan et al., 1995²⁷⁹) have found a positive relationship between an increase in their intake (for example, through fish oil) and improvement of insulin sensitivity. As mentioned previously, an increase in consumption of these fatty acids seems to be associated with a reduction in risk of death for cardiac events and stroke (see Hu F.B., 2001²⁸⁰ and Harris et al., 2003²⁸¹).

In addition, some studies have found that long-chain n-3 fatty acid intake can lead to an increase in glycemia, but recent meta-analyses (Friedberg et al., 1998²⁸²; Montori et al., 2000²⁸³)

have shown that this effect is not significant.

Despite the fact that numerous findings demonstrate quite clearly the positive potential of dietary intake of n-3 and n-6 fatty acids, sufficient evidence does not exist to reach a detailed prevention-related definition for the best n-3/n-6 acid ratio within the habitual diet.

The effect of unsaturated trans fatty acids (which originate in the hydrogenation process of vegetal oils) seems similar to that identified for saturated fatty acids, which is an increase in LDL cholesterol in blood. Beside this, trans fatty acids also reduce the presence of HDL cholesterol in blood (Katan et al., 1995)²⁸⁴.

Numerous studies have demonstrated that a high trans fatty acid diet can increase the risk of type 2 diabetes (see Salméron et al., 2001²⁸⁵) and increase post-prandial insulinemia in individuals with type 2 diabetes (Christiansen et al., 1997²⁸⁶).

In terms of dietary cholesterol, numerous studies on both diabetic and healthy individuals have shown a noticeable increase in plasma cholesterol as the amount of dietary cholesterol consumed increases (Weggemans et al., 2001²⁸⁷; Romano et al., 1998²⁸⁸; Toeller et al., 1999²⁸⁹).

In addition, intake of dietary cholesterol seems closely correlated to cardiovascular disease risk. Some studies (including once again, Toeller et al., 1999) have shown that increased intake of total fats, saturated fats and dietary cholesterol is associated with a greater frequency of cardiovascular disease, fiber intake reduce this relation.

Several information related to the effect of changes in the amount of saturated fats, trans fats and dietary cholesterol consumed on plasma lipids, have been taken from studies undertaken on non-diabetic individuals because not enough data were available for diabetic ones.

Proteins

At the current time, there does not appear to be sufficient scientific evidence in support of the existence of long-term benefits of diabetes prevention and cure from an intake of proteins higher than the habitual diet one (15-20% of the overall caloric level). In most Western countries, protein consumption is 10-20% of daily caloric intake, equal to approximately 0.8-2.0 g/kg of body weight per day.

Numerous studies have shown that for healthy individuals and those affected by type 2 diabetes, the glucose produced by metabolism of dietary proteins consumed does not generate an immediate increase in glucose in the blood, but does effect the insulin response, causing it to rise (see Franz et al., 2002²⁹⁰ and Gannon et al., 2001²⁹¹).

Some studies (including Gannon et al., 2003, 2004²⁹²) have found a negative relationship between concentrations of glucose and insulin and an amount of proteins very high (above 20% of

the total caloric intake). Not only these diets reduce these levels of concentration, but they also reduce appetite and increase a sense of satiety, thus helping in the control of body weight.

Despite the fact that similar scientific results do exist, on the whole they do not yet seem sufficiently analyzed (as noted by the ADA in its recent position statement entitled "Nutrition recommendations and interventions for diabetes" issued January 2008), nor are the long-term effects of high-protein diets on the regulation of caloric intake and body weight, or the ability of individuals to actually follow such diets for protracted periods of time.

Without entering too deeply into this point, it is interesting to note that protein content is relevant in terms of the development of one of the main cardiovascular complication of diabetes, diabetic nephropathy²⁹³.

Despite the fact that some studies have highlighted the existence of possible correlation between the quantity of protein intake and diabetic nephropathy, there does not seem to be general agreement on the findings of studies conducted on the link between restricting the amount of protein consumed and critical aspects of diabetic nephropathy (primarily albuminuria and filtered glomerulus). In some cases, there seem to be discrepancies between the relationships noted and in others the significance of the findings appears limited.

Generally, in terms of the reduction in the protein content derived from diet, it should be noted that individuals with diabetes (or at serious risk to it) often show an increase in protein turnover (basically the relationship between protein utilized - or eliminated in the case of diabetic nephropathy - and protein consumed). Therefore, an excessive reduction in overall protein content does not seem positive for these individuals (Nair et al., 1983²⁹⁴; Gougeon et al., 1994²⁹⁵; Gougeon et al., 1997²⁹⁶; Gougeon et al., 1998²⁹⁷). As seen previously, although its reduction could have beneficial results, protein content should not be less than 0.6 g/kg of ideal weight per day since a lower intake level would seem to create potential malnutrition problems.

Micronutrients

In the current situation - as also noted by Guerrero-Romero et al. (2005)²⁹⁸ and Kligler et al. (2004)²⁹⁹ - there does not appear to be sufficient evidence produced to-date by long-term clinical trials aimed at identifying both health safety and potential positive role of chromium, magnesium and antioxidants in a preventive or therapeutic approach to type 2 diabetes. To a certain extent, findings of the various studies seem to be contradictory or, in some cases, not sufficiently significant.

In its recent report, "*Diet, nutrition and the prevention of chronic diseases*" the WHO also confirms that currently there is no adequate scientific confirmation to support the hypothesis that chromium and magnesium are able to provide a form of protection against type 2 diabetes risk.

For individuals not affected by diabetes, prospective studies indicate that antioxidants, vitamins and foods rich in these substances (such as fruit, vegetables, walnuts and berries) are able to guarantee protection against cardiovascular disease (see Fraser et al., 1992³⁰⁰; Gaziano et al., 1995³⁰¹; Gillmann et al., 1995³⁰²; Hu et al., 1998³⁰³; Joshipura et al., 1999³⁰⁴; Liu et al., 2000³⁰⁵; Joshipura et al., 2001³⁰⁶; Kris-Etherton et al., 2001³⁰⁷; Liu et al., 2001³⁰⁸; Albert et al., 2002³⁰⁹; Bazzano et al., 2002³¹⁰).

In addition, insufficient presence in the body of chromium, potassium, magnesium and zinc would seem to worsen carbohydrate intolerance. Results of some recent studies (Cefalu et al., 2004³¹¹; Ryan et al., 2003³¹²; Althuis et al., 2002³¹³), confirm the existence of positive effects on glycemic levels and glucose intolerance management through an increase in chromium intake.

Empiric observation (see McNair et al., 1982³¹⁴ and Tosiello et al., 1996³¹⁵) has shown that diabetes is significantly correlated to the observation of a reduced magnesium levels in the blood. In any case, once again here, if some circumstances directly tied to individuals already affected by diabetes are excluded³¹⁶, there does not seem to be sufficient scientific proof to support a positive role for increased intake of magnesium in preventing type 2 diabetes.

Diabetes is often associated with a lack in the body of micronutrients which underscores the importance for diabetics or those at-risk to follow a balanced diet that contains sufficient vitamins and minerals. However, there does not seem to be sufficient scientific evidence to-date (as noted also by the WHO) to identify unequivocal relationships between intake of given quantities of vitamins and minerals and risk of diabetes or correlated diseases.

In fact, in terms of antioxidants, numerous clinical trials conducted have noted the lack of evident benefits to glycemic control from the introduction on doses of vitamin E, C and carotene and other integrators with antioxidant properties at levels in excess of those found in a balanced, varied diet (see Franz et al., 2002³¹⁷; Hasanain et al., 2002³¹⁸ and Lonn et al., 2002³¹⁹).

In addition, some available data (see Kris-Etherton et al., 2004³²⁰) does not seem to support the hypothesis of a positive effect in terms of reducing cardiovascular risk of the supplementation of antioxidants through dietary supplement, and numerous studies have not identified any direct benefit traceable to chromium supplementation into the diet of individuals suffering from type 2 diabetes or glucose intolerance, both in terms of glycemia management and body weight control (Gunton et al., 2005³²¹; Kleefstra et al., 2006³²² and Pittler et al., 2003³²³).

Alcohol

Some studies (see Howard et al., 2004³²⁴) have shown that moderate intake of alcohol at meals does not generate any significant serious effect on the level of glucose in the blood or concentration of insulin.

High levels of alcohol consumption has been correlated—independently of the body mass index—to a higher waist-to-hip ratio (Dallongeville et al., 1998³²⁵) and the carbohydrates consumed with the alcohol seem to increase plasma glucose. According to some studies (Kerr et al., 1990³²⁶ and Pownall et al., 1999³²⁷), alcohol also seems capable of increasing trygliceridemia and the risk of hypoglycemia.

Despite these findings, moderate alcohol consumption seems to have a potentially positive effect on insulin sensitivity (Davies et al., 2002³²⁸; Greenfield et al., 2003³²⁹; Sierksma et al., 2004³³⁰) and would seem to be correlated to a reduction in the risk of coronary events (Howard et al., 2004³³¹ and Ajani et al., 2000³³²) and stroke (Sacco et al., 1999³³³), to an increase in HDL cholesterol levels in the blood and to a reduction in lipid oxidation and coagulation indices (through the action of antioxidant substances in some alcoholic beverages).

Some studies (Mukamal et al., 2003³³⁴ and Gaziano et al., 1999³³⁵) have demonstrated, in particular, that modest intake of alcohol has a more positive effect if consumed on a regular basis compared with a situation in which it is consumed on fewer occasions but in greater amounts. However, these studies have not indicated any significant connection between the time of day of consumption in terms of meals/type of alcoholic beverage and positive effects of the alcohol itself.

As was also mentioned by the WHO, currently-available evidence does not make it possible to credit moderate alcohol consumption with preventive properties for type 2 diabetes. Considering the scientific findings produced to-date, there does not seem to be conclusive data in terms of the most appropriate level of alcohol consumption for diabetic individuals or those strongly at-risk. Therefore, the recommendation of all major international scientific associations is similar to that given to the population at-large (for a study that examines this, see Burger et al., 2000³³⁶).

In light of the findings of the studies analyzed, the table below summarizes their results in terms of the connection between diet and diabetes.

Figure 26. Summary of major findings on life styles and diet factors and the risk of developing diabetes

Evidence	Decreased risk	Increase in risk
Convincing	Voluntary weight loss in overweight and obese people	Overweight and obesity
	Physical activity	Abdominal obesity Physical inactivity
Probable	Dietary fiber	Saturated fats
Possible	Wholegrain cereals	
	n-3 fatty acids	Total fat intake
	Low glycaemic index foods	Trans fatty acids
	Moderate alcohol	
Insufficient	Vitamin E Chromium Magnesium	Excessive alcohol

Source: The European House-Ambrosetti re-elaboration of WHO, "Diet, Nutrition and the Prevention of Chronic Diseases", 2003

2.2.3 Major findings in international studies about the relation between diet and cancer

Tumors are caused by a multitude of factors, some of which are known, but others of which are still unknown to the international scientific/medical community.

Smoking tobacco, following an unhealthy diet, consuming alcohol, physical inactivity, infections, hormonal factors and radiation are all factors which can trigger cancer.

One of the key non-food causes is tobacco smoke. Tobacco smoke increases the normal risk of each individual to contract lung cancer by about 30 fold³³⁷. It is responsible for 80% of lung cancer cases in developed countries³³⁸ and it is the most common type of tumor on a world level³³⁹. Tobacco smoke is also one of the main risk factors in cancer of the mouth, larynx and esophagus. In studying the triggering causes of pancreatic cancer, Calle³⁴⁰ obtained results which indicate that tobacco smoke is a factor that substantially increases the risk of tumors of the pancreas.

The industrialization process in developing countries and resulting increase in living standards means that the types of tumors found in developing countries and developed countries are increasingly similar, especially those caused by diet-related factors. Between 2000 and 2020, the number of cancer cases in developing countries is expected to increase by 73%, while in developed countries an increase of 29% is forecast.

Some studies³⁴¹ have forecast that the adoption of improper dietary habits represents an incidence factor of 30% in cancer in industrialized countries, second only to tobacco smoke. This incidence is still around 20% in developing countries³⁴², but could increase significantly faced by the probable change in future dietary habits and already seen in developed countries.

The number of tumors seen in a population and the relative percentage rate varies on the basis of the countries examined, type of diet and life style. The *International Agency for Research on Cancer*³⁴³ has indicated overweight and physical inactivity as the factors which account for between 20% and 35% of cases in the onset of breast, colon, renal and esophageal cancer.

To date, the scientific studies published have identified a fairly limited number of links between diet and cancer risk.

Obesity and overweight

Long-term, but also short-term conditions of obesity and overweight represent factors that increase the risk of various types of tumors.

The *International Agency for Research on Cancer*³⁴⁴ has indicated overweight and obesity as factors that augment the risk of colorectal cancer. A subsequent study by Calle³⁴⁵ confirmed the relationship between obesity and colorectal cancer, although it is noted that this relationship is more pronounced in men. Again in reference to colorectal cancer, the studies by Cummings and Bingham³⁴⁶ noted how the type of diet adopted accounts for over 80% of the differences seen in the rates of colorectal cancer within the populations of the various countries analyzed around the world. In other words, the onset of this type of tumor depends very strongly on the type of diet followed. On a worldwide level, the rates of colorectal cancer are ten times higher in developed countries than in developing countries. Only in the United States where the percentage of obese and overweight people is very high does colorectal cancer represent the second most prevalent cause of death by tumor³⁴⁷.

Analyzing the risk factors for oral cavity tumors, Brown³⁴⁸, indicated that overweight and obesity increase the risk of esophageal adenocarcinoma³⁴⁹.

In a study conducted by Michaud³⁵⁰ overweight and obesity emerge as risk factors also for pancreatic tumors, especially if coupled with high consumption of meat and low percentage of vegetables in the diet.

For breast cancer, many studies, including those by Radimer³⁵¹, Trentham-Dietz³⁵², Carmichael³⁵³ and Stephenson³⁵⁴, once again indicate that overweight, especially in adulthood, is one of the factors in the increase of the risk of breast tumors.

Overweight and obesity increase the risk of endometrial tumors, as seen in the studies by Amant³⁵⁵, while Bergstrom³⁵⁶ stressed that this risk is approximately three times higher in obese women compared with those of normal weight.

Once again in the studies conducted by Bergstrom³⁵⁷, in 30% of cases overweight and obesity are triggering factors in renal cancer.

Although the etiology of renal cancer is still little known,

in 2002 the *International Agency for Research on Cancer*³⁵⁸ indicated that there is sufficient evidence to demonstrate that overweight is a risk factor in the onset of renal cancer.

To summarize, overweight and obesity are factors that increase the risk linked to the onset of mouth cavity, colorectal, breast, pancreatic, endometrial and renal cancer.

Alcoholic beverages

In developed countries, the main diet-related risk factor for tumors of the mouth, larynx and esophagus, is the consumption of alcoholic beverages. Tobacco smoking added to alcohol consumption account for over 75% of all tumors of the oral cavity³⁵⁹.

The results of the study by McKillop³⁶⁰ showed that excessive consumption of alcohol is a risk factor in the onset of liver cancer, probably through the development of cirrhosis of the liver.

Smith-Warner³⁶¹ have also indicated how an increase in daily consumption of alcohol increases the risk of breast cancer. Other studies by Hamajima³⁶² and Feigelson³⁶³ have produced the same findings. Generally, even if this latter connection is not well known, studies by Dorgan³⁶⁴ indicate that the relationship between alcohol and breast cancer can be linked through the increase in levels of some estrogens.

In conclusion, Giovannucci³⁶⁵, in a number of alcohol-specific studies, showed how consumption of alcoholic beverages is linked to a greater risk in the onset of colorectal tumors.

Consumption of alcoholic beverages constitutes an increased risk factor for oral cavity, liver, breast and colorectal cancer.

Fruit and vegetables (dietary fiber)

The *International Agency for Research on Cancer*³⁶⁶ has found that approx. 60% of oral cavity tumors are probably correlated to a lack of micronutrients caused by a diet lacking in fruits and vegetables.

In studying the causes of colorectal tumors, Potter³⁶⁷ noted a weak connection with fruit and vegetable consumption. Also in a meta-analysis study by Jacobs³⁶⁸, a weak connection between consumption of dietary fiber and reduction in the risk of colorectal tumors was found.

More recent studies by Mikels³⁶⁹ and Bueno de Mesquita³⁷⁰ have shown contradictory findings, some of which indicate an inverse relationship between consumption of fruit and vegetables and colorectal cancer, others which show that there is no clear-cut relationship between fruit and vegetable consumption and colorectal cancer.

Studies by Schatzkin³⁷¹ and Alberts³⁷² based on a sample of individuals who, for 3 to 4 years were given supplementary servings of dietary fiber, fruit and vegetables and had the amount of fats in their diet reduced, did not note any relationship between these foods/nutrients and risk of colorectal cancer.

In reference to the same studies, it is possible that the discrepancy in findings and lack of connection between fruit, vegetables, dietary fiber and colorectal tumors depends both on the differences between the studies in relation to the type of dietary fibers analyzed, as well as their methods of classification in the nutrient table, but also by the fact, as indicated in the study by Terry³⁷³, that the positive connection between consumption of fruit and vegetables and reduction of colorectal tumors was seen in those individuals with diets with low fruit and vegetable intake.

On an overall level, even if a clear-cut relationship does not exist, the results of medical-scientific studies indicate that consumption of fruit and vegetables probably reduces the risk of colorectal tumors.

Gonzalez³⁷⁴, analyzing the risk factors for gastric cancer, noted that consumption of fruit and vegetables plays a protective role against stomach tumors.

In a recent study, Bandera³⁷⁵ suggested that a diet composed of high levels of fruit and vegetables reduces the risk of endometrial cancer.

Many studies³⁷⁶ showed that fruit and vegetables also play a protective role against lung cancer. However, it should be noted that the apparent protective role of fruit and vegetables could be justified by the fact that smokers (the no. 1 risk factor in lung cancer), on a whole, consume less fruit and vegetables than non-smokers.

Finally, Key³⁷⁷ and Smith-Warner³⁷⁸, analyzing determining factors for breast cancer, did not note any particular relationship with fruit, vegetables and dietary fiber.

On a general level, the results of medical-scientific studies indicate that regular consumption of fruit, vegetables and dietary fiber aids in reducing the risk of oral cavity, gastric, colorectal and endometrial cancer.

Fresh meat, cured meat and sausage

The international medical-scientific community agrees on the fact that some aspects of Western diet, and, specifically, consumption of fresh meat, cured meat and sausage, is a factor in increased cancer risk.

In a meta-analysis study by Norat³⁷⁹, what emerged was that a high level of cured meat and a high fat content diet augments the risk of colorectal tumors. Other studies³⁸⁰ did not reveal positive connections between colorectal cancer and the consumption of poultry (white meat) and fish.

Shuurman³⁸¹, Chan³⁸² and Michaud³⁸³ found that elevated consumption of red meat and animal products has a positive correlation with the development of prostate cancer. Studies by Kolonel³⁸⁴ and Rodriguez³⁸⁵ also confirmed the positive relation between red meat and prostate cancer.

In conclusion, a study by Michaud³⁸⁶ shows that a high amount of meat in the diet is a risk factor for pancreatic cancer.

Folate, vitamins, beta-carotene, selenium, calcium and lycopene

From analysis by Giovannucci³⁸⁷ on determining factors in colorectal cancer, it emerged that high intake of folate and vitamins reduces the risk of colorectal cancer. In specific studies on vitamin D, Giovannucci³⁸⁸ once again found that intake of vitamin D could prevent the onset of colorectal cancer.

On a general level, medical-scientific studies in identification of causes and factors in lung cancer risk have produced controversial and, often, contradictory results. Numerous observational studies³⁸⁹ have found that individuals who contract lung cancer generally have a diet with low beta-carotene intake, while Hennekens³⁹⁰, Omenn³⁹¹ and international study groups³⁹² have tested the link between beta-carotene and the onset of lung cancer without discovering any particular connection.

Studies conducted by Heinonen³⁹³ and Clark³⁹⁴ have demonstrated that beta-carotene supplements do not affect the risk level for prostate cancer, but supplements of vitamin E and selenium can have positive effects.

Studies by Bonithon-Kopp³⁹⁵ and Baron³⁹⁶ indicate that a high level of calcium in the diet could have a preventive function for colorectal cancer and also be a prevention factor in recurrence of tumors in the same individual.

On the other hand, studies by Giovannucci³⁹⁷ have shown that supplemental or high intake of calcium in the diet increase the risk of recurrence of very aggressive prostate cancer. On the contrary, Kristal³⁹⁸ has shown that lycopene, a substance found in tomatoes, is a protective factor in prostate cancer.

Salt and salt-preserved foods

In a number of studies conducted on an international level and on the Asian continent, Ferlay³⁹⁹ and Yu⁴⁰⁰, observed that nasopharyngeal cancer is especially common in East Asia. This situation was connected to high consumption levels of salted fish (in traditional Chinese style), in particular during childhood⁴⁰¹.

Palli⁴⁰² and Kelley⁴⁰³ found that increased risk of gastric cancer is associated with high consumption levels of salt-preserved foods, cured meats and pickled foods.

Very hot foods and beverages

Analyzing the causes of esophageal cancer, Sharp⁴⁰⁴ found that there is a significant correlation between consumption of very hot foods and beverages and increase in the risk of tumors in the oral cavity.

In other words, the results of the study showed that intake of very hot beverages and food is a risk factor for oral cavity cancer.

Regular physical activity

The number of tumors seen in a population and the relative percentage rate varies on the basis of the countries examined and type of diet, but above all from personal habits.

The *International Agency for Research on Cancer*⁴⁰⁵ has indicated that physical inactivity, together with overweight, are factors which account for between 20% and 35% of cases of breast, colorectal, renal and esophageal cancer.

Specific studies by Martinez⁴⁰⁶ and Hardman⁴⁰⁷ have shown that regular physical activity is linked to a significant reduction in colorectal cancer.

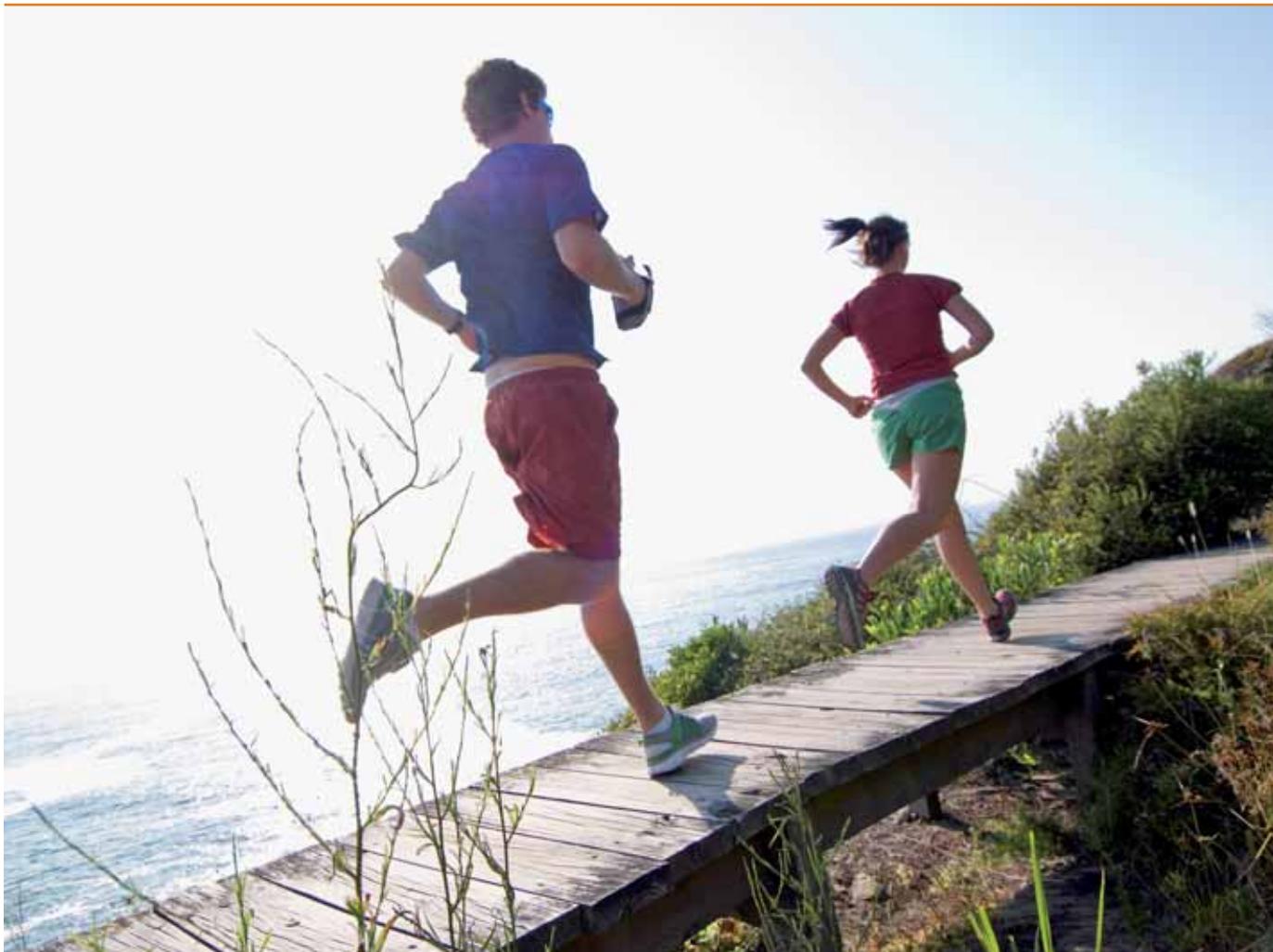
Generally, a lifestyle which includes adequate physical activity is a factor that reduces cancer risk.

In light of the findings of the studies analyzed, the table below summarizes their results in terms of the connection between diet and prevention of cancer.

Figure 27. Summary of major findings on life styles and diet factors and the risk of developing cancer

Evidence	Decreased risk	Increased risk
Convincing	Physical activity (colon cancer)	Overweight and obesity (oesophagus, colorectum, breast, endometrium, kidney)
		Alcohol (oral cavity, pharynx, larynx, oesophagus, liver, breast)
		Chinese-style salted fish (nasopharynx cancer)
Probable	Fruits and vegetables (oral cavity, oesophagus, stomach, colorectum cancer)	Preserved meat (colorectum cancer)
		Salt-preserved foods (stomach cancer)
		Salt (stomach cancer)
		Very hot drinks and food (oral cavity, pharynx, oesophagus cancer)
Possible/insufficient	Fibre	Animal fats
	Soya	Nitrosamines
	n-3 Fatty acids	
	Vitamins B ₂ , B ₆ , B ₁₂ , C, D, E	
	Calcium, zinc and selenium	
	Carotenoids	
	Non-nutrient plant constituents (e.g. flavonoids, isoflavones, lignans)	

The European House-Ambrosetti re-elaboration of WHO, "Diet, Nutrition and the Prevention of Chronic Diseases", 2003



NOTE PART A

1. Source: "2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases", World Health Organization 2008
2. Obesity is defined as an excess of body fat in relation to lean mass, in terms both of quantity and distribution in precise points of the body. Classification of the population in terms of weight is accomplished using the Body Mass Index (BMI) which is considered the most representative for the presence of excess body fat. The BMI is calculated as the ratio between weight (kg) and height (m) squared. (Source: Centro Nazionale di Epidemiologia, Prevenzione e Promozione della Salute - Istituto Superiore di Sanità Roma, 2004)
3. National Institutes of Health (NIH), Obesity Research Task Force: "Strategic Plan for NIH Obesity Research", August 2004
4. Trust for America's Health and Robert Wood Johnson Foundation: "F as in Fat: how obesity policies are failing in America", July 2009
5. WHO Technical Report Series 916. Diet, nutrition and the prevention of chronic diseases. Report of a Joint FAO/WHO Expert Consultation. World Health Organization, Geneva, 2003
6. For example, heart attack, hypertension, thrombosis, aneurism, stroke, etc.
7. Source: "Cardiovascular diseases", Fact sheet no. 317, February 2007, World Health Organization
8. Source: "Heart Disease & Stroke Statistics. 2009 Update at-a-glance", American Heart Association, 2009
9. The standardized rate makes it possible to compare different time periods irrespective of the various distributions in terms of the age of the population over the different time periods. It is an indicator created "artificially" that no longer corresponds to the actual value, but has been adapted to compare death rates between different time periods by age bracket
10. Source: Foot D., Lewis R., Pearson T., Beller G., "Demographics and cardiology, 1950-2050", Journal of the American College of Cardiology, Volume 35, Issue 5, 2000
11. Source: "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009
12. This indicates the years each deceased person would have lived if he/she had reached the life expectancy age
13. Source: Centro Nazionale di Epidemiologia, Prevenzione e Promozione della Salute - Istituto Superiore di Sanità Roma, 2004
14. Source: "Documento di iniziativa per promuovere le strategie e gli interventi di prevenzione cardiovascolare in Italia", SIPREC - Società Italiana per la Prevenzione cardiovascolare, 2008
15. DRG (Diagnosis Related Group) refers to the classification system for patients released from hospitals for severe problems, based on like-ailment groups, that is utilized as the basis for financing to hospital districts
16. Source: "Documento di iniziativa per promuovere le strategie e gli interventi di prevenzione cardiovascolare in Italia", SIPREC - Società Italiana per la Prevenzione cardiovascolare, 2008
17. These include, among others, smoking, high blood pressure, obesity and overweight, sedentary life style, etc.
18. Source: "Heart Disease and Stroke Statistics - 2009 Update", The American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Circulation, 2008
19. Hospital costs alone total 150.1 billion dollars
20. Source: "Cardiovascular diseases", Fact sheet no. 317, February 2007, World Health Organization
21. Source: "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009
22. Source: "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009
23. This primarily involves hours of assistance received by patients with coronary or cerebral-vascular disease by non-salaried workers
24. Source: Censis, "Monitor Biomedico 2007"
25. Source: "Documento di iniziativa per promuovere le strategie e gli interventi di prevenzione cardiovascolare in Italia", SIPREC - Società Italiana per la Prevenzione cardiovascolare, 2008
26. Prevalence measures the number of individuals (in a population) affected by a particular disease at that given moment
27. The vast majority of cases (85-95%) involve type 2 mellitus diabetes, or non-insulin dependent diabetes
28. Source: "Diabetes Atlas", International Diabetes Federation, 2009 (<http://www.eatlas.idf.org/>)
29. According to the International Diabetes Federation, the level is 5.8%
30. The metabolic syndrome (also known as the X syndrome, or insulin-resistance syndrome) is diagnosed when a person exhibits three or more of the following conditions: abdominal obesity (abdominal circumference greater than 103 cm for men and 88 cm for women), high levels of triglycerides in the blood, low levels of HDL cholesterol (low density lipoproteins), high blood pressure and high fasting glucose levels in the blood (although there are differences between Italian and international organizations in exactly specifying these criteria)
31. This syndrome is present in approx. 90% of patients with type 2 mellitus diabetes
32. Source: The European Food Information Council; <http://www.eufic.org/index/it/>
33. Source: International Obesity Task Force, June 2005
34. "Economic Costs of Diabetes in the U.S. in 2007", American Diabetes Association, Diabetes Care, Volume 31, Number 3, March 2008
35. "Health & the EU Lisbon Agenda - High Returns on Health Investment", May 2006
36. Source: "Global Cancer Facts&Figures 2007", American Cancer Society
37. Source: World Health Organization, Fact Sheet no. 297, February 2009
38. Number of new cases recorded each year
39. Source: "Rapporto Osservasalute 2008. Stato di salute e qualità dell'assistenza nelle regioni italiane", Università Cattolica del Sacro Cuore, 2008
40. Source: "Global Cancer Facts&Figures 2009", American Cancer Society, 2009
41. To evaluate the social-economic impact of tumors, an index called DALY (Disability Adjusted Life Years), originally developed by the World Health Organization, is used
42. Source: "The burden and cost of cancer", Annals of Oncology 18 (supplement 3), European Society for Medical Oncology, 2007
43. Source: "The burden and cost of cancer", Annals of Oncology 18 (supplement 3), European Society for Medical Oncology, 2007
44. Source: Lévy C., Bonastre J., "The cost of chemotherapy", Bull Cancer 2003 Nov
45. Source: "The burden and cost of cancer", Annals of Oncology 18 (supplement 3), European Society for Medical Oncology, 2007
46. Source: Bosanquet N., Sikora K., "The economics of cancer care in the UK", BMJ, 2003
47. Source: Mackay J., Jemal A., Lee N.C., Parkin M., "The Cancer Atlas", American Cancer Society, 2006
48. ISDOC study group, "Actual and preferred place of death of cancer patients. Results from the Italian survey of the dying of cancer (ISDOC)", Journal of Epidemiology and Community Health 2006
49. Source: Fondazione Istud and Department of Oncology of the Policlinico Umberto I, 2007
50. World Health Organization, "Healthy Living", 1999
51. Source: World Health Organization, "The World Health Report 2002 - Reducing risks, Promoting Healthy Life"
52. Data from 2000. Source: World Health Organization, "The World Health Report 2002 - Reducing risks, Promoting Healthy Life"
53. DALYs (Disability-Adjusted Life Years) is a statistical index developed by the WHO to express in percentage terms the number of years of life in good health lost because of a disease
54. Source: World Health Organization, "The World Health Report 2002 - Reducing risks, Promoting Healthy Life"
55. Source: World Health Organization, "The World Health Report 2002 - Reducing risks, Promoting Healthy Life"
56. Source: World Health Organization, "World Health Statistics 2008"
57. Source: World Health Organization, "Noncommunicable diseases now biggest killers", May 2008
58. Source: World Health Organization, "Do lifestyle changes improve

- health?"; January 2009
59. Data from 2000. Source: World Health Organization, "The Tobacco Atlas", 2002
 60. Source: World Health Organization, "The Tobacco Atlas", 2002
 61. Source: World Health Organization, "Diet and physical activity: a public health priority"
 62. Source: World Health Organization, "Diet and physical activity: a public health priority"
 63. Numerous scientific studies were published in World Health Organization - "Chronic diseases and health promotion"
 64. Nizal Sarrafzadegan et al, "Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran", Bulletin of the World Health Organization, Volume 87, Number 1, January 2009
 65. The spread of tumors is discussed in section 1.4
 66. Doll R., Peto R., "The causes of cancer", Oxford Medical Publications, 1981
 67. Source: Water Footprint Network
 68. World Health Organization, "North Karelia Project"
 69. World Health Organization, "Diet, Nutrition and the Prevention of Chronic Diseases"
 70. World Health Organization, "Obesity and overweight"
 71. Source: Lindstrom, "Diabetologia", 2006
 72. Source: FAO/WHO, "Scientific Update on carbohydrates in human nutrition: conclusions", 2007
 73. Reddy KS. Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. *Public Health Nutrition*, 2002, 5:231-237
 74. Linoleic acid is found in sunflower and corn oil
 75. Linoleic acid is quite rare and is found in low quantities in common types of vegetable oils
 76. Oleic acid is 75% of the acids in olive oil
 77. Typical of fiber-based diets
 78. Folate is necessary for the synthesis, repair and functioning of DNA and RNA, the prime "building blocks" of life. Therefore, folate is necessary for the production and maintenance of new cells, and is particularly important during periods of rapid growth, such as childhood and pregnancy. A slight lack of folate is also tied to an increase in homocysteine amino acid levels in the blood which is an emerging risk factor for cardiovascular disease and stroke, as shown in the study by JJ Strain and L. Dowey carried out in 2004 and entitled "B-vitamins, homocysteine metabolism and CVD", published in the Proceedings of the Nutrition Society
 79. Kris-Etherton P, Summary of the scientific conference on dietary fatty acids and cardiovascular health: conference summary from the nutrition committee of the American Heart Association. *Circulation*, 2001, 103:1034-1039
 80. Grundy SM, Vega GL. Plasma cholesterol responsiveness to saturated fatty acids. *American Journal of Clinical Nutrition*. 1988, 47:822-824; Katan MJ, Zock PL, Mensink RP. Dietary oils, serum lipoproteins and coronary heart disease. *American Journal of Clinical Nutrition*, 1995, 61 (Suppl. 6):1368--1373
 81. Myristic acid is found in nutmeg, coconut oil and fats of dairy products
 82. Palmitic acid is contained in palm oil, meat and dairy products
 83. Hu FB et al. Dietary fat intake and the risk of coronary heart disease in women. *New England Journal of Medicine*, 337:1491-1499, 1997; Xu J, Eilat-Adar S, Loria C, Goldbourt U, Howard BV, Fabsitz RR, Zepher EM, Mattil C, Lee ET, Dietary fat intake and risk of coronary heart disease: the Strong Heart Study, *The American Journal of Clinical Nutrition*, 84(4):894-902, 2006
 84. Trans fatty acids exist in reduced amount in nature and are found in meat and dairy products, with virtually the entire amount generated during the hydrogenation process. The change in structure of the fats contained in foods obtained through hydrogenation makes it possible to extend product shelf life and guarantee freshness while reducing production costs. In its "trans" form, fatty acid not only increases the level of LDL lipoproteins, the so-called "bad cholesterol", but it also reduces the "good" HDL that protects the cardiovascular apparatus by helping the body to eliminate cholesterol
 85. Mensink, R P and Katan, M B, Effect of dietary trans fatty acids on high-density and low-density lipoprotein cholesterol levels in healthy subjects. *N. Engl. J. Med.*, 323:439-445, 1990
 86. Sundram, K; Anisah, I; Hayes, K C; Jeyamalar, R and Pathmanathan, R. Trans (elaidic) fatty acids adversely impact lipoprotein profiles relative to specific saturated fatty acids in humans. *J. Nutr.*, 127:514S-520S, 1997; Wood, R; Kubena, K; O'Brien, B; Tseng, S e Martin, G, Effect of butter, mono- and polyunsaturated fatty acid-enriched butter, trans fatty acid margarine and zero trans fatty acid margarine on serum lipids and lipoproteins in healthy men. *J. Lipid Res.*, 34:1-11, 1993
 87. www.nasonline.org
 88. Institute of medicine, Letter report on dietary reference intakes for trans fatty acids. National Academy of Sciences, USA, July 2002
 89. Willett, W C; Stampfer, M J; Manson, J E; Colditz, G A; Speizer, F E; Rosner, B A; Sampson, L A and Hennekens, C H, Intake of trans fatty acids and risk of coronary heart disease among women. *Lancet*, 341:581-585, 1993
 90. Ascherio, A; Hennekens, C H; Buring, J E; Master, C; Stampfer, M J and Willett, W C, Trans fatty acids intake and risk of myocardial infarction. *Circulation*, 89:94-101, 1994
 91. Koletzko, B. and T. Decsi 1997. Metabolic aspects of trans fatty acids. *Clinical Nutrition* 16:229-237.
 92. Oomen CM et al. Association between trans fatty acid intake and 10-year risk of coronary heart disease in the Zutphen Elderly Study: a prospective population based study. *Lancet*, 357:746-751, 2001
 93. Willett WC, Intake of trans fatty acids and risk of coronary heart disease among women. *Lancet*, 341:581-585, 1993
 94. Katan MB. Trans fatty acids and plasma lipoproteins. *Nutrition Reviews*, 58:188-191, 2000
 95. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are polyunsaturated fatty acids of the omega 3 family. Unlike other omega 3 fatty acids, EPA and DHA are not essential fatty acids, but it is believed they play a very important role in the health of individuals because they play a positive role in synthesizing good eicosanoids. EPA and DHA are especially present in fish fats (100 grams of salmon, trout, sardines, mackerel, herring or tuna contain an amount that varies between 1.5 and 3 grams of omega 3). Although they are not essential fatty acids, it has been demonstrated that they are fundamental nutrients for proper development and maintenance of good health by reducing the risk of cardiovascular disease and lowering the level of triglycerides
 96. Mori TA, Beilin LJ. Long-chain omega 3 fatty acids, blood lipids and cardiovascular risk reduction. *Current Opinion in Lipidology*, 12:11-17, 2001
 97. GISSI-Prevenzione investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. *Lancet*, 354:447-455, 1999 (www.gissi.org)
 98. Marckmann P, Gronbaek M., Fish consumption and coronary heart disease mortality. A systematic review of prospective cohort studies. *European Journal of Clinical Nutrition*, 53:585-590, 1999.
 99. Burr ML et al. Effects of changes in fat, fish and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet*, 2:757-761, 1989.
 100. Zhang J, Fish consumption and mortality from all causes, ischemic heart disease, and stroke: an ecological study. *Preventive Medicine*, 28:520-529, 1999.
 101. Hu FB, Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. *American Journal of Clinical Nutrition*, 69:890-897, 1999
 102. Ascherio A et al. Dietary fat and risk of coronary heart disease in men: cohort follow-up study in the United States. *British Medical Journal*, 313:84-90, 1996
 103. Anderson JW, Hanna TJ. Impact of nondigestible carbohydrates on serum lipoproteins and risk for cardiovascular disease. *Journal of Nutrition*, 129:1457-1466, 1999
 104. Truswell AS. Cereal grains and coronary heart disease. *European Journal of Clinical Nutrition*, 56:1-14, 2002
 105. Rimm EB, Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. *Journal of the American Medical Association*, 275:447-451, 1996
 106. Ness AR, Powles JW. Fruit and vegetables, and cardiovascular disease: a review. *International Journal of Epidemiology*, 26:1-13, 1997.
 107. Liu S, Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. *American Journal of Clinical*

- Nutrition, 72:922-928, 2000.
108. Joshipura KJ, Fruit and vegetable intake in relation to risk of ischemic stroke. *Journal of the American Medical Association*, 282:1233-1239, 1999.
 109. Gilman MW et al. Protective effect of fruits and vegetables on development of stroke in men. *Journal of the American Medical Association*, 273:1113-1117, 1995.
 110. Appel LJ et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *New England Journal of Medicine*, 336:1117-1124, 1998
 111. <http://www.chd-taskforce.de>
 112. Yusuf S et al. Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *New England Journal of Medicine*, 342:154-160, 2000
 113. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20 536 high-risk individuals: a randomized placebo-controlled trial. *Lancet*, 2002, 360:23-33
 114. Egger M, Schneider M, Davey-Smith G. Spurious precision? Meta-analysis of observational studies. *British Medical Journal*, 1998, 316:140-144
 115. Brouwer IA, Low dose folic acid supplementation decreases plasma homocysteine concentrations: a randomized trial. *American Journal of Clinical Nutrition*, 1999, 69:99-104
 116. Ueland PM et al. The controversy over homocysteine and cardiovascular risk. *American Journal of Clinical Nutrition*, 72:324-332, 2000. Nygard O et al. Total plasma homocysteine and cardiovascular risk profile. The Hordaland Homocysteine Study. *Journal of the American Medical Association*, 274:1526-1533, 1995
 117. <http://www.channing.harvard.edu>
 118. Rimm EB et al. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women. *Journal of the American Medical Association*, 279:359-364, 1998
 119. Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *British Medical Journal*, 325:1202-1208, 2002
 120. Keli SO. Dietary flavonoids, antioxidant vitamins, and incidence of stroke: the Zutphen study. *Archives of Internal Medicine*, 156:637-642, 1996
 121. Hertog MGL. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet*, 342:1007-1011, 1993
 122. Gibbs CR, Lip GY, Beevers DG. Salt and cardiovascular disease: clinical and epidemiological evidence. *Journal of Cardiovascular Risk*, 7:9-13, 2000
 123. Law MR, Frost CD, Wald NJ. By how much does salt reduction lower blood pressure? III--Analysis of data from trials of salt reduction. *British Medical Journal*, 302:819-824, 1991
 124. Tuomilehto J. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. *Lancet*, 357:848-851, 2001
 125. Cutler JA, Follmann D, Allender PS. Randomized trials of sodium reduction: an overview. *American Journal of Clinical Nutrition*, 65:643-651, 1997
 126. Midgley JP. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *Journal of the American Medical Association*, 275:1590-1597, 1996
 127. Tian HG et al. Changes in sodium intake and blood pressure in a community based intervention project in China. *Journal of Human Hypertension*, 9:959-968, 1995
 128. Forte JG. Salt and blood pressure: a randomized trial. *Journal of Human Hypertension*, 3:179-184, 1989
 129. Sacks FM. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *New England Journal of Medicine*, 344:3-10, 2001
 130. Whelton PK. Effects of oral potassium on blood pressure. a meta-analysis of randomized controlled trials. *Journal of the American Medical Association*, 277:1624-1632, 1997
 131. Ascherio A. Intake of potassium, magnesium, and fiber and risk of stroke among US men. *Circulation*, 98:1198-1204, 1998
 132. Khaw KT, Barrett-Connor E. Dietary potassium and stroke-associated mortality. A 12-year prospective population study. *New England Journal of Medicine*, 316:235-240, 1987
 133. Kris-Etherton PM. The effects of nuts on coronary heart disease risk. *Nutrition Reviews*, 59:103-111, 2001
 134. Hu FB, Stampfer MJ. Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence. *Current Atherosclerosis Reports*, 1:204-209, 1999
 135. Crouse JR. Randomized trial comparing the effect of casein with that of soy protein containing varying amounts of isoflavones on plasma concentrations of lipids and lipoproteins. *Archives of Internal Medicine*, 159:2070-2076, 1999
 136. Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease. *Journal of Nutrition*, 130 (Suppl.):653-711, 2000
 137. Anderson JW, Smith BM, Washnok CS. Cardiovascular and renal benefits of dry bean and soybean intake. *American Journal of Clinical Nutrition*, 70:464-474, 1999
 138. Rimm EB. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *British Medical Journal*, 319:1523-1528, 1999
 139. Tverdal A. Coffee consumption and death from coronary heart disease in middle-aged Norwegian men and women. *British Medical Journal*, 300:566-569, 1990
 140. Pietinen P. Changes in diet in Finland from 1972 to 1992: impact on coronary heart disease risk. *Preventive Medicine*, 25:243-250, 1996
 141. European Association for the Study of Diabetes (EASD), Gruppo di Lavoro italiano Associazione Medici Diabetologi - Diabete Italia - Società Italiana di Diabetologia (AMD-DI-SID), American Diabetes Association (ADA), WHO
 142. Eriksson K.F., Lindgarde F.: Prevention of type 2 (non insulin dependent) diabetes mellitus by diet and physical exercise. *Diabetologia* 34: 891, 1991
 143. Goldstein D.J.: Beneficial health effects of modest weight loss. *Int. J. Obes.* 16: 397-415, 1992
 144. Brage S., Wedderkopp N., Ekelund U., et al. the European Youth Heart Study (EYHS): Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children. *Diabetes Care* 27: 2141, 2004
 145. St-Onge M.P., Janssen I., Heymsfield S.B.: Metabolic syndrome in normal-weight Americans. *Diabetes Care* 27: 2222, 2004
 146. Tuomilehto J et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, 2002, 344:1343-1350
 147. Knowler WC et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention of metformin. *New England Journal of Medicine*, 2002, 346:393-403
 148. Colditz GA et al. Weight as a risk factor for clinical diabetes in women. *American Journal of Epidemiology*, 1990, 132:501-513
 149. Després JP et al. Treatment of obesity: need to focus on high-risk abdominally obese patients. *British Medical Journal*, 2001, 322:716-720
 150. Chan JM et al. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care*, 1994, 17:961-969
 151. Boyko EJ et al. Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. *Diabetes Care*, 2000, 23:465-471
 152. Després JP. Health consequences of visceral obesity. *Annals of Medicine*, 2001, 33:534-541
 153. Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell JQ, Wheeler M: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148-198, 2002
 154. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukkaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M: Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*, 344:1343-1350, 2001
 155. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM: Reduction in the incidence of type 2 diabetes with lifestyle intervention of metformin. *N Engl J Med* 346: 393-403, 2002
 156. Hu FB, Manson JE, Stamper MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle and the risk of type 2 diabetes mellitus in women. *New Engl J Med* 2001; 345:790-7
 157. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang

- H, Bennett PH, and Howard BV. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997; 20:537-44
158. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian with Impaired Glucose Tolerance (IDPP-1). *Diabetologia* 2006; 49:289-97
 159. Manson JE et al. A prospective study of exercise and incidence of diabetes among US male physicians. *Journal of the American Medical Association*, 1992, 268:63-67
 160. Kriska AM et al. The association of physical activity with obesity, fat distribution and glucose intolerance in Pima Indians. *Diabetologia*, 1993, 36:863-869
 161. Helmrich SP et al. Physical activity and reduced occurrence of non-insulindependent diabetes mellitus. *New England Journal of Medicine*, 1991, 325:147-152
 162. McAuley K.A., Williams S.M., Mann J.I., et al.: Intensive lifestyle changes are necessary to improve insulin sensitivity: a randomised intervention trial. *Diabetes Care* 25: 445, 2002
 163. Klein S, Sheard NF, Pi-Sunyer X., Daly A., Wylie-Rosett J, Kulkarni K., Clark NG: Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies: a statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. *Diabetes Care* 27:2067-2073, 2004
 164. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, Szapary PO, Rader DJ, Edman JS, Klein Nutrition recommendations and interventions S74 DIABETES CARE, VOLUME 31, SUPPLEMENT 1, JANUARY 2008 S: A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 348: 2082-2090, 2003
 165. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF: The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med* 140:778-785, 2004
 166. For this, see the recent position statement published by the ADA: "Nutrition recommendations and interventions for diabetes", January 2008
 167. Ryan DH, Espeland MA, Foster GD, Haffner SM, Hubbard VS, Johnson KC, Kahn SE, Knowler WC, Yanovski SZ: Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. *Control Clin Trials* 24:610-628, 2003
 168. The "exchange diet", especially advised to diabetic patients, is based on the necessity of a varied diet while maintaining the share of various nutrients constant. Foods have been divided into groups with similar nutritional properties. A balanced diet is created on the basis of which substitutions may be made from within the exchange list (of food groups). For example, if a certain total of grams of bread (carbohydrates) are part of the diet, these can be substituted by a corresponding quantity of another food on the same list (potatoes, pasta, rice, polenta, breadsticks, etc.). (Source: Progetto Diabete)
 169. Van Gaal L., Rillaerts E., Creten W., De Leeuw I.: Relationship of body fat distribution pattern to atherogenic risk factors in NIDDM. *Diabetes Care* 11: 103, 1988
 170. Lean M.E.J., Han T.S., Morrison C.E.: Waist circumference as a measure for indicating need for weight management. *Br. Med. J.* 311: 158, 1995
 171. Scottish Intercollegiate Guidelines Network Guidelines No. 69: Obesity in children and young people. SIGN, 2003. www.show.scot.nhs.uk/guidelines/fulltext/69.html
 172. WHO Technical Report Series 916. Diet, nutrition and the prevention of chronic diseases. Report of a Joint FAO/WHO Expert Consultation. World Health Organization, Geneva, 2003
 173. Note the position statement of the ADA on this: "Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications", January 2002
 174. Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV: Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr* 34:362-366, 1981
 175. Willett W.C., Manson J., Liu S.: Glycemic index, glycemic load, and risk of type 2 diabetes. *Am. J. Clin. Nutr.* 76: 274S, 2002
 176. Among low glycemic index food (<51) it is possible to find: dry chickpeas (10), cherries (22), barley, bread with cereals seeds (27), lentils (30), pasta (40), oranges, apples and pears (38-44), all bran (51), pumpernickel bread (51). Among medium glycemic index food (from 56 to 69) it is possible to find: wholemeal rice (55), basmati rice (58), oat (65), wholemeal bread (69). Among high glycemic index food it is possible to find: white bread (70), potatoes (93).
 177. Frost G., Wilding J., Beecham J.: Dietary advice based on the glycaemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet. Med.* 11: 397, 1994
 178. Brand J., Colagiuri S., Crossman S., Allen A., Roberts D., Truswell A.: Low-glycemic index foods improve long-term glycemic control in NIDDM. *Diabetes Care* 14: 95, 1991
 179. Fontvieille A., Rizkalla S., Penformis A., Acosta M., Bornet F., Slama G.: The use of low glycaemic index foods improve metabolic control of diabetic patients over five weeks. *Diabet. Med.* 9: 444, 1992
 180. Wolever T., Jenkins D., Vuksan V., et al.: Beneficial effect of a low glycaemic index diet in type 2 diabetes. *Diabet. Med.* 9: 451, 1992
 181. Jensinks D., Kendall C., McKeown-Eyssen G., et al.: Effect of a Low Glycemic Index or a High Cereal Fiber Diet on Type 2 Diabetes: A Randomized Trial. *JAMA*, December 17, 2008- Vol 300, No. 23
 182. Liese AD, Schulz M, Fang F, Wolever TM, D'Agostino RB Jr, Sparks KC, Mayer-Davis EJ: Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the Insulin Resistance Atherosclerosis Study. *Diabetes Care* 28:2832-2838, 2005
 183. Sheard NF, Clark NG, Brand-Miller JC, Franz MJ, Pi-Sunyer FX, Mayer-Davis E, Kulkarni K, Geil P: Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement of the American Diabetes Association. *Diabetes Care* 27:2266-2271, 2004
 184. Wylie-Rosett J, Segal-Isaacson CJ, Segal-Isaacson A: Carbohydrates and increases in obesity: does the type of carbohydrate make a difference? *Obes Res* 12 (Suppl. 2):124S-129S, 2004
 185. Buyken AE., Toeller M., Heitkamp G., et al. and the EURODIAB IDDM Complications Study Group: Glycemic index in the diet of European outpatients with type 1 diabetes: relations to HbA1c and serum lipids. *Am. J. Clin. Nutr.* 73: 574, 2001
 186. Riccardi G., Clemente G., Giacco R.: Glycemic index of local foods and diets: the Mediterranean experience. *Nutr. Rev.* 61: S56, 2003
 187. On this issue, see, among others, Foster et al., 2003 and Samaha et al., 2003; this lack of efficacy is probably also due to the fact that low-carbohydrate diets normally a rich in fats, with a consequent potential negative effect on long-term maintenance of optimum body weight and insulin sensitivity (see Vessby et al., 2001; Toeller et al., 2001 and Shah et al., 1996)
 188. Garg A.: High-monounsaturated fat diets for patients with diabetes mellitus: a meta-analysis. *Am. J. Clin. Nutr.* 67 (suppl.): 577S, 1998
 189. For this, see the recent position statement published by the ADA: "Nutrition recommendations and interventions for diabetes", January 2008
 190. Salmeron J et al. Dietary fiber, glycemic load and risk of NIDDM in men. *Diabetes Care*, 1997, 20:545--550. Salmeron J et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *Journal of the American Medical Association*, 1997, 277:472-477
 191. Meyer KA et al. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *American Journal of Clinical Nutrition*, 2000, 71:921-930
 192. Mann J. Dietary fibre and diabetes revisited. *European Journal of Clinical Nutrition*, 2001, 55:919-921
 193. Tuomilehto J et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, 2002, 344:1343-1350
 194. Knowler WC et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention of metformin. *New England Journal of Medicine*, 2002, 346:393-403
 195. Appleby P.N., Thorogood M., Mann J.I., Key T.J.: Low body mass index in non-meat eaters: the possible roles of animal fat, dietary fibre and alcohol. *Int. J. Obes.* 22: 454, 1998
 196. Buyken AE., Toeller M., Heitkamp G., et al. and the EURODIAB IDDM Complications Study Group: Nutrient intakes as predictors of body weight in European people with type 1 diabetes. *Int. J. Obes.* 25: 181S, 2001

197. McKeown N.M., Meig S.J.B., Liu S., Saltzman E., Wilson P.W.F., Jacques P.F.: Carbohydrate nutrition, insulin resistance, and the prevalence of the Metabolic Syndrome in the Framingham Offspring Cohort. *Diabetes Care* 27: 538, 2004
198. Mann J. Dietary fibre and diabetes revisited. *European Journal of Clinical Nutrition*, 2001, 55:919-921
199. Mann J. Lawrence lecture. Lines to legumes: changing concepts of diabetic diets. *Diabetic Medicine*, 1984, 1:191-198
200. Simpson HRC et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet*, 1981, 1:1-5
201. Chandalia M et al. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *New England Journal of Medicine*, 2000, 342:1392-1398
202. Salmeron J et al. Dietary fiber, glycemic load and risk of NIDDM in men. *Diabetes Care*, 1997, 20:545-550. Salmeron J et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *Journal of the American Medical Association*, 1997, 277:472-477
203. Lousely S.E., Jones D.B., Slaughter P., Carter R.D., Jelfs R., Mann J.L.: High carbohydrate/high fibre diets in poorly controlled diabetes. *Diabet. Med.* 1: 21, 1984
204. Simpson R.W., Mann J., Eaton J., Carter R.D., Hockaday T.D.R.: High-carbohydrate diets and insulin dependent diabetics. *Br. Med. J.* 2: 523, 1979
205. Simpson H.C.R., Carter R.D., Lousley S., Mann J.L.: Digestible carbohydrate - an independent effect on diabetic control in type II (non-insulin dependent) diabetic patients? *Diabetologia* 23: 235, 1982
206. Perrotti N., Santoro D., Genovese S., Giacco A., Rivellese A., Riccardi G.: Effect of digestible carbohydrates on glucose control in insulin dependent patients with diabetes. *Diabetes Care* 7: 354, 1984
207. Mann J.: Lines to legumes: changing concepts of diabetic diets. *Diabetic Med.* 1: 191, 1984
208. Mann J.: Dietary fibre and diabetes revisited. *Eur. J. Clin. Nutr.* 55: 919, 2001
209. Sargeant L.A., Khaw K.T., Bingham S., et al.: Fruit and vegetable intake and population glycosylated haemoglobin levels: the EPIC-Norfolk Study. *Eur. J. Clin. Invest.* 55: 342, 2001
210. Fontvieille A., Rizkalla S., Penformis A., Acosta M., Borneo F., Slama G.: Separate influence of dietary carbohydrate and fibre on the metabolic control in diabetes. *Diabetologia* 26: 116, 1984
211. Simpson H.C.R., Carter R.D., Lousley S., Mann J.L.: A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1: 1, 1981
212. Chandalia M., Garg A., Lutjohann D., von Bergmann K., Grundy S.M., Brinkley L.J.: Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *N. Engl. J. Med.* 342: 1392, 2000
213. Rimm E.B., Ascherio A., Giovannucci E., Spiegelman D., Stampfer M.J., Willet W.C.: Vegetable, fruit and cereal fiber intake and risk of coronary heart disease among men. *J.A.M.A.* 275: 447, 1996
214. Bazzano L.A., He J., Ogden L.G., Loira C.M., Whelton P.K., National Health and Nutrition Survey I Epidemiological Follow-up Study: Dietary fiber intake and reduced risk of coronary heart disease in US men and women: The National Health and Nutrition Survey I Epidemiological Follow-up Study. *Arch. Intern. Med.* 163: 1897, 2003
215. Wu H., Dwyer K.M., Fan Z., Shircore A., Fan J., Dwyer J.H.: Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. *Am. J. Clin. Nutr.* 78: 1085, 2003
216. Pereira M.A., O'Reilly E., Augustsson K., et al.: Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies. *Arch. Intern. Med.* 164: 370, 2004
217. Metabolic syndrome is defined as the simultaneous presence of three or more of the following conditions: abdominal obesity (abdominal circumference greater than 102 cm for men and 88 cm for women), high levels of triglycerides in the blood (greater than or equal to 150 mg/dl), low levels of HDL cholesterol (less than 40 mg/dL for men, less than 50 mg/dL for women), high blood pressure (greater than or equal to 130/85 mm Hg) and high fasting glucose levels in the blood (greater than or equal to 100 mg/dL). (Source: American Heart Association)
218. Poppitt S.D., Keogh G.F., Prentice A.M., et al.: Long term effects of ad libitum low-fat highcarbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome. *Am. J. Clin. Nutr.* 75: 11, 2002
219. Raben A., Vasilaras T., Moller A., Astrup A.: Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am. J. Clin. Nutr.* 76: 721, 2002
220. Franz M.J., Bantle J.P., Beebe C.A., Brunzell J.D., Chiasson J.L., Garg A., Holzmeister L.A., Hoogwerf B., Mayer-Davis E., Mooradian A.D., Purnell J.Q., Wheeler M.: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148-198, 2002
221. Bantle J., Raatz S., Thomas W., Georgopoulos A.: Effects of dietary fructose on plasma lipids in healthy subjects. *Am. J. Clin. Nutr.* 72: 1128, 2000
222. Raben A., Vasilaras T.H., Moller A.C., Astrup A.: Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am J Clin Nutr* 76:721-729, 2002
223. Meyer K.A., Kushi L.H., Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR: Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr* 71:921-930, 2000
224. Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB: Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. *Am J Clin Nutr* 80:348-356, 2004
225. Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D: Dietary fiber intake and glycemic index and incidence of diabetes in African-American and white adults: the ARIC study. *Diabetes Care* 25: 1715-1721, 2002
226. Liese AD, Roach AK, Sparks KC, Marquart L, D'Agostino RB Jr, Mayer-Davis EJ: Whole-grain intake and insulin sensitivity: the Insulin Resistance Atherosclerosis Study. *Am J Clin Nutr* 78:965-971, 2003
227. Joshipura K.J., Hu F.B., Manson J.E., et al.: The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann. Intern. Med.* 134: 1106, 2001
228. Sargeant L.A., Khaw K.T., Bingham S., et al.: Fruit and vegetable intake and population glycosylated haemoglobin levels: the EPIC-Norfolk Study. *Eur. J. Clin. Invest.* 55: 342, 2001
229. Lipoproteic changes (increase in triglyceridemia and reduction in HDL cholesterol levels) contribute significantly to increasing the risk of vascular events in overweight and obese individuals and seem decidedly more common in individuals with visceral obesity than those with simple obesity. (Source: Andrea Poli, Fondazione Italiana per il Cuore)
230. Mayer EJ et al. Usual dietary fat intake and insulin concentrations in healthy women twins. *Diabetes Care*, 1993, 16:1459-1469
231. Lovejoy J, DiGirolamo M. Habitual dietary intake and insulin sensitivity in lean and obese adults. *American Journal of Clinical Nutrition*, 1992, 55:1174-1179
232. Feskens EJM et al. Dietary factors determining diabetes and impaired glucose tolerance. A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care*, 1995, 18:1104-1112
233. Marshall JA et al. Dietary fat predicts conversion from impaired glucose tolerance to NIDDM. The San Luis Valley Diabetes Study. *Diabetes Care*, 1994, 17:50-56
234. Feskens E.J.M., Virtanen S.M., Räsänen L., et al.: Dietary factors determining diabetes and impaired glucose tolerance. A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care* 18: 1104, 1995
235. Bo S et al. Dietary fat and gestational hyperglycaemia. *Diabetologia*, 2001, 44:972-978
236. Feskens EJM, Kromhout D. Habitual dietary intake and glucose tolerance in euglycaemic men: the Zutphen study. *International Journal of Epidemiology*, 1990, 19:953-959
237. Parker DR et al. Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: the Normative Aging Study. *American Journal of Clinical Nutrition*, 1993, 58:129-136
238. Pérez-Jiménez F, López-Miranda J, Pinillos M.D., et al.: A Mediterranean and a highcarbohydrate diet improve glucose metabolism in healthy young persons. *Diabetologia* 44: 2038, 2001
239. Summers L.K.M., Fielding B.A., Bradshaw H.A., et al.: Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. *Diabetologia* 45: 369, 2002

240. Thomsen C, Rasmussen O, Lousen T, et al.: Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *Am. J. Clin. Nutr.* 69: 1135, 1999
241. Thomsen C, Storm H, Holst JJ, Hermansen K.: Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *Am. J. Clin. Nutr.* 77: 605, 2003
242. Vessby B, Uusitupa M, Hermansen K, et al.: Substituting dietary saturated fat with monounsaturated fat impairs insulin sensitivity in healthy men and women: the KANWU Study. *Diabetologia* 44: 312, 2001
243. Uusitupa M et al. Effects of two high-fat diets with different fatty acid compositions on glucose and lipid metabolism in healthy young women. *American Journal of Clinical Nutrition*, 1994, 59:1310-1316
244. Vessby B et al. Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia. *European Journal of Clinical Nutrition*, 1980, 10:193-202
245. Folsom AR et al. Relation between plasma phospholipid saturated fatty acids and hyperinsulinemia. *Metabolism*, 1996, 45:223-228
246. Vessby B, Tengblad S, Lithell H. Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70-year-old men. *Diabetologia*, 1994, 37:1044-1050
247. Vessby B et al. The risk to develop NIDDM is related to the fatty acid composition of the serum cholesterol esters. *Diabetes*, 1994, 43:1353-1357
248. Salmeron J et al. Dietary fat intake and risk of type 2 diabetes in women. *American Journal of Clinical Nutrition*, 2001, 73:1019-1026
249. Meyer KA et al. Dietary fat and incidence of type 2 diabetes in older Iowa women. *Diabetes Care*, 2001, 24:1528-1535
250. Katan M.B., Zock P.L., Mensink M.P.: Dietary oils, serum lipoproteins, and coronary heart disease. *Am. J. Clin. Nutr.* 61: 1368S, 1995
251. Howell W.H., McNamara D.J., Tosca M.A., Smith B.T., Gaines J.A.: Plasma lipid and lipoprotein responses to dietary fat and cholesterol: meta analysis. *Am. J. Clin. Nutr.* 65: 1747, 1997
252. Mensink R.P., Zock P.L., Kester A.D.M., Katan M.B.: Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL-cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* 77: 1146, 2003
253. Vessby B, Gustafsson I-B, Boberg J, Karlström B, Lithell H, Werner I.: Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia. *Eur. J. Clin. Invest.* 10: 193, 1980
254. Vessby B, Uusitupa M, Hermansen K, et al.: Substituting dietary saturated fat with monounsaturated fat impairs insulin sensitivity in healthy men and women: the KANWU Study. *Diabetologia* 44: 312, 2001
255. Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell JQ, Wheeler M: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148-198, 2002
256. Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen YD, Grundy SM, Huet BA, et al.: Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. *JAMA* 271: 1421-1428, 1994
257. Katan M.B., Zock P.L., Mensink M.P.: Dietary oils, serum lipoproteins, and coronary heart disease. *Am. J. Clin. Nutr.* 61: 1368S, 1995
258. Howell W.H., McNamara D.J., Tosca M.A., Smith B.T., Gaines J.A.: Plasma lipid and lipoprotein responses to dietary fat and cholesterol: meta analysis. *Am. J. Clin. Nutr.* 65: 1747, 1997
259. Mensink R.P., Zock P.L., Kester A.D.M., Katan M.B.: Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL-cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* 77: 1146, 2003
260. Heine R.J., Mulder C., Popp-Snijders C., van der Meer J., van der Veen E.A.: Linoleic-acidenriched diet: long term effects on serum lipoprotein and apolipoprotein concentrations and insulin sensitivity in non-insulin dependent diabetic patients *Am. J. Clin. Nutr.* 49: 448, 1989
261. Storm H, Thomsen C, Pedersen E, Rasmussen O, Christiansen C, Hermansen K.: Comparison of a carbohydrate-rich diet and diets rich in stearic or palmitic acid in NIDDM patients. *Diabetes Care* 20: 1807, 1997
262. Cox C, Mann J, Sutherland W, Chisholm A, Skeaff M.: Effects of coconut oil, butter, and safflower oil on lipids and lipoproteins in persons with moderately elevated cholesterol levels. *J. Lipid Res.* 36: 1501, 1995
263. Garg A.: High-monounsaturated fat diets for patients with diabetes mellitus: a meta-analysis. *Am. J. Clin. Nutr.* 67 (suppl.): 577S, 1998
264. Rasmussen O.W, Thomsen C, Hansen K.W, Versterlund M, Winther E, Hermansen K.: Effects on blood pressure, glucose, and lipid levels of a high-monounsaturated fat diet compared with a high-carbohydrate diet in NIDDM subjects. *Diabetes Care* 16: 1565, 1993
265. Thomsen C, Rasmussen O.W, Hansen K.W, Vesterlund M, Hermansen K.: Comparison of the effects on the diurnal blood pressure, glucose, and lipid levels of a diet rich in monounsaturated fatty acids with a diet rich in polyunsaturated fatty acids in type 2 diabetic subjects. *Diabet. Med.* 12: 600, 1995
266. Pérez-Jiménez F, López-Miranda J, Pinillos M.D, et al.: A Mediterranean and a highcarbohydrate diet improve glucose metabolism in healthy young persons. *Diabetologia* 44: 2038, 2001
267. Thomsen C, Rasmussen O, Lousen T, et al.: Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *Am. J. Clin. Nutr.* 69: 1135, 1999. Thomsen C, Rasmussen O, Christiansen C, et al.: Comparison of the effects of a monounsaturated fat diet and a high carbohydrate diet on cardiovascular risk factors in first degree relatives to type-2 diabetes. *Eur. J. Clin. Nutr.* 53: 818, 1999
268. Bonanome A, Visona A, Lusiani L, et al.: Carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus: effects of a low-fat, high carbohydrate diet vs a diet high in monounsaturated fatty acids. *Am. J. Clin. Nutr.* 54: 586, 1991
269. Luscombe N.D., Noakes M, Clifton P.M.: Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM. *Eur. J. Clin. Nutr.* 53: 473, 1999
270. Rodrigues-Villar C, Manzaneres J.M., Casals E, et al.: High monounsaturated fat, olive oil-rich diet has effects similar to a high-carbohydrate diet on fasting and postprandial state and metabolic profiles of patients with type 2 diabetes. *Metabolism* 49: 1511, 2000
271. Toeller M, Buyken A.E, Heitkamp G, Cathelineau G, Ferriss J.B, Michel G, and the EURODIAB IDDM Complications Study Group: Nutrient intakes as predictors of body weight in European people with type 1 diabetes. *Int. J. Obes.* 25: 1815, 2001
272. Poppitt S.D., Keogh G.F, Prentice A.M., et al.: Long term effects of ad libitum low-fat highcarbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome. *Am. J. Clin. Nutr.* 75: 11, 2002
273. Feskens E.J.M.: Can diabetes be prevented by vegetable fat? *Diabetes Care* 24: 1517, 85, 2001
274. Hu F.B., van Dam R.M., Liu S.: Visceral adiposity and risk of type 2 diabetes: the role of types of fat and carbohydrate. *Diabetologia* 44: 805, 2002
275. Marshall J.A., Bessesen D.H.: Dietary fat and the development of type 2 diabetes. *Diabetes Care* 25: 620, 2002
276. Salmeron J et al. Dietary fat intake and risk of type 2 diabetes in women. *American Journal of Clinical Nutrition*, 2001, 73:1019-1026
277. Meyer KA et al. Dietary fat and incidence of type 2 diabetes in older Iowa women. *Diabetes Care*, 2001, 24:1528-1535
278. Mann J, Lean M, Toeller M, Slama G, Uusitupa M, Vessby B. on behalf of the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD): Recommendations for the nutritional management of patients with diabetes mellitus. *Eur. J. Clin. Nutr.* 54: 353, 2000
279. Pan DA et al. Skeletal muscle membrane lipid composition is related to adiposity and insulin action. *Journal of Clinical Investigation*, 1995, 96:2802-2808
280. Hu F.B.: The role of n-3 polyunsaturated fatty acids in the prevention and treatment of cardiovascular disease. *Drugs Today* 37: 49, 2001
281. Harris W.S., Park Y, Isley W.L.: Cardiovascular disease and long-chain omega-3 fatty acids. *Curr. Opin. Lipidol.* 14: 9, 2003

282. Friedberg C.E, Janssen M.J, Heine R.J, Grobbee D.E.: Fish oil and glycemic control in diabetes. A meta-analysis. *Diabetes Care* 21: 494, 1998
283. Montori V.M., Farmer A., Wollan P.C., Dinneen S.F.: Fish oil supplementation in type 2 diabetes: a quantitative systematic review. *Diabetes Care* 23: 1407, 2000.
284. Katan M.B., Zock P.L., Mensink M.P.: Trans fatty acids and their effects on lipoproteins in humans. *Ann. Rev. Nutr.* 15: 473, 1995
285. Salméron J., Hu F.B., Manson J.A., et al.: Dietary fat intake and the risk of type 2 diabetes in women. *Am. J. Clin. Nutr.* 73: 1019, 2001
286. Christiansen E., Schnider S., Palmvig B., Tauber-Lassen E., Pedersen O.: Intake of a diet high in trans monounsaturated fatty acids or saturated fatty acids. Effects on postprandial insulinemia and glycemia in obese patients with NIDDM. *Diabetes Care* 20: 881, 1997
287. Weggemans R.M., Zock P.L., Katan M.B.: Dietary cholesterol from eggs increases the ratio of total cholesterol to highdensity lipoprotein cholesterol in humans: a meta-analysis. *Am. J. Clin. Nutr.* 73: 885, 2001
288. Romano G., Tilly-Kiesi M.K., Patti L., et al.: Effects of dietary cholesterol on plasma lipoproteins and their subclasses in IDDM patients. *Diabetologia* 41: 193, 1998
289. Toeller M., Buyken A., Heitkamp G., Scherbaum W.A., Krans H.M.J., Fuller J.H. and the EURODIAB IDDM Complications Study Group: Associations of fat and cholesterol intake with serum lipid levels and cardiovascular disease: The EURODIAB IDDM Complications Study. *Exp. Clin. Endocrinol. Diabetes* 107: 512, 1999
290. Franz M.J, Bantle J.P, Beebe CA, Brunzell J.D, Chiasson J.L, Garg A, Holzmeister L.A, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell J.Q, Wheeler M: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148-198, 2002
291. Gannon MC, Nuttall JA, Damberg G, Gupta V, Nuttall FQ: Effect of protein ingestion on the glucose appearance rate in people with type 2 diabetes. *J Clin Endocrinol Metab* 86:1040-1047, 2001
292. Gannon MC, Nuttall FQ, Saeed A, Jordan K, Hoover H: An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. *Am J Clin Nutr* 78:734-741, 2003. Gannon MC, Nuttall FQ: Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. *Diabetes* 53:2375-2382, 2004
293. Diabetic nephropathy is the renal manifestation of the damage caused to all the small arteries in the body by failure to correct hyperglycemia. (Source: Dipartimento di Medicina Interna, Università degli Studi di Perugia; Istituto per lo studio e la cura del diabete)
294. Nair K.S., Garrow J.S., Ford C., Mahler R.F., Halliday D.: Effect of poor diabetic control and obesity on whole body protein metabolism in man. *Diabetologia* 25: 400, 1983
295. Gougeon R., Pencharz P.B., Marliss E.B.: Effect of NIDDM on the kinetics of whole-body protein metabolism. *Diabetes* 43: 318, 1994
296. Gougeon R., Pencharz P.B., Sigal R.J.: Effect of glycemic control on the kinetics of whole-body protein metabolism in obese subjects with non-insulin-dependent diabetes mellitus during iso- and hypoenergetic feeding. *Am. J. Clin. Nutr.* 65: 861, 1997
297. Gougeon R., Marliss E.B., Jones P.J., Pencharz P.B., Morais J.A.: Effect of exogenous insulin on protein metabolism with differing nonprotein energy intakes in type 2 diabetes mellitus. *Int. J. Obes.* 22: 250, 1998
298. Guerrero-Romero F, Rodriguez-Moran M: Complementary therapies for diabetes: the case for chromium, magnesium, and antioxidants. *Arch Med Res* 36:250-257, 2005
299. Kligler B: The role of the optimal healing environment in the care of patients with diabetes mellitus type II. *J Altern Complement Med* 10 (Suppl. 1):S223-S229, 2004
300. Fraser G.E., Sabate J., Beeson W.L., Strahan T.M.: A possible protective effect of nut consumption on risk of coronary heart disease: the Adventist Health Study. *Arch. Intern. Med.* 152: 1416, 1992
301. Gaziano J.M., Manson J.E., Branch L.G., Colditz G.A., Willett W.C., Buring J.E.: A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly. *Ann. Epidemiol.* 5: 255, 1995
302. Gillmann M.W., Cupples L.A., Gagnon D., et al.: Protective effect of fruits and vegetables on development of stroke in men. *J.A.M.A.* 273: 1113, 1995
303. Hu F.B., Stampfer M.J., Manson J.E., et al.: Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. *B.M.J.* 317: 1341, 1998
304. Joshipura K.J., Ascherio A., Manson J.E., et al.: Fruit and vegetable intake in relation to risk for ischemic stroke. *J.A.M.A.* 282: 1233, 1999
305. Liu S., Manson J.E., Lee I.M., et al.: Fruit and vegetable intake and risk of cardiovascular disease: the Women' Health Study. *Am. J. Clin. Nutr.* 72: 922, 2000
306. Joshipura K.J., Hu F.B., Manson J.E., et al.: The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann. Intern. Med.* 134: 1106, 2001
307. Kris-Etherton P.M., Zhao G., Binkoski A.E., Coval S.M., Etherton T.D.: The effect of nuts on coronary heart disease risk. *Nutr. Rev.* 59: 103, 2001
308. Liu S., Lee I.M., Ajani U., Cole S.R., Buring J.E., Manson J.E.: Intake of vegetables rich in carotenoids and risk of coronary heart disease in men: the Physicians' Health Study. *Int. J. Epidemiol.* 30: 130, 2001
309. Albert C.M., Gaziano J.M., Willett W.C., Manson J.E.: Nut consumption and decreased risk of sudden cardiac death in the physicians' health study. *Arch. Intern. Med.* 162: 1382, 2002
310. Bazzano L.A., He J., Ogden L.G., et al.: Fruit and vegetable intake and risk of cardiovascular disease: the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. *Am. J. Clin. Nutr.* 76: 93, 2002
311. Cefalu WT, Hu FB: Role of chromium in human health and in diabetes. *Diabetes Care* 27:2741-2751, 2004
312. Ryan GJ, Wanko NS, Redman AR, Cook CB: Chromium as adjunctive treatment for type 2 diabetes. *Ann Pharmacother* 37:876-885, 2003
313. Althuis MD, Jordan NE, Ludington EA, Wittes JT: Glucose and insulin responses to dietary chromium supplements: a meta-analysis. *Am J Clin Nutr* 76:148-155, 2002
314. McNair P, Christiansen M.S., Christiansen C., Madsbad S., Transbol I.: Renal hypomagnesaemia in human diabetes mellitus: its relation to glucose homeostasis. *Eur. J. Clin. Invest.* 12: 81, 1982.
315. Tosiello L.: Hypomagnesemia and diabetes mellitus: a review of clinical implications. *Arch. Intern. Med.* 156: 1143, 1996.
316. It has been hypothesized that reduced presence of magnesium is associated (see Sjogren A., Floren C.H., Nilsson A.: Magnesium deficiency in IDDM related to level of glycosylated hemoglobin. *Diabetes* 35: 459, 1986; De Leeuw I., Vertommen J., Abs R.: The magnesium content of the trabecular bone in diabetic subjects. *Biomedicine* 29: 16, 1978) with two pathologies frequently found in diabetic patients, neuropathy (family of complications involving the nervous systems) and retinopathy (pathology of the blood vessels of the retina; it is the most frequent and precocious of diabetes complications). See Engelen W., Bouten A., De Leeuw I., De Block C.: Are low magnesium levels in type 1 diabetes mellitus associated with electromyographical signs of polyneuropathy? *Magn. Res.* 13: 197, 2000; McNair P, Christiansen C., Madsbad S., et al.: Hypomagnesemia, a risk factor in diabetic retinopathy. *Diabetes* 27: 1075, 1978. In light of this evidence, some studies (including De Leeuw I., De Block C., Van Gaal L.: Long term Mg supplementation influences favourably the natural evolution of neuropathy and retinopathy in Mg depleted type 1 diabetic patients. *Diabetologia* 46: A396, 2003) have identified the possibility that increasing magnesium intake (for example, through consumption of foods rich in it, such as whole grains, walnuts, etc.) could reduce the risk of developing neuropathy and retinopathy. However these hypotheses haven't been confirmed by international studies
317. Franz M.J, Bantle J.P, Beebe CA, Brunzell J.D, Chiasson J.L, Garg A, Holzmeister L.A, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell J.Q, Wheeler M: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 25:148-198, 2002
318. Hasanain B, Mooradian AD: Antioxidant vitamins and their influence in diabetes mellitus. *Curr Diab Rep* 2:448-456, 2002
319. Lonn E, Yusuf S, Hoogwerf B, Pogue J, Yi Q, Zinman B, Bosch J, Dagenais G, Mann JF, Gerstein HC: Effects of vitamin E on cardiovascular and microvascular outcomes in high-risk patients with diabetes: results of the HOPE study and MICRO-HOPE substudy. *Diabetes Care* 25:1919-1927, 2002

320. Kris-Etherton PM, Lichtenstein AH, Howard BV, Steinberg D, Witztum JL: Antioxidant vitamin supplements and cardiovascular disease. *Circulation* 110: 637-641, 2004
321. Gunton JE, Cheung NW, Hitchman R, Hams G, O'Sullivan C, Foster-Powell K, McElduff A: Chromium supplementation does not improve glucose tolerance, insulin sensitivity, or lipid profile: a randomized, placebo-controlled, double-blind trial of supplementation in subjects with impaired glucose tolerance. *Diabetes Care* 28:712-713, 2005
322. Kleefstra N, Houweling ST, Jansman FG, Groenier KH, Gans RO, Meyboom-de Jong B, Bakker SJ, Bilo HJ: Chromium treatment has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population: a randomized, double-blind, placebo-controlled trial. *Diabetes Care* 29: 521-525, 2006
323. Pittler MH, Stevinson C, Ernst E: Chromium picolinate for reducing body weight: meta-analysis of randomized trials. *Int J Obes Relat Metab Disord* 27:522- 529, 2003
324. Howard AA, Arnsten JH, Gourevitch MN: Effect of alcohol consumption on diabetes mellitus: a systematic review. *Ann Intern Med* 140:211-219, 2004
325. Dallongeville J, Marecaux N, Ducimetiere P, et al.: Influence of alcohol consumption and various beverages on waist girth and waist-to-hip ratio in a sample of French men and women. *Int. J. Obes.* 22: 1178, 1998
326. Kerr D, Macdonald I.A., Heller S.R., Tattersall R.B.: Alcohol causes hypoglycaemic unawareness in healthy volunteers and patients with Type 1 (insulin dependent) diabetes. *Diabetologia* 33: 216, 1990
327. Pownall H.J., Ballantyne C.M., Kimball K.T., Simpson S.L., Yeshurum D., Grotto A.M.: Effect of moderate alcohol consumption on hypertriglyceridemia. *Arch. Intern. Med.* 159: 981, 1999
328. Davies M.J., Baer D.J., Judd J.T., Brown E.D., Campbell W.S., Taylor P.R.: Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women. *J.A.M.A.* 287: 2559, 2002
329. Greenfield J.R., Samaras K., Jenkins A.B., Kelly P.J., Spector T.D., Campbell L.V.: Moderate alcohol consumption, estrogen replacement therapy, and physical activity are associated with increased insulin sensitivity: is abdominal adiposity the mediator? *Diabetes Care* 26: 2734, 2003
330. Sierksma A., Patel H., Ouchi N., et al.: Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor- α , and insulin sensitivity. *Diabetes Care* 27:184-189, 2004
331. Howard AA, Arnsten JH, Gourevitch MN: Effect of alcohol consumption on diabetes mellitus: a systematic review. *Ann Intern Med* 140:211-219, 2004
332. Ajani U.A., Gaziano J.M., Lotufo P.A., et al.: Alcohol consumption and risk of coronary heart disease by diabetes status. *Circulation* 102: 500, 2000
333. Sacco R., Elkind M., Boden-Albala B., et al.: The protective role of moderate alcohol consumption on ischemic stroke. *J.A.M.A.* 281: 51, 1999
334. Mukamal K.J., Conigrave K.M., Mittleman M.A., et al.: Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men. *N. Engl. J. Med.* 348: 109, 2003
335. Gaziano J.M., Hennekens C.H., Godfried S.L., et al.: Type of alcoholic beverage and risk of myocardial infarction. *Am. J. Cardiol.* 83: 52, 1999
336. Burger M., Brönstrup A., Pietrzik K.: Alkohol und Krankheiten. Abschlussbericht zum Forschungsvorhaben des Bundesgesundheitsministeriums für Gesundheit. Schriftenreihe des Bundesministeriums für Gesundheit Band 134; NOMOS Verlagsgesellschaft Baden-Baden 2000
337. Biesalski HK, Bueno de Mesquita B, Chesson A, Eur Consensus Statement on Lung Cancer: risk factors and prevention. *Lung Cancer Panel. CA Cancer J Clin*, 48:167-176, 1998
338. Reducing Tobacco Use: A Report of the Surgeon General. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2000
339. Jemal A, Siegel R, Ward E, Cancer statistics, *CA Cancer J Clin* 2006;56:106-130, 2006
340. Calle EE, Murphy TK, Rodriguez C, Diabetes mellitus and pancreatic cancer mortality in a prospective cohort of United States adults. *Cancer Causes Control*, 9:403-410, 1998
341. Doll R, Peto R. Epidemiology of cancer. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Oxford, Oxford University Press, 197-221, 1996
342. Willet MC. Diet, nutrition, and avoidable cancer. *Environmental Health Perspectives*, 103 (Suppl. 8):S165-S170, 1995
343. Weight control and physical activity. Lyon, International Agency for Research on Cancer (IARC Handbooks of Cancer Prevention, Vol. 6), 2002
344. Overweight and lack of exercise linked to increased cancer risk. In: Weight control and physical activity. Lyon, International Agency for Research on Cancer, (IARC Handbooks of Cancer Prevention, Vol. 6), 2002
345. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *N Engl J Med*, 348:1625-1638, 2003
346. Cummings JH, Bingham SA. Diet and the prevention of cancer. *British Medical Journal*, 317:1636-1640, 1998
347. Jemal A, Siegel R, Ward E, Cancer statistics, *CA Cancer J Clin* 2006;56:106-130, 2006
348. Brown LM, Adenocarcinoma of the esophagus: role of obesity and diet. *Journal of the National Cancer Institute*, 87:104-109, 1995
349. Malignant tumor of the epithelial cells organized in gland-like structures
350. Michaud DS, Physical activity, obesity, height, and the risk of pancreatic cancer. *Journal of the American Medical Association*, 286:921-929, 2001
351. Radimer KL, Ballard-Barbash R, Miller JS, Weight change and the risk of late-onset breast cancer in the original Framingham cohort. *Nutr Cancer*, 49:7-13, 2004
352. Trentham-Dietz A, Newcomb PA, Egan KM, Weight change and risk of postmenopausal breast cancer (United States). *Cancer Causes Control*, 11:533-542, 2000
353. Carmichael AR, Bates T. Obesity and breast cancer: a review of epidemiologic evidence. *Breast*, 13: 85-92, 2004
354. Stephenson GD, Rose DP. Breast cancer and obesity: an update. *Nutr Cancer*, 45:1-16, 2003
355. Amant F, Moerman P, Neven P, Endometrial cancer. *Lancet*, 366:491-505, 2005
356. Bergstrom A, Overweight as an avoidable cause of cancer in Europe. *International Journal of Cancer*, 91:421-430, 2001
357. Bergstrom A, Obesity and renal cell cancer, a quantitative review. *British Journal of Cancer*, 85:984-990, 2001
358. Vainio H, Bianchini F. Weight Control and Physical Activity, vol. 6. Lyon, France: International Agency for Research Cancer Press, 2002
359. Cancer: causes, occurrence and control. Lyon, International Agency for Research on Cancer, (IARC Scientific Publications, No. 100), 1996
360. McKillop I, Schrum L., Alcohol and Liver Cancer, Department of Biology, University of North Carolina at Charlotte, Charlotte, 2005
361. Smith-Warner SA, Alcohol and breast cancer in women: a pooled analysis of cohort studies. *Journal of the American Medical Association*, 279:535-540, 1998
362. Hamajima N, Hirose K, Tajima K, Alcohol, tobacco and breast cancer—collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer*, 87:1234-1245, 2002
363. Feigelson HS, Jonas CR, Robertson AS, Alcohol, folate, methionine, and risk of incident breast cancer in the American Cancer Society Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev*, 12:161-164, 2003
364. Dorgan JF et al. Serum hormones and the alcohol-breast cancer association in postmenopausal women. *Journal of the National Cancer Institute*, 93:710-715, 2001
365. Giovannucci E, Alcohol, low-methionine, low-folate diets, and risk of colon cancer in men. *Journal of the National Cancer Institute*, 87:265-273, 1995
366. Cancer: causes, occurrence and control. Lyon, International Agency for Research on Cancer, (IARC Scientific Publications, No. 100), 1996; Food, nutrition and the prevention of cancer: a global perspective. Washington, DC, World Cancer Research Fund/American Institute for Cancer Research, 1997
367. Potter JD, Steinmetz K. Vegetables, fruit and phytoestrogens as

- preventive agents. In: Stewart BW, McGregor D, Kleihues P, eds. *Principles of chemoprevention*. Lyon, International Agency for Research on Cancer, 61-90 (IARC Scientific Publications, No. 139), 1996
368. Jacobs DR, Whole-grain intake and cancer: an expanded review and meta-analysis. *Nutrition and Cancer*, 30:85-96, 1998
369. Michels KB, Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *Journal of the National Cancer Institute*, 92:1740-1752, 2000
370. Bueno de Mesquita HB, Ferrari P, Riboli E (on behalf of EPIC Working Group on Dietary Patterns), Plant foods and the risk of colorectal cancer in Europe: preliminary findings. In: Riboli E, Lambert R, eds. *Nutrition and lifestyle opportunities for cancer prevention*. Lyon, International Agency for Research on Cancer, 89-95 (IARC Scientific Publications, No. 156), 2002
371. Schatzkin A, Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *New England Journal of Medicine*, 342:1149-1155, 2000
372. Schatzkin A, Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Phoenix Colon Cancer Prevention Physicians' Network. *New England Journal of Medicine*, 342:1156-1162, 2000
373. Terry P, Fruit, vegetables, dietary fiber, and risk of colorectal cancer. *Journal of the National Cancer Institute*, 93:525-533, 2001
374. Gonzalez CA, Vegetable, fruit and cereal consumption and gastric cancer risk. *IARC Sci Publ*, 156:79-83, 2002
375. Bandera EV, Kushi LH, Conside DM, The association between food, nutrition, physical activity and the risk of endometrial cancer and underlying mechanisms. In support of the Second WCRF/AICR Report on Food, Nutrition, Physical Activity and the Prevention of Cancer, 2007
376. American Cancer Association, American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention: Reducing the Risk of Cancer With Healthy Food Choices and Physical Activity, 2006
377. Key TJ, Allen NE, Nutrition and breast cancer. *Breast*, 10 (Suppl. 3):S9-S13, 2001
378. Smith-Warner SA, Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. *Journal of the American Medical Association*, 285:769-776, 2001
379. Norat T, Meat consumption and colorectal cancer risk: a dose-response meta-analysis of epidemiological studies. *International Journal of Cancer*, 98:241-256, 2002
380. Food, nutrition and the prevention of cancer: a global perspective. Washington, DC, World Cancer Research Fund/ American Institute for Cancer Research, 1997
381. Schuurman AG, Animal products, calcium and protein and prostate cancer risk in The Netherlands Cohort Study. *British Journal of Cancer*, 80:1107-1113, 1999
382. Chan JM, Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. *American Journal of Clinical Nutrition*, 74:549-554, 2001
383. Michaud DS, A prospective study on intake of animal products and risk of prostate cancer. *Cancer Causes Control*, 12:557-567, 2001
384. Kolonel LN, Fat, meat, and prostate cancer. *Epidemiol Rev*, 23:72-81, 2001
385. Rodriguez C, McCullough ML, Mondul AM, Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev*, 15:211-216, 2006
386. Michaud DS, Physical activity, obesity, height, and the risk of pancreatic cancer. *Journal of the American Medical Association*, 286:921-929, 2001
387. Giovannucci E, Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. *Annals of Internal Medicine*, 129:517-524, 1998
388. Giovannucci E, The epidemiology of vitamin D and colorectal cancer: recent findings. *Curr Opin Gastroenterol*, 22:24-29, 2006; Giovannucci E, Liu Y, Rimm EB, Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. *J Natl Cancer Inst*, 98:451-459, 2006
389. Nutritional Aspects of the Development of Cancer. Report of the Working Group on Diet and Cancer of the Committee on Medical Aspects of Food and Nutrition Policy. London, The Stationery Office, (Report on Health and Social Subjects, No. 48), 1998; Fruits and Vegetables, vol. 8. Lyon, France: International Agency for Research on Cancer, World Health Organization; 2003
390. Hennekens CH, Lack of effect of long-term supplementation with betacarotene on the incidence of malignant neoplasms and cardiovascular disease. *New England Journal of Medicine*, 334:1145-1149, 1996
391. Omenn GS, Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *New England Journal of Medicine*, 334:1150-1155, 1996
392. Beta Carotene Cancer Prevention Study Group The Alpha-Tocopherol. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *New England Journal of Medicine*, 330:1029-1035, 1994
393. Heinonen OP, Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. *Journal of the National Cancer Institute*, 90:440-446, 1998
394. Clark LC, Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. *British Journal of Urology*, 81:730-734, 1998
395. Bonithon-Kopp C, Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial. European Cancer Prevention Organisation Study Group. *Lancet*, 356:1300-1306, 2000
396. Baron JA, Calcium supplements and colorectal adenomas. Polyp Prevention Trial Study Group. *Annals of the New York Academy of Sciences*, 889:138-145, 1999
397. Giovannucci E, Liu Y, Stampfer MJ, Willett WC, A prospective study of calcium intake and incident and fatal prostate cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15:203-210; Giovannucci E, Rimm EB, Wolk A, Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res*, 58:442-447, 1998
398. Kristal AR, Cohen JH. Invited commentary: tomatoes, lycopene, and prostate cancer. How strong is the evidence? *American Journal of Epidemiology*, 151:124-127, 2000
399. Ferlay J, Globocan 2000: cancer incidence, mortality and prevalence worldwide. Version 1.0. Lyon International Agency for Research on Cancer, 2001
400. Yu MC, Nasopharyngeal carcinoma: epidemiology and dietary factors. In: O'Neill IK, Chen J, Bartsch H, eds. *Relevance to human cancer of N-nitroso compounds, tobacco smoke and mycotoxins*. Lyon, International Agency for Research on Cancer, 39-47 (IARC Scientific Publications, No. 105), 1991
401. Some naturally occurring substances: food items and constituents, heterocyclic aromatic amines and mycotoxins. Lyon, International Agency for Research on Cancer, (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 56), 1993
402. Palli D, Epidemiology of gastric cancer: an evaluation of available evidence. *Journal of Gastroenterology*, 35 (Suppl. 12):S84-S89, 2000
403. Kelley JR, Duggan JM, Gastric cancer epidemiology and risk factors. *J Clin Epidemiol*, 56:1-9, 2003
404. Sharp L, Risk factors for squamous cell carcinoma of the oesophagus in women: a case-control study. *British Journal of Cancer*, 85:1667-1670, 2001
405. Weight control and physical activity. Lyon, International Agency for Research on Cancer, (IARC Handbooks of Cancer Prevention, Vol. 6), 2002
406. Martinez ME, Giovannucci E, Spiegelman D, Leisure-time physical activity, body size, and colon cancer in women. Nurses' Health Study Research Group. *J Natl Cancer Inst*, 89:948-955, 1997
407. Hardman AE, Physical activity and cancer risk. *Proceedings of the Nutrition Society*, 60:107-113, 2001

Part B: interpretation keys

3. ANALYSIS OF GUIDELINES FROM MAJOR INTERNATIONAL SCIENTIFIC BODIES AND INSTITUTES

On the basis of what has emerged from the published scientific studies analyzed in Chapter 2, this chapter will provide dietary and life style guidelines to be adopted to prevent the main chronic diseases.

3.1 Dietary guidelines for prevention of cardiovascular disease

WHO - WORLD HEALTH ORGANIZATION

Saturated, unsaturated and trans fatty acids

- The findings of the studies analyzed show that consumption of saturated fatty acids increases the risk of cardiovascular disease.
- For a diet that reduces this risk, the general goal is to consume, at most, 10% of daily caloric intake in saturated fats for normal individuals, reducing this to a maximum of 7% for those at high-risk. In addition, within this context, if an individual already consumes less than 10% of his or her daily caloric allowance in saturated fats, this amount should be maintained and not increased.
- In order to promote good functioning of the cardiovascular system, the diet should be comprised of a low content of trans fatty acids, in other words, avoid consumption of hydrogenated fatty acids which should be less than 1% of the total daily caloric allowance of an individual. This is particularly true for developing countries where, given their low cost, hydrogenated fatty acids are widely utilized.
- Again, the diet should be comprised of between 6% and 10% of polyunsaturated fatty acids. The optimal balance would be reached by consuming a quantity of n-6 polyunsaturated fatty acids between 5% and 8% and n-3 polyunsaturated fatty acids between 1% and 2%.
- Since scientific studies indicate that fats should represent an overall percentage of 15% and 30% of the daily caloric allowance, the missing percentage should consist of monounsaturated fats, such as oleic acid (an acid extra-virgin olive oil is very rich in).
- In conclusion, recommendations concerning the percentage and amount of fats to be consumed daily vary on the basis of each individual (age, sex, life style, etc.) but on a general level it is better to limit intake of fat to prevent overweight and obesity that increase the risk of cardiovascular disease.

Figure 28. Recommendations for fats consumption

Type of fatty acid	Daily allowance
Saturated fatty acid	<10% for all populations <7% for individuals at high risk
Trans fatty acids	<1% for all populations
Monounsaturated fatty acids	10%-17% for all populations
Polyunsaturated fatty acids	6%-10% for all populations: - 5%-8% of n-6 polyunsaturated fats for all populations - 1%-2% of n-3 polyunsaturated fats for all populations

Source: World Health Organization, "Diet, Nutrition and Prevention of chronic disease", 2003

Fiber and phytonutrients (fruits and vegetables)

- Fiber, phytonutrients and potassium (found primarily in fruit and vegetables), contribute to the health of the cardiovascular system.
- Study findings recommend that between 400 and 500 grams of fruit and vegetables be consumed each day in order to reduce the risk of coronary disease, stroke and high arterial pressure.

Sodium and potassium

- Consumption of sodium (salt) and potassium as part of a daily diet has an impact on blood pressure and, as a result, their quantity should be controlled with the goal of reducing the risk of coronary disease and stroke.
- The daily target amount of salt (sodium chloride) is approx. 5 grams⁴⁰⁸. This is the quantity that allows to maintain the cardiovascular system healthy.
- Because sodium tends to increase blood pressure, unlike potassium which tends to lower it, the amount of potassium should be set at a level that maintains the ratio between amount of sodium intake and amount of potassium intake to a value of 1⁴⁰⁹.

Eicosapentaenoic and docosahexaenic acids (fish)

- Regular consumption of fish (a food rich in eicosapentaenoic and docosahexaenic acids) - corresponding to 1-2 servings per week - has beneficial effects for coronary disease and, more generally, in the prevention of cardiovascular disease.
- The ideal portion should provide 200/500 milligrams of eicosapentaenoic acid and docosahexaenic acid⁴¹⁰ which are found in salmon, trout, sardines, mackerel, herring and tuna. It is strongly recommended that vegetarians have an adequate quantity of alpha-linolenic acid.

Alcohol

- Low or moderate consumption of alcohol (1 glass of wine or beer for women and 2 glasses for man per day) protects from coronary disease, while the risk of other cardiovascular diseases is influenced negatively by alcohol consumption.
- For this reason, scientific studies generally do not pronounce themselves in favor of its consumption.

Physical activity

- One of the most important factors in prevention of cardiovascular disease is regular physical activity for at least 30 minutes per day, almost every day of the week.
- Studies show that lifestyles with adequate physical activity register an inverse risk of cardiovascular disease, especially coronary disease.

AMERICAN HEART ASSOCIATION, EUROPEAN SOCIETY OF CARDIOLOGY, SOCIETÀ ITALIANA DI CARDIOLOGIA

In terms of what kind of life style to adopt, the most authoritative international scientific bodies and institutes⁴¹¹ have identified a number of points of behavior to adopt to promote health of the cardiovascular system, in conjunction with the recommendation given above.

Recommended life styles and behavior

- engage in at least 30 minutes of physical activity each day⁴¹²;
- know your own caloric needs in terms of calories per day in order to adopt a diet that maintains and promotes your ideal weight;
- know the calorie values of foods you eat;
- reduce as much as possible the amount time in front of the television or personal computer;
- weigh yourself regularly and be involved in physical activity;
- try to incorporate physical movement into everyday activity (take the stairs instead of the elevator, go by foot or bicycle for short distances, etc.);
- do not smoke;
- if you drink, try not to exceed two glasses of alcohol (beer, wine, etc.) per day for men and one for women.

Dietary guidelines that reduce the risk of cardiovascular disease

- Check the nutritional information (carbohydrates, proteins and fats) on foods as you shop, selecting those with lower fat content;
- Make fresh fruit and vegetables part of your regular diet, preferably without the addition of salt or sugar;
- For snacks, substitute high-calorie foods with fruit and vegetables;
- Increase intake of dietary fiber through consumption of legumes and grains;
- Choose vegetable oil instead of animal fats (butter, lard);
- Limit consumption of highly-sugared beverages (normally those in cans);

- Reduce consumption of bakery products;
- Choose milk and dairy products with low-fat content;
- Reduce the amount of salt in your diet, including by reducing the use of sauces and condiments;
- Remove the skin before eating poultry;
- Choose fruit over fruit juice.

With the goal of **reducing the risk of cardiovascular disease** for the population as a whole, **the results of the studies conducted must be diffused** in a widespread and useful way in terms of public opinion, but it is essential that every entity involved (institutions, local government, the health care system) implement initiatives aimed at facilitating the achievement of the set goals.

In fact, only if **all those involved in the food chain**, in their own way **promote action to support a healthy, balanced diet**, the desired results will be achieved.

Within this context, an effective policy is not only aimed at informing the end-consumer of the relative benefits or risks of consuming certain foods or nutrients, but must also provide for an active, positive, involved role for the entire agricultural-food chain, public catering services, health care system and local and national government bodies.

These groups must be fully aware and informed of the potential problems for public health deriving from poor diet and the advantages to be had from correct diet; in the areas for which they are responsible they must commit themselves to adopt the guidelines and recommendations that emerge from international medical-scientific studies in order to improve the health of the country's citizens.

Given below are the main recommendations divided by sector.

Recommendations from health sector employees, such as doctors and nutritionists, towards their patients should:

- follow the recommendations given above in terms of the type of diet to be followed;
- encourage and promote regular physical activity in young people and adults;
- calculate the body mass index and check that it is in line with the age and height of the patient;
- discourage cigarette smoking;
- encourage moderate consumption of alcohol in those who drink regularly.

In line with study findings, the public catering sector should:

- point out the caloric content for each dish served while also providing in a simple and easy-to-comprehend manner the recommended daily servings of the nutrients in each dish;
- reduce serving size;
- rework dish ingredients to reduce the calorie, sodium, saturated fatty acid and trans fatty acid content;
- increase the selection of vegetable-based dishes;

- increase the selection of fruit-based dishes;
- offer the choice in some dishes to replace fried foods with those that are boiled (e.g., potatoes);
- offer whole-grain dishes (pasta, rice, bread) and encourage their consumption.

For the food processing industry, the main recommendations are:

- reduce the sugar and salt content in the preparation of foods;
- reduce/eliminate hydrogenated fats (main source of trans fatty acids)
- increase mono- and polyunsaturated fats instead of saturated fatty acids;
- increase the types of whole-grain foods available to the consumer;
- pack foods in single-serving packages;
- develop packaging methods that preserve freshness and flavor to promote consumption of fresh fruit and vegetables without adding preservatives or substances such as sodium.

For school and corporate lunchrooms, the main recommendations are:

- serve students and employees foods with limited caloric content, sugar, trans fatty acids and sodium;
- adopt policies that discourage cigarette smoking in areas where people work;
- for schools: include in the weekly class program various types of physical activity, including after school.

And, finally, in terms of government, their involvement is fundamental for:

- developing and implementing educational courses/programs at school and in the workplace that can inform about the risks tied to poor diet;
- building bicycle and pedestrian paths to promote individual travel by other than motorized means;
- promoting policies that increase the availability of healthy food (which is generally more expensive) also to low-income individuals.

3.2 Dietary guidelines for prevention of diabetes

Presented below are the guidelines for a correct approach to diabetes prevention proposed, primarily by the WHO (summarized in the previously-mentioned report, *"Diet, nutrition and the prevention of chronic diseases"*), by the European Association for the Study of Diabetes (EASD), the Gruppo di Lavoro Italiano Associazione Medici Diabetologi - Diabete Italia - Società Italiana di Diabetologia (AMD-DI-SID) and by the American Diabetes Association (ADA).

WHO - WORLD HEALTH ORGANIZATION

Guidelines for diabetes prevention

- Prevention and treatment of overweight and obesity, especially in individuals at-risk.

- Maintain an optimal BMI (within the range of what are considered normal limits). For the adult population, this means maintaining the BMI between 21 and 23 kg/m² to avoid weight gain (> 5kg) during adult years.
- Voluntary weight reduction in overweight and obese individuals with glucose intolerance.
- Regular physical activity at a moderate or intense level (for example, fast walking) for an hour per day, most days of the week.
- Ensure that intake of saturated fatty acids is not more than 10% of the daily calorie allowance and, for high-risk individuals, the share of calories from fats overall must be less than 7% of the total caloric intake.
- Consume an adequate amount of dietary fiber through regular consumption of whole grains, legumes, fruit and vegetables. It is recommended that at least 20 g of fiber be consumed each day.

EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES (EASD)

General guidelines for diabetes prevention

- Avoiding overweight and engaging in regular physical activity are the best ways to reduce the risk of type 2 diabetes.
- In overweight individuals, weight loss and maintaining that loss are the central point in life style modification aimed at reducing the risk of type 2 diabetes.
- The composition of dietary macronutrients to reduce risk of type 2 diabetes is as follows: total fats < 30% of caloric intake, saturated fats < 10% of caloric intake, fiber > 15g/1000 Kcal.

In particular, in terms of macro- and micronutrients, European guidelines primarily indicate:

Caloric balance and body weight

- In overweight individuals (BMI > 25 kg/m²), the amount of calories must be lowered and amount of energy consumed increased in order to bring the BMI into the recommended limits.
- Reducing weight (-10%) improves the glycemic value, the arterial pressure and prevents diabetic disease.
- It is important to ensure that lost weight is not regained.
- In general, in individuals with a BMI at normal limits (18.5-25 kg/m²) specifying the optimal calorie level is not necessary.
- Total caloric intake must take into consideration the activity level of the individual.
- Reduction in consumption of high-caloric foods, especially those rich in saturated fats and simple sugars, makes it possible to lose weight without having to specify a calorie limit.

Carbohydrates

- Carbohydrate intake can vary between 45% and 60% of total calories.
- The exact amount within this range depends on the metabolism of each individual.

- Vegetables, legumes, fruit and whole grains must be an integral part of the diet.
- When the amount of carbohydrates tends towards the upper recommended limits, it is especially important that fiber-rich foods with low glycemic index be recommended.
- There is no justification for recommended diets with a very low carbohydrate content.
- Among foods with carbohydrate content, those rich in complex carbohydrates with a low glycemic index should be preferred when the other nutritional characteristics are suitable.
- If desired and if glycemic levels are satisfactory, moderate intake of “added sugars” (up to 50g/day) can be part of the diet. Nonetheless, as with the population as a whole, consumption of “added sugars” should not exceed 10% of caloric intake. Lower levels could be useful for those who must lose weight.
- Consumption of foods naturally rich in fiber must be encouraged. The amount of fiber consumed should be ideally 40 g per day (or 20 g/1000 kcal/day) or more, and approximately one half should be water-soluble. Positive benefits can also be obtained with lower levels which, for some, are even more acceptable. Daily consumption of at least 5 servings of vegetables or fruit with high-fiber content and at least four servings of legumes per week will help to provide the minimum amount of fiber recommended.
- Grains should be whole grain to the extent possible and rich in fiber.

Fats

- Total consumption of fats must not exceed 35% of the total daily caloric intake. For overweight individuals, overall consumption of fats < 30% of daily calories could facilitate weight loss.
- Saturated fatty acids and unsaturated trans fatty acids must provide less than 10% of total daily calories. Lower consumption (< 8%) is recommended if LDL cholesterol levels are high.
- Oils rich in monounsaturated fatty acids are a useful source of fats and, as preferred, can furnish between 10 and 20% of total caloric intake.
- Polyunsaturated fatty acids must not exceed 10% of total caloric intake.
- Consumption of 2-3 servings of fish per week (preferably fish rich in fats) and vegetal n-3 fatty acids (for example, rape oil, soy oil, walnuts and some leafy green vegetables) aid in attaining an adequate consumption level of n-3 fatty acids.
- The amount of cholesterol must not exceed 300 mg/day and must be further reduced in the presence of high plasma concentrations of LDL cholesterol.

Proteins

- Protein consumption should provide 10-20% of total daily caloric intake (in individuals without signs of nephropathy).

- There are no scientific findings sufficient to provide recommendations on the type of proteins to be preferred.

Micronutrients: antioxidants, vitamins, minerals

- Consumption of foods naturally rich in antioxidants (tocopherols, carotenes, vitamin C, flavonoids, polyphenols, phytic acid), micronutrients (iron, zinc, iodine, selenium) and other vitamins should be encouraged.
- Daily consumption of a large variety of vegetables and fruit should be encouraged because these foods represent a rich source of many vitamins and antioxidants.
- Regular consumption of whole grain bread, grains and fat-rich fish will cover the requirements of other water-soluble and lipo-soluble vitamins.
- As in the population as a whole, individuals with diabetes or those at-risk for diabetes, must reduce their salt intake to less than 6 g/day. A further reduction could be appropriate for individuals with high blood pressure.

Alcohol

- Moderate consumption of alcohol (up to 10 g/day for women and 20 g/day for men) is acceptable.
- Alcohol consumption must be limited in overweight, hypertensive and hypertriglyceridemic individuals.

GRUPPO DI LAVORO ASSOCIAZIONE MEDICI DIABETOLOGI - DIABETE ITALIA - SOCIETÀ ITALIANA DI DIABETOLOGIA (AMD-DI-SID)

General guidelines for diabetes prevention

- Avoiding overweight and engaging in regular physical activity (20-30 minutes per day or 150 minutes per week) are the best ways to reduce the risk of type 2 mellitus diabetes in individuals with reduced glucose tolerance.
- People with diabetes or those with altered glucose tolerance must receive individual medical-nutritional advice from a dietitian preferably part of a diabetes team and with specific competence in diabetes.
- Nutritional advice must take into consideration the personal needs and openness to change of the people with altered glucose tolerance or mellitus diabetes.
- Individuals with reduced glucose tolerance must be encouraged to modify their eating habits as follows:
 - reduce the total amount of fats (< 30% of daily caloric intake) and especially saturated fatty acids (< 10% of daily caloric intake);
 - increase the amount of vegetal fiber (at least 15 g/1000 Kcal).
- Vegetables, legumes, fruit and grains—foods characteristic of the Mediterranean diet—must be included in the diet. It is important to encourage the use of fiber-rich foods and those with a low glycemic index, particularly if the diet is rich in carbohydrates.
- There is no evidence for recommending the use of “dietetic” foods by diabetics.
- In individuals who are obese and with reduced glucose tolerance who have failed in changing their life style or for

whom it is not applicable, pharmacologic treatment could be considered, even though this is less effective than working on life style change.

In particular, in terms of macro - and micronutrients, Italian guidelines primarily indicate:

Overweight and obesity

- Weight loss is recommended for all adults that are overweight (BMI 25.0-29.9 kg/m²) or obese (\geq 30.0 kg/m²).
- The primary approach towards weight loss is to modify life style, which includes a reduction in calorie intake and increase in physical activity. A modest reduction in calorie intake (300-500 kcal/day) and a modest increase in energy expenditure (200-300 kcal/day) allow for slow but constant weight loss (0.45-0.90 kg/week).
- Recommended physical activity is: 30-45 minutes per day of moderate aerobic activity for 3-5 days per week (goal: 150 min/week). Higher levels of physical activity, equal to at least one hour per day of moderate activity (walking) or 30 minutes per day of more vigorous activity (jogging) may be necessary to obtain effective long-term weight loss.

Carbohydrates

- The total amount of carbohydrates introduced into the diet on a daily basis must provide between 45 and 60% of total daily caloric intake.
- Within these limits, personal metabolism must determine the correct amount for each individual.
- Low-carbohydrate diets are not recommended (i.e., less than 130 g/day) in individuals with diabetes or those at-risk.
- Both the quantity and quality of dietary carbohydrates can influence the glycemic response. Controlling the total quantity of carbohydrates through use of exchange diets or those that count carbohydrates, is a key strategy in obtaining glycemic control.
- As in the population at-large, for individuals at-risk or with diabetes the total amount of saccharose should not exceed 10% of the total daily caloric intake introduced through foods. Lower amounts may be useful for those who must lose weight.
- Sweeteners (saccharine, aspartame, acesulfameK, sucralose) are safe when consumed in moderate daily amounts.
- The glycemic index could be a useful indicator in the choice of carbohydrate-rich foods to include in the diet.
- High fiber-content foods should be encouraged. Ideally, the amount of fiber introduced into the diet should be more than 40 g/day (or 20 g/1000 kcal/day), the majority of which must be soluble.
- Daily consumption of 5 servings of vegetables or fruit and 4 servings per week of legumes can be useful in providing minimum fiber requirements.

Proteins

- In individuals without a history of nephropathy, the introduction of proteins must provide 10-20% of total daily dietary caloric intake.

- In individuals with any kind of chronic kidney disease, the amount of protein must be limited to the recommended dose (0.6-0.8 g/kg), in order to reduce the risk of evolution of the nephropathy.

Fats

- Fats must not be more than 30% of the total daily dietary caloric intake. In overweight individuals, introducing fats at a level of less than 30% of total daily caloric intake could facilitate weight loss.
- The daily amount of saturated fats must be less than 10% of total calories. Lower levels (< 7%) could be useful if LDL cholesterol is > 100 mg/dl.
- Oils rich in monounsaturated fatty acids are an important source of fats and, depending on the preferences of individual patients, can provide between 10 and 20% of total daily dietary caloric intake.
- Intake of trans fatty acids must be minimized (< 1%).
- Polyunsaturated fatty acids must not be more than 10% of the total daily dietary caloric intake.
- Dietary cholesterol must not exceed 300 mg/day and may be further reduced if LDL cholesterol is > 100 mg/dl.

Alcohol

- Moderate introduction of alcohol (up to 10 g/day for women and 20 g/day for men) is acceptable.

Micronutrients: antioxidants, vitamins, minerals

- Introduction of foods naturally rich in antioxidants, microelements and other vitamins must be encouraged. Introducing these nutrients requires the promotion of fruit and vegetables on a daily basis.
- Habitual supplementation with antioxidants, such as vitamins E, C and β -carotene, is not recommended given the lack of results about their long-term efficacy and safety.
- As in the population at-large, for individuals with diabetes or at-risk, daily salt consumption must be kept to under 6 g/day.

AMERICAN DIABETES ASSOCIATION (ADA)

General guidelines for diabetes prevention

- Individuals with diabetes or at-risk must receive a personalized "medical nutrition therapy", preferably prepared by a trained dietitian with experience in dietary treatment for diabetics.
- The indications should take into consideration the needs, openness to change and capacity to make changes of each individual with diabetes or at-risk.
- For individuals at high-risk for developing type 2 diabetes, structured programs are recommended that stress a change in life style, including modest weight loss (7% of body weight) and regular physical activity (150 mins/week), together with a dietary strategy which includes reduction in dietary intake of calories and fats; these programs can, in fact, reduce the risk of developing diabetes.

- Individuals at high-risk for type 2 diabetes must be encouraged to follow the recommendations of the US Department of Agriculture (USDA) for consumption of fiber (14 g fiber/1,000 Kcal) and foods with whole grain flours (half of the grains consumed).

In particular, in terms of macro- and micronutrients, American guidelines primarily indicate:

Overweight and obesity

- Weight loss is recommended for all overweight or obese individuals, diabetics or those at-risk.
- In the short-term (up to 1 year), both a low-carbohydrate diet and diet with low-fat content and limited caloric intake can be efficacious.
- Physical activity and changes in behavior are important parts of weight loss programs and are very useful in maintaining ideal weight.

Carbohydrates

- For good health, the adoption of a dietary plan is encouraged that includes carbohydrates from fruit, vegetables, whole grains, legumes and skim milk.
- The average amount of carbohydrates on a daily basis must be approx. 130 g/day.
- Monitoring of carbohydrates through carbohydrate counting, exchanges or estimates based on experience, remains a basic strategy in gaining control over glycemia levels.
- In diabetic individuals, the use of the glycemic index and glycemic load can provide an additional modest advantage in glycemic control compared with what can be obtained by considering only total carbohydrates.
- Foods containing sugar are not advised against as long as they do not cause the overall calorie intake limit to be exceeded.
- The fructose naturally found in fruit, vegetables and other foods is not advised against.
- As in the population at-large, individuals with diabetes or at-risk are encouraged to consume a wide variety of foods containing fiber, such as legumes, fiber-rich grains (≥ 5 g fiber/serving), fruit, vegetables and whole grain products. In any case, there is no evidence to suggest that individuals with diabetes or at-risk should be recommended to consume higher levels of fiber than those indicated for the population at-large (14 g/1000 kcal).
- Alcohol sugars and non-nutritive sweeteners are safe when consumed within the limits established by the Food and Drug Administration (FDA).

Proteins

- For individuals with diabetes or those at-risk without kidney problems there is no reason to suggest that the normal level of protein consumption (15-20% of overall caloric intake) be modified.
- At the current time, high-protein diets are not recommended as a weight-loss method since their long-term effects have

not yet been adequately scientifically ascertained.

Fats

- The amount of saturated fats must be less than 7% of total calories.
- Intake of trans fatty acids must be minimized.
- In individuals with diabetes or those strongly at-risk, limiting intake of dietary cholesterol to less than 200 mg/day appears useful.
- Consumption of two or more servings of fish per week (with the exception of fried fish) is recommended as it appears to guarantee adequate intake of n-3 polyunsaturated fatty acids.

Alcohol

- If a diabetic individual or one strongly at-risk decides to consume alcohol, it should be limited to a moderate daily amount (a glass or less per day for adult women and two glasses a day or less for adult men).

Micronutrients: antioxidants, vitamins, minerals

- There does not seem to be sufficient evidence of a positive preventive/therapeutic effect for diabetes deriving from assumption of vitamins or minerals in cases in which individuals do not exhibit a lack of them.
- Daily supplements of antioxidants, such as vitamins E and C and carotene are not recommended given the lack of results about their long-term efficacy and safety.
- The use of chromium-based supplements is not recommended in diabetics or individuals strongly at-risk or those who are obese because the benefits of these supplements have not been proven.

3.3 Dietary guidelines for prevention of cancer

On the basis of what has emerged from the published scientific studies analyzed, this chapter will provide dietary and life style guidelines to be adopted to reduce cancer risk.

WHO - WORLD HEALTH ORGANIZATION

On a general level, above and beyond the characteristics of each type of tumor, the main recommendations to emerge from medical-scientific studies indicate that to reduce cancer risk, it is advisable to:

- maintain the Body Mass Index⁴¹³ between 18.5 and 25kg/m²;
- maintain regular physical activity for most days of the week. 60 minutes per day of intense/moderate activity such as, for example, a walk or bicycle ride, are required to maintain ideal body weight;
- occasionally engage in more intense physical activity, such as a long run;
- do not exceed one glass of wine, beer or other alcoholic drink per day;
- regulate the amount of salt in the daily diet;
- do not undergo long-term hormone treatments;

- minimize exposure to toxins contained in mushrooms and molds;
- consume approx. 400 grams of vegetables and fruit each day;
- regulate consumption of preserved meats;
- do not consume foods and beverages when they are very hot.

The scientific studies, selected from the most prestigious international publications and in the forefront of research, concentrated on the analysis of individual nutrients and components (such as, beta-carotene, vitamins and calcium), as well as directly on certain categories of foods, such as preserved meats, salt-preserved fish, fruit and vegetables.

**INTERNATIONAL AGENCY FOR RESEARCH ON CANCER,
AMERICAN CANCER ASSOCIATION, FEDERATION OF
EUROPEAN CANCER SOCIETY**

In terms of the life style adopted, the most authoritative international scientific bodies and institutes⁴¹⁴ have identified and drawn up clear and comprehensible guidelines for both individuals as well as local and national government, which provide the results of the studies in a clear way and give concrete indications on actions to be taken to reduce the risk of cancer.

The main recommendations are:

- maintain ideal body weight throughout life;
- adopt a life style that includes adequate physical activity;
- adopt a balanced diet centered on consumption of fruit and vegetables;
- limit consumption of alcoholic beverages.

More specific guidelines have also been provided for each recommendation.

Maintain ideal body weight throughout life

- know the calorie content of foods consumed and balance caloric intake with physical activity (energy expenditure);
- avoid excessive weight gain, even if ideal weight is subsequently returned to;
- for those currently overweight, reach and maintain ideal weight.

Adopt a life style that includes adequate physical activity

- for adults, engage in medium-to-high intensity physical activity⁴¹⁵ at least 30 minutes per day for at least 5 days per week. it is preferable to reach a level of 45-60 minutes per day;
- for adolescents, engage in medium-to-high intensity physical activity at least 60 minutes per day for at least 5 days per week;
- when possible, use the stairs instead of the elevator;
- when possible, use a bicycle or walk to reach your destination;
- during working hours, take a break for physical exercise, such as stretching or a quick walk;
- physically go over to work colleagues to communicate

- information rather than sending mail messages;
- go dancing with your companion or friends;
- choose vacations that include sports activity over those that do not (vacations “lying on the beach”);
- wear a pedometer each day with the goal of increasing the distance traveled;
- enroll in sports activity;
- use a treadmill or exercise bicycle while watching television;
- play with your children or friends;
- plan the above activities with the goal of gradually increasing their duration and frequency.

Adopt a balanced diet centered on consumption of fruit and vegetables

- consume few and small servings of high-calorie foods;
- be aware that foods with low-fat content are not necessarily low-calorie foods;
- eat fruit and vegetables as a snack instead of potato chips, ice cream, doughnuts and sweets;
- consume at least five portions of fruit each day, varying the type;
- choose low-calorie foods when eating out;
- limit consumption of fried food;
- consume pasta and bread made with whole grain flour rather than pasta and bread made with white flour;
- reduce consumption of bakery products;
- limit consumption of red meat and cured meats;
- consume fish and chicken rather than beef, pork and lamb;
- become aware of the correct serving sizes for each food.

In terms of this last point, the table below provides the ideal values for each serving of food. Serving indicates the ideal quantity for each type of food for each meal consumed during the day.

Figure 30. Ideal serving size

Food	Quantity per serving
Fruit	1 banana, 1 apple, 1 orange Half a cup of fruit salad 1 fruit juice
Vegetables	1 plate of raw salad Half plate of cooked vegetables
Grains	1 slice of bread 30 grams of grains Half plate of rice/pasta
Legumes	Half plate of dried legumes 10 grams of nuts
Dairy products and eggs	1 glass of milk 1 carton of yogurt 45 grams of cheese 1 egg
Meat	60-80 grams of red meat, chicken, fish

Source: American Cancer Association

Limit consumption of alcoholic beverages

- do not consume alcoholic beverages;
- those who do drink should not exceed two glasses of alcohol (beer, wine, etc.) per day for men and one for women.

As already noted in reference to cardiovascular disease, with the goal of reducing the risk of cancer for the population as a whole, the results of the studies conducted must be diffused in a widespread and useful way in terms of public opinion, and it is essential that every entity involved implement initiatives aimed at facilitating the achievement of the set goals.

Towards this end, the food industry, public catering services and local and national government bodies are asked to provide an active, positive and involved role. Therefore, it is recommended that:

- very long work days be limited in order to allow time for meal preparation;
- the time dedicated to recreational and leisure activities be increased;
- availability and accessibility of parks, bike and pedestrian paths be augmented;
- policies and actions which increase the availability of healthy food (which is generally more expensive) also to low-income individuals be promoted.
- policies and actions aimed at increasing availability and accessibility of sports facilities be promoted.

3.4 Summary of guidelines for a healthy diet aimed at preventing the risk of main chronic diseases

As can be seen from analysis of the dietary guidelines proposed by the major international scientific bodies, there are many aspects which converge in terms of diet in the prevention of major chronic diseases.

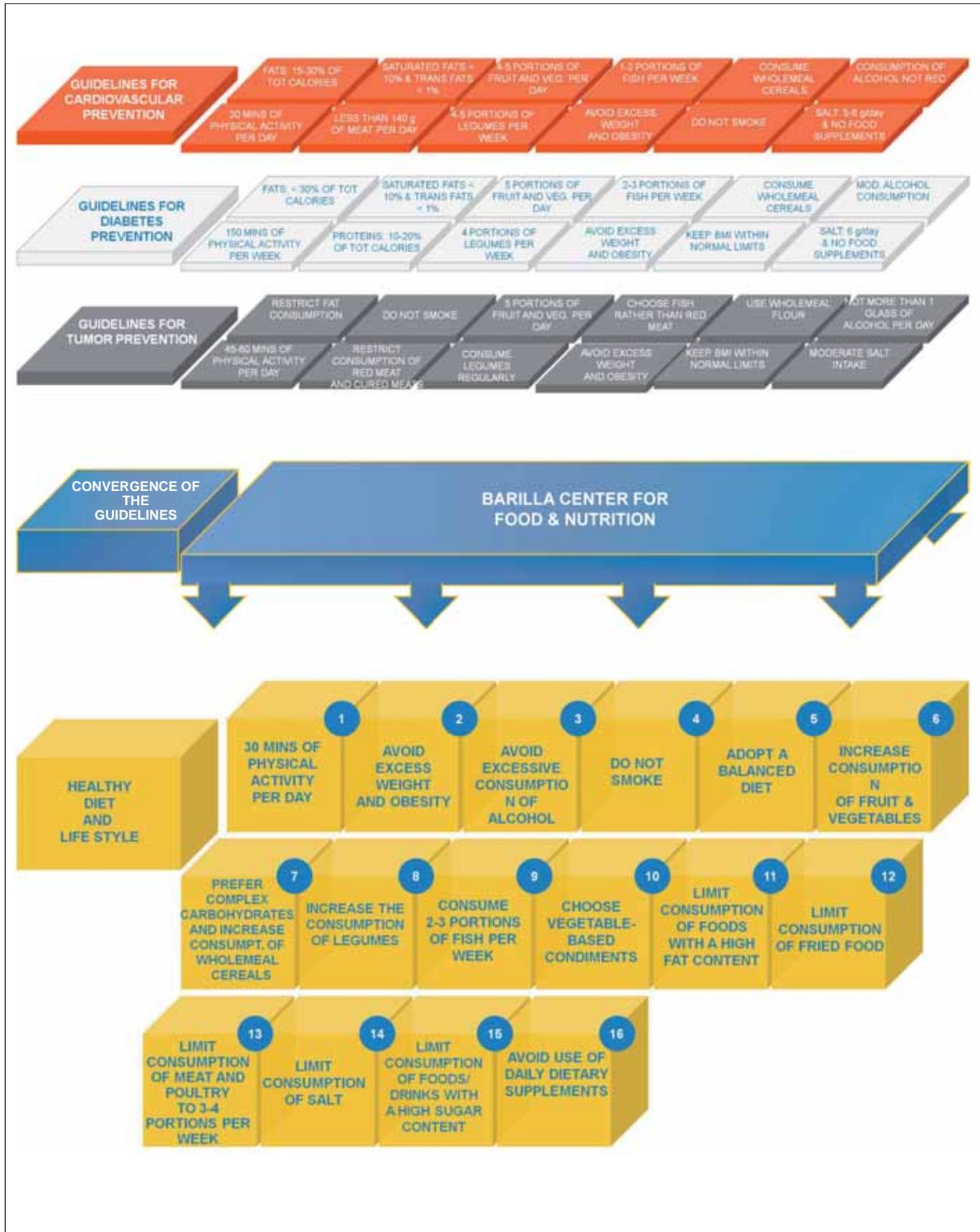
From a comparative analysis we can outline which behavior and life styles should be adopted for a healthy diet with an overall preventive function towards the risk of cardiovascular disease, diabetes and cancer⁴¹⁶.

Lifestyle, behavior and diet

- Engage in **regular physical activity** for 30 to 60 minutes per day of medium (e.g., walking or bicycle riding) or high intensity (e.g., running, swimming, team sports) for most days of the week.
- **Avoid being overweight/obese** both for short periods and over the long-term (including regaining excess weight that may have been lost).
- **Avoid excess alcohol consumption** (no more than one glass for women and two glasses for men).
- **Do not smoke.**
- Adopt a **balanced diet** in which the overall caloric intake is regulated, and which has the right mix of macro- and micronutrients.

- **Increase** (up to approx. 400g/day) consumption of fruit and vegetables, especially those rich in dietary fiber: Consume 4-5 servings of fruit/vegetables per day, including as replacement for other snacks.
- **Prefer complex carbohydrates sources and increase the consumption of whole grains** (e.g., bread, pasta, breadsticks made with whole grain flours).
- **Consume 2-3 servings of fish each week.**
- **Limit consumption of foods/beverages with high sugar content** (e.g., baked goods and soft drinks).
- **Limit consumption of foods with high fat content** (e.g., hot dogs, sauces, creams, dairy products, cured meats), preferring "low-fat" products (such as low-fat yogurt and skim milk).
- **Utilize vegetable-based condiments** (vegetable oils) instead of condiments with high animal fat content (butter, lard, margarine).
- **Limit consumption of fried food.**
- **Increase consumption of legumes** (2-3 servings per week).
- **Limit consumption of meat and poultry to 3-4 servings per week.**
- **Limit the use of added salt** over that normally contained in foods (do not utilize more than 5-6 g of added salt, equal approx. to a half teaspoon).
- **Avoid use of daily dietary supplements.**

Figure 31. Summarizing scheme of the methodology used to analyze the guidelines that state the convergence of a healthy diet and lifestyle with the prevention of chronic diseases



4. ADHERENCE OF THE MOST WIDESPREAD DIETARY REGIMENS TO THE GUIDELINES DRAFTED FOR THE WELL-BEING OF PEOPLE

The summary of the above-described guidelines has led to the pinpointing of a series of behavior patterns to be adopted in order to safeguard against the onset of chronic diseases. As widely demonstrated by the numerous scientific studies presented so far - that show the positive relationship existing between dietary practices and health - a fundamental part of these suggestions is linked to a correct and healthy diet.

The guidelines and the instructions provided by the leading international scientific bodies - **the comparative analysis of which forms the central theme of the research effort conducted, inasmuch as it has enabled the demonstrating of a substantial convergence in dietary habits useful for the prevention of tumors, cardiovascular and metabolic diseases, as a starting point for more efficacious and more unified prevention strategies** - cannot however result in the identification of a single, perfect, hypothetical perfect food diet able to supply the maximum benefit in terms of health and prevention of disease. In fact, there are reasons linked to typical local products, gastronomic traditions, the customs and uses of each and every Country or region of the world⁴¹⁷ that would make it unrealistic and, in any case, wrong to attempt to spread an ideal meta-diet.

In actual fact, the guidelines and the instructions should not be interpreted as an attempt to launch a standardization process of dietary regimens or an attempt to promote a single nutritional approach. Quite the reverse, in fact, as a series of cultural factors and typical gastronomic traditions exist in the regions of the world that should be promoted and optimized on the basis of the indications formulated by the world of science. Essentially, in order for food to improve people's state of health, actions and strategies have to be put into practice geared at encouraging the rediscovery of regional diets and their more wholesome nutritional components, all in the light of the most recent scientific knowledge.

Through efforts to simplify, useful for identifying dietary tendencies on a global scale, three wide-reaching gastronomic traditions may be identified in the world, each of which is distinguished by its own peculiar traits. The Mediterranean model, the North American model and the Asian model (which embraces a number of important traditions and cultures, from the Japanese, to the Vietnamese to the Chinese).

The **Mediterranean diet** is the most widely adopted food model in the Countries of the Mediterranean area, particularly in Italy, Spain, Portugal, Greece and France.

It is a food model that distinguishes itself for its nutritional balance. Its first four components (fruit, vegetables, products derived from cereals, milk and derivatives) present a balanced division both in terms of quantities consumed (from 200 to 260 grams per day per food) and in terms of proportion with respect to daily consumption (the sum of the first four components

exceeds 40% of the daily intake). As we shall observe more in detail as the present chapter continues, the Mediterranean diet is acknowledged by many nutritionists and food scientists to be one of the best diets, in an absolute sense, as regards physical well-being and the prevention of chronic diseases, particularly cardiovascular diseases.

In general, its strict adherence to the recommendations suggested at a scientific level, make the Mediterranean model **one of the most efficacious diets in terms of well-being and prevention of disease**.

The **North American diet** - i.e. the food model widespread throughout the United States and Canada - is now under the scrutiny of the world of science, worried by the serious phenomenon presented by the exponential growth of obesity and metabolic diseases in the United States.

This phenomenon seems to depend on excess food consumption (equivalent to 2,600 grams per day against the approx. 2,000 grams per day of the Mediterranean and Japanese models) and on the unbalanced nutritional composition of the diet, that tends in particular towards an excessive consumption of red meat and sweet things, 11.7% and 7.1% of the daily total intake, respectively⁴¹⁸.

It is, essentially, a diet, for the most part, rich in proteins and sugars, not properly counterbalanced with a sufficient intake of fruit and vegetables. Due to these characteristics, the North American diet diverges greatly from the recommendations and guidelines formulated by leading international scientific bodies and needs, today, to be duly reviewed and integrated.

This is amply demonstrated by the tendencies recorded over the last thirty years, that show how the calories consumed by the average American have increased by 25% daily, accompanied by an increase in the consumption of food with a high calorie content. As a consequence of this change in dietary habits, 65% of Americans today are overweight, a huge increase on the value recorded in the Eighties, which was equivalent to 46% of the population⁴¹⁹.

The **Japanese diet**⁴²⁰ - taken as an example of the dietary practice prevalent in the Countries of Eastern Asia - favors the consumption of cereals, which occupy 24% of the total daily intake, and fish. As far as the latter food component is concerned, consumption is equivalent to 107 grams per day, much higher than the 45 grams present in the Mediterranean diet and the 18 grams of the North American diet. This diet, in terms of food components, is very similar to the Mediterranean diet, also as regards preparation (relatively low incidence of fried foods). It is a diet typified by richness of mineral salts, omega 3, phosphorus and polyunsaturated fats deriving, first and foremost, from the consumption of fish.

This demonstrates how it is possible for widely differing dietary regimens to adhere to the principles ratified by medical science.

What we are keen to achieve in this chapter is not so much to make an in-depth comparison between food models, an endeavor

that would require an entire research paper in itself, but - in the light of the results obtained until now and of the introductory remarks made - to attempt an initial rapid evaluation of the adherence of the food model closest to Southern European Countries (the so-called Mediterranean diet) to the guidelines analyzed, interpreting the dietary habits of this area in a dynamic manner, in virtue of the continuing changes underway in the everyday reality of food choices.

The Mediterranean diet and the Mediterranean adequacy index

The idea and the concept of a Mediterranean diet was established in 1939 by the medical nutritionist Lorenzo Piroddi, who was the first to understand the connection between food and diabetes, bulimia and obesity⁴²¹.

Subsequently, in the fifties, Ancel Keys⁴²², a medical-scientist from the University of Minnesota College of Food, came to Italy during the second War World and became aware of something that, at the time, seemed very strange. The less affluent (the so-called poor) in the small towns of Southern Italy, who survived prevalently on bread, onions and tomatoes were much healthier not only than the citizens of New York, but also than their own relations who had emigrated to the United States in the previous years.

The nutritional value of the Mediterranean diet has been scientifically demonstrated by the famous "seven countries study"⁴²³ directed by Keys. In this study, the diets adopted by the populations in seven Countries were compared in order to determine their benefits and critical points.

From the results obtained from the "seven countries study" the associations between type of food diet and risk of onset of chronic disease were discovered⁴²⁴. As emerged from the results, the high level of saturated fatty acids and cholesterol in the blood represents a factor capable not only of explaining the differences in mortality rates, but also of predicting the future rates of coronary disease in the populations analyzed⁴²⁵.

The final result of the "seven countries study" indicated that the best dietary regime was that practiced by the inhabitants of Nicotera, in Calabria, who adopted the "Mediterranean" dietary regimen. The population of Nicotera (Calabria), of Montegiorgio (Marches) and the inhabitants of Campania had a very low level of cholesterol in the blood and a minimum percentage of coronary diseases thanks to the dietary regimen adopted, based on olive oil, bread and pasta, garlic, red onions, aromatic herbs, vegetables and very little meat.

From the first "seven countries study" till today, many other studies have analyzed the characteristics and the associations between dietary habits adopted and the onset of chronic disease⁴²⁶. Since the mid-nineties, moreover, a current of thought has been developed, investigating the association between dietary habits and longevity⁴²⁷.

In general, what emerges is that the adoption of a Mediterranean, or similar, diet, provides a protective factor

against the most widespread chronic diseases. In the studies conducted, the concept of the Mediterranean diet was translated, in concrete terms, into a dietary regimen characterized by: a high consumption of vegetables, pulses, fruit and nuts, olive oil and cereals (which in the past were prevalently wholemeal); a moderate consumption of fish and dairy products (especially cheese and yogurt) and wine; a low consumption of red meat, white meat and saturated fatty acids⁴²⁸.

With the aim of measuring the adherence or divergence of a diet from the Mediterranean diet, various Mediterranean adequacy indices have been developed, as the studies published in literature judge the Mediterranean diet to be one of the best for the prevention of chronic diseases.

Trichopoulou⁴²⁹, after having created an index that quantifies adherence to the Mediterranean diet on a scale from 0 to 9 (where the maximum value means maximum adherence and vice versa), found an inverse association between the score obtained by a population and the mortality rates of the more elderly people.

Also from the studies of Panagiotakosa⁴³⁰ it emerged that the increase in the level of adherence to the Mediterranean diet was significant for the prediction of cases of hypertension, hypercholesterolemia, diabetes and obesity in adults. An increase of approx. 20% of adherence to the Mediterranean diet⁴³¹ reduces the onset of cardiovascular diseases by 4% in the course of ten years.

Other studies conducted by Trichopoulou⁴³² showed how adherence to the Mediterranean diet produces significant reductions in the overall mortality rates of the population, especially in deaths due to cardiovascular diseases and tumors. The same results emerge also from the recent studies of Mitrou⁴³³ conducted for ten years on a sample of over 380,000 Americans.

In the specific case of coronary diseases, De Longeri⁴³⁴ demonstrated how the Mediterranean diet reduces the risk of heart attack by 72%. The results of the studies of Fung⁴³⁵ have confirmed, once more, the cardioprotective effects of the Mediterranean diet. In a recent meta-analysis study by Sofi⁴³⁶ it emerged that the Mediterranean diet provides a protective factor against all causes of mortality and, in the specific instance, towards those connected with cardiovascular diseases and tumors, but also towards Parkinson's and Alzheimer's disease.

Notwithstanding the results of these studies indicate that the dietary pattern to aim at for a healthy life is the Mediterranean diet, since the fifties, that is since the first study by Keys, the entire Mediterranean area, Italy included, has witnessed a gradual growing away from this diet in favor of less healthy dietary habits.

In fact, with reference to the Italian case, the results of the Fianza studies⁴³⁷ have shown how the Mediterranean adequacy index in the two symbol cities has dropped dramatically: in

Nicotera it was 7.2 in 1960, dropping to 2.2 by 1991, while in Montegiorgio where it was 5.6 in 1965, it had dropped to 3.9 by 1991. The rejection of the Mediterranean diet is clearly noticeable also in the main Italian cities⁴³⁸.

Baldini⁴³⁹, in a recent study on conditions in Spain and Italy, observed how the younger generations seem, gradually and constantly, to grow away from the Mediterranean diet in favor of new dietary trends generally characterized by foods with a high fat content. In addition to being correlated with reduced physical activity, excess weight and obesity in Italy and Spain also seem to be correlated to the rejection of the Mediterranean diet.

Last but not least, a study presented in July of 2009, by the Italian Association of Dietetics and Clinical Nutrition and by the Grana Padana Nutritional Observatory, confirmed the tendency to grow away from the Mediterranean diet. In Italy, in fact, the Mediterranean adequacy index is around 1.44, a far cry from the 7.2 of Nicotera in 1960 and from the 5.6 of Montegiorgio in 1965.

In this context, Lombardy has a Mediterranean adequacy index of 1.32, the lowest in Italy. In other words, the calorie intake deriving from the foods typical of the Mediterranean diet in Lombardy is 53% (compared with the 56% of the other regions), while that deriving from foods not included in the Mediterranean diet reaches 47% (compared with the 44% of the rest of Italy).

The result is that, notwithstanding the Lombardy Region's reputation as an "excellence" in the oncological field, as it offers its citizens access to advanced screening programs and top level treatments, health in this area is considerably at risk: in Lombardy each year 30.7 persons per 10,000 inhabitants die of tumors, against a national average of 28.6.

In conclusion, it may be seen how the Mediterranean food model is close to and consistent with food guidelines for the prevention of the main chronic diseases, published by the leading international scientific institutes and bodies and presents, therefore, in its entirety, a vast and consolidated scientific base. For this reason, the Mediterranean model has been taken as a reference point for the various studies conducted on the relationship between food and chronic disease.

A worrying tendency that has been gaining ground over recent years, also in Italy, is that of the rejection of the guidelines of this type of dietary practice.

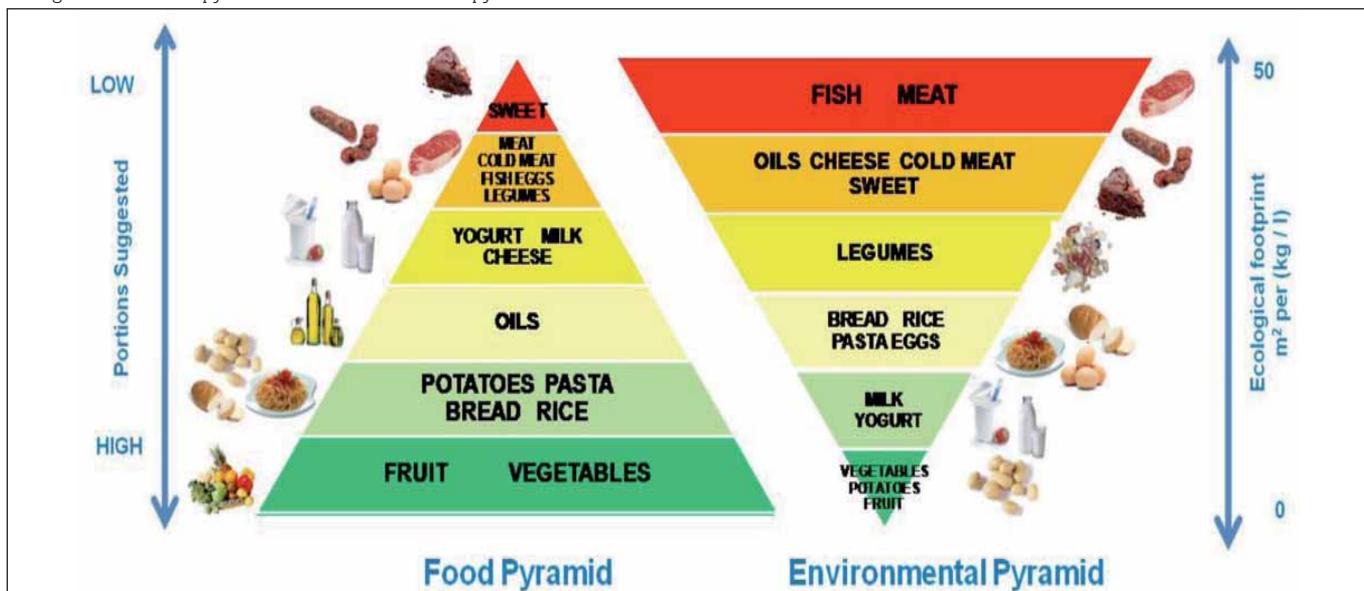
It is absolutely indispensable to promote a series of actions and policies geared at combating and containing the progressive rejection of the Mediterranean diet in the Countries of Southern Europe, which corresponds to an impoverishment of the dietary habits of the entire population. It is also necessary to spread knowledge on nutritional issues and to increase food culture in the population, with the aim of preventing, on the one hand, the onset of chronic diseases that cause - each year throughout the world - millions of deaths and billions of Euro in costs to the various national health systems and, on the other, to demonstrate and divulge to people a series of indications, suggestions and behavior patterns that will help contribute to the maintenance of a lasting state of well-being.

Food and Environmental Pyramid

The Mediterranean food model is consistent not only with the guidelines for the prevention of chronic diseases, but also - at the same time - is characterized by its minimum environmental impact.

It appears to be very interesting matching the traditional Food Pyramid with an "environmental pyramid" built considering the environmental burden (measured through

Figure 32. The food pyramid and the environmental pyramid



Source: The European House-Ambrosetti re-elaboration of different sources

the Ecological Footprint) of each food. In this way, it is possible to obtain a “reversed pyramid”, where at the apex, positioned on the bottom, we find low environmental impact foods (first of all fruits, but also milk, yogurt and cheese, fish, eggs and vegetables and, at an upper level, pasta and rice), with high beneficial value in terms of ill prevention; at the bottom - which is positioned on the top - we find food (especially meat and sweets) which production implies an higher consumption of environmental resources, and whose nutrients imply an increase of chronic diseases’ risk.

With regard to this issue, please see the Position Paper on “Water Management” and “Climate Change, agriculture and food” published by Barilla Center for Food & Nutrition in 2009.

5. COST AND BENEFITS OF INVESTMENT IN PREVENTION

The analysis that follows⁴⁴⁰ is intended to stimulate reflection on the **benefits of increasing resources destined for prevention in terms of reduced public health expenditure** (added to this, naturally, are also the benefits of improved individual state of health).

According to the OECD, the category **prevention expenditure** includes services provided to improve the overall state of health of the population, as opposed to treatment-related services. Typical prevention services are vaccination campaigns, screening programs and public awareness policies (e.g., promotion of healthier life styles). The OECD stresses that their classification does not include all areas pertaining to public health in its widest sense, such as environmental protection. Other sources⁴⁴¹, starting from a wider-ranging definition of health prevention services, arrive at a higher amount. The decision to utilize the data supplied by the OECD was based on the need to guarantee an acceptable level of international comparability of the data, as well as the fact that the classification of prevention expenditure utilized is closer to that of the objectives of this report.

This analysis takes into consideration **overall prevention expenditure** and not just prevention directly tied to dietary-related choices. This methodological decision is based on two considerations.

The first is the **close relationship between “non-dietary” prevention** (screening programs, control of risk factors for main chronic diseases, medical counseling to establish the best dietary program for each individual, etc.) **and correct diet**.

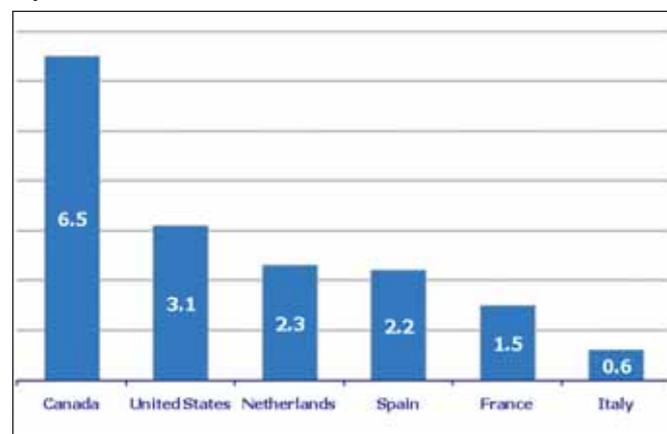
In fact, in drawing up their dietary guidelines for prevention of main chronic diseases, the most highly-esteemed international medical associations define as essential elements for success regular control over primary risk factors, involvement of medical specialists in preparing the best dietary plan for each patient, and providing individuals at-risk with professional medical help to guarantee that prevention and short-term results are also maintained over the long-term.

The second, largely technical in nature, is the **impossibility of being able to measure** statistically:

- the amount of prevention expenditure directly invested for only medical-dietary purposes in the strictest sense (as has been seen, dietary prevention is an integral part of other necessary analysis procedures, evaluations and information that are also repeated over time and which cannot theoretically be defined as “dietary initiatives”, although they are a necessary consequence);
- the part of the improvement in the health of the individual (and, therefore, in public health expenditure) due solely to changes in dietary habits (composition of daily diet), excluding the concurrent effect on the final result of the activity defined above as “non-dietary prevention”. There is only one long-term variable (required to measure changes association with prevention): reduction in the incidence of chronic disease in the population and consequent reduction in health care expenditure. The internal “composition” of that effect cannot be broken down into a measurable component.

As seen in the figure below, in Italy, prevention expenditure represents only a marginal amount of public health expenditure if compared with other countries. In 2006 it was 0.6% of public health expenditure, compared with 6.5% in Canada, 3.1% in the United States, 2.3% in The Netherlands, 2.2% in Spain and 1.5% in France.

Figure 32. Prevention expenditure as a percentage of public health expenditure, 2006



Source: The European House-Ambrosetti re-elaboration of data from the OECD “Health Data 2008”, December 2008

The goal of the analysis conducted was to estimate the extent of the benefit and how long it took to manifest itself on the basis of empirical evidence seen on an international level. Specifically, the analysis took into consideration five OECD member countries: Canada, France, The Netherlands, Spain and the United States⁴⁴².

Because the OECD classification criteria are based on defining prevention as distinct from treatment-related health services, to estimate the benefit of investment in prevention, the

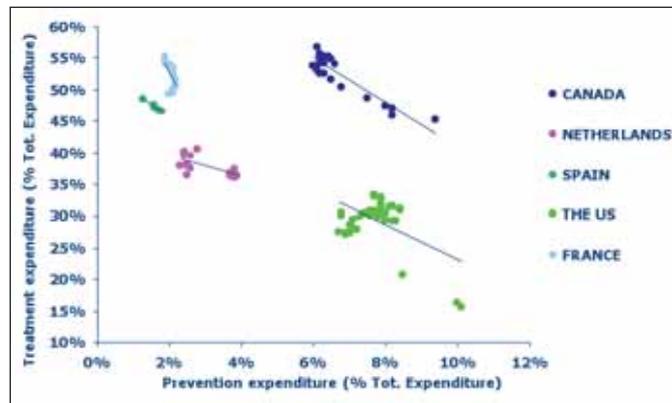
correlation between prevention expenditure and treatment and rehabilitation services expenditure was analyzed.

From analysis of data from the past (Figure 33) it can be seen that there is an inverse relationship between prevention expenditure and treatment/rehabilitation services expenditure in subsequent years.

Specifically, a 1% increase in the ratio of prevention expenditure to public health expenditure was correlated to a 3% reduction in the percentage of expenditure destined to treatment and rehabilitation services.

Taking into consideration different time frames in which benefits could be noted, the best statistical correlation between variation in percentage of prevention expenditure and variation in expenditure for treatment/rehabilitation services was seen to be within a period of 10 years.

Figure 33. Correlation between prevention expenditure and treatment expenditure

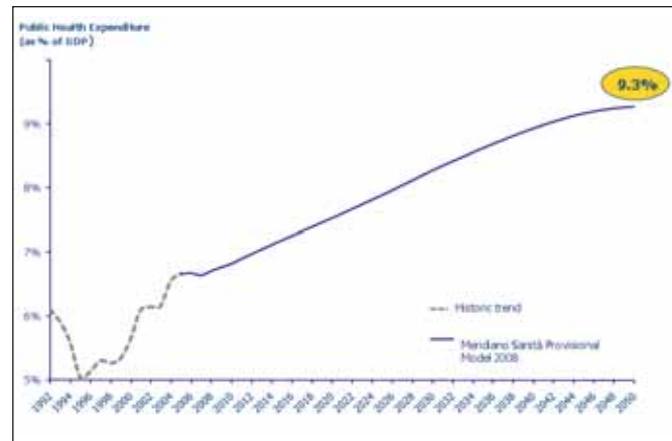


Source: The European House-Ambrosetti, "Meridiano Sanità - Le coordinate della salute. Final Report", November 2008

In conclusion, analysis from past years shows a multiplier for treatment/rehabilitation service expenditure of -3 times the investment in prevention and the maximum manifestation of the benefit within a period of 10 years.

The results of the analysis performed on international data from the past were then applied to forecasts for public health expenditure in Italy to the year 2050. As a result of demographic and economic factors⁴⁴³, the public health expenditure to the year 2050 was estimated to be over 262.8 billion euros, equal to 9.3% of GDP in 2050 (Figure 34).

Figure 34. Forecast model of public health expenditure in Italy to the year 2050



Source: The European House-Ambrosetti, "Meridiano Sanità - Le coordinate della salute. Final Report, November 2008

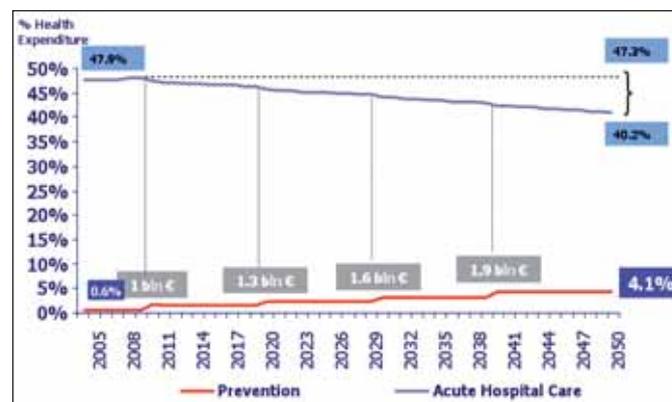
For the estimate of the impact of the increase in prevention investment, the following hypotheses were formulated:

- a multiplier for treatment/rehabilitation services of -3 times the investment in prevention;
- manifestation of the benefit within a period of 10 years;
- impact of the benefit as a decrease in expenditure for acute hospital care⁴⁴⁴;
- a constant multiplier in terms of the absolute value of investment in prevention⁴⁴⁵.

The extent and type of prevention investment are arbitrary choices. As a baseline case, a structural increase of the prevention expenditure/public health expenditure ratio of 1% every 10 years was hypothesized.

Figure 35, provides a summary of the prevention investment trend and its impact on health care expenditure for treatment/rehabilitation services.

Figure 35. Prevention investment trend and impact on treatment/rehabilitation services expenditure



Source: The European House-Ambrosetti, "Meridiano Sanità - Le coordinate della salute. Final Report", November 2008

The red line shows the trend in prevention expenditure; the “steps” at 10-year intervals are the structural increments caused by the 1% in the prevention expenditure/public health expenditure ratio (the grey boxes above each step show the actual value of the structural increment in relation to the year it was effected). Following the structural increments every 10 years, and applying the same average annual growth rate for the public health expenditure, in 2050 the prevention expenditure will absorb 10.7 billion euros and amount to 4.1% of public health expenditure.

In the medium-to-long term period, the structural increase in prevention expenditure will lead to a **reduction in the impact of acute hospital care expenditure on overall health care expenditure**. In 2006, hospital services accounted for 47.9% of public health expenditure. Without the “prevention effect”, for the period 2006-2050, they are expected to decrease slightly to 47.3% of health care expenditure (dotted blue line). As a consequence of prevention investment, a net reduction in hospital services expenditure is forecast, expected to be at a level of 40.2% of public health expenditure in 2050 (solid blue line).

By the year 2050, the decision to structurally increase prevention investment will require an expenditure of 9.3 billion euros⁴⁴⁶, but will generate a benefit in terms of reduced treatment/rehabilitation services expenditure of 26.4 billion euros.

The net benefit by the year 2050 of a structural increase of 1% in the prevention expenditure/public health expenditure ratio is estimated to be 17.1 billion euros, equal to a reduction of 0.6 percentage points in the ratio of public health expenditure to GDP, which would thus decrease to 8.7%.

5.1 A specific example

An example of how these benefits can be attained can be seen in the question of reducing blood pressure.

From the studies by Lewington⁴⁴⁷ carried out on a sample of over 1 million adults, it was seen that an increase, even a small one, in blood pressure (2 mmHg) would produce for the entire population an increase of 7% in the risk of coronary death and an increase of 10% in stroke risk.

Current dietary trends lead to consumption of foods that increase blood pressure. Recent data from the Atlante Italiano delle Malattie Cardiovascolari show that in Italy, 32% of the population is hypertensive and approx. 16% is at the limits of hypertension.

Within this context and faced by the above-mentioned trends, actions and policies must be implemented that can modify the life style and diet of the population.

On a concrete level, there are a number of solutions for solving the problem of high blood pressure in the population⁴⁴⁸.

- Adopting a low-sodium diet would bring about a reduction in blood pressure of 2-8 mmHg. Therefore, even taking into consideration only the baseline case, it would avoid the increase of 7% in the risk of coronary death and 10% in stroke risk generated by an increase of 2 mmHg, as shown in the studies by Lewington;
- Adopting a vegetable-rich diet would produce a reduction in blood pressure of between 8 and 14 mmHg;
- a life style with regular physical activity would reduce arterial pressure by between 2 and 4 mmHg;
- a weight reduction of 10Kg would bring about a reduction in pressure of approx. 5-20 mmHg.

In Europe, the overall economic impact of cardiovascular disease for 2006 was approx. 192 billion euros⁴⁴⁹. More specifically, costs for heart disease total 49 billion euros per year (about one-quarter of the total) and those related to stroke to 38 billion euros (approx. one-fifth of the total).

Adoption of a low-sodium (salt) diet alone **would avoid the 7% increase in coronary death risk**, equivalent to **3.4 billion euros per year** of costs saved in Europe, and **10% stroke risk**, equivalent to **3.8 billion euros per year** of costs saved in Europe.

In total, **reducing salt in the diet** (one of the factors tied to high blood pressure), **the benefits for European health care systems would be around 7.2 billion euros each year**.

NOTE PART B

408. World Health Organization, *Diet Nutrition and the Prevention of Chronic Disease*, Geneva 2003.
409. World Health Organization, *Diet Nutrition and the Prevention of Chronic Disease*, Geneva 2003.
410. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are present in fish fats (100 grams of salmon, trout, sardines, mackerel, herring or tuna contain an amount that varies between 1.5 and 3 grams of omega 3).
411. American Heart Association, European Society of Cardiology, Società Italiana di Cardiologia.
412. The most important factor in reducing the risk of cardiovascular disease is physical activity which, from the studies conducted, has an inverse correlation to cardiovascular disease, especially coronary disease. Therefore, an increase in physical activity corresponds to a reduction in the risk of cardiovascular disease.
413. The Body Mass Index is a biometric value expressed as the ratio between an individual's mass and height and is utilized as an indicator of ideal weight status. Range values are the same for both men and women.
414. International Agency For Research On Cancer, American Cancer Association, Federation Of European Cancer Society
415. By medium-intensity physical activity is meant walking, dancing, riding a bicycle, riding a horse, playing golf, cutting grass and gardening. By high-intensity physical activity is meant running, bicycle racing, engaging in aerobic dance in a gym, jumping, swimming, playing ball, tennis, basketball and engaging in manual labor, such as pruning trees in the yard, building furniture, masonry work, digging or carrying heavy weights.
416. These behaviour and lifestyles are consistent with the recommendations expressed by the Italian National Research Institute for Food and Nutrition (INRAN).
417. See, for example, for Italy, the Guidelines for a healthy Italian diet, of the National Research Institute for Food and Nutrition - INRAN, of 2003.
418. Agriculture Fact Book, Profiling Food Consumption in America, 2002
419. National Institute of Health, Strategic Plan for nih obesity research, 2004
420. The Japan Dietetic Association, National Nutrition Survey, 2001
421. *Cucina Mediterranea. Ingredienti, principi dietetici e ricette al sapore di sole*, Mondadori, Milano, 1993.
422. Ancel Benjamin Keys (1904-2004) American physician and physiologist is famous for having been one of the main advocates of the benefits of the Mediterranean diet for combating a large number of widespread diseases in the West, particularly cardiovascular diseases.
423. Keys A, Aravanis C, Blackburn H, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Karvonen MJ, Kimura N, Menotti A, Mohacek I, Nedeljkovic S, Puddu V, Punsar S, Taylor HL, Van Buchem FSP, Seven Countries. A Multivariate Analysis of Death and Coronary Heart Disease. 1980. Harvard University Press, Cambridge, MA and London. 1-381; Toshima H, Koga Y, and Blackburn H. Lessons for Science from the Seven Countries Study. 1995. Springer Verlag, Tokyo.
424. Keys A, Aravanis C, Blackburn HW, Van Buchem FSP, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Karvonen MJ, Kimura N, Lekos D, Monti M, Puddu V, Taylor HL. Epidemiologic studies related to coronary heart disease: characteristics of men aged 40-59 in seven countries. *Acta Med Scand* 1967 (Suppl to vol. 460) 1-392.
425. Keys A., Coronary heart disease in seven countries. *Circulation* 1970 (Suppl to vol.41) 1-211. Kromhout D, Menotti A, The Seven Countries Study: A Scientific Adventure in Cardiovascular Disease Epidemiology. 1994. Brouwer. Utrecht.
426. World Cancer Research Fund. Food, nutrition and the prevention of cancer: a global perspective. Washington, D.C.: American Institute for Cancer Prevention, 1997. Willett WC. Diet and coronary heart disease. In: Willett WC, ed. *Nutritional epidemiology*. 2nd ed. New York: Oxford University Press, 1998
427. Nube M, Kok FJ, Vandenbroucke JP, van der Heide-Wessel C, van der Heide RM. Scoring of prudent dietary habits and its relation to 25-year survival, *Journal of American Diet Association* 1987; Kant AK, Schatzkin A, Harris TB, Ziegler RG, Block G. Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, *American Journal of Clinical Nutrition* 1993; Farchi G, Fidanza F, Grossi P, Lancia A, Mariotti S, Menotti A. Relationship between eating patterns meeting recommendations and subsequent mortality in 20 years, *Journal Clinical Nutrition* 1995; Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Diet and overall survival in the elderly, *BMJ* 1995; Huijbregts P, Feskens E, Rasanen L, Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and the Netherlands: longitudinal cohort study, *BMJ* 1997; Kouris-Blazos A, Gnardellis C, Wahlqvist ML, Trichopoulos D, Lukito W, Trichopoulou A. Are the advantages of the Mediterranean diet transferable to other populations? A cohort study in Melbourne, Australia, *Br J Nutr* 1999; Kumagai S, Shibata H, Watanabe S, Suzuki T, Haga H. Effect of food intake pattern on all-cause mortality in the community elderly: a 7-year longitudinal study, *Journal Nutrition Health Aging* 1999; Osler M, Schroll M. Diet and mortality in a cohort of elderly people in a north European community, *International Journal of Epidemiologic* 1997; Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women, *JAMA* 2000; Lasheras C, Fernandez S, Patterson AM. Mediterranean diet and age with respect to overall survival in institutionalized, nonsmoking elderly people, *American Journal Clinical Nutrition* 2000; Osler M, Heitmann BL, Gerdes LU, Jørgensen LM, Schroll M. Dietary patterns and mortality in Danish men and women: a prospective observational study, *Journal of Nutrition* 2001; Michels KB, Wolk A. A prospective study of variety of healthy foods and mortality in women, *International Journal of Epidemiol* 2002.
428. Willett WC, Sacks F, Trichopoulou A, Mediterranean diet pyramid: a cultural model for healthy eating, *American Journal of Clinical Nutrition*, 1995.
429. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Diet and overall survival in the elderly, *BMJ* 1995.
430. Panagiotakos D., Pitsavos C., Arvanitic F., Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore, *Preventive Medicine*, Volume 44, Issue 4, April 2007.
431. The scale used in the study runs from 0 to 55, so an increase of 10 points on the Mediterranean adequacy index is equivalent to an increase of approx. 20%.
432. Trichopoulou A., Costacou T., Bamia C., Trichopoulos D., Adherence to a Mediterranean Diet and Survival in a Greek Population, *The New England Journal of Medicine*, Volume 348, N° 26, 2003.
433. Mitrou PN, Kipnis V, Thiebaut Ac, Reedy J, Subar AF, Wirfalt E, Flood A, Mouw T, Hollenbeck AR, Letizmann M, Schatzkin A. Mediterranean dietary pattern and prediction of all-cause mortality in a U.S. population: results from the NIH-AARP Diet and Health Study, *Archives of Internal Medicine*. 2007.
434. De Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N., Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study, *Circulation*, 1999.
435. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *American Journal of Clinical Nutrition*, 2005.
436. Sofi F, Cesari F, Abbate R., Gensini G., Casini A., Adherence to Mediterranean diet and health, *BMJ*, July, 2008.
437. Fidanza A., Fidanza F, Mediterranean Adequacy Index of Italian diets, *Public Health Nutrition*, 2004.
438. The Mediterranean adequacy index, thus calculated, compares the calories consumed through foods belonging to those typical of the Mediterranean diet with those not belonging to the Mediterranean diet, by creating a division. An index of 2 means that for each calorie consumed through a food not belonging to the Mediterranean diet, two calories of a food belonging to the Mediterranean diet are consumed.
439. Baldini M., Pasqui F, Bordoni A., Maranesi M., Is the Mediterranean lifestyle still a reality? Evaluation of food consumption and energy expenditure in Italian and Spanish university students, *Public*

- Health Nutrition, 2008.*
440. Analysis conducted by The European House-Ambrosetti as part of the project "Meridiano Sanità - Le coordinate della salute", developed for Pfizer Italia under the scientific supervision of an Advisory Board comprised of Innocenzo Cipolletta, Elio Guzzanti, Giacomo Vaciago and Umberto Veronesi
441. For example, the Agenzia per i Servizi Sanitari Regionali (ASSR)
442. The choice of these countries was dictated by the availability extensive, complete and comparable statistical data; for Italy this requirement is not present because a sufficiently extensive data base from the past is not available.
443. The model took into consideration two aspects whose evolution and interaction will determine the trend in public health expenditure over the near future. The first is demographics-related, i.e., the connection to the number and breakdown of the population by sex and age. The second is economics-based and tied to the tendency (seen in all advanced countries) towards an increase in overall health expenditure (public and private) that is more than proportionate to the growth in GDP. For a detailed description of the method and results of the health expenditure forecast model, please see: The European House-Ambrosetti, "Meridiano Sanità - Le coordinate della salute. Final Report, November 2008
444. The hypothesis that prevention manifests itself as a decrease in expenditure for any type of service defined in the context of the forecast model does not impact on the total value of the benefit, but rather on the division of health expenditure among different types of services.
445. This assumption is reasonable taking into consideration the modest level of investment in prevention and its low impact on public health expenditure. For high values of prevention investment and/or its impact on public health expenditure, it is reasonable to think that the benefit trend would decrease with the increase in the amount invested.
446. The difference between prevention expenditure by the year 2050 (10.7 billion euros) and the resources deriving from the structural investment (9.3 billion euros) represents the 2050 forecast for prevention expenditure already extant for the year 2006.
447. Lewington, et al. *Lancet*. 2002;360:1903-1913.
448. Chobanian A et al, *JAMA* 2003.
449. Source: "European cardiovascular disease statistics 2008", British Heart Foundation; Health Promotion Research Group, Department of Public Health, University of Oxford; Health Economics Research Centre, Department of Public Health, University of Oxford, 2009

Part C: recommendations

6 AREAS OF INITIATIVE

Before formulating a number of specific, final recommendations as the outcome of this report, we believe it useful to briefly review the **premises and logic** behind it. In particular, three existing situations formed the basis of the methodological approach utilized:

■ **THE GROWING IMPORTANCE OF PREVENTION WITHIN HEALTH CARE POLICY OVERALL.** Recent decades have seen a significant shift in the focus of medical activity in the treatment of disease and its prevention.

Over the last fifty years, in parallel with the more general and extraordinary improvement in treatment techniques (both pharmacological and surgical), there has been an overwhelming awareness of the enhanced efficiency and **efficacy** of prevention efforts compared with equivalent assistance to individuals already ill.

Enhanced efficacy because prevention allows for better overall results, also thanks to the intrinsic nature of working to aid a wider portion of the population than is the case with medical treatment; enhanced **efficiency** because it costs less. It is for this latter reason that prevention is one of the main lines of action for the future in guaranteeing the sustainability of health care systems affected by ever-growing levels of investment and operating costs, as is the case in virtually all countries of the Western world.

It is for this reason that our report is focused on prevention; we are convinced of the fact that this is an essential area for the future of medicine with extremely significant social spin-offs which have only been marginally explored to-date;

■ **THE INCREASED AWARENESS OF THE IMPACT OF LIFE STYLE AND DIET, IN PARTICULAR, ON PERSONAL HEALTH.** It was only in the second half of the last century that the first observational studies that stressed the connection between individual behavior and onset of disease began to appear. This provided scientific confirmation of the extremely close tie between individual choices and their consequences for health, and examination began of the underlying social, environmental and cultural factors.

The area of dietary habits emerged, in particular, as one of those most connected to the quality of life and

health of individuals and, therefore, also one of the most promising in terms of obtainable results. In this regard (as already noted at the start of this chapter), dietary habits and life styles play a decisive role in the prevention of **each of the three main families of noncommunicable disease (cancer, cardiovascular disease, diabetes and metabolic syndrome)**;

■ **THE DIFFICULTY IN IMPLEMENTING SUITABLE PREVENTION POLICIES AND SEARCH FOR BEST PRACTICES IN THIS AREA.** As shown by the overall alarming situation (see Chapter 1) characterized by the increased impact on a global scale of the major diseases afflicting humanity, there exist objective difficulties in translating the enormous amount of medical-scientific knowledge available into **policies and plans of action capable of having a concrete effect on individual behavior and, therefore, to contain over time the number of people who become ill.**

In fact, in recent years, the situation has worsened, including in contexts in which it seemed that major efforts had been initiated to reduce the incidence of certain diseases.

Unquestionably, this means that our scientific knowledge must be refined even further in order to improve our understanding of the causes behind disease. But, at the same time, it suggests that we must reflect more profoundly on how the knowledge already available can be better utilized and how to glean from it approaches and more concrete lines of action than those currently in place.

Within the context of these baseline considerations, our report concentrates on the issue of **prevention**, examining in particular the area of **diet** - which constitutes the specific area of study of our Research Center - and offers **concrete proposals for the future** in the form of the recommendations presented below. These, then, have been respectively the perimeter of our research and the goals of the study.

Above and beyond the decision to present the *state of the art* in terms of the selected goal of the study, what has emerged from the research done? Which elements are worth noting as points-of-departure to provide useful dietary suggestions for the future?

Briefly, two major points seem to have emerged. First of all, we noted that, within the scientific community, there is a growing conviction that **connection between life styles and health is very direct and very intense**.

A person's life style choices can have a devastating impact on health (the most blatant example being that of smoking), just as they can aid in protecting the person from the risk of serious diseases. In terms of individual choices, diet plays a decisive role. As we have attempted to show in this report, there is a high level of knowledge of the consequences of consuming, or failing to consume, various types of nutritional substances in terms of each macro family of noncommunicable diseases.

In addition (and this is even more interesting than the first point), analysis of the **guidelines** drawn up by the world's top scientific bodies showed a **high level of agreement in terms of practical operational recommendations**, irrespective of the disease under examination. In other words, there exist **life styles and diets which, when followed simultaneously and in parallel, can minimize risk of cancer, cardiovascular disease, diabetes and metabolic syndrome**. This finding is an important one because it creates the conditions for sending clear, direct and detailed information to the public about preferred dietary choices and life styles.

The fact that these conclusions could be reached while moving in parallel in three different areas of study (cancer, cardiovascular disease, metabolic dysfunction), demonstrates once again how useful the attempt to **create a codified system of knowledge in contiguous but separate areas** can be. In fact, it is also sometimes possible to contribute to generating new knowledge by attempting to bring together elements that are already known but rarely interpreted from an integrated and overall standpoint.

These findings suggest further, very important, courses of study and areas of action.

In our view, there are four priority areas for action and these are outlined below. They are:

1. PROMOTE HEALTHY EATING STYLES IN AN EFFECTIVE MANNER, ON THE BASIS OF THE MOST AUTHORITATIVE SCIENTIFIC STUDIES

The most interesting point to emerge from an analysis of the guidelines of the most authoritative scientific bodies and institutes is the surprising **convergence towards very solid dietary models of behavior which, to simplify, could be defined as the so-called "Mediterranean diet"**. Moderate consumption of alcohol, modest serving sizes, reduced calorie, salt, saturated fatty acid and trans fatty acid content, wide selection of fruit and vegetable-based dishes, fish, whole grains and cereals high in complex

carbohydrates, vapor cooking methods rather than frying and minimum consumption of meats and cured meats: these are the main, intersecting recommendations for preventing risk in a wide range of cardiovascular and metabolic disease and cancer.

The way in which food is consumed also plays a fundamental role. An average length of meal time adequate to giving the body time to allow the sensation of satiety to arrive at the brain is required. Otherwise, as in the case of compulsive or excessively fast eating, it would not be noted in time and this would result in excessive caloric intake. In addition, the progress in scientific studies tends to confirm the growing link between how foods are consumed and the nutritional consequences for the body.

Briefly stated, there exists a **correct dietary style** that is scientifically appropriate for safeguarding people from noncommunicable diseases. This dietary style (and this is a further finding that emerged over the course of the interdisciplinary studies conducted by the Barilla Center for Food & Nutrition) not only provides effective medical protection for people, but is also **environmentally-friendly**. Scientific findings in terms of *water management* and *climate change* (see the "Water Management" and "Climate Change, Agriculture and Food" position papers) demonstrate how implications of the production choices tied to dietary styles have significant impact on the environment, from both a positive and negative standpoint. In the second position paper cited we were able to construct the environmental pyramid associated with the well-known food pyramid, thus showing how a healthy, balanced diet has a low environmental impact as measured in terms of its overall footprint.

Transition towards more correct dietary models that are coherent with the macro-model cited will not be easy. The food industry must rethink a part of its productive processes and there are many players in the food chain who should also re-evaluate their role. What is at stake, however, including in economic terms (see Chapters 1 and 5), is too important to not embark down this road in a decisive way.

What is needed is concerted communication from government, scientific bodies and the medical community so that individuals can modify their view of the importance of dietary styles and be more aware of the issue. Our first recommendation is, therefore, the following: an invitation to follow more assiduously the guidelines that emerge over time from scientific studies and to implement all the initiatives required for these to become a reality.

2. IMPROVE AVAILABLE SCIENTIFIC KNOWLEDGE

The patrimony of scientific knowledge regarding diet is already very extensive and continues to grow.

Nonetheless, the concrete possibility does exist to make a noteworthy improvement in our level of understanding of the dynamics between food and health. We offer here a number of “cutting-edge” areas of study which we believe to be especially promising:

- expand studies regarding mechanisms of aging and cell repair. We know, in fact, that the incidence of noncommunicable disease is correlated to the state of health (inflammation level) of some cells in the body. In particular, study of the pre-inflammation and inflammation states could be one of the most promising fields of research given the multiple connections between these and the diseases under consideration, diabetes *in primis*. There is increasingly convincing evidence of the close tie between state of health of cells and the nutritive intake of an individual, although it has not yet been possible to clearly define all the relationships and processes involved in this dynamic;
- delve more deeply into the **gene-nutrient-food** relationships in order to have a focused and systematic understanding of the mechanisms of interaction between different nutrients and genes which are identified and recognized as study progresses, and which play an important role in the prevention or cause of various diseases. These studies will open new opportunities to increase the efficacy of certain food choices to maintain quality of life over time and for the well-being of individuals;
- expand and focus scientific studies on individuals who have **some risk factors typical of the onset of the diseases** under study at any given time (cardiovascular, cancer, diabetes), recognizing these people as being those most relevant and interesting for analysis and identification of the main relationships between diet and health. In fact, from a preventive standpoint, analysis of existing correlations between consumption (in different quantities, ways and times) of macro- and micronutrients and the development/course of various diseases in relation to individuals already affected by these diseases does not seem that open to generalization in order to formulate dietary recommendations aimed at their prevention. Similarly, analysis of the effects of dietary variation in healthy individuals does not seem able, by itself, to constitute an adequate information base in formulating prevention guidelines given that these individuals (because they are in good health) would not seem to be the ideal sample for investigation;
- systematically promote study on the question of **calorie restriction** to have a more in-depth understanding of what our bodies truly require from a dietary standpoint;
- promote **increasingly integrated and interdisciplinary research approaches** between the various branches of knowledge that study nutritional issues.

From an operational standpoint, for Italy, in our view the best way to approach the problem consists in the creation

of a “**national research network**” comprised of the top university research centers (both in Italy and abroad) capable of guaranteeing adequate focus, rationalization and optimization of research funds and, above all, a precise definition of research strategy. This network should have a double purpose: one focused on **basic research to best understand the “food-individual” interaction; the other applied research with significant interaction-guidance from the food industry.**

This should make it possible to create mixed university/industry research teams that are more efficacious and efficient, in order to propose projects eligible for EU funding as part of various basic programs. It would also offer the possibility of creating a number of specialized research body spin-offs to promote both major and more rapid findings for industry and the growth of talented researchers who see their ideas and hunches become concrete, thus improving the “cross-breeding” necessary between industry and research centers.

Given the importance of the food sector to our economy, there exist all the preconditions required to launch a major national project capable of bringing together scientific research, technological development and economic growth. In fact, Italy has the ideal characteristics to offer itself as a candidate for becoming the country of reference on a worldwide level in this field.

3. ADOPT SOCIAL-HEALTH CARE POLICIES AIMED AT SPREADING HEALTHY DIETARY BEHAVIOR

The main problem of the guidelines by the scientific bodies is their **ability to have an impact on individual behavior**. This despite the fact that there have been significant efforts to render the recommendations comprehensible.

In our view, the following things need to be worked on:

- make scientific knowledge available by translating it into precise and comprehensible recommendations that can be adopted by families and individuals **under the specific circumstances of their daily lives**. There should be no fear in entering into people’s everyday lives and providing specific recommendations that can help them face their daily experiences. People often eat out and even when they eat at home, they increasingly make use, at least partially, of pre-packaged foods. This is the reality of the situation that must be faced if we want to obtain results;
- involve the medical community in the diffusion of healthier dietary behavior. The **family doctor**, in particular, could become the invaluable transmission belt for more correct eating habits. This would require a significant investment and increased awareness (on all levels) of the importance of this theme;
- ask the **food industry to implement coherent strategies**

and operational plans, providing incentive for the possibility of performing scientific and technological research and work constructively on various issues on the table which involves it (for example, progressive improvement of nutritional profiles, food with specific functionality and improvement of density nutrition);

- work more intensively and better on the issue of **communication with the public** (covered in the next recommendation).

In summary, social-healthcare policies must be rethought within this context because around the guidelines, with their tremendous scientific value, a **more wide-ranging** and articulated project could be created that would have a real impact on individual behavior.

4. IMPROVE COMMUNICATION PROCESSES TO ADOPT LIFE STYLES AND DIETARY BEHAVIOR IN LINE WITH AVAILABLE SCIENTIFIC KNOWLEDGE

What is currently known about diet is already sufficient to create a massive, all-pervasive and scientifically unassailable communication campaign on a global scale

that could lead to saving a very high number of human lives and improve the quality of life on our planet.

For this, we need to be aware of the cost to society of the spread of noncommunicable diseases and convince ourselves of the need to undertake exceptional investment in grass-roots communication programs that can aid people in choosing and implementing a correct dietary style.

From this standpoint, involving young people in our schools through the **introduction of dietary studies** would appear to be a simple initiative, but one with enormous potential. Prevention and healthy dietary practices cannot just be handed down through the generations; it must be taught starting in elementary school. It is a fundamental and civic element for personal health, that can provide a boost in reinforcing a prevention-oriented perspective. Towards this end, programs for the school curriculum would need to be prepared relating to food, diet, prevention and the Mediterranean-style diet.

However, the food industry should, at the same time, promote communications standards in line with the guidelines for a healthy diet.

	Scientific Bodies/ Research Centres/Universities	Policy Makers	Companies/ Economic operators	Individuals/ Consumers
Promote and adopt healthy diets, following the most trustworthy scientific studies	Make the guidelines for an healthy diet more usable and easily applicable	Identify innovative communication solutions, able to affect individuals behaviour	Define strategies and implement operational plans in line with healthy lifestyle practices	Develop a growing awareness on the importance of diet and nutrition for a healthy life; encourage institutions and companies to adopt responsible behaviour
Improve the scientific knowledge available	Investigate deeply the relationship between diet and prevention; promote multidisciplinary groups, Universities-companies	Promote basic research and further develop applied research; Encourage and realize the framework for the creation of multidisciplinary groups, Universities-companies	Promote investments in applied research and encourage the creation of multidisciplinary groups Universities-companies	
Adopt socio-sanitary policies aimed to spread healthy dietary behaviour		Improve the usability of the scientific knowledge and of the guidelines for a healthy lifestyle in all the areas where the public power is involved in (schools, hospitals, canteen, etc.)		
Improve communication processes in order to promote the adoption of lifestyles and dietary behaviour in line with the best scientific knowledge available		Spread to the whole population the guidelines developed by scientific bodies; Promote the study of diet and food culture at school	Spread nutritional information and good dietary habits through all available communication channels (web, advertisement, packaging, etc.)	

 = OWNER

REFERENCES

- ADA, "Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications", January 2002
- ADA, "Nutrition recommendations and interventions for diabetes", January 2008
- Agriculture Fact Book, "Profiling Food Consumption in America", 2002
- Ajani U.A., Gaziano J.M., Lotufo P.A., et al., "Alcohol consumption and risk of coronary heart disease by diabetes status", *Circulation* 102: 500, 2000
- Albert C.M., Gaziano J.M., Willett W.C., Manson J.E., "Nut consumption and decreased risk of sudden cardiac death in the physicians' health study", *Arch. Intern. Med.* 162: 1382, 2002
- Alberts D.S., "Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas", *Phoenix Colon Cancer Prevention Physicians' Network. New England Journal of Medicine*, 342:1156-1162, 2000
- Althuis M.D., Jordan N.E., Ludington E.A., Wittes J.T., "Glucose and insulin responses to dietary chromium supplements: a meta-analysis", *American Journal of Clinical Nutrition* 76:148-155, 2002
- Amant F., Moerman P., Neven P., "Endometrial cancer", *Lancet*, 366:491-505, 2005
- American Cancer Association, "American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention: Reducing the Risk of Cancer With Healthy Food Choices and Physical Activity", 2006
- American Cancer Society, "Global Cancer Facts&Figures 2007"
- American Diabetes Association, "Economic Costs of Diabetes in the U.S. in 2007", *Diabetes Care*, Volume 31, Number 3, March 2008
- American Heart Association, "Heart Disease & Stroke Statistics. 2009 Update at-a-glance", 2009
- Anderson J.W., Hanna T.J., "Impact of nondigestible carbohydrates on serum lipoproteins and risk for cardiovascular disease", *Journal of Nutrition*, 129:1457-1466, 1999
- Anderson J.W., Smith B.M., Washnok C.S., "Cardiovascular and renal benefits of dry bean and soybean intake", *American Journal of Clinical Nutrition*, 70:464-474, 1999
- Appel L.J. et al., "A clinical trial of the effects of dietary patterns on blood pressure", DASH Collaborative Research Group. *New England Journal of Medicine*, 336:1117-1124, 1998
- Appleby P.N., Thorogood M., Mann J.I., Key T.J., "Low body mass index in non-meat eaters: the possible roles of animal fat, dietary fibre and alcohol", *International Journal of Obesity*, 22: 454, 1998
- Ascherio A. et al., "Dietary fat and risk of coronary heart disease in men: cohort follow-up study in the United States", *British Medical Journal*, 313:84-90, 1996
- Ascherio A., "Intake of potassium, magnesium, and fiber and risk of stroke among US men", *Circulation*, 98:1198-1204, 1998
- Ascherio A., Hennekens C. H., Buring J.E., Master C., Stampfer M.J., e Willett W.C., "Trans fatty acids intake and risk of myocardial infarction", *Circulation*, 89:94-101, 1994
- Associazione Medici Diabetologi - Diabete Italia - Società Italiana di Diabetologia (AMD-DI-SID)
- Baldini M., Pasqui F., Bordonni A., Maranesi M., "Is the Mediterranean lifestyle still a reality? Evaluation of food consumption and energy expenditure in Italian and Spanish university students", *Public Health Nutrition*, 2008
- Bandera E.V., Kushi L.H., Conside D.M., "The association between food, nutrition, physical activity and the risk of endometrial cancer and underlying mechanisms. In support of the Second WCRF/AICR Report on Food, Nutrition, Physical Activity and the Prevention of Cancer", 2007
- Bantle J., Ratz S., Thomas W., Georgopoulos A., "Effects of dietary fructose on plasma lipids in healthy subjects", *American Journal of Clinical Nutrition* 72: 1128, 2000
- Baron J.A., "Calcium supplements and colorectal adenomas", *Polyp Prevention Trial Study Group, Annals of the New York Academy of Sciences*, 889:138-145, 1999
- Bazzano L.A., He J., Ogden L.G., Loira C.M., Whelton P.K., "National Health and Nutrition Survey I Epidemiological Follow-up Study: Dietary fiber intake and reduced risk of coronary heart disease in US men and women: The National Health and Nutrition Survey I Epidemiological Follow-up Study", *Arch. Intern. Med.* 163: 1897, 2003
- Bazzano L.A., He J., Ogden L.G., et al., "Fruit and vegetable intake and risk of cardiovascular disease in US adults: the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study", *American Journal of Clinical Nutrition* 76: 93, 2002
- Bergstrom A., "Obesity and renal cell cancer, a quantitative review", *British Journal of Cancer*, 85:984-990
- Beta Carotene Cancer Prevention Study Group The Alpha-Tocopherol, "The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers", *New England Journal of Medicine*, 330:1029-1035, 1994
- Biesalski H.K., Bueno de Mesquita B., Chesson A., Eur Consensus Statement on Lung Cancer, "Risk factors and prevention", *Lung Cancer Panel. CA Cancer J Clin.* 48:167-176, 1998
- Bo S., et al., "Dietary fat and gestational hypoglycaemia", *Diabetologia*, 2001, 44:972--978
- Bonanome A., Visona A., Lusiani L., et al., "Carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus: effects of a low-fat, high carbohydrate diet vs a diet high in monounsaturated fatty acids", *American Journal of Clinical Nutrition* 54: 586, 1991
- Bonithon-Kopp C., "Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial", *European Cancer Prevention Organisation Study Group. Lancet*, 356:1300-1306, 2000
- Bosanquet N., Sikora K., "The economics of cancer care in the UK", *BMJ*, 2003
- Boyko E.J. et al., "Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans", *Diabetes Care*, 2000, 23:465--471
- Brage S., Wedderkopp N., Ekelund U., et al. the European Youth Heart Study (EYHS), "Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children", *Diabetes Care* 27: 2141, 2004
- Brand J., Colagiuri S., Crossman S., Allen A., Roberts D., Truswell A., "Low-glycemic index foods improve long-term glycemic control in NIDDM", *Diabetes Care* 14: 95, 1991
- British Heart Foundation, "European cardiovascular disease statistics 2008", Health Promotion Research Group, Department of Public Health, University of Oxford
- Brouwer I.A., "Low dose folic acid supplementation decreases plasmahomocysteine concentrations: a randomized trial", *American Journal of Clinical Nutrition*, 1999, 69:99--104
- Brown L.M., "Adenocarcinoma of the esophagus: role of obesity and diet. *Journal of the National Cancer Institute*", 87:104-109, 1995
- Bueno de Mesquita H.B., Ferrari P., Riboli E. (on behalf of EPIC Working Group on Dietary Patterns), "Plant foods and the risk of colorectal cancer in Europe: preliminary findings"
- Burger M., Brönstrup A., Pietrzik K., "Alkohol und Krankheiten. Abschlussbericht zum Forschungsvorhaben des Bundesgesundheitsministeriums für Gesundheit. Schriftenreihe des Bundesministeriums für Gesundheit Band 134", NOMOS Verlagsgesellschaft Baden-Baden 2000
- Burr M.L., et al., "Effects of changes in fat, fish and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART)", *Lancet*, 2:757-761, 1989
- Buyken A.E., Toeller M., Heitkamp G., et al. EURODIAB IDDM Complications Study Group, "Glycemic index in the diet of European outpatients with type 1 diabetes: relations to HbA1c and serum lipids", *American Journal of Clinical Nutrition* 73: 574, 2001
- Calle E.E., Murphy T.K., Rodriguez C., "Diabetes mellitus and pancreatic cancer mortality in a prospective cohort of United States adults. *Cancer Causes Control*", 9:403-410, 1998
- Calle E.E., Rodriguez C., Walker-Thurmond K., Thun M.J., "Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults", *N Engl J Med*, 348:1625-1638, 2003
- Carmichael AR, Bates T., "Obesity and breast cancer: a review of the literature", *Breast*, 13: 85-92, 2004
- Cefalu W.T., Hu F.B., "Role of chromium in human health and in diabetes", *Diabetes Care* 27:2741-2751, 2004
- Census, "Monitor Biomedico 2007"
- Chan J.M. et al., "Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men", *Diabetes Care*, 1994, 17:961--969
- Chan J.M., "Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study", *American Journal of Clinical Nutrition*, 74:549-554, 2001
- Chandalia M. et al., "Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus", *New England Journal of Medicine*, 2000, 342:1392--1398

- Christiansen E., Schnider S., Palmvig B., Tauber-Lassen E., Pedersen O., "Intake of a diet high in trans monounsaturated fatty acids or saturated fatty acids. Effects on postprandial insulinemia and glycemia in obese patients with NIDDM. *Diabetes Care*", 20: 881, 1997
- Clark L.C., "Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial", *British Journal of Urology*, 81:730-734, 1998
- Colditz G.A. et al., "Weight as a risk factor for clinical diabetes in women", *American Journal of Epidemiology*, 1990, 132:501--513
- Cox C., Mann J., Sutherland W., Chisholm A., Skeaff M., "Effects of coconut oil, butter, and safflower oil on lipids and lipoproteins in persons with moderately elevated cholesterol levels", *J. Lipid Res.* 36: 1501, 1995
- Crouse J.R., "Randomized trial comparing the effect of casein with that of soy protein containing varying amounts of isoflavones on plasma concentrations of lipids and lipoproteins", *Archives of Internal Medicine*, 159:2070-2076, 1999
- Cucina Mediterranea, "Ingredienti, principi dietetici e ricette al sapore di sole", Mondadori, Milano, 1993
- Cummings JH, Bingham SA., "Diet and the prevention of cancer", *British Medical Journal*, 317:1636-1640, 1998
- Cutler J.A., Follmann D., Allender P.S., "Randomized trials of sodium reduction: an overview", *American Journal of Clinical Nutrition*, 65:643-651, 1997
- Dallongeville J., Marecaux N., Ducimetiere P., et al., "Influence of alcohol consumption and various beverages on waist girth and waist-to-hip ratio in a sample of French men and women", *Int. J. Obes.* 22: 1178, 1998
- Davies M.J., Baer D.J., Judd J.T., Brown E.D., Campbell W.S., Taylor P.R., "Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women", *J.A.M.A.* 287: 2559, 2002
- De Leeuw I., De Block C., Van Gaal L., "Long term Mg supplementation influences favourably the natural evolution of neuropathy and retinopathy in Mg depleted type 1 diabetic patients", *Diabetologia* 46: A396, 2003
- De Leeuw I., Vertommen J., Abs R., "The magnesium content of the trabecular bone in diabetic subjects", *Biomedicine* 29: 16, 1978
- De Lorgeril M., Salen P., Martin J.L., Monjaud I., Delaye J., Mamelle N., "Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study", *Circulation*, 1999
- Despre's J.P. et al., "Treatment of obesity: need to focus on high-risk abdominally obese patients", *British Medical Journal*, 2001, 322:716-720
- Despre's J.P., "Health consequences of visceral obesity", *Annals of Medicine*, 2001, 33:534--541
- Doll R., Peto R., "The causes of cancer", Oxford Medical Publications, 1981
- Doll R., Peto R., "Epidemiology of cancer. In: Weatherall D.J., Ledingham J.G.G., Warrell D.A., eds", Oxford textbook of medicine. Oxford, Oxford University Press, 197-221, 1996
- Dorgan J.F. et al., "Serum hormones and the alcohol--breast cancer association in postmenopausal women", *Journal of the National Cancer Institute*, 93:710-715, 2001
- Dowey L., "B-vitamins, homocysteine metabolism and CVD", *Proceedings of the Nutrition Society*
- Egger M., Schneider M., Davey-Smith G., "Spurious precision? Meta-analysis of observational studies", *British Medical Journal*, 1998, 316:140--144
- Engelen W., Bouten A., De Leeuw I., De Block C., "Are low magnesium levels in type 1 diabetes mellitus associated with electromyographical signs of polyneuropathy?", *Magn. Res.* 13: 197, 2000
- Eriksson K.F., Lindgarde F., "Prevention of type 2 (non insulin dependent) diabetes mellitus by diet and physical exercise", *Diabetologia* 34: 891, 1991
- European Association for the Study of Diabetes (EASD)
- European Society for Medical Oncology, "The burden and cost of cancer", *Annals of Oncology* 18 (supplement 3), 2007
- FAO/WHO, "Scientific Update on carbohydrates in human nutrition: conclusions", 2007
- Farchi G., Fidanza F., Grossi P., Lancia A., Mariotti S., Menotti A., "Relationship between eating patterns meeting recommendations and subsequent mortality in 20 years", *Journal Clinical Nutrition* 1995
- Farmer A., Montori V., Dinneen S., Clar C., "Fish oil in people with type 2 diabetes mellitus. *Cochrane Database Syst Rev*", CD003205, (meta-analys, lipider. TG ner, LDL chol upp), 2001
- Feigelson H.S., Jonas C.R., Robertson A.S., "Alcohol, folate, methionine, and risk of incident breast cancer in the American Cancer Society", *Cancer Prevention Study II Nutrition Cohort*, *Cancer Epidemiol Biomarkers Prev*, 12:161-164, 2003
- Ferlay J., Globocan 2000, "Cancer incidence, mortality and prevalence worldwide. Version 1.0", Lyon International Agency for Research on Cancer, 2001
- Feskens E.J.M., "Can diabetes be prevented by vegetable fat?", *Diabetes Care* 24: 1517, 85, 2001
- Feskens E.J.M., Virtanen S.M. Räsänen L., et al., "Dietary factors determining diabetes and impaired glucose intolerance. A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study", *Diabetes Care* 18: 1104, 1995
- Feskens E.J.M., Kromhout D., "Habitual dietary intake and glucose tolerance in euglycaemic men: the Zutphen Study", *International Journal of Epidemiology*, 1990, 19:953-959
- Fidanza A., Fidanza F., "Mediterranean Adequacy Index of Italian diets", *Public Health Nutrition*, 2004
- Folsom A.R. et al., "Relation between plasma phospholipid saturated fatty acids and hyperinsulinemia. *Metabolism*", 1996, 45:223--228
- Fondazione Istud e Dipartimento di Oncoematologia del policlinico Umberto I, 2007
- Fontvieille A., Rizkalla S., Penformis A., Acosta M., Bornet F., Slama G., "The use of low glycaemic index foods improve metabolic control of diabetic patients over five weeks", *Diabet. Med.* 9: 444, 1992
- Foot D., Lewis R., Pearson T., Beller G., "Demographics and cardiology, 1950-2050", *Journal of the American College of Cardiology*, Volume 35, Issue 5, 2000
- Forte J.G., Pereira Miguel J.M., Pereira Miguel M.J., de Padua F., Rose G., "Salt and blood pressure: a community trial", *Journal of Human Hypertension*, 3:179-184, 1989
- Foster G.D., Wyatt H.R., Hill J.O., McGuckin B.G., Brill C., Mohammed B.S., Szapary P.O., Rader D.J., Edman J.S., "Klein Nutrition recommendations and interventions", *S74 DIABETES CARE, VOLUME 31, SUPPLEMENT 1, JANUARY 2008 S: A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med* 348: 2082-2090, 2003
- Franz M.J., Bantle J.P., Beebe C.A., Brunzell J.D., Chiasson J.L., Garg A., Holzmeister L.A., Hoogwerf B., Mayer-Davis E., Mooradian A.D., Purnell J.Q., Wheeler M., "Evidence- based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications", *Diabetes Care* 25:148-198, 2002
- Fraser G.E., Sabate J., Beeson W.L., Strahan T.M., "A possible protective effect of nut consumption on risk of coronary heart disease: the Adventist Health Study", *Arch. Intern. Med.* 152: 1416, 1992
- Friedberg C.E., Janssen M.J., Heine R.J., Grobbee D.E., "Fish oil and glycemic control in diabetes", *A meta-analysis. Diabetes Care* 21: 494, 1998
- Frost G., Wilding J., Beecham J., "Dietary advice based on the glycaemic index improves dietary profile and metabolic control in type 2 diabetic patients", *Diabet. Med.* 11: 397, 1994
- Fung T.T., McCullough M.L., Newby P.K., Manson J.E., Meigs J.B., Rifai N., Willett W.C., Hu F.B., "Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction", *American Journal of Clinical Nutrition*, 2005
- Gannon M.C., Nuttall F.Q., "Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes", *Diabetes* 53:2375-2382, 2004
- Gannon M.C., Nuttall F.Q., Saeed A., Jordan K., Hoover H., "An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes", *American Journal of Clinical Nutrition* 78:734-741, 2003
- Gannon M.C., Nuttall J.A., Damberg G., Gupta V., Nuttall F.Q., "Effect of protein ingestion on the glucose appearance rate in people with type 2 diabetes", *J Clin Endocrinol Metab* 86:1040-1047, 2001
- Garg A., Bantle J.P., Henry R.R., Coulston A.M., Griver K.A., Raatz S.K., Brinkley L., Chen Y.D., Grundy S.M., Huet B.A., et al., "Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus", *JAMA* 271: 1421-1428, 1994
- Garg A., "High-monounsaturated fat diets for patients with diabetes mellitus: a meta-analysis", *Am. J. Clin. Nutr.* 67 (suppl.): 577S, 1998
- Gaziano J.M., Hennekens C.H., Godfried S.L., et al., "Type of alcoholic beverage and risk of myocardial infarction", *Am. J. Cardiol.* 83: 52, 1999
- Gaziano J.M., Manson J.E., Branch L.G., Colditz G.A., Willett W.C., Buring J.E., "A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly", *Ann. Epidemiol.* 5: 255, 1995

- Gibbs C.R., Lip G.Y., Beevers D.G., "Salt and cardiovascular disease: clinical and epidemiological evidence", *Journal of Cardiovascular Risk*, 7:9-13, 2000
- Gillmann M.W., Cupples L.A., Gagnon D., et al., "Protective effect of fruits and vegetables on development of stroke in men", *J.A.M.A.* 273: 1113, 1995
- Giovannucci E., "Alcohol, low-methionine, low-folate diets, and risk of colon cancer in men", *Journal of the National Cancer Institute*, 87:265-273, 1995
- Giovannucci E., "Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study", *Annals of Internal Medicine*, 129:517-524, 1998
- Giovannucci E., Liu Y., Rimm E.B., "Prospective study of predictors of vitamin D status and cancer incidence and mortality in men", *J Natl Cancer Inst*, 98:451-459, 2006
- Giovannucci E., Liu Y., Stampfer M.J., Willett W.C., "A prospective study of calcium intake and incident and fatal prostate cancer", *Cancer Epidemiol Biomarkers Prev* 2006;15:203-210
- Giovannucci E., Rimm E.B., Wolk A., "Calcium and fructose intake in relation to risk of prostate cancer", *Cancer Res*, 58:442-447, 1998
- Giovannucci E., "The epidemiology of vitamin D and colorectal cancer: recent findings", *Curr Opin Gastroenterol*, 22:24-29, 2006
- GISSI-Prevenzione investigators, "Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial", *Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. Lancet*, 354:447-455, 1999
- Goldstein D.J., "Beneficial health effects of modest weight loss", *Int. J. Obes.* 16: 397-415, 1992
- Gonzalez C.A., "Vegetable, fruit and cereal consumption and gastric cancer risk", *IARC Sci Publ*, 156:79-83, 2002
- Gougeon R., Marliss E.B., Jones P.J., Pencharz P.B., Morais J.A., "Effect of exogenous insulin on protein metabolism with differing nonprotein energy intakes in type 2 diabetes mellitus", *Int. J. Obes.* 22: 250, 1998
- Gougeon R., Pencharz P.B., Marliss E.B., "Effect of NIDDM on the kinetics of whole-body protein metabolism", *Diabetes* 43: 318, 1994
- Gougeon R., Pencharz P.B., Sigal R.J., "Effect of glycemic control on the kinetics of whole-body protein metabolism in obese subjects with non-insulin-dependent diabetes mellitus during iso- and hypoenergetic feeding", *Am. J. Clin. Nutr.* 65: 861, 1997
- Greenfield J.R., Samaras K., Jenkins A.B., Kelly P.J., Spector T.D., Campbell L.V., "Moderate alcohol consumption, estrogen replacement therapy, and physical activity are associated with increased insulin sensitivity: is abdominal adiposity the mediator?", *Diabetes Care* 26: 2734, 2003
- Grundty S.M., Vega G.L., "Plasma cholesterol responsiveness to saturated fatty acids", *American Journal of Clinical Nutrition*, 1988, 47:822-824
- Guerrero-Romero F., Rodriguez-Moran M., "Complementary therapies for diabetes: the case for chromium, magnesium, and antioxidants", *Arch Med Res* 36:250-257, 2005
- Gunton J.E., Cheung N.W., Hitchman R., Hams G., O'Sullivan C., Foster-Powell K., McElduff A., "Chromium supplementation does not improve glucose tolerance, insulin sensitivity, or lipid profile: a randomized, placebo-controlled, double-blind trial of supplementation in subjects with impaired glucose tolerance", *Diabetes Care* 28:712-713, 2005
- Hamajima N., Hirose K., Tajima K., "Alcohol, tobacco and breast cancer-collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease", *Br J Cancer*, 87:1234-1245, 2002
- Hardman A.E., "Physical activity and cancer risk. Proceedings of the Nutrition Society", 60:107-113, 2001
- Harris W.S., Park Y., Isley W.L., "Cardiovascular disease and long-chain omega-3 fatty acids", *Curr. Opin. Lipidol.* 14: 9, 2003
- Hasanain B., Mooradian A.D., "Antioxidant vitamins and their influence in diabetes mellitus", *Curr Diab Rep* 2:448-456, 2002
- Heart Protection Study Collaborative Group, "MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20 536 high-risk individuals: a randomized placebo-controlled trial", *Lancet*, 2002, 360:23-33
- Heine R.J., Mulder C., Popp-Snijders C., van der Meer J., van der Veen E.A., "Linoleic-acid-enriched diet: long term effects on serum lipoprotein and apolipoprotein concentrations and insulin sensitivity in non-insulin dependent diabetic patients", *Am. J. Clin. Nutr.* 49: 448, 1989
- Heinonen O.P., "Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial", *Journal of the National Cancer Institute*, 90:440-446, 1998
- Helmrich S.P. et al., "Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus", *New England Journal of Medicine*, 1991, 325:147-152
- Hennekens C.H., "Lack of effect of long-term supplementation with beta-carotene on the incidence of malignant neoplasms and cardiovascular disease", *New England Journal of Medicine*, 334:1145-1149, 1996
- Hertog M.G.L., "Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study", *Lancet*, 342:1007-1011, 1993
- Howard A.A., Arnsten J.H., Gourevitch M.N., "Effect of alcohol consumption on diabetes mellitus: a systematic review", *Ann Intern Med* 140:211-219, 2004
- Howell W.H., McNamara D.J., Tosca M.A., Smith B.T., Gaines J.A., "Plasma lipid and lipoprotein responses to dietary fat and cholesterol: meta-analysis", *Am. J. Clin. Nutr.* 65: 1747, 1997
- Hu F.B., "The role of n-3 polyunsaturated fatty acids in the prevention and treatment of cardiovascular disease", *Drugs Today* 37: 49, 2001
- Hu F.B., Stampfer M.J., Manson J.E., et al., "Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study", *B.M.J.* 317: 1341, 1998
- Hu F.B., van Dam R.M., Liu S., "Diet and risk of type 2 diabetes: the role of types of fat and carbohydrate", *Diabetologia* 44: 805, 2002
- Hu F.B., et al., "A prospective study of egg consumption and risk of cardiovascular disease in men and women", *Journal of the American Medical Association*, 281:1387-1394, 1999
- Hu F.B., et al., "Dietary fat intake and the risk of coronary heart disease in women", *New England Journal of Medicine*, 337:1491-1499, 1997
- Hu F.B., "Fish and omega-3 fatty acid intake and risk of coronary heart disease in women", *American Journal of Clinical Nutrition*, 69:890-897, 1999
- Hu F.B., Manson J.E., Stamper M.J., Colditz G., Liu S., Solomon C.G., Willett W.C., "Diet, lifestyle and the risk of type 2 diabetes mellitus in women", *New Engl J Med* 2001;345:790-7
- Hu F.B., Stampfer M.J., "Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence", *Current Atherosclerosis Reports*, 1:204-209, 1999
- Huifregts P., Feskens E., Rasanen L., "Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and the Netherlands: longitudinal cohort study", *BMJ* 1997
- Institute of medicine, "Letter report on dietary reference intakes for trans fatty acids", National Academy of Sciences, USA, July 2002
- International Agency for Research on Cancer, "Cancer: causes, occurrence and control", Lyon, (IARC Scientific Publications, No. 100), 1996
- International Agency for Research on Cancer, "Overweight and lack of exercise linked to increased cancer risk. In: Weight control and physical activity", Lyon, 2002
- International Diabetes Federation, "Diabetes Atlas", 2009
- International Obesity Task Force, database
- ISDOC, "Actual and preferred place of death of cancer patients. Results from the Italian survey of the dying of cancer (ISDOC)", *Journal of Epidemiology and Community Health* 2006
- ISS, database
- Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - INRAN, "Linee Guida per una sana alimentazione italiana", 2003
- Jacobs D.R., "Whole-grain intake and cancer: an expanded review and meta-analysis", *Nutrition and Cancer*, 30:85-96, 1998
- Jemal A., Siegel R., Ward E., "Cancer statistics", *CA Cancer J. Clin.* 2006;56:106-130, 2006
- Jenkins D.J., Wolever T.M., Taylor R.H., Barker H., Fielden H., Baldwin J.M., Bowling A.C., Newman H.C., Jenkins A.L., Goff D.V., "Glycemic index of foods: a physiological basis for carbohydrate exchange", *Am J Clin Nutr* 34:362-366, 1981
- Jensinks D., Kendall C., McKeown-Eyssen G., et al., "Effect of a Low Glycemic Index or a High Cereal Fiber Diet on Type 2 Diabetes: A Randomized Trial", *JAMA*, December 17, 2008, Vol 300, No. 23
- Joshi K.J., Ascherio A., Manson J.E., et al., "Fruit and vegetable intake in relation to risk for ischemic stroke", *J.A.M.A.* 282: 1233, 1999
- Joshi K.J., Hu F.B., Manson J.E., et al., "The effect of fruit and vegetable intake on risk for coronary heart disease", *Ann. Intern. Med.* 134: 1106, 2001
- Kant A.K., Schatzkin A., Graubard B.I., Schairer C., "A prospective study of diet quality and mortality in women", *JAMA* 2000
- Kant A.K., Schatzkin A., Harris T.B., Ziegler R.G., Block G., "Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up", Study,

- American Journal of Clinical Nutrition 1993
- Katan M.B., Zock P.L., Mensink M.P., "Dietary oils, serum lipoproteins, and coronary heart disease", *Am. J. Clin. Nutr.* 61: 1368S, 1995
- Katan M.B., Zock P.L., Mensink R.P., "Trans fatty acids and their effects on lipoproteins in humans", *Ann. Rev. Nutr.* 15: 473, 1995
- Katan M.B., "Trans fatty acids and plasma lipoproteins", *Nutrition Reviews*, 58:188-191, 2000
- Katan M.J., Zock PL, Mensink RP, "Dietary oils, serum lipoproteins and coronary heart disease", *American Journal of Clinical Nutrition*, 1995, 61(Suppl. 6):1368--1373
- Keli S.O., "Dietary flavonoids, antioxidant vitamins, and incidence of stroke: the Zutphen study", *Archives of Internal Medicine*, 156:637-642, 1996
- Kelley J.R., Duggan J.M., "Gastric cancer epidemiology and risk factors", *J. Clin. Epidemiol.* 56:1-9, 2003
- Kerr D., Macdonald I.A., Heller S.R., Tattersall R.B., "Alcohol causes hypoglycaemic unawareness in healthy volunteers and patients with Type 1 (insulin dependent) diabetes", *Diabetologia* 33: 216, 1990
- Key T.J., Allen N.E., "Nutrition and breast cancer", *Breast*, 10(Suppl. 3):S9-S13, 2001
- Keys A., Aravanis C., Blackburn H.W., Van Buchem F.S.P., Buzina R., Djordjevic B.S., Dontas A.S., Fidanza F., Karvonen M.J., Kimura N., Lekos D., Monti M., Puddu V., Taylor H.L., "Epidemiologic studies related to coronary heart disease: characteristics of men aged 40-59 in seven countries", *Acta Med Scand* 1967 (Suppl. to vol. 460) 1-392
- Keys A., Aravanis C., Blackburn H., Buzina R., Djordjevic B.S., Dontas A.S., Fidanza F., Karvonen M.J., Kimura N., Menotti A., Mohacek I., Nedeljkovic S., Puddu V., Punsar S., Taylor H.L., Van Buchem F.S.P., "Seven Countries. A Multivariate Analysis of Death and Coronary Heart Disease", 1980. Harvard University Press, Cambridge, MA and London. 1-381
- Keys A., "Coronary heart disease in seven countries", *Circulation* 1970 (Suppl. to vol.41) 1-211
- Khaw K.T., Barrett-Connor E., "Dietary potassium and stroke-associated mortality. A12-year prospective population study", *New England Journal of Medicine*, 316:235-240, 1987
- Kleefstra N., Houweling S.T., Jansman F.G., Groenier K.H., Gans R.O., Meyboom-de Jong B., Bakker S.J., Bilo H.J., "Chromium treatment has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population: a randomized, double-blind, placebo-controlled trial", *Diabetes Care* 29: 521-525, 2006
- Klein S., Sheard N.F., Pi-Sunyer X., Daly A., Wylie-Rosett J., Kulkarni K., Clark N.G., "Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies: a statement of the American Diabetes Association", *The North American Association for the Study of Obesity - the American Society for Clinical Nutrition. Diabetes Care* 27:2067-2073, 2004
- Kligler B., "The role of the optimal healing environment in the care of patients with diabetes mellitus type II", *J. Altern Complement Med* 10 (Suppl. 1):S223-S229, 2004
- Knowler WC et al. "Reduction in the incidence of type 2 diabetes with lifestyle intervention of metformin", *New England Journal of Medicine*, 2002, 346:393-403
- Koletzko, B., Decsi T., "Metabolic aspects of trans fatty acids", *Clinical Nutrition* 16:229-237
- Kolonel L.N., "Fat, meat, and prostate cancer", *Epidemiol Rev*, 23:72-81, 2001
- Kouris-Blazos A., Gnardellis C., Wahlqvist M.L., Trichopoulos D., Lukito W., Trichopoulou A., "Are the advantages of the Mediterranean diet transferable to other populations? A cohort study in Melbourne, Australia", *Br J Nutr* 1999
- Kris-Etherton P., "Summary of the scientific conference on dietary fatty acids and cardiovascular health: conference summary from the nutrition committee of the American Heart Association. *Circulation*", 2001, 103:1034--1039.
- Kris-Etherton P.M., "The effects of nuts on coronary heart disease risk", *Nutrition Reviews*, 59:103-111, 2001
- Kris-Etherton P.M., Lichtenstein A.H., Howard B.V., Steinberg D., Witztum J.L., "Antioxidant vitamin supplements and cardiovascular disease", *Circulation* 110: 637-641, 2004
- Kriska A.M., et al., "The association of physical activity with obesity, fat distribution and glucose intolerance in Pima Indians", *Diabetologia*, 1993, 36:863--869
- Kristal A.R., Cohen J.H., "Invited commentary: tomatoes, lycopene, and prostate cancer. How strong is the evidence?", *American Journal of Epidemiology*, 151:124-127, 2000
- Kromhout D., Menotti A., "The Seven Countries Study: A Scientific Adventure in Cardiovascular Disease Epidemiology", 1994
- Kumagai S., Shibata H., Watanabe S., Suzuki T., Haga H., "Effect of food intake pattern on all-cause mortality in the community elderly: a 7-year longitudinal study", *Journal Nutrition Health Aging* 1999
- Lasheras C., Fernandez S., Patterson A.M., "Mediterranean diet and age with respect to overall survival in institutionalized, nonsmoking elderly people", *American Journal Clinical Nutrition* 2000
- Law M.R., Frost C.D., Wald N.J., "By how much does salt reduction lower blood pressure? III--Analysis of data from trials of salt reduction", *British Medical Journal*, 302:819-824, 1991
- Lean M.E.J., Han T.S., Morrison C.E., "Waist circumference as a measure for indicating need for weight management", *Br. Med. J.* 311: 158, 1995
- Lee Y.M., Haastert B., Scherbaum W., Hauner H., "A phytosterol-enriched spread improves the lipid profile of subjects with type 2 diabetes mellitus: a randomized controlled trial under freelifing conditions", *Eur J Nutr* 42:111-117, 2003
- Lévy C., Bonastre J., "The cost of chemotherapy", *Bull Cancer* 2003 Nov
- Lewington, et al. *Lancet*. 2002;360:1903-1913
- Liese A.D., Roach A.K., Sparks K.C., Marquart L., D'Agostino R.B., Jr, Mayer-Davis EJ, "Whole-grain intake and insulin sensitivity: the Insulin Resistance Atherosclerosis Study", *Am J Clin Nutr* 78:965-971, 2003
- Liese A.D., Schulz M., Fang F., Wolever T.M., D'Agostino R.B., Jr, Sparks KC, Mayer-Davis EJ, "Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the Insulin Resistance Atherosclerosis Study", *Diabetes Care* 28:2832-2838, 2005
- Lindstrom, "Diabetologia", 2006
- Liu S., "Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study", *American Journal of Clinical Nutrition*, 72:922-928, 2000
- Liu S., Lee I.M., Ajani U., Cole S.R., Buring J.E., Manson J.E., "Intake of vegetables rich in carotenoids and risk of coronary heart disease in men: the Physicians", *Health Study. Int. J. Epidemiol.* 30: 130, 2001
- Lonn E., Yusuf S., Hoogwerf B., Pogue J., Yi Q., Zinman B., Bosch J., Dagenais G., Mann J.F., Gerstein H.C., "Effects of vitamin E on cardiovascular and microvascular outcomes in high-risk patients with diabetes: results of the HOPE study and MICRO-HOPE substudy", *Diabetes Care* 25:1919-1927, 2002
- Lousely S.E., Jones D.B., Slaughter P., Carter R.D., Jelfs R., Mann J.I., "High carbohydrate/high fibre diets in poorly controlled diabetes", *Diabet. Med.* 1: 21, 1984
- Lovejoy J, DiGirolamo M., "Habitual dietary intake and insulin sensitivity in lean and obese adults", *American Journal of Clinical Nutrition*, 1992, 55:1174--1179
- Luscombe N.D., Noakes M., Clifton P.M., "Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM", *Eur. J. Clin. Nutr.* 53: 473, 1999
- Mackay J., Jemal A., Lee N.C., Parkin M., "The Cancer Atlas", American Cancer Society, 2006
- Mann J. Lawrence lecture, "Lines to legumes: changing concepts of diabetic diets", *Diabetic Medicine*, 1984, 1:191--198
- Mann J., "Dietary fibre and diabetes revisited", *Eur. J. Clin. Nutr.* 55: 919, 2001
- Mann J., "Lines to legumes: changing concepts of diabetic diets", *Diabetic Med.* 1: 191, 1984
- Manson J.E., et al., "A prospective study of exercise and incidence of diabetes among US male physicians", *Journal of the American Medical Association*, 1992, 268:63-67
- Marckmann P., Gronbaek M., "Fish consumption and coronary heart disease mortality. A systematic review of prospective cohort studies", *European Journal of Clinical Nutrition*, 53:585-590, 1999
- Marshall J.A., Bessesen D.H., "Dietary fat and the development of type 2 diabetes", *Diabetes Care* 25: 620, 2002
- Marshall J.A., et al., "Dietary fat predicts conversion from impaired glucose tolerance to NIDDM", *The San Luis Valley Diabetes Study. Diabetes Care*, 1994, 17:50--56
- Martinez M.E., Giovannucci E., Spiegelman D., "Leisure-time physical activity, body size, and colon cancer in women", *Nurses' Health Study Research Group. J Natl Cancer Inst.* 89:948-955, 1997
- Mayer E.J., et al., "Usual dietary fat intake and insulin concentrations in healthy women twins", *Diabetes Care*, 1993, 16:1459--1469
- McAuley K.A., Williams S.M., Mann J.I., et al., "Intensive lifestyle changes are necessary to improve insulin sensitivity: A randomised controlled

- trial", *Diabetes Care* 25: 445, 2002
- McKeown N.M., Meig S.J.B., Liu S., Saltzman E., Wilson P.W.F., Jacques P.F., "Carbohydrate nutrition, insulin resistance, and the prevalence of the Metabolic Syndrome in the Framingham Offspring Cohort", *Diabetes Care* 27: 538, 2004
- McKillop I., Schrum L., "Alcohol and Liver Cancer", Department of Biology, University of North Carolina at Charlotte, Charlotte, 2005
- McNair P., Christiansen C., Madsbad S., et al., "Hypomagnesaemia, a risk factor in diabetic retinopathy", *Diabetes* 27: 1075, 1978
- McNair P., Christiansen M.S., Christiansen C., Madsbad S., Transbol I., "Renal hypomagnesaemia in human diabetes mellitus: its relation to glucose homeostasis", *Eur. J. Clin. Invest.* 12: 81, 1982
- Mensink R.P., Zock P.L., Kester A.D.M., Katan M.B., "Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL-cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials", *Am. J. Clin. Nutr.* 77: 1146, 2003
- Mensink R.P., Katan M.B., "Effect of dietary trans fatty acids on high-density and low-density lipoprotein cholesterol levels in healthy subjects", *N. Engl. J. Med.*, 323:439-445, 1990
- Meyer K.A., Kushi L.H., Jacobs D.R. Jr, Slavin J., Sellers T.A., Folsom A.R., "Carbohydrates, dietary fiber, and incident type 2 diabetes in older women", *Am J Clin Nutr* 71:921-930, 2000
- Michaud D.S., "A prospective study on intake of animal products and risk of prostate cancer", *Cancer Causes and Control*, 12:557-567, 2001
- Michaud D.S., "Physical activity, obesity, height, and the risk of pancreatic cancer", *Journal of the American Medical Association*, 286:921-929, 2001
- Michels K.B., "Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers", *Journal of the National Cancer Institute*, 92:1740-1752, 2000
- Michels K.B., Wolk A., "A prospective study of variety of healthy foods and mortality in women", *International Journal of Epidemiol* 2002
- Midgley J.P., "Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials", *Journal of the American Medical Association*, 275:1590-1597, 1996
- Mitrou P.N., Kipnis V., Thiebaut A.C., Reedy J., Subar A.F., Wirfalt E., Flood A., Mouw T., Hollenbeck A.R., Letizmann M., Schatzkin A., "Mediterranean dietary pattern and prediction of all-cause mortality in a U.S. population: results from the NIH-AARP Diet and Health Study", *Archives of Internal Medicine*, 2007
- Montori V.M., Farmer A., Wollan P.C., Dinneen S.F., "Fish oil supplementation in type 2 diabetes: a quantitative systematic review", *Diabetes Care* 23: 1407, 2000
- Mori T.A., Beilin L.J., "Long-chain omega 3 fatty acids, blood lipids and cardiovascular risk reduction. *Current Opinion in Lipidology*", 12:11-17, 2001
- Mukamal K.J., Conigrave K.M., Mittleman M.A., et al., "Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men", *N. Engl. J. Med.* 348: 109, 2003
- Nair K.S., Garrow J.S., Ford C., Mahler R.F., Halliday D., "Effect of poor diabetic control and obesity on whole body protein metabolism in man", *Diabetologia* 25: 400, 1983
- National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, "Reducing Tobacco Use: A Report of the Surgeon General. US Department of Health and Human Services", 2000
- National Institutes of Health (NIH) - Obesity Research Task Force, "Strategic Plan for NIH Obesity Research", August 2004
- Ness A.R., Powles J.W., "Fruit and vegetables, and cardiovascular disease: a review", *International Journal of Epidemiology*, 26:1-13, 1997
- Nizal Sarrafzadegan et al., "Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran", *Bulletin of the World Health Organization*, Volume 87, Number 1, January 2009
- Norat T., "Meat consumption and colorectal cancer risk: a dose-response meta-analysis of epidemiological studies", *International Journal of Cancer*, 98:241-256, 2002
- Nube M., Kok F.J., Vandenbroucke J.P., van der Heide-Wessel C., van der Heide R.M., "Scoring of prudent dietary habits and its relation to 25-year survival", *Journal of American Diet Association* 1987
- Nutritional Aspects of the Development of Cancer, "Report of the Working Group on Diet and Cancer of the Committee on Medical Aspects of Food and Nutrition Policy, London, The Stationery Office, 1998
- Nygard O., et al., "Total plasma homocysteine and cardiovascular risk profile. The Hordaland Homocysteine Study", *Journal of the American Medical Association*, 274:1526-1533, 1995
- Omenn G.S., "Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease", *New England Journal of Medicine*, 334:1150-1155, 1996
- Omen C.M., et al., "Association between trans fatty acid intake and 10-year risk of coronary heart disease in the Zutphen Elderly Study: a prospective population based study", *Lancet*, 357:746-751, 2001
- Osler M., Heitmann B.L., Gerdes L.U., Jørgensen L.M., Schroll M., "Dietary patterns and mortality in Danish men and women: a prospective observational study", *Journal of Nutrition* 2001
- Osler M., Schroll M., "Diet and mortality in a cohort of elderly people in a north European community", *International Journal of Epidemiologic* 1997
- Palli D., "Epidemiology of gastric cancer: an evaluation of available evidence", *Journal of Gastroenterology*, 35(Suppl. 12):S84--S89, 2000
- Pan D.A., et al., "Skeletal muscle membrane lipid composition is related to adiposity and insulin action", *Journal of Clinical Investigation*, 1995, 96:2802--2808
- Pan X.R., Li G.W., Hu Y.H., Wang J.X., Yang W.Y., An Z.X., Hu Z.X., Lin J., Xiao J.Z., Cao H.B., Liu P.A., Jiang X.G., Jiang Y.Y., Wang J.P., Zheng H., Zhang H., Bennett P.H., Howard B.V., "Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance", *The Da Qing IGT and Diabetes Study*, *Diabetes Care* 1997;20:537-44
- Panagiotakos D., Pitsavos C., Arvanitaki F., "Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore", *Preventive Medicine*, Volume 44, Issue 4, April 2007
- Parker D.R., et al., "Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: the Normative Aging Study", *American Journal of Clinical Nutrition*, 1993, 58:129-136
- Pereira M.A., O'Reilly E., Augustsson K., et al., "Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies", *Arch. Intern. Med.* 164: 370, 2004
- Pérez-Jiménez F., López-Miranda J., Pinillos M.D., et al., "A Mediterranean and a highcarbohydrate diet improve glucose metabolism in healthy young persons", *Diabetologia* 44: 2038, 2001
- Perrotti N., Santoro D., Genovese S., Giacco A., Rivellese A., Riccardi G., "Effect of digestible carbohydrates on glucose control in insulin dependent patients with diabetes", *Diabetes Care* 7: 354, 1984
- Pietinen P., "Changes in diet in Finland from 1972 to 1992: impact on coronary heart disease risk", *Preventive Medicine*, 25:243-250, 1996
- Pittler M.H., Stevinson C., Ernst E., "Chromium picolinate for reducing body weight: meta-analysis of randomized trials", *Int J Obes Relat Metab Disord* 27:522- 529, 2003
- Poppitt S.D., Keogh G.F., Prentice A.M., et al., "Long term effects of ad libitum low-fat highcarbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome", *Am. J. Clin. Nutr.* 75: 11, 2002
- Potter J.D., Steinmetz K., "Vegetables, fruit and phytoestrogens as preventive agents", *International Agency for Research on Cancer*, 61-90 (IARC Scientific Publications, No. 139), 1996
- Pownall H.J., Ballantyne C.M., Kimball K.T., Simpson S.L., Yeshurum D., Grotto A.M., "Effect of moderate alcohol consumption on hypertriglyceridemia", *Arch. Intern. Med.* 159: 981, 1999
- Raben A., Vasilaras T.H., Moller A.C., Astrup A., "Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects", *Am J Clin Nutr* 76:721-729, 2002
- Radimer K.L., Ballard-Barbash R., Miller J.S., "Weight change and the risk of late-onset breast cancer in the original Framingham cohort", *Nutr Cancer*, 49:7-13, 2004
- Ramachandran A., Snehalatha C., Mary S., Mukesh B., Bhaskar A.D., Vijay V., "The Indian Diabetes Prevention shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian with Impaired Glucose Tolerance (IDPP-1)", *Diabetologia* 2006; 49:289-97
- Rasmussen O.W., Thomsen C., Hansen K.W., Versterlund M., Winther E., Hermansen K., "Effects on blood pressure, glucose, and lipid levels of a high-monounsaturated fat diet compared with a high-carbohydrate diet in NIDDM subjects", *Diabetes Care* 16: 1565, 1993
- Reddy K.S., "Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. *Public Health Nutrition*", 2002
- Riccardi G., Clemente G., Giacco R., "Glycemic index of local foods and diets: the Mediterranean experience", *Nutr. Rev.* 61: S56, 2003
- Riccardi G., Rivellese A., Pacioni D., Genovese S., Mastranzo P., Mancini

- M., "Separate influence of dietary carbohydrate and fibre on the metabolic control in diabetes", *Diabetologia* 26: 116, 1984
- Rimm E.B., Ascherio A., Giovannucci E., Spiegelman D., Stampfer M.J., Willet W.C., "Vegetable, fruit and cereal fiber intake and risk of coronary heart disease among men", *J.A.M.A.* 275: 447, 1996
- Rimm E.B., et al., "Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women", *Journal of the American Medical Association*, 279:359-364, 1998
- Rimm E.B., "Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors", *British Medical Journal*, 319:1523-1528, 1999
- Rimm E.B., "Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men", *Journal of the American Medical Association*, 275:447-451, 1996
- Rodrigues-Villar C., Manzaneres J.M., Casals E., et al., "High monounsaturated fat, olive oil-rich diet has effects similar to a high-carbohydrate diet on fasting and postprandial state and metabolic profiles of patients with type 2 diabetes", *Metabolism* 49: 1511, 2000
- Rodriguez C., McCullough M.L., Mondul A.M., "Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort", *Cancer Epidemiol Biomarkers Prev*, 15:211-216, 2006
- Romano G., Tilly-Kiesi M.K., Patti L., et al., "Effects of dietary cholesterol on plasma lipoproteins and their subclasses in IDDM patients", *Diabetologia* 41: 193, 1998
- Ryan D.H., Espeland M.A., Foster G.D., Haffner S.M., Hubbard V.S., Johnson K.C., Kahn S.E., Knowler W.C., Yanovski S.Z., "Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes", *Control Clin Trials* 24:610-628, 2003
- Ryan G.J., Wanko N.S., Redman A.R., Cook C.B., "Chromium as adjunctive treatment for type 2 diabetes. *Ann Pharmacother* 37:876-885, 2003
- Sacco R., Elkind M., Boden-Albala B., et al., "The protective role of moderate alcohol consumption on ischemic stroke", *J.A.M.A.* 281: 51, 1999
- Sacks F.M., "Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet", *New England Journal of Medicine*, 344:3-10, 2001
- Salmeron J., et al., "Dietary fat intake and risk of type 2 diabetes in women", *American Journal of Clinical Nutrition*, 2001, 73:1019-1026
- Salmeron J., et al., "Dietary fiber, glycemic load and risk of NIDDM in men. *Diabetes Care*", 1997, 20:545-550
- Sargeant L.A., Khaw K.T., Bingham S., et al., "Fruit and vegetable intake and population glycosylated haemoglobin levels: the EPIC-Norfolk Study", *Eur. J. Clin. Invest.* 55: 342, 2001
- Schatzkin A., "Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas", *Polyp Prevention Trial Study Group. New England Journal of Medicine*, 342:1149-1155, 2000
- Schulze M.B., Liu S., Rimm E.B., Manson J.E., Willett W.C., Hu F.B., "Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women", *Am J Clin Nutr* 80:348-356, 2004
- Schuurman A.G., "Animal products, calcium and protein and prostate cancer risk in The Netherlands Cohort Study. *British Journal of Cancer*", 80:1107-1113, 1999
- Scottish Intercollegiate Guidelines Network Guidelines No. 69, "Obesity in children and young people", SIGN, 2003
- Sharp L., "Risk factors for squamous cell carcinoma of the oesophagus in women: a case-control study", *British Journal of Cancer*, 85:1667-1670, 2001
- Sheard N.F., Clark N.G., Brand-Miller J.C., Franz M.J., Pi-Sunyer F.X., Mayer-Davis E., Kulkarni K., Geil P., "Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement of the American Diabetes Association", *Diabetes Care* 27:2266-2271, 2004
- Sierksma A., Patel H., Ouchi N., et al., "Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity", *Diabetes Care* 27: 184-189, 2004
- Simpson H.C.R., Carter R.D., Lousley S., Mann J.L., "Digestible carbohydrate - an independent effect on diabetic control in type II (non-insulin dependent) diabetic patients?", *Diabetologia* 23: 235, 1982
- Simpson H.C.R., Simpson R.W., Lousley S., et al., "A high carbohydrate leguminous fibre diet improves all aspect of diabetic control", *Lancet* 1: 1, 1981
- SIPREC - Società Italiana per la Prevenzione cardiovascolare, "Documento di iniziativa per promuovere le strategie e gli interventi di prevenzione cardiovascolare in Italia", 2008
- Sjogren A., Floren C.H., Nilsson A., "Magnesium deficiency in IDDM related to level of glycosylated haemoglobin", *Diabetes* 35: 459, 1986
- Smith-Warner S.A., "Alcohol and breast cancer in women: a pooled analysis of cohort studies", *Journal of the American Medical Association*, 279:535-540, 1998
- Sofi F., Cesari F., Abbate R., Gensini G., Casini A., "Adherence to Mediterranean diet and health", *Adherence to Mediterranean diet and health*, *BMJ*, July, 2008
- Stephenson G.D., Rose D.P., "Breast cancer and obesity: an update", *Nutr Cancer*, 45:1-16, 2003
- Stern L., Iqbal N., Seshadri P., Chicano K.L., Daily D.A., McGrory J., Williams M., Gracely E.J., Samaha F.F., "The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial", *Ann Intern Med* 140:778-785, 2004
- Stevens J., Ahn K., Juhaeri, Houston D., Steffan L., Couper D., "Dietary fiber intake and glycemic index and incidence of diabetes in African-American and white adults: the ARIC study", *Diabetes Care* 25: 1715-1721, 2002
- St-Onge M.P., Janssen I., Heymsfield S.B., "Metabolic syndrome in normal-weight Americans", *Diabetes Care* 27: 2222, 2004
- Storm H., Thomsen C., Pedersen E., Rasmussen O., Christiansen C., Hermansen K., "Comparison of a carbohydrate-rich diet and diets rich in stearic or palmitic acid in NIDDM patients", *Diabetes Care* 20: 1807, 1997
- Summers L.K.M., Fielding B.A., Bradshaw H.A., et al., "Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity", *Diabetologia* 45: 369, 2002.
- Sundaram K., Hornstra G., Houwelingen A.C., Kester A.D., "Replacement of dietary fat with palm oil: effect on human serum lipids, lipoproteins and apolipoproteins", *Br. J. Nutr.*, 68:677-692, 1992
- Sundram K., Anisah I., Hayes K.C., Jeyamalar R., Pathmanathan R., "Trans (elaidic) fatty acids adversely impact lipoprotein profiles relative to specific saturated fatty acids in humans", *J. Nutr.*, 127:514S-520S, 1997
- The American Heart Association Statistics Committee and Stroke Statistics Subcommittee, "Heart Disease and Stroke Statistics - 2009 Update", *Circulation*, 2008
- The European Food Information Council, database
- The European House-Ambrosetti, "Meridiano Sanità - Le coordinate della salute. Rapporto Finale", novembre 2008
- The Japan Dietetic Association, "National Nutrition Survey", 2001
- Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease. *Journal of Nutrition*, 130(Suppl.):653-711, 2000
- Thomsen C., Rasmussen O., Lousen T., et al., "Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects", *Am. J. Clin. Nutr.* 69: 1135, 1999
- Thomsen C., Rasmussen O.W., Hansen K.W., Vesterlund M., Hermansen K., "Comparison of the effects on the diurnal blood pressure, glucose, and lipid levels of a diet rich in monounsaturated fatty acids with a diet rich in polyunsaturated fatty acids in type 2 diabetic subjects", *Diabet. Med.* 12: 600, 1995
- Tian H.G., et al., "Changes in sodium intake and blood pressure in a community based intervention project in China", *Journal of Human Hypertension*, 9:959-968, 1995
- Toeller M., Buyken A.E., Heitkamp G., Cathelineau G., Ferriss J.B., Michel G., EURODIAB IDDM Complications Study Group, "Nutrient intakes as predictors of body weight in European people with type 1 diabetes", *Int. J. Obes.* 25: 1815, 2001
- Toshima H., Koga Y., Blackburn H., "Lessons for Science from the Seven Countries Study", 1995. Springer Verlag, Tokyo
- Tosiello L., "Hypomagnesemia and diabetes mellitus: a review of clinical implications", *Arch. Intern. Med.* 156: 1143, 1996
- Trentham-Dietz A., Newcomb P.A., Egan K.M., "Weight change and risk of postmenopausal breast cancer (United States)", *Cancer Causes Control* 11:533-542, 2000
- Trichopoulos A., Kouris-Blazos A., Wahlqvist M.L., "Diet and overall survival in the elderly", *BMJ* 1995
- Trichopoulos A., Orfanos P., Norat T., Bueno-de-Mesquita B., Ocke M.C., Peeters P.H., van der Schouw Y.T., Boeing H., Hoffmann K., Boffetta P., Nagel G., Masala G., Krogh V., Panico S., Tumino R., Vineis P., Bamia C., Naska A., Benetou V., Ferrari P., Slimani N., Pera G., Martinez-

- Garcia C., Navarro C., Rodriguez-Barranco M., Dorronsoro M., Spencer E.A., Key T.J., Bingham S., Khaw K.T., Kesse E., Clavel-Chapelon F., Boutron-Ruault M.C., Berglund G., Wirfalt E., Hallmans G., Johansson I., Tjonneland A., Olsen A., Overvad K., Hundborg H.H., Riboli E., Trichopoulos D., "Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study", *BMJ* 330:991, 2005
- Trichopoulou A., Costacou T., Bamia C., Trichopoulos D., "Adherence to a Mediterranean Diet and Survival in a Greek Population", *The New England Journal of Medicine*, Volume 348, N° 26, 2003
- Trust for America's Health and Robert Wood Johnson Foundation: "F as in Fat: how obesity policies are failing in America", July 2009
- Truswell A.S., "Cereal grains and coronary heart disease", *European Journal of Clinical Nutrition*, 56:1-14, 2002
- Tuomilehto J., et al. "Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance", *New England Journal of Medicine*, 2002, 344:1343-1350
- Tuomilehto J., "Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study", *Lancet*, 357:848-851, 2001
- Tuomilehto J., Lindstrom J., Eriksson J.G., Valle T.T., Hamalainen H., Ilanne-Parikka P., Keinanen-Kiukaanniemi S., Laakso M., Louheranta A., Rastas M., Salminen V., Uusitupa M., "Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance", *N Engl J Med* 344:1343-1350, 2001
- Tverdal A., "Coffee consumption and death from coronary heart disease in middle-aged Norwegian men and women", *British Medical Journal*, 300:566-569, 1990
- Ueland P.M., et al., "The controversy over homocysteine and cardiovascular risk", *American Journal of Clinical Nutrition*, 72:324-332, 2000
- Università Cattolica del Sacro Cuore, "Rapporto Osservasalute 2008. Stato di salute e qualità dell'assistenza nelle regioni italiane", 2008
- Uusitupa M., et al., "Effects of two high-fat diets with different fatty acid compositions on glucose and lipid metabolism in healthy young women", *American Journal of Clinical Nutrition*, 1994, 59:1310-1316
- Vainio H., Bianchini F., "Weight Control and Physical Activity", vol. 6. Lyon, France: International Agency for Research Cancer Press, 2002
- Van Gaal L., Rillaerts E., Creten W., De Leeuw I., "Relationship of body fat distribution pattern to atherogenic risk factors in NIDDM", *Diabetes Care* 11: 103, 1988
- Vessby B., et al., "Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia", *European Journal of Clinical Investigation*, 1980, 10:193-202
- Vessby B., et al., "The risk to develop NIDDM is related to the fatty acid composition of the serum cholesterol esters", *Diabetes*, 1994, 43:1353-1357
- Vessby B., Tengblad S., Lithell H., "Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70-year-old men", *Diabetologia*, 1994, 37:1044-1050
- Vessby B., Uusitupa M., Hermansen K., Riccardi G., Rivellese A.A., Tapsell L.C., Nansen C., Berglund L., Louheranta A., Rasmussen B.M., Calvert G.D., Maffetone A., Pedersen E., Gustafsson I.B., Storlien L.H., "Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: the KANWU study", *Diabetologia* 44: 312-319, 2001
- Vessby B., Gustafsson I-B., Boberg J., Karlström B., Lithell H., Werner I., "Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia", *Eur. J. Clin. Invest.* 10: 193, 1980
- Wald D.S., Law M., Morris J.K., "Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis", *British Medical Journal*, 325:1202-1208, 2002
- Wang C., Harris W.S., Chung M., Lichtenstein A.H., Balk E.M., Kupelnick B., Jordan HS., "n-3 fatty acids from fish or fish-oil supplements, but not {alpha}-linolenic acid, benefit cardiovascular outcomes in primary- and secondary-prevention studies: a systematic review", *Am J Clin Nutr* 84:5-17, 2006
- Water Footprint Network, database
- Weggemans R.M., Zock P.L., Katan M.B., "Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: a meta-analysis", *Am. J. Clin. Nutr.* 73: 885, 2001
- West S.G., Hecker K.D., Mustad V.A., Nicholson S., Schoemer S.L., Wagner P., Hinderliter A.L., Ulbrecht J., Ruy P., Kris-Etherton P.M., "Acute effects of monounsaturated fatty acids with and without omega-3 fatty acids on vascular reactivity in individuals with type 2 diabetes", *Diabetologia* 48:113-122, 2005
- Whelton P.K., "Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials", *Journal of the American Medical Association*, 277:1624-1632, 1997
- WHO Technical Report Series 916, "Diet, nutrition and the prevention of chronic diseases. Report of a Joint FAO/WHO Expert Consultation", World Health Organisation, Geneva, 2003
- Willett M.C., "Diet, nutrition, and avoidable cancer", *Environmental Health Perspectives*, 103(Suppl. 8):S165-S170, 1995
- Willett W.C., Manson J., Liu S., "Glycemic index, glycemic load, and risk of type 2 diabetes", *Am. J. Clin. Nutr.* 76: 274S, 2002
- Willett W.C., "Intake of trans fatty acids and risk of coronary heart disease among women", *Lancet*, 341:581-585, 1993
- Willett W.C., Sacks F., Trichopoulou A., "Mediterranean diet pyramid: a cultural model for healthy eating", *American Journal of Clinical Nutrition*, 1995
- Willett W.C., "Diet and coronary heart disease", Oxford University Press, 1998
- Willett, W.C., Stampfer M.J., Manson J.E., Colditz G.A., Speizer F.E., Rosner B.A., Sampson L.A., Hennekens C.H., "Intake of trans fatty acids and risk of coronary heart disease among women", *Lancet*, 341:581-585, 1993
- Wolever T., Jenkins D., Vuksan V., et al., "Beneficial effect of a low glycaemic index diet in type 2 diabetes", *Diabet. Med.* 9: 451, 1992
- Wood R., Kubena K., O'Brien B., Tseng S., Martin G., "Effect of butter, mono- and polyunsaturated fatty acid-enriched butter, trans fatty acid margarine and zero trans fatty acid margarine on serum lipids and lipoproteins in healthy men", *J. Lipid Res.*, 34:1-11, 1993
- World Bank Organization, Fact Sheet No. 297, February 2009
- World Cancer Research Fund, "Food, nutrition and the prevention of cancer: a global perspective", Washington, D.C., American Institute for Cancer Prevention, 1997
- World Health Organization 2008, "2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases"
- World Health Organization, "Cardiovascular diseases", Fact sheet n° 317, February 2007
- World Health Organization, "Diet and physical activity: a public health priority"
- World Health Organization, "Diet Nutrition and the Prevention of Chronic Disease", Ginevra 2003
- World Health Organization, "Do lifestyle changes improve health?", January 2009
- World Health Organization, "Healthy Living", 1999
- World Health Organization, "Noncommunicable diseases now biggest killers", maggio 2008
- World Health Organization, "North Karelia Project"
- World Health Organization, "Obesity and overweight"
- World Health Organization, "The Tobacco Atlas", 2002
- World Health Organization, "The World Health Report 2002 - Reducing risks, Promoting Healthy Life"
- World Health Organization, "World Cancer Report", Edited by Stewart B.W., Kleihues P., IARC Press, Lyon, 2003
- World Health Organization, "World Health Statistics 2008"
- Wu H., Dwyer K.M., Fan Z., Shircore A., Fan J., Dwyer J.H., "Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study", *Am. J. Clin. Nutr.* 78: 1085, 2003
- Wylie-Rosett J., Segal-Isaacson C.J., Segal-Isaacson A., "Carbohydrates and increases in obesity: does the type of carbohydrate make a difference?", *Obes Res* 12 (Suppl. 2):124S-129S, 2004
- Xu J., Eilat-Adar S., Loria C., Goldbourt U., Howard B.V., Fabsitz R.R., Zephier E.M., Mattil C., Lee E.T., "Dietary fat intake and risk of coronary heart disease: the Strong Heart Study", *The American Journal of Clinical Nutrition*, 84(4):894-902, 2006
- Yu M.C., "Nasopharyngeal carcinoma: epidemiology and dietary factors", *International Agency for Research on Cancer*, 39--47 (IARC Scientific Publications, No. 105), 1991
- Yusuf S., et al., "Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators", *New England Journal of Medicine*, 342:154-160, 2000
- Zhang J., "Fish consumption and mortality from all causes, ischemic heart disease, and stroke: an ecological study", *Preventive Medicine*, 28:520-529, 1999



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