

EGEA

THIRD EDITION

Rome – Italy – May 18th - 21st , 2005

International Conference on Health Benefits of Mediterranean Diet

From scientific evidence to health prevention actions

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Preface

This is the third edition of EGEA, the International Conference on the Health Benefits of a Mediterranean Style Diet. Progressively, this Conference is taking an important place at the crossroads of scientific evidence and health prevention actions. The aim is to establish a consensus on an effective strategy to prevent and control chronic diseases such as obesity, diabetes, cardiovascular diseases and cancer, which are becoming, according to the World Health Organization, leading causes of morbidity and mortality around the world. Like infectious diseases, these chronic diseases could be, and should be, prevented and controlled on a mass scale by the preservation or creation of healthy environments, including healthy food systems. Such prevention, however, faces difficulties stemming from the diversity and economic consequences of the environmental factors involved, including the changing nature and quality of food supplies, food advertising, marketing, promotion and food pricing. With the increasing number of meals taken away from home, time limitations of consumers, the food industry has responded by increasing the number of convenience foods and the availability of prepared meals, together with an increase in portion sizes and per capita availability of fat and added sugar. EGEA constitutes a unique and valuable opportunity for the convergence of multidisciplinary approaches, from basic science, health, agriculture, communication, to global prevention policies. Two round tables are being organized to share experiences on various strategies available and to define guidelines for health nutrition policies which could be implemented at the general population level. With the participation of the best world specialists on these issues, the support of the French and Italian Ministries of Health and IARC-WHO, this conference is fully in line with the global strategy of the World Health Organization concerning nutrition, physical activity and health. It is my sound conviction that this conference will again be a success story!

Pr. Ambroise MARTIN

Professor of Nutrition, University of Lyon,
member of the steering committee of the French national nutrition health policy (PNNS)

— *An official opening talk was held prior to the scientific lectures on Wednesday, May 18th , 2005, featuring Mr Laurent Damiens, Director of Aprifel and Dr Saida Barnat, Head of the Scientific Department of Aprifel, who welcomed their distinguished guests.*

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Romano MARABELLI

Director General, Directorate General for Veterinary Health and Food, Ministry of Health, Rome, Italy

It is an honor for us to host this conference, as well as an honor for the Italian Health Ministry to take an active part in the event, as part of its great interest for key aspects of the obesity issue such as lifestyle, diet and food security.

Let me introduce the matter that will later be discussed by my colleague Pr. Greco: I would like to remind you of the goals that were set in 2004 by the World Health Organization towards the implementation of a global strategy for healthy diets and lifestyles worldwide, as the WHO acknowledged the social and economic role and possible benefits of traditional diets and lifestyles.

During the 2004 Assembly of the WHO, some of the most urgent issues were raised before Member States such as: the need for national goals to be set, and for an implementation schedule to be determined, as well as national guidelines for diet and physical activity and specific indicators for the monitoring and evaluation of actions undertaken. And most of all need to find appropriate measures in order to maintain and promote traditional food and lifestyles.

I would also like to underline, as a food security expert, that, when talking about traditional food, we refer exclusively to the foods that live up to our modern security standards. It would definitely be dangerous to imagine less safe processes for these products.

The issue of overweight and obesity is a growing problem in Europe, and has increased by 25% between 1994 and 1999 in Italy, according to available data for the year 1999. The most important consequences of the phenomenon in terms of non-contagious diseases include cardiovascular diseases, type II diabetes, some cancers, osteoporosis and dental caries. All of these are linked with unhealthy diets. Eating disorders in women aged 12-25 include anorexia (0.3% to 0.5%) bulimia (1 to 3%) and others (6%).

Italy has tackled this issue through national health plans, specifically the 2003-2005 plan that aims at a better lifestyle, and more prevention and communication around health issues (point 9). Awareness campaigns were also led in schools through actions targeting children and through physicians. National awareness campaigns have also been launched in the country.

In 2002, in coordination with the Ministry of Education, we focused on prevention of children's eating disorders. In 2003, the goal was to encourage people to maintain a healthy diet. Awareness campaigns were conducted through television and other media in order to promote lower caloric intake, higher physical activity and healthy diets such as the Mediterranean diet.

The 2004 campaign specified what healthy diet and physical activity really mean thanks to a press campaign which promoted healthy lifestyles. This year, in 2005, we have started a campaign that offers a 5-points programme for a healthy lifestyle: more fruit, vegetables and water, less fat, a greater diversity, a less sedentary lifestyle and smaller servings.



This is the work that has been achieved to date by the Italian Health Ministry and the Italian government through its various services and ministries. It certainly is an ambitious project, as it aims at very sensitive targets such as the youth and demands therefore strong, positive and significant commitment.

In this context, this Roman Conference is a great opportunity for us to evaluate together during the next three days the possible common strategies to be implemented in Italy and the rest of Europe.

Thank you.

Ferdinando ROMANO

President of the National Institute for Research on Food and Nutrition (INRAN), Italy

Thank you for this invitation. It is an honour to be here at this meeting in Rome.

I would like to begin with something that I believe is extremely important regarding the issue we are discussing today. This is a mission statement from the incredible recognition and information of chronic diseases conducted for the FAO in 2003. It says that the cost to the world of the current and projected epidemic of chronic disease related to diet and physical inactivity dwarfs all other health costs. Let us take into account that the situation regarding diet is a major emergency today. To give a rough estimate of the cost of obesity in the United States, I am told that obesity costs about 1.7% of the gross national product in the United States. The estimate is much lower in Italy because we have a much lower rate of obesity: it is about 0.24% of the gross national product. We are talking only about the health costs of obesity.

Everybody knows how important nutrition is in the development of these types of diseases: we have 41% of the main diseases with nutrition as a major determinant, and another 38% for whom nutrition plays a role. Consensual literature data reported that dietary factors account for 30% of cancers in industrialised countries.

The concept of Mediterranean dietetic style became famous after 1986 Time Magazine appearance and since that time it has been deeply investigated. This slide is another example of pyramid graphical representation showing the comparison between Mediterranean diet and northern Europe and the United States dietetic style. The latter is practically reverse than the former, according to this comparison.

Numerous and solid scientific evidence demonstrating that the major nutrients that characterise the Mediterranean diet have a beneficial effect on health exist. For example, convincing evidences exist on health benefits of fish and fish oils. A good overview of the scientific evidence of the protective effects of fruit and vegetable is provided by WHO. Actually these data should be updated but the results are still valid.

THE 9 POINTS OF MEDITERRANEAN STYLE

- high olive oil consumption
- high consumption of legumes
- high consumption of cereals, mostly whole grain
- high consumption of fruits
- high consumption of vegetables
- MODERATE wine/alcohol consumption
- moderate consumption of dairy products
- moderate to high consumption of fish, poultry
- low consumption of meat and meat products



There are some clear evidences of the beneficial effect of the Mediterranean diet. This is the recently published Epic study, and some scientists participating in the study are attending this

meeting This study explored the effect of the Mediterranean diet on survival among older people demonstrating how the Mediterranean diet as a whole was associated with a lower death rate.

I would like to mention other few papers. This last year paper considers the Mediterranean diet together with healthy lifestyle habits – moderate alcohol use, no smoking, and physical activity. All these factors lowered the mortality rate for all causes of about 50%.

Another effect of the Mediterranean diet is on circulating homocysteine concentration. The Mediterranean diet is able to lower the homocysteine concentration in blood in heterozygous and homozygous genotypes that having high homocysteine level.

In this other study published in 1998, a randomised clinical trial showed that the Mediterranean diet has been able to prolong survival and protect against cancer.

At this point, we have a lot of evidence on the health benefits of Mediterranean diet. The major question arising now is what is going on today? Professor Marabelli has told us that obesity is a major problem, in our country too. For example, recent data showed that 9% of Italians are obese and more than 50% of older Italians are overweight. Obesity is more and more a paediatric problem regarding one third of Italian children (36%) that resulted overweight with 11% of them clearly obese.

The Mediterranean areas are still Mediterranean, so what is happening? Are we still following a Mediterranean diet?

This is an Italian study assessing the so-called Mediterranean score. The Mediterranean score is a score between 0 and 8. When the score is between 4 and 8, the diet is Mediterranean. With a score between 0 and 3, there is no Mediterranean-style diet. The figures show that the score has gradually been decreasing since 1961. Presently, the score is 3 meaning that we are no longer following a Mediterranean diet in Italy.

There has been a lot of educational campaigning and a lot of efforts to reposition the Mediterranean diet as the central diet for our nutritional lifestyle. It might be that all the efforts made up to now have not been as effective as we would have expected.

The current situation regarding the Mediterranean diet should induce us to think hard about what should be done in terms of an effective educational campaign. We still have some insights on the WHO/FAO report. First of all, the public health action to prevent the adverse consequences of inappropriate dietary patterns and physical inactivity is now urgently needed.

The second point is applied research. This is an important issue because the most challenging task now is to match the demand from the general population and the results of the research. The applied research should provide convincing evidence and useful tools to guide effective interventions.

The third point is how to induce changes in nutritional habits, how to move back to a Mediterranean dietetic style. Changes can only be initiated through effective communication. What does effective communication mean? This is a crucial point because

we, as scientists, must address and reach the general population. Effective communication means bridging the gap between technical experts, policymakers and the general public. At the moment with our educational campaigns, we are producing a strong awareness among the general public on the problems of how to have a healthy lifestyle in terms of nutrition. What, in our opinion, is still lacking is an adequate production of tools for the general public to put into practice the correct information. For example, we know the benefits of antioxidants, but in which way consumers could monitor their antioxidant intake? What means more fruit and vegetables? Compared to what? We should think about how the general public can put all this information into practice in their daily lives. This is a crucial point leading us able to transform our educational campaign in intervention strategies with production of practical tools to put the information into practice in daily lives.

The fourth point is related to the fact that as scientists, we are generally used to communicate in terms of science and our information is often given to people from a scientific point of view, which could be not easily understandable. The point is to give simple and clear messages.

The last point has been covered before, and is related to the level of involvement of different stakeholders. Governments need to work together with the private sector, official health bodies, consumer groups, academics, the religious community and other non-governmental bodies in order to obtain the best results. It is necessary as a moral imperative, that concerted actions will be structured between all the stakeholders to be effective in modifying the current lifestyle in terms of nutrition and to go back to a real Mediterranean diet.

Thank you.

Donato GRECO

Director General of Health Prevention, Ministry of Health, Rome, Italy

I come from Naples, the capital of the Italian Mediterranean diet. I would like to take this opportunity to remind you that within the original campaign origin, one of the most relevant studies ever made on the health effects of the Mediterranean diet was launched, and many scientists from the US and Italy helped in the study.

As I think we are going to be overwhelmed with the 'dietary story' over the next few days, I thought I would use the next five minutes to tell you some other news about what Italy is trying to do.

After 29 years in science, I moved to implementation because I felt strongly about this enormous gap between what we know should be done and what is done.

We have seen that there is a gap in this country, in your country, as everywhere. We have known for a long time that we should eat more fruit, that we should not smoke, and that we should walk for an hour a day, but in fact there is little evidence that the population is moving, rather a lot of evidence that the population is going the other way. So we have to do something about this impact gap. Of course, I do not have a solution – otherwise I would not be here.

We are trying to create a new programme with a new institution to try to get science messages through to the population. This is why our parliament approved through a new law last year the Italian CCM, Il Centro nazionale per la prevenzione e il Controllo delle Malattie [The national centre for prevention and control of diseases]. It is a network between the regions and the many institutions to build our capacity to work together in a network. Our mission is to help attain assessment, surveillance and response in coordination with the regions. Each of the 21 independent health authorities of the country are becoming more and more independent. They have their own ministers, parliament and funds (funds are not managed in Rome anymore, but remain where they are collected.)

So we have training to do, presentation, networking, and information feedback. It is a very heavy mission. To start with, we have been given 6 tasks: infectious diseases, health promotion, environment and climate, vaccines and vaccination, road and domestic accidents, and bio-terrorism. This covers the country's major health problems.

We have a small additional budget on top of our main budget which allows us and the network to function. This fund is granted every year and is protected against any cuts by the government or treasury minister.

We have a national plan for active prevention, the word 'active' being a message we would like each citizen to hear; we want to reach them in their homes.

Of course, when we speak about these diseases, we are speaking about the major causes of disease: 250,000 deaths caused by cardiovascular disease and more than 1 million sick people every year at any given moment. Diabetes is now our great challenge: according to our treasury calculations, our entire health budget in the next ten years will be barely sufficient to pay for diabetes only – let alone the rest!

The National Plan of Active Prevention (NPAP) :

- Cardiovascular Risk
- Diabetes
- Obesity
- Cancer Screenings
- Vaccinations
- Accidents



Our actions must include cancer screening. I have just come from the World Health Assembly in Geneva in which cancer control was one of the items discussed, and again, diet is crucial, as one third of cancers are associated with diet.

What are our main points? Smoking: I am proud and pleased to say that we are now one of the leading countries in the world for combating smoking because we have approved a quite stringent and effective law that forbids smoking in all public places. Believe it or not, despite our 'illegal' attitude – we do not usually like to respect red lights – the Italian population is accepting this law very happily. We have figures showing a minor drop in consumption of cigarette sales of about 10% a month, and out of the many tens of thousands of police inspections of restaurants and bars, less than 3% were fined for irregularities. The population is happy about the restriction of smoking in public places. However, we are not forbidding smoking: this is not a law against smokers; it is a law against passive smoking to protect the non-smokers. Things are going very well.

Health Promotions and Life Styles

- SMOKING
- PHISICAL ACTIVITY
- NUTRITION
- ALCOHOL



Physical activity: over the next few days you will hear in different presentations how people are not inclined to move and walk.

Nutrition, of course, is a major issue, as has already been mentioned by other colleagues.

As in many other European countries, alcohol is our problem, but I am pleased to say that our total alcohol consumption over the last ten years has decreased by more than 20%. We are drinking better and drinking less, and we are not much fond of spirits. Although alcohol consumption is going down, Italy, like most countries, do have a huge problem with alcohol and smoking among the young – youngsters love beer and there are many new pubs springing up, even in Rome.

There is good news, however. In general, all programmes are applied to Rome and nothing happens in other regions. However a few months ago the 21 regions signed a pact with the State to engage in this national active prevention plan for three years from 2005 to 2007. (The plan is the one I showed you earlier). What is also important is that 1,320 million euros have been set aside for these five items, including nutrition and physical activity. Historically, this has never happened. This is part of Italy's 90-billion-euros health budget, not an

enormous amount, but significant enough so that there is no longer any justification for the 250 local authorities or the 21 regions not to act in accordance with the national guidelines which aggressively address the risk-factors we will be speaking of over the next few days. For once, the money is directed at the target – which sounds very simple, but that never happens in this country! The regions have to start implementing this action next month – otherwise they do not receive the funds.

Finally, there is a mechanism to assist regions as well as a verification mechanism whereby each region has to be periodically certified on the active prevention plan within its own territory to get its quota of money. I am quite hopeful and believe that this mechanism will make it difficult to deny or divert the money to pay for other things.

This is a heavy task and I strongly hope that over the next few days of this meeting, we will go in the direction that Italy is ultimately trying to take to fill the gap between science and the benefits to the citizen. Thank you.

Elio RIBOLI

Head of the Nutrition and Hormones Group, International Agency for Research on Cancer (IARC-WHO), Lyon, France

Thank you. It is a great pleasure being with you for the third edition of EGEA. I would like to give special thanks to my Italian colleagues for their excellent collaboration and support for the organisation of this conference in Rome.

Professor Greco raised a very important point in his talk: we need to find points of contact between what is known and the application of what is known. The carcinogenesis of tobacco was clearly demonstrated by 1955 and it has taken half a century to implement laws to limit the use of tobacco. When I say 'limit the use', I mean to forbid the use of tobacco. So if what we know about nutrition is not immediately translated into public health, we should look at the history of tobacco and understand that it takes time to change people's minds and to stand against economic interests.

Coming from cancer research, why are we interested in nutrition? When I started working on cancer research in the late '70s in Milan at the National Cancer Institute, the idea was that cancer was basically due to chemicals in the environment. The main task of cancer researchers was to identify chemical and physical carcinogens. However, epidemiologic studies came in and started bringing evidence that chemical carcinogens did not explain the huge differences that we see around the world in the incidences of some cancers. These differences are clearly not due to chemical carcinogens in human beings. For example, colorectal cancer is much more frequent in North America, Europe and Australia than, for example, in Africa or Southeast Asia, and there is no evidence whatsoever that colorectal cancer is due to chemical carcinogens in human beings.

On the other hand, incidence rates of stomach cancer have the opposite image of colorectal cancer. The incidence of stomach cancer is very low in North America – where it is actually the lowest in the world, and in North-African countries, (two regions that have very little in common) – and it is also very low in Australia. This is exactly where colorectal cancer is most frequent.

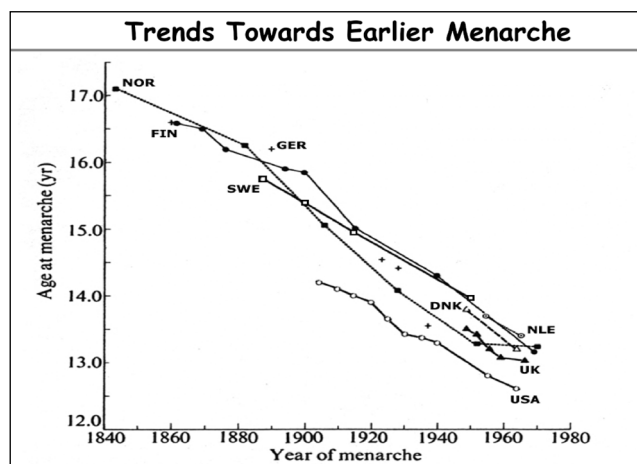
Cancer is not a single disease, and this has to be considered to articulate our efforts for prevention. Cancer is a very large family of different diseases with completely different causes, and therefore should be addressed with different prevention strategies. For example, let us take as example the two most common cancers in women around the world. Breast cancer is very common in North America in more or less the same regions where colorectal cancer is very common. However, the incidence of cervical cancer, or cancer of the uterine cervix, is just the opposite: the incidence is very low in North America, Australia and China, but very high in some regions like Central America, the east coast of Africa and India.

In addition there are major changes in risk occurring around the world, both in the positive and in the negative direction. Let us take India and Western Europe as example. There are now very good population-based cancer registries some regions of India, which provide very good measure of the incidence of cancer in that population.

The incidence rate of colon cancer in Western Europe is 44 new cases per 100,000 people per year. There is 1 case per 100,000 people per year in this region of India. Rates of breast cancer are 78 and 14 per 100,000 women per year respectively – that means 780 new cases per 1 million women, as compared to 140. The incidence of cervical cancer is much higher in India – 67 cases

in India versus 10 cases per 100 000 women in Western Europe. However, the year 2000 was the first year with more breast cancer than cervical cancer cases in Bombay. So the more the economic situation evolves and the hygienic condition improves, the more cervical cancer (which is a sexually transmitted cancer – 100% are due to the papilloma virus) goes down, but the incidence of the cancers that are typical of the western life style (breast cancer, colon cancer) increases. Differences in incidence rates clearly indicate that lifestyle and environment are extremely important in determining the risk of cancer, and I draw your attention to colon cancer. Basically, that means that with an Indian diet and the Indian physical expenditure characteristics, colon cancer is almost non-existent. That gives some clues for the identification of the causes of colon cancer.

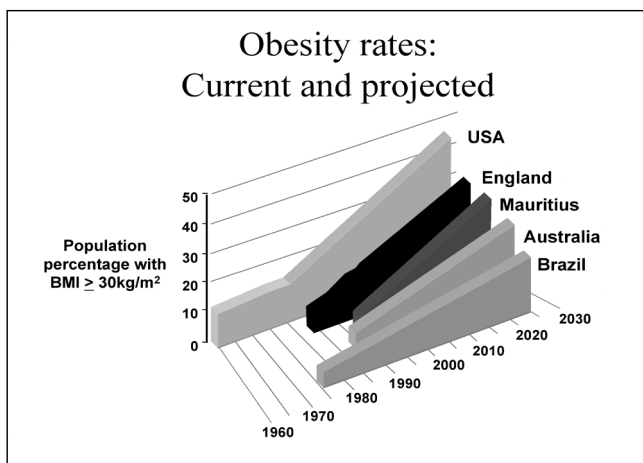
We are used to thinking that the environment changes – and this is absolutely true – but we are less used to think how the environment has changed the human race. This figure shows the height of young men (18 to 19 years old) on their entry into the army in the Netherlands, Denmark, Sweden and Norway in 1860, while the average height of men in the EPIC-Netherlands study is 187 cm. That means that in 150 years, the average height of men has increased by 22 cm in the Netherlands. This is a major change in the anthropometric, metabolic and hormonal characteristics of human beings – higher than the changes occurred in the previous 20,000 years based on the characteristics of skeletons found in fossil places.



Another impressive change is the age at the menarche. This figure shows the mean age at menarche as recorded in Norway, Finland, Germany, Sweden, Denmark, the Netherlands, the UK and the United States. Until the middle of the last century, it was absolutely normal and physiologic for a girl to have the first menses at around age 17: now it is considered normal to have the first menses at around age 12. However, what is normal is not physiological, because normality means frequency. The fact that it happens frequently does not necessarily mean that it is physiologically normal. What is common is not necessarily good, because another difference between these women is that the women now have a 200% increase in their risk of breast cancer compared with women 50 years ago. The 4-year difference in anticipation of sexual maturation is totally non-physiological. The causes of this are well known – excessive weight increase, lack of physical activity and high protein consumption. We are very concerned about the hole in the ozone

layer, but relatively little attention has been paid to the huge changes body growth, and that 'taller is better' is not true in medicine.

The third point I would like to touch is obesity. In addition of being taller we are becoming heavier. The prevalence of obesity in different regions of the United States in 1991 was 12%. In 1998, over 20% of the population is obese in the United States. That is a dramatic epidemic. It is progressing a little more slowly in Europe but the increase in obesity in the UK is approaching what was observed in the United States.



Obesity was thought to be a problem of rich countries but obesity is increasing also in developing countries. Brazil is one of the

countries with the largest proportion of obese people, particularly in the poor rural areas.

These are the results of a European Commission study. The aim was to determine the proportion of subjects that practiced some kind of regular physical activity, including walking, in different countries. A very high proportion of the study population does not practice any type of physical activity in southern Europe. That matches the figures presented about the high prevalence of obesity in children in southern Europe.

It has been estimated that this obesity epidemic will increase by millions the number of people living with diabetes. It is expected that the prevalence will be multiplied by 5, or even more.

Obesity is a big problem, together with overweight, and it is increasing globally. It affects developed and developing countries. Some colleagues wrote in "Living with our genes" this very interesting statement: 'If obesity were an infectious disease, like tuberculosis or AIDS, it would be declared a national emergency and would become the target of a medical war. Instead, doctors treat the various diseases caused by obesity, but not the underlying cause – that is, the obesity.' All the attention is focused on the diseases due to obesity and the metabolic syndrome, but it is very important to put together research on aetiology and research on intervention.

We have the opportunity over the next few days to be together, to exchange, to go from science to public health and vice versa, and to have an interesting discussion. I look forward to a very interesting conference, and thank you again for being here with us.

Dietary energy density as a guide to food choices and weight management

Barbara ROLLS

Department of Nutritional Sciences, The Pennsylvania State University, USA

I have divided my talk into the three stages of weight change: weight gain, weight loss, and weight maintenance. I am going to begin by speaking about whether we can find diets which promote satiety and prevent weight gain.

In the field of study of food intake, most of the focus in the past has been on macro-nutrients. We all hear talk of high-protein and low-carbohydrate diets: Dr Astrup is going to expand on this theme later during his presentation.

There are many food properties that can affect satiety and satiation, including sensory properties, physical-chemical properties, and viscosity. Today, I shall concentrate on energy density, or the calories or joules per gram. We all know how the different nutrients can be divided in terms of energy density, with fat being the most energy dense at 9 calories per gram, followed by carbohydrates and protein at 4 calories per gram, and fibre at between 1 1/2 and 2 1/2 calories per gram. However, relatively little attention has been paid to the water which has 0 calories per gram.

Water is the largest component of food and as a result, water has the greatest impact on how much food we eat. This leads to some interesting suggestions in terms of satiety and satiation.

As a simple example of the power of water to influence the amount of food that one can eat, we can compare grapes and raisins, essentially the same foods: a grape is dehydrated to produce a raisin. If we compare 100 calorie portions, we see that the grape portion is eight times heavier in weight than the raisin portion. This does not mean that you should not eat raisins; it simply means that they represent a far smaller portion for the same number of calories, and, furthermore, it is probably easier to overeat raisins than grapes.

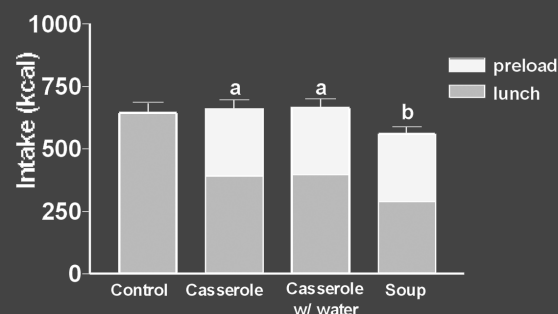
This is relatively easy to understand, but it becomes more complicated and requires greater care to explain that water also has the power to reduce the energy density of high-fat foods. Therefore, if, for example, we take one gram of fat and one gram of water and add them together, we halve the energy density. This is why a food like cheese, in which one third of the calories derive from fat, has the same energy density as a food like pretzels which is just made up of carbohydrates: the pretzels are dry, the cheese has a higher water content.

In order to study satiety, we give a preload – a first course. After a given interval during which we can track hunger and fullness, we study the impact of that preload on the types and amounts of food eaten during an ad libitum test meal.

I am going to share with you information about a few of the studies that we have carried out on satiety. In one study, we looked at the effects of water either in a food or consumed as a beverage on subsequent food intake. People came to our laboratory on three different occasions and they consumed a preload. Each preload had 270 calories, and consisted of a chicken and rice casserole. On one occasion they were given the chicken and rice casserole alone, on another occasion they drank a 10 oz. glass of water with the casserole, and on another occasion we gave them the casserole and the water cooked together as a soup. Therefore, the second and third preloads contained the same ingredients. They were also tested with no first course at all, which constituted our base-line control condition. Fifteen minutes after they had started to eat, we

gave them a second course. In this graph, we see the calories from the preloads and what they ate at lunch. It can be seen that drinking water together with the casserole had no additional impact on intake at lunch, but that when the water was cooked into the food, it had an additional impact in reducing intake by around 100 calories – the people felt just as full and satisfied and did not eat more later in the day to compensate for that calorie difference. Therefore, water in food enhances satiety.

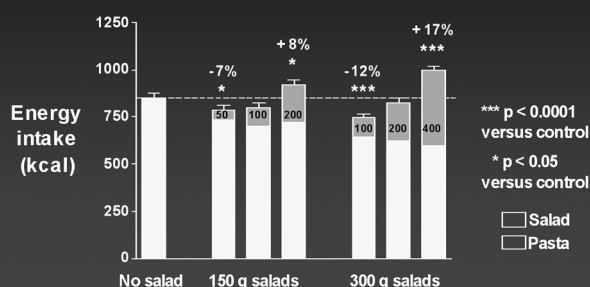
Water within a food, but not consumed as a beverage, reduced intake



Rolls, Bell & Thorwart, *American Journal of Clinical Nutrition*, 70:448-455, 1999

We conducted another study using salad as a first course. We were interested in using two different portions of salad, three different energy densities, and three different calorie levels. We could also compare portion size with the same number of calories using a small salad and a large salad which contained 100 or 200 calories respectively. We reduced the calories and energy density by using lower fat dressings and cheeses; it is therefore primarily achieved through fat reduction. People were allowed to eat as much pasta as they wanted in the subsequent test meal. Our findings are shown on this graph. It can be seen that the portion size, the energy density, and the calories in the salad had a significant impact on how much was consumed in total during the meal. A person consuming a large portion of a low-calorie salad ate 12% less during the total meal compared to a person consuming no first course at all: therefore, they gained an extra course in the meal and consumed fewer calories. On the other hand, a person consuming a high-calorie large salad consumed 17% more.

Intake was influenced by both energy density and portion of salad

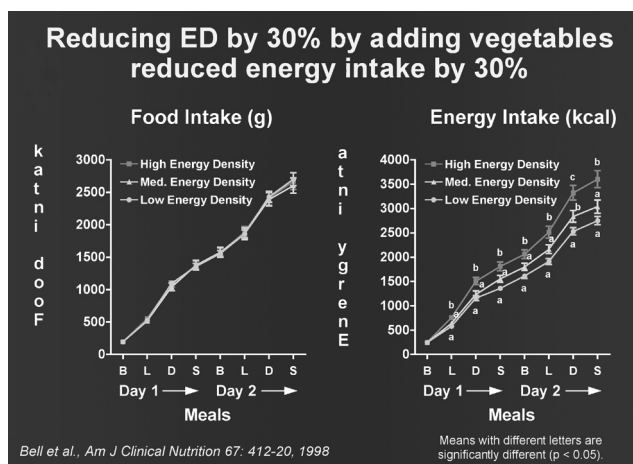


Rolls, Roe & Meengs, *Journal of the American Dietetic Association*, 104, 1570-1576, 2004

The basic conclusion to be drawn in this case is that 'bigger is better' if it is low calorie: the 100 calorie salads that were bigger reduced intake more. Therefore 'eat less' is not always the best message: sometimes, if a food is low calorie, it is better to eat more as it displaces the higher calorie options later in the meal.

The other method we use to study intake is to test satiation. We let people eat as much as they want. This is more difficult than other methodologies as we have to ensure that the palatability and sensory properties between the foods being compared are the same, as people eat more of one food if they like it more, regardless of our manipulation.

In this study, we gave people all their meals in the laboratory over two days. We had three different levels of energy density: low, medium and high. We used mixed dishes such as pasta and casseroles so that we could lower the energy density by adding more vegetables. The weight of food consumed over the two days is shown and the results are self-evident. What people tend to do in this kind of situation where they can eat as much or little as they wish, and where the foods are matched for palatability, is to eat the same amount. Therefore, if the energy density is lowered, people spontaneously consume fewer calories. When we reduced the energy density by circa 30% by adding more vegetables, people spontaneously ate 30% fewer calories over the two days and they felt equally full and satisfied. Therefore, adding water- and fibre-rich vegetables to meals spontaneously reduces energy intake without any change in levels of hunger or satisfaction.



We have been talking about energy density, but yesterday we heard that we should also consider portion size. We have carried out a series of studies on the effects of portion size on energy intake. In one study, we varied the portion size of all of the foods available to our subjects over three periods of two days each. Once again, study participants ate all of their meals in the laboratory. During one two day test there were standard portions which were based on what people should typically eat, and on recommendations on food packaging, and so on. Then during the other two day tests there were two bigger portion conditions in which all available foods were either 50% or 100% greater than the standard portions. The subjects did not see the portions side by side and surprisingly, most people are unaware of the fact that we were varying the portion size. What we found when we increased the portion size by 100% was that women ate 500 calories more on day 1 and 500 calories more on day 2 than when they had the standard portions. Men ate 800 calories more on day 1 and 800 calories more on day 2. Therefore, portion size has an important effect on energy intake.

However, it is not just portion size that is important: it is the combination of portion size and energy density which influences

our food intake. We have carried out several studies to examine how energy density and portion size interact to influence energy intake. In one such study completed only recently, we asked people to eat all of their meals in the laboratory over a two day period. There was enough food to ensure that their intake was not limited simply because we were giving them small portions. We carried out this test over four different weeks, two days at a time under the following conditions:

- Standard energy density, standard portion size;
- Portion size reduced by 25%, standard energy density;
- Energy density reduced by 25%, standard portion size;
- Reduced portion size by 25% and reduced energy density by 25%.

We used foods that are commonly available. One aim of this study was to send a message to the food industry that small changes can have an impact on intake, so we used foods like pizza, pasta, sandwiches and so on. The energy density of the foods was varied, for example, by decreasing the cheese and increasing the vegetables on pizza. The differences in portion size and energy density were subtle, and the subjects never saw the portions side by side.

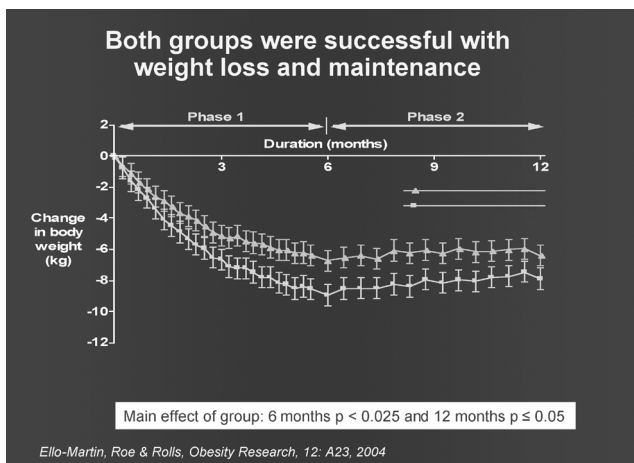
Reducing both portion size and energy density of all foods led to significant and independent decreases in energy intake over two days. A 25% decrease in portion size led to a 10% decrease in energy intake, and a 25% decrease in energy density led to a 24% decrease in energy intake. The effects on energy intake were additive and sustained over the two days. Thus, when portion size and energy density were reduced together over the two days, people ate 800 calories less on day 1 and 800 calories less on day 2, spontaneously eating 1 600 calories less over a two-day period. There were no differences in levels of hunger or fullness. Therefore, this is a strategy that could be used to reduce food intake and that would be acceptable to consumers, as long as palatability and cost were not affected.

I would like to talk about the strategies that can be used to enhance satiety and reduce energy density. Reducing fat intake does reduce energy density, but I think that it is important to emphasise that people should not reduce fat intake to such an extent that they do not enjoy their food; the message of 'healthy fat' should be emphasized. Intake of high-water and high-fibre foods does need to be increased, and these are the types of foods that we recommended in the Mediterranean diet. Portion control needs to be emphasized in the case of energy-dense foods – for higher fat foods and foods with low moisture content. We have also carried out a number of studies that demonstrate that calories from beverages add to food calories. It is also important to eat adequate amounts of lean protein: Dr Arne Astrup will tell you that protein helps to enhance the satiety of foods.

We have been discussing how to enhance satiety and weight gain. What about weight loss? We have recently completed a clinical trial where we compared two different strategies for reducing the energy density of the diet over a one-year period. We randomly selected 97 women. One half of the group was told to reduce fat intake and to restrict portions – typical of the kind of advice that has been given for years. The other group, the energy density group, was given a more positive message: to eat more fruit and vegetables, soups and wholegrain foods, and to eat as much as they wanted of foods very low in energy density. This group was taught the principles of energy density and to use portion control for energy dense foods. Neither group counted calories or fat grams; they were only given instructions as to what foods they should eat.

These are the results for weight loss over the year for those who completed the study. We can see that the number of completers was similar in both groups. After six months the low-fat group

had lost circa 15 pounds of weight, and the low-energy-density group had lost circa 20 pounds. Both groups regained circa 1^{1/2} pounds over the remaining six months. The groups remain statistically different over this time period. We have just finished our analysis of the diet records that we asked everyone to keep. Both groups showed a similar reduction in fat intake – which is logical, as both groups were given the same information regarding fat. However, the low-energy-density group ate more fruit and vegetables, which meant that the energy density was different between the groups, as we had hoped, and the low-energy-density group did eat a low-energy-density diet. The very interesting and positive message resulting from this study is that the low-energy-density group lost more weight, but they were eating more food in terms of food weight. Clearly, this can help people to avoid the sense of hunger and deprivation that often comes with weight management.



There have been very few studies that have focused on maintenance. Obviously, this formed a part of our studies over the last six months, but it is clear that there is a real need for far more long-term studies on weight maintenance. One of the main problems in studying weight maintenance is that of establishing adherence. Dr. Roland L. Weinsier pioneered the low energy density approach at the University of Alabama, and they are still

analysing results and running a weight loss clinic there. Their approach is to recommend unlimited fruit and vegetables with fat restriction. They have reported that people following this advice were successful in not regaining weight in the long term, and they have reported more recent studies with similar results. Therefore, these studies are promising, but we clearly need more data.

We are working with the CDC examining nationally representative data from CSFII, which consists of self-reported intake data from 7 500 Americans. Dr Jenny H. Ledikwe, a post-doctoral fellow, is going to present these data here. She has looked at people who eat more than 30% of their diet as fat, or less than 30% of their diet in the form of fat. She has then divided these two groups in accordance with their intake of fruit and vegetables to look at the energy density of their diets. The results show a significant impact of fruit and vegetables on energy density of the diet. It is possible to eat a higher fat diet and have a lower energy density diet if you eat enough fruit and vegetables. This may help to explain the Mediterranean diet and how people can manage their weight eating slightly higher fat: they eat a lot of fruit and vegetables. Indeed we find that the higher fat groups eating large amounts of fruit and vegetables have a lower percentage of obesity than the lower fat diet groups who are not eating large amounts of fruit and vegetables.

In conclusion, it is starting to become clear, and the policy-making organisations, such as the World Health Organisation (WHO) with their dietary guidelines, are starting to take note of this, that energy density can have a powerful impact on our intake and on body weight. I think that the data clearly demonstrate that combining increased intake of low-energy dense foods, such as fruit and vegetables, with moderate reductions in fat intake is an effective strategy for weight loss. Furthermore, we now know that reducing energy density by eating more fruit and vegetables can affect a variety of dietary patterns, even those that are relatively high in fat, and whilst we have not been able to show all of this data, Dr. Ledikwe has also shown that a low-energy-density diet is better in terms of diet quality.

Questions

Member of the audience

I found the range for low, medium and high energy density very limited. Am I correct in thinking that a ratio greater than 1 calorie per gram is considered to be high energy density?

Barbara ROLLS

We consider very low-energy-density foods to be less than 0.6 calories per gram, and low-energy-density foods to be 0.6 to 1.5 calories per gram. Dr Jenny H. Ledikwe and colleagues published a paper recently in the Journal of Nutrition on how to look at energy densities of national data sets. It is complicated because beverages have to be considered in a different way because they have a disproportionate impact on energy density; therefore, we exclude beverages when determining the typical energy density of diets. We find that even a small difference in energy density can have a significant impact on daily energy intake. Therefore, it is important to think about small changes and to start eating at least slightly more fruit and vegetables.

Optimal dietary strategies for weight management

Arne ASTRUP

Department of Human Nutrition, Royal Veterinary and Agricultural University, Frederiksberg, Denmark

Thank you very much for inviting me to this beautiful place. I am enjoying my visit to Rome and also hope to do a little tourism whilst I am here.

The background to this presentation and to these discussions is the global epidemic of obesity. This can be seen by the differences between body shapes in Paris and New York, which are immediately apparent. Even last night, we saw that there are major differences in the prevalence of obesity between countries, and I think that Denmark and the Netherlands are amongst the countries with the lowest rates of obesity. However, we see from records that obesity did not really exist in Denmark sixty years ago and now we have a prevalence rate of 7.4%. It can be seen all over the world, and even though we are some years behind the United States and the United Kingdom, where we would prefer the problem to remain, we see that there is an upwards trend, and we are beginning to witness substantial problems ourselves in this respect.

Today, we are talking about diets, but I think the problem is also caused by our inactivity and low levels of daily physical activity. Sixty years ago, we could probably eat approximately 500 calories more every day without gaining weight due to high energy expenditure, but today, because energy expenditure is so low, it is difficult to consume the same amount of food as before. I think that this is an important part of the problem and needs to be acknowledged

I shall not focus on portion size today as we have already heard about that and also about energy density, which are two of the very important aspects to consider. The problem that remains is how to use these findings to prevent further weight gain and obesity.

Some years ago, we carried out some meta-analyses on the randomised trials looking at fat reduction, which is reduction of energy density, even though we did not focus on energy restriction. There was strong evidence to suggest that, in the short term at least, there was spontaneous reduction in caloric intake and a slight weight reduction in normal weight to overweight subjects, and a significant weight reduction in obese subjects if they reduced energy density by reducing the fat content of the diet. There has been some controversy about the long term effects, but I believe this is because there are very few good studies on this and, more importantly, very few studies with active intervention.

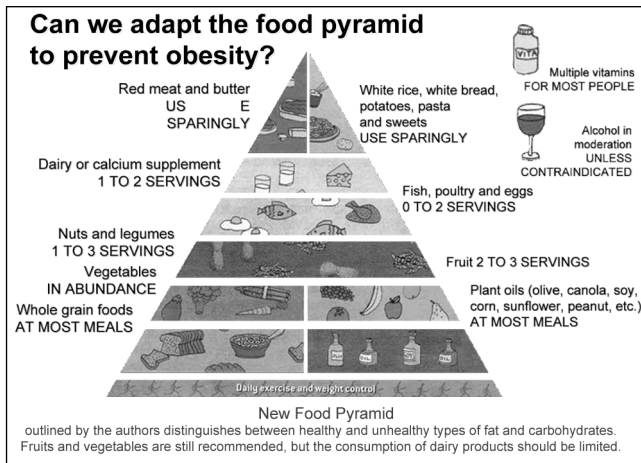
Dr Boyd Swinburn's study in New Zealand included active intervention over a period of one year with a control group using low fat food. The group lost circa 3 1/2 kilo, which is what we would expect given the meta-analyses that we had carried out, but what is also apparent is that once the active intervention ended, people started to regain weight and within five years, they had regained all of the weight that they had lost. Some people have interpreted this data to mean that this low fat, low energy density approach does not work in the long term and that there has to be some adaptation. I think it is obvious that this is not the case because, as for every treatment, be it drug treatment, dietary change or lifestyle change, it does not work beyond the time that it is being carried out: therefore, as soon as the intervention ends, people resume their old habits that made them fat. Therefore, the real problem is how to make people sustain dietary change and increased levels of daily physical activity: this is the real challenge.

Another study has shown that this Indo-Mediterranean diet seems not only to produce spontaneous weight loss but also to reduce cardiovascular mortality amongst high-risk groups. When I showed this slide during a meeting recently, I was told that this study does not really exist and when someone asked for the data, they were told that all the records were eaten by termites. Therefore, I am not sure whether it actually did take place, but I like the data and I liked the study.



I think that it is also important, when talking about low fat diets, to emphasize that the non-fat component of the diet is extremely important. For example, if the fat reduction was made up by an increased consumption of sugar from soft drinks, it would probably be a problem. There are quite good epidemiological observational studies which demonstrate that those consuming high levels of sugar-rich soft drinks are at a higher risk of gaining weight and developing obesity and type 2 diabetes in the long term. When we carried out small randomised trials on this, where we compared sugar-rich with artificially sweetened soft drinks, we were surprised to see that even over a relatively short time period of ten weeks, there was a dramatic weight change. It seems that calories from sugar-rich soft drinks were simply added to the daily energy intake: there was no compensation at all. Therefore, it appears that the body did not recognize the calories entering the body through sugar-rich drinks, which seems to be different from the case of sugar in solid foods. I do not have all of the data with me here, but blood pressure also went up by between 6 and 8 mm of mercury and the amount of C-reactive Protein in the sugar group was doubled. It could not all be explained by the differences in weight loss, so it would seem that there is some adverse effect, not only on body weight but also on the inflammatory process and diabetes amongst those with high levels of soft drink consumption. By analogy, a low fat diet including a lot of soft drinks might be fattening and also have many other adverse effects on health.

One of the latest developments is this new food pyramid, which includes many 'good' foods such as fruit and vegetables and wholegrain foods. I have to admit being concerned that the potato is placed towards the top and by the recommendation to increase levels of 'healthy' fat consumption. I think that this would be the perfect diet for a very active person who has never had any weight problems. However, this would increase the energy density in a sedentary person who is having weight problems, and I am uncertain as to what would happen.



We are currently implementing a large-scale study in Copenhagen in collaboration with the food pyramid inventor, Dr Walter Willet, over a one-year period, to see which of the two pyramids is the most successful in maintaining weight loss. The results will be published at the beginning of next year. One of my personal concerns is that if potatoes are held to be fattening and we are told that it is better to eat avocados and nuts and so on, what about the energy density? I have seen no evidence to support the claim that it is better for the appetite and satiety to eat the much higher energy dense avocados and nuts. As Barbara Rolls told us, the volume and weight of food seem to be extremely important determinants of body weight control, so I believe that it is important that we see some randomised trials first. I cannot exclude the possibility that there is some magic in almonds and olives and avocados, and there is some evidence to suggest that it may be more complex than we believe today, but we need to have more concrete evidence before recommending that people change their diets; otherwise, we may exercise more harm than good.

Another one of the latest trends is the glycaemic index in dieting. It was originally invented to assist type 2 diabetics as a means of improving glycaemic control, but now it is increasingly used for weight control. It is heavily promoted for weight control, and I am convinced that it is good to choose low glycaemic index foods, but I am not certain that it can contribute towards weight maintenance and weight loss in people. There are many other problems: as soon as carbohydrates are mixed with fats and protein, something strange that we used to do in most of our meals, the effect on the glycaemic index of the carbohydrates seems to be eliminated, whereas the effect of the fats and the protein remains far more significant.

We recently carried out a study where we examined forty different European typical breakfast meals. We used this table to predict the glycaemic index and then measured it in twenty subjects each time – not a substantial number, but sufficient for our purposes. Our greatest concern was that there was really no relationship between the predicted and the measured glycaemic index, and when we tried to correlate the two, no significant correlation could be found. Therefore, it would seem to be of little use to advise consumers to keep a glycaemic bible in their bag and to check all their foods before buying them, because as soon as they are mixed with fat and protein, the values change completely. I am rather sceptical with regard to the use of glycaemic indexes in this respect.

Another part of the idea for using the glycaemic index is that a significant rise in insulin adversely affects metabolism and appetite control. However, this is not substantiated by most studies, and I can show you the meta-analysis that we have not

yet published, measuring postprandial glucose and insulin, where we have compared glucose and insulin response with the postprandial satiety feeding. It is interesting to note that there is quite a strong positive correlation between insulin and satiety, so that means that a substantial increase in insulin response postprandially would lead to a sense of satiety. We know from many other studies that insulin is a central satiety hormone, so it is not logical to think that it is dangerous and that a potato should have an adverse effect because it stimulates insulin.

We did not carry out the meta-analysis in order to address this issue, but because we have seen in smaller studies that this association seems to be disrupted in obese subjects so they do not have the same relationship. This may be due to central insulin resistance, but we should not necessarily consider insulin increase as an abnormal or adverse phenomenon: we should view it in a more positive light as simply being a part of the physiological response. However, it is quite a complex issue.

I promised to talk about some of these low carbohydrate diets. In reality, if one examines them carefully – with the exception of the Atkin's diet, which consists of carbohydrate elimination – most of the books combine a reduction of carbohydrates and usually an increase in proteins, and the Palaeolithic diet recommends cutting out all potatoes and grains. My personal opinion is that these diets are extremely boring, and most dieters would not be able to sustain such a diet on a long term basis, even though they may be of interest scientifically. However, returning to the Atkin's diet trials again, there is no doubt that the low carbohydrate diets are quite effective in inducing weight loss. This weight loss is a fat loss, and there is no real adverse cardiovascular or diabetes effect, at least in the short term whilst the weight loss is occurring. However, it does not really seem to work on a long term basis, and when we carried out our analysis, which we have published during the last six months, one of the problems was that there seemed to be adverse effects such as cramps, headache, diarrhoea, weakness and so on, and it would seem that this is due to the lack of carbohydrates: when the brain has to use ketone bodies instead of glucose, this leads to headaches and the like.

Ultimately, my main concern is that the long term impact of these diets will lead to very low consumption of fruit and vegetables which may increase the risk of cancer and other such diseases, but we would never be able to see this from short term trials and would require biological studies.

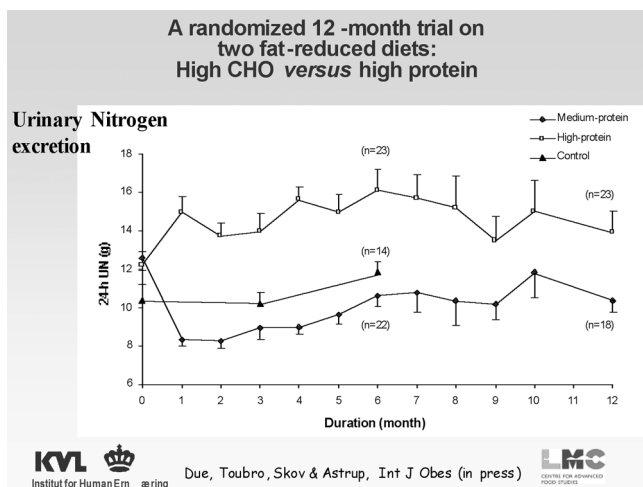
However, the real denominator of these diets is the very high level of protein, specifically between 30 and 50% of food intake, and it would seem that protein is far more satiating than carbohydrates and fat. To conclude on low carbohydrate diets, risk factors are improved but long term studies do not show that they are better than 'low-fat' diets. There are the adverse effects that we have discussed and also the predicted long term adverse effects of cardiovascular risk factors and cancers because as soon as weight loss stops, we would expect to see the adverse effects of the high saturated fat intake and the very low intake of fruit and vegetables and wholegrain foods on cardiovascular risk factors. However, perhaps it would be possible to use less extreme variations of these diets by increasing protein intake slightly at the expense of foods with low wholegrain content, such as white bread.

A paper that has recently been published in obesity reviews is an epidemiological study looking at the changes in different cultures in obesity prevalence and also in the macronutrient composition of the diet. What can be seen with changes in energy density is that with increased fat content, there is a slight increase in obesity prevalence; with a change in carbohydrate levels, there is a slight decrease; and there is an inverse association between

changes in protein content in the diet and obesity prevalence. This suggests that a slight increase in protein content is beneficial and would seem to reduce obesity prevalence. The slide that I am showing now suggests that additional studies demonstrate that protein is more satiating than carbohydrates and fat, and that even with the same energy density and calories, there is a slightly higher sensation of satiety and fullness after high protein meals. This could be of interest for weight and obesity management.



We carried out a one-year trial on this subject, where we studied high protein diets – although when I use the term ‘high-protein’, I am referring to a diet where 25% of the calories are derived from protein, which is far lower than what is recommended by many of the low carbohydrate diet books. Our control group was on a high carbohydrate diet where 12% of the diet was constituted by protein, which is a ‘normal’ level. We used a supermarket model with 1 500 different food items. The most effective system to ensure adherence to a diet is to provide the subjects with all foods free of charge and to use the bar codes to control the nutrient composition of the diet. I will not enter into too much detail but it was an effective system. A good biological marker of different protein intakes was that urinary-nitrogen excretion increased on the high protein diet, and that it decreased on the low protein diet.



We can see that there was extremely good compliance during this six-month period, but as soon as the free of charge food system was ended, compliance began to decrease. In any case, the results show that the high protein diet lead to far better weight loss, even though there was no real control of these diets and no calorie control, and people ate until they felt satiated. Our only instruction was that they adhere to the protein ratios.

During the first six months this group lost significantly more weight and they really did lose fat: almost twice as much as the normal protein diet. Subsequently, between the sixth and twelfth month, when there was no control through the supermarket system, they tended to regain weight, but there was far better weight loss compared to the control group. Therefore, it would seem to have some relevance.

Of secondary importance during the study was the intra-abdominal fat, and we were quite surprised to see that a high protein diet seemed to reduce the visceral fat of the subjects. In the beginning, we were unsure as to whether we could trust that this was a real finding and wondered whether it was just a coincidence, but the result seems to be correct. I have just seen an American study which suggests that there seems to be something in dairy protein which seems to reduce visceral fat, and this is very intriguing. There is another aspect to dairy protein that I would like to discuss: calcium intake.

There is talk of how calcium seems to reduce body weight and this theory is mostly based on epidemiological and animal studies and a few human intervention trials by an American group. We are trying to carry out some control studies to understand how calcium produces weight loss, if indeed it does, and how it affects energy balance. We have been unable to see any effect on energy expenditure and fat oxidation. However, there was an effect – and I asked my laboratory technician to carry out a specific analysis to verify this – which measures the faecal fat and energy outputs in both high and low dairy protein and calcium. We can see that with an increase in calcium intake of dairy products from 500 mg to 1,500 mg per day, there is an increase in fat excretion from 5% to 18% of intake, which is sufficient to play a role in body weight regulation on a long term basis. This is approximately 100 calories that are lost spontaneously, and now we are carrying out further studies to understand its interaction with the fat content of the diet, and other calcium-related tests, although so far we have not been able to ascertain whether calcium has any effect on appetite and on energy expenditure. We can see in this graph that there does not seem to be a dramatic effect but there is an effect. We had a symposium about this in Copenhagen and there were articles about it in newspapers, and I think that this is a positive message for young girls who are afraid of milk because they think that it is fattening; if it is the low fat version, it seems that it may have the opposite effect. We have been unable to find any adverse effects of this protein diet on the bones, kidneys and so on after twelve months.

Of course, this does not mean that we would recommend that everyone increases the meat intake as it probably would not be a good idea, but in terms of assisting in the control of body weight, I think that it could be something for us to consider if ensuring more fruit and vegetables, a reduction in energy density of the diet and of the portion size at the same time. Obviously, we are all concerned about whether there might be a higher risk of cancer if we recommended this.

However, I note that the Institute of Medicine has recently increased the upper safe range for protein intake in adults to 35%, and it has also increased dramatically for children compared to what we considered to be safe in the Scandinavian countries. Only one or two months ago, the Harvard Medical School in Boston also increased their recommendations for type 2 diabetics, as well as for overweight and the obese with impaired glucose, from an allowance of 20 to 30% protein. Therefore, there definitely seems to be a tendency to accept and recommend more protein in the diet, and of course, this makes it all the more important that we consider if this presents any adverse effects.

Personally, I would like to see more long term control studies. Together with partners in Europe and the United States, we will probably conduct a large-scale intervention study in whole families with obese parents and their overweight children, and there will probably be three centres in the United States running the same protocol. The study will consist of five different levels, including normal protein and high protein in type 2 diabetes subjects, and will also include the use of the

glycaemic index to try to understand what the roles of protein and the glycaemic index are for body weight control. This study will investigate weight regain principally and we hope to gain more information. Also, the epidemiological part of the diagnosis will address some of the above issues in terms of the glycaemic index and protein. I hope that this will contribute to our understanding of the optimal diet for weight control. Thank you for your attention.

Questions

Member of the audience

Thank you for this extremely interesting speech. I would like to ask you about these high protein diet results. Did you also measure the energy expenditure? Maybe the subjects began to exercise more. Did you measure energy output as well as input?

Arne ASTRUP

Yes, we have done some 24-hour energy expenditure studies in this area. Our findings were that protein increases body weight by 3 to 4% on a daily basis, but we were unable to see any change in physical activity and it seems to be more a case of the body weight increasing. This is only information gathered on a short term basis and we do not have any long term studies addressing this issue. Hopefully, this study will allow us to examine this issue in more detail.

Obesity, socio-economic status and food intake in children

Marion HETHERINGTON

School of Psychology, University of Liverpool, UK

I would like to speak to you about obesity, socio-economic status and food intake in children. Arne Astrup has set the scene for global epidemic of obesity admirably, and what I would like to do is to discuss recent evidence gathered in Scotland on socio-economic status and food intake in young children. I would also like to introduce and consider some intervention work that we have carried out previously in a school setting.

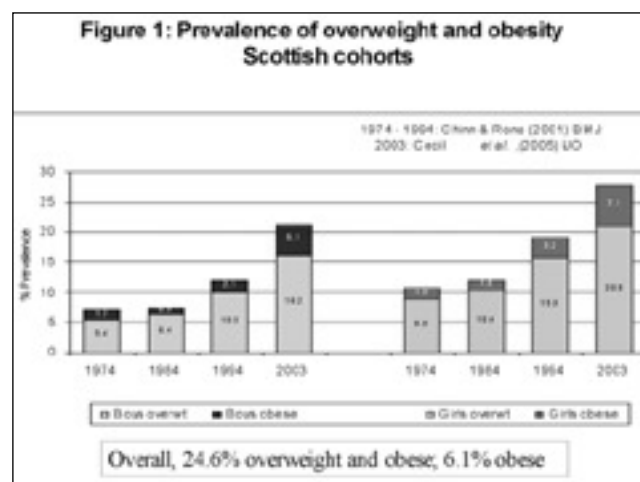
My speech is divided into four sections. I would first like to consider socio-economic status and obesity as a worldwide problem. Then I specifically wish to address the issue of obesity prevalence and the role of the socio-economic status in Scottish school children. I would like to continue from this theme to discuss some of the differences in food choices that children from high and low socio-economic status make. Finally, I would like to describe a whole-school intervention that was carried out a few years ago in an attempt to increase the consumption of fruit and vegetables amongst Scottish children, who could benefit from following a more Mediterranean diet.

Data from Dr Tim Lobstein and colleagues from the International Obesity Taskforce show very clearly that approximately 10% of the world's children are carrying excess body fat. These data demonstrate very well that this is no longer an issue which concerns Western and industrialised societies alone, but that childhood obesity is on the increase worldwide and is now recorded increasingly in developing countries. Moreover, there is an increase in overweight prevalence globally, including countries such as China, and, of course, increasing prevalence in the United Kingdom and the United States continues unabated.

In the case of the United Kingdom, childhood obesity and overweight prevalence has almost tripled in the last decade. Overweight prevalence according to family income levels presents quite an interesting and complicated relationship because it seems – and data from Jane Wardle supports this idea – that higher socio-economic status in Western industrialised countries protects against overweight and obesity, whereas the opposite is the case in developing countries such as Brazil. Therefore, it would seem that in developing countries, a higher socio-economic status is a risk factor for obesity, whereas in the United States and the United Kingdom, higher socio-economic status actually confers a protective benefit against obesity and overweight.

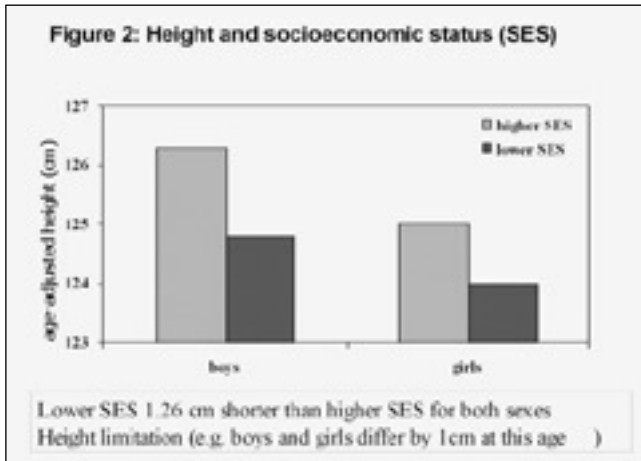
My interest in examining socio-economic status in children arose from a larger collaborative study on genotyping of children in Scotland (see Cecil et al., references). Essentially, the purpose of this study was to examine PPAR- γ , which is a protein involved in fat cell differentiation. We studied 2 454 children from Northeast Scotland and we characterised their genotype with respect to variants of PPAR- γ . Having genotyped the children, we then carried out energy expenditure studies on 100 children who were enriched for 3 PPAR- γ variants. In the beginning, we only considered socio-economic status incidentally as a part of the whole picture and we looked at BMI in relation to their socio-economic status. The average age of the child was 7.4 years old, and the majority of the children were of normal weight. However, when we plot the data gathered on a chart, it can be seen that there is an extremely significant increase in prevalence of obesity and

overweight compared to the National Survey data of 1994. We have also found that this is a conservative estimate because most of the parents of the heaviest and most overweight children would not give permission for their children to be included in the study (Figure 1).



If we show this data against previous survey data taken in Scotland published in the British Medical Journal, we see that the increase in overweight and obesity prevalence is significant, and that in Scotland, childhood obesity and overweight is increasing at an exponential rate. From the original group, it can be seen that 1 in 4 children is overweight and the total percentage is 6.1 for obesity, taking boys and girls into together. In order to define the socio-economic status of the group, we used a Scottish Parliament proxy of socio-economic status by looking at free meal entitlement. The Scottish Parliament publishes details of the number of children entitled to free meals for each school and this reflects the numbers of socially-excluded and poor children. In the initial group that we examined, we found that the schools were bi-modally distributed in the group: 1 000 of the children were from low socio-economic status groups, according to above average free meal entitlement, and 1 400 of the children were of high socio-economic status, because their schools had below average free meal entitlement.

When we looked at these children in more detail, we found that having a higher socio-economic status produced a lower level of obesity. In fact, the lower socio-economic status children were 65% more likely to be obese than the higher socio-economic status children. The income level was inversely related to overweight and obesity, and this is particularly true for girls: this is a finding that confirms previous work on socio-economic status and childhood obesity. Indeed, income level is a stronger predictor of childhood obesity than sex. However, when we looked at this data in more detail, we found that the children from the lower socio-economic status families were not heavier in weight. There was no difference in age and sex-adjusted weight between the groups, the difference was in height, such that there was growth limitation amongst the children from the lower socio-economic status groups (Figure 2).

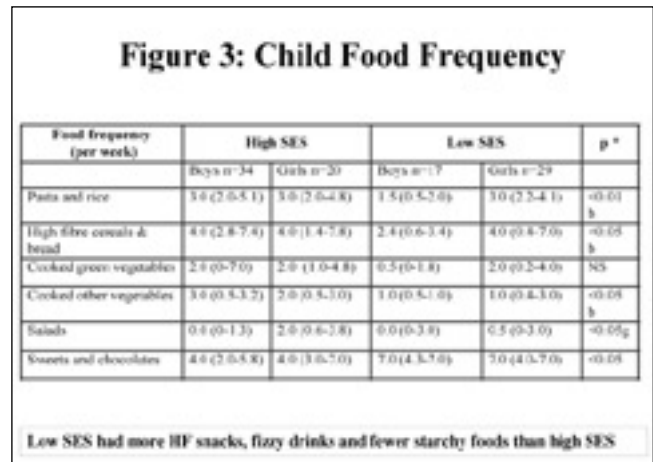


We can see from the figure that the higher socio-economic status boys and girls were taller than their lower socio-economic status counterparts. Overall, the difference amounts to approximately 1.26 cm, which is quite significant because at this age, boys and girls tend to differ by approximately 1 cm, so the growth limitation in this group is of a greater magnitude than that expected on the basis of sex differences. The socio-economic status difference in height was quite apparent across a range of BMIs: the higher socio-economic status children were always taller, irrespective of whether they were lean or obese. In conclusion, since the height difference is observed across all levels of BMI, we can infer that growth rates were possibly similar in the children but that there was a specific influence of poverty on growth limitation, and we are able to observe from our calculations that individuals from low income families were approximately 65% more likely to be overweight than children of higher socio-economic status. These children weighed the same as the more affluent children of the same age, but were 1.26 cm shorter. Before I proceed to talk about these children in more detail, I wish to say that if the children from the low socio-economic status background are shorter, this is clearly related to the maternal diet during pregnancy. Therefore, whilst the quality of the diet may produce some differences in height during the lifetime of the child, growth limitation is determined in part by maternal diet during pregnancy.

In the second phase of this study, we were able to investigate a group of 100 children more closely. We took body composition measures, total energy expenditure, resting energy expenditure and several types of energy intake measurement. We had food frequency questionnaires completed by the children's parents – mainly by the mothers – and we also had 24 hour energy intake recorded by recall using a multiple-pass method. Of the 100 children that we studied in further detail, the boys and girls were similar in overweight and obesity status as the original cohort, and these are higher values for BMI and percentage body fat than those published previously for Scottish cohorts.

In this sample, we found that child adiposity was closely associated with maternal adiposity, but we also further investigated the dietary patterns of the children in terms of food frequency between low and high socio-economic status children. We found that there were significant differences in the number of portions of food consumed according to status. This was particularly true with pasta and rice – the high starch foods – with lower socio-economic status boys eating far fewer portions than high socio-economic status boys. Similarly, there was a significant difference in the consumption of high fibre cereals and bread. Boys in this sample never ate salads, irrespective of whether they were of high or low socio-economic status. We also found that high energy snacks were eaten more frequently amongst low socio-economic status children. Low socio-economic status

children had more high fat snacks, more fizzy drinks and fewer starchy foods than the higher socio-economic status children. What was apparent was that in this cohort, all of the children were consuming fewer than the 'five-a-day' fruit and vegetable portions, and they were consuming far more high fat snacks than recommended by the United Kingdom government. The low socio-economic status children of both sexes had a higher frequency of consumption of sweets and chocolate and as a result, they were consuming fewer healthy options and more energy dense snacks (Figure 3).



As some children were eating far less fruit and vegetables than recommended and as this conference concerns the health benefits of the Mediterranean diet, I thought it would be useful if I talked to you about an intervention that we carried out in order to attempt to improve the amount of fruit and vegetables being eaten in schools in Scotland with a high level of socio-economic deprivation. For this intervention, we used materials developed for us by D.C. Thomson using the 'Bash Street Kids' popular cartoon characters known to many, if not most, Scottish children. In the materials, these characters were depicted eating fruit and vegetables and these were included in curriculum materials and posters around the schools in a whole-school approach. We incorporated materials that teachers could use with the children to encourage fruit and vegetable consumption, and we limited high fat snacks from the tuck shops and offered fruit and vegetables instead. We were also able to instigate some changes into the provision of meals at school through catering by offering vegetable soups, fruit salads and fresh fruits as part of the school meals, and we gave newsletters to the parents to encourage fruit and vegetable consumption at home. Therefore, we used intervention materials across a number of different domains through newsletters, posters, curricular materials, and so on.

The materials developed for this intervention are all available on the Food Standards Agency website, and teachers in the United Kingdom can download these materials if they wish to use them in their classrooms see:

<http://www.food.gov.uk/interactivetools/educational/>.

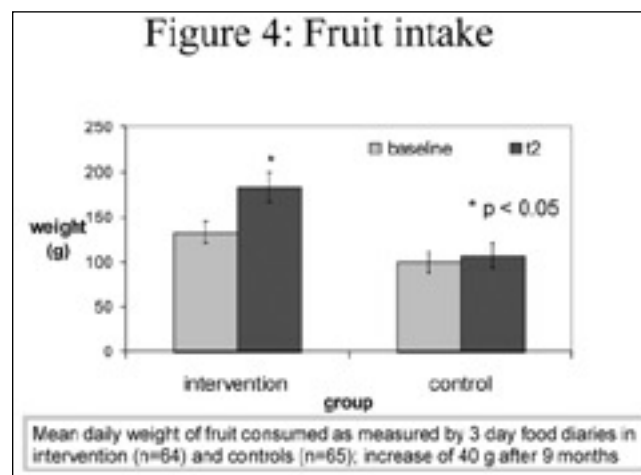
We measured fruit and vegetable intake using three-day parental food diaries; we examined food preference ratings from the children and asked them to taste the foods and tell us how much they liked the foods we were using; we also looked at the success of the tuck shops by comparing control schools with intervention schools; and then we looked at fruit and vegetable consumption using parental frequency questionnaires. There were two control schools and two intervention schools which were matched for socio-economic status but in fact, all of the schools involved in the study had a higher free meal entitlement than average, and the postcode indicators of the families revealed that the majority of children came from low socio-economic status families. Sixty-four children were included in the intervention for the diary part of

this study, and sixty-five in the control schools. As these were relatively young children, when measuring food preferences, we used facial expressions so that the children could tell us how much they liked or disliked fruit and vegetables along with other types of snack foods.

We found there was a small but significant increase in liking for foods like grapes and drinks like orange juice, and a very slight but significant decline in liking for foods like chocolate. In terms of actual food intake, the diaries showed that there was a very modest if significant increase in fruit intake in children in the intervention schools, so the mean daily weight of fruit consumed as measured by the food diaries showed a modest increase of approximately 40 grams (Figure 4). This was after 9 months of a very intensive whole-school intervention. Therefore, the effect was relatively limited (see Anderson et al., 2005 for more detail).

The whole-school approach had a modest success in increasing fruit intake, but did not have any impact on vegetable intake at all. Since this study was conducted, the Scottish Parliament has developed a programme called 'Hungry for Success', and what they have done is to completely change the culture of school meals in all Scottish schools by reducing the amount of deep-fried and high fat foods and increasing daily fresh vegetables and fruit in every part of the school meal programme. This is in line with WHO recommendations to change societal attitudes and behaviour.

In conclusion, I would like to say that socio-economic status is strongly predictive for obesity, that risk of obesity in our data derived from shorter height rather than weight measurements linked to maternal as well as childhood diet, and finally, interventions such as the one I have just described, are only moderately successful unless they are linked to larger public health solutions. It will be interesting to see whether fruit and vegetable intake has increased amongst Scottish children in five years' time to resemble the Mediterranean diet more closely as a result of the new 'Hungry for Success' programme. Thank you.



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Questions

Barbara ROLLS

Thank you, Marion. Did the Scottish government spend a large sum of money on the 'Hungry for Success' programme?

Marion HETHERINGTON

I do not know the exact cost of the programme, although I believe that it has been quite expensive to develop. However, I think that they will see a return on this investment because more children are taking school dinners now.

Member of the audience

Thank you for your interesting speech. Could you describe in more detail the 'Hungry for Success' programme, such as the food culture change, when it started, and the kinds of things that they are changing in the culture?

Marion HETHERINGTON

I have only just returned to Scotland, so I am quite new to the programme myself. Essentially, they have completely revamped the whole school meal system. For example, there are still competitive tenders for school meals in England, and much of this is very low cost, high energy density food such as 'Turkey Twizzlers', which have been written about in the press recently in England.

What they have done in Scotland is to completely change the nutritional quality of the diet offered to children. For instance, there is a red, a blue and a green tray and the children have to choose one of these trays, or a 'grab and go', which is a packed lunch. Each day, the children have to choose one of these three trays or a 'grab and go', and each of these meals has a fruit and a vegetable content, be it salad, cooked vegetables, soup or fresh fruit. There has also been a move towards more traditional cuisines: for example, the children have home-made bread baked on the school premises. This programme is at an early stage at the moment as it was rolled out at the beginning of this year, but I have watched my own children coming home really excited about school meals. I would have thought that was impossible before but it is because there is so much choice and so much dietary variety.

Barbara ROLLS

Are they monitoring what is happening?

Marion HETHERINGTON

I hope and assume that they are.

Barbara ROLLS

It would be a great opportunity lost if they did not.

Member of the audience

I heard two weeks ago in a meeting in London that Scotland has invested £64 million into this programme, which is wonderful.

Prevention of obesity: is it ever too late to start?

Jaap SEIDELL

Free University of Amsterdam, Faculty of Earth and Life Sciences and VU University Medical Center (VUmc), Amsterdam, The Netherlands

Thank you, Dr Rolls. I would also like to thank the organisers of this wonderful symposium for inviting me to Rome. I see that it is a beautiful day outside and we are sitting inside listening to a speech on obesity prevention, when we should be outside walking, running and eating healthy Mediterranean food!

What I am going to do is to follow on from what has already been said. I am not going to discuss nutrition too extensively, but rather whether or not we are doing the right things at the right time for the right people.

This occurred to me because we are now witnessing an explosion in interest on the part of public health officials, ministries of health and organisations such as the European Union regarding the necessity of doing something very soon about the prevalence of obesity. The trend is invariably leaning towards directing all funding towards preventing obesity in children, which is, of course, applauded by everyone. Therefore, there has been a series of studies such as those that Dr Hetherington has just discussed carried out in schools.

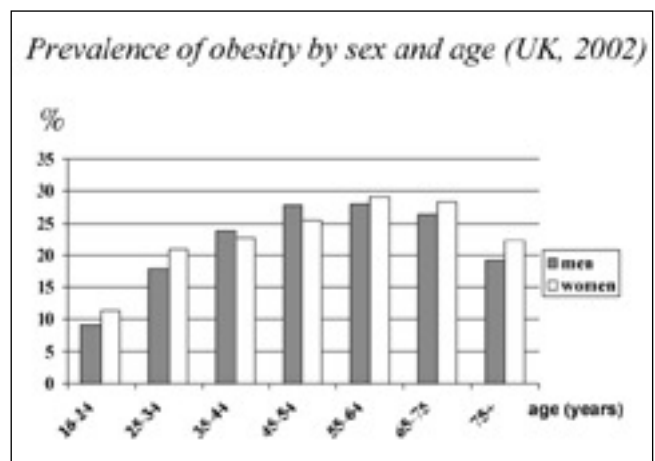
However, we have found that it is quite difficult to sustain the effects of these interventions over a long period of time and it has to be carried out quite intensively in order to achieve reasonable effects on body weight and health outcomes, and an even longer period of time to achieve a long term health benefit. We have noticed that due to the fact that all funding is being channelled into childhood obesity prevention programmes, there is no money left to focus on other groups. Childhood obesity prevention is very well-funded by organisations. For example, the World Health Organization (WHO), as a consequence of the obesity reports and chronic diseases strategies, is concentrating almost exclusively on children. Of course, the reason for this is that we are witnessing increases in childhood obesity which are quite dramatic and horrendous and need to be stopped, and I believe that this is a problem that deserves our attention. However, we may be missing out important categories.

The reasons we are concentrating on children are as follows: firstly, we all think that prevention should start early as habits start early and are more difficult to change later on, and if it is not started early, the benefits will not be reaped; secondly, it is assumed, especially by public health experts, that it is more difficult to change habits in adults, and that once you are an adult you are either a physically active or a sedentary person and that this cannot be changed; thirdly, that once adults have insulin resistance and risk factors for cardiovascular disease, that these factors are irreversible; and lastly, there is a strong school of thought that for middle-aged and for older people in particular, the worst thing that can happen to them is that they lose weight – this is particularly emphasised in Geriatrics and Gerontology – and also, many seem to think that it is a less important consideration for older people than for young people.

What I wish to convey to you is that there are some considerations that need to be taken into account. One of these is that obesity starts in young adults, but the prevalence of obesity is actually quite low in most populations studied across Europe, and obesity only begins to reach high proportions in adulthood. Adult weight gain is in itself an independent predictor of the weight status of an adult of most obviously related health outcomes, such as diabetes, breast cancer, cardiovascular

disease, and other chronic diseases. The risk of potentially preventable non-communicable diseases increases with age; that is to say that diabetes is much more common amongst older people than amongst younger people. It is my opinion that if we wish to talk about interventions, we have to ensure that they are not only effective, but also cost-effective: they are efficient and deliver long term health improvements, rather than just costing large amounts of money without any real impact.

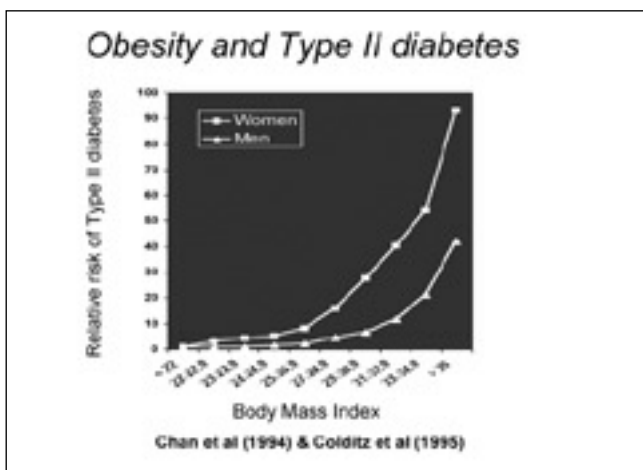
When we are talking about the prevalence of obesity, we look at the relationship of obesity with age, and we see that in the United Kingdom there is already a large amount of obesity amongst young adults at circa 5-10%, but this increases sharply until middle-age to circa 25%, and then decreases after the age of sixty or sixty-five. Many conclude from these statistics that obesity disappears with age and people lose weight and the problem is resolved. However, it has to be remembered that these figures are all based on cross-sectional data; it is a snap-shot of the population looking at the whole population and the prevalence of obesity and obesity in younger people plotted on a graph. This is done in almost every country to describe the relationship between age and trackers. The older people included in this data were born during a completely different time in the 1930s and 1940s as these are records from the Second World War in the UK and in continental Europe: there was not much obesity, as Dr Astrup mentioned using his military conscript data.



Therefore, we are trying to develop a more sophisticated methodology to look at age, period and cohort effects. We have examined different studies over time, and following individual people over time. This slide shows that if we start with people in the 1980s at the age of twenty-five, they will gain a lot of weight. If we examine people aged thirty-five in the 1980s and follow them up the chart, they start at this level. We see that people, who are now thirty-five years of age ten years later at this point on the graph, are already six kilos heavier than the people who were thirty-five ten years earlier. It can also be seen, when looking at the association between age and body weight, that there is an increase in body weight with age and that then it seems to drop. As a result, the cross-sectional data seems to suggest that there is weight loss with age. However, if you look at people longitudinally, it can be seen that they continue to gain weight even amongst the older age-groups.

Therefore, cross-sectional data alone is misleading and needs to be examined together with longitudinal data to see the dynamics of obesity. From this, we see that the real weight gain is different from the picture shown by cross-sectional data, and thirty-five year old people are 5 or 7 kilos heavier at this point than their elders were ten years earlier. There is a continuous increase in all age groups. The rate of increase is lower, but we can also see that the major weight gain actually takes place during early adulthood, with people gaining in the order of 6 or 7 kilos over a ten year period during early adulthood. If we look at BMI, we see that there is an increase in BMI for every age group, although the starting level is higher for older age groups, of course.

Why is this important? One of the points I mentioned earlier is that if a person has a higher BMI at a young age, there is a higher risk of diabetes. However, this is really dependent on whether or not there is subsequent weight gain, because if the person maintains their weight, then, there is little knock-on effect in terms of diabetes. However, if there is a high BMI of 24 at the age of twenty-one and there is a weight gain of more than 11 kilos, which is very common in our populations, then there is a real synergy and the risk of diabetes increases exponentially. Therefore, it is not just a matter of the starting level of obesity but also what happens in adulthood that is important. It is especially important because the relationship between the body mass index and diseases such as type 2 diabetes are curvilinear and increase exponentially. As a result, middle-aged people who have a relatively high starting level of BMI and who continue to gain weight have a very high risk of developing diabetes. Dr Tuomilhto will discuss this further when he will talk about the diabetes prevention intervention study in Finland, but if the persons gain as much as 3% of their body weight, which is usually circa 2 or 3 kilos, their risk of diabetes is doubled over a period of five years. These are people who are already overweight, insulin-resistant or glucose-intolerant and a small change in bodyweight doubles their risk of diabetes.



Why is so little emphasis being placed on the middle-aged and elderly groups of the population when discussing prevention? Perhaps it is because it is less attractive. Is it because we believe that adults have their own responsibility and should take care of their own lives? Or because the relative risks of disease seem to decrease with age because there is a common perception that hypertension and body weight are less of a risk factor with age? Of course, we are not thinking about this in a sophisticated way. We have to think about the different types of risk. In a paper recently published in the International Journal of Obesity, they showed that the relative risk of obesity for hypercholesterolaemia decreased with age, and the conclusion was that obesity was not a real problem in older people and that we should focus our attention on younger people. Of course, this is wrong. It occurs because clinicians and others are trained to

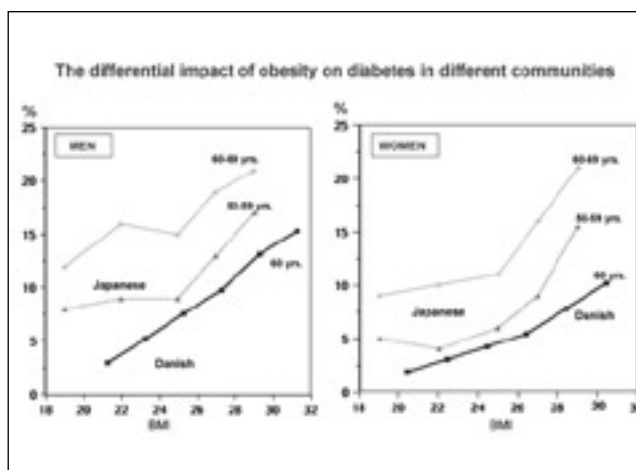
think about relative risks in terms of how their patients can benefit from a treatment, and almost invariably papers published about public health and epidemiology present findings in terms of relative risk. However, in public health, attributable risk is far more important.

At the risk of labouring my point, I wish to present you an example. On the graph, these are two different age groups, and this is the risk of obesity or the risk of coronary heart disease with obesity. This is the age of forty-five and this is the age of seventy-five. Here, we can see that the prevalence of obesity increases sharply and the relative risk is decreasing. This is an accurate picture of what actually happens: obesity seems to be less of a problem in older people in terms of relative risk than in younger people, but the actual risk of coronary heart disease is actually much higher. If we look at the attributable risk, that is to say the number of cases of coronary heart disease that can actually be attributed to obesity in older and younger people, we can see that it is actually 20% in the older people and less than 10% in younger people. For many medical students, it is difficult to think that something that is less of a risk factor in terms of relative risk might be more important in terms of public health. Therefore, obesity in older age is actually an enormous public health problem in terms of absolute risk, attributable risk, and the number of patients who develop disease.

Estimated 10-Year Risk of Incident Coronary Heart Disease in Younger And Older Individuals with or without Obesity

Age, yrs	Obesity	Prev.	Absolute Risk	Relative Risk	Excess Risk	Attributable Risk
45	No	90%	5%	-	-	-
	Yes	10%	10%	2.0	5%	9.1%
75	No	50%	20%	-	-	-
	Yes	50%	30%	1.5	10%	20%

As a result, it is important that we do not focus only on these relative risks, which are often cited in studies to demonstrate that the relative risks of obesity in old age diminish, as it does not mean that obesity is less of a problem for society. This can be seen on this graph, which demonstrates that the absolute incidence of type 2 diabetes is actually higher at every BMI level in age groups of fifty to fifty-nine and sixty to sixty-nine.



Therefore, when considering the possibility of a long-term intervention of ten years, if you would like to see that there are health benefits from the intervention and real cost-effectiveness, I would say that the potential health gain and cost-effectiveness will be far more effective if the focus is on older people rather than on younger people. If the £64 million in Scotland could be spent only once, would it be wise to invest it only in childhood programmes? I am not purporting that the school programmes should not be implemented as I believe that they are enormously important, but I am concerned that we are neglecting the rest of the population.

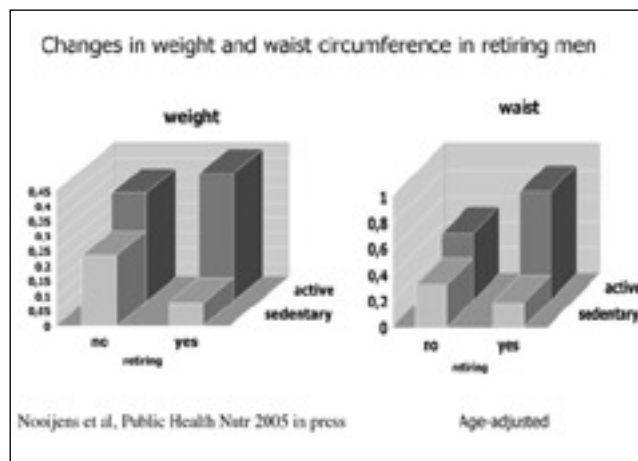
Rather than just concentrating on school-based interventions alone, what we are now doing is to start interventions in all of these age groups, and these are all groups that are vulnerable to incidence of obesity that is changing their lifestyles quite considerably and who have a high risk of developing obesity-related complications. We are currently implementing interventions in young adult people where there is a significant change in their lifestyle and who do not focus on physical activity and nutritional behaviour: they are also the prospective parents of our new generation of young children. This relates back to one of the problems that we noticed in our school-based interventions, that even when we were able to stimulate the interest of the children, if they went home to parents who were not interested at all, the effect is actually quite negligible. The parents have to be involved and young adults are in themselves a high risk group because it is at this time that they gain weight. Pregnancy is also very important and there is very little guidance as to how women can avoid excess weight gain and weight gain retention after pregnancy and we are currently running interventions for these women. Smoking-associated programmes are also extremely important, and I am also going to talk to you about work-site programmes, as well as a group that is extremely important in numbers because of the aging of the 'baby-boomers' in our societies: people who have retired.

Let me give you a few examples. One is the work-site prevention of weight gain, where we are running different interventions situations with randomised studies in approximately a dozen different situations. This is an example of the type of studies that we are carrying out. We are carrying out randomised studies and they favour physical activity, particularly when we look at all the other lifestyle factors as well. There is a reference group which is a control group which only receives written information.

We are looking at a large variety of output measures. One of them is body fat and body mass index as cardiovascular disease risk factors. What we find is that if work-sites take up these physical activities and healthy lifestyle programmes, it does not make a difference to body mass index and moderate physical activity, but it does influence vigorous physical activity, cardio-respiratory fitness and body composition: these are the effects that we witness in intervention studies with the introduction of physical activity – no change in body mass index but an improvement in body composition. Now, if you consider how we could motivate people from companies to do these kinds of interventions, we need only look at days of sick leave. After some time, it starts to become apparent that the number of days sick leave for the intervention group is reduced by about 7 days. The cost benefit of doing this for a company is that whilst they must pay during the first year for the intervention and counselling and so on, they start to regain that investment during the second year due to improvements in absenteeism and sick leave and the like. When companies see this, they start to wake up to the benefits that this can bring to them in the long term.

Another group that I mentioned earlier is people who are retiring from their occupations. We have followed numbers of these cohorts and we divide them into two groups: there are the office

workers with sedentary jobs on the one hand, and the manual workers with physical activity during work on the other. In all of these cases, there is a sharp reduction in the hours that they work upon retirement; they suddenly have thirty hours less work per week. One can imagine that in the case of a manual worker, it is a challenge to compensate for the loss of thirty hours of physical activity during the week in their leisure time in terms of energy balance and in terms of preventing obesity. When they stop working, they increase their household activity – but not significantly, according to what their wives tell you – and they do one and a half hour's of odd jobs. Instead of working between thirty and forty hours per week, they take up household activities and manual activities around the house for approximately five hours per week, but this still means that they have lost circa twenty-four hours of physical activity and this loss needs to be compensated for, either by means of a reduction in energy intake or by means of equivalent energy expenditure. Unfortunately, this rarely happens. In the case of people with sedentary jobs, when they retire their body weight decreases because they are more active physically than when they were working, and this has a favourable effect on their body weight and energy balance. However, in the case of people retiring from active jobs, there is a weight gain, and there is a sharp increase in waist circumference. To my knowledge, this was the first study that was carried out studying body composition and disease risk, and the absolute risk of type 2 diabetes and metabolic syndrome and all kinds of other diseases that will be discussed during this symposium can be seen: they are actually dramatically deteriorating and they have full metabolic syndrome within one to two years.



Do we know what kind of nutritional and behavioural factors might be important? What we have seen is that there are a number of factors that may be important. In terms of nutrition, frequency in fruit consumption is beneficial, and if they increase their sugar, sweets and soft drinks their body weight increases, if they increase their fibre intake there is less of a weight gain, and if they take up cycling and odd jobs excessive weight gain is avoided. However, these factors are marginal and do not really compensate for the total effect of retirement. The same can be seen for waist circumference, although waist circumference tends to be an even more reliable indicator than body weight in these age groups. Again, physical activity helps to prevent weight gain.

It seems that there is little interest in funding agencies and the ministries of health in different European countries, but health organisations involved with the 55+ age groups are increasingly interested in contributing in the area of physical fitness, nutrition and wellness, and I think that we need to teach people how to deal with changes in their lives and how to prevent sharp increases in obesity.

Therefore, my message is that obesity prevention is possible. However, the common perception is that it is especially possible with children because an early start is a guarantee of success for the long term, whereas we find that it is extremely difficult to sustain the effects of school-based interventions on a long term basis due to the fact that it has to be continued throughout each class in every school to be effective. However, there are some critical moments in life that make people very vulnerable and very accessible to health interventions, and they provide opportunities for obesity prevention in older age groups as well.

The message is that we need to work on obesity prevention at every stage of life. It is not sufficient to concentrate on children alone and think that once school meals are changed, they will eat healthily forever. It is necessary to work at work-sites, on retirement, on specific groups that are vulnerable to the development of type 2 diabetes and obesity. The life course approach is necessary and is being emphasised by the World Health Organization (WHO), but many public health agencies have not adopted this approach. I believe that we need to realize

that obesity is an exceptionally important predictor of health in older people. Even though the relative risks of disease with increasing body mass and its decrease in ageing, the total burden of disease associated with people with moderate overweight and obesity in older people is enormous, and much higher than in younger children.

Of course, the famous Geoffrey Rose prevention paradox has not really entered into our discussion about the prevention of obesity but it needs to be reiterated: the cost-effectiveness of interventions will probably be more favourable in older ages compared to childhood obesity prevention programmes. Of course, we need more than just words, we need results. Next year, I should be able to present most of the results of the intervention studies that we have done in pregnant women, young adults, work-sites and in older people, but we really need more studies in these populations in order to understand what is happening and how we can prevent obesity and especially the associated disorders that follow on from it. Thank you for your attention.

— Questions —

Barbara ROLLS

Thank you for an extremely comprehensive overview. Are there any questions?

I would also like to ask the speakers to come up onto the stage during this question and we will have an open forum for five minutes after it.

Member of the audience

You emphasise the difference between the absolute risk and the relative risk and you state that the cost-effectiveness of concentrating on older people rather than on younger people would be higher, but this is only because you are taking absolute risk as your measure. However, if your measure is the number of years of life lost, the picture would be completely different. It does matter whether the same numbers of absolute risk occur at the age of thirty or at my age of seventy. I am in a good position not to argue too much in favour of everyone because otherwise you would dedicate all resources to old people as the risks increase in a never-ending circle for this group of the population.

Member of the audience

Before your answer to this comment, whilst I think that your presentation is extremely interesting, I would also like to argue this point. It is similar to working with smokers: if you want to have an immediate improvement in lung cancer rates, you only work with people who are over fifty years of age; however, if you want to prevent health damage and the number of years of life lost due to tobacco, you must concentrate on teenagers. I am sure that we both understand this point. The issue is whether we must confine ourselves with very limited resources for prevention, or whether we want to fight for there to be more resources for prevention, instead of pulling resources from the young for the old.

Jaap SEIDELL

I understand your concern. The point that I would like to make is that we should not only implement childhood obesity prevention programmes as I think that if we only concentrate on school-based intervention and stop everything else, this would not be effective. The example of smoking is a little different because the age of onset of smoking and the outcome of disease occurs many years later, whereas we see that in middle-aged people the change in weight and the occurrence is very closely linked, almost instantaneous; this is very different from the example of smoking and lung cancer. However, I do accept what you are trying to say and I am not saying that we should not carry out programmes for the prevention of obesity to prevent a large number of life years in health terms, but I think that the middle-aged are like the lost generation. Governments are investing all their money in the generation that will have the benefits from now, but what about the rest of the population? Can anything be done for them to prevent obesity-related diseases? We should also not forget old people and people going into retirement, as there are huge health benefits to be gained.

Discussion

Member of the audience

All the studies presented here report upon an increase in obesity at the beginning of the Eighties, whereas it was almost non-existent before. During these years, we witnessed the dramatic increase of hypermarkets, the modification of the supply routes and the advent of a plethora of sweetened and fatty snack bars, dairy desserts, sweetened drinks, soft drinks, and cooked dishes for which it is difficult to evaluate the energy density. These omnipresent and low-cost products promote obesity. You implement many initiatives at the consumer level – elderly persons, children, parents and pregnant women - but as long as the plethora of these foods remains the same, people will be faced with difficulties in modifying their dietary habits. Should the governments not push the food industry to put on offer more traditional products, unprocessed fresh fruit and vegetables and as well to limit the broadcast of advertisements targeting children? It would undoubtedly be more effective.

Barbara ROLLS

I think it is clear that the food industry could do more to offer foods that would help us to eat more healthily, and this is a challenge that we all need to work towards. In the United States, the subsidies programmes also present a significant problem. However, it is not going to be easy. Professor Adam Drewnowski and I sit on a panel mandated by the Food and Drug Administration and we meet with the food industry policy makers and the food industry is being very forthcoming about the challenges that they face. They find that as soon as they label a food as healthy, it makes the product unpopular and the public does not want to eat it. Therefore, it would seem that the challenge is to ensure that people eat more healthily in spite of themselves. I call it 'stealth health': we have to introduce it without people seeing us do it. We all want them to eat more fruit and vegetables and wholegrain and so on, but how can we make them want this food? This is the real challenge.

Member of the audience

Thank you for your intervention. I understand perfectly the problem in so-called wealthy European countries, but it is also present in developing countries. Obesity and diabetes concern particularly the poor within rich countries. However, the poor within developing countries will also undergo this shock in a few years. We must thus think of this now. But I will pose the problem differently. The statistical studies which were presented must be regarded as experimental data to study and correlate with others. There is enough evidence and information to enable a thorough analysis of the problem. The relation between the body mass index and diabetes is well known. However, is diabetes a consequence of weight gain? In this case, how can we explain that elderly people, generally less obese, are more sensitive to diabetes? Couldn't one say that people sensitive to weight gain are also sensitive to diabetes? In consequence, are the cardiovascular problems of coronary diseases related to obesity? Is obesity related to incipient diabetes? Don't these elements have the same origin? These questions deserve to be asked. Thank you.

Barbara ROLLS

I am sorry that none of us speak much French. Does anyone else have any comments about the food industry whilst we are waiting for a translation of this point?

Thank you for those comments. Does anyone else have any comments?

Member of the audience

I think that these are actually excellent points which deserve further discussion. Of course, this is why many of these new initiatives are actually occurring in developing countries such as Latin America, Africa and especially in Asia, where I think there is now an explosion of type 2 diabetes, heart disease and overweight. It is much more complicated than we initially thought: we are exporting our own European and Western data to third world countries and that may be totally inappropriate. How do we define obesity in Asian countries for instance? The governments there have already recognised that there is a developing public health catastrophe in terms of type 2 diabetes, and if nothing is done until everyone reaches a BMI of 30, about 80% of Indians will have type 2 diabetes: this is not a very effective way of looking at the treatment and prevention of obesity. Therefore, we must be careful about taking our data to other countries. We need to be extremely careful.

Member of the audience

My comment relates to the responsibility of the food industry. I am a researcher and I am not involved in the food industry at all. I think that we should also talk about the responsibility of research and results. What we heard this morning about protein is extremely important and maybe we are not fully aware that we are undergoing a revolution in our knowledge of the relative importance of the balance between carbohydrates, fat and protein. I studied water concentration at the end of the seventies when the dogma was that what was bad in our diets was fat and protein. The food industry, particularly in North America and some parts of Europe, reacted to this message by producing low fat foods which were high in sugar. Therefore, in a way, science gave the wrong message by saying that what was wrong with our diets was fat and protein. Some consumers followed this message and started to buy low fat, which is also low in protein, high-sugar diets. We now have clear evidence that this is the worst diet possible from the point of view of obesity, the development of diabetes, and possibly the development of cancer. Therefore, whereas our colleague and friend Donato Greco said yesterday that we need to act, I would also say that we need to obtain better scientific data because if we act on incomplete scientific data, we do more harm than good. It is very important to realise that if we need to do more, we also need to know more, rather than just proceeding in an ideological manner. Ideology does not sit comfortably with science.

Arne ASTRUP

I think that these are wise words, and it is clear that we need much more robust information before we change recommendations and issue new advice to the public. On the other hand, we need to advise people today.

As far as the low fat story is concerned, the problem was that when the recommendations on reducing fat in the diet were being made, we did not really understand the importance of energy density because what we saw was that in many of the products there was a too great reduction in fat, but the caloric content and energy density was not reduced. Therefore, these foods were not really effective because energy density was not reduced. However, we have seen beneficial changes in many countries in that people have changed their consumption to lean versions with dairy and meat products where energy density is reduced dramatically; people are choosing the lean versions. If there had not been this reduction in fat, there would have been a more dramatic increase in obesity in many countries.

However, I believe that you are right that we should be more careful in the future. I think that all low carbohydrate food is a problem as it really is not sensible, and there is no evidence to suggest that it is beneficial for the population in the long term, either in terms of body weight regulation or reducing the risk of type 2 diabetes. It is important that we tell the industry that it should not follow this advice because we do not believe that there is any evidence to support it.

Member of the audience

I would just like to say that we are now attending a new catastrophe due to incorrect information on glycaemic index, and is now being followed by the food industry as they are starting to look at fructose, because it has been said that it does not increase the glycaemic index. We know that there is fructation just as there is glycation. Fructose in fruit is not a problem but if you add large quantities of fructose, then you paralyse all the enzymatic and protein systems and I think that it would be difficult to sustain the consequences of this new movement.

Member of the audience

I think that these are extremely important points and I think that what has been said is quite clear. Whatever we do, even in the case of isolated studies, is abused by the food industry because the commercial market is misleading and the message can be misunderstood by the population. The glycaemic index is an example of this. That is why what WHO did is so important: they examined food-based dietary guidelines, food patterns and non-communicable diseases, and did not just concentrate on one isolated phenomenon. It is important that diabetes, cancer, heart disease and so on be examined in an integrated manner so that we are not promoting a type of diet that is helpful in preventing weight gain but is deleterious in terms of cancer. I think that this is the main problem with recommendations stemming from research.

For example, if we find that dairy protein is extremely beneficial in preventing weight gain and we advise people to increase their low fat milk and their dairy protein intake to high levels, this could be extremely dangerous in terms of cancer risk. What we need is someone who integrates all of this information in order to ensure that we continue to see outside the box of disease-specific nutrients and disease-specific relationships.

Barbara ROLLS

I think that we need to emphasize the consensus that we all feel. What emerges in the press is when we disagree and any outrageous remarks and things that are unexpected. As health professionals we have a responsibility to keep emphasising the points that we do agree on, and I think that it is safe for us to encourage the public to eat more fruit and vegetables, wholegrain, high fibre foods and lean proteins: many of these products form the basis of the Mediterranean diet and I think that we have to keep repeating this message as there will always be someone trying to sell snake oil to the public.

Observational studies of dietary factors and the metabolic or insulin resistance syndrome

Nick WAREHAM

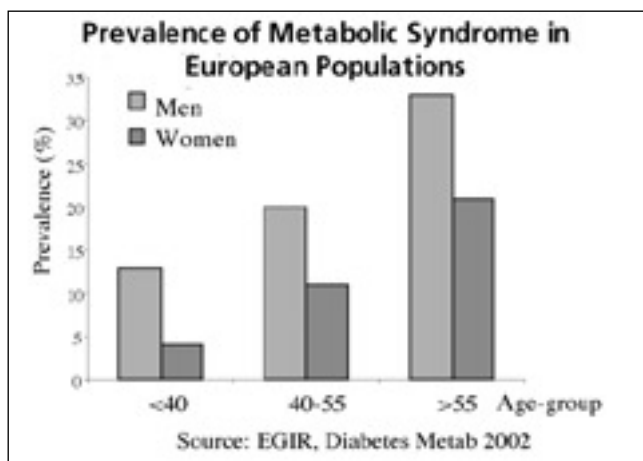
MRC Epidemiology Unit, Elsie Widdowson Laboratory, Cambridge, UK

It is my pleasure to introduce the second session today. My name is Nick Wareham and I am the director of the Medical Research Council Epidemiology Unit in Cambridge. This session is a small but perfectly formed session on metabolic syndrome and diabetes, which is squeezed between the expanding session on obesity and the double session on cardiovascular disease this afternoon. We have tried to structure this session slightly differently from the other sessions. We are taking an epidemiological perspective on the issues of diet, metabolic syndrome and diabetes by first concentrating on observational data for the two conditions separately, and then considering trial data.

I am going to talk about diet and the metabolic syndrome using data only from observational studies. As everyone in this audience is no doubt aware, metabolic syndrome is a loose clustering of related metabolic diseases comprising abnormal glucose regulation, insulin resistance, dyslipidaemia, principally of low HDL cholesterol and hypertriglyceridemia, hypertension and obesity: both total and central obesity.

There has been a continuing controversy in the literature about which of these features are central to the condition. We have conducted factor analysis using longitudinal data to examine how the different factors change over time. It is perfectly clear from these studies that the central determining factor of this syndrome is the degree of obesity and that drives the other factors listed on this chart. When we come to consider the dietary factors that relate to the syndrome, we cannot exclude that some of them may be mediated through obesity and some of them may be independent, and this is the main focus of our discussions today.

What ecological data do we have from studies examining the prevalence in different populations of metabolic syndrome and relating that to dietary factors, such as the proportion of the population eating a Mediterranean style diet? One of the problems that we are encountering is that we do not actually have the data to answer this question. It is only recently that we have started to obtain data about the prevalence of metabolic syndrome across European countries. Some of this originates from studies such as the DECODE study which was led in part by Jaakko Tuomiheto which was a consortium of population-based studies all performed after 1980 and all of which included both men and women and an age range of at least two decades.



One of the key prerequisites in these studies was that all of the participants had to have a two-hour 75 gram oral glucose tolerance test. Colleagues from the EGIR group reported a few years ago that the prevalence of the metabolic syndrome in European populations was greater in men than in women and that it was clearly highly age-dependent.

The EGIR group demonstrated their preference for different definitions of the syndrome as they chose the WHO definition of the syndrome, which includes a measure of insulin resistance. As the European group for studying insulin resistance, it is not surprising that they preferred that definition as opposed to others, such as the American ATP 3 definition, which focuses more on the five factors that I demonstrated previously, excluding insulin resistance. One of the difficulties here is that we have different definitions of the syndrome and indeed, only a few weeks ago another definition of the syndrome was announced by the International Diabetes Federation. This definition differs from some others in that it places obesity at the centre of the syndrome. A person is defined as having the syndrome if they have obesity plus two or more of the following factors: raised triglyceride, raised blood pressure, reduced HDL cholesterol, or abnormal glucose regulation. It is clear that the definition depends on the existence of obesity, and then the other factors are regarded as metabolic consequences of obesity. One of the difficulties is that this definition was only announced in April 2005, and there have not yet been many epidemiological studies describing prevalence. However, I know that Jaakko and his team have looked at the prevalence of metabolic syndrome in European populations using this definition and it is clear that one of the observations is that the prevalence will rise markedly if this definition is used. Indeed, using this definition, 37% of the population can be defined as having the syndrome. I think that the level of that prevalence really questions whether such a definition has clinical utility because it would be extremely difficult to treat nearly 40% of the population on an individual basis. Another issue is whether condensing this syndrome into a unitary dichotomous definition, which defines people as either having the syndrome or not, is useful when we are considering aetiology. I am convinced that it is useful to do this to make a political point about the importance of this syndrome, that it is associated with the risk of diabetes, cardiovascular disease and many other disorders. However, is it important clinically to label 40% of the population as having a syndrome? By condensing it in this manner, it is also possible that we limit our own thinking about the different aetiology of the subtypes of this syndrome.

I would like to discuss what we know about diet and metabolic syndrome in relation to specific nutrients, concentrating on fat and carbohydrate, looking at some specific foods and then moving on to dietary patterns. Then, I would like to consider whether there is any residual confounding in these observational data by key lifestyle factors, such as physical activity, alcohol consumption and smoking. Finally, I shall talk about effect modification by genes.

With regard to fat, there was a review last year conducted by Dr Riccardi, and I think some of the other groups from Italy who are here today such as Dr Rivellese. They reviewed a number of epidemiological studies, most of which were cross-sectional, and which included some by Dr Edith Feskens, who is also here

today. On the whole, they demonstrate that increased levels of saturated fat are associated with decreased insulin sensitivity. In general, total fat is positively associated with higher fasting insulin levels, a good proxy measure for insulin resistance. Increased saturated fat specifically is associated with increased insulin levels and higher polyunsaturated fat tends to be associated with lower insulin levels.

The biological mechanism is largely unknown but may well be related to altered fatty acid composition of cellular membranes which may directly affect insulin resistance. There is some suggestion in the literature of effect modification by physical activity. There have been some studies that suggest that the two factors – alteration of the composition of dietary fat and physical activity – are more than additive and the two factors may be synergistic. We examined this association ourselves in the Ely study and related fasting levels of insulin in non-glycaemic individuals who were stratified by the PS ratio in the diet and by physical activity level. We dichotomised this into high and low, but actually the measure was an objective assessment of physical activity energy expenditure by individually calibrated heart rate monitoring, so it was a careful measure of physical activity. We were able to demonstrate that there was no evidence of effect modification. This kind of study looking at the combined effects of physical effect and diet are the way forward, as we have tended to concentrate on the two factors in isolation and it is clear that from a public perspective, it is important to know how dietary and physical activity factors may combine, and whether there are any additional benefits of changing both together. There is also an important research agenda to be pursued in relation to the timing of foods and physical activity, about which we have little information at present.

If we consider carbohydrates, it can be seen that the literature on carbohydrate intake and the prevalence of metabolic syndrome is extremely sparse and there are very few studies, even fewer which are longitudinal. However, I would like to report one study, the Framingham study that was reported by Nicola Mckeown in Diabetes Care last year. She related wholegrain intake and the prevalence of the metabolic syndrome by stratifying it by the quintiles of carbohydrate source. She showed an inverse relationship which remains statistically significant after adjustment for age and sex, smoking, total energy expenditure, alcohol, proportion of saturated fat, multivitamin use and physical activity. Therefore, there was quite extensive adjustment for possible confounding factors, although, of course, residual confounding continues to be an issue, particularly for some of these difficult but important factors, such as physical activity.

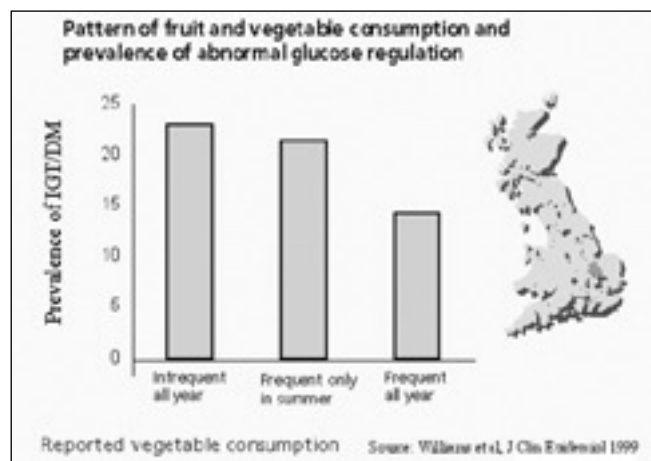
She went on to look at cereal fibre intake and the prevalence of the syndrome, and here we can see that the trend is slightly clearer and that the P value for trend is of greater statistical significance. This association survives adjustment for the same confounding factors and survives adjustment for the wholegrain intake, suggesting that the association with wholegrain intake is explained by cereal fibre. There was no association at all with total carbohydrate. This group examined the glycaemic index and the prevalence of the metabolic syndrome and demonstrated a positive association – those with the highest glycaemic index having approximately a 40% increased risk of having the metabolic syndrome after adjustment for the same factors as before. However, the confidence intervals are wide and the P value for trend is quite marginal. In this study, there was no association at all with glycaemic load rather than with glycaemic index.

I would like to move on to ask the question that I posed at the beginning of my talk, which was whether there are any disadvantages to considering studies, such as the one I have just

discussed, where the outcome is condensed into a single binary condition – the metabolic syndrome. I believe that there could be instances where a food or a nutrient could be associated with one aspect of the metabolic syndrome and not with another, and that if we only conduct studies where we condense the syndrome to a binary state, we may miss those. This may be the case for salt intake, which is clearly more closely related to hypertension than the other factors but may be related in some studies to insulin sensitivity. It may also be true for fish oil intake, which would seem to have an association with lower triglyceride, but less of an association with hyperglycaemia. It is my belief that there is an argument for looking at the elements of the syndrome in isolation and then looking at the syndrome etiologically in combination, as if we only look at one or the other we may fail to include important information.

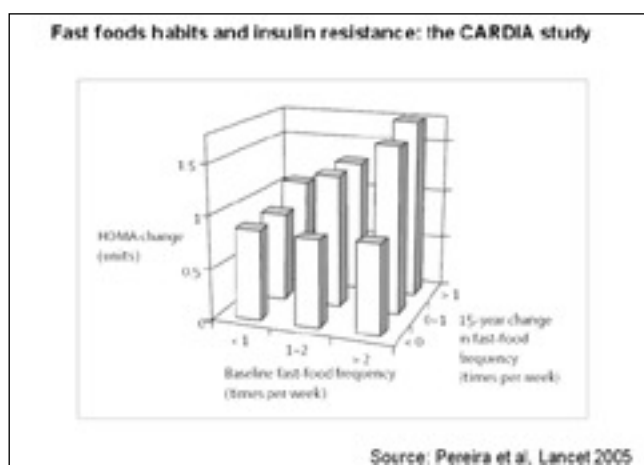
Looking at other types of foodstuff, one of the foods that has been examined is dairy intake and how it relates to dietary fibre and insulin resistance. This is one of the few longitudinal studies using more than 3 000 black and white subjects aged thirty, who have been studied for ten years in four United States' metropolitan areas. In this analysis, insulin resistance syndrome was defined as two or more of the components being abnormal: glucose homeostasis, obesity, elevated blood pressure and dyslipidaemia. What Mark Pereira and colleagues were able to demonstrate a few years ago was that compared to a reference group, who were defined as those who had high fibre intake and high dairy intake, individuals who were classified as having low fibre intake and low dairy intake had nearly a sevenfold increase in risk which survived adjustment for the factors that are listed on the right hand side of this graph. This is an intriguing observation which obviously needs to be tested in other populations. To my knowledge, there have not been any other reports of a similar nature and it may be that this is related to the calcium, magnesium or potassium intake; it could be that there is an element of alteration in satiety by the lactose, protein or fat content of dairy foods; it could be that dairy foods alter the glycaemic index; it could be that there is some compound in dairy foods that has an impact on the metabolic syndrome; or, of course, it could be the result of residual confounding. Unfortunately, observational data of this type will never resolve this issue, which can only ever be resolved by trials.

What about fresh fruit and vegetable intake, a key element of the Mediterranean diet? In the EPIC Norfolk study, we used a measure of biomarker of fresh fruit and vegetable intake and the plasma vitamin C concentration and have demonstrated that this is quite strongly inversely related to glycated haemoglobin, a measure of glycaemic control. In the Ely study, we went on to look at the pattern of reported fresh fruit and vegetable consumption and the prevalence of abnormal glucose regulation,



which suggested that those individuals who had frequent consumption throughout the entire year had the lowest risk of diabetes, and that there was an intermediate level of risk in those individuals who had frequent consumption only during the summer months. It may be that part of the association between the Mediterranean diet and disease risk is not just mediated by average consumption through the year but by whether or not there are periods where people eat that diet and periods when they do not. Therefore, examining the patterning of dietary intake of fresh fruit and vegetables is important because we tend to focus on averages rather than on seasonality.

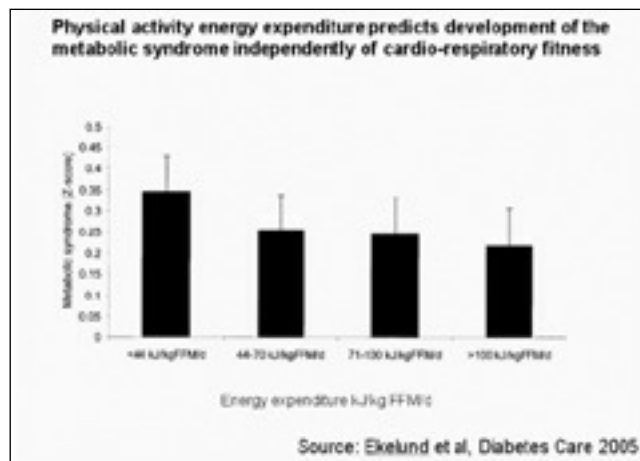
It is clear that fresh fruit and vegetable intake and the other elements of the diet that I have just described are not uncorrelated, and in the same way that others have looked at the patterning of the diet and the relationship to diabetes risk, we looked at patterning of diet in relation to previously undiagnosed diabetes and features of the metabolic syndrome five years ago. One of the principle components that emerged discriminated those who had a high fruit, salad and fish consumption and those who ate lots of fried food, sausages, potatoes and fried fish. The first component was associated with a significant reduction of the risk of undiagnosed diabetes, and that was independent of age, sex and smoking, but most importantly, of body mass index. Therefore, there may be future work to be carried out looking at the patterning of the diet in relation to the metabolic syndrome, as this is still an unexplored field. One element of the pattern of the diet is, of course, the consumption of fast foods. Earlier this year, Mark Pereira and colleagues, in the CARDIA study, looked in a longitudinal way at the baseline reported frequency of consumption of fast foods, and then the change in that reported measure of fast food consumption over fifteen years. For those individuals who had a baseline consumption of under once a week and did not change over those fifteen years, there is a marked difference in the HOMA over this fifteen year period compared to those who started with a high baseline consumption and then increased and had the highest level of HOMA, which is a measure of insulin sensitivity. This is a single study which needs to be replicated in other studies.



Now the focus of this conference is on the Mediterranean diet, and so I looked through the literature for a summary paper that might describe the association between people adhering or not adhering to the Mediterranean diet and the prevalence of metabolic syndrome. I stand to be corrected but I could only find one study, which was carried out in Greece, the ATTICA study, which looked at just over 1 000 men and 1 000 women who were over eighteen years of age and were free of cardiovascular disease and diabetes. In this study, metabolic syndrome was defined using the ATP3 criteria, and the overall prevalence was 20%. The association with the Mediterranean diet in this study was 0.81

with fairly wide confidence intervals, but it was statistically significant. The authors also demonstrated a marked association with physical activity, and noted that those in the highly physically active group had a reduction of risk of 30%. This leads one to consider whether it is possible to fully remove the effects of physical activity and residual confounding in these studies because typically it is not measured particularly well in epidemiological cohorts. This is a topic of considerable interest because we carried out a systematic review at the beginning of this year on the relationship between physical activity and insulin resistance. We identified thirty-nine cross-sectional studies in adults, thirty of which demonstrated a strong inverse association and fifteen studies in children and adolescents, seven of which demonstrated an inverse association, but of those seven, six were reporting fitness rather physical activity. Therefore, there is a real need for further work to be carried out describing the relationship between physical activity and fitness and insulin resistance in children. It should also be noted that there were only four adult prospective cohort studies, so little is known about physical activity and the development of insulin resistance in adults.

Therefore, we set out to study this several years ago in the Ely study. We have just reported our findings in Diabetes Care on the relationship between physical activity, energy expenditure and the development of metabolic syndrome, independent of factors such as obesity and cardio-respiratory fitness. Energy expenditure, here, is expressed in kilojoules per kilogram fat-free mass per day, as measured by individually calibrated heart rate monitoring. We were able to demonstrate an inverse relationship with those people who had the most everyday energy expenditure progressing least in terms of a Z score computation of the metabolic syndrome. Therefore, this provides some evidence that objectively measured energy expenditure is strongly related to the risk of the progress of the metabolic syndrome.



We also reported last year in Diabetes Care the relationship between physical activity and fitness and metabolic syndrome risk in children, demonstrating that, if you stratify those on the graph in the darker grey colour as unfit and those in the white colour who are fit, those with the highest risk are those who are both inactive and unfit. The slope of the relationship between activity and the metabolic score is steeper amongst the unfit than it is amongst the fit. This is an observation that we have also demonstrated with adults. It may be that people who are naturally fit, but not particularly active, are somehow protected from the metabolic consequences of obesity due to their fitness. It suggests that those who are really most at risk are those who are unfit and inactive. This may help us to understand the aetiology and it may also help us to understand who we need to target.

Finally, what about the prospect of studying the modulation of the relationship between diet and the metabolic syndrome by

genetic factors? The clearest example of such a study is one that has been alluded to already this morning, which is PPAR- γ a gene critically involved in the process of adipocyte differentiation. This is a very good biological target for gene-nutrient interaction, because the natural ligand is a fatty acid and the degree of affinity to the receptor is affected by the length of the fatty acid and the degree of saturation. We speculated a few years ago that there would be interaction between a common variant in this gene and the ratio of polyunsaturated to saturated fat in the diet on insulin resistance, and demonstrated here that people who are the adult carriers appear to be more responsive to change diet. Obviously, I cannot really say this because this is only observational data, but this observation has now been replicated in a number of other studies and critically in a number of other trials. Therefore, perhaps the focus for the future should be not only to look more closely at the relationship between dietary factors and the metabolic syndrome, but also how those dietary factors are modified by genes, and for the moment, it seems best to concentrate on genes that are biologically plausible, such as PPAR- γ .

Of course, one would really like to move from qualitative studies, where the outcome is a measure of insulin resistance, to more clinically meaningful outcomes, such as the incidence of type 2 diabetes. However, in order to do this, it is necessary to have very large studies tested within large cohorts, and I think

that it is only studies such as EPIC Europe, which have the size and the number of samples collected at baseline and the characterisation of diet, which will be able to study the interaction between genes like PPAR- γ , dietary factors like the ratio of polyunsaturated to saturated fat in the diet, and the incidence of clinical meaningful disease such as diabetes.

In summary, I think that this field has been somewhat bedevilled by difficulties with the diverse definitions of the syndrome. This has been aided with the important announcement of the International Diabetes Foundation definition, which correctly places obesity as a prerequisite for the condition, and then adds on the metabolic consequences. I think that whilst this is good for politics and descriptive epidemiology, we have to be careful that this does not obstruct etiological thinking and we may need to look at some individual components of the syndrome in addition. There is clearly limited prospective data and the studies that have been undertaken have been small. However, the associations are most consistent for the amount and type of dietary fat, there is some consistent data for wholegrain intake and there is some data on the pattern of diets, suggesting that the Mediterranean diet is indeed protective for this syndrome. Thank you.

As the chairman as well as the speaker, I can now take your questions.

—Questions—

Member of the audience

Thank you for that wonderful overview. I think that what is so counter-productive is the existence of the different definitions of metabolic syndrome which all emphasise different factors. Of course, we know that if a person has more risk factors, their increased risk of cardiovascular disease will increase more.

My question is that looking at these International Diabetes Foundation criteria, not only is central obesity very prominent but it has very low cut-off points. Taking our own data into consideration of people aged fifty and older, approximately 75% of them, and perhaps more, will have a waist circumference which is higher than the circumference shown on that graph. Why did they change that cut-off point?

Nick WAREHAM

I was not part of that group and I am not in a position to defend the criteria, but I believe that Jaakko Tuomilheto was. Is that correct, Jaakko? Could I suggest that you answer that question?

Jaakko TUOMILHETO

The reason for this was simply that the risks demonstrated in observational studies start at that level and this was why it was considered to be the appropriate level. Of course, many people say that this will include too many people, but the fact is that certain health risks related to diabetes start at that level and that therefore it should be considered as a cut-off point.

Nick WAREHAM

Thank you, Jaakko. Perhaps we can discuss this later but I think that it is debatable whether it is useful to define so many people as having the syndrome and I wonder whether this cut-off point should not be changed.

Member of the audience

You mentioned that the group consuming fish and fresh fruit had better health outcomes as opposed to those consuming fried foods and sugar. Do you not think that the consumption of smoked salmon and strawberries in England is a marker of social class, and that the health outcomes could be linked to financial and other resources as a result?

Nick WAREHAM

That analysis was adjusted for social class.

The previous member of the audience

It is difficult to do that because we use income and education as proxies for social class and never ask information about assets.

Nick WAREHAM

You are talking about a residual confounding by social class, which is a possibility. You are quite right.

Member of the audience

What about drugs in the treatment of the metabolic syndrome?

Nick WAREHAM

There are drugs which affect insulin sensitivity. I would have thought that one of the driving forces in having a definition of 40% of the population as having a disease is the hope of some that there may be a medical therapy for this. I personally think that this is not a very useful school of thought. It is a public health problem and we need to find public health methods of treating it, as it would be extremely difficult to medicate 40% of the population. Clearly, there is a role for drugs, but I think that we have to be very careful that the debate is not driven by the drug industry.

Member of the audience

Thank you for a wonderful presentation. If you think about the clinical aspect of this issue, it really is important for public health awareness and for politics for us to have the right numbers. The prevalence may be high, but this is not practical for clinical purposes. Is it useful to have any definition of metabolic syndrome for clinical practice?

Nick WAREHAM

I am not sure that it is very useful in clinical practice where we increasingly treat people on the basis of risk and the reduction of risk expected on the basis of therapy. We know that the relationship between many of these metabolic measures and cardiovascular risk is linear rather than curvilinear, so there is no point at which the risk is eliminated. This contrasts sharply with the risk between glycaemia and the microvascular complications of diabetes, which is flat and then increases steeply. In that instance, it is possible to identify people who are at risk and need to be treated. However, this is not the case for many of these metabolic parameters. It is not that we dichotomise into those who are and who are not at risk, some people simply are more at risk. The question is where we draw the line as to who needs treatment individually and where to say that a public health approach is needed. This is what we need to discuss and it is a question of economics.

The previous member of the audience

I have been listening to the debate so far regarding sensitivity, specificity and health economics approaches to these definitions. This needs to be done.

Nick WAREHAM

There is so little data, though. If we knew how to change the population levels of metabolic syndrome, we would not be here today.

The previous member of the audience

Of course, but if it could be done, it would reduce central obesity.

Nick WAREHAM

Yes.

Member of the audience

You mentioned that you measured fitness. What is your definition of fitness? Is it based on body mass index?

Nick WAREHAM

I should probably have mentioned earlier that the measure we used for fitness was cardio-respiratory fitness, which was assessed by sub-maximal or VO₂ max test on a treadmill as a measurement of oxygen consumption. You are right that we need to be careful to be precise when using terminology.

Diet and type 2 diabetes from observational studies

Frank HU

Department of Nutrition, Harvard School of Public Health, Boston, USA

I would like to thank the organisers for inviting me to this wonderful symposium.

I would like to start my talk by introducing the three cohort studies that we are carrying out at Harvard, because much of the data that I will be presenting today derives from these studies. These cohorts (Nurses' Health Study, Nurses' Health Study II, and Health Professionals' Follow-up Study) have followed approximately 300 000 men and women, over a period of twenty to thirty years. We have collected dietary information using validated food frequency questionnaire every two to four years, and because of the prospective design, we have the ability to look at long term dietary intake in relation to risk of type 2 diabetes in these populations. This work has established that obesity is the single most important risk factor for type 2 diabetes. Therefore, the question now is whether the association between any of the dietary factors and type 2 diabetes is independent of obesity.

I am going to talk about macronutrients first. All the analyses I mention were adjusted for body mass index, as I just mentioned, to see whether the effect of dietary factors are over and above the effects of overweight and obesity. This is an analysis that we carried out several years ago looking at the association between different types of fat and the risk of type 2 diabetes in the Nurse's Health Study. In the first model, there are four different types of fat: saturated, monounsaturated, polyunsaturated, and trans-fat. The analyses were adjusted for age, family history of diabetes, BMI, alcohol, smoking and physical activity, as well as for protein and total intake. In this kind of model, the effects of dietary fat can be interpreted as the substitution of a certain percentage of fat for the equivalent percentage of carbohydrate, because total energy and protein intakes are held constant, so all that is left out is carbohydrates.

Model	RR* (95% CI)	P-Value
Model 1		
Saturated fat (5% of E)	0.97 (0.86-1.10)	0.68
Monounsaturated fat (5% of E)	1.05 (0.91-1.20)	0.52
Polyunsaturated fat (5% of E)	0.63 (0.53-0.75)	<0.001
Trans fat (2% of E)	1.39 (1.25-1.67)	0.0006
Model 2		
Animal fat (5% of E)	0.98 (0.95-1.02)	0.35
Vegetable fat (5% of E)	0.79 (0.74-0.84)	<0.001
Model 3		
Total fat (5% of E)	0.98 (0.94-1.02)	0.24

Adjusted for age, family history, BMI, alcohol, PA, protein, total energy intake

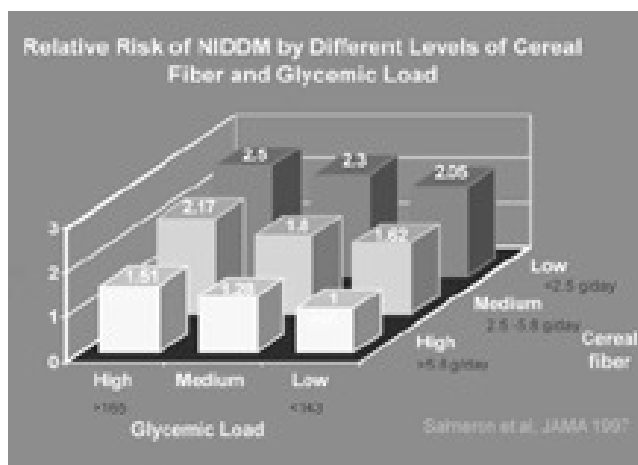
Salmanson et al. AJCN 2001

When we compared different types of fats with carbohydrates – of course, most of the carbohydrates in American diets are refined carbohydrates – saturated and monounsaturated fat were not associated with an increased risk of type 2 diabetes. This is not surprising because refined carbohydrate is a risk factor for diabetes. However, polyunsaturated fat was significantly associated with a decreased risk whereas trans-fat was associated with an increased risk. Consistent with the polyunsaturated fat

results, vegetable fat is significantly associated with a lower risk of diabetes. However, when we looked at the total amount of fat in the diet, after adjusting BMI and other risk factors, there was no appreciable association between total fat and the risk of type 2 diabetes.

Now I will discuss the role of carbohydrates. The conventional wisdom based on the chemical structure of carbohydrates is that simple carbohydrates are bad and complex carbohydrates are good. However, we know that in the case of many refined carbohydrates, particularly refined starch from white bread, digestion occurs far more quickly than for some of the simple sugars. The new classification places more emphasis on the biological effects of whole food, using the glycaemic index, glycaemic load, and whole grains vs. refined grains.

As you know, the concept of glycaemic index is complex and is still controversial. Some people completely embrace the glycaemic index and use it as the only yardstick to classify good versus bad foods, which can be very misleading; there are others who completely dismiss this concept, which is also not consistent with the evidence that we have. In our cohorts, we found a strong association between the glycaemic index and the glycaemic load and a risk of type 2 diabetes and coronary heart disease. The glycaemic load represents both the quantity and quality of carbohydrates, and in this analysis we found a significant association between increase in glycaemic load and the risk of type 2 diabetes independent of cereal fibre. As expected, those who eat a very high glycaemic load diet with very small amounts of cereal fibre have the highest risk of developing diabetes.

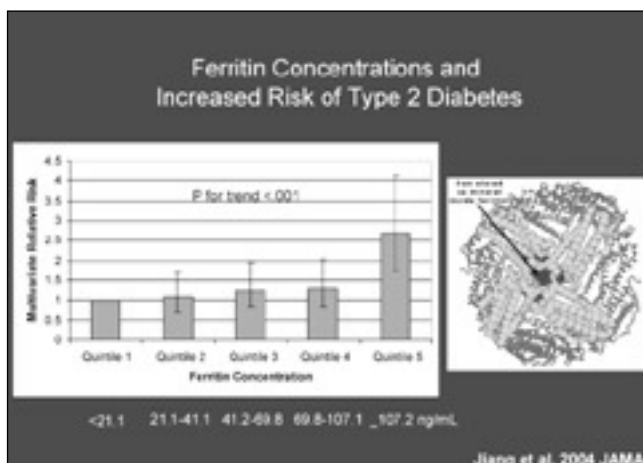


The relationship between omega-3 fatty acids and diabetes is unsettled. Animal studies have shown that long-chain omega-3 fatty acids improve insulin sensitivity, and cross-sectional studies have shown a positive association between long-chain omega-3 fatty acids in muscle cell membranes and insulin sensitivity. However, prospective epidemiological studies have not found an association between fish consumption and risk of type 2 diabetes. There was a modest inverse association between omega-3 fatty acid consumption and type 2 diabetes in the Nurses' Health Study, but after adjusting for BMI and other risk factors, this association completely disappeared.

I would like to move on to discuss micronutrients, especially chromium, magnesium and iron. In a recent study published in *Diabetes Care*, we looked at the mean chromium concentration in toenails for the three groups (healthy subjects, diabetic patients without cardiovascular disease, and diabetic patients with cardiovascular disease). The reason why we wanted to measure chromium concentration in toenails was that it is not possible to measure dietary chromium consumption as the variability is so great across different foods, whereas the chromium concentration in toenails could reflect long term intake of chromium. In this analysis, we found that people with diabetes had significantly reduced chromium levels compared to healthy controls and that people with diabetes and cardiovascular disease had further decreased chromium concentration. This does not prove a causal relationship, but several clinical trials have shown beneficial effects of chromium supplementation on insulin sensitivity and cardiovascular risk factors. However, I do not think that we have enough evidence to recommend regular chromium supplementation as a preventive strategy for diabetes at this point. There are several important dietary sources of chromium including whole grains, nuts, green leafy vegetables and coffee, all of which have all been associated with a decreased risk of diabetes.

There are more epidemiological studies on magnesium than on chromium in relation to the risk of type 2 diabetes. The results are generally consistent and several large studies, including ours, have found an association between increasing magnesium consumption and a reduced risk of diabetes. Like chromium, magnesium is an important co-factor for the insulin signalling pathway. People who eat large quantities of refined carbohydrate sugar need more chromium and magnesium to process the sugar. Unfortunately, the intake of these micronutrients is actually decreased during the refining process.

Iron and diabetes has become a very interesting area of research. Several years ago, a very small Finnish study found a positive association between ferritin concentration and the risk of type 2 diabetes. Last year, we published a paper with almost 800 cases and more than 1 000 controls, in which we found a positive significant association between ferritin concentration and the risk of type 2 diabetes. I would like to point out that the ferritin concentration for the vast majority of subjects was within the normal range. It is known that people hereditary haemochromatosis have extremely high ferritin levels and most of them will eventually develop diabetes. As for mechanism, iron is a catalyst for the formation of free radicals in the body, so the increased diabetes risk may be due to the increased oxidative stress.

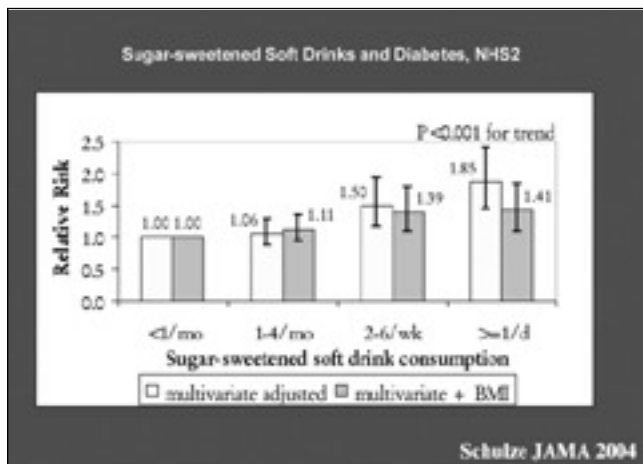


We proceeded to look at dietary intake of iron and the risk of diabetes and in these analyses, we specifically focused on heme iron, which comes from animal products, especially red and processed meat. Heme iron is a very important dietary determinant of ferritin levels. We found a very striking positive association between higher heme iron intake and the risk of diabetes, even after adjusting for red meat and processed meat, suggesting that this association is not explained by other components in those meats. What is interesting is that the association between dietary iron and diabetes may be modified by the HFE genotypes. We found that the association between heme iron and diabetes was only present among those who carry either C282Y or H63D variant genotypes, but not among those who carry the wild genotypes. This is biologically plausible because if a person eats large quantities of iron and also has the genotypes that facilitate iron absorption, the combination puts this person at a very high risk of developing diabetes.

I shall now address the subject of foods and food patterns. As many of you are aware, there has been very consistent observational data, mostly prospective studies, between nut consumption and coronary heart disease. At least five large cohort studies have found a strong inverse association between nut consumption and the risk of coronary heart disease. Metabolic trials have also found that increasing nut consumption reduced total and LDL cholesterol. In addition, we found that higher nut consumption was associated with a decreased risk of diabetes. What is interesting is that this association is actually independent of body mass index. We found an inverse association across different categories of BMI – even for those who were overweight and obese, higher nut consumption is associated with a reduced risk of type 2 diabetes. One of major concerns about increasing nut consumption is weight gain because it is a high fat food. However, we did not find increased weight gain with higher nut consumption. In fact, there seemed to be an inverse association, and several other studies have also found an inverse association between nut consumption and body mass index. We know that although nuts contain a large amount of fat, they consist mostly of good fats: monounsaturated and polyunsaturated fats. Even peanuts, whilst technically not a nut but a legume, have a similar fatty acid profile as other types of nuts, and the nutrient profile of peanut butter is no different from peanuts. These results provide further evidence that the type or quality of fat is more important than the total amount of fat in determining the risk of diabetes and coronary heart disease.

The evidence for whole grains is also very consistent. Several prospective studies over the last few years have demonstrated that a higher consumption of whole grains reduces the risk of type 2 diabetes and cardiovascular disease.

Higher consumption of sugar-sweetened soft drinks has been associated with increased obesity in children. In the study published recently in *JAMA*, we looked prospectively at the relationship between soft drinks and type 2 diabetes in the Nurses' Health Study II. It can be seen that those who consumed at least one can of sugar-sweetened soft drinks per day had an 80% increased risk of developing diabetes compared to those who rarely consumed soft drinks. What is interesting is that the association remained significant even after adjusting for body mass index, although it was somewhat attenuated. This result suggests that the association between soft drinks and diabetes is not entirely mediated through overweight and obesity.



There has been consistent epidemiological data on the protective effects of coffee on type 2 diabetes. The first study was conducted in a Dutch cohort, followed by at least eight cohort studies from the United States of America and Scandinavian countries. Most of these cohort studies have demonstrated that higher coffee consumption is associated with lower risk of type 2 diabetes, in both men and women. Compared to the lowest category (<math><2</math> cups/day), the risk reduction is approximately 35% in the highest category (7 to 8 cups per day in European studies, and approximately 5 to 6 cups per day in the American studies). At the moment, we still are unsure as to which components of coffee are responsible for the risk reduction; it could be caffeine or the very high amount of antioxidants, especially chlorogenic acid or, as I mentioned earlier, coffee also contains high amounts of chromium and magnesium.

The data on alcohol and type 2 diabetes has also been extremely consistent. There is a protective effect amongst moderate alcohol drinkers – consuming 5 grams to less than 3 drinks per day is associated with 30% lower risk of type 2 diabetes. However, if a person drinks more than 3 drinks per day, the risk actually increases.

There has also been consistent data on the consumption of processed meats and the risk of type 2 diabetes. Processed meats include hot dogs, bacon and hamburgers. In our cohorts and also in a few other studies, higher consumption of processed meats, once a day for example, is associated with a 40 to 50% increased risk of type 2 diabetes. Processed meats are also associated with other unhealthy diet and lifestyle factors, which could confound the results. However, when adjusted for the Western dietary pattern, the association still remains.

Recently, we found a significant decreased risk of diabetes with higher dairy consumption. Most of the protection comes from low fat and non-fat dairy products. We found no association between high fat dairy products and a risk of type 2 diabetes. As Nick Wareham has mentioned, we still do not know which component of dairy products contributes to decreased insulin resistance or type 2 diabetes. The public health implications of these findings are not clear: although dairy products may have beneficial effects on insulin resistance, hypertension, or type 2 diabetes, they may also have detrimental effects in terms of sex hormone-related cancers. Therefore, we need to be very careful in recommending high amounts of dairy to prevent diabetes.

To look at the cumulative effects of the different foods and food groups, we used principle component analysis or factor analysis, as Nick Wareham mentioned, to define the dietary patterns. In our cohorts, we have identified two major patterns: one is the 'prudent pattern', and the other is the 'Western pattern'. The prudent pattern is characterised by fruits and vegetables, legumes, fish, seafood and whole grains, whereas the Western pattern is characterized by red meat, processed meat, potatoes, French fries, butter, refined grains and high fat dairy. We created two factor scores for each individual in the cohort, and then looked at the factor scores in relation to different disease outcomes. For type 2 diabetes, we found a clear positive association between the Western dietary pattern and the risk of diabetes, and this finding is consistent with the results for individual foods and individual nutrients. For the prudent pattern, the association was not very clear: there was a slight inverse association but the trend was not statistically significant. The prudent pattern is much more protective for other outcomes such as coronary heart disease and colorectal cancer. The Western pattern also increased the risk of colorectal cancer and coronary heart disease.

To summarise our findings regarding dietary factors and type 2 diabetes, I think that we are now in a better position to understand the protective factors as well as risk factors based on the results from multiple prospective epidemiological studies. There is good evidence that higher consumption of refined carbohydrates reflected by a higher glycaemic index, glycaemic load or refined grain products, is associated with increased risk of diabetes. Trans fat is a risk factor for insulin resistance, metabolic syndrome and type 2 diabetes. Saturated fat is more complicated: if you compare saturated fat with refined carbohydrates, both are bad and as a result, it would be difficult to notice any real difference. However, a comparison of saturated and polyunsaturated fat demonstrates an increased risk of diabetes with higher consumption of saturated fat. Therefore, from a public health point of view, we need to recommend a reduction in saturated fat, replaced by unsaturated fatty acids. As I have mentioned, there is now quite strong evidence that processed meat is a risk factor for diabetes. There is also strong evidence for the so-called 'protective factors' such as polyunsaturated fat, cereal fibre and whole grains. The results for omega-3 fatty acids are less clear. The results for nuts, peanut butter and coffee are very intriguing and they need to be studied further, especially in metabolic studies. The evidence for alcohol is overwhelming so I do not wish to elaborate on that point further. I think there is a very complex public health message for dairy, but it is important for us to understand which dairy components or substances contribute to a decreased risk in type 2 diabetes.

What do we go from here? Clearly, we need replications from other cohort studies. We already have very good replications for whole grains and for coffee, but we need more replications for dairy. These results from epidemiological studies should inspire more metabolic studies of individual dietary components and the risk of insulin sensitivity. We need to understand the mechanisms behind the association between certain dietary factors and the risk of type 2 diabetes. Ideally, we should conduct randomised trials using diabetes as end-point for all dietary components that I have just mentioned. However, this would probably not be feasible due to lack of compliance and perhaps also ethical issues, unless there were a supplement or a pill. Therefore, at this point, we probably have to rely on the consistency of the epidemiological studies and the results from metabolic studies to evaluate the casual relationships between dietary factors and type 2 diabetes. Thank you very much.

Questions

Member of the audience

Thank you for this overview. Could I ask whether you have any data on tea consumption?

Frank HU

We did look at tea consumption and the risk of diabetes but we did not find any association. The amount of caffeine and antioxidants in tea is far lower than in coffee. The reason that coffee has a very strong taste and flavour from coffee is due to the fact that there is a very high amount of antioxidants, especially chlorogenic acid.

Member of the audience

What about polyphenols, polyphenolics and antioxidants?

Frank HU

We were not able to look at individual polyphenols. It is not possible to differentiate the individual components within the products.

Edith FESKENS

In relation to alcohol, I think that you are right in concluding that moderate amounts are protective and this has been shown in many studies, but given the Mediterranean focus of this conference, were you able to look at the different types of alcoholic drinks?

Frank HU

We did look at this. The results were similar to those for coronary heart disease. The beneficial effects on diabetes are due to the alcohol itself rather than other components of the beverages. Basically, our data do not reveal any significant differences according to different types of alcoholic drinks.

Edith FESKENS

I see. Then that would also refer to the polyphenol question. With regard to the dietary cholesterol which was on your list for risk factors and which I found myself in studies almost ten years ago, you did not explain this. I never reached a satisfactory conclusion on this point and I am interested to know what your thoughts are on this issue.

Frank HU

It is ironic that cholesterol turns out to be a stronger risk factor for diabetes than for coronary heart disease. The results are consistent across our own cohorts and several other studies in showing that higher consumption of cholesterol is a risk factor for type 2 diabetes and for insulin resistance. However, I do not know what the underlying mechanism is. There is speculation that it may work through ApoCIII, because people with underlying insulin resistance have a defect in ApoCIII so that they have compromised ability to clear cholesterol from the body.

Dietary interventions and the metabolic syndrome

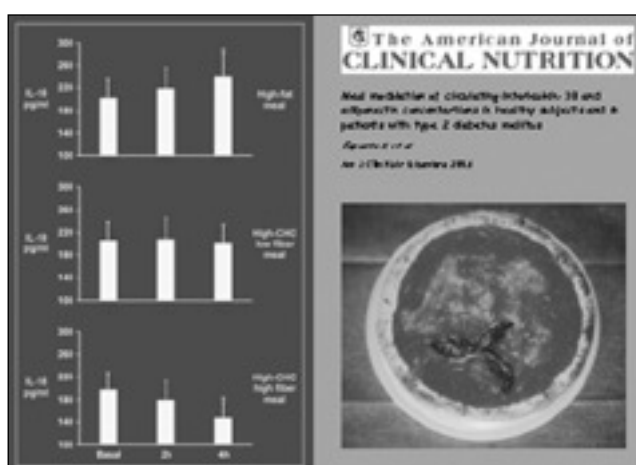
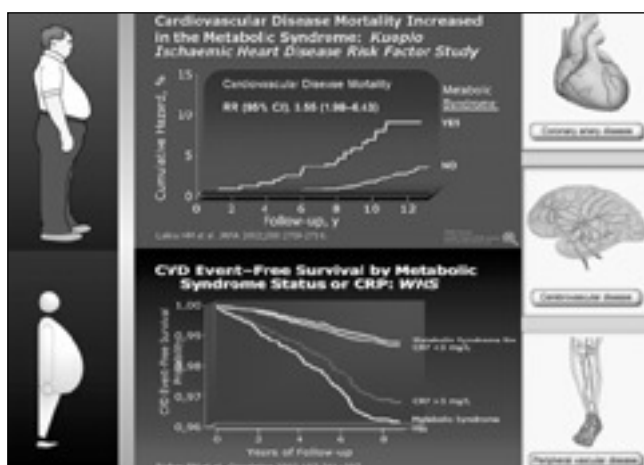
Dario GIUGLIANO

Second University of Naples, Chair and Division of Metabolic Diseases, Department of Geriatrics and Metabolic Diseases, Naples, Italy

Good morning, bonjour! Thank you very much, Nick, for inviting me to attend this exciting symposium. The subject of my presentation is dietary intervention and the metabolic syndrome. First of all, I would like to begin by stating the obvious. It is obvious that during the last twenty years, there has been a decrease in coronary artery events among the population. A study from England and Wales showed a 70% decrease in coronary heart disease mortality; at the same time, there was a correlating increase in diabetes and obesity that augment the risk of coronary heart disease. This is particularly important because both obesity and diabetes are pathological conditions included in the diagnosis of the metabolic syndrome.

resistance and endothelial dysfunction, leads to diabetes, the metabolic syndrome and atherosclerosis. This is a working hypothesis, which is supported by several clinical and epidemiological studies.

Inflammation is now regarded as a link for many chronic diseases such as cancer, heart disease, and also for neurological diseases, such as Alzheimer's disease. However, my speech is about diet. Unhealthy diets may play an important role in increasing the incidence of chronic and metabolic diseases through the production of free radicals, oxidative stress and inflammation.



Prospective epidemiological studies have demonstrated that people with the metabolic syndrome have an increasing relative risk of cardiovascular disease. These observations mainly come from two studies – one Finnish and one American. They show a three times greater risk of developing cardiovascular disease mortality and a cardiovascular event. In Italy, the prevalence of the metabolic syndrome amongst adults is about 23%, very close to the prevalence of 24% reported in the U.S. applying the criteria of adults treatment panel III (ATP III). It is important to recognise that people with the metabolic syndrome have an association not only with classic risk factors, but also with emerging risk factors. For example, in 180 patients with metabolic syndrome, we found with the increase of components of metabolic syndrome, a parallel decrease in insulin sensitivity and endothelial function – and endothelial dysfunction is one of the first signs of atherosclerosis – associated with an increase of inflammatory burden. Therefore, insulin resistance, inflammation and endothelial dysfunction go hand-in-hand in these persons.

We have also shown a decrease of anti-inflammatory potential in people with the metabolic syndrome. Interleukin 10 is a cytokine which has a central anti-inflammatory activity: people with the metabolic syndrome, irrespective of whether or not they are obese, have lower circulating levels of interleukin 10. The working hypothesis we developed claims for the presence of an imbalance between pro-inflammatory cytokines (IL-6, IL-18, TNF- α), and anti-inflammatory cytokines (adiponectin and interleukin 10), the two anti-inflammatory cytokines, facilitating the generation of a pro-inflammatory milieu that, through insulin

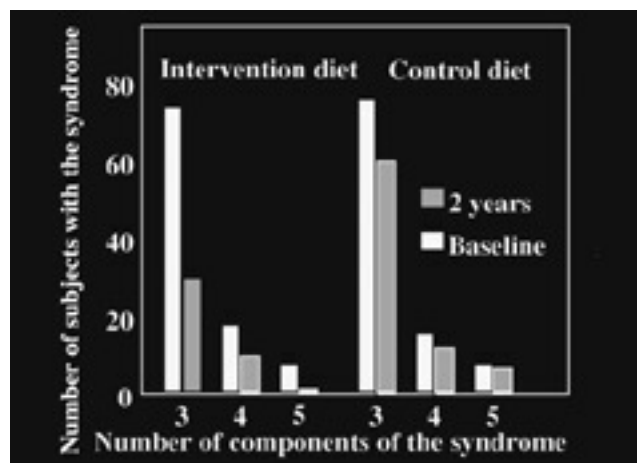
We compared two isocaloric meals, one high-fat, continental meal and one high-carbohydrate meal. Being a Neapolitan, I chose pizza. These two isocaloric meals contain approximately 750 calories. When a normal person eats pizza, there is no change in glucose and triglyceride levels, but when the same subject eats a high-fat meal, its triglycerides go on the raise. These responses are amplified in the diabetic patient who presents rapid and prolonged swings of glucose and triglyceride levels after both meals. In both normal people eating the high-fat meal, and diabetic people eating both meals, we observed circulating markers of endothelial activation, such as adhesion molecules, and inflammation, such as tumour necrosis factor, and interleukin 6, going on the raise. Depending on what one eats, endothelium does not work well during the postprandial phase, which lasts four to six hours. We also compared high-fat meals, with and without antioxidant-rich foods: the addition of natural food or antioxidant-rich foods was able to smooth the adverse effects of the high-fat meal on the endothelium.

The type of carbohydrate is also important. We compared the effects of two types of pizza: a refined-grain pizza, and a whole-grain pizza. The high carbohydrate, low-fibre meal did not change the circulating level of interleukin 18, which is involved in plaque destabilization and coronary heart events; however, increasing the amount of fibre in the meal (high-carbohydrate, high-fibre meal) was associated with reduced levels of IL-18. Thus, it is possible to modulate inflammation through appropriate foods.

It is important to recognise that the postprandial phase is important because an increase in glucose and lipids can produce a stress to our endothelia through many mechanisms, including activation of protein kinase C, protein glycation, oxidative stress, and so on. We have provided evidence that hyperglycaemic spikes may be proinflammatory. In normal people, when a hyperglycaemic clamp is introduced, i.e. when the plasma concentration of glucose is acutely increased with exogenous glucose infusions, the level of some proinflammatory cytokines, such as interleukin 6 and tumour necrosis factor- α , increased. These hyperglycaemic spikes are similar to that occurring in type 2 diabetes after a meal. Moreover, the increase in tumour necrosis factor- α and the decrease in endothelial functions are strictly correlated, providing a mechanistic explanation for the deleterious effects of foods on vessels. So, a diet rich in fat (saturated or trans-fat), and rapidly-absorbed glucose, especially when associated with the lack of natural antioxidants, may produce some mechanisms that are linked to the occurrence of atherosclerosis.

However, I wish to move on to show you the results of an intervention study with people with metabolic syndrome. We compared the effect of two different types of diet in people with metabolic syndrome. People were chosen when having at least three criteria from the adult treatment panel tree for out-patients population. The first 90 people ate a control diet containing less than 30% of energy from fat, less than 10% of energy from saturated fat, and less than 300 milligrams of cholesterol. For the intervention studies, people were recommended to increase their intake of fruits and vegetables, nuts, and whole grain. After two years of observation, there was a difference between the intervention diet and the control diet. There was an increase in fibre intake in patients of the intervention study, a decrease in saturated fat, an increase in monounsaturated fat, a decrease in omega 3 and omega 6 fatty acids ratio, an increase in consumption of fruit, vegetables, nuts and legumes, olive oil and whole grains.

Concerning the effect on the biochemical parameters, there was a decrease in triglycerides and total cholesterol, associated with an increase in HDL cholesterol. Blood pressure also decreased. C-reactive protein, which is a sensitive marker of inflammation decreased by 1 mg/dl. C-reactive protein has been considered a marker of inflammation to date. However, we have enough evidence to suggest that C-reactive protein may be a mediator of inflammation. The most important finding, at least in the clinical setting, was that the prevalence of metabolic syndrome in those patients with 3, 4 or 5 components of the syndrome was reduced by about one half by the end of the study: about 45 patients did



not have the features of metabolic syndrome at the end of the experiment. Therefore, this study may be seen as a prevention of later diabetes.

To summarise, diets that favour large increases in postprandial glucose, free fatty acids and triglycerides, raise the inflammatory burden, which in turn may increase the risk of the metabolic syndrome, type 2 diabetes, and atherosclerosis. This seems particularly important if one take into account the following percentages are alarming: two-thirds of American adults are overweight; more than 30% are obese; almost 8% are diabetic; nearly 25% have metabolic syndrome; and almost 45% of women and 30% of men are seeking to lose weight each year.

Speaking about the Mediterranean diet, three scientific organisations – the American Cancer Society, the American Diabetes Association and the American Heart Association – used a few words in issuing their general prevention guidelines for adults to eat at least five servings of fruit and vegetables per day. Is this enough? The recommended six servings in Denmark may be a better goal.

In relation to the history of the Mediterranean diet, grain, oil and wine are considered to be important foods. Burned foods found in Pompeii include nuts, bread, vegetables and lentils, olives, and, as we can see from the famous fresco, wine. Finally, a last word for Ancel Keys, perhaps the father of the Mediterranean diet, who left us in 2004, as a centenarian. A living museum of the Mediterranean diet has been dedicated to his memory in Pioppi, South Italy. Thank you very much.

Questions

Member of the audience

With respect to the statistics that you gave for the American population, do you have similar data for Italians?

Dario GIUGLIANO

Prevalence of obesity and overweight is quite similar in Italy as for the United States and is rising. I used the United States data because I had more recent data and also because the quantity of people affected is greater. In Italy, the prevalence of the metabolic syndrome is circa 23% of the adult population.

Member of the audience

Often quoted, the Mediterranean diet is a healthy diet. With regard to the dairy products, it is difficult to believe that the Cretan, or the Mediterranean, do not eat milk and goat's milk cheese. The children consume a great quantity of milk. There are certainly studies on the biological and biochemical composition of various fresh milks and out of powder. Could you make a comment on this point?

Dario GIUGLIANO

The speaker was asking about goat dairy products. I do not really have any experience with relation to such products. However, the most fitting adjective I have found for the Mediterranean diet is 'frugal', because the Mediterranean diet was a frugal diet and 'frugal' comes from the Latin word frugis, which means 'product of the heart'. It is very important to recognise that the products of the heart are vegetables, fruits and grain. However, 'frugal' is not a word that is fitting with our society today.

Member of the audience

I am grateful that you put forward the inflammatory factors in obesity, metabolic syndrome and cardiovascular disease, but would you agree that it is a vicious circle in the sense that all of these processes also increase inflammation? We could say the same perhaps for the process of antioxidant status: if there is a lack of antioxidant intake, these processes are favoured, but having more fat would also trap more vitamin and soluble antioxidants, so it is an auto-aggravating situation.

Dario GIUGLIANO

In my view, inflammation is the key point. Inflammation may be a key point in our understanding of the relationship between the diet and some of the effects that you mentioned. I should like to stress that we do not know what triggers the whole process: perhaps it is the obesity; perhaps it is the diet, or the ingestion or consumption of macronutrients which may be responsible for the obesity, for insulin resistance and endothelial dysfunction, which are the precursors for type 2 diabetes, atherogenesis and so on. Therefore, the theory that I have presented claims that the macronutrients that we eat every day and the food choices that we make are important in the future of our vessels.

Member of the audience

I just wanted to try to answer the question about goat dairy products. There is some data that suggests the fatty acid content of goat's milk and cheese could be somewhat different from cow's milk and cheese, especially in the content of omega 3 fatty acid that could be higher.

Dietary interventions and risk of type 2 diabetes

Jaakko TUOMILHETO

National Public Health Institute, Diabetes and Genetic Epidemiology Unit, Department of Epidemiology and Health Promotion, Helsinki, Finland

Thank you very much, Nick. Ladies and gentlemen, I am extremely grateful to have been invited here. It is always a pleasure to come from cold Finland to the South, not only for reasons of food but also the climate.

In my presentation I will concentrate on preventive aspects of type 2 diabetes. We have heard much about the observational data, the risks and the benefits of various dietary components in relation to type 2 diabetes. Type 2 diabetes is a disease which has a very strong genetic component. Most people carry genes that permit type 2 diabetes to develop. The lifetime risk in the European population is circa 50%, and many more people have milder forms of hyperglycaemia during their lifetime. Of course, what is important is that this genetic susceptibility can be modified by lifestyle and that we can identify individuals who are in the process of developing diabetes and who have impaired glucose tolerance, which is in the middle of the process between normal glycaemia to type 2 diabetes. We have already heard about lifestyle-related risk factors and these operate in different ways: I shall talk briefly about this. Most of my presentation will focus on the data from our randomised controlled trial, 'Finnish Diabetes Prevention Study', which was published a few years ago. Today I will present not only those but also new data.

The aim of the study was to determine whether we could, using a lifestyle intervention, prevent or delay the development of type 2 diabetes in middle aged people who had impaired glucose tolerance and who were obese. We randomised individuals either to a standard reference group, which received some advice as to how to reduce health risks, or to another group, which received intensive lifestyle intervention.

Why did we carry out such a study in Finland? Finland is a country which is located in the north. Quite recently, there was a reference to the Finnish lifestyle in 'Science', and as you may read, the diet consumed by Finland in the past was certainly not a Mediterranean one.

In the study population, the selection criteria were middle-aged individuals, with an average bodyweight of 90 kilos, an average waist circumference of 100 cm or more, and elevated two hour glucose, and if we use the metabolic syndrome classification based on the previous American National Cholesterol Education Program Adult Treatment Panel III, about 75% of the individuals had metabolic syndrome.

According to the baseline data regarding diet: these individuals at high risk of type 2 diabetes consumed less carbohydrates than recommended; fat intake was higher and dietary fibre intake was lower than recommended; physical activity were low, much lower than recommended for a healthy lifestyle. Therefore, it is no wonder that these individuals had impaired glucose tolerance.

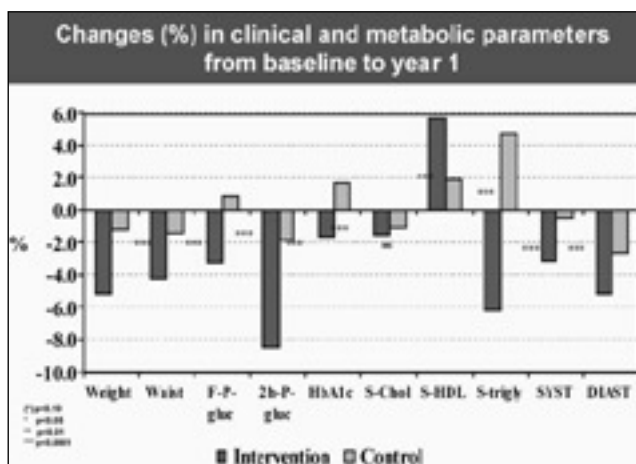
The five main aims of the intervention in the intervention group of the Finnish Diabetes Prevention Study were: to reduce bodyweight, reduce fat intake, change the type of fat that people were eating, increase the dietary fibre intake to at least 15 grams per 1 000 kilocalories, and to introduce half an hour of exercise, which could be aerobic or muscle-strengthening.

How did we try to reach these intervention goals? By way of example, for the reduction of overweight, there were several

strategies used in the intervention. The key people administering the intervention in five clinics that we had were dietitians or nutritionists, and there was also a study nurse and a physician meeting individuals at least once a year, but the dietician was the main interface for the intervention. With regard to the change in saturated fat intake, we tried to increase the non-fat dairy products and substitute them for the high fat products, along with the other initiatives. In relation to total fat intake, we promoted Finnish rapeseed oil, which has similar content than olive oil, but is locally made, and we also encouraged fish consumption. In terms of fibre intake, bread (mostly rye) is the most important source of dietary fibre in Finland, constituting circa 40% of dietary fibre consumption, although we also consume large quantities of oats, porridge and other similar products. We also promoted the consumption of fruit, berries and vegetables.

The physical activity programme was based on promoting everyday life physical activities which do not require extra time but which can be fitted in with peoples' lifestyles, including dancing. We also provided the opportunity to use a gymnasium with a supervised resistance-training programme for free, which was used by most people.

The intervention strategy was to achieve as much as we could during the first year, and to maintain the new habits for the following years. It can be seen that we achieved statistically significant changes in fat intake, total fat, saturated fat and in dietary fibre. The protein intake increased slightly and this was due to the fact that fat intake was reduced, so people obviously ate higher protein foods and meats. Vigorous physical activity increased more in the intervention group. It can be seen that the control group, who received health leaflets and related general information, also changed to some extent. As a result of changes in diet and physical activity, in all the components or the parameters of the metabolic syndrome improved, especially the two hour postprandial glucose level, which was reduced by 8%. Also, bodyweight decreased by circa 4 kilos and waist circumference decreased by circa 4cm. Triglycerides and HDL cholesterol also showed favourable changes. Thus all components of the metabolic syndrome improved. Changes in bodyweight resulted in expected changes in blood pressure: a loss in bodyweight of 1 kilo usually corresponds to a change by 1 mm Hg change in systolic blood pressure.



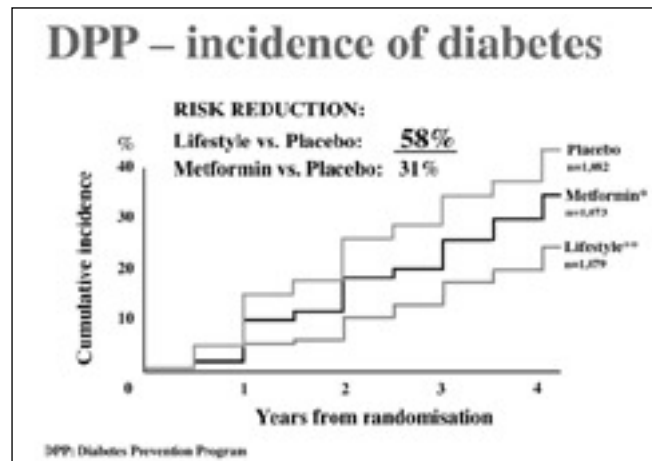
Correlations between the changes in weight and waist circumference with the metabolic parameters were not high, the highest correlations being 0.3. Therefore, lifestyle intervention comprised factors other than reduction in weight and waist circumference alone which also contributed to the changes in the glucose, lipids and blood pressure. The correlations between weight changes and dietary changes are not extremely high at circa 0.15 and 0.02, but are still statistically very significant. The risk of diabetes depended on the bodyweight change: in the individuals who gained weight by more than 1%, the risk over a three-year period was doubled compared to those whose weight did not change at all. Those who reduced bodyweight by more than 7% had a 75% to 80% lower risk of diabetes than those individuals whose weight did not change. This is in keeping with findings from earlier observational studies. Weight control is extremely powerful for the risk of diabetes and its prevention.

What about the other factors? In relation to dietary fibre, even though we only had approximately 500 individuals in the study, we were able to show that the higher the intake of dietary fibre, the more positive the outcome was, and it was highly statistically significant. Total fat intake also demonstrated a highly statistically significant increase in the risk of diabetes in those people who ate large quantities of fat, particularly saturated fat. When we combined fat and dietary fibre, it was interesting to observe that in comparison with individuals with both a low fat high fibre diet, those with a low fat diet but a low fibre intake had an increased risk of diabetes by almost 50%.

It seems that fat intake is a very important determinant of diabetes, and moreover, it seems that if we combine high fat intake with a low fibre intake, the risk of type 2 diabetes is the lowest. There is a difficulty to distinguish between the people who change their dietary fat intake from those who increase their dietary fibre intake, since usually when fat intake increases fibre intake decreases and vice versa, and therefore it is quite difficult to isolate independent effects of these dietary changes.

Baseline variables, such as body mass index, influenced the benefit of the intervention. Those with the lowest body mass index of circa 29, had a 70% benefit from the intervention, whereas there was a 40% reduction in the risk of diabetes in the most obese subjects in the intervention group compared to the control group. Therefore, the message is that it is important to begin risk modification as early as possible; the earlier a person starts, the better the benefits.

Weight change is important but when people are losing weight it is for a reason: either they are consuming more energy or they eat less. There was a clear correlation in this intervention study: the more that people exercised, the more bodyweight changed. Therefore, it is very difficult to state which component of this kind of multifactorial lifestyle intervention is producing its beneficial effects. With regard to the targets that we had for the individuals, it is important to realise that a lifestyle intervention must be a total package. Some individuals have more difficulties with certain components of these lifestyle issues than others and therefore the intervention strategies have to be modified on an individual basis. However, it was interesting to observe that amongst the individuals who achieved four or all five of the targets for lifestyle intervention, none developed diabetes: there was 100% protection where the intervention was followed properly. Therefore, we can conclude that lifestyle intervention in the prevention of diabetes is extremely powerful if carried out properly. Had we not intervened and if all five targets had not been pursued, circa 35% of high-risk individuals would have become diabetic over a three-year period.



There was a diabetes prevention programme (DPP) going on at the same time in the United States, but it started a few years later. We had similar study protocols for lifestyle because when we designed our protocols in Finland, we had a consultant from the United States (Dr. W.C. Knowler). Thus, our protocol was available to the investigators in United States and as a result, we were fortunate enough to have two studies with a similar design, although implemented differently and in different countries. The DPP revealed the same reduction in risk of diabetes as we observed in Finland: 58% relative risk reduction. In addition to lifestyle intervention the DPP also used metformin in a separate arm, a drug that lowers blood glucose; metformin resulted in a circa 30% risk reduction. In the DPP, all ethnic groups benefited similarly from the interventions, whether in the form of a drug or a lifestyle intervention.

There was also an earlier study in China, in Da Qing city, which also showed a 40-50% reduction in the risk of diabetes using lifestyle intervention. This was not an individually randomised study, although the clinics were randomised, and as a result there were some doubts as to the viability of the data. In Sweden, lifestyle intervention also seemed to work with a 50 to 60% reduction in the risk of diabetes, but there were some problems with the follow-up of these individuals and the compliance between the different individuals. There was also another Swedish intervention study, which showed a 50% reduction in the risk of diabetes with diet and exercise, but there was no individual randomisation as people could choose whether or not to join lifestyle intervention.

Let us examine the dietary changes in the US DPP, where the results were similar to ours. In general, the energy intake reduced for the intervention group. There was also a fall in body weight in the control group. Interestingly, also in the metformin group, body weight was reduced significantly. It was interesting to note that in the DPP, even though there was a significant difference in the change in dietary fibre between groups, there was hardly any increase in dietary fibre in the intervention group, but a decrease in the control group: this is quite revealing in terms of dietary patterns in America.

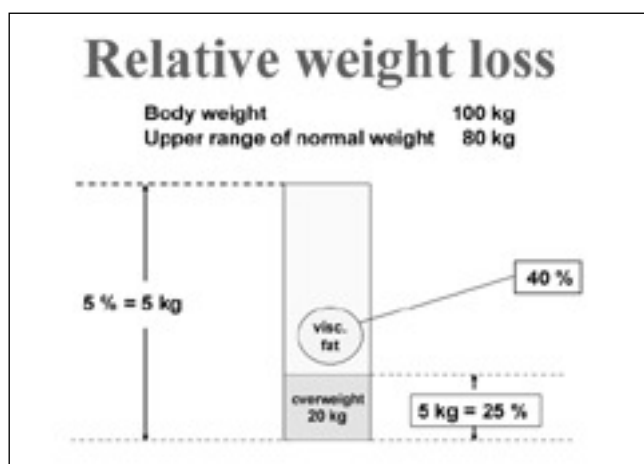
In terms of food item changes in the DPP, the main change for the lifestyle intervention group was the reduction of sweets. There was also a reduction in grains, although this may be due to the lack of non-sweet bread in the United States and the proliferation of sweet buns and rolls, which were not to be consumed in the lifestyle change intervention.

Glucose levels vary during the day. In the individuals with impaired glucose tolerance (IGT), the postprandial glucose levels were particularly elevated and fasting glucose levels were usually normal. Using continuous glucose monitoring, we tried

to evaluate the changes in glucose levels during the day using a glucose monitor which measures during three days glucose in peripheral tissue every three minutes, and then presenting it in graph form. We took the individuals from the DPS and provided them diet with a high or low glycaemic index. After the randomised trial period, we invited people to join this glucose monitoring study, and more than 70 people participated. With the high glycaemic diet in these with IGT glucose levels increased after breakfast at its highest peak to almost 11mmol/l, which is at the level of diabetes. The pattern was similar after lunch and dinner, although the typical pattern is that after lunch, the glucose levels remain at a higher level for the rest of the day and do not return to normal.

When the same individuals received the low glycaemic index diet, the curves were less variable, and during most of the day the peaks are small, unless they were given the glucose load, at which point the levels increased significantly again. Therefore, it seems that by modifying the type of carbohydrates consumed, it is possible to control glucose levels and postprandial glucose levels in people who have impaired glucose tolerance.

We now have the trial data to demonstrate convincingly that diabetes can be prevented in high-risk individuals with IGT. The lifestyle changes required are rather small, so can they be used in everyday life? We had an approximately 5% reduction in bodyweight in these individuals. The typical man had an initial bodyweight of 100 kilos at the beginning and had a 5 kilo reduction in bodyweight. Given that the upper range normal weight is 80 kilos, this 5% reduction may seem very small.



However, this should be considered in another light: if the man has 20 kilos overweight and loses 5 kilos, his overweight has

reduced by 25%, not by 5%. Moreover, we already know that when weight reduction begins, initially there is more decrease in visceral fat; in this scenario it would have reduced by about 40%. Therefore, a seemingly small change in bodyweight in these individuals means a quite significant change in the fat patterning in their bodies.

There are many more questions to be answered. For instance, (i) how much does it cost to prevent a case of type 2 diabetes, (ii) whether benefits are long-lasting, and (iii) whether lifestyle intervention is cost-effective. We have shown that lifestyle intervention is feasible and produces beneficial changes in metabolic parameters, and that required lifestyle changes do not need to be extreme and could therefore be achieved by most of the people. In terms of the duration of the benefit, we have followed the individuals on a one-yearly basis and compared with the results that were originally published 4 years ago, there is no sign of disappearance of the initial effects of the intervention. In fact, the difference between the groups is becoming even more significant, even though the subjects in the intervention group were left on their own after the formal trial period was over. Thus, the intervention has long-lasting effects. In trials like the metformin arm of the DPP and other trials using anti-diabetic drugs to reduce the risk of diabetes, the effect largely disappears as soon as the drug is no longer administered. This is not surprising because the drug provides a pharmacological mechanism to control glucose, whereas in the lifestyle intervention we influenced the causal factors, and when this is done properly, the intervention provides long-term effects.

We are carrying out a cost-effective analysis of the intervention at the moment, and this has already been done by the DPP. The DPP results showed that the intervention was cost-effective even though their intervention was more labour-intensive than what is possible in real life. A very small amount of money, approximately 10-20 euros or dollars, is needed to prevent a case of diabetes with a 12 month intervention, so it is definitely cost-effective. Since the results in the Finnish DPS were similar to those in the DPP, but intervention was much less intensive, the results from the cost-effectiveness analysis will be certainly very positive.

Ladies and gentlemen, I have tried to convince you that lifestyle intervention is a very effective method for type 2 diabetes prevention in high risk individuals. Dietary advice must be combined with efforts to increase physical activity. It is important to study the importance of different dietary components and the individual effects of those components, but I think that this is more of an academic exercise. I think that we know most of the issues important for the prevention of type 2 diabetes in the population in general. Thank you.

—Questions—

Member of the audience

Could we have more practical information about the intensive lifestyle counselling?

Jaakko TUOMILHETO

We have published a paper in Diabetes Care which contains a full description of the intervention (Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, Uusitupa M, Tuomilehto J for the Finnish Diabetes Prevention Study Group. The Finnish Diabetes Prevention Study (DPS). Lifestyle, intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26: 3230-3236).

Member of the audience

I wonder whether it is possible to increase the body mass index and to reduce the risk of developing diabetes at the same time by converting the fat into muscle.

Jaakko TUOMILHETO

Theoretically, I believe that you could, although I am not sure how this would be done in practice. After evaluating the effect of physical activity and adjusting for bodyweight and body mass index changes, we could clearly show that physical activity independently reduced the risk of diabetes. However, in our study, there were no individuals who would have increased their body mass index and decreased their risk. I think it is rather theoretical.

Introduction

Salvatore PANICO

Dipartimento di Medicina Clinica e Sperimentale, Università di Napoli, Federico II, Naples, Italy

This afternoon, we shall talk about cardiovascular disease, which is classically related to the Mediterranean diet. The hypothesis for the diet was born on the basis of a cross-cultural investigation which included seven countries and which was the seminal work by Ancel Keys.

You will certainly be aware of Ancel Keys but may not know the details of the first steps of the Seven-country Study. The study was actually designed in Naples, the city where I live. During the last part of World War II, Ancel Keys and Paul Dudley White, the cardiologist of the US General Eisenhower, were very surprised to see so few myocardial infarction patients in hospitals there compared to Boston hospitals. Thereafter, some 15 years later the SCS started, including also Italian small villages.

Today, the issues of how much and with what components we should encourage people to eat according to the Mediterranean-type diet are still crucial.

This session is dedicated, in the first part, to the experimental evidence on the benefits of recommended dietary regimen or dietary components. Then, the reasoning on the evidence of protective effects other than through lipids will be presented, and finally, some reflections will be provided on the preventive potential of the adherence to a Mediterranean-type diet, with special respect to Mediterranean countries.

Therefore, I offer the floor to the first speaker, Dr Marchioli, who is from the Mario Negri Sud Institute in Italy. He will present the paper 'Cardiovascular risk, n-3 PUFA, and dietary habits after myocardial infarction: the GISSI-Prevention study'.

Cardiovascular risk, n-3 PUFA, and dietary habits after myocardial infarction: the GISSI – Prevention study

Roberto MARCHIOLI

Laboratory of Clinical Epidemiology of Cardiovascular Disease, Consorzio Mario Negri Sud, Santa Maria Imbaro (CH), Italy

Mr Chairman, ladies and gentlemen, dear colleagues, I am supposed to give you a short summary of the new results of the trial, including the experimental results of the trial, and some additional information about dietary habits.

Firstly, the design of our trial was as follows: patients with a risk of myocardial infarction within three months received dietary and lifestyle counselling, drug therapy prescribed at that time, consisting mainly of aspirin and beta blocker inhibitors. They could then be randomised to one of four groups: omega-3 fatty acids, vitamin E, the combination, or no treatment at all. After six months, patients returned for their first clinical visit following randomisation, and if their blood cholesterol was higher than 200 milligrams per decilitre, they could be randomised in a nested randomised trial testing the efficacy of pravastatin in these patients. Patients were followed for 42 months following randomisation. However, the second trial was brought to a close because it duplicated other trials, such as the walk-up study and the CARE trial. When the CARE trial was published in the New England Journal of Medicine, we decided that it was not ethical to allow patients who had myocardial infarction to continue with high blood cholesterol and no cholesterol-lowering treatment at all; therefore, the trial was closed. However, when we closed the trial, we did have some results relating to pravastatin: there was a 20% reduction of LDL cholesterol and there was also some reduction of total mortality, but it was not significant because we closed the trial.

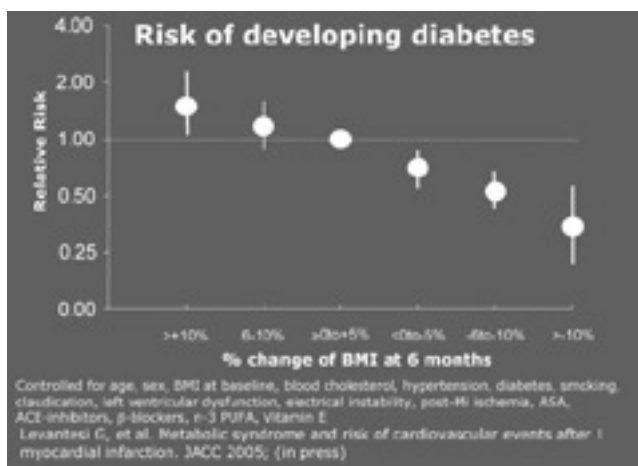
In relation to the main study on omega-3 fatty acids and vitamin E, we had interesting results. Patients were enrolled within 25 days (median value) of their myocardial infarction and none of them had a severe prognosis, as we excluded patients with malignancy or with severe congestive heart failure. They had a mean age of 60 years and a mean age at infarction of 52, and this was why we excluded patients with severe heart failure, and then we have LDL cholesterol of 136 and so on. In relation to other characteristics, 42% were smokers before myocardial infarction, 14% were diabetics and 36% had hypertension. As to pharmacological treatment, there was clearly a change in the use in the cholesterol-lowering trial between the baseline situation and at the end of the study because of the effect of the nested trial on pravastatin. However, at the end of the study, approximately 80% of patients were taking aspirin, and 40% were taking ACE inhibitors or beta blockers.

The results on omega-3 fatty acids (because vitamin E did not improve prognosis in these patients) were as follows: there was a 15% reduction of death plus non-fatal infarction or stroke, and a 20% reduction of cardiovascular death plus major non-fatal end points. These were the two main points that were established in the protocol. However, we conducted a series of additional analyses, and we realised that there was a slight, but not significant, reduction in fatal myocardial infarction and non-fatal stroke but there was an important reduction of total mortality through cardiovascular death of up to 30%, and for sudden death of up to 44%. This was associated with an early onset of this benefit within three months for total mortality, and within four months for sudden death, and this was why we

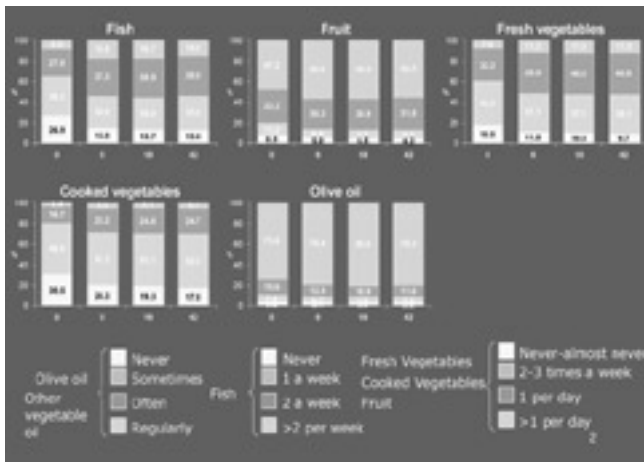
thought that one of the main mechanisms through which omega-3 fatty acids could act could be through their anti-arrhythmic properties, but this has not been demonstrated yet. However, there was no change in blood lipids – there was only a 3% reduction of triglycerides, which was statistically significant but small compared to the magnitude of the benefit on total mortality.

GISSI-Prevenzione was mainly a prevention project, and patients were also given counselling about healthy lifestyles, including physical activity, diet and so on. When we look at the data relating to smoking, we can see that even after six months following myocardial infarction, 12% of patients were still smoking and this proportion had increased up to 16% by the end of the study. Therefore, we can see that it is not easy to modify lifestyle habits, as we all know. I must also emphasise that if we look at the body mass index at the beginning of the GISSI-Prevenzione study, we can see that there are a number of patients who are overweight or obese.

If we look at the modification of body mass index at six months and its relationship with the probability of developing diabetes, we can see that compared to the reference category of those not gaining weight or gaining little weight, if the patient sustains significant weight gain, there is an increase in the risk of becoming diabetic; if the patient decreases in weight, there is a clear decrease in the risk of becoming diabetic. We can see that modifying lifestyle habits has important consequences.



Unfortunately, we did not collect information about physical activity but we did collect some information about diet. Since GISSI-Prevenzione was a pragmatic trial to be conducted by cardiologists, we had to be very pragmatic about the collection of information about diet and as a result, we used a very simple food frequency questionnaire with simple markers of dietary habits regarding intake of cooked and raw vegetable, fruit and so on, and the frequency of their consumption during the week. With this approach, we collected information relating to circa 11 000 patients over 42 months.

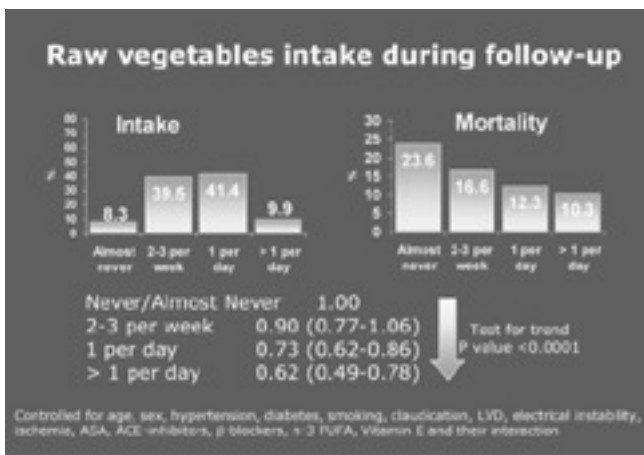


We can see on the graph, that we have the intake of fish at the baseline in this column. The green and orange parts of the column indicate those patients consuming fish once or more than twice per week respectively. We can see that if we examine the progress at six months, eighteen months and forty-two months, there is an increase in intake of fish that was maintained during follow-up. Therefore, there was an improvement of dietary health in relation to fish, but this pattern was also present for other foods such as fruit, cooked vegetables, fresh vegetables and olive oil: there was an overall improvement of dietary health. Even intake of olive oil increased after myocardial infarction, a surprising factor given that the study was performed in Italy where the level of consumption of olive oil is already high.

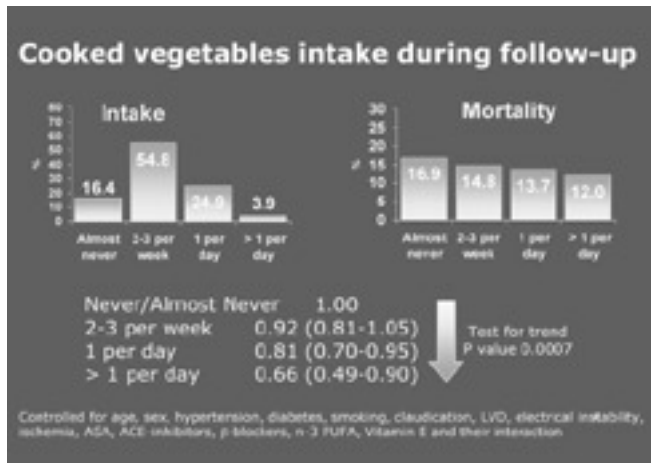
What did we do? We performed a number of multivariate analyses adjusting for main potential confounding factors, and we calculated a dietary score using the numbers that can be seen in the boxes on the graph in order to obtain higher scores for people with better dietary health. In this way, we were able to analyse the data of circa 11 000 patients and obtain information relating to total mortality for approximately 6 years of follow-up, which represents circa 60 000 person-years of follow-up.

In this graph, we can see the average food intake during follow-up or the improvement of diet during follow-up. About 80% of patients ate fruit at least once per week, and this was slightly associated in univariate analysis to a lower mortality, but on performing multivariate analysis we saw a 27% reduction in mortality for patients eating fruit more than once per day, with a highly significant P value for the trend test.

We performed the same analyses for other foods. In relation to raw vegetables, approximately 50% of patients had a high intake of raw vegetables, and this was clearly associated with lower mortality. This information was confirmed by means of multivariate analysis, with a 38% reduction in the risk of death.



In the case of cooked vegetables, 30% of patients ate cooked vegetables at least once per day. There was a slight association with a lower mortality and again, it was statistically significant with more than 30% reduction of total mortality.



In relation to fish intake, circa 50% of the patients ate fish at least twice per week and this was associated with lower mortality. This was confirmed by means of multivariate analysis with almost 30% reduction in mortality.

In relation to olive oil, many of the patients used olive oil regularly, as I mentioned before, and this was associated with a reduction in total mortality.

Interestingly, we also obtained data for other seed plant oils, as people were also regularly using other seed plant oils, and there was an inverse association with mortality, i.e. the risk increased, and this was confirmed through multivariate analysis.

Although butter intake is not high in Italy, we did obtain data for butter and we found an association with high risk of death and despite the low numbers, it was statistically significant. With regard to cheese, there was no clear association with total mortality.

For wine intake, there was an association with moderate intake of wine, that is to say that was a lower mortality in those who had a moderate intake of wine.

The results for coffee were that there was a significant increase in risk of death in patients who drunk more than 4 cups of coffee per day.

These were the results for foods individually, but as we needed to summarise the dietary patterns of these patients, we calculated the score using healthy foods alone, such as fruit, fresh vegetables, cooked vegetables, fish and olive oil. As I have already mentioned, there was an association between the score and the total mortality, that is to say that the higher the score, the better the diet and the lower the total mortality. This kind of result was also confirmed through subgroup analysis, and there was similar association for the dietary score in patients according to gender, age, drug therapy or experimental drugs like omega-3 PUFA and Vitamin E used during the trial.

In conclusion, to summarise the results of the dietary score, if we present them in terms of quartiles of the score, there was a 40% reduction in the highest quartile of patients who had the best dietary habits. Thank you for your attention.

— Questions —

Member of the audience

Would you exclude that those individuals adhering to the dietary recommendations more closely would also be those who took their drugs more regularly than the others?

Roberto MARCHIOLI

Yes, we did carry out an analysis looking at this point and there was such an association. However, we adjusted for the intake of drugs, such as the compliance to experimental treatment, and we obtained similar results.

Member of the audience

I would like to ask you a question relating to your results for coffee. They are not part of the score as I understand, but I am interested in coffee because as we heard earlier, we have seen an inverse association between coffee and the risk of diabetes. You have mentioned that it is associated with an increased risk of mortality. Could you tell me what causes of death could be associated with coffee? Do you have any information regarding the types or properties of coffee that are concerned? For example, we know that boiled coffee increases LDL cholesterol, and perhaps this is a part of the mechanism. Or is it related to an increase in blood pressure?

Roberto MARCHIOLI

In relation to your question, we have a problem of proxies because there were people who did not stop smoking, and people who resumed smoking during the period, and this could be associated with a higher intake of coffee. Therefore, this result is quite complex. This was what we saw. Personally, I think that the best way is to look at the whole dietary pattern rather than just concentrating on the intake of one food.

Changing dietary pattern reduces CVD risk

Evidence from primary prevention trials

Edith FESKENS

National Institute of Public Health and the Environment Centre for Nutrition and Health, Bilthoven, The Netherlands

Thank you for your kind invitation to attend this conference. The task that has been set for me is extremely difficult as I was asked to talk about changing dietary patterns and how they reduce cardiovascular disease risk. The problem is that I was asked to focus specifically on the evidence from primary prevention trials and this will be difficult, as I will explain to you later. The question should really be reformulated to ask whether there is any evidence from primary prevention trials that this is the case. However, I would like to use the next 20 minutes to discuss the importance of this topic.

Firstly, I should like to pay my respects to Ancel Keys, who is no longer amongst us. Together with Paul Dudley White, he was the first to acknowledge the fact that there are so many interesting aspects to the lifestyle and diet here in the Mediterranean area. That is also why he chose to live here after his retirement after spending several periods of his life here. In collaboration with Daan Kromhout, I have been working on the Seven Countries Studies for almost fifteen years, and what Ancel Keys found was very important in saying that in Italy, Greece, Corfu, Crete, in the former Yugoslavian republics, their average saturated fat intake is quite low and the mortality rate from coronary heart disease is quite low. He was one of the first to acknowledge that the Mediterranean diet may be very important in the prevention of coronary heart disease and other cardiovascular diseases.

We analysed the data of the Cretan participants of the Seven Countries Study and looked at how they ate in 1960, and we returned to Crete to buy Cretan foods, including traditional foods that are not eaten so much now, such as the leaves and greens which are traditionally eaten in Crete. I shall not talk about this issue but Daan Kromhout may be able to expand further on this topic later when we have the data ready.

Obviously, we all know that there are many items that can be beneficial within the Mediterranean diet. We all think that there must be a healthy combination of these foods. Almost eight years ago, we published a paper on the Finnish, Italian and Netherlands' cohorts of the Seven Countries Study showing that a healthy diet, as calculated using the Healthy Diet Indicator, is associated with reduced mortality. This was especially so in the case of Italy. It was less clearly visible in the cohort in the Netherlands and this may also be the effect of the disadvantage of an observational study: in the Netherlands study, amongst the elderly men participating, the range of exposure was limited in terms of healthy diet and most of them ate an unhealthy diet. The Italians had a much higher score, which was associated with lower mortality rates.

As an epidemiologist, I can tell you that I do not spend all of my days fishing in my computer. However, we do have to acknowledge that carrying out observational research is not a fishing expedition.

The hallmark study on the benefits of a Mediterranean diet on recurrent myocardial infarctions is of course the Lyon Diet Heart Study.

Unfortunately, they did not have complete dietary information for all the participants in the experimental and control group, but the basic results indicated that they used more monounsaturated

fatty acids (MUFA) and more alpha-linolenic acid and had higher fish fatty acid intake, and less linoleic acid. Looking at their data and their results on plasma acid, they say that the intake of alpha-linolenic acid is particularly important in explaining this reduced risk.

I would like to draw your attention to another more recently published study, which is the 'Indo-Mediterranean diet heart study'. This study is similar to the 'Lyon heart diet study' but was carried out in a larger population with 1 000 patients in an area in India. They used the end points fatal and non-fatal myocardial infarction and sudden cardiac death, and also obtained very convincing data on reduced risk in the patients in the intervention. They did have extensive dietary information available for their intervention group, and the intervention was aimed at eating more fruit and vegetables, nuts, whole grains, mustard and soy bean oil. It is to be remembered that this was being carried out not in a Mediterranean area but in India, and they had a higher PS ratio with this result. [Note by the speaker added in the proofs of the transcription: there are now serious doubts on the validity of this study- see the editorial 'Expression of concern: Indo-Mediterranean Diet Heart Study' by Richard Horton, *The Lancet*, p 354-356].

This is a secondary prevention study. We do not know, or perhaps we do not need to know, whether this would be successful in non-patients or in primary prevention. What about the possibility of using the Mediterranean diet in primary prevention of cardiovascular disease? To my knowledge, there are no studies on real events at end points, although, of course, there are many studies on markers for risk. When I looked into these studies, some of which we carried out ourselves, I found that they did not always look at the whole Mediterranean dietary pattern, even if they used the name, often simply taking elements from the diet such as using olive oil rather than saturated fat. They have often been small-scale studies. However, I think that it is worthwhile to discuss the results of these kinds of studies.

The first paper that I noticed was written by a group from Cordoba, who found some interesting results. They conducted a four-week intervention but they only used olive oil versus saturated fat and did not include other elements of the Mediterranean diet. However, they found reductions in LDL and HDL cholesterol and increased insulin sensitivity. This is an extremely good paper from *Diabetologia* written several years ago. In a smaller study, they found reductions in flow associated fat of dilatation, i.e. an improvement in endothelial dysfunction, and in some, but not in the biochemical, markers of endothelial dysfunction. Once again, the study was extremely interesting and well implemented, but an intervention of only four weeks and using olive oil alone.

Then, there was a group in Quebec, led by Professor Lemieux, which carried out a twelve-week intervention on 71 women, whereby the advice given was based on a Mediterranean dietary pattern with people increasing their use of olive oil alone. They found reduced LDL and reduced oxidated LDL, but they did not use a control group, which is necessary for such an intervention.

The second study on this slide was a study that I was involved in myself which was carried out in collaboration with the University of Groningen in the Netherlands. This was the Margarin Study, in which we tried to implement a small-scale Lyon diet heart study with risk factors as an end point. It was only a two-year study in 282 high risk subjects. We advised them quite intensively as to how to modify their diet into a more Mediterranean dietary pattern. Fish and fruit and vegetable intake increased, but if we looked at the risk factors such as serum lipids, hypertension or clotting factors, we could not find any associations. This was a pity. Perhaps the intervention group was small, but with 282 high risk patients, we would have expected some results. This was also a good study, because within this design we also randomised within linoleic acid margarine versus alpha linolenic acid margarine, but that is another story.

Professor Lairon will be happy today as I mentioned to him this morning that I shall also talk about the Medi-RIVAGE study, for which some results were published two years ago. They carried out an intervention in Marseille on 212 subjects. It was a randomised parallel trial and the outcome was the risk factors that have been published. They really did use a Mediterranean diet intervention, changing the fatty acid profile, increasing fish, fruit and vegetables and fibre, and the control diet was a low fat, low cholesterol diet. When we compare the results, they demonstrated larger reductions in total LDL cholesterol, larger reductions in fasting insulin and fasting glucose, triglycerides and postprandial triglycerides, and they also showed a reduction in the intervention group in body mass index.

Therefore, we have seen some developments in the field and some improvements can be seen. There is a study that has already been discussed by Dario Giugliano this morning that I would just like to mention again. It was a very good study. It concerned patients with metabolic syndrome and introduced the whole Mediterranean diet in their approach. They carried out a two-year follow-up for markers of endothelial dysfunction and vascular inflammation. They increased whole grains, fruits, vegetables, walnuts and olive oil with very interesting results, as we heard this morning. Therefore, I do not need to repeat the results but would like to point out that, once again, the Mediterranean diet group lost weight, as was the case in the Medi-RIVAGE study, sustained improvements in risk factors and improvements in the prevalence of metabolic syndrome.

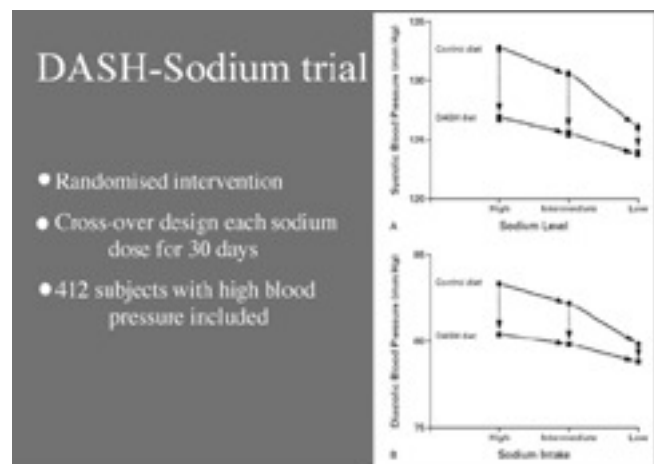
I read an abstract book from the Athens meeting last month that was organised by Professor Trichopoulou, and I found an abstract on a pilot study carried out by a Spanish group called the PREDIMED study. I have only read the abstract and therefore I do not know very much about it, but it is interesting as it is a fairly large study covering 600 people – elderly people with asymptomatic cardiovascular disease, or pre-risk factors or diabetes. It is a randomised trial with intensive behavioural counselling, a nutrition education on the Mediterranean diet, plus free supply of virgin olive oil or nuts, and there is a control group. The results are that compliance has been good and there have been reductions in blood pressure, LDL cholesterol, a marker of endothelial function and a marker of sub-clinical inflammation, and a rise in HDL cholesterol. Unfortunately, the abstract does not mention body mass, glucose or insulin, so I am very curious about this study. Perhaps there is someone in the audience who knows more about it.

Finally, for this part of our talk, I would like to refer you to Poster 26. We are planning a controlled intervention ourselves with rigorous control of food intake. We will compare it with a high MUFA diet and we would like to study the Mediterranean diet. We have not yet decided what to do about alcohol and we welcome your advice as to which Mediterranean diet we should use for this intervention.

With regard to the Mediterranean diet as a whole, there have been studies and there have been risk factors, but they have not been too large yet. There are also other important dietary patterns which may have favourable effects. The Mediterranean diet seems very good, also from observational studies, but there are other possibilities, such as the DASH diet, which is the dietary approach to stop hypertension, and the PORTFOLIO diet for the lipids.

This slide shows the DASH diet pyramid, which has already been tested and published several years ago. It contains plenty of vegetables and fruit, grains, seafood, low fat dairy, legumes, beans, nuts and seeds, oils and a small amount of sweets. I should mention that when we look at blood pressure and at coronary heart disease, there are some interesting results for the sweet category, especially for chocolate. We have found that the more chocolate a person eats, the better their blood pressure is and the lower their risk of coronary artery disease. Perhaps we should examine this category of sweets in more detail.

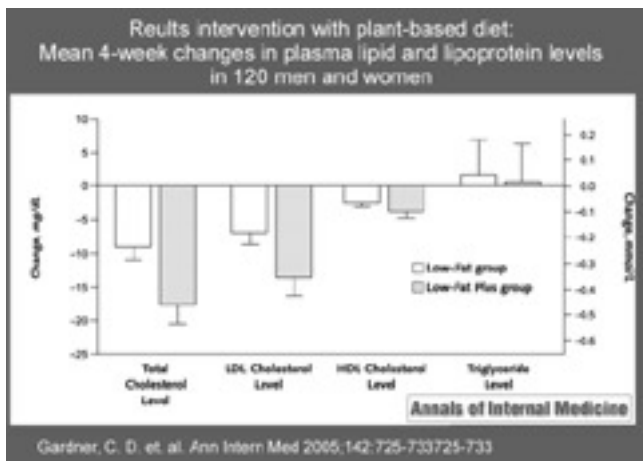
Here are the results of the additional DASH sodium trial, which is very important and which finally settled the dispute about sodium: sodium really is important for reducing blood pressure. Here we see the results for systolic and diastolic for the control diet. There is clearly a difference with the DASH diet with lower blood pressure, and this is true for every dose of sodium: high, medium or low. This was carried out on 412 subjects. Therefore, this is the DASH diet as it is advertised: vegetables and fruit, grains, some dairy products and no salt.



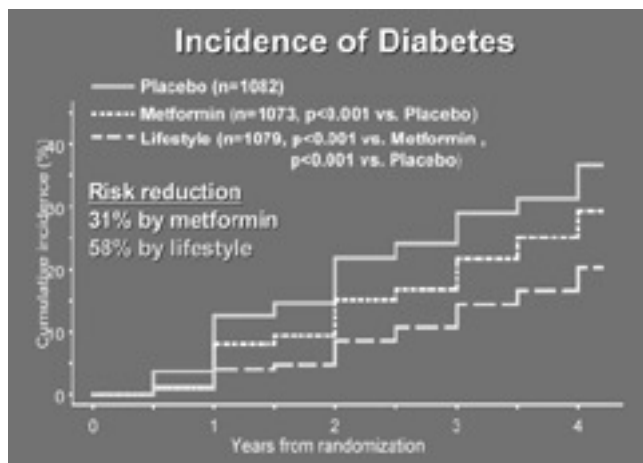
The second diet that I would like to discuss with you is also a diet that you must have come across. This is based on the work of people, such as David Jenkins, who worked on this Portfolio eating plan containing viscous fibres, soy protein, plants, cereals, and nuts such as almonds. He showed that the Portfolio diet may be as effective as statins and also reduces C-reactive protein, a sub-clinical inflammation. I saw a paper of his published in the 'American Journal of Clinical Nutrition' and there is a copy of it outside in the hall for you all.

David Jenkins noticed that his diet – which is quite rigorous because it contains all these types of foods which could be classified as 'functional foods' – may be slightly more expensive than just using the plant-based diet. This paper was published very recently, and I have not included it yet within my abstract. In this slide, we can see the four-week changes in plasma, lipids and lipoproteins in 120 men and women: a reduction in total cholesterol (both low fat diets – this is the plus group with the plant-based diet) and a larger reduction in LDL cholesterol. These results are quite impressive in the sense that there is not a large difference, so it is not as effective as Jenkin's diet, but it

only uses plant foods and grains which are readily available, so I believe that the implications of this are quite important.



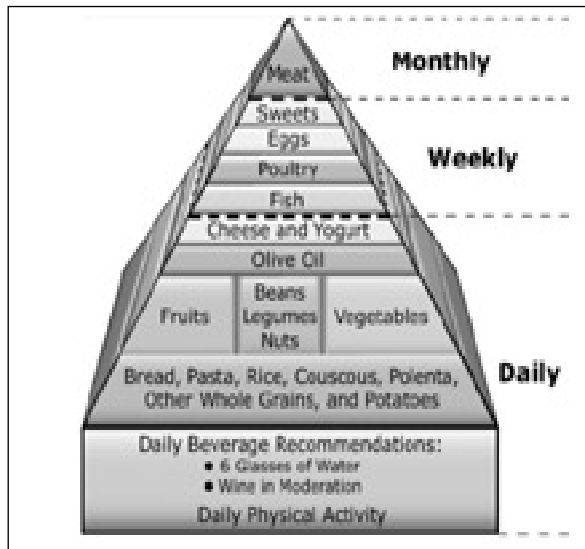
Insulin, diabetes, insulin-resistance and glucose are also risk factors for coronary heart disease. Therefore, when thinking about primary intervention it would be possible to consider these types of studies. This was explained very well by Professor Tuomilhto, so I will not discuss it too much. However, I would like to draw your attention to the fact that risk reduction by lifestyle was even greater than the risk reduction by metformin, and as Professor Tuomilhto demonstrated, after discontinuation of the study, the risk reduction by lifestyle was maintained, whereas with metformin it came down again to the level of the placebo group.



We carried out this type of study ourselves with Professor Tuomilhto in a small group in order to carry out more physiological tests. We did a randomised trial and used the national guidelines for a healthy diet with reduced saturated fat, increased vegetables and fruit and fibre, and we increased physical activity and supervised training. Of course, there was also a control group for the study.

Like Professor Tuomilhto, we only saw a 5% reduction in body weight on this programme, although when looking at the results of the 2-hour glucose, which is an independent risk factor for coronary heart disease, we see a steady increase in 2-hour glucose for the control group as the cohort becomes older, and a very large decline during the first year for the intervention group, and this difference between the two groups remains. Impaired glucose tolerance almost disappears in the intervention group, at least during the three-year follow-up.

One of the things that we have been discussing this morning is how we can make our interventions more cost-effective, and this is an extremely important issue. This slide includes the Mediterranean diet here, like the pyramid that you will all know, and includes physical activity here, beverages over there, wine and glasses of water over here, cheese and yoghurt are here, and it does not include any negative comments on tea and coffee.



The point that I would like to make is that all this may be successful in the Mediterranean area and is more or less similar to what the people there are eating know, or at least to what their grandparents ate, but to change the populations in the Netherlands in such a way will demand significant work and resources. Therefore, whilst we agree that this whole pattern is very important, we would still like to understand which one of all of these layers is crucial and should be of primary focus, as it is quite difficult for many to eat a Mediterranean diet in our country.

Therefore, more interventions of good methodological quality are needed (and we are trying to carry out a small one ourselves) because interventions really are the proof of the pudding. Perhaps I do not need to remind you about the confusion that we have now, for example, on the use of vitamin E and beta-carotene, observational studies that show preventive effect, intervention studies that show nothing, or about hormone replacement therapy? Or do we know enough and can we simply tell our people to eat as close to a Mediterranean diet as they can? I do not know. Which components are really essential? I would like to know, but I would also like to know which combinations are best as I am convinced that the key lies within the combinations.

In the Netherlands, we have an ongoing debate regarding whether or not we should use more or less dairy products. We believe that it may protect against diabetes, there is some evidence to suggest that it may not be good for hormone-dependent cancers, and there is some debate as to whether it is good or bad for osteoporosis. It is an interesting discussion because, as you know, dairy products are not part of the Mediterranean dietary pattern.

Finally, who would be interested in funding a large-scale primary prevention study on the Mediterranean diet with disease end points such as cardiovascular diseases, as we need to know where we can get the money for such research? Perhaps we can convince the European Union to fund such work. In addition to well-know European observational cohorts such as EPIC, we also need further intervention studies. Thank you.

Questions

Franco BERRINO

I would like to discuss the basis of your parameters. You included potatoes and polenta. I know that potatoes are very high on the glycaemic index and that maize is very high in starch and I wonder whether these two arguments bear any relation to the Mediterranean tradition. Perhaps the chairman can say whether the Mediterranean tradition included potatoes. I think that there are sometimes strange definitions of the Mediterranean tradition.

Edith FESKENS

Perhaps the chairman can answer first as I believe that potatoes are not really part of the Mediterranean tradition.

Salvatore PANICO

Potatoes are definitely not part of the Mediterranean tradition.

Edith FESKENS

Potatoes are the most important staple in our country. The glycaemic index of potatoes varies according to their preparation, and this can be confusing. In general, our approach for the dieticians is that they reduce the potato intake slightly and replace them with pasta or brown rice. This is the practical approach in our country. As far as couscous and polenta are concerned, they are not consumed much in the Netherlands, so I do not know much about them. As far as I know, polenta is typical of northern Italy. I do not believe that it is fibre rich.

Member of the audience

We need to refer to the traditional Mediterranean diet as it was in the 1960s in Crete, as this was the best example. However, we need to realise that these people at that time were very poor peasants from a small village in Crete with a very traditional poor diet, and these people were farmers and had very high levels of physical activity. It is a good reference, but if you would like to plan an intervention study now, with people with very low levels of physical activity, I believe that it is far more complex. Therefore, I believe that we do need to refer to the Mediterranean diet so that everyone uses the same parameters, but it needs to be adapted to context, as few would tolerate the traditional Mediterranean diet. Furthermore, if you wish to transfer the Mediterranean diet to a northern country, this also presents some challenges. For example, in the south we do not use the potato much as we use more greens. In the north, the situation is different. This merits important discussion.

Edith FESKENS

I would like to add, before someone else asks me, that potatoes are the most important source of vitamin C in our country, not because they contain large quantities of vitamin C but because we consume so much of them, far more than vegetables and fruits. Therefore, we have to be very careful not to throw out the potatoes and replace them with pasta. We need to maintain a balance.

Member of the audience

I have two questions relating to fish. Could you clarify whether there was any fish in the Indo-Mediterranean diet? Secondly, we have heard about GISSI, but there were two trials on fish in the United Kingdom: DART 1 and DART 2. Whereas DART 1 demonstrated a protective effect, DART 2 showed a significant adverse effect in the fish group. Do you have any views on this?

Edith FESKENS

With regard to the Indo-Mediterranean diet, I would need to refer to the paper as I did not pay too much attention to fish consumption, although I assume that they did use fish because they increased their long chain PUFA and I would imagine that this came from fish as well as oils, and I believe that the intake increased.

In relation to your question about fish, the evidence from the GISSI Prevenzione, and from some other trials examining sudden cardiac death, is quite impressive. In reference to the DART 1 study, I did not find anything for dietary fibre. I do not know about the DART 2 trial. I think that what is becoming clear is that fish does not work very well for non-fatal end points, but it is far clearer for the arrhythmia-related end points in sudden cardiac death. Therefore, I think that the primary end point in your trial affects the relative risk that you will observe in a fish intervention. However, I cannot remember exactly how DART 2 worked. I cannot imagine that increasing fish or n-3 fatty acids is detrimental for any disease that I know of.

The previous member of the audience

I cannot remember either, although it does raise LDL.

Edith FESKENS

It raises LDL, but it has to be an extremely high dose, so it would be important if you were using fish or fish oil alone. The American Heart Association recommends that 3 grams of fish oil per day is acceptable, although it says that the person should be under a physician's supervision, and up to 1 gram per day is recommended for any person, and that is reasonable. I have not seen any evidence of increased LDL or increased glucose levels with these moderate levels.

Member of the audience

I would like to add a comment regarding DART 2. As far as I know, they had difficulties with their study because they needed more than seven years to recruit their patients and they had to stop the trial for one year because they did not have enough funding. As a result, we do not know what happened to the patients followed by general practitioners.

Elio RIBOLI

Perhaps my question should wait until the final session, as I think it would be useful to discuss on why we are discussing the Mediterranean diet. It is one thing to discuss what the Mediterranean diet is from a historical and gastronomy point of view for which we need to look according to region and time: potatoes and tomatoes were not consumed that much in the 1700s in southern Europe.

The other issue is which components of a Mediterranean diet help prevent chronic diseases. There is a risk that sometimes the debate on what is historically accurate replaces the debate on which components help to prevent cardiovascular diseases.

Mediterranean diet and CVD: beyond cholesterol

Angela RIVELLESE

Department of Clinical and Experimental Medicine, University Federico II, Naples, Italy

Good afternoon. Firstly, I would like to thank Dr Panico and the organisers of this conference for inviting me to speak about the Mediterranean diet and cardiovascular disease: beyond cholesterol.

Like the previous speaker, I would like to start by discussing the Seven Countries Study, which is an obvious starting point when discussing the Mediterranean diet. Since the beginning of these studies, it was clear that there was an extremely significant difference for coronary heart disease mortality between Mediterranean and non-Mediterranean countries. This difference was ascribed to the different dietary habits. For many years, the beneficial effects of the Mediterranean diet was attributed mainly to its hypocholesterolemic action, but although this action is important, it is not enough to fully explain the beneficial effects of the Mediterranean diet in reducing cardiovascular risk. In fact, in the same Seven Countries Study at the same level of plasma cholesterol, there was a very large difference in mortality for cardiovascular disease, which suggested that plasma cholesterol is not the only way to explain differences in cardiovascular mortality. Moreover, the very impressive effects of the Mediterranean-style diet used in the Lyon Diet Heart Study on cardiovascular and non-cardiovascular mortality were obtained without any change in plasma cholesterol. Therefore, we have to consider whether the Mediterranean diet may act in reducing cardiovascular risk not only for its action on plasma cholesterol but also because this kind of diet may beneficially influence other mechanisms.

In my presentation, I shall focus especially on the possible effects that the most typical components of the Mediterranean diet may have on some of these mechanisms. In particular, I shall focus on insulin sensitivity, postprandial metabolism, both lipid and glucose metabolism, which are now considered to be more than simply new and emerging cardiovascular risk factors. Of course, one of the main components of the Mediterranean diet is monounsaturated fat, derived mainly in this kind of diet from olive oil. The beneficial effects of monounsaturated fat compared to saturated fat on classical risk factors, such as blood pressure and plasma cholesterol, is well-established, but what are the effects of a diet rich in monounsaturated fat on insulin sensitivity, and why is the possibility of influencing insulin sensitivity considered to be so important?

Insulin resistance is now considered to be a very well-established risk factor. Insulin resistance may lead to arteriosclerosis through many mechanisms, some very well-known as blood glucose or plasma lipid abnormalities, and other newer, such as oxidative stress, muscle cell proliferation, and so on. Therefore, the possibility of modulating and reducing insulin resistance means the possibility of improvement of all these other mechanisms, resulting in a synergistic amplified effect in the reduction of cardiovascular risk. We tried to clarify this point – the possibility of influencing insulin sensitivity by substituting monounsaturated fat with saturated fat – in this multi-centre international study, called the KANWU study, performed in five different centres in Europe.

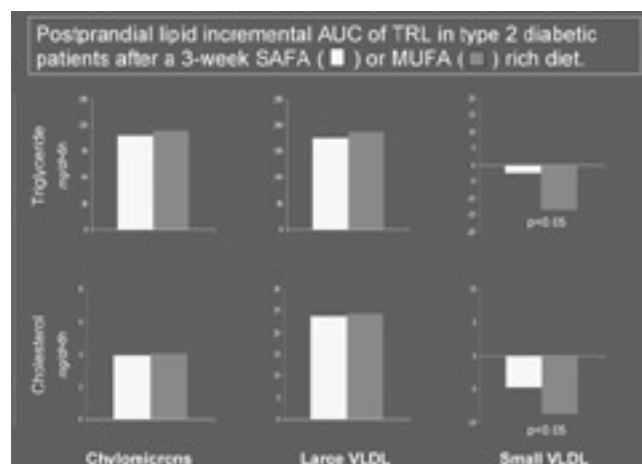
In this study, 162 healthy people were randomly assigned to two kinds of diet: a diet rich in saturated fat, with approximately 17% of total energy from saturated fat, and a diet rich in monounsaturated fat, with approximately 22% of total energy from monounsaturated fat. At the end of a three-month period,

some parameters, including insulin sensitivity, were evaluated. In relation to the effect on insulin sensitivity, the high saturated fat diet significantly deteriorated insulin sensitivity in these healthy people, whilst the high MUFA diet significantly improved insulin sensitivity, with a significant difference between the two diets of more than 20%, although this only occurred in the group with a moderate total fat intake, less than 37% of total energy. The beneficial effect of the high monounsaturated fat diet was completely lost when the total fat intake was higher than 37% of energy. Therefore, it seems that one component of the Mediterranean diet – monounsaturated fat – is able to improve also insulin sensitivity in healthy people, but only when the amount of total fat is not very high.

I do not wish to speak about fish or fish oil too much, but I would like only to underline that in the KANWU study, where people following the two diets were randomized to a moderate supplementation with fish oil [2.7 grams per day] or placebo, fish oil supplementation did not change at all insulin sensitivity. Therefore, the beneficial effects of fish oil on the reduction of cardiovascular risk must be related to other effects of this dietary component.

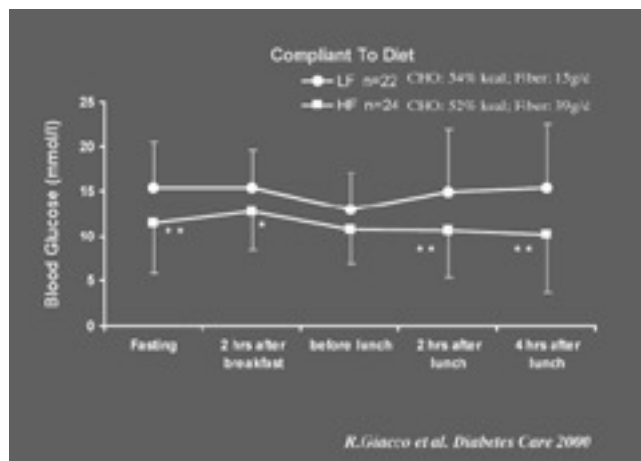
Another new and emerging cardiovascular risk factor is postprandial lipid abnormalities. This aspect has attracted a lot of attention over the last few years because human beings spend large periods of time in a postprandial state. Abnormalities in the postprandial metabolism are mainly characterised by an increased concentration and prolonged residence time of small particles of remnant particles in particular, both of endogenous and exogenous origin, and these particles are considered to be highly atherogenic as they can trigger the atherosclerotic process at different levels. In truth, the effects of monounsaturated fat compared to saturated fat on postprandial lipid metabolism has not been studied in depth, and the results of these studies were extremely conflicting, with some showing a higher postprandial chylomicron increase after the MUFA diet, but especially after acute experiments.

We have started to study this matter using the same diet as that used in the KANWU study, this time in type 2 diabetic patients with a cross-over design. The two diets were followed for three weeks. Here are the preliminary results on 11 type 2 diabetics in relation to the six hour postprandial incremental area of chylomicrons, large VLDL and small VLDL, after a standard meal rich in saturated fat, which were given to patients at the end of the two dietary periods.



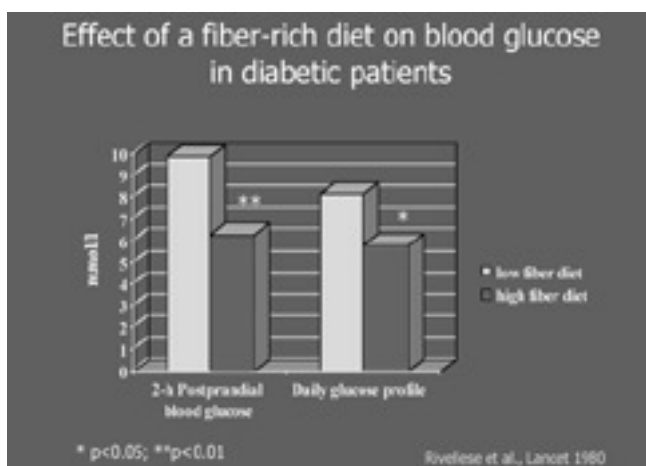
It can be seen that there is no difference for the cholesterol and triglyceride incremental areas with respect to chylomicrons and large VLDL. In relation to the small VLDL, which includes the large parts of remnant particles and which tends to decrease during the postprandial period, there is a significant high reduction after the MUFA diet, which suggests that a monounsaturated fat rich diet may induce a small but significant decrease in these remnant particles. Therefore, to summarise the first part of my talk, it can be said that monounsaturated fat, as opposed to saturated fat, certainly reduces LDL cholesterol and blood pressure, but may also improve insulin action and may reduce postprandial lipoprotein remnants.

Let us consider the other typical component of the Mediterranean diet: dietary carbohydrates. I think that it is very important to evaluate the possible beneficial effects of carbohydrates on insulin sensitivity, postprandial blood glucose or lipid metabolism, because there have been several studies over the last few years that have shown that carbohydrates may have a detrimental effect on these parameters. When we talk about carbohydrates, it is important to remember that carbohydrates are a very heterogeneous family of foods. It should also be remembered that the quality of carbohydrates is more important than the quantity. In fact, it is only when both of these aspects are considered, using the glycaemic load of the diet, that a clear relationship with cardiovascular risk is evident, in the sense that the higher the glycaemic load of the diet, the higher the cardiovascular risk, at least in overweight or obese women. Therefore, it is important to reduce the glycaemic load of the diet, which may be achieved by choosing the right carbohydrate rich foods, that is foods rich in dietary fibre. Again, it is important to look at the possible effects of this kind of diet not only on LDL cholesterol, blood pressure and so on, but also on insulin sensitivity, postprandial blood glucose and postprandial lipid metabolism. It has recently been shown that a diet rich in fibre with low glycaemic index foods is able to improve insulin sensitivity significantly, also in type 2 diabetes patients, characterised by a long-standing state of very high insulin resistance, which is very difficult to change.

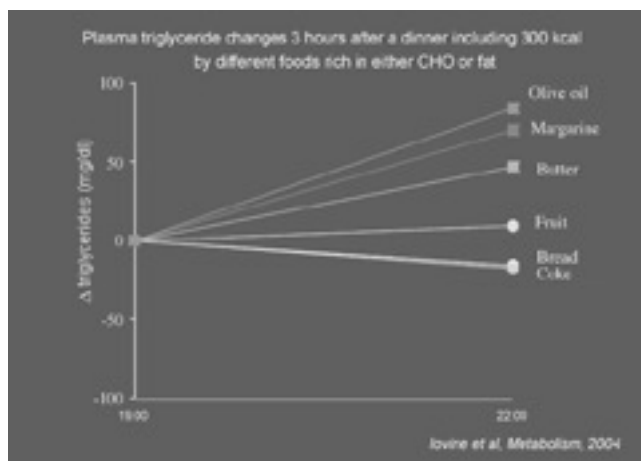


We can see that after six months on a high fibre diet, type 1 diabetic patients show a daily blood glucose profile that is significantly lower compared to the daily blood glucose profile of type 1 diabetic patients on a low fibre, high glycaemic index diet, and this result is even more significant in the postprandial period. The relevance of this effect on postprandial blood glucose, which is also present in non-diabetic subjects, was not really understood when these studies were performed. Only recently this aspect has been fully understood, when it has been demonstrated that postprandial blood glucose levels may be considered as an independent cardiovascular risk factor. This effect has been further emphasised by the results of the acarbose: the treatment with acarbose reduces significantly the incidence of cardiovascular events compared to placebo. These results come from a post hoc analysis; therefore, they should be considered with prudence. However, it is important to remember that acarbose reduces postprandial blood glucose levels and that this effect is very similar to the one obtained with foods rich in fibre and with a low glycaemic index.

Another point that I would like to consider is the effect of carbohydrate rich foods on postprandial lipid metabolism. We already know that high carbohydrate diets increase fasting triglycerides and this has been considered an adverse effect with respect to cardiovascular risk. However, very little is known about the effects of carbohydrates and the different kinds of carbohydrates on postprandial lipid metabolism. We have started to examine the possible effects using acute experiments looking at the changes in triglycerides in hypertriglyceridemic subjects after a standard dinner containing 300 calories derived from different foods rich in either carbohydrates or fat.



Moreover, one of the most important effects of this kind of diet is the improvement of blood glucose control. This improvement is mostly due to the fact that this kind of diet is able to significantly reduce postprandial blood glucose levels. In this study, after a short period of intervention, there was reduction of more than 20%. The effects of this kind of diet are also evident after a longer intervention period, as shown in the study on this slide.



It can be seen that 3h changes in triglycerides are significantly higher in the group receiving foods rich in fat compared to the changes in triglycerides obtained after foods rich in carbohydrates. This suggests that during the postprandial period, at least, the main determinant of the rise in triglycerides is the amount of fat rather than that of carbohydrates. Moreover, the quality of the carbohydrates may also be important, not only for the purposes of moderating blood glucose control after a meal but also with respect to postprandial lipid metabolism.

This is shown in another acute experiment where the rise of plasma triglycerides, of APO B100, which is the apoprotein of endogenous lipoproteins, and the rise of Apo B48, which is the apoprotein of exogenous lipoproteins, are significantly lower after a meal containing a large proportion (17 grams) of slowly digestible carbohydrates compared to the increase of these parameters obtained after a meal with the same total amount of carbohydrates, but with a lower proportion of slowly digestible carbohydrates.

This suggests that the quality of the carbohydrate may be important in modulating postprandial lipid response in relation to lipids of both exogenous and endogenous origin. Therefore, to

summarise this second part of my presentation, it can be said that high fibre low glycaemic index foods certainly reduce LDL cholesterol, but they may also improve insulin action and reduce postprandial blood glucose as well as postprandial exogenous and endogenous lipoprotein.

In conclusion, I think that it is possible to say that a Mediterranean diet or, more in general, a healthy diet, which should be tailored to fit the dietary habits also of non-Mediterranean countries, may have an impressive effect on the reduction of cardiovascular risk since the ideal combination of the different foods acts synergistically throughout different mechanisms. However, I believe that it is also important to stress that when we speak about the Mediterranean diet, we are referring to the Mediterranean diet followed by Mediterranean people of, at least 50 years ago. If we believe that it is important to adopt this kind of diet, it is also essential to consider that we should try to optimise this kind of diet by choosing the foods that maximise the reduction of cardiovascular risk. I would further like to stress that 50 years ago, levels of physical activity were much higher and it is therefore necessary to adapt the amount of food to the actual needs.

Thank you very much for your attention.

Questions

Member of the audience

I would like to make a comment on your first slide, which was a study looking at cholesterol and heart disease mortality across Mediterranean countries. I think that this study underestimates the true impact of saturated fat because it appears to show the same cholesterol levels with much lower mortality in the Mediterranean than there is in the north of Europe. However, I think that this is because they relied on a single measure of cholesterol, whereas if there were a regression to the mean, the lines become shorter and steeper, and then it is no longer clear whether there is a real difference at each cholesterol level. We should not downgrade the major importance of saturated fat and cholesterol.

Angela RIVELLESE

I completely agree. I do not wish to suggest that the hypocholesterolemic action is not important, but we must also consider the other possible effects in order to be able to choose the right foods and adopt a diet that can maximise its effects on the reduction of cardiovascular risk.

Didier CHAPELOT

I would like to make a comment on the importance of the postprandial diet. It is really related to the first question. In general, HDL or LDL cholesterol levels are considered as independent factors because they are measured at the fasting state and it is a reflection of lipid synthesis but in fact, it is very important, it happens after meals every day, which is also the case for glycaemia, so fasting glycaemia is an artefact, which only occurs for a few hours at the end of the night. The same can be said for lipids. After breakfast, the baseline for triglycerides will not be reached until the end of the night. Of course, it is possible to measure triglyceride in the fasting state at 7 o'clock in the morning, but it is just a reflection. What is most important is what is happening after every meal in terms of metabolic response. In this respect, abnormal accumulation within the circulation of glucose and also triglyceride with lipoprotein is the most important thing in terms of long term effects on health. This is also the reason why, depending on the study, markers that are measured in the fasting state tend to be different because what is important is the dynamic during the postprandial state, which is effectively much more difficult to measure.

Angela RIVELLESE

The problem is the measurement of these parameters in the postprandial state.

Member of the audience

Do you have any data enabling a distinction between different categories of fibres, such as soluble fibres or insoluble fibres coming from fruits or whole grains, on these effects?

Angela RIVELLESE

In relation to the metabolic studies, soluble fibre rich foods are more effective. However, it is also important to remember that in observational studies, and epidemiological studies, the relationship with cardiovascular risk is particularly present with cereal fibre. Therefore, I think that both are important and act through different mechanisms.

Cardiovascular disease preventable fraction in the population through adherence to Mediterranean diet

Salvatore PANICO

Dipartimento di Medicina Clinica e Sperimentale, Università di Napoli, Federico II, Naples, Italy

I would like to begin by talking about one of the main issues of this meeting: moving from research to action. One of the questions that need to be asked is whether it is necessary to promote dietary change when we can rely on effective drugs which favourably modify these factors. We already heard the story about the magic hormone replacement therapy, which was considered for decades to be a solution for the prevention of coronary disease in post-menopausal women. Now, it is the era of statins. We know that they are very potent and effective drugs against cholesterol, inflammatory markers, blood pressure and even cancer. Public health has the major task to qualify all these pieces of scientific information as effective and convenient on the large scale as well as to raise the issue of feasibility both in terms of costs of and compliance to the suggested solutions.

I would like to show you some slides looking at the situation in the United States but which can also be applied to Europe.

If we take the main three risk factor distribution statistics and apply the current evidence-based guidelines on the risk factors, using either American or European guidelines, there are large amount of people between the ages of 45 and 64 taking more than one drug – and if we look at those over 65, there are very few people without drugs. The problem is that with all these indications, the situation can become confusing and it becomes possible to lose the desired direction. We also know that there could be a pill (known as the polypill) that could prevent 80% of coronary heart attacks: a pill composed of all of these drugs, which are effective and, when combined, could reduce the risk of strokes by 80%. We also know that we could use selected food items as pills (known as the polym meal), even though this idea was not taken seriously when it was initially published in the British Medical Journal. Therefore, we are facing the possibility of extremely important levels of prevention of coronary heart disease, and cardiovascular disease in general, simply by taking a pill or by using food items like components of a pill – you would take a clove of garlic and a piece of chocolate like a pill.

The problem is that we like to eat for pleasure, especially in Europe, and food cannot be dealt with like a medical remedy. Therefore, if we wish to have a basis for reasonably effective preventive action in public health, we must take into account that diet and dietary habits need to be considered as a whole. There are some issues which need to be considered, such as the modernity of the Mediterranean diet, which is now very different from the original Cretan diet. Is it still protective? Then, there is the problem of the visibility and the application of this diet. There are two main problems involved here: one is internal and derives from the fact that even in Mediterranean countries, investors in industrial food preparation rank profit as their top priority above consumer sales. The other problem relates to external issues, such as the transferability of the Mediterranean diet to other cases and contexts. There is also the problem of lack of experiments, as already suggested today: there are no experiments in the use of the Mediterranean diet using our end points. Do we need this? Then, there is the problem of looking at the size of the Mediterranean diet effect now. For this reason, I will start with some recent data on a Mediterranean cohort study within the framework of the EPIC Italy collaboration and which is important in order to establish the weight of the argument for the modern Mediterranean diet. This data was collected in the 1990s.

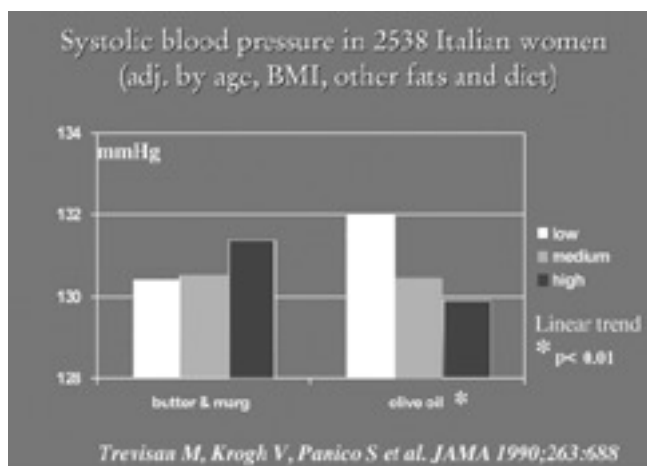
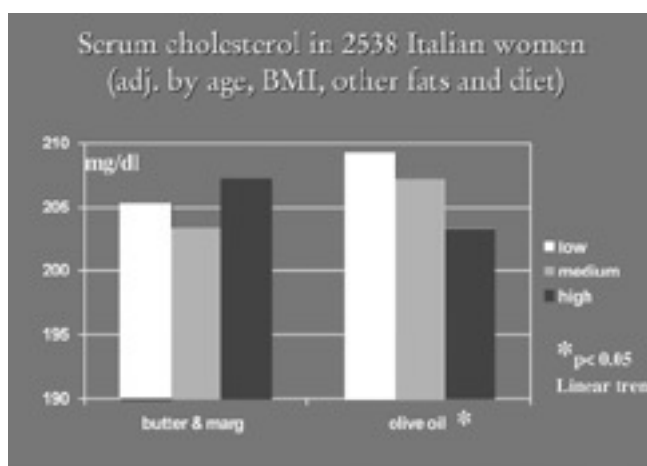
The EPIC Italy collaboration included centres spreading from northern Italy to southern Italy. These are the groups who produced this data and I would like to thank them for this data. These are the numbers: there are almost 50 000 people under observation and another 52 000 women. For the women cohort, we have tried to study the incidence of cardiovascular disease and the effect that diet has on it. They have used a dietary lifestyle questionnaire, anthropometry, blood pressure, and a vital statistics follow-up. This slide shows the well-known Mediterranean index score and these are the 9 items that we have used to compose the score, whose origin comes from the work of Greek colleagues, using the median value of the distribution of these components and using a score of 0/1 according to the position in respect to the median value.



This is what has been done to collect and validate data on the incidence: use of hospital admission data and in-cohort surveys. We know that incidence data are crucial for cardiovascular disease because case control studies are difficult to interpret. As to mortality we have examined all fatal cases, starting with the death certificate and then assigning the diagnosis. As to incidence of non-fatal cases, we have validated the data case by case according to medical notes. We have observed 129 cases of ischemic heart disease; then we have performed a statistical analysis on the incidence data, using the Mediterranean index as the variable to evaluate, and making adjustments for age, location, status, education, body mass index, levels of physical activity, smoking, total energy intake, risk factor status and history of angina. We have used different models, including treatment for risk factors, with no meaningful changes of the results. There is significant reduction of ischemic heart disease incidence according to the different tertile of distribution of the Mediterranean index: the risk is almost halved in the group with the highest adherence to the Mediterranean style.

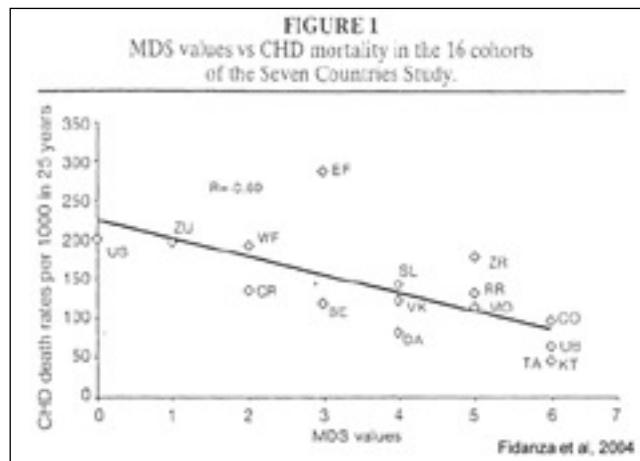
We have applied this risk estimates to achieve attributable risk at population level to know something more in terms of public health. Going through from the first tertile, which includes the diet scores up to 3 (an indication of the lowest adherence to the Mediterranean style), it is possible to prevent 28.5% of coronary events: these events include myocardial infarction and coronary re-vascularisation.

However, as known by epidemiologists, there are some problems of precision and interpretation of the estimate which are linked to the use of a simple formula. Firstly, it is problematic to extrapolate population attributable risk from epidemiological studies. Sometimes, all these risks are calculated using components deriving from different sources, which is not the case here. Another issue is the lack of confidence intervals: We have improved the precision of the estimate by using a specific multivariate formula that enabled us to adjust all the variables together in the evaluation of the population attributable risk. We estimated a 27.4 preventable fraction in the passage from the low- to the high adherence tertile: we had a high proportion of the events among the exposed in the first tertile (including the women who followed less a Mediterranean-type diet), more than 61%.



These results come from the first investigation on a female Mediterranean cohort, as most cohorts are male, or if they are female, they tend to be in North America or Central Europe. This data confirms that in the 1990s, women on what we know now as the modern Mediterranean diet, whilst not the traditional one, were still protected. This was consistent with data from studies on random samples of the Italian population 15 years ago, which showed that, the major risk factors, like cholesterol, systolic blood pressure, and glycemia, were lower in people consuming more olive oil than butter and margarine, as indicator of a Mediterranean dietary style.

To look at the Mediterranean picture, examining recent data from Greece and Spain, in case control studies, we see that adherence to Mediterranean diet, measured through a Mediterranean index, provide protection toward acute coronary syndrome. In a recent analysis of the data from Seven Country Study, the Mediterranean score provide comparable results for risk reduction in men.



Therefore, given the risk reduction through the Mediterranean diet, the one we have now, it appears that there is no variability in the three Mediterranean countries as far as coronary disease is concerned. I think that it is reasonable to assume that the estimation we have provided (almost one woman over four) can be saved from ischemic heart disease just going through a feasible passage: increasing consumption of at least one or two of the nine dietary items characterising the Mediterranean type of diet. This is of public significance.

For the purposes of comparison, I would like to talk about the Nurses study, which also took into account this relationship with attributable risk. Whilst it did not concentrate on diet alone, having a diet score in the upper two quintiles, non-smoking nurses performing vigorous exercise have a risk reduction higher than ours with 54% of population attributable risk.

Another comparable estimation of the risk reduction, performed in a Dutch population, indicates that the prevented proportion of individuals with chronic disease - using fruit and vegetable indicators - is about 16% (focusing on mortality from cardiovascular disease).

I have two final comments and then we shall open the discussion.

- Even in "modern times" Mediterranean type diet appears a feasible, safe and effective tool for preventive action against cardiovascular disease, especially coronary, in the population living in the Italy, Spain and Greece (the olive oil congregates).
- The size of preventable fraction of cardiovascular disease - mainly coronary - is significant and approximate one third of the total events, for simple changes in dietary habits.
- This estimate provides important public health information to decide on the adoption of more "chronically oppressive" tools like drugs and selected food items promotion.
- Eating for better health still may means eating to be pleased and happy.

Are there any questions? Perhaps you would just like to have an open discussion.

Questions

Frank HU

That was very interesting data. I have a question regarding the individual components of the Mediterranean diet. As you know, the overall dietary score in the original Greek study had significant benefits in terms of total mortality, cancer and cardiovascular mortality. However, none of the individual components showed any significant effects. Did you look at the association between individual components of the Mediterranean dietary score and coronary heart disease?

Salvatore PANICO

We carried out analyses relating to this, and we know that the ratio between monounsaturated and saturated fat and alcohol consumption are the main significant components of this score, at least as far as our cohort is concerned.

Member of the audience

This question is very interesting. With regard to the "Mediterranean diet" - also known in the south of the Mediterranean and the south of France - the onion and garlic are often regarded as the most important food. One often intends to say that the presence of garlic and onion in a house moves away the disease. It is completely possible to live by consuming olive oil and flours of durum wheat, like in 'couscous' or bread. My parents and grandparents lived with onion, garlic, bread and olive oil. Garlic was evoked like a food making it possible to decrease the blood pressure but the onion also reduces the sugar rate in the diabetes. They are important food of the Mediterranean meal.

Salvatore PANICO

I can confirm this empirical experience and scientific evidence on the protective factor of onions and garlic on these two risk factors. I would like to say that when we talk about the dietary index, we are discussing comprehensive patterns. If we wish to talk about single food items, this is another matter. We need to know much more about all of them, and the extent to which people would be ready to start consuming certain items on the basis of recommendations. Would anyone else like to make a comment?

Edith FESKENS

I would also like to comment on this matter. In relation to garlic, we have seen that there has been an analysis showing some beneficial effects. It is being sold in our country as 'The Pill', and I know that in our elderly men's study over the seven countries, many people use these garlic pills even though they do not have any disease. There was greater opportunity to study the health effect of onions and we carried out some extensive studies on the micronutrients amongst these components in the diets, such as red wine, apples and onions, and we showed that the higher the intake of the flavanols, the lower the risk of coronary heart disease. In our study, this was mostly due to consumption of tea and apples, but we did not consume as many onions so they were not studied in the same amount of detail. However, I think that it would be really interesting to see what is in these vegetables and fruit.

Member of the audience

I have a question for the whole panel. If we are now promoting the Mediterranean type diet, is it a diet that everyone, from children to the elderly, should follow? There are so many differences between people, their habits, whether or not they smoke, their genetic make-up and metabolisms and so on. Should we really be promoting one diet?

Roberto MARCHIOLI

I agree with you that there are different Mediterranean diets. If we think about the diets in Greece and Italy 50 years ago, we can see that they were very different from diets in those countries today. However, as Salvatore Panico said earlier, the so-called Mediterranean diet is good for health.

I would like to answer your question with a question that a cardiologist asked me when we were asking cardiologists to join the GISSI Prevenzione trial. He asked: 'But why are we going to study fish oil in Italy when we have so much olive oil?' My answer to him was that as we had so much olive oil, perhaps we needed some fish oil. There could be a mix of the two situations: cultural dietary habits associated with lower cardiovascular mortality; and in addition, an improvement of the diet, with some pieces taken from other protective dietary habits.

Angela RIVELLESE

I think that it is important to promote not necessarily a Mediterranean diet, but a healthy diet on the basis of all of our knowledge. This diet then needs to be tailored to fit the dietary habits of different populations. Some of the typical and most important components of this diet should be a reduction of foods rich in saturated fat compensated by an increase in foods rich in fibre and using the low glycaemic index. This is the basis, and all the other minerals and vitamins come naturally with this kind of dietary pattern. This may seem very simplistic, but I think that it is important to ensure that the message is clear.

Edith FESKENS

I am a member of a national health council for the recommended dietary allowances and I have been on the committee for dietary fibre. I think it is clear that what we advise in terms of nutrition for adults is different from what we advise for children. Of course, it is necessary to look at the personal make-up, age and body weight of each person.

Speaking of body weight, one of the intriguing things I have found is that people on the Mediterranean diet had a lower body mass index and as a result, they lost weight. This is intriguing because it is important and it is also contradictory to what I remember seeing. For example, in the EPIC cohorts in Spain, the prevalence of obesity in women and children is quite high. Therefore body weight is very difficult to manage, but it does have to be managed as a first priority.

Finally, with regard to genetic susceptibility, we all carry the genes that make us susceptible to type 2 diabetes and obesity, as Jaakko Tuomilhto explained this morning. There are people who are more susceptible to certain types of cancer or other types of disease. We need to look at this in more detail, but I think that this would be very costly and we need to provide advice to the general public. There may be people who do not respond very well, but this information is not dangerous to anyone. However, we can be optimal by refining what we already know, such as typical genetics, but this is a difficult area and I do not predict that there will be any real progress in this area in the next few decades.

CVD diet visavi other CVD risk factors

Göran BERGLUND

Department of Clinical Sciences, Malmö University Hospital, Malmö, Sweden

I am the chairman of the last session (CVD – II). We will start the session on dietary factors and cardiovascular disease. I shall start with an introduction to put dietary factors into perspective along with the other cardiovascular risk factors of which you are aware, and look at how important diet is compared to smoking and so on. Margaret Leosdottir, from Iceland, will then continue with energy and fat intake and their relationship to cardiovascular disease. Rodolfo Saracci will subsequently present a recent paper on the EPIC heart study. Finally, Dr Schulze from Germany will talk to us about dietary patterns and the risk of cardiovascular disease.

I would encourage everyone to ask any questions they may have as they arise at the end of each presentation.

Let us quickly look at the well-known array risk factors of cardiovascular disease: age, male gender, smoking, blood pressure, lipids, diabetes, low physical activity, low social status, and markers of inflammation such as the CRP. We have already discussed dietary factors and we have seen many slides on this subject today. They are: the high intake of saturated fat, the low impact of monounsaturated and polyunsaturated fat, low intake of fruit and vegetables, low intake of fibre, and high energy intake, which is something that we would also like to present some data on.

The epidemiological cornerstone for the dietary-cardiovascular relationship starts with the Seven Countries Study, as already mentioned by several speakers here today, and I will provide some more critical information on this study as it has been so very important to the whole area of dietary recommendations for the last 20 years.

We all know the Western Electric study from the Stamler group, the Framingham study, and the Oslo Intervention study, all three of which were carried out in 1981. The latter showed a 50% reduction of the multivariate intervention, data that has been very difficult to replicate.

I will give some data from two more recent studies – the Health Professional Follow-up Study and the Nurses Health Study – in order that we may examine how the large-scale American East Coast studies work and what results they have obtained.

I shall also examine the INTERHEART study in more detail to put the dietary factors into perspective compared to smoking, hypertension, diabetes, lipids etc.

There is also the beacon of light offered by the EPIC Heart Study that is now ripe to bear results, and we will hear the first results on anthropometry here today from Rodolfo Saracci.

The current dietary guidelines are also being shown on the slide: total fat intake < 30, total saturated fat <10. In addition, in the American Heart Association paper, there are some very strong statements claiming that saturated fat intake is the principle dietary determinant of LDL. It is quite difficult to find a scientific basis on which to base such a statement, considering all the studies conducted to date. Cholesterol intake <300, 2 fish servings per week, five servings of fruit and vegetables per day, limitation of salt to less than 6 grams per day – which is easier said than done – and limit alcohol with no more than 2 units per day for men and 1 for women: these were the 2001 guidelines.

I will comment briefly on the Seven Countries Study. There is an impressive array of well-known epidemiologists behind this study. The main results were that all death rates were negatively related to the ratio of the monounsaturated to saturated fatty acids. Furthermore, the inclusion of that ratio with classic risk factors – age, blood pressure and others – accounted for 85% of the variance in deaths from all causes, almost all variance of the coronary heart disease mortality, 55% of the variance for cancer and 66% of the variance for strokes.

I will focus mainly on all-cause mortality and coronary heart disease mortality. A very encouraging statement comes at the end of the conclusion. With olive oil as the main fat, all-cause mortality rates and coronary heart disease rates were low. This is very encouraging for this audience here, as well as for the Italian and Greek populations.

The aim was to relate each nutrient contributing to energy to deaths from all-causes, and death from coronary heart disease, stroke and cancer. There were 11 000 men aged 40-59 years old in 15 cohorts. In most centres they came from very rural areas. The Dutch cohort was a random sample of all men in Zutphen; the US and Rome cohorts were railroad men, and the Serbian men were largely from an agricultural cooperative. There was a very high participation rate of 90%. We will never see that again. In Scandinavia we have seen the participation rates go down from 75% to 60% to 40% as new populations come into our country.

I would like to put this into perspective by focusing on a number of points. EPIC has individual dietary data on over 500,000 people. In the Seven Country study, dietary data was collected from between thirty and fifty men in each cohort. Each centre had slightly different methods. An important part of the Seven Countries Study was that all food and drinks were weighed and recorded for seven days in the participating centres. Duplicate samples were sent to the laboratory for chemical analysis. There was also a spread over seasons, which is very important in this type of study.

They observed very striking differences in the 50-year death rates between the participating countries. Look at the coronary heart disease death rates from East Finland to Crete. Today we never see these differences. I looked carefully at the diagnosis of the cause of death. In some cohorts, only a minority died from coronary heart disease or cancer. It is difficult to see the validity of the diagnosis here and it is also difficult to see what they really died from. When looking at rural areas one also has to question whether the vital status is really valid in this study. Furthermore, are the data from East Finland to Crete really compatible with longevity data from the larger areas these samples are taken from? I think these are very important questions.

The well-known finding here is that if you take the ratio of monounsaturated to saturated fat, you can explain 72% of the observed deaths. This is a very strong correlation and is due to the fact that the results are the mean of the cohorts, so this is an ecological study and not individual data here.

When it comes to the same analysis ratio for monounsaturated to saturated fat for coronary heart disease mortality, they can explain only 44% of the observed deaths here by this ratio. This means that there are some discrepancies in the findings.

When you add classic risk factors of age, body mass index, systolic blood pressure, cholesterol and the number of cigarettes smoked, you can explain nearly 100% of the variation in a highly complex chain of events that leads to death from myocardial infarction.

Reading the Seven Countries Study now, with all the new knowledge around, it should be remembered that this is an ecological study that uses population means. Very few subjects were used to obtain dietary means and the dietary methods differ between centres. One could postulate that the centres were representative of Europe at that time and probably not at all of the Europe of today. Furthermore, the design overestimates true associations because population means are used. However it has had a huge impact throughout the Western World on dietary recommendations.

It is important to remember that risk of saturated fat intake should be mediated through a high serum cholesterol level. A high saturated fat intake should increase your serum cholesterol. Most feeding studies show that, but they are short-term and do not offer much information about long-term effects. However most studies within cohorts have had difficulty in showing any relationship between saturated fat intake and serum cholesterol levels, even if you take several cholesterol measurements. We have this problem in the Swedish populations that I am aware of and work with; we have great difficulty in showing significant correlation. This could be due to regression dilution bias, although this could be a way to explain something that has not been found.

The next generation of studies, the Health Professionals Follow-Up Study published in 1996, showed no association between total fat and coronary heart disease. In these East Coast studies there were no association between saturated fat intake and coronary heart disease, but there was a negative association between monounsaturated fat and coronary heart disease: it showed that the more monounsaturated fat you eat the lower your risk of coronary heart disease. The same is true for polyunsaturated fats, but the opposite is the case for trans-fatty acids, which increase the risk of coronary heart disease. This is a large study on men with a long follow-up and carries considerable weight.

Diet vis-à-vis other CVD risk factors

- **The Health Professionals Follow-up Study**
- No association between total fat and CHD
- Ditto for saturated fat intake and CHD
- Monounsaturated fat intake negatively associated with CHD
- Polyunsaturated fat intake negatively associated with CHD
- Trans fatty acids positively associated with CHD

The same is true for women – the Nurses' Health Study had 80 000 participants. Multivariate regression analysis including cardiovascular disease risk factors and fat sub-classes. Quintiles 5 to 1 showed no significant association between total fat intake; saturated fat CHD, and monounsaturated fat and CHD. Polyunsaturated fat and trans-unsaturated fat are strongly significant and are negative and positive respectively.

Diet vis-à-vis other CVD risk factors

The Nurses Health Study (n=80.082)

Quintiles, multivariate logistic regression in-cluding CVD risk factors and fat subclasses

	p for trend
• Total fat intake and CHD	0.50
• Saturated fat and CHD	0.37
• Monounsaturated fat and CHD	0.37
• Polyunsaturated fat and CHD	0.003
• Trans unsaturated fat and CHD	0.002

I will finish by discussing the INTERHEART study in order to put the dietary factors in perspective with the other strong cardiovascular risk factors. INTERHEART is a case control study. It carries weight as it has 15 000 hospitalised myocardial infarctions, which means that at least 40% of the study in cardiac deaths are not included, but it is impressive nonetheless. The participants are from 52 countries from all continents. The design could be open to question with regard to controls. The odds ratios and the population relative to the risk have been calculated. For myocardial infarction, this was done using nine modifiable risk factors: smoking, history of hypertension or diabetes, waist/hip ratio, diet, physical activity, consumption of alcohol, apo B to apo A1 ratio and social factors. The last of these is a difficult score to understand as many questions are incorporated in this psychosocial score.

With regard to the results, 90% of the variation in men and almost 95% in women could be explained for the population relative to the risk figures. Smoking, the apo B to apo A1 ratio and diabetes were all strong risk factors, however they explained different components of the population attributable risk, as these have high prevalences in the population. The same is true of psychosocial factors: one third of the risk can be explained by psychosocial factors. The only significant dietary factor was the daily fruit and vegetable intake, which came out with 14% of the population's attributable risk. Alcohol consumption and physical activity were also significant but account for lesser degrees of the population's attributable risk. This provides a good estimate of the importance of various risk factors for having a myocardial infarction.

In summary, nine modifiable risk factors accounted for most of the risk in both men and women. They conducted a good analysis showing this was true for all continents, both sexes and all ages. Intake of fruit and vegetables explains 14% of the variation of risk; findings suggest that changes in lifestyle (because all of these things were modifiable) have the potential to prevent the majority of premature cases of myocardial infarction. The question is to what extent diet could contribute to the risk decrease.

In my view, the old ecological analyses of prospective cohorts do not form a very valid base for dietary recommendations. The more recent cohort studies do not really show clear-cut results for some major dietary factors. In my view, we need to continue this work; we need large prospective cohort studies. Most importantly, we need dietary intervention studies to be able to design effective programs for the prevention of cardiovascular disease. Bearing this in mind, I am glad that we have the EPIC study with more than 500 000 participants on which we have dietary data.

Are there any questions?

Questions

Franco BERRINO

I would like to challenge your proposal. I imagine that you agree that saturated fat has something to do with the level of cholesterol in the blood.

Göran BERGLUND

The problem is that it is very hard to show that in free-living people.

Franco BERRINO

But there is evidence that by modifying the diet and reducing saturated fat the cholesterol goes down.

Göran BERGLUND

All the feeding studies show that to be true. For the observational studies there is probably some form of regression dilution bias and it is hard to assess how big that bias is.

Franco BERRINO

Yes, because cholesterol is related to cardiovascular disease. Perhaps it is our ability to measure saturated fat with questionnaires that explains that conundrum.

Göran BERGLUND

This is at least one possibility.

Energy and fat intake and CVD risk

Margret LEOSDOTTIR

Department of Medicine, Lund University, Malmö University Hospital, Malmö, Sweden

The topic of my talk is “Energy and fat intake and cardiovascular disease risk”. I will focus mainly on fat intake but also briefly mention energy intake. I will start by going over dietary recommendations on fat and examining how they look today. Then I will spend most of my time talking about our research and results from Malmö. I will then try and put our results in perspective with other similar studies conducted in the field, and then conclude with a hypothetical idea of how dietary guidelines for cardiovascular disease should look.

Scientific studies on cardiovascular disease began in the early 20th century with animal studies, where you could see that by feeding research animals a fatty diet you made the animals atherosclerotic. With regard to human studies, one of the first studies was Ancel Keys’ Seven Countries Study, which showed that high intakes of animal foods (excluding fish) increased the risk of coronary heart disease and also showed a high monounsaturated/saturated fat ratio being beneficial in preventing coronary heart disease.

These findings were later strengthened by dietary intervention studies, mostly with surrogate endpoints such as blood lipid levels. However, results from epidemiological studies conducted at this time and later were not as convincing – especially not concerning total fat and saturated fat intake. Many of these studies had non-significant findings.

Nevertheless, dietary guidelines started appearing at a similar time, generally promoting low fat diets with special emphasis on saturated fats. The core message of the dietary guidelines today remains unchanged: reduce fat intake to less than 30% of total energy intake and saturated fat to less than 10% of total energy intake. These recommendations are seen in the American Heart Association guidelines. The same goes for most nationally used guidelines – although these are of course released to promote general health and do not focus only on cardiovascular disease. All the same, they have the same core message: reduce total fat to less than 30% of total energy intake and saturated fat and trans-fatty acids to less than 10%, monounsaturated fat to 10%-15%, and polyunsaturated fat to 5%-10%.

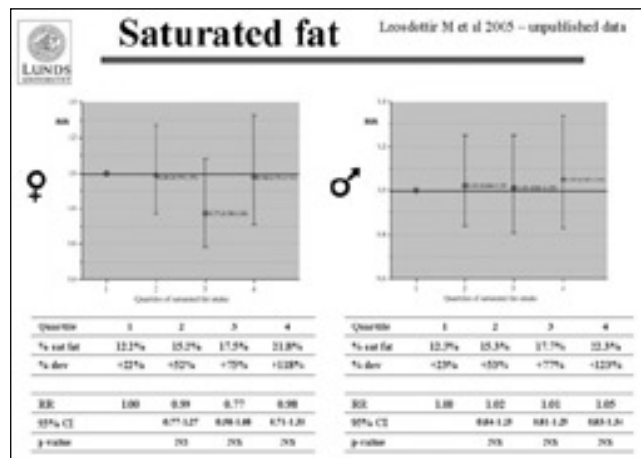
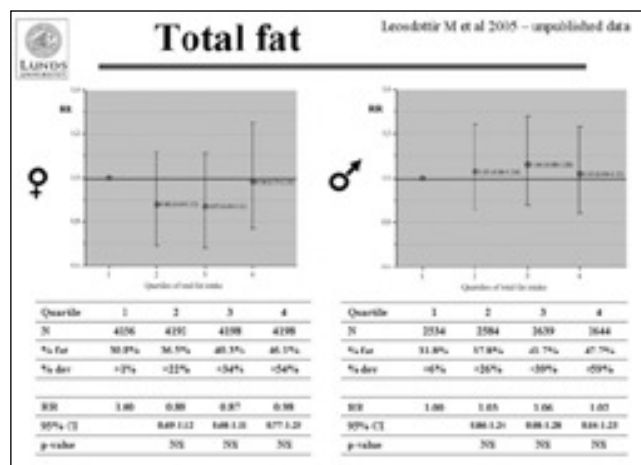
With regard to total energy intake, reference values are given in most dietary guidelines. These are usually acquired from biological studies on humans on energy expenditure and not on disease or mortality data. In Swedish dietary guidelines reference values are around 2 700 kilocalories per day for grown men and 2 200 kilocalories per day for women.

I now come to our Malmö study: the Malmö diet and cancer study is one of the EPIC cohorts. It was designed in the early 1990s to detect dietary factors in relation to cancer risk. The cohort includes just over 28 000 middle-aged individuals who were living at the time in Malmö – the third largest city in Sweden. Sixty-one per cent were women. Dietary composition was evaluated with a food frequency questionnaire and a seven-day menu diary. A physical examination was conducted, blood samples were drawn, and each subject answered an extensive questionnaire regarding lifestyle, disease history, etc.

The aim of the current analysis we have been doing on the Malmö diet and cancer material was to examine whether total energy intake, total fat intake, saturated, monounsaturated or

polyunsaturated fat intake are independent risk factors for cardiovascular disease and mortality. We divided the material into quartiles of energy and fat intake, respectively, using the first quartiles as a reference groups. We adjusted for age, smoking, physical activity, socio-economic status, marital status, dietary fibre, alcohol consumption, systolic blood pressure and body mass index. Endpoints were cardiovascular events: acute coronary events or ischaemic strokes, fatal or non-fatal, and we calculated relative risks with the Cox regression model.

During a follow-up time of 8.4 years, 1 556 endpoints were registered. Results for total fat can be seen in figure 1. In the first quartile for women and for men, subjects were eating approximately in accordance with dietary guidelines. Individuals in the fourth quartiles were ingesting 46%-48% fat as a proportion of total energy intake. As seen on the graphs, there was no significant difference between the quartiles concerning cardiovascular disease risk. The same was observed for saturated fats (figure 2). Individuals in the first quartiles received on average 12% of their total daily energy from saturated fats, compared to 20% in the fourth quartiles –over 100% more than recommended. Still we did not observe any increase in cardiovascular disease risk.



Also, for monounsaturated and polyunsaturated fat there was no significant difference between the quartiles. Note though that there is a significant limitation to the unsaturated fat analysis, which will be mentioned shortly.

We also looked at the ratio between the saturated and unsaturated fats in a similar way as was done in the Seven Countries Study, where individuals in the first quartiles had the most beneficial ratio – the highest intake of unsaturated as opposed to saturated fat – and those in the fourth quartile had the least beneficial ratio. No significant difference between the quartiles was observed.

Concerning total energy, individuals in the third quartiles ingested approximately in line with dietary guidelines, and those in the fourth quartile ingested 20%-30% more than recommended. No increase in risk was observed for individuals in the fourth quartiles.

Taken together, we observed that individuals getting more than 30% of daily energy from total fat and more than 10% from saturated fat did not have increased cardiovascular disease risk – even individuals receiving 45%-50% of their daily calories from fat or 20% from saturated fat did not have increased risk. Benefits of ingesting relatively large amounts of unsaturated fat were not observed in our cohort, and men and women ingesting 20%-30% more calories than recommended did not have an increased risk.

There are some important considerations to be taken into account. Firstly, the subjects were already middle-aged at a baseline, or between 55 and 57 years old. This can be of significance, as other studies have indicated that dietary factors are more important at an earlier age. For example, the recently published 20-year follow-up from the Nurses' Health Study showed this, as did the Framingham Study. Another limitation in the Malmö material is that trans-fatty acids were not registered as a separate variable and are thus included into the monounsaturated and, to some extent, polyunsaturated fat variables, which can have confounded the results considerably.

I will come to the matter of trans-fatty acids again shortly, but first, a quick mention of the sources of unsaturated fatty acids, which is also very important when talking about the effect of unsaturated fat on health and cardiovascular disease risk. In the average Malmö diet, most monounsaturated fats come from dairy products and margarines, while in the Mediterranean diet for example, the monounsaturated fats come mostly from olive oil. These are two completely different types of fat which are coupled to different dietary patterns. This must be taken into account when drawing conclusions from dietary studies.

Returning to the trans-fatty acids - data from the 20-year follow-up publication of the Nurses' Health Study shows clearly the harmful effects of trans-fatty acids in the diet, giving an increased risk of coronary heart disease. As you can imagine, when combining trans-fatty acids and unsaturated fat variables as unfortunately was done in the Malmö Diet and Cancer study, it is maybe not surprising that we did not observe any significant beneficial effects of unsaturated fats in the diet.

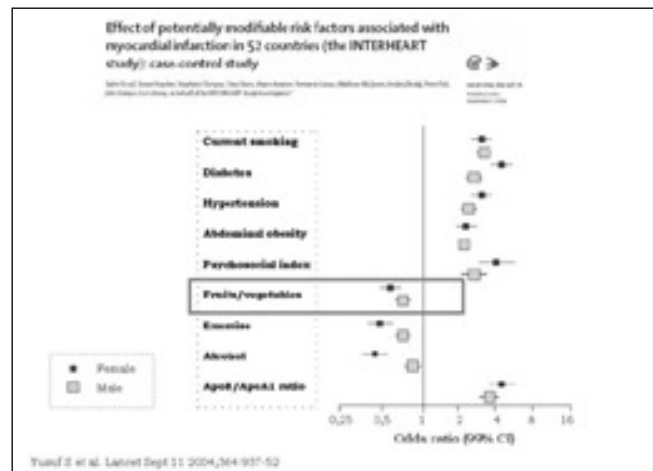
Another thing I would like to point out from the Nurses' Health Study are the results obtained on total fat and saturated fat, which as in our study had no significant effects on coronary heart disease risk.

With that in mind, I would like to return to the Swedish dietary guidelines which, like many other dietary guidelines, group together saturated and trans-fatty acids in the recommendations, saying that you should limit these two types of fat to under 10%. This in my opinion is not fair to the saturated fatty acids, as these

two types of fat do not have comparable effects on health.

Another thing that should be taken into account, when discussing the effect of dietary fat on health and on cardiovascular disease, is what characterises the individuals who eat fatty foods? One very important factor is fibre intake – we know that fibre is protective against cardiovascular disease. Data from our own material shows that with increasing fat intake, one can observe a significant decrease in fibre intake for both men and women. The effects of fibre on cardiovascular disease were shown very clearly in the Health Professionals' Follow-Up Study in their multivariate analysis. When fibre intake was added to their multivariate adjustment model a significant drop in the risk for the upper quintiles of fat intake was observed. The same pattern was observed for saturated fats.

With this in mind I will return to the previous epidemiological studies just to point out that adjustments for fibre intake were generally not made in these. Vegetables and fruit are also a very important thing to think about when looking at dietary fat and cardiovascular disease. Analysis from the Malmö diet and cancer study material shows across quintiles of fat intake how intake of fruit and vegetables decreases and, as we know and have heard a lot about here today, fruit and vegetables protect against cardiovascular disease. This is a very important thing to take into account when looking at such data. The INTERHEART study depicted the effect of fruit and vegetables on cardiovascular disease very nicely (figure 3). As was talked about earlier, fruit and vegetables were the only dietary factor that showed some significance in their analyses, underlining the importance of taking this into account when evaluating cardiovascular disease risk.



We should also bear in mind that individuals who eat fatty foods also eat more on average, and that people who eat calorie rich foods often eat relatively fatty foods. Smokers and individuals of lower socio-economic classes also often eat fattier foods. All these factors are important when looking at the fat-cardiovascular disease relationship. Perhaps instead of looking at fat as the culprit, we should look at the behaviour (both the dietary and lifestyle behaviour) of those who eat fatty foods and how those factors are coupled to cardiovascular disease.

To conclude, current internationally used dietary guidelines on total and saturated fat intake are not strongly scientifically supported when it comes to cardiovascular disease risk. Saturated and trans-fatty acids do not have a comparable effect on health and as such do in my opinion not deserve the same treatment when it comes to dietary advice. Fat intake is strongly coupled to intake of dietary fibre, fruit and vegetable intake, all of which have proven cardio-protective effects. This could have considerably biased results of previous epidemiological studies on the effect of dietary fat on cardiovascular disease incidence.

If basing dietary advice concerning cardiovascular disease on the degree of scientific evidence available, one should stress a diet rich in fruit, vegetables and fibre with a focus on fat quality and not fat quantity.

For the ideal dietary guidelines, if we try to prioritize the factors that have the strongest scientific evidence, I would say that we need to stress that people adjust energy intake to energy expenditure, avoiding over-consumption of calories. They should maintain a balanced diet including calories from all energy sources including fat, but shifting fat consumption toward

non-hydrogenated, unsaturated fat from plant sources and from fish. They should avoid trans-fatty acids entirely and, even though I have not covered this in my topic, they should shift carbohydrate consumption away from refined carbohydrates to more complex ones, and prioritize vegetable, fruit and fibre-rich products in the diet.

Finally, it is perhaps not ideal to talk about dietary guidelines, but rather about lifestyle guidelines, because diet is inevitably coupled to lifestyle factors and we should take this into consideration.

Questions

Member of the audience

Having served on several expert panels trying to figure out what the totality of evidence is, I would like to remind you that you are reporting the results of one cohort study. I personally obtained identical results concerning fatty acids 10 years ago from the ATBC trial, except that we did find trans-fatty acids to be harmful – which we know – so I ask that before you spread this new information further, you remind the audience that you are reporting the analysis of one cohort study.

Margret LEOSDOTTIR

This is of course true, and it is not my intention to “spread news”, but to represent results from our study and other similar ones to this audience of fellow researchers gathered here today. However, I think we have to critically evaluate the scientific evidence we have from all studies on the diet-heart relationship and that is what I was trying to do here.

Frank HU

You found an inverse association between energy intake and coronary heart disease. This result is consistent with several previous studies, so the interpretation of total energy in these kinds of studies is not just about calories but is a marker for increased physical activity. Here, the data tells us that increase in physical activity is associated with decreased risk of coronary heart disease, so the results are not really surprising – the interpretation is just more complicated.

My second comment is related to saturated fat. I think we probably put too much emphasis on saturated fat. Even though we know that saturated fat increases HDL cholesterol but it also increases LDL cholesterol, it does not have a very strong impact on the ratio of HDL cholesterol to LDL cholesterol. This ratio, as we know, is the strongest predictor of coronary heart disease. Also, if you compare saturated fat with refined carbohydrates, it actually decreases triggers for this. This is why if you compare saturated fat with carbohydrate, which is mostly refined carbohydrate, you are not expected to see a major impact, as has been found in the Seven Countries Study.

Margret LEOSDOTTIR

Concerning energy intake, I agree with what you have said, and this is perhaps why I have not gone into detailed discussion about our energy findings. These are in line with other findings. This is a very complicated relationship between not only physical activity, but also basal metabolic rate, spontaneous body movements, vitality and premature ageing. These all affect total caloric intake, so it's a very complex relationship that is perhaps hard to assess through epidemiological studies. I also agree on the matter of saturated fats.

Edith FESKENS

This was an intriguing presentation. I have some comments. Firstly, to follow up on the energy issue, one of the factors which may play a role is under-reporting by overweight people. I think one of the main problems we have with observational studies looking at diseases which are associated with being overweight may be under-reporting. It may also be beneficial to look not at cardiovascular disease in total but coronary disease and stroke, because there are different ideologies from a dietary point of view. You talk about the Seven Countries Study: I think you do the study an injustice because there was an adjustment in the study for fibre and an adjustment for vegetables and fruit that appeared in later publications. What we saw in the publications was that rates within the ecological study were explained by saturated fat, smoking and the intake of flavinols, such as creatine in foodstuffs, tea and red wine, and indeed, that was taken into account.

I am on the Netherlands Health Council involved in preparing the recommended dietary allowances. The recommendations for dietary fibre we are currently preparing in the Netherlands are the first recommendations based on epidemiological data. So far, all the recommendations (and I am sure that this is also the case in Sweden) have not been looked at from the point of epidemiological studies of cohorts because of the problems of confounding causation etc. They all looked at intervention trials and there were recommendations made for trans-fatty acids and saturated fatty acids, which are separate in most countries, and for all the types of fatty acids in the studies by Martine Katan, for example, which are exactly the same as was done by Ancel Keys in the 1950s with regard to total cholesterol, LDL and triglycerides and HDL from saturated fat, monounsaturated fat and polyunsaturated fat. Only the trans-fatty acids have additional influence on CHD apart from the lipoproteins, so it is worth mentioning them separately.

Results from the EPIC Heart

Rodolfo SARACCI
 Italy & IARC-WHO
 IFC-National Research Council, Pisa, Italy
 International Agency for Research on Cancer, Lyon, France

Thank you. My presentation will be in two parts. The first will be a rapid overview of the EPIC study design. I have borrowed several slides from Dr Elio Riboli who has been the co-ordinator for more than 15 years and was the initiator of this study. I think it will be useful for his presentation tomorrow, and that of Dr Marzano, if I pave the way by presenting a summary for those of you who are not familiar with the structure of the study. Then, as a way in which this study, which originated focusing on cancer, can be used to probe questions of ideological intervention in the cardiovascular area, I will examine some of the preliminary results on the anthropometric indices. The EPIC heart collaboration is the EPIC-based study on cardiovascular disease which has started looking in particular at systolic heart disease.

We move on to the simple and basic public health principle which we have already touched upon today. Obviously each person can eat only one diet. We have seen recent recommendations by the American Heart Association, the Diabetes Association and the American Cancer Society. Finally if you think in terms of what the cardiovascular epidemiologists (unlike most of the other epidemiologists) call primordial prevention for the general population, you obviously have to give some general advice to the general population. Does that not imply that you then have to target special sub-groups, for example if you have subjects that are in pre-diabetic conditions or other special groups?

The EPIC heart study's strengths are both from the research viewpoint – the EPIC infrastructure of larger exposure of variables and also biospecimens and uniform study criteria – and from the public health viewpoint. The results for both ischaemic heart disease or other endpoints and cancer will be obtained in the same population from the same methods. This is one advantage, to the extent that one often has to take evidence from different types of studies and collate them into what appear to be translatable recommendations in the form of guidelines.

The ten EPIC heart countries are the same as for the major EPIC countries and are all located here in Western Europe. There are 23 collaborating centres in the EPIC heart study and they are in the same countries. Some countries have only two centres and others more; some large countries, such as France, have a nationwide collection in a special cohort of female teachers. Other countries have centres which are geographically distributed – Italy and Spain, for example. The samples that have been taken are in a sense opportunity samples that were suitable for collecting from a very large cohort in the different countries.

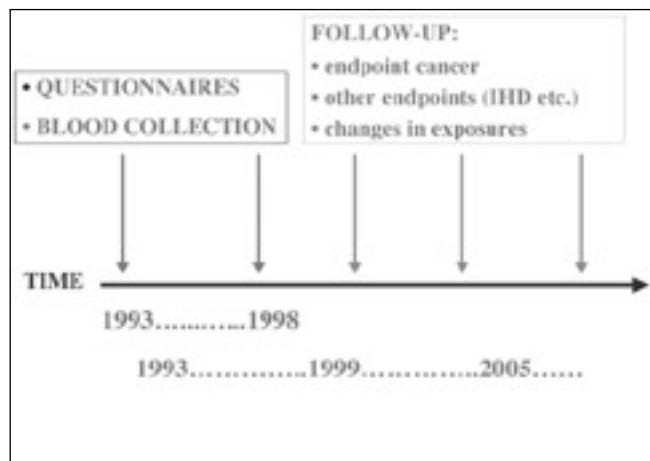
Lifestyle and personal history was taken from questionnaires and addressed questions of tobacco, alcohol, reproductive history, occupation, past and present illnesses, medication, physical activity and socio-economic status variables. We then took the anthropometric measurements: height, weight, waist, hip, and sitting height. Not all the measurements are available for the whole cohort (as I will comment on later) and an additional measurement of blood pressure is also available.

One of the interesting things about EPIC is that there are two dietary measurements in the sub-samples. There is the main

dietary question on usual diet from each of the 1/2 million subjects with methods which are based on the same principle, although the actual articulation of the questions is different in different countries to make allowances for local circumstances. These are designed to rank the subject from high to low. Then, there is a second measurement in a 7% sub-sample comprising approximately 38 000 cohort subjects. This is intended to offer an instrument of standardisation, or rather of calibration, of the question of measurement against the common standard, which was a very laborious activity. This was carried out by nutritionists from the different countries and a central group of nutritionists at the IARC. It gives very detailed open-ended reporting on over 3 000 foodstuffs and 700 recipes. It is designed to calibrate data measurement in two ways: to re-scale between centres the absolute quantities (the top quartile in Sweden of fat that corresponds in Italy and to which absolute amount) and for attenuation purposes (when one studies the relationship between exposure and the outcome – cancer or other endpoints).

The EPIC blood collection in storage contains plasma, serum, buffy coat and red blood cells. There is a bank of approximately 300 000 subjects centrally collected and approximately 100 000 total subjects for which it is available. Some biological specimens are available – close to 400 000, if I am correct – about 80% of the total cohort of about 1/2 million. Not all of them have this banking in Lyon but the samples are available.

The physical system that has been used for long-term sample storage is in liquid nitrogen in the central bank. This may be to do with the design of the study: this is a collection typical of the different cohorts which have worked on a rolling system depending on when each cohort started. They started between 1993 and 1998 and the follow-up has now begun.



The follow-up includes cancer and other endpoints – ischaemic heart disease, stroke etc. – with questions on their own changes in exposure. While this was a study initially designed for investigating cancer, it has also been designed to obtain cancer incidence figures via cancer registries or similar systems for the active follow-up and registration of incident cases. For the other endpoints, for the time being the only form in which these

endpoints come is mortality: causes of death for ischaemic heart disease stroke, diabetes etc. It would be good to investigate further, but this is one of the limitations of the study.

I will now consider ischaemic heart disease, which is the first of the other endpoints which has been considered. There are a number of analyses which are in progress. In fatal cases ischaemic heart disease ICD 9 410-414 ICD 10, I 20, I 24. We have left out the sudden death category in the ICD 9 7 8 9 7 8 8 7 8 9 as there were so few cases that for practical purposes it was not interesting to put them in.

The non-fatal cases will form a new additional database, with the same ICD categories in two steps. The first step will comprise diagnosis as available at participating centres. We are fortunate that at a number of participating centres (for reasons totally independent of EPIC), collection of incident cases of myocardial infarction or stroke, or both, was going on. This was a lucky coincidence.

Step two: later on, we will have procedures for standardising the diagnosis for the future collection of the incidence cases. We are now concentrating on the first part: the fatal cases. In fact, the EPIC heart collaboration design and work plan those from the exposure and anthropometric questions, and data from all cohorts are analysed. We will do the same on fatal and non-fatal cases as soon as we have the incoming new database. There will then be laboratory studies on phenotypic and genetic biomarkers using the method case control design.

At the present, statistical analyses are in progress depending on the interest of the different members of the group. We have to set statistical analysis in motion using anthropometric

and questionnaire data: anthropometry, meat and processed meat, fish, dairy products, fruit and vegetables, nuts, alcohol, blood pressure and tobacco smoking. There are nine different groups working in different centres on this set of exposure variables. We will have these results by the end of the year and we will publish our findings early next year.

I will now talk about anthropometry, simply because that is what I have mainly been involved with. I would like to point out some of the present limitations we have because of the deaths. The number of ischaemic heart disease deaths includes death rates here in the different centres. There are two slides about this. You can see that the numbers are quite small by centre. Though the total is 1 500, this is largely driven by some centres. We cannot really hope therefore at this stage to be able to make a consistent verification as to what we find throughout these centres. There is an additional aspect which is in this representational limitation. If we want to exclude those who had a previous myocardial infarction, namely a myocardial infarction revealed by the questionnaire at the time of enrolment, the size comes down.

There is a third limitation to the anthropometric data: not all the data are uniformly available for all the centres. We really need to have the non-fatal cases as soon as possible to obtain meaningful statistics.

There are various interesting aspects to the anthropometric variables. The first two are the merits of this variable: they are markers of adult energy, metabolism and balance and they are markers of adult material metabolism and lipocytes, and we know what they do. We had a presentation this morning in particular in which we heard about obesity and visceral fat and their possible implications in a series of metabolic steps in the pro-inflammatory process were examined.

There is a third point of interest: markers for physiological adult and pre-adult processes prior to the time of subject enrolment. This applies to all studies, like the EPIC studies, which do not have birth cohorts, and now there are birth cohorts being included. However, we would like to see whether the results can be replicated, and out of the few markers that one has available, although their status is an initial status rather than having a clear meaning, they are just the anthropometric variables. From a public health viewpoint they are easily measured by health monitoring instruments and in fact they are very much advocated as such, particularly in developing countries, as a means of monitoring the next wave of likely diseases to affect the population.

The total cohort I showed you before in detail by centre is a total of 463 000 subjects. If you calculate the ratio, you find that the average follow-up is approximately 6 years, and ischaemic heart disease deaths are a little more than 1 500 up to now. This is a large number, but it is inadequate for certain types of comparison and sub-analysis that one would like to do. The preliminary analyses were done using the Cox proportional hazard model using age as the time-based variable. These are stratified by sex and centre, including alcohol, smoking, education and physical activity as independent variables. Shown here are the results for these two variables, weight and height, or BMI. These are available for virtually every subject in the cohort.

First, I will show you how the confounders – alcohol, smoking, education and physical activity – behave in the Cox proportional hazard model equations. These are summarised concisely in a single table. The other ratios are shown here as highest versus lowest exposure category for each one. This is not the best way of expressing alcohol because the open category, which is 40g or more, includes the fact that the risk increases, and the penultimate category, the next to the highest, had another even

Number of IHD deaths and crude death rates (per 100,000 p-y) by centre and sex [1]

Centre	Deaths		Rate	
	M	F	M	F
1.France	-	13	-	3.6
2.Florence	10	3	53.6	5.3
3.Varese	5	6	39.7	9.6
4.Ragusa	8	-	42.2	-
5.Turin	9	2	21.8	5.8
6.Naples	-	2	-	6.0
7.Asturias	11	-	55.5	-
8.Granada	5	5	42.5	13.6
9.Murcia	14	2	52.7	5.5
10.Navarra	19	3	54.6	9.7
11.San Sebastian	15	1	55.7	3.5

Number of IHD deaths and crude death rates (per 100,000 p-y) by centre and sex [2]

Centre	Deaths		Rate	
	M	F	M	F
11.Cambridge	315	118	361.8	114.3
12.Oxford	133	99	162.3	35.5
14.Bilthoven	42	11	63.9	13.8
15.Utrecht	-	29	-	27.1
16.Greece	79	26	200.4	45.4
17.Heidelberg	71	18	109.3	13.4
18.Potsdam	72	10	110.4	10.1
19.Malmö	179	57	244.6	51.9
20.Umeå	63	11	84.6	13.1
21.Aarhus	22	7	72.9	22.3
22.Copenhagen	47	10	65.7	12.4
23.Norway	-	9	-	6.1

lower ratio of 0.58. Then, it goes up. That just gives you an idea that things are going in the right direction. This is smoking. Now look at the educational level, which is 0.45. Physical activity, which is a global index that pools together recreational, occupational and home activity, does not seem to stand out. Let us look at the anthropometrics. Weight has been adjusted in this equation, and here is one fifth of that distribution. We give actual values for males and females but this is a combined one adjusted by stratification. Weight risk goes up from 1 to 1.88 and there is a very highly significant trend. Height has a spectacular inverse association, which has been observed in many studies, but here it is really quite impressive and is consistent in both sexes. When weight and height are replaced by body mass index in a separate equation, without putting everything together, again BMI comes out very much as the weight was before, and in fact the meaning of the BMI is simply that you consider height as a disturbing variable; you cancel it out and you have the weight aspect of the adiposity.

Both height, which has a declining ratio in the last quintile, and educational level are two variables which are fixed by the age of 20. As I said before, not all anthropometric indexes are available in the whole cohort. Waist and hip ratio are available for almost the totality of the cohort, but sitting height at 20 years of age, which really would complete the set, are available from far fewer people.

I conducted an exploration into waist and hip data on a sub-sample that was considerably smaller simply because the guiding variable was sitting height and therefore it reduced the sample down to around 500, or just one third of the total we showed before. Preliminary analyses used the same Cox model and weight/height ratio and then the waist/hip ratio, or alternatively, BMI and waist/hip ratio. When waist/hip ratio is inserted into the equation and adjusted for alcohol, education, physical activity, etc., in the equation in which weight and height are present you can see that the waist/hip ratio has an independent contribution

here. When it is inserted in the equation in which BMI appears instead of these two variables, you can see an independent contribution with a highly significant trend in weight and height: weight retains its independent contribution in that equation in which you have waist/hip ratio, and height is still a slightly less marked trend but is still quite significant. You should bear in mind that the significance of this sample is badly affected by the fact that it represents only 500 events.

I then worked on an ambitious exercise looking at leg length. Existing evidence is confusing. In literature, leg length should help to split the period that comes before you are 8, to 20, when your height is fixed in a sub-period because the leg grows particularly in the pre-pubertal period. When adult, you have a trunk to leg ratio of about 1:1, but at birth the trunk represents about two thirds of total height. The responsibility of the inverse relationship of height with ischaemic heart disease, which is clear here and has been shown by other studies, has been tentatively attributed to leg length, and therefore inferentially to possible nutritional influences taking place during the pre-pubertal period.

The results observed here were the other way around, but the sample was small, so I would be curious to see when we look at more data what the results will be and whether they will be different. None of these results are particularly significant.

This is where we stand now. The anthropometric data will be refined and completed and we will try to use all the sub-cohort available for this using all measurements for the subject: waist, hip and also sitting height at age 20. We need to work out some function of age at 20 which can also be inserted in the equation; that is the programme that we have. We will carry out a second step of the same exercise as soon as the new database on non-fatal cases is in, and then there is a separate part of the programme which targets on the laboratory component.

Göran BERGLUND

I think that there will be a very interesting development in the EPIC cohort. I see how the plans are for both biomorphics and for genetic analysis and how big the sample will be within half a year's time with more than 7 000 myocardial infarctions, which will give us impressive power to detect even small differences.

Dietary patterns and risk of CVD

Matthias SCHULZE

German Institute of Human Nutrition, Dept. of Epidemiology, Nuthetal, Germany

I have the pleasure of giving the last talk on dietary patterns and the risk of CVD today and I will focus largely on cohort studies and not on intervention studies. In observational studies, we usually measure food intake with an FFQ or with other assessment methods. One strategy is to relate the intake of single food items or food groups to the risk of CVD. Another strategy is to derive through food composition tables the intake of nutrients and to relate those nutrients or constituents of food items to CVD risk. A third approach, which has been used more and more commonly within the last five or ten years, is the analysis of overall dietary patterns which reflect the consumption of different foods and nutrients in composition, and therefore reflect the effects of overall diet and cumulative effects of these components. In terms of observational studies, there are essentially two different strategies for defining these dietary patterns. The first uses prior information on possible or known effects of single components or nutrients or food items on risk, and this information is used to define a dietary index or score: a classic example is the Mediterranean diet score. The second method, the exploratory method, uses the data at hand and data reduction techniques, cluster analysis and principal component analysis, to define the common patterns that exist in the study population of interest.

Another technique, which is called reduced rank regression, uses both prior information and data at hand to define these patterns, and this method has recently been introduced by our group from Potsdam. I will give two examples of its application on CVD.

The first question is whether dietary patterns relate to CVD risk markers, and there are several metabolic pathways by which diet may relate to the risk of CHD which could be considered here. We have heard about one study already today: the Mediterranean style diet may affect blood pressure, blood lipids and also inflammatory markers. These effects are independent of effects on body weight. So, even though subjects in the intervention group lost more weight than those in the control group – the effects on inflammatory markers, for example, were independent of this.

There are also observational studies which link dietary patterns to cardiovascular risk markers. One such example comes from the National Health and Nutrition Examination Survey in the United States which identified two patterns. One is the Western pattern, which is high in processed meats, red meat and high in dairy. This pattern is related to somewhat lower HDL cholesterol but also to lower folate levels and higher HbA1c and higher insulin levels. On the other hand, an American healthy pattern, mainly consisting of vegetables and salad dressing, did not show any appreciable associations with these risk markers.

There are three more studies which relate overall dietary patterns in an observational setting to cardiovascular risk markers, and two of them come from the Harvard group [Figure 1]. In both studies, the Western and the prudent patterns were observed by using factor analysis or principal component analysis. While the Western pattern was associated with risk markers such as higher insulin, C-peptide and leptin, higher homocysteine or lower folate levels and also inflammatory markers, the prudent pattern showed somewhat opposite effects on these risk markers. The Morgen Study from the Netherlands identified three patterns. The cosmopolitan pattern is somewhat similar to the prudent pattern in the US, but with more vegetables. The traditional and

refined foods patterns both share components of the Western pattern in the United States. What the investigators saw is that the cosmopolitan pattern was associated with lower blood pressure and higher HDL cholesterol, while the traditional and refined foods pattern was associated with a biomarker profile that reflected a higher risk of CVD. These effects were adjusted for known risk factors and potential confounding factors.

Study (author)	Population	Patterns/Method	Associations
Health Professionals Follow-up Study (Sung and Alu) (See Year 2002, 2004, 05)	84k men	2 Cluster-based factor analysis	7 insulin, C-peptide, leptin, and homocysteine; 7 folate
		Western (meat and only processed meats, high fat dairy products, and refined grains)	7 folate; 7 insulin and homocysteine
MORGEN Study (van't Hof-Grootenboer et al.) (See Year 2002, 7/2006, 05)	29 750 adults	2 Cluster-based factor analysis	7 blood pressure; 7 HDL-cholesterol
		Cosmopolitan (processed vegetables, whole grains, fish, nuts, and fruit)	7 blood pressure, LDL-cholesterol, total cholesterol, glucose
		Traditional (more whole grains, vegetables and less of low fat dairy and fruit)	7 total cholesterol
Nurses' Health Study (Savage-Cox et al.) (See Year 2002, 06/2007, 05)	752 women	2 Cluster-based factor analysis	7 CRP, E-selectin, sICAM-1, sVCAM-1
		Western (meat and only processed meats, high fat dairy products, and refined grains)	7 CRP and E-selectin
		Prudent (more fruits, vegetables, whole grains, and products)	

figure 1

The second line of evidence comes from observational studies on dietary patterns and the risk of CVD. I would like to acknowledge the two secondary prevention trials published so far on the Mediterranean style diet and the risk of cardiovascular disease. However, most of the evidence for primary prevention comes exclusively from observational studies. One good example is the Health Professionals Follow-Up Study, in which the prudent pattern was associated with a decreased risk of CHD and the Western pattern showed a positive association with the risk of CVD. This was not totally explained by nutrients which may be related to this pattern. Both patterns were associated with risk after adjustment for these nutrients.

Another example comes from EPIC-Greece where a diet score predefined as a Mediterranean diet was related to all-cause mortality but especially to mortality from coronary heart disease. This was again adjusted for potential confounding factors and anthropometric measures [Figure 2].

Variable	No. of Deaths/ No. of Participants	Hazard Ratio for Death (95% CI)		
		Crude	Age and Sex-Adjusted	Fully Adjusted
Death from any cause	275/22,043	1.74 (1.61-1.88)	1.79 (1.65-1.91)	1.75 (1.64-1.87)
Death from coronary heart disease	147/22,043	1.63 (1.51-1.76)	1.74 (1.61-1.87)	1.67 (1.57-1.78)
Death from cancer	107/22,043	1.11 (1.04-1.18)	1.10 (1.03-1.18)	1.10 (1.03-1.18)

(Trichopoulos et al., N Engl J Med 2003; 349: 2599 - 608)

figure 2

There are many more observational studies on CHD and this table shows some which used predefined dietary scores. A study by Kant and colleagues recommends a food score essentially based on fruit and vegetables, whole grains, lean meats and poultry, which was related to a decreased CHD mortality. Stamper and colleagues used a dietary score based on six nutrients which have been shown to reduce CHD. This score was also related to decreased CHD risk. The other three studies evaluated the healthy eating index – which is based on the new USDA dietary guidelines - or the modified Healthy Eating Index. The Healthy Eating Index was associated with MI and stroke risk. The alternative healthy eating index was more strongly related to these endpoints.

Four other studies derived dietary patterns using exploratory methods – in this case, with principal component analysis. There are two studies from the Nurses' Health Study which is similar to the Health Professionals' Study. They define two patterns, both the Western and the prudent pattern. The prudent pattern was consistently associated with a decreased risk of CHD, while the Western pattern was associated with an increased risk. The same was the case for stroke. In the studies by Osler and colleagues, they defined two factors by principal component analysis and also a predefined dietary score. While the prudent pattern was associated with CHD mortality, it was not associated with CHD. The Western and the healthy food index were not related to either CHD mortality or total CHD risk.

Using principal component analysis in one particular data set always gives the same patterns, no matter what kind of disease you are interested in. So using the Nurses' Health Study data will give the Western or the prudent pattern, no matter whether we look at CHD or diabetes or different sorts of cancers. This approach is probably not optimal in defining the best dietary patterns in the sense of reducing CHD risk or reducing the risk of other chronic diseases.

It might be useful to use an approach that somehow incorporates prior information. This can be done using a newer technique called reduced rank progression. Basically, you can define a set of CVD risk markers – so-called responses. The method tries to define dietary patterns which explain variance in these responses or cardiovascular risk markers. This should give dietary patterns which may be more strongly related to cardiovascular risk. This method can also be adopted to other endpoints using different sets of biomarkers.

One study, published by our group last year, looked at different blood lipids, C-peptide, and the inflammatory marker C-reactive protein, and used this set of biomarkers to define a dietary pattern using this new technique.

The data came from the CORA study, which is a case control study on myocardial infarction in women in northern Germany. What we observed was that the dietary pattern was related to lower HDL cholesterol and much higher C-peptide and C-reactive protein levels where there was no relation with LDL cholesterol and lipoprotein(a). The food groups which contributed to this pattern were red meat, poultry, sauce, margarines, and "other vegetable fats and oils", which is somewhat surprising. This "other fats and oils" group does not include olive oil. There were, however, negative correlations with plant-based foods, such as vegetarian dishes, vegetables, whole grains, and also with wine. In this case control study this pattern was very strongly related to the risk of myocardial infarction. However, these data are probably too good to be true and this result is to be reproduced in a prospective setting.

We have just finished working on a different data set. This is the same study - the CORA study - but using a different set of

responses which are related to the homocysteine pathway. We were able to derive a pattern which was related to higher folate levels, higher vitamin B12 levels and lower homocysteine levels. The food groups that contributed to this pattern were mainly mushrooms, olive oil, fruits, wine, vegetables, nuts and whole grains, while fried potatoes were negatively associated with this pattern [Figure 3].

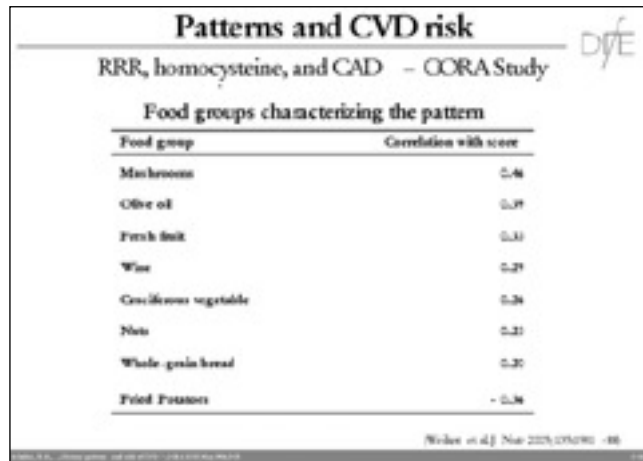


figure 3

This pattern was associated with a decreased risk of myocardial infarction in the study [Figure 4].

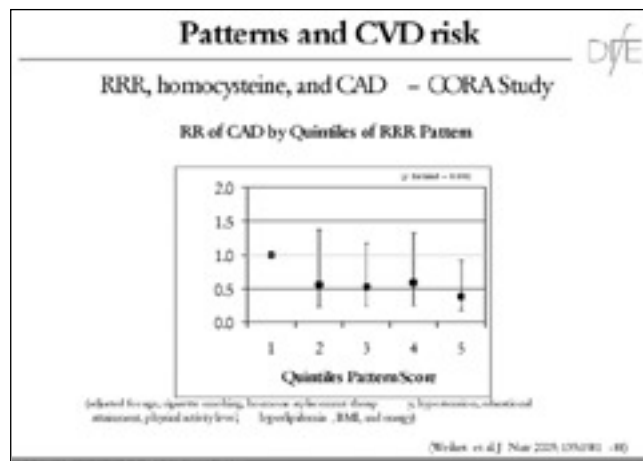


figure 4

We tried to replicate this finding in a prospective study, using data from the EPIC-Potsdam centre, which is a prospective cohort study. With about 27 000 participants free of CHD at baseline, we observed 157 incident myocardial infarction cases until April 2004. Fortunately, CORA uses the same FFQ (Food Frequency Questionnaire) as used in EPIC-Potsdam, so it should not prove problematic to assess dietary intake between both studies. We tried to mimic the pattern we observed in CORA by using the food items I mentioned before to define a dietary pattern score based on the previous results. In this prospective EPIC-Potsdam study there was still a significant trend for a decreased risk with this pattern, although the risk was somewhat smaller than we had observed in the CORA study. This, of course, was adjusted for a number of confounding factors.

In summary, there are many observational studies which show that a Western style diet comprising red and processed meats and refined grains is associated with both risk markers of CVD and an increased risk, and on the other hand that plant-based diets rich in fruits and vegetables, whole grains and also healthy sources of fat reduce the risk of cardiovascular disease by

affecting blood pressure, inflammation and lipoproteins. If we are looking at studying more dietary patterns in relation to cardiovascular disease in observational settings, the application

of this new pattern method may be a good chance to do so, despite the ongoing interest in factor analysis and cluster analysis in this field.

Questions

Edith FESKENS

Thank you for your very nice overview. I am very interested in your reduced rank regression, which I think is a very good method.

The Ministry of Public Health recently asked us to look at dietary patterns and dietary indexes, so we looked at the literature a little bit like you did. Their question was as follows: which type of nutrient-related or diet-related problem is worst in the Netherlands? They could then use this dietary index to pinpoint the biggest problem for our diet in the Netherlands. If they conduct monitoring studies and they observe a reduction in folate or beta-carotene intake, for example, what should they dedicate most attention to and what should they put their money into? This was their question. They asked us whether we could look into this matter and look at dietary indexes from that point of view, which, as you can imagine, is very difficult.

But I would like to challenge you. Could we use dietary indexes, factor analysis, principal component analysis or even reduced rank regression to weight the various dietary components to see which dietary components have the greatest weight to predict longevity and then focus on that dietary component? This is a different way to use the indexes.

Matthias SCHULZE

I think it is very hard to go from an overall dietary pattern, which we observed, to focusing on single components. This is precisely the opposite of what you intend by evaluating dietary patterns. It is of course the case that some food items contribute more to a dietary pattern and some contribute less to a pattern, which may indicate that something is more important or less important. I do not believe that it is worthwhile to conduct factor analysis and principal component analysis, because this method only focuses on defining a pattern that explains variance among the food items. That meat intake is slightly better explained by the pattern than refined grain intake is insignificant from a health point of view; it does not explain whether the pattern is related to a disease or not.

Edith FESKENS

Perhaps I can ask a second question. This is also directed to Professor Trichopoulou. If you look at these dietary indexes, for example the Mediterranean dietary score or the healthy eating index, you judge the diet, awarding one or two points for the highest group for olive oil or the groups for vegetables and fruits. Has anyone ever looked at weighing coefficients of these various components? We simply add them up and end up with a minimum of zero and a maximum of 10 points, for example, so that unhealthy fruit carries the same weight as unhealthy alcohol. What is your opinion on that?

Matthias SCHULZE

I think that this is a very good idea. If you are aware of nutrients or specific foods which have been shown to relate to a disease and the effect and attributable risk is known, then this should be incorporated by putting weights on them, so that alcohol and plant food oils will not carry the same weight in such a score.

Edith FESKENS

Where should we get those weights? From EPIC?

Matthias SCHULZE

Not by evaluating overall dietary patterns. I think that needs to be done in studies looking at the specific nutrients or foods.

Göran BERGLUND

Are there other questions?

Antonia TRICHOPOLOU

Thank you for giving me the opportunity to speak briefly about the Mediterranean diet score. We have also been working on principal components. In the Mediterranean diet score, in contrast to the principal components analysis, there is a real diet behind the Mediterranean diet score – a diet which exists and is clearly defined. In the context mentioned and according to the request of your Ministry of Health, what we have done is to analyse the traditional Mediterranean diet based on the Mediterranean diet score for seven days. At the end of those seven days, we observed that the traditional Mediterranean diet offers many many more nutrients than the diet habitually mentioned in our dietary guidelines. You would be surprised to know that we consume equal amounts of catechins as the Netherlands, but catechins are sourced from ten different vegetables – in the Netherlands, catechins are mainly sourced from tea – so that means something for the synergistic effects of the various components of the pattern. I think that there is a long way to go before we can decipher the beneficial effects of the traditional Mediterranean diet.

Göran BERGLUND

Thank you all. In this session we have analysed the effect of important sub-classes of fat intake and also put the finger on a new and important pattern tool to be used in the future analysis of foods and risk of disease. It will be very interesting in the EPIC study, which has centres from Athens to Tromsø in Norway, to see how this new tool can be used for better evaluation of risks. Thank you.

Sophie VILLERS

General Direction of Nutrition, Ministry of Agriculture, France

Good morning. I have the pleasure to represent Mr. Bussereau, the French Minister of Agriculture, to this third international conference on health benefits of the Mediterranean diet. On behalf of Mr. Bussereau, let me apologize for his absence today, and thank the Italian Health Ministry, which provided, with the French Ministry, great support to this conference, granting us this great Roman venue, at the heart of the Mediterranean culture. Let me also address our special thanks to Pr. Antonio Trakatellis, representative of the European Parliament, Mr. Wilfried Kamphausen, from the DG Sanco, and Mr. Elio Riboli, who is the president of this morning session and whose EPIC study is a great reference.

I am happy to open this session, which, I hope, will result in concrete actions to encourage balanced and diversified food consumption. Such an objective will not be reached without a consistent food policy from producers to consumers, which stands for a priority in the view of the current Minister.

“Nutrition is our first medicine”, said Hippocrates. This does not mean that food should be regarded as a drug, but it stresses the fact that a diverse, well-balanced and pleasant diet that matches our specific needs is a way to remain healthy. As shown in more and more studies, in particular the 2003 WHO report on nutrition and prevention of non-contagious diseases, the relationship between nutrition and health is incontestable. Yet we must remain cautious not to medicalize food to avoid confusion in the mind of consumers. It is essential to promote dietary models such as the Mediterranean diet. Those not only emphasize the importance of dietary balance through food diversity but are built on cultural references that represent reliable landmarks for consumers, thus allowing for a better understanding and effectiveness of the message. Because of our lifestyle and the lack of connection between food and consumers, people have lost their nutritional landmarks. The dietary model approach is an important tool in policies that aim at fighting chronic diseases and obesity in particular. Such an approach covers various aspects of diet and nutrition, thus guiding consumers towards healthy choices, notably through food balance and awareness of the link between what we eat and what we are. Taste, pleasure, food culture, food origin, production and preparation that impact on health, all prove important. I hope all Mediterranean countries share this view. This seemed obvious in the debate around the tentative regulation on allegations at the European council. Southern European countries have asked that we take food cultures and traditions into account while elaborating nutritional profiles, in order for these to be easily achievable and to avoid confusion. This positive approach of food promotes the role of several types of foods for our health, according to the well-balanced combination of a diversity of foods. We must keep this essential idea in mind, which also underlies the French nutritional policy: there are no good or bad foods but they are more or less adequate diets for our needs and appropriate nutritional behaviors.

But how about implementing a new food policy? Informing consumers on possible benefits of a rich and well-balanced diet is not enough. Once nutritional recommendations based on nutritional models have been developed, the issue of behavioral changes remains. Concrete measures must be implemented by the authorities and the private sector in order to promote such changes. Nonetheless, their effectiveness still depends on our ability to integrate them into a real food strategy.

This will be discussed during the afternoon session, but we may already underline that food policy lies at the crossroads of health policy and agricultural policy. Thus, it is essential to seek overall consistency of public interventions in the field of food and nutrition. In France, the PNNS, National Program for Health and Nutrition, which will be presented by the vice-president of the supervising committee Mr. Hercberg, translates such an effort towards consistency. Beside his role in the definition and implementation of actions defined by the PNNS, the Minister is also required to help provide consumers with a high-quality food supply. The ministers of Agriculture and Health must also ensure the availability of high-quality foods. The services of the General Direction for food and nutrition are working on the implementation of the concept of accessibility through concrete actions at the level of supply and demand. When we recommend consumption of at least 5 pieces of fruit and vegetables a day, we also must ask other questions, such as: are fruit and vegetables easily accessible to consumers? Are they tasty, easy to eat on the go? How can they be prepared and complemented? To answer these questions, the Ministry of Agriculture, together with field professionals, has created pilot programs which aim at improving control over prices and nutritional quality of products, as well as the convenient aspects of their consumption and proximity of distribution points. The question of employees' lunch cannot be neglected either. Nowadays, special attention must be put on school restaurants as well. Thus, measures such as fruit distributions in schools are currently under consideration. Actually, school restaurants have already received specific nutritional recommendations; the General Direction of food and nutrition is currently evaluating their implementation and will strengthen the mechanism if necessary.

Together with the authorities, all actors must come together to conduct effective field activities. As far as field work is concerned, I would like to stress the importance of partnerships and voluntary actions on the side of economic actors. This is also the view of the European Commission which is currently working with several European federations within the framework of the network for common actions for nutrition, physical activity and health. Mr. Kamphausen will probably tell you more about this.

It is possible to achieve synergies among fields towards the promotion of diversity, balance and pleasure in dietary habits as a whole. I would like to thank each and every French field for their dynamic role in this regard. The Minister encourages them to build local partnerships in order to facilitate information and accessibility of basic products within the framework of nutritional education activities. As an example, I would like to mention EPODE (Network for the prevention of childhood obesity). Local authorities are conducting local actions with partners from the health, education and production sectors, so that children can be encouraged to modify their dietary behaviors, exercise more and that overweight/obese children find counseling. Production fields naturally play a great part in this multi-partnership and local approach. In this regard, I would like to thank APRIFEL for organizing this international conference over the years, as well as for its various actions towards the improvement of fruit and vegetables accessibility. This afternoon's presentations will allow us to underline the role of agro-food industries in the supply and distribution of foods of high nutritional quality. Despite the constraints, French companies have shown their awareness and are working, either individually or collectively, to attain this goal. The PNNS

provides a framework for all types of actions. In that sense, companies have, for example, voluntarily agreed on the reduction of salt content of processed food.

As a conclusion, let me thank again all actions that bring partners together on a voluntary basis in order to promote diversity, balance and pleasure in dietary habits through the improvement of supply and dietary habits.

In this regard, all the links of the food chain are concerned: farmers, transformers, distributors, consumers, researchers and education actors. We will mobilize all actors towards the fight against non-contagious diseases which are unfortunately spreading steadily in our populations. However, the fight will be all the more successful as we keep in mind that food plays a role in our “nutrition”, our “health” but also in our “dreams”. Thank you very much.

Introduction

Elio RIBOLI

International Agency for Research on Cancer (IARC-WHO), Nutrition and Hormones Group, Lyon, France

We wish to thank Ms Sophie Villers, from the French Ministry of Agriculture, for her participation and her important declarations which show serious, active and long-term commitment to the implementation of the French National Program for Nutrition and Health (PNNS). France is one of the few European countries to have developed such a plan as a framework for intervention towards better nutritional standards, food quality and health. This cutting-edge approach should be adopted by other European countries.

I would like to elaborate on one of the ideas that were raised earlier regarding the medicalization of food. Today, as more and

more messages seem to encourage a health benefits based approach in food consumption, we tend to forget that our consumption should be essentially driven by the taste of foods we eat. Of course, eating does play a part in the improvement of our lifestyle but it should not be perceived as an obligation or duty.

Let us open the first session of the day, on the relationship between food and cancer. We will hear four interventions about four types of cancer. I will introduce these sessions with the EPIC study whose main characteristics were presented yesterday by my colleague and friend Rodolfo Saracci.


Where do we stand in the search for the nutritional causes of cancer?

Elio RIBOLI

International Agency for Research on Cancer (IARC-WHO), Nutrition and Hormones Group, Lyon, France

The presentations will essentially be based on EPIC results. EPIC is a prospective study on approximately half a million subjects. The study was conceived in the early 90s, when I was working with Rodolfo Saracci at the Unit of Epidemiology at the International Center for Cancer Research, WHO, Lyon. We were seeking proper actions to be conducted by the United Nations centre in France, in order to improve knowledge of nutrition and cancer while capitalizing on our international and European outreach. We then adapted the concept of the Seven Countries Study on cancer with a more modern approach. We wanted to investigate the relationship of nutrition, cancer and other chronic diseases by studying individuals' dietary habits and their relation to several cancerous and non-cancerous pathologies.

EPIC		
Collaborating Centres and Participating Subjects		
	Participating Subjects	
	Questionnaire	Q + Blood
France	74 824	28 053
Italy	47 749	47 725
Spain	41 440	39 579
U.K.	87 942	43 141
Netherlands	40 072	36 318
Greece	28 555	28 483
Germany	53 091	50 678
Sweden	53 826	53 781
Denmark	57 054	56 131
Norway	37 215	31 000
Total	521 448	414 389



We also intended to make use of the great variability in terms of diet and lifestyles from the North to the South of Europe. Since they were already conducting similar studies, three Scandinavian cohort studies joined EPIC.

A prospective study requires means and time in order to collect data on lifestyles and habits of the subjects. A follow-up mechanism had to be implemented. In Europe, we have an excellent network of cancer databases that allows for the close monitoring of the half-million of individuals that participate to the study. It thus becomes possible to study the link between cancer, coronary diseases – and soon, diabetes – with data about lifestyle and other characteristics about the subjects before and at the time of inclusion in the study.

EPIC is the first study in the world to have collected blood and DNA samples in order to analyse the relationships between genetic and diseases in all the cohort.

EPIC is an EU-financed consortium that gathers 24 centres and was created fifteen years ago. It is managed by an executive committee that represents the EU countries. As a group and in a very friendly manner, these centres actually planned and prepared the scientific implementation of the project. Initially conceived as a cancer-oriented project, EPIC was gradually broadened to include other chronic diseases and conditions. Some members of the project are here with us: Antonia Trichopoulou, University of Athens, who is responsible for the 'Epic Elderly', Ken Derlee, who has just received new

contributions from the EU for studies about the dietary recommendations, Rodolfo Saracci, who initiated the "cardiovascular" side of the project with EPIC HEART, and Nick Wareham from the Cambridge Medical Research Council, in charge of the "diabetes" component.

At the beginning of our study, we had 14 000 subjects with diabetes. During the follow-up, more than 15 000 have developed the disease. This is turning to be the most important study ever conducted with a sample of 30 000 diabetics. We are also analyzing total mortality, i.e. general survival, which is one of the best indicators of the relation between lifestyle and life expectancy. A specific sub-project on obesity titled EPIC PANACEA is also underway and we are very hopeful that the EU will support it.

A half-million study is not an easy thing to manage. It was built upon a huge database with thousands of variables for each subject, as well as a network of biological databanks, which makes it the most important biological databank for biomedical research in the world. All samples were stored at -196°C .

This morning's presentations were based on the outcomes of EPIC and other studies of diagnosed cancers for which we had reliable data for the first 6-7 years of follow-up. We rely on precise data for 28 000 cases of cancer.

Nutrition and Cancer, IARC, 2003	
Follow-up of EPIC subjects, 1994-2003	
28,091 incident cancers (updated 30 April 2004)	
Breast	6844
Colon-rectum	2198
Prostate	1746
Lung	1551
Corpus uteri	890
Cervix uteri	685
Ovary	738
Stomach	631
Upper GI Tract	437
Pancreas	405
Kidney	421

As a conclusion, I would like to share with you the scientific approach we have been following along the project. Research relies on ideas. Yesterday, a speaker stressed that research has nothing to do with chance. The relationship between hormones and breast cancer, or the protection against cancer through specific foods should be integrated in etiological and biological models. To do this, a prospective study, with nutritional, anthropometric and metabolic components, and with biological samples, constitutes a useful scenario.

The concept of "evidence-based medicine" is very important. Replication, i.e. the repetition of studies among diverse populations, proves essential. EPIC does allow for replication since it was led in 10 countries simultaneously. Replication therefore stands for an implicit component of the project.

Above all, we should never forget that, unlike laboratory mice, people have their own lifestyles, which may vary and are linked to dietary habits. We are conducting such a research on the relationship between nutrition and health because we all share

the desire to see our work benefit the people; in other words, we want to see scientific results translated into public health measures, to avoid pointless projects. This is a long-term process that will require broad-based support and participation.

Nutrition, steroid hormones and breast cancer

Franco BERRINO

Istituto Nazionale per lo Studio e la Cura dei Tumori, Epidemiology Unit, Milano, Italy

Thank you very much and good morning. The history of hormones and breast cancer is a very long one. The relationship between ovarian activity and breast cancer has been known for over a century, but it has been in the last 50 years that many different hypotheses came out and started fighting one against the other. There have been many hormonal hypotheses on breast cancer. Almost each hormone has been considered by different authors in different periods as responsible for the growth of breast cancer, either for the initiation, promotion or progression of breast cancer. Now things are a bit clearer.

In 2002, the Endogenous Hormones and Breast Cancer Collaborative Group put together all the available prospective data on hormones and cancer in post-menopausal women (nine prospective studies with biological banks carried out in Italy, Japan, UK, and the United States). The results were based on over 600 cases of cancer that occurred in these nine cohorts. For several types of oestrogens there is a clear trend of increasing risk with increasing plasma concentrations. However, not only oestrogens are involved in breast cancer aetiology; androgens are involved too, at about the same strength of association (Figures 1 and 2).

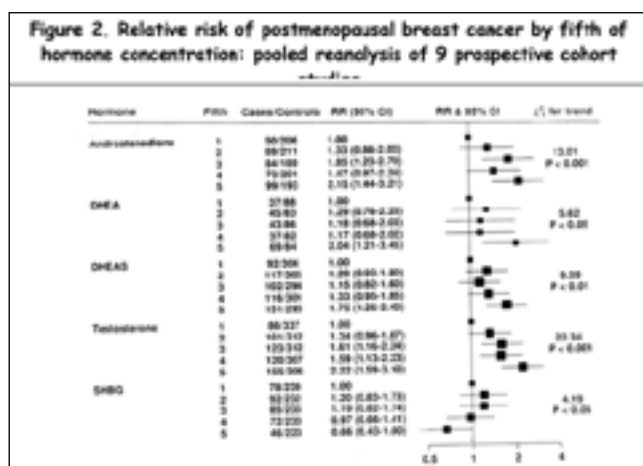
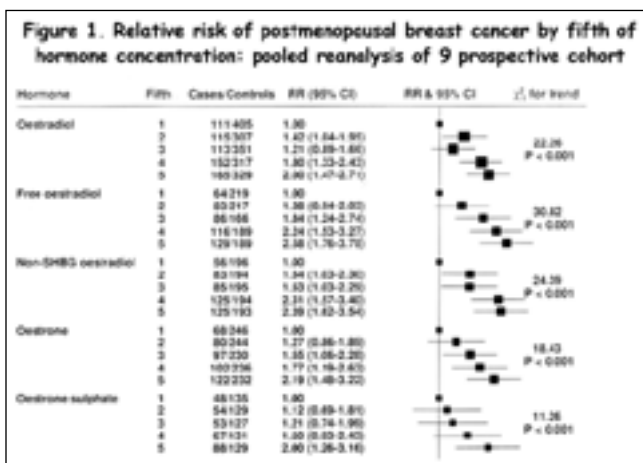
exactly what the mechanisms are for these different hormones, but we can say beyond reasonable doubt that an increased level of sex hormones is associated with an increased risk of breast cancer.

Recently, the European Prospective Investigation into Cancer and nutrition (EPIC) confirmed all these results in post-menopausal women, with almost exactly the same results as in the pooled analysis, in a single study with over 600 incident breast cancer cases. In this analysis we excluded all the women that were under hormone replacement treatment. So we know fairly well what is the pattern of endogenous hormones associated with post-menopausal breast cancer.

Things are much more difficult before the menopause because the hormone levels vary over the ovarian cycle. It is actually a mess: we would have to take blood every day of the cycle to understand anything, and even that would not be easy to interpret. Things are difficult in particular for studying the role of progesterone, which is only produced in the second half of the cycle. Its levels may vary a lot depending on when blood is taken in this phase of the cycle: in a normal 28-day cycle progesterone is usually high between the 20th and 24th day of the cycle, but if the cycle is shorter, these days could be at the end of the cycle, when progesterone is low. If the cycle is long, these days could be near the ovulation when progesterone is also low, so it is really very difficult to plan a study of this type. The issue is important because there are conflicting theories about the role of progesterone in breast cancer: according to one theory, a well-functioning ovary producing progesterone in the second half of the cycle is associated with a lower risk; according to another theory, a normal production of progesterone is associated with an increased risk.

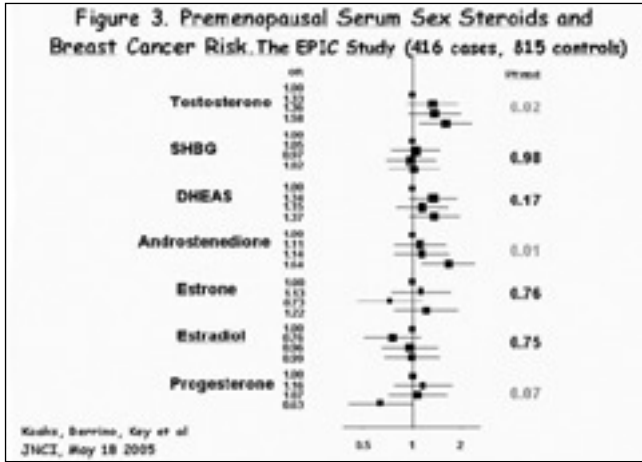
Our ORDET (Hormones and Diet) prospective cohort study is relatively small compared to the huge volume of studies such as EPIC: we recruited only 11 000 women, 5 000 post-menopausal and 6 000 pre-menopausal, but blood was collected from fasting women, between 8 and 9 o'clock in the morning, between the 20th and 24th day of the menstrual cycle, and we also collected the date of the previous and the following menses. To synchronise the moment of blood collection of cases and controls over the cycle we took into account in the analysis the length of the cycle, the distance from the subsequent menses, and the LH/FSH levels, which may indicate if blood was taken near the ovulation. We also excluded women who had menstrual irregularities suggestive of perimenopause, for whom it is very difficult to interpret the menstrual phase. The results showed a strong association with total testosterone, but an even stronger association with progesterone – in the sense that women with a high progesterone level have a significantly lower risk of breast cancer (Micheli et al., 2004). This, however, was based on a small number of cases.

A much larger study on breast cancer cases occurred in pre-menopausal women recruited into the EPIC study has just been published. This study very neatly confirms that the level of androgens – the level of testosterone in particular – is associated with pre-menopausal breast cancer risk, and that the level of progesterone is negatively associated (Figure 3) (Kaaks et al., 2005). When the analysis was restricted to pre-menopausal women younger than 50 years of age at recruitment in order to avoid perimenopausal irregularities, the protective association of



This is not only because androgens are a precursor of oestrogens. When androgen levels are adjusted for oestrogen levels, and vice versa, both maintain a significant association. We do not know

progesterone was more evident. Unfortunately, the EPIC study did not collect blood in a given day of the cycle but the dates of previous and subsequent menses were usually available and we could work on over than 400 cases, so we were able to produce robust analyses that corroborated the results of the ORDET study. Before menopause there was no association with oestrogen levels (Figure 2).



So we now have a clear pattern of association: after the menopause, breast cancer is associated with androgens and oestrogens; before the menopause, there is a positive association with androgens, a negative association with progesterone, and no association with the level of oestrogens. This does not mean that oestrogens are not important before the menopause – they are always very high and always at a level sufficient to promote the development of breast cancer. After the menopause, we see an important effect of a doubling of the level of oestrogens – a doubling of the level of oestrogens after the menopause still means that it is ten times less than the level of oestrogens before the menopause. However, oestrogens cannot be used as a risk indicator before menopause.

The history of progesterone is a long history. The hypothesis was that a normal menstrual cycle would be protective, while chronic anovulation syndrome associated with an increased production of androgens and a luteal insufficiency. The hypothesis was formulated in the early 1960s. In 1964, Professor Grattarola, from our institute published a study in which he evaluated anovulation with endometrial biopsies. He found that breast cancer patients very frequently had a proliferative hyperplasia of the endometrium in the second half of the cycle instead of a secretory one.

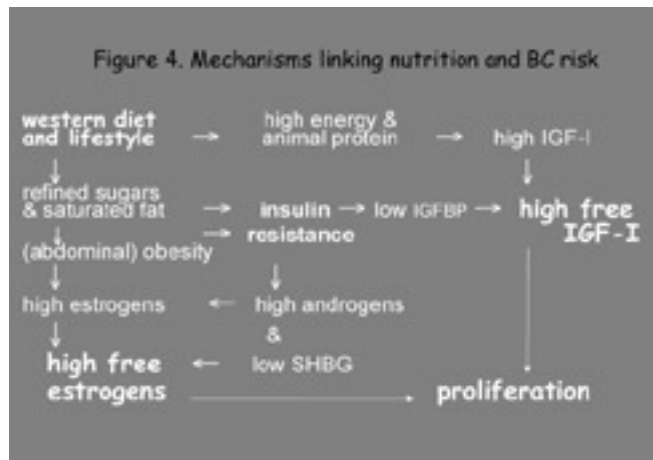
Twenty years later, Dr Secreto from our institute published a case-control study based on the measurement of testosterone and progesterone in blood, and the results were consistent with the original hypothesis.

Again, 20 years later in 2004, Dr Micheli published our first interpretable results on pre-menopausal women and breast cancer, confirming that high androgens and low progesterone are associated with breast cancer risk. The EPIC study now corroborates this hypothesis.

Also a recent publication on the risk associated with hormonal replacement therapy in the French section of the EPIC study – the E3N prospective study of 100 000 teachers in France – falsify the hypothesis that progesterone may increase breast cancer risk. France is the unique country where a natural progesterone – the micronised progesterone – has been widely used in the hormonal replacement treatment of menopausal symptoms. In all other

countries, particularly in North America and northern Europe, the progestins associated to oestrogens have been of a different type – medroxyprogesterone is being used mainly in North America and nortestosterone derivatives in northern Europe. The association of oestrogens plus progestins was usually found associated with an increased breast cancer risk. The risk is very high with nortestosterone derivatives that have a strong androgenic activity, and a moderately high with medroxyprogesterone acetate that has less androgenic activity. The French study did not evidenciate any increased risk when natural progesterone was used, but confirmed the increased risk with synthetic progestins. These results corroborate our hypothesis that natural progesterone is not a risk factor for breast cancer, and that actually women who have a normal menstrual activity are at lower risk.

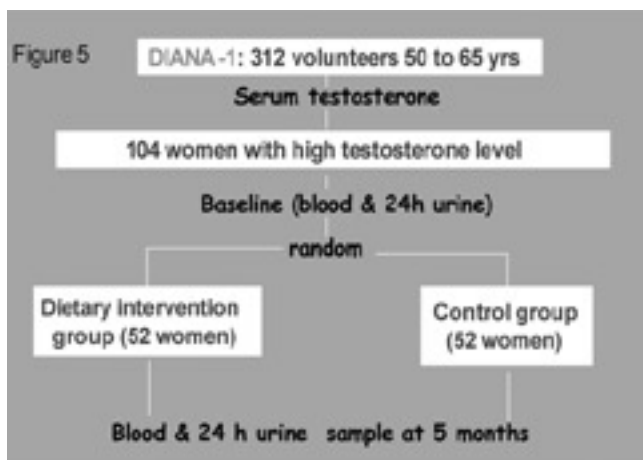
Another field of research on hormones and growth factors in breast cancer aetiology has to do with the glucose metabolism. In our study, we found a significant association (only in pre-menopausal women) with glycaemia (within the normal range), some association with insulin and a significant association with the level of IGF-I. Other studies have found the same. It appeared at the beginning that this association was prevalent only in pre-menopausal women; other studies suggested that there is also an association after the menopause. However, there are some inconsistencies in these results. Also, the genes involved in the synthesis of insulin and IGF-I and in the regulation of these factors are being systematically examined, but again, there is no strong association with the genetic effect, at least up to now, while there is some association with the dietary pattern. In particular dietary proteins, mainly animal proteins and milk proteins are associated with a somewhat higher level of IGF-I in the blood.



On the basis of this knowledge, we developed the hypothesis that we might modify the level of sex hormones and growth factors by modifying the dietary style. Figure 4 illustrates a simplified mechanistic interpretation of the relationship of western diet with breast cancer: western diet is associated with high energy and animal proteins that determine a high level of IGF-I; western diet is associated with refined sugars and fat that in turn are associated with insulin resistance; insulin has a gonadotropic activity, stimulates the synthesis of androgens in the ovary, and inhibits the synthesis of SHBG, the sex hormone binding globulin that regulate the bioavailability of circulating androgens and oestrogens; insulin, moreover, inhibits two of the IGF binding proteins. This means that both oestrogens and IGF, which co-operate for the proliferation of epithelial breast cells, including breast cancer cells, are more available.

According to the above rationale we designed a first randomised dietary intervention study – the DIANA (diet and androgens)

study. We randomised 104 women who were in the upper tertile of the blood distribution of testosterone, and we modified the diet of half of them. We measured the level of hormones in the blood and urine again after five and a half months (Figure 5).



The dietary intervention was a diet based mainly on unrefined cereals, a lot of pulses and vegetables, no sugar, and a little meat, cheese and milk, based on the traditional Mediterranean diet and macrobiotic recipes. We avoided foods such as white bread, potatoes and cornflakes, and we used highly satiating food. All of these women lost some weight – 4 kilograms on average – and we found that they tended to eat less just because the diet we proposed was fairly satiating. These women came twice a week to eat with us and to follow kitchen courses. We organised 50 different menus in order to show that we may have a wide variety in the diet even with these principles. Their testosterone decreased, together with free oestradiol, insulin and glucose, and also cholesterol and triglycerides went down. On the contrary SHBG and IGFBP1 and 2 went up. IGF-I, however, did not change significantly, perhaps because we did not decrease protein in this diet – we just shifted from animal to vegetable proteins.

Questions

Elio RIBOLI

Thank you, Franco. You cannot present everything in half an hour, but could you say a few words on what make you think that these results are important for public health? In this randomised trial, you started with changes in diet and lifestyle. To what extent do you think these changes are within the reasonable reach of feasibility for the normal population?

Franco BERRINO

In this study, we put a lot of effort into changing these women's diet in a radical way, and we invested a lot in psychological assistance. However, there is more and more evidence that all the factors defining metabolic syndrome – high blood pressure, low HDL, high triglycerides, high glycaemia and waist circumference – are associated with breast cancer. As you saw yesterday, there are several ways that are not necessarily dramatic to improve metabolic syndrome. Metabolic syndrome is associated in women with a high testosterone level, and so it is reasonable to hypothesise that an even less dramatic change will reduce incidence and improve survival.

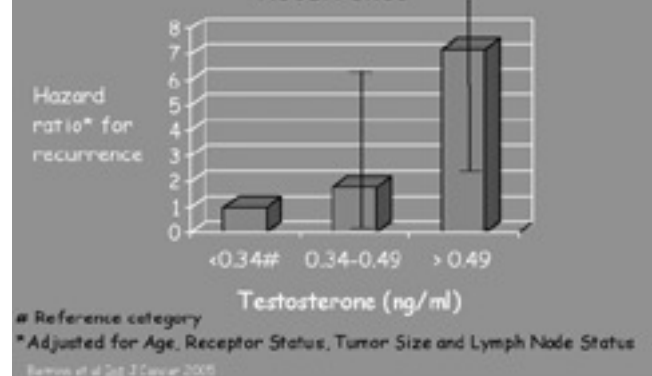
Nick WAREHAM

One of the things we observe from diabetes epidemiology is marked variation in the prevalence around the world, with some particular populations having an extraordinarily high prevalence. The question is really an ecological one: does that variation map at all to breast cancer incidence?

Franco BERRINO

I would say yes, the diabetes map is quite consistently superposable on the breast cancer incidence map. The relationship between diabetes and breast cancer is a little confused. It did not appear in the old studies, but then I was very impressed by a study showing that women with breast cancer had a higher risk of diabetes. This is interesting because the problem is not that diabetes per se increases the risk of breast cancer, but the pre-diabetic condition, when insulin is still high, may increase the risk. At the end, when the pancreas is not producing more insulin in sufficient quantities, there is probably not a strong association.

Figure 6. Testosterone and Breast Cancer Recurrence



The second trial we carried out (DIANA 2) was with breast cancer patients. The study included 110 disease free breast cancer patients who followed our diet for one year and the incidence of recurrence, including of local recurrence, distant metastasis and contra-lateral breast cancer, was recorded over 5.5 years. Previous studies had suggested that several diet-related factors may affect the recurrence of breast cancer: obesity, weight gain during adjuvant treatment, hyperinsulinemia. The results of our study showed that also high serum testosterone is a major determinant of breast cancer prognosis (Figure 6). To a lesser degree, also oestradiol, body weight, glycaemia, as well as the presence of metabolic syndrome affected prognosis.

The numbers are small, but when we classified women according to whether they succeeded in reducing their testosterone level from above the median value to below the median, those who succeeded had a lower frequency of recurrences (Berrino et al., 2005) suggesting that breast cancer patients may reduce their risk of recurrence through a change in their diet. Thank you very much.

Elio RIBOLI

There is a study within EPIC where we investigated and measured the C-peptide. C-peptide is a small peptide that belongs to the insulin molecule that is removed from insulin, and then insulin becomes biologically active. C-peptide is a good marker in blood of a high insulin production level by the pancreas. We measured the C-peptide in blood samples collected many years before the development of breast cancer and in women who did not develop breast cancer. We are now analysing the result and we find that a high level of C-peptide is associated with a significant increase in the incidence of breast cancer, which means multiplying by 2.5 – the high level versus the normal level – in women older than 65 or 70. There is a weaker association in women between 50 and 60, and there is almost no association, or no effect, below 50.

This is extremely important if we think that overweight does not increase the risk of breast cancer before the menopause, while overweight is strongly associated with an increase in breast cancer after the menopause, and in a way, C-peptide is closely related to overweight. So we have a situation where overweight after the menopause and what is called insulin-resistance, which is a poor utilisation of insulin and glucose by the organism, are associated with breast cancer.

Member of the audience

In relation to the level of testosterone in the intervention with the Mediterranean and macrobiotic diet, I would like to know something more about the combination of the two diets and what you mean exactly by macrobiotic intervention.

Franco BERRINO

Next time, we will organise lunch using the DIANA diet for you to see that it can be appreciated by everyone.

The typical diet we used was a vegetable soup or a mixed salad, followed by a main dish, with cereals every day, like wheat, rice, buckwheat, millet or barley, and with various kinds of pulses and cooked vegetables. There was also a desert almost every day, which was made without sugar, milk, butter or fats. There was a wide variety of macrobiotic deserts and also a lot of nuts. We are fairly confident that the recommended dietary allowance was respected for all essential nutrients.

We are now carrying out the DIANA 3 study on young women – this is a low-protein diet with just 9% of calories from proteins – in order to see if we are able to act more on IGF-I.

Member of the audience

Do you mean vegetable proteins or also animal proteins?

Franco BERRINO

Mainly vegetable proteins – these women are advised to have animal protein only once a week.

Diet, obesity, physical activity and colorectal cancer

Teresa NORAT

International Agency for Research on Cancer, Unit of Nutrition and Cancer, Lyon, France

I will present some of the results from the EPIC study on the association of diet and colorectal cancer. Some of the results are preliminary and some of the results have already been published. Specifically, I will present the preliminary results on obesity and physical activity, fruit and vegetable intake, and dairy products intake; and I will present our published results on fibre (with a new update), and meat, fish and poultry.

Colorectal cancer represents one of the most frequent causes of cancers in the world. We can see in the figure the rates of incidence and mortality of colorectal cancer in developed and developing countries. The rates are increasing in developing countries. Changes in incidence rates together with studies in migrant populations showing that the rates in the immigrant population approach the rates of the host population have suggested that colorectal cancer risk is related to lifestyle.

In EPIC, we have the advantage of having cohorts from 10 different countries, which allowed us to investigate populations with very diverse dietary practice. We have followed the subjects for cancer incidence and mortality through cancer registries in 7 of the participating countries, while we have a combination of methods to identify incidence and mortality for colorectal cancer in three other countries through active follow up. To date, we have been able to identify close to 1 800 cases of colorectal cancer that we have included in the analyses presented here.

Recently, an important meeting was held at the International Agency for Research on Cancer to evaluate the evidence concerning the association of overweight, obesity and physical activity with risk of several cancers. This table used for the expert group in that meeting, showing the results of all case-control and cohort studies published at that time, shows that subjects in the highest level of physical activity, compared with subjects in the lower level of physical activity, had a reduced risk of colorectal cancer.

In EPIC, we have collected information about work-related, household and leisure time physical activity in the participants at recruitment through questionnaires. Measuring physical activity in population studies is very difficult. The studies that have been published have measured physical activity using different questionnaires, but the measurements have not been validated in most of those studies. We have collected the frequency and duration of different types of physical activity, but we do not have measurements of the intensity for many activities. We know how many hours a person walks by week, for example, but we do not know the speed the person walks at. As in other studies, our results are subjected to measurement error.

In EPIC, physical activity at work was classified by level of intensity as sedentary activity, standing, manual or heavy manual activity. For non-occupational activities, the metabolic equivalent of energy expenditure (Mets) was applied. The participants in EPIC were categorized in quintiles of Mets and an index of total physical activity created by combining occupational and non-occupational levels of activities. We used this index to investigate the association of physical activity with colon and rectal cancer risk.

Here we see the results of the study on colon cancer in males. The inverse trend of colon cancer risk across categories of inactive, moderately inactive, active, and very active subjects are statistically significant. The trend in women was in the same

direction but not significant. However, the results for men and women are not statistically different, so we could combine them. When men and women are combined, we observe a significant inverse trend between colon cancer risk and physical activity. The subjects who were classified as active in our study had a relative risk of 0.77 compared to the inactive, while for rectal cancer, as in other studies, we do not see any association.

Colorectal cancer and physical activity : combined household, recreational and occupational activity. Preliminary results from EPIC

	Colon		
	Males (n=177)	Females (n=77)	All (n=254)
Inactive	1	1	1
Moderately inactive	0.90 (0.67-1.20)	0.98 (0.70-1.35)	0.96 (0.75-1.09)
Moderately active	0.83 (0.62-1.11)	0.86 (0.66-1.13)	0.84 (0.68-1.01)
Active	0.80 (0.58-1.17)	0.73 (0.49-1.10)	0.77 (0.59-1.01)
p-trend	0.18	0.12	0.02

	Rectum		
	Males (n=93)	Females (n=30)	Both (n=123)
Inactive	1	1	1
Moderately inactive	0.98 (0.69-1.39)	1.06 (0.72-1.57)	1.01 (0.71-1.33)
Moderately active	0.96 (0.68-1.35)	1.17 (0.80-1.73)	1.03 (0.80-1.32)
Active	0.80 (0.50-1.27)	1.17 (0.68-2.07)	1.02 (0.71-1.46)
p-trend	0.18	0.43	0.41

ORs & regressions adjusted for age, height, weight (quintiles adjusted for men) and central, alcohol consumption (quintiles), smoking status (never, former, current smoker), smoking, educational level, (2 g/day), fibre and red meat intake and stratified by centre. In women, adjusted for use of hormone replacement therapy

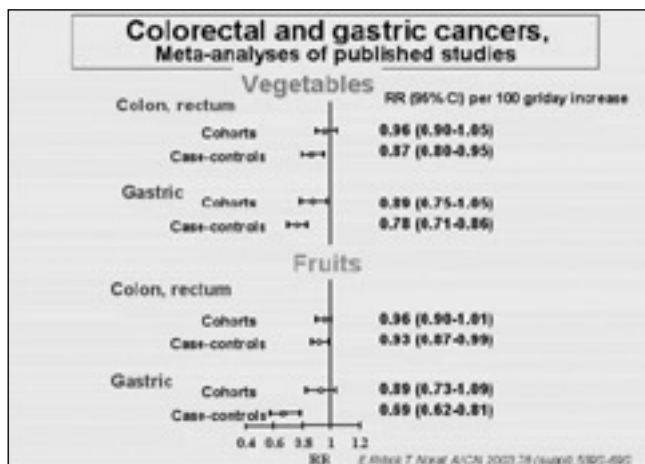
These analyses has been adjusted for age, height, weight, alcohol consumption, smoking status, educational level, dietary fibre and red meat intake, and stratified for center. We also adjusted for the use of hormone replacement therapy in women.

In this figure, extracted from the IARC report on overweight and physical activity, we observe the relationship between body mass index and risk of several cancers in published cohort studies. The values are the relative risk when comparing groups of subjects with the highest level of body mass index versus the lowest level of body mass index in each of the studies. The comparisons are not strictly the same across studies, but in most of the studies, the highest level was "higher than 28 kg/m²" versus "less than 22 kg/m²" of body mass index. We can appreciate the positive association between body mass index and colon cancer risk.

In these preliminary results of EPIC, we observe a significant positive trend between colorectal cancer and body mass index; increasing body mass index is associated with significant increased colon cancer risk in men, but this trend is not significant in women in EPIC. Rectal cancer risk is not associated to body mass index in this population. This is consistent with most of the other studies.

When we analysed an index of abdominal obesity – the ratio of waist to hip circumferences – we observed that in both men and women, the ratio of waist to hip is significantly positively associated to the risk of colon cancer in women and men.

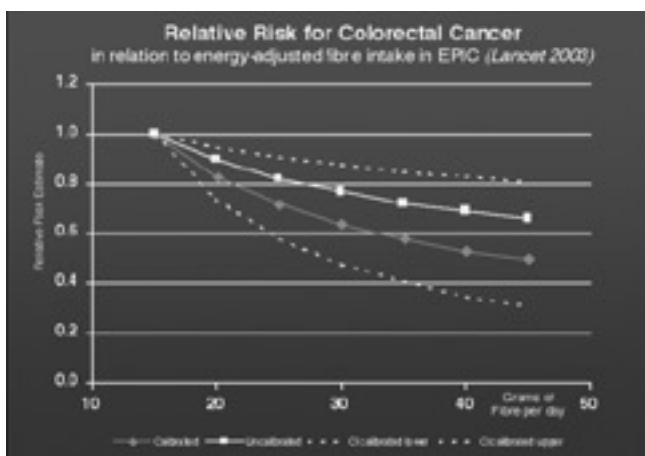
The association of colorectal cancer with fruits and vegetables has been investigated in several case-control and cohort studies. We published a meta-analysis of published studies showing that the overall results of case-control studies suggested a significant association between vegetable intake and colorectal cancer, but that this association was not confirmed by cohort studies, for which the overall results showed an inverse but not significant association.



The analyses on fruits and vegetables we are showing are preliminary and include only the cases reported until five years ago. We are now re-analysing the information, with the latest update. In the preliminary analyses, we observed a significant inverse trend for vegetables and for fruits and vegetables combined, while no association was observed with fruits.

We published a paper about the association of nuts and seed intake with colon cancer risk in EPIC, showing an inverse association of nuts intake and colon cancer risk in women but not in men. These results have to be confirmed by other studies.

The study of the association of dairy products and colorectal cancer in EPIC is ongoing. Interestingly, our first results are consistent with the results of the Pooling Project of cohorts, published last year. In EPIC, we observe an inverse association of milk intake and colorectal cancer risk, and inverse but not significant for cheese and yoghurt. The analysis was adjusted for sex, energy intake, height, weight, physical activity, alcohol consumption, smoking status, dietary fibre, folic intake, red and processed meat. We are working in the classification of the dairy items to differentiate milk according to its fat content in EPIC.

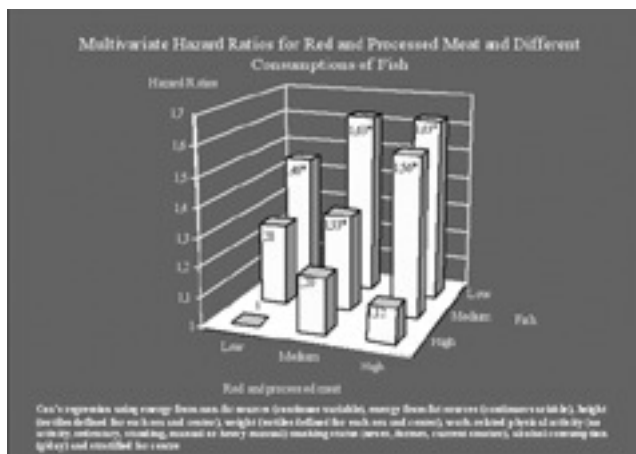


The results on the association of dietary fibre and colorectal cancer risk were published in the Lancet two years ago. The hypothesis that dietary fibre is protective against colorectal cancer is a well established hypothesis, but most of the recent studies have not found an association between dietary fibre and colorectal cancer risk. There is a wide variability of fibre intake across countries. Most of the fibre comes from cereals in EPIC but vegetables and fruits are other important sources. The results published in Lancet showed a significant inverse association between fibre intake and risk of colon but not rectal cancer. Why have these results not been found in other cohorts? We think that the wide range of fibre intake in the EPIC population allowed us

to detect this effect. We repeated recently the analysis with two more years of follow-up and in addition, we adjusted for the dietary folate for which we could not adjust in the first analysis, and we obtained exactly the same results as in our first paper, which are mainly that the association of fibre is mainly with tumours of the left colon, is not significant with tumours of the right colon, and there is no association with risk of cancer of the rectum. With almost 700 more case subjects and a better adjustment, we see the same protective effect of dietary fibre against colon cancer as in the previous study.

The first cohort study that published that the risk of colon cancer was positively associated with high red meat consumption was the Nurse's Health study in 1990. Several studies have replicated this finding. The ecological correlation between meat consumption and the incidence of colon cancer was already showed in an interesting article published in 1975. These two maps show the concordance of geographical distribution of red meat intake and colorectal cancer risk. These are based on updated information on cancer incidence from IARC, and estimates of food availability from FAO. We published a meta-analysis of case control and cohort studies, showing that colorectal cancer risk was inversely although no significantly associated with fish, no associated with poultry, and positively significantly associated with the consumption of processed meat and fresh and processed meat combined. Processed meat is a very heterogeneous category in which you can find sausages, dried sausage, raw and cooked ham, different types of bacon and other types of processed meat. Most of the processed meat at the time the studies were published was from pork. There is a high heterogeneity of consumption of fish, red meat, processed meat and poultry in the EPIC population. Interestingly, the consumption of processed meat in Greece is the lowest in EPIC. The highest consumption of processed meat in EPIC is in the German countries. The consumption of red meat is the highest in the nordic countries; the consumption of fish is the highest in Spain and some of the nordic countries.

In EPIC, we observe a significant increase of colorectal cancer risk associated to the intake of processed meat, and red and processed meat combined. There is no association with poultry. There is a significant inverse association with fish intake, and we see a significant protective effect associated to the consumption of fish. To investigate if the increased risk associated to red and processed meat, or the protective effect of fish, were explained by displacement of red meat by fish and vice versa, we did cross-classified analysis categorising the subjects according to the intake of red and processed meat – low, medium and high – and simultaneously to the intake of fish, in low, medium and high intakes. The protective effect of fish is observed for all the levels of intake of red and processed meat. The subjects with a high consumption of red meat and a low consumption of fish have a relative risk of colorectal cancer of 1.63 compared to subjects with a low consumption of red and processed meat and a high consumption of fish.



Since we observed a protective effect of fibre and subjects who eat more red and processed meat tend to eat less fibre, we did a similar analysis combining the consumption of fibre with the consumption of red and processed meat, and there was no statistical interaction.

There are well established mechanisms supporting the role of fibre in the protection against colorectal cancer: There are suggestive mechanisms supporting the role of meat in the

association of colorectal cancer, in particular the presence of some carcinogens formed during the cooking of meat at high temperatures for long periods of time, and the endogenous formation of nitroso-compounds, that can be mutagenic. In the EPIC study we observe a positive association of red and processed meat and an inverse with dietary fibre. Our results suggest that fish could be protective against colorectal cancer. Thank you.

Questions

Franco BERRINO

My question refers to poultry, for which you showed an insignificant negative association. I wonder if this negative association would disappear if you adjust for red meat. I would like to ask you what could be the reason why red meat could increase the risk and poultry does not increase the risk. Poultry also contains haeme iron in different quantities according to the type of poultry, and heterocyclic amines are formed while cooking poultry. The type of fat is different, but the type of fat does not seem very important for the risk of colon cancer. What is your idea about that?

Teresa NORAT

You are right, when red meat and poultry are together in the model the non-significant association with poultry is even more attenuated. When beef, pork and lamb are together in the same model, only the association with pork remains significant. When ham, sausages and bacon are in the same model, none of them explained the association independently. There are no clear mechanisms to show why processed meat should increase the risk more than red meat, but we do know from the metabolic studies conducted in Cambridge that in subjects fed with red meat there is an increase in total apparent nitroso-compound in the faeces – this is catalysed by iron coming from haem iron, but not for inorganic iron – while no increase in the total nitroso-compound in the faeces is observed in subjects fed with white meat. This study has been published and is probably the most supportive of our results.

Regarding the formation of carcinogens in meat, fish and poultry when they are cooked, these hypotheses have been explored in a few epidemiological studies. We do not see an association with fish and poultry, although there are heterocyclic amines in fish and in poultry. This can be explored in association studies in subjects with certain polymorphisms of metabolic enzymes participating in the activation of these carcinogens. The Colorectal Cancer Group has recently published a study in which they studied genotypes associated to the carcinogen activation and their results are not supportive of the effect of heterocyclic amines. I think that the endogenous nitrosation in the presence of haem iron iron could explain the association with red meat. We do not have a hypothesis to explain why processed meat should increase the risk more than fresh red meat, although we have observed that in our meta-analysis.

The other interesting topic related is dietary patterns. We have a project on dietary pattern. It is very interesting that the apparent noxious effect of red meat was attenuated in subjects with a high consumption of fibre. These results need replication.

Member of the audience

Could you recap your preliminary results done on fruits and vegetables and maybe give a little more detail?

Teresa NORAT

As I said, these results are preliminary. At that time, we only had about 700 case subjects. We do not know what the results are now with a longer follow-up. Preliminary, we observed an inverse association of vegetables, and fruit and vegetables combined with colorectal cancer risk. When we examined the different types of vegetables, the association was significant with green leafy vegetables. However, there are questions of measurement error and we cannot exclude that measurement error of intake varies according to the type of vegetable, at least in European populations. If the association exists, it is probably weak, because several other studies have not found a significant association.

Member of the audience

I have a brief question on the protective effect of milk. Is there any chance that the cases would have avoided milk for some reason, for example hyper-lactation or something like that, or just not feeling well so they avoid milk?

Teresa NORAT

The proportion of non-consumers of milk in our population is very low – so low that we could not make a category of non-consumers.

Elio RIBOLI

I interpreted the question in a different way, but I will pose another question anyway. Did you look at the association with milk specifically for the cases occurring in the first few years of observation? I understood that some bowel dysfunction that may be related to that diagnosis could modify the milk consumption.

Teresa NORAT

In almost all the cases, the diagnosis is after the first two years of follow-up. Thu, the results are very much driven by the cases diagnosed after the first two years.

Elio RIBOLI

To follow this question on changes in diet, this may be related to symptoms preceding the appearance of the disease. What we systematically do in EPIC and other cohort studies is that we look at the association with the cases that are diagnosed during the first year, and those during the second period of either 3 to 4 years or 5 to 6 years. There is no real indication that this has any impact on the association with disease risk and sometimes it becomes even stronger.

Member of the audience

I would like to add to Elio's comment that in our cohort, we never see a difference, excluding or not cases diagnosed during the first 2 or 3 years.

I would like to ask if you have looked at butter consumption.

Teresa NORAT

Butter is highly correlated with dairy product intake but we did not see a significant association. I do not remember the exact figures of hazard ratios. The problem with butter is also measurement error.

The previous member of the audience

Because in our data, I was seeing an inverse association as well.

Teresa NORAT

I think we have a non-significant inverse association, I am not sure now, but I interpreted it as driven by the correlation with dairy products.

Coming back to the haeme iron hypothesis, we did an analysis of offal intake and we did not see any association. I think you published a paper recently on liver and colorectal cancer recently. Would you like to comment on it?

The previous member of the audience

We have been studying black pudding, which has a very high concentration of haeme iron, and we see a very strong association with this special food item, and with haeme iron – our intake level of liver is very low so we could not recognise an association.

Elio RIBOLI

The catalysing effect of haeme iron on the endogenous formation of nitrogenic compounds that has been clearly shown by metabolic studies on volunteers I think are of major importance for the mechanistic interpretation of what happens in the lumina and in the colon, and that corroborates very nicely for the first time the results of our epidemiological study.

Vegetarianism and cancer risk

Tim KEY

Cancer Research Epidemiology Unit, University Oxford, UK

I would like to thank the organisers for inviting me to Rome for this meeting. I would like to speak about vegetarianism and cancer risk, and I am going to speak on that topic even though there is not an awful lot of data on that specific question.

I will start off by making clear what we are talking about with vegetarianism. This is the definition: vegetarians do not eat meat or fish of any type. Sometimes people forget bacon or sausages or salami, but vegetarians do not eat any meat, and that includes poultry, and they do not eat any fish at all. That is the definition I will be working with this morning.

We also have a sub-group of vegetarians called vegans, who do not eat any animal products – they do not eat any animal products, do not eat any dairy products and they do not eat eggs.

I am going to divide my talk into 5 sections. I will start by telling you why there has been interest in the possibility that the vegetarian diet might alter the chance of getting cancer. Then I will explain what data we have to look at the questions, then a little about what vegetarians actually eat – how does their diet differ from that of people who are not vegetarians in terms of foods and nutrients that might be relevant to cancer? I will then move on to the actual data we have on cancer rates, focusing on the 3 common cancers that have been focused upon at this morning's meeting as well that we think might be related to diet particularly, which are colorectal, breast and prostate. I will then draw some conclusions.

In terms of where this hypothesis comes from, I think it really dates back to the work of people like Armstrong and Doll in the 1970s looking at the ecological associations between what different populations ate around the world and their cancer rates. We have seen some of those data earlier this morning.

I would like to show some data from that publication for colon cancer rates in men in 23 countries around the world. I have put the correlation coefficients for four animal foods – meat, animal protein, eggs and milk – and also for cereals. Dr Teresa Norat showed the slide of the correlation with meat; that slide she showed you corresponds to the correlation coefficient of 0.85, so a very strong correlation. Countries where they were eating a lot of meat in 1965 had high colon cancer rates. There were also quite strong positive correlations with an estimate of animal protein (0.74), and also with eggs and milk, whereas cereals had a moderately strong negative correlation – those countries where people ate a lot of cereals had lower rates of colon cancer. So you could say that people who do not eat meat and eat a lot of cereals, a vegetarian diet, might not get colorectal cancer. There are similar correlations, but not quite as strong, for both breast and prostate cancer. So there had been an underlying idea that a vegetarian diet might be protective against these 3 common cancers.

I would like to make one more comment on this question because when we are looking at vegetarians now – and that really means that the data we have is from vegetarians living in industrial countries like Britain and America – these people's diet has very little in common with that of the poor semi-vegetarians who were living in the countries that had the low colon cancer rates in this slide – places like old-time Japan, rural China, India, etc. These were countries where the population were poor; a lot of them would have liked to eat meat but they could not afford it. The

western vegetarians have got lots of money, they eat as much as they want of everything, and the vegetarians who are not vegans actually eat eggs and milk by definition. You can see here that although the correlation with meat is the highest, we have also got positive correlations with both eggs and milk. So the hypothesis is not very well thought out and maybe we should really be focusing within western society on vegans, because these are people who have zero intakes of all the animal products and they are probably a little closer in terms of nutrition to the old-time low-risk populations.

In terms of what data we have to look at, there are quite a lot of, what we might call cross-sectional studies, where a group of vegetarians and a group of meat-eaters living in the same place and compared them – compared their diets, weighed and measured them, took blood samples and conducted biochemistry. There are quite a lot of data of this type, but obviously that does not tell you about cancer rates.

In terms of studies that have real data on cancer in vegetarians, there are very few. There are a few cohort studies and these are cohorts where a large percentage of the people in the cohort were vegetarian because that is the way it was designed. For example, in the Seventh Day Adventists cohorts, the Seventh Day Adventist Church recommends that a healthy diet should have zero or low amounts of meat and fish, so a lot of Seventh Day Adventists are vegetarians and if you recruit a cohort among those people, you can compare the people who do not eat meat with those who do eat meat. However, they are fairly similar in terms of other background, because it would be unhelpful if we compared vegetarians with national rates because they would be different in so many ways.

We have a few cohorts of that type: we have the Seventh Day Adventists, two older British cohorts set up in the 1970s and 1980s, a small German cohort. There are two case-control studies of breast cancer using Indians, where a large proportion of the people were vegetarian. Finally, we have one component of the EPIC study – the EPIC-Oxford cohort – where we deliberately went out to recruit as many vegetarians as possible. We have ended up with about 65 000 people in EPIC-Oxford, and about half of those people do not eat meat. That is the largest cohort so far where we have data on people who do and do not eat meat that have been recruited in the same way from a broadly similar background.

I will show you some data from all these cohorts, but I will particularly concentrate on EPIC-Oxford as a source for showing you some descriptions about what vegetarians eat. In the total cohort at EPIC-Oxford we have 34 000 meat eaters and 10 000 people that we call fish eaters – people that do not eat meat but do eat fish. That may be a little confusing as you might think that these people eat fish all the time, but they do not eat an awful lot of fish, it is just that they are vegetarians who will eat fish. If you look at their fish intake, it is similar to that of the meat eaters. Then we have the strict vegetarians, about 19 000, who do not eat fish or meat, and then about 2 500 vegans.

These are data from the whole EPIC-Oxford cohort on intake of a few foods and nutrients, starting with fruit. We have them in four groups: meat, fish, vegetarians and vegans, men and women. Fruit intake in the whole cohort is relatively high compared with an average British person, because they have all

shown some sort of health consciousness and keenness to enter a study on diet and cancer. We can see that in both the men and women, the fish eaters and vegetarians have a higher fruit intake than the meat eaters, and that the vegans have the highest intake. The women eat a bit more fruit than the men. You will notice that although the vegetarians are a bit higher than the meat eaters (it is not a very big difference so they are not eating twice as much fruit, they are just eating a bit more), the vegans eat quite a lot more fruit. That same pattern keeps recurring: the vegetarians are always a little different from the meat eaters, the fish eaters always look almost exactly the same as the vegetarians, and the vegans are always at the extreme end and usually more different from the vegetarians than the vegetarians are from the meat eaters.

If we look at vegetables, not including legumes – which means beans, pulses and potatoes – they have very similar patterns, though relatively high intakes of vegetables for Britain: identical intakes in the fish eaters and vegetarians, which are a bit higher than the meat eaters, and then the vegans with the highest intake.

If we look at legumes – which means pulses, beans, lentils and includes soya beans, which is quite important in the vegans – then we find a much bigger difference, where the vegetarians are eating more than the fish eaters (probably because they have eaten beans instead of fish), and the vegans are eating much more (because legumes are a major source of protein and calories for the vegans). So there you see some quite extreme differences.

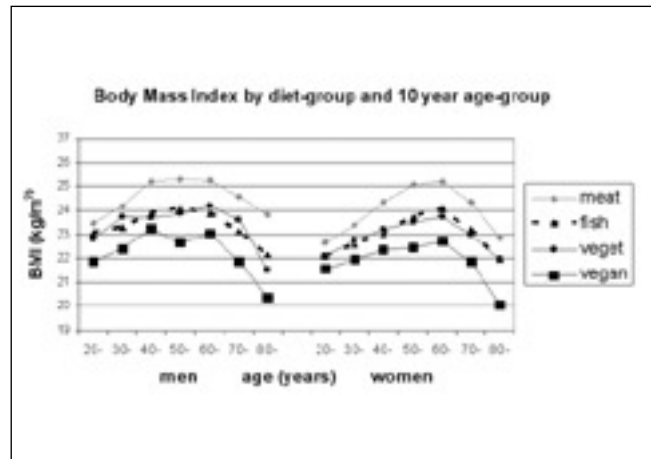
If we look at total fat intake, it does not vary much between the groups, but saturated fat does. Again, we have the same sort of pattern: fish eaters and vegetarians appear identical (they are lower than the meat eaters but the difference is really quite small, going down from 10.5% to 9.5% of energy from saturated fat – a highly significant difference but one that probably would not translate into much impact in this case on heart disease), whereas the vegans have really quite an extreme difference with their saturated fat intake at about half of that in the other groups.

For fibre intake, again there is a similar pattern: a fairly even trend across the groups with the vegans having the highest intake and being really substantially higher than that of the meat eaters, whereas the vegetarians' intake of fibre is higher, but only a little higher. If you think about the data that Dr Norat showed earlier on fibre and colorectal cancer, where you are looking at people in the top fifth of the whole population of EPIC compared to the bottom fifth, that difference in fibre intake from top to bottom fifth is much, much bigger than this little difference between vegetarians and meat eaters – so they do eat more fibre, but it is not hugely more.

Folic correlated with fibre with a similar trend, so a bit higher in the vegetarians, quite a lot higher in the vegans.

Finally, in terms of the cross-sectional data, this is body mass index in the 4 diet groups. We have men on the left and women on the right, and the mean body mass index in the groups in each 10-year age group at the time of recruitment into EPIC-Oxford. The first thing to note is that overall, our cohorts are relatively slim compared to the British average, with body mass indexes around 23 or 24, and obesity being rather rare.

You can see that in all the diet groups, people get fatter as they get older until they are in their sixties, and then people in their seventies and eighties get thinner again. That has been seen commonly in other studies, so whatever you eat, you get fatter on average. So you can see that there are big differences between the diet groups, both in men and women: the meat eaters are the fattest, the vegans the thinnest, and the fish eaters and vegetarians are in the middle and almost exactly the same as each



other. The difference here is about 1 unit between the groups, so compared to the meat eaters, the fish eaters and vegetarians are about 1 unit of BMI thinner, and the vegans are about 2 units thinner. When we come back to thinking about cancer, they are a bit thinner, therefore they should get less cancer of certain types, but 1 unit of BMI would not give you a very big reduction in risk.

Now I will focus on colorectal cancer. The problem we have been discussing this morning with colorectal cancer, in terms of trying to make sense of what variables to look at and how the whole pattern fits together, is that we do not yet have a well-established intermediate biochemical marker that links exposure with risk. With heart disease we have serum cholesterol; with breast cancer, as Dr Berrino showed you this morning, we have oestradiol, at least in post-menopausal women, and some other hormones. In colorectal cancer there are a lot of hypotheses, but we do not really know what to focus on in terms of intermediate markers.

I will show you a couple of things for which we have some data. At EPIC-Oxford, we looked at the frequency of bowel movements in the different dietary groups. The axis here is the mean number of bowel movements per week – once a day would give you a value of 7 – and we have it in the 4 diet groups. The first thing to notice is that men are ahead of women – men have about one more bowel movement a week than women – and that has been seen in other studies. If you look within the diet groups, this is based on 21 000 people in this analysis so there are very highly statistically significant differences. The fish eaters and the vegetarians have a higher frequency of bowel movements than the meat eaters, and the vegans are the highest, with about 2 more a week than the meat eaters both in men and in women. In fact we looked in this database at other things, including fibre, and diet group was by far the strongest predictor of bowel movement frequency – fibre went in the expected direction but was not as strong as diet group. It could be that is because we cannot measure fibre as accurately as we can measure diet group, but I think it may be because it is not just fibre – some of the foods that the vegans eat may have particularly strong effects on the bowel, particularly things like pulses, soya beans, etc.

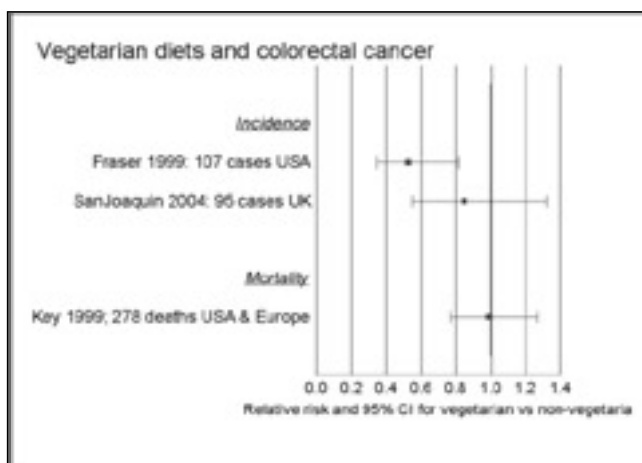
Other people have looked at other characteristics. This is another British study (not EPIC) looking at 3 indices of characteristics of faeces that might be important in colorectal cancer. There were 3 groups: white omnivores, white vegetarians, and Indian vegetarians. You can see that looking at faecal weight, it was higher in the vegetarians, and much higher in the British Indian women than in the British white women.

If we look at pH in the faeces, this is very impressive. This is relative to the meat eaters at 100%. This is a highly significant difference in that the Indian vegetarians have a more acidic pH

in the faeces than the white omnivores. This could be important because the pH determines the rate of metabolism of things like primary bile acids and secondary bile acids. There is one secondary bile acid, deoxycholic acid, which some people have suggested might be a causal factor in colorectal cancer, and the faecal levels of this are lower in both vegetarian groups than in the meat eaters.

You would think that there seem to be lots of factors in terms of colorectal cancer epidemiology that are going in the direction that the vegetarians should have less colorectal cancer: if the meat is important as you saw this morning, where you have the zero meat intake, they also have a slightly higher intake of fibre, fruit and vegetables, they are less constipated, etc., so you would think that they should have less colorectal cancer.

We do not have very much data. These are all prospective data sets looking at the rates of colorectal cancer in vegetarians compared with non-vegetarians within the same cohort. This study is within the cohort of the Seventh-day Adventists living in California, and we find a significantly lower incidence of colorectal cancer in the vegetarians than in the meat eaters in that cohort – 107 cases. We published last year, from the old Oxford vegetarian study on 95 cases, a non-significantly lower incidence of colorectal cancer in the vegetarians than the meat eaters in that old British study.



The other thing we published on is mortality, which give you bigger numbers – 300 deaths here – and this is bringing together all the data in the world on the cohort studies of vegetarians. Three of those studies did not have any data on incident cases, so we therefore looked at mortality as an index of risk because the mortality for colorectal cancer is quite high. Here, we saw a relative risk of exactly 1, so the mortality from colorectal cancer in these cohorts was identical in the vegetarians compared with the non-vegetarians. The results are still compatible with some reduction in mortality in vegetarians, but the point estimate is 1.

I quite often read books or articles saying that vegetarians have less colorectal cancer than meat eaters, but as far as I know, this is all the data there is in the world. It is hard to say that is true; it may be that there is a difference, but the evidence is not there.

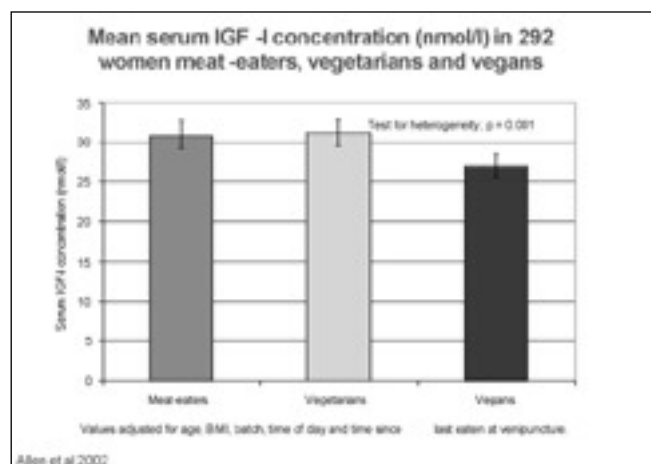
Regarding breast cancer, as Dr Berrino showed you, we are a lot further forward in some ways in terms of intermediate risks, like hormones. I will show you some data on hormone levels in vegetarians, focusing on oestradiol and then on IGF-I.

As we have seen, high levels of oestradiol in the blood definitely predict breast cancer risk in post-menopausal women. The data we have for pre-menopausal women do not show this

association, but there are serious measurement error problems in these women.

This is data from EPIC-Oxford where we looked at the oestradiol level in 1 100 women – meat eaters, vegetarians and vegans – and we split them into pre and post-menopausal. In pre-menopausal women, there was absolutely no difference between the groups that we could detect. In post-menopausal women, the vegetarians and vegans have very slightly lower blood levels of oestradiol than the meat eaters. Though it was not statistically significant, it is lower. It should be lower because they are a bit thinner, and if you adjust for the body mass index, that slight difference is eliminated. We conclude that there is no evidence that among pre-menopausal women oestradiol levels in vegetarians and vegans are different from those of meat eaters. They are very slightly lower in post-menopausal women, probably purely because they are a little bit thinner.

When we looked at IGF-I, the results were more interesting. We saw absolutely no difference in IGF-I between meat eaters and vegetarians, but the vegans have a highly significantly lower IGF-I. The difference is not very big at about 12%. However, I think a 12% difference in a hormone level is quite important because hormone levels are controlled by various means of homeostasis, and it normally takes a lot to shift them because you need the hormones to function. So a difference of 12% could be rather important. We cannot say why that difference is, but our analysis suggests it is most likely due to the difference in the type of protein intake. The protein intake in the vegans is low, but more than that, the intake of essential amino acids is lower. We do not think it is the energy intake because we have adjusted for BMI and for energy intake and it makes no difference, but we think it because of the difference in animal protein. If you think back to the definition, the gross dietary difference between vegetarians and vegans is dairy products – vegans do not eat them, vegetarians do – so it may be that the difference is due to dairy products.



There are slightly more data for breast cancer than for colorectal cancer because we have these 2 case-control studies focusing on Indian women. The first study was from California: there was a slightly, but not significantly, lower breast cancer incidence in the vegetarians. The data for the Indians do not suggest a difference. In the study that was actually done in India, the breast cancer incidence was insignificantly higher in the vegetarians; and in the British study, the risk was a bit lower but it was not significant.

In the mortality study, where we brought together all the data in the world from the cohorts of vegetarians, we found the risk of breast cancer was more or less identical in vegetarians as in non-vegetarians. I would say that overall, there is really little

evidence that breast cancer differs between vegetarians and non-vegetarians. It is not just western vegetarians in this case; we also have the data for Indian-type vegetarian diets.

Prostate cancer has some parallels with breast cancer in that hormones are likely to be very important, but we have not got quite as far in sorting out hormones in prostate cancer. The data that exist at the moment are rather weak on the main androgen testosterone, but there is a suggestion that there is a metabolite of testosterone that is an index of what is going on in the prostate itself that may be higher in men who get prostate cancer. There is also a little more data on IGF-I, suggesting it may increase prostate cancer risk. We have looked at both these types of hormones according to diet group.

For the sex hormones, we have a highly significant difference: vegans have significantly higher blood testosterone levels than meat eaters. In fact, this is potentially misleading because although testosterone is significantly higher in the vegans, the reason is because they have higher blood levels of SHBG, the sex hormone binding globulin. If you have more SHBG in your blood, you should have more testosterone because it is bound to the SHBG. The important fact is that the factor that is controlled by feedback in men is the level of free testosterone. Here, there is absolutely no difference between the 3 diet groups – it is identical in the vegans and the meat eaters. The vegans do have higher levels of SHBG and we are not sure why they are higher. Part of it is because they are thinner, but it may be because they have lower glycaemic index diets with therefore less insulin production, we are not sure. We are sure that the reason that testosterone is higher is because SHBG is high and free testosterone does not differ and androstenediol glucuronide is an index of what is actually happening in the prostate, and that did not differ either. Maybe that is to be expected because androgen levels are well controlled by feedback – they have to be controlled – and it seems that the dietary changes do not impact on the hormone levels.

However, when we looked at IGF-I, we saw results nearly identical to what I have shown you for women. The scale here has been truncated and the difference is not as huge as it might look. The results are highly significant here: the vegetarians and the meat eaters have absolutely the same levels of IGF-I, which is what we saw in the women, but the vegans have lower levels of IGF-I. As with the women, the most obvious thing is that the meat eaters and the vegetarians people eat dairy products, and the vegan men do not eat dairy products.

There is hardly any data on prostate cancer and vegetarians. The Seventh Day Adventists study published some data on incidence – 180 cases – and there is no significant difference, although the rate was slightly lower in the vegetarians. We looked at mortality in all 5 cohorts and despite having all the data in the world on prostate cancer mortality, we only had 137 deaths and the point estimate was close to 1. There is really no suggestion that prostate cancer is different in vegetarian men compared to meat eating men.

The main message emerging is that we need a lot more data – there is just not enough to draw conclusions. EPIC-Oxford will produce some, although it is still not really going to be big enough to answer all the questions; we will have to continue to try to pool all the data in the world.

I will just show you this one slide on the current situation in EPIC-Oxford. This is all cancers combined, because we do not really have enough to split it up. We have 1 400 incident of cancers in EPIC-Oxford. Splitting it up between the diet groups, if you take the meat eaters as the reference point, all cancer rates in the fish eaters and vegetarians and vegans are a little lower

than the cancer rates in the meat eaters (this is after adjusting for smoking and age, etc.). So, this is not obviously explained by known confounding factors but none of them are statistically significant.

The conclusions are really quite brief. In terms of definite risk factors, I think the only absolutely certain thing is obesity that really consistently studies have shown that, on average, vegetarians are little thinner than meat eaters living in the same place. The definite evidence is that obesity does increase the risk of some types of cancer, particularly breast cancer, endometrial cancer, and adenocarcinoma of the oesophagus. As there is a little less obesity, therefore there should be a little less of those types of cancer among vegetarians. However, we will not see that difference in these types of studies because the effect on the relative risk will only be a few per cent. It is probably true that it is happening but we cannot detect it.

Turning to probable risk factors, vegetarians by definition have a zero intake of meat, their fibre intake is a little higher than that of meat eaters, and so they get less constipation. These sorts of factors may well reduce colorectal cancer, but the data we have got have not established that this is true. The data we have do not show that colorectal cancer is different between vegetarians and average meat eaters. That does not rule out the results we saw this morning that people with a very high intake of meat have an increased risk, because we are comparing only with the average. Nevertheless, it does not seem to me to fit very well, because you would think that if meat was really important, people who have not eaten meat for 20 years really would have a lower risk – and they do not.

The sex hormones do not really look different between the dietary groups, and I think that is because homeostasis works. However, the results on IGF in vegans could be potentially important. We have seen very clearly, both in men and women, lower IGF levels in vegans. If you think back to the start of this whole story and the aetiological studies, the populations that have had low rates of these western country cancers were the populations with low intakes of animal products and certainly not eating a lot of dairy products, so they may be closer to a western vegan-type diet in terms of a lower intake of animal proteins – the link there could be IGF-1, but we need a lot more information to be sure there is anything important going on.

Conclusions

- Definite risk factor
 - **Less obesity** - will reduce risk for several cancers
- Probable risk factors
 - **Zero meat intake**
 - **High fibre intake** } - might reduce colorectal cancer?
 - **Less constipation** }
 - **Low IGF-I in vegans** - might reduce breast & prostate?
- Cancer rates
 - **Inconclusive** whether lacto-vegetarian diets affect cancer risk
 - **Almost no data** for vegans

The cancer data are really inconclusive on whether lacto-vegetarian diets have any effect on cancer rate. For vegans, there is a biochemical suggestion that there could be more important things going on, but there are almost no data at all on cancer rates in vegans so it is anybody's guess what they are. Thank you.

Questions

Elio RIBOLI

Thank you for this excellent review on vegetarianism and cancer.

Domenico PALLI

You mentioned 20 years as the length of time you have studied vegetarian subjects. I imagine that only a very small minority will have been raised from childhood as vegetarians. Most of these people will have decided at some time in their life to switch from meat eating to non-meat eating. Do you have any official information on this point?

Tim KEY

That is a very important point. I took the 20 years as an example but we do in fact have the data. You are right that in the British studies there are not many people who were raised from birth as vegetarians – there are some, but that is quite rare. I think that in our cohort the average was maybe 10 or 15 years, it is fairly long term. We looked at whether people had just become vegetarian and the bulk of them were quite long term. In the Seventh Day Adventists cohort quite a lot of them were vegetarians from childhood – in fact, they used the age at baptism into the church as a surrogate measure. In future we need to present those data more carefully.

We did publish something on body mass index showing that the long-term vegetarians were thinner and the short-term vegetarians were not.

Member of the audience

I did not understand the association between the consumers of meat, which is a protein, and the testosterone, which is a steroid hormone. The steroid hormone is generally synthesized by the acetate, which enters the luteal cells, and is transformed into cholesterol at the REL level, then in delta-5-pregnenolone at the mitochondrion level, to lead to the REL which gives testosterone. The testosterone would possibly come from the fatty acids, which are proteins. Consequently, why the testosterone rate would increase in the meat consumers?

Elio RIBOLI

The question is whether you could explain what is behind the association you have reported between meat consumption and testosterone levels. The questioner went into some detail about the production of testosterone by the Leydig cells and expressed scepticism about why there should be a link between meat consumption and testosterone levels.

Tim KEY

We were a bit surprised by this result because the hypothesis coming from world literature was that vegetarians, and maybe particularly vegans, might have lower testosterone levels in their blood. I do not know why, but that was the hypothesis. As you can see, this study is in 750 men. There were 250 men in each group: 250 vegans, 250 meat eaters. So there is a lot of statistical power and it is by far the biggest study in the world of this type. We found a highly significant difference in that the vegan men have higher testosterone levels than the meat eating men.

I think your question was that you did not believe that could be true, because where do they make the testosterone? Well, I think they do make it, because if you study testosterone levels in a bull, you will find they are quite high – and the bull is eating grass!

You do not get testosterone from meat; all these steroid hormones come from cholesterol. Everybody has cholesterol in their blood. The vegans have cholesterol in their blood – they have less than meat eaters because they eat less saturated fat, they are eating zero cholesterol. They have about 20% less cholesterol in their blood but that is hugely enough cholesterol to make as much testosterone as you would ever need, so I think the level of testosterone in the blood is in no way limited by what you are eating – every man should have enough nutrients to make plenty.

I think it is controlled by feedback, where the brain detects the amount of free testosterone in the blood and if there is not enough, it tells the testes to make a bit more. The system works.

Elio RIBOLI

I think this question is important because it addresses the fundamental design of research. There are many ways of investigating a biochemical and the chronological phenomenon. One way is to observe: you take men, women, obese people, lean people, and you measure something. You may find, as many studies have found, that obese men have lower testosterone than lean men. This is an observation, so it is what you see.

The second step is explaining why: what the biological mechanism is and why you see it. Researchers often find things that may be unexpected. This is extremely important because research progresses only when you find something you do not expect, because that springs theories and new observations. There is growing evidence that people with diabetes have a low incidence of prostate cancer – a big study on 650 000 Americans has found a 25% lower incidence of prostate cancer in men with diabetes. That shows that there are sometimes things you do not expect, so you then try to understand the mechanism behind. One American said that the difference between a researcher and a believer is that the researcher believes what he sees and the believer sees what he believes. It can be puzzling because it is contrary to what one might have expected.

Member of the audience

I wonder if you would comment on your Oxford meat eaters. You showed figures for the percentage of energy from saturated fatty acids, and that looked to be quite low – in fact lower than the mean that would be shown from the national diet and nutrition survey in the UK. Is part of the problem that you have particularly healthy meat eaters in Oxford?

Tim KEY

I would not use the word 'problem', but to some extent you are right. I would expect the people in the cohort to be a bit healthier than the average person in that country. The difference is more in our cohorts in EPIC-Oxford because we deliberately tried to recruit people with unusual diets. So in recruiting vegetarians, a lot of the people, when we were trying to recruit vegetarians, were meat eaters. They are certainly all shades, but they do have a relatively healthy diet compared with the average British person. We do have subgroups among the men so as in every other cohort, if we split those men up we will have some with higher saturated fats and some with lower. What you say is partly right, but if you look at saturated fat, we clearly still have a big difference within the cohorts because we have the vegans.

The other comment, which I probably should not make because it puts the spanner in the works of a lot of epidemiology, is that these data are from the food frequency questionnaire. The British EPIC questionnaire is an adaptation of the Nurses' health study questionnaire used in all the Harvard studies, and I think the estimates of some of these nutrients are not very accurate, particularly for saturated fats, which I believe are coming out a bit low. We have some data from the food diaries where both the total fat intake and the saturated fat intake, as estimated from the food diaries, are quite a bit higher than these data from the food frequency questionnaire. The difference between the diet groups remains more or less the same, which is why I felt it was alright to show it. The UK targets – that the government says we should not eat more than 10% energy from saturated fat – suggest the meat eaters are almost there on average. I think they are not; I think they are probably about 12%.

Member of the audience

According to different studies the amount of iron would be an important factor increasing colon cancer. From other Canadian and Japanese studies, the way the meat is cooked has an effect on the iron content. Do you have any data on this?

Tim KEY

In terms of the second question about the way of preparing the meat, we do not have data available on that from the food frequency questionnaire but we do have it from the food diaries, which we also have in Britain and we are coding that information at the moment.

Turning to the first question about iron, the situation is really quite complicated. If you look at iron intakes in the diet groups, it is a bit like the testosterone story in that the highest iron intake in our cohort is in the vegans. It is because a lot of plants do have quite a lot of iron in them, but it may be that much of that is not absorbed. The lowest iron intake is in the vegetarians, because they do not eat meat, and dairy products have almost no iron in them.

Coming back to colorectal cancer and iron, if iron was important then the vegetarians should have a slightly lower risk, but I think the difference would not be enough to be detectable. You are right that there is a lot of interesting work going on at the moment, but we are a long way from knowing whether iron has any relevance to colorectal cancer.

Elio RIBOLI

Research being done in Cambridge clearly indicates that the iron from vegetable sources does not work as a catalyser for endogenous N-nitrosation.

Franco BERRINO

I refer to the slide for sugar and carbonated drinks, which are not particularly healthy foods. Do vegans eat a lot of sugar?

Tim KEY

That is quite a hard question to answer because of the way the food tables are constructed. If you look at total sugar in the British food tables, the vegans come out at about the same as the meat eaters, but that includes fruits. You cannot get added sugar – like sucrose – out of the food table. We tried to do it by estimating which foods provide it. I think the vegans do eat a little less sugar, so they are slightly more health conscious in a way, but some of them eat very large amounts of fruit or dried fruit because they get hungry and they need to get calories from something, and one calorie-dense food is dried fruit. If sugar is bad for you, then it may not be that vegans are in a good position.

Elio RIBOLI

In a parallel analysis we have done on dietary habits in EPIC, we have seen that the vegetarians have a lower consumption of cakes and sweets compared to the non-vegetarians in the Oxford cohort.

Member of the audience

My question is about the morbidity and mortality rates you showed for the different types of cancer – the morbidity and mortality data. The mortality data were in general less conclusive. Nevertheless, you placed quite some emphasis on the mortality data, and I think it was because of the sample size because this was a bigger sample size. I am wondering about the value of such a finding. Is that not probably strongly biased by the assessment by death certificates which means that the cause of death is not properly assessed? Furthermore, does it rather show the successful medical treatment more than anything else?

Tim KEY

You are right that mortality is not the perfect thing to study if you are interested in incidence. It can be used in some cases as a reasonable surrogate; it depends on the cancer and the situation. The reason we used this was because we had 3 cohorts that had mortality data but did not have incidence figures, so the only thing we could look at was mortality. The mortality from colorectal cancer should be correlated with incidence. For some cancers, like prostate, there is an argument that it is better to look at mortality than incidence, because it eliminates the very small tumours that have a very good prognosis. I do not say that the mortality is excellent data for looking at risk but if there was a large difference between the vegetarians and the meat eaters in colorectal cancer, you would see lower mortality.

Member of the audience

What you say is very interesting but do you have any information about familial cancer history in this group? There is now a significant difference between non-vegetarians and vegetarians and vegans and this is surprising because we are always seeing low-risk recommended diets that are similar for cardiovascular disease and cancer. Maybe the difference in familial cancer history is also important in these 3 groups.

Tim KEY

We have not looked at that, but I only spoke about cancer because that was the title. We also published on coronary heart disease from the same studies, and there we found a highly significant difference. When we looked at mortality from ischemic heart disease in all the cohorts in the world – combined cohorts of about 80 000 people with a few thousand deaths from heart disease – there was an absolutely clear difference that the vegetarians had lower mortality from heart disease. There is an effect but that was not the topic this morning.

Mediterranean diet and cancer risk

Domenico PALLI

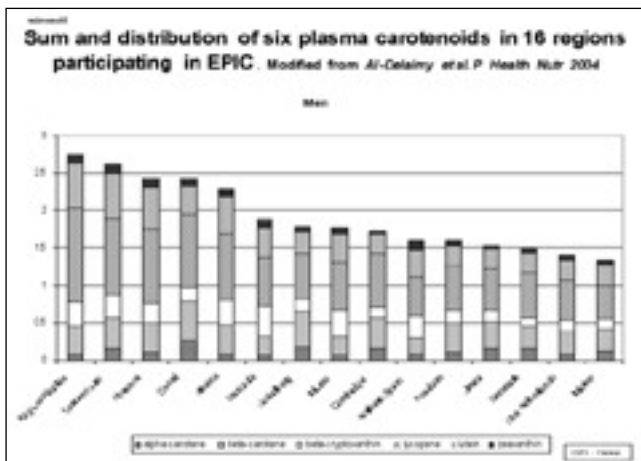
Molecular and Nutritional Epidemiology Unit, Cancer Research and Prevention Centre (CSPO), Scientific Institute of Tuscany, Florence, Italy

I would like to thank the organisers for giving me the opportunity of giving this lecture.

Actually, the Mediterranean diet concept is not very well defined and we may find hundreds of definitions. In general, it has been associated with a reduced risk of cardiovascular disease. More recently, however, the possibility that this dietary model might protect from cancer has become more and more popular among researchers and in the lay press. We focus on this issue because a traditional Mediterranean dietary model might help to optimise the combination of protective dietary components, leaving out the detrimental ones or keeping these detrimental habits to a minimum.

Among the hundreds of definitions, I would like to focus on foods from plant sources and olive oil.

These results were published last year on the journal *Public Health Nutrition* (Al-Delaimy et al., 2004): this is a cross-sectional study. Each bar represents the average plasma levels of the 6 major carotenoids in a sample of 100 men across 15 different areas participating in the EPIC study. In first place, you see men from southern Italy, northern Italy, central Italy, Oxford (which has a high component of vegetarians), Greece, Granada (southern Spain), and so on. On the other side, you see the minimum levels found in Scandinavia and the Netherlands. The different components are basically alpha-carotene levels, which are greatly consumed in European countries, beta-carotene, beta-cryptoxanthin, which is at a very high level in Granada, southern Spain, because of orange and citrus fruit components, and then we have other carotenoids, particularly lycopene and lutein with high values in Italian participants.



This is the picture among women, again with each bar based on 100 women (in 16 local cohorts, including France where only women were enrolled), ranked according to the total sum of plasma carotenoids. Again, the highest levels are found in southern Italy, northern Italy, central Italy, Oxford, Greece, and then the other centres.

Irrespective of a very precise definition of a Mediterranean-style diet, when we measure some dietary components, we find some

differences between populations living in different areas of Europe. Dr Riboli in his introduction on the first day mentioned the problem of decreasing age at menarche and increasing height. This slide is taken from another study, again across EPIC centres, and we see that women participating in EPIC in the three Mediterranean countries – Italy, Spain and Greece – were shorter in earlier cohorts. We see an increase in the adult height, but this increase is in parallel with the increase shown by northern and central European females (Onland-Moret et al., 2005).

There is no clear definition of the Mediterranean diet, you can either focus on some relevant component of a diet or you can use a Mediterranean diet score. Several projects have focused on cancer mortality and we also tried to carry out some analyses on cancer risk.

A paper recently published in the *New England Journal* by A. Trichopoulou reported that apart from a protective effect on the overall survival, a multivariate model showed that there was a reduced risk of mortality from cancer in the Greek component of the EPIC study, just applying the Mediterranean diet score proposed by that group.

Another study showed that if you count the number of protective factors, including a sort of Mediterranean score for diet, there was a significant protection from cancer-specific mortality in elderly Europeans.

On the other hand, when we think in terms of fruit and vegetables, we think of the natural and most relevant components of the Mediterranean diet. We were a little disappointed with the paper published recently by another group from the US because it came out that for fruit and vegetable consumption the strong benefits were restricted to cardiovascular disease but were not evident for cancer, which is our primary target.

Thus, we applied the Mediterranean index to the EPIC Italy cohorts (47,000 adults from 5 centres across the country) and also focus on the overall consumption of fruit and vegetables in this relatively large national series.

We have already seen this map of Italy. The interesting fact is that we have two centres in southern Italy with a very Mediterranean-style diet. We have Florence in between, and then we have two centres in northern Italy with more continental habits. The interesting fact is that because of socio-economic reasons in the 1950s and 1960s, a lot of people from southern Italy migrated to Turin and Milan and other industrialised areas in northern Italy. Approximately one third of current residents in these areas originated from southern Italy, so this is a nice mix.

Overall, we have approximately 47 000 adults participating in Italy – 15 000 men and 32 000 women (Palli et al., 2003). We have recently updated for 1 500 newly diagnosed cases of cancer which were diagnosed after enrolment. Women represent three quarters of our series and you see that there are 3 cancers in females for each case of cancer in men. There are two major types of cancer: more than 500 cases of breast cancer, and 150 cases of colorectal cancer. The other cases are evenly distributed among other sites.

Age at diagnosis is another relevant aspect: approximately 10% of our cases have been diagnosed in subjects older than 65 years of age, so the bulk of our cases were diagnosed before 65 years of age. This is the distribution according to the length of follow-up and you see that most of the cases have at least 3 or 4 years of follow-up.

This is the basic multivariate model. We adjusted for educational level, smoking history, and some basic anthropometric measurements, which were all taken by us at enrolment according to a standard protocol.

What comes out in this EPIC-Italy analysis is that the trend over the quintiles of total vegetable consumption is statistically significant, although the effect of moving from one quintile to another is quite small. Even more statistically significant is the inverse association between leafy vegetable consumption over the quintiles and total cancer risk. Root vegetables – mostly carrots – show a significant inverse association, while there is no effect for tomatoes and for another potentially interesting category, as cabbages.

We also used the Mediterranean score proposed by our Greek colleague. We substantially adopted their model and these are the results. Again, we have a statistically significant trend over the categories, although no single category is statistically different from the unit. But there is some suggestion that the highest category – those really adopting a Mediterranean-style diet – have an approximately 40% reduction in total cancer risk.

Association between the Mediterranean SCORE and total cancer risk in the frame of the follow up of 44,865 volunteers enrolled in the EPIC-Italy study (1993-98) (1,488 incident cancer).

EPIC - ITALY			
Mediterranean SCORE	Relative Risk [^]	IC 95%	p
0-1	1		
2-3	0.96	0.79-1.16	0.63
4-5	0.85	0.70-1.04	0.11
6-7	0.88	0.70-1.09	0.23
8-9	0.62	0.33-1.15	0.13
P for trend			0.02

[^] Relative risk estimated by Cox regression models stratified by centre, sex and birth cohort, including terms for smoking history, education level, weight, height, total calories (log).

CSPC - Firenze

Association between quintiles of food consumption and total cancer risk in the frame of the follow up of 44,865 volunteers enrolled in the EPIC-Italy study (1993-98) (1,488 incident cancer cases).

EPIC - ITALY			
FOODS GROUPS / FOODS	RELATIVE RISK [*]	IC 95%	P for trend
Vegetables (all types)	0.95	0.91-0.99	0.02
- Leafy vegetables (total)	0.95	0.91-0.98	0.005
- Root vegetables	0.96	0.92-0.99	0.04
- Tomatoes	0.98	0.94-1.02	0.41
- Cabbages	0.97	0.94-1.01	0.19

^{*} Relative risk estimated by Cox regression models stratified by centre, sex and birth cohort including terms for smoking history, education level, weight, height, total calories (log) and each food separately (quintiles).

CSPC - Firenze

In terms of micro-nutrients, these are very preliminary results, but we can show that there was a stronger inverse association with the total fibre consumption. In terms of micro-nutrients with antioxidant capacity, the most relevant result was the inverse association with beta-carotene, although there was a limited association for folic acid. Leafy vegetables are a very good source of folic acid in this population which, at least at the moment, has a very low proportion of subjects taking vitamin supplements.

Association between the intake of fiber and selected micronutrients (in quintiles) and total cancer risk in the frame of the follow up of 44,865 volunteers enrolled in the EPIC-Italy study (1993-98) (1,488 incident cancer cases).

EPIC - ITALY			
Nutrient	Relative Risk [^]	IC 95%	p
Fiber	0.94	0.89-0.99	0.02
Folic acid	0.96	0.91-1.01	0.14
β-carotene	0.96	0.92-0.99	0.02

[^] Relative risk estimated by Cox regression models stratified by centre, sex and birth cohort, including terms for smoking history, education level, weight, height, total calories (log) and each nutrient separately (quintiles). The RR shows the modification of the risk associated with the increase of one logarithmic unit.

Most of our cases were females and the most relevant type was breast cancer, so we focused on breast cancer. Recently, in the Journal of the American Medical Association, there was a negative meta-analysis concluding that fruit and vegetables consumption in adults was not significantly associated with a reduced breast cancer risk. More recently, the EPIC consortium published a negative study at the European level focused on breast cancer, which again was published by the Journal of the American Medical Association (van Gils et al., 2005). Here we focused on the updated series of breast cancer cases among the 32 000 women enrolled in EPIC-Italy. We present some data after exclusion of approximately 10% of the cases that were diagnosed immediately after enrolment in the cohort. We ended up with a series of 480 breast cancer cases. The age distribution is quite young – just 10% of all breast cancer cases were diagnosed at the age of 65 or older, so these are relevant cases in younger adults. According to menopausal status at enrolment, you see that we now have an equal balance between women who were enrolled in a pre-menopausal status or who were already post-menopausal, with a small group in between.

These are the person-years accumulated by our cohort and the distribution of the cases. You see that after excluding the first 6 months, most of the cases had a follow-up of at least 4 or 5 years.

This is the more complex model we used to adjust for dietary variables. We included terms for education level, reproductive history, age at menarche, menopausal status and anthropometry. Again, you see that height was a statistically significant predictor of breast cancer risk in our population.

These are the main results. We found a suggestion of a protective effect of the total consumption of vegetables in this Italian population, although that was particularly strong in terms of the leafy vegetables, either raw or cooked. There was no other association, in particular with tomatoes. You may have seen a negative paper published in the last few months on cancer aetiology by an American group. The paper also measured lycopene in blood and there was no association with breast cancer.

Association between quintiles of food consumption and Breast Cancer risk in the frame of the follow up of 30,153 volunteers enrolled in the EPIC-Italy study (1993-98) (477 incident breast cancer cases). (1)

EPIC-ITALY			
FOODS GROUPS / FOODS	RELATIVE RISK*	IC 95%	P for trend
Vegetables (all types)	0.93	0.87-1.00	0.06
- Leafy vegetables (total)	0.92	0.86-0.98	0.01
- raw	0.93	0.87-0.99	0.04
- cooked	0.92	0.86-0.99	0.02
- Root vegetables	0.97	0.91-1.04	0.35
- Tomatoes	1.02	0.95-1.09	0.55
- Cabbages	0.96	0.90-1.03	0.25

*Relative risk estimated by Cox regression models stratified by centre and both cohort, including terms for education level, age at menarche, number of children, menopausal status, weight, height, total calories (kg) and each food separately (quintiles).

We also took into account other aspects of dietary habits in this female population, and the only relevant result we have is this borderline significant positive association with the consumption of potatoes. You may remember that there was some discussion yesterday on vegetables and potatoes (potatoes are not included in the category of vegetables).

The other key point of the Mediterranean diet is olive oil, but it is very difficult to measure the consumption of olive oil and that is why we think our results are inconclusive. On the other hand, seed oils, which mean all other vegetable oils, consumed in this female population have, if any, some positive association with breast cancer risk.

These results on the inverse association we have found between the consumption of vegetables and breast cancer are in substantial agreement with a recently published paper by the Milan group led by Franco Berrino. They had an approach based on dietary patterns and they found that patterns characterised by a high consumption of raw vegetables and olive oil was strongly inversely associated with the risk of breast cancer.

We have done some analysis in our local cohort in Florence evaluating the association between dietary habits and high mammographic breast density, which is a condition that is very

frequent in adult women and which has been consistently associated with increased breast cancer risk. We again found an inverse association with the consumption of total vegetables, and particularly leafy vegetables (Masala et al., 2005).

Before finishing, I would like to mention that in terms of Mediterranean diets and cancer, there is a strong interest among researchers about intervention studies with specific food items and the use of biomarkers, particularly tomatoes and olive oil. This is a protocol of a study published by a group from Milan in the British Journal of Nutrition (Porrini et al., 2005). The size of the study is moderate because they have only 26 volunteers and they used a commercial drink based on tomatoes. The expectation was that the consumption of tomato components (mainly lycopene) by this drink would decrease the oxidative damage, and they found that there was a significant reduction.

Again, I would like to remind you of the particular distribution of lycopene levels across European countries: the highest levels are found in southern Italy and other Mediterranean areas.

Olive oil has repeatedly been reported to be inversely associated with the risk of cancer, and very recently we carried out a small cross-over intervention study in Florence. We assigned women to use extra-virgin olive oils with a very high concentration of hydroxytyrosol and natural phenolic compounds, in comparison to a similar extra-virgin olive oil with low levels of hydroxytyrosol and natural phenolic compounds.

We have been able to show that this population was compliant, and we can show that the urinary excretion of biomarkers of consumption of this metabolite increased during the consumption of high extra-virgin olive oil and decreased during the consumption of low extra-virgin olive oil (Salvini et al., submitted). So these interventions are feasible in the Italian population and other populations also. Also, in terms of oxidative damage, we found a statistically significant difference between the Comet assay results in the two study phases. The problem with this study is that it is quite small because it is very difficult to raise funds to run large intervention trials.

To conclude this presentation, we are convinced that components of a Mediterranean-style diet may play a role in cancer prevention and we urgently need well planned interventions trials. Thank you for your attention.

Questions

Member of the audience

How can you explain that in the Italian small sub-cohort you can see the inverse association and in the whole of EPIC you can not?

Domenico PALLI

This is a very relevant question because it is the same question we have asked ourselves. At some primary point in the analysis of the European data, we had this inverse association only in Italy. It was the only country where breast cancer was inversely associated with total vegetable consumption. Then we updated the central database. In different countries we use different tools to collect data, so some of the information detail is lost when we use the central database. We have recently updated the follow-up in Italy so we have a slightly larger series, and we find these results, which were already evident at the very beginning at the European level. However, I agree with you that we have to better investigate why there is this apparent contrast with the common analysis.

We focused on vegetables and it is possible that the quality, variety, the seasonal distribution system and conditions in which vegetables are on the market in Italy, and other areas with locally-grown products, are essentially different from what happens in other countries where the market provides you with vegetables grown far away. This is a possible explanation.

Also, vegetables in Italy tend to be consumed with olive oil, so it is not clear if we are measuring the effect of one or the other. What is strongly evident to me is that we are unable to capture the real food intake but we would need to understand better the details of olive oil consumption, because it is very difficult, and also the types of olive oil vary in different areas – it is not homogenous, even across Italy. We have to work more on these issues, but at least these results are promising.

The previous member of the audience

As I understand it, in this model you tried to adjust for olive oil.

Domenico PALLI

No. These are multivariate analyses with just one dietary component.

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Introduction

Lorelei DI SOGRA

Director of the 5 a Day Programme, National Cancer Institute, NIH, DHHS, Bethesda, USA

Welcome to this afternoon's session. This session will leap from the scientific evidence to health promotion and disease prevention actions taking place around the world. We will talk about what is happening in 5 different countries. We are talking about action: how do we take the science and move it into action to change and improve eating behaviour.

The subject of this afternoon's session will focus on ways and actions to increase fruit and vegetable consumption. As many of you know, we have 15 years of scientific literature telling us how important it is to increase our fruit and vegetable consumption. All populations around the world are eating many less fruits and

vegetables than they need for good health. Many countries have national nutritional policies that recommend 5 servings of fruits and vegetables a day or to double fruit and vegetable consumption. We also have the WHO recommendations, again promoting increased fruit and vegetable consumption.

This afternoon, we will look at 5 actions that are taking place to try to increase fruit and vegetable consumption.

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Communication

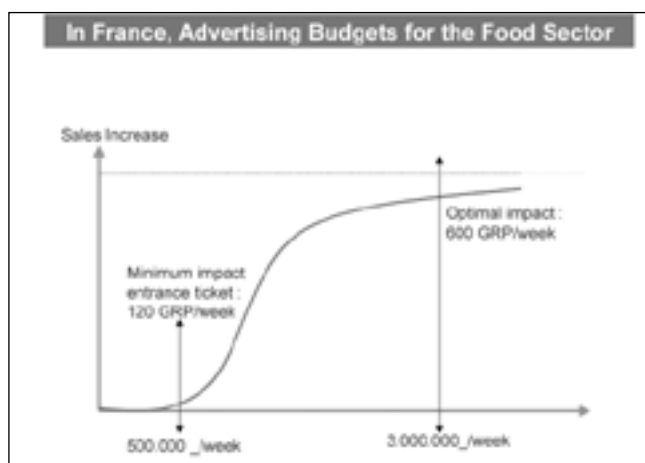
Laurent DAMIENS

Director of Aprifel, Agency for Research and Information on Fruit and Vegetables, Paris, France

Thank you. Advertising is a powerful tool to change food behaviour. Fruit and vegetable consumption has decreased in developed countries over the last 40 years. In France, the drop in fruit and vegetable consumption has averaged 1% per year. The reduction was dramatic in the 1970s and has been slightly decreasing since 1980. At the same time, the French population has increased by 13%. Therefore, fruit and vegetable consumption per capita has dropped significantly over the last 40 years to an average drop of 2% per year.

During the same period, consumption of industrialised foods such as soft drinks, sweets and chocolates, and dairy products, increased substantially. The two major increases in the last three decades are ice-creams, sweets, and soft drinks. The consumption of ice-creams and sweets has increased by a factor of 14, amounting to a 1 500% increase, and soft drink consumption, by a factor of 6, that is to say, a 700% increase.

One of the main reasons for these consumption increases is advertising. With advertising, the more you invest, the more you sell with the well-known AIDA model on the advertising response curve on sales. When you start to invest in advertising, it does not have any initial effect on sales until it reaches a minimum investment level – and only then you will have a significant improvement in your sales before it reaches an optimal level.

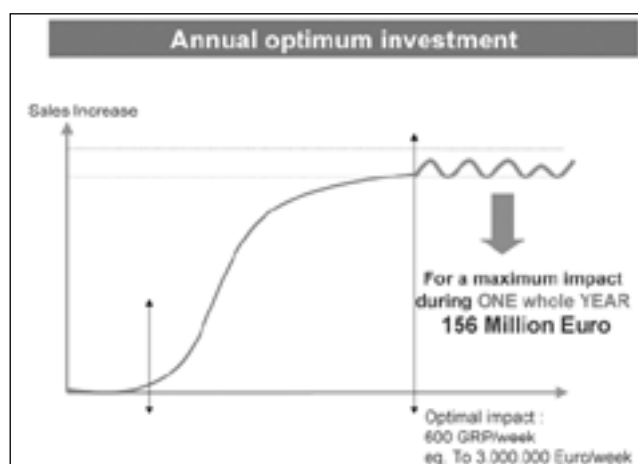


In advertising budgets for the food sector in France, the minimal impact entrance ticket is calculated to be 500 000 euros per week. So, if you invest under 500 000 euros per week it does not have any effect on your sales.

For the food sector in France, the optimum impact is calculated to be at a level of 3 million euros per week. If you calculate the optimum annual budget you need to invest in advertising for maximum impact for a whole year, you need to spend 156 million euros.

Who can afford to spend over 150 million euros each year? Certainly no company in the fruit and vegetable sector, that is for sure. However, the extremely profit-driven industry can. If you take the yoghurt industry, the chocolate industry, the biscuit or cheese industries, the coffee or tea industries,

can invest well over 150 million euros per year, which is the optimum advertising investment. If you take the two main investors in advertising in France: Danone spends 440 million euros a year, and Nestlé spends over 300 million euros. This is double the optimum investment for advertising for a whole year in France.



Do increasing advertisement investments go along with increased consumption? Little by little, the consumption increases have a considerable impact on food behaviour and on food behavioural changes. As scientific evidence points out, the need to increase fruit and vegetable consumption by investing in fruit and vegetable advertising for health issues has become an absolute necessity. However, the economics of the fruit and vegetable sector make this level of minimum investment impossible for any individual company, as the fruit and vegetable sector is made up of thousands of small companies – in France, we have over 127 million small units. Therefore, only public-private collective partnerships would make it possible.

This is what we are trying to achieve in France: a public-private partnership of fruit and vegetable advertising with the European Commission, the French Ministry of Agriculture and Food, and the whole-fruit and vegetable companies grouped together within our association. The total budget for this public-private partnership for advertising is 18 million euros for 3 years – funded 50% by the EU, 20% by the French Ministry of Agriculture and Food, and 30% by the fruit and vegetable companies.

Despite this partnership, we come to a quite limited budget of 6 million euros a year. Therefore, we have to know our target audience for advertising: to the 35 year olds and under, and more specifically those under 25 that we presume is the group with the lowest fruit and vegetable consumption level – what we used to call the ‘new adults’. We can only afford to invest in 3 waves a year of 2 or 3-week campaigns each.

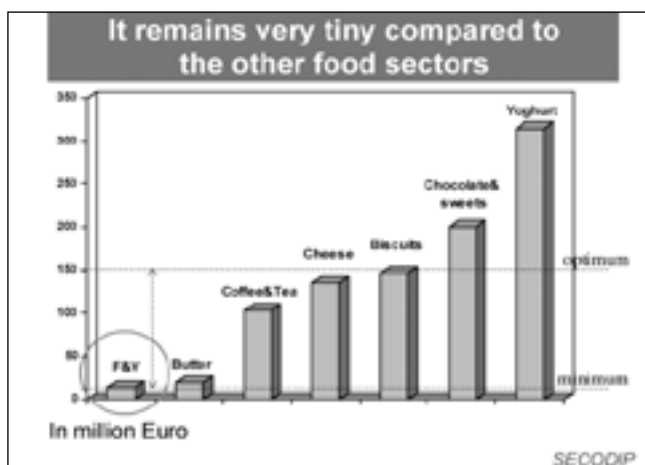
Here is the advertisement (DVD presentation).

These are not guidelines, as you can see. Nor is it education. The objective is to include fruit and vegetable consumption into modern lifestyle.

What impact has it had? The impact of our advertising on youth has been positive. We increased the consumption of fruit and vegetables

in the targeted youth group by 10% last year compared to the previous year, and by 11% in 2004 compared to 2003. For the rest of the population, however, the consumption slightly decreased.

The power of the media is such today that advertising is a powerful tool not only for industrialised food products, but also for fresh fruit and vegetables. However, with our budget level we can only work on a small restricted target. When we do the calculations, we would need 20 times this budget to have a substantial impact on the whole population. Our current budget is under 1% of the total for food advertising in France, but our fruit and vegetable advertising investment in France represents 0.86% of the whole-food sector advertising, which is very tiny compared to the other food sectors. As we are at the limit of the minimum impact, we have a little impact on consumption.



In conclusion, healthy foods like fruit and vegetables are totally isolated in an unbalanced food market for economic reasons. Advertising plays an essential part in this competitive disadvantage. Hence, government authorities have introduced measures to balance this situation to increase the fruit and vegetable advertising impact on consumer behaviour. My suggestions to increase the fruit and vegetable advertising impact are:

- 1) decrease the cost of advertising for fruit and vegetables, and
- 2) increase public financial support for fruit and vegetable advertising.

How could we decrease the cost of fresh fruit and vegetable advertising? In France, we could correct through a “grande cause” status or “general interest” status like the Max Avalor Café for fair trade, who have a 50% discount on advertising for the coffee; or through free public service announcements, as in Canada (our friends in Canada do not pay to advertise for fruit and vegetables); or indeed in the US, like the ‘Drink Milk’ campaign, where they did not have to pay anything because it was also free advertising.

The other possibility is to increase public financial support. Three ideas:

- we would like to reverse the dramatic downward trend in EU financing of fruit and vegetable advertising – it was 6 million euros last year for fruit and vegetable advertising for all the countries in Europe; it dropped to 4 million this year.
- we could create special sections for fruit and vegetable advertising at national level, based on the fact that the fruit and vegetable sector is in a disadvantaged economic position regarding advertising investment, which is why consuming fruit and vegetables has become a health issue.
- finally, in public-private partnerships for the fruit and vegetables advertisement the rate of public support could be up to 90%.

Promoting fruit & vegetables through schools - A European perspective

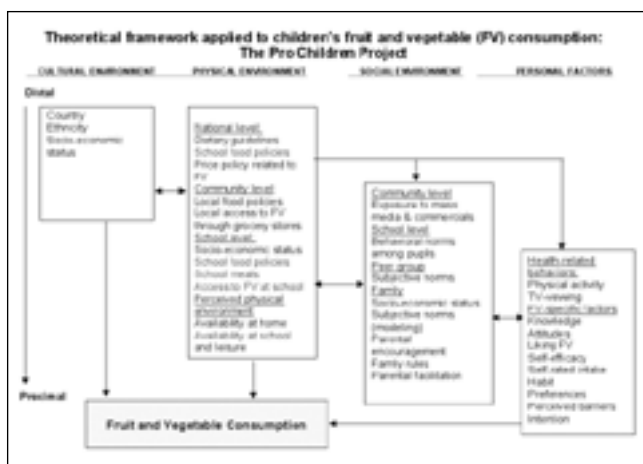
Knut-Inge KLEPP

Department of Nutrition, Faculty of Medicine, University of Oslo, Oslo, Norway

The focus of this talk is how we can promote increased fruit and vegetable consumption within schools across Europe. Our work could be labelled as action research and I will draw mainly on research results and experience from two large ongoing projects: the Pro-Children project, which is an EU-funded project taking place in 9 countries, from Iceland in the north to Portugal and Spain in the south; and also a large study conducted in Norway called the 'Fruit and Vegetables Make the Marks' study.

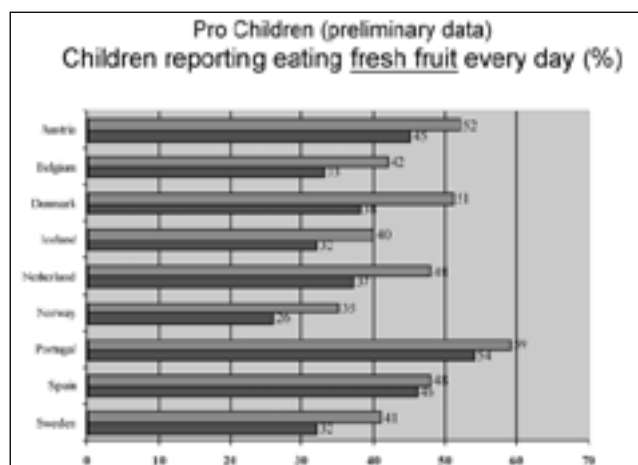
The main objectives of both of these studies have been to develop and test effective strategies to promote increased consumption of fruit and vegetables among schoolchildren and also their parents. In the Pro-Children study, we did surveys of national representative samples of pupils, and also their parents, in order to identify important determinants of fruit and vegetable consumption. In this study we also tested intervention programmes in three different settings, i.e. in Spain, the Netherlands and Norway.

A comprehensive model was used in the Pro-Children project in order to map out different determinants for fruit and vegetable intake (Figure 1). We labelled the cultural environment, looking at country, ethnicity, socio-economic status, the physical environment, social environment and also personal factors. Under the physical environment, we are collecting data on school food policies at the national level and also at the school level, looking to see what the guidelines and policies are, how the school meals are provided and what is the availability of fruit and vegetables. We are also assessing the availability of fruit and vegetables at the student level.



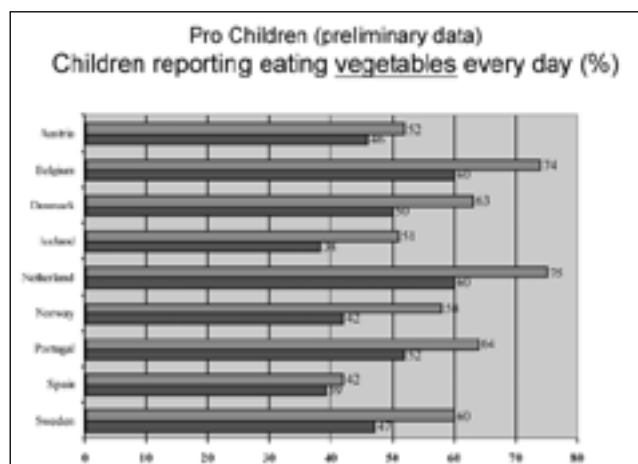
The Pro-Children intervention programme is a comprehensive programme where we are targeting the school, the family and the community. Within the school we have the classroom curriculum that has been implemented by the teacher. We focus on the school environment making fruits and vegetables more readily available. We have special school events and also special project committees that help promote the programme and facilitate its implementation within the schools. We also target the school meals. I will then in this presentation focus on what we are doing in terms of increasing the availability in the schools.

In October-November 2003, we conducted the national surveys. Here I present the proportion of children who say they eat fresh fruit at least once a day, so not meeting the guidelines but still eating about once a day. As can be seen from Figure 2, only about half of all the students say they eat fruit at least once a day. We did see some differences between the countries: the Portuguese children reported the highest frequency of eating fruit; and it was lowest in Norway. So here we see the north/south gradient that we know has existed historically in terms of fruit consumption in Europe.



For both fruits and vegetables, we see a clear gender difference: in all countries the girls report a higher consumption of fruit and also of vegetables.

When it came to vegetables, there was less of a north/south gradient and it was actually Spain which had the lowest proportion of children who reported eating vegetables every day, indicating that there are rapid changes taking place in some countries.



In the previous presentation it was mentioned that overall consumption in the developed countries has been going down. I should say that in the northern countries, such as Iceland and

Norway, fruit and vegetable consumption has substantially increased over the past few decades, with the overall vegetable consumption in Norway for example being doubled over the past 50 years.

We assessed availability at school level by asking the children whether they were able to buy or get free fruits and vegetables at school. We found that while there were differences across countries, overall the perceived availability is rather low, in that only small portions of students report that fruits are available on a daily basis at school. Austria had the highest proportion saying that they were easily available, and they were basically not available at all in the Netherlands.

We also saw large differences when it came to vegetables being available at school. Here it is Sweden that stands out with vegetables available every day as part of their free school meal, and the Netherlands again is at the bottom.

In the Pro-Children project, we tried to make vegetables more readily available. There is a school meal in Spain but the proportion of children that can participate varied quite a bit. However, we tried to increase fruits and vegetables being part of the school meals. Then, a special fruit break was introduced where all the children could get apples, oranges, bananas or tangerines. This was provided free by local distributors to start with but was subsequently taken over by the parents, and this program was continued throughout the school year. A large proportion of teachers and students reported this to be a positive experience.

In the Netherlands there is no organised school meal and pupils usually do not eat at school. We introduced a fruit break and all intervention schools received free fruit or vegetables once a week delivered by local retailers.

Some schools introduced special fruit breaks, other pupils ate the fruit and vegetable during their usual breaks, and some were even allowed to take it home with them – which was not our intention, but that was how it was implemented. Both teachers and children reported enjoying these breaks and the main complaint was that there were too many apples and too little variation.

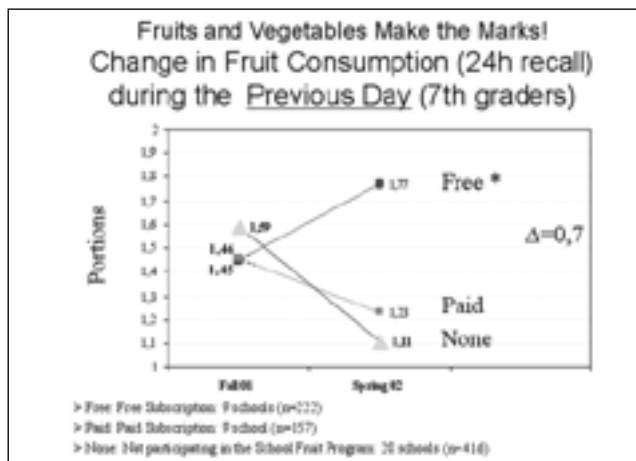
In Norway, we have had a school fruit programme in place on a pilot basis since the mid-1990s and it is now offered throughout the country. This is a subscription programme where parents pay about 2.50 Norwegian Kroner per day (~ 0.30 per day) for their child to receive an apple, pear, carrot, banana or orange at lunchtime.

There has been a large increase in the number of students participating in this, but while there are about 35% to 40% of schools participating, it tends to be the smaller schools which participate, and we are still only reaching about 10-15% of the total student population with this programme.

In the National programme we have tried to address some of the complaints and issues that have been raised. These include that there is a lack of variation and that schools do not have proper storage facilities. This has been addressed by introducing a rotating menu securing variation, providing storage facilities and boxes for easy distribution within the school, as well as better information to parents about the programme.

In the Fruit and Vegetable Make the Mark study, we were able to offer this programme for free to students in 9 schools in one of the counties. We saw a very clear effect of the programme. Figure 4 shows that there was a strong increase in the proportion

of foods eaten the previous day among those receiving the program for free. The students whose parents paid for the subscription also increased their consumption, but due to the low proportion of parents who participated, the impact on the school level was modest. Students whose parents did subscribe had a higher consumption level of fruit and vegetables even prior to the programme. For students at schools with no programme, we see a strong decrease, in part due to seasonal variation.



In this study, we have been able to follow the students for one more year, and we see that the effects obtained after the first year were sustained into the second year, even though the intervention stopped after the first year. There was a clear positive long-term effect one year later, with about 25% to 30% overall increase in consumption compared to the comparison group. We find this to be a very encouraging result.

I also want to point out that in Norway the National Nutrition Council's have been looking at ways for funding a free national fruit programme. In 2001, the sales tax on food was cut in half by the government. The council argued at the time that energy-dense, nutrient poor items (such as sugar-sweetened soft drinks) should be exempt from such a price reduction. Unfortunately, we were not listened to. In 2003, the sale of soft drinks in Norway just from grocery stores and petrol stations amounted to about 5.5 billion Norwegian Kroner. Thus, today the Government is losing about 500 million Norwegian Kroner just on sales tax on soft drinks. The estimated annual cost of a free school fruit programme for all school children is in comparison only about 400 million Norwegian Kroner.

In conclusion, the availability of fruit and vegetables at school varies considerably across Europe, and increasing the availability of fruits and vegetables for schoolchildren through subscription programmes and fruit breaks appear popular with pupils and teachers in very different settings.

The evaluation of the Norwegian school food programme demonstrates that providing free fruits and vegetables to children significantly increase their consumption, and this increase was sustained a year after the programme ended.

The paid school fruit programme, however, increased consumption among the subscribers, but the participation tended to be too low for it really to have an impact, and it could end up actually increasing the social inequalities seen in eating habits.

Our recommendation is that schoolchildren should be offered free fruits and vegetables during the school day as part of a healthy snack break.

Acknowledgement

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The Fruit and Vegetables Make the Marks study is funded by the Norwegian Research Council.

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The fruit and vegetable snack program in the United States: A case study in policy development

Lorelei DI SOGRA

Director of the 5 a Day Programme, National Cancer Institute, NIH, DHHS, Bethesda, USA

Good afternoon. I am Lorelei DiSogra the Director of the 5 A Day programme at the National Cancer Institute in the United States.

I am going to talk to you about the Fruit and Vegetable Snack Programme in the United States, following up on what Professor Klepp has just mentioned. My purpose is to illustrate how results from research can lead to policy development. I'll be sharing one example from the United States and discussing how we intend to continue to build on this effort.

The Fruit and Vegetable Snack Programme in the US was started in 2002. It started with a vision from one of our Congressmen. About five years ago, all of us in 5 a Day programmes around the world (there are now more than 30 of these programmes) began to shift our attention and priority to environmental and policy changes that will increase fruit and vegetable consumption consistent with global and national health and nutrition recommendations.

In the United States we have a political champion for nutrition policy changes. At a national conference in the autumn 2001, Senator Harkin expressed his vision that every student should have a fresh fruit or vegetable snack every day at school. About 8 months later Senator Harkin took the opportunity to add legislative language authorizing a pilot fresh fruit and vegetable program for the 2002-2003 school year along with 6 million dollars of funding to the U.S. 2002 Farm Bill. The legislation specified the 4 states to implement the pilot fruit and vegetable snack program. In addition, the United States Department of Agriculture selected one Indian Tribal Organization to also participate in the pilot. Ninety-seven dollars per student was allocated for the pilot and 54 000 students participated in the fruit and vegetable snack program during the 2002/2003 school year. The fruit and vegetable snack was provided to students free and could not compete with school lunch, so in most cases it was offered in the morning.

For young children in elementary school, one serving of the fruit and vegetable snack was delivered to the classroom each day. Schools reported little or no waste and estimated that elementary school children increased their fruit and vegetable consumption by approximately 1-serving per day. In middle and high schools, a kiosk (large table) was set up in a central location in the school. The fruit and/or vegetable snack was put on the table and the table was refilled throughout the day. Students could come and take whatever they wanted. Many of the middle and high schools reported that students returned several times throughout the day and estimated that the program increased fruit and vegetable consumption by 2 to 3 servings a day. Increasing consumption by 2-3 servings per day is very significant, because it demonstrates that a school fruit and vegetable snack program can help close the gap between current fruit and vegetable consumption and national nutrition recommendations.

The funding for the pilot program was for only one year. Therefore, it was critical to ensure that the programme was implemented as effectively as possible in order to demonstrate

success and to serve as a building block for future funding and policy development.

In 2004 the fresh fruit and vegetable snack programme was expanded and received 9 million dollars of permanent funding. Although the 9 million dollars was very important, the fact that the funding was permanent was even more critical. The 2004 expansion provided funding for 8 states (25 schools/state) and 3 Indian Tribal Organisations. It is important to note that during the 2002 pilot, it was demonstrated that the snack programme could be successfully implemented for less money per student than had been appropriated therefore the 2004 legislation provided 60 dollars per student per year.

How did we go from a 1-year pilot to permanent funding? Hopefully, you can apply some of what worked in the US experience in your own countries. You need political champions and you need to cultivate them very well. You need cooperation between all the sectors in government – health, agriculture and education – so those ministries collaborate together. You need a diverse coalition of committed partners that will fight to increase funding and expand the programme. You need advocacy and lobbying. One recommendation I would make is to get out and start to advocate for what you know is going to make a difference in terms of public health. Turn national nutrition recommendations into policy actions; become an advocate in your own country, creating new political champions as you go along. In the US we started with a political champion from the Democratic Party, but for the last 5 years the Republican Party has controlled the White House and Congress, so you need to build support among all political parties in your country. You need to work aggressively to create those political champions, political will and ownership among all political parties. You need strategic leadership, must be willing to take risks, and market results relentlessly to everybody who will listen – the media, politicians and other advocates – and you need passion and commitment to build these programmes from the ground up.

From Vision... to Pilot ... to Policy

- Political Champion
- Collaboration: Health and Agriculture
- Diverse Coalition of Committed Partners
- Advocacy and Lobbying
- Creating New Political Champions, Building Political Will and Ownership
- Strategic Leadership and Risk Taking
- Market Results to Drive Political Will
- Passion and Commitment





I work for the National Cancer Institute in the Department of Health and Human Services, and we took it upon ourselves to

engage the Department of Agriculture in these our efforts. We created a formal relationship through a Memorandum of Understanding (MOU). That MOU says that the Department of Agriculture and the Department of Health will work together on efforts to increase fruit and vegetable consumption in the United States. Before the ink was dry, before the signatures were even on the Memorandum of Understanding (which is only about 4 pages long), we immediately started to put that MOU into operation for environmental change strategies.

Collaboration: Health & Agriculture

- 5 A Day Partners meet with political appointees at Department of Agriculture
- Health takes responsibility for building relationship with Agriculture. ... "Can we work together to increase F/V consumption?"
- Health & Agriculture establish official relationship thru Memorandum of Understanding (MOU)

We focused immediately on what the Department of Agriculture could do in schools that would increase the availability and the accessibility of fruit and vegetables. We were very aggressive in our thinking about these issues and how we wanted to see them implemented. The funding for the snack programme in 2002 provided an excellent opportunity for the Department of Health and the Department of Agriculture to collaborate and we used the positive outcome of that collaboration as a model for successfully working together in the future.

Many organizations on the national level were driving this policy change. The National Cancer Institute, the Produce for Better Health Foundation, the Department of Agriculture, the United Fresh Fruit and Vegetable Association, School Nutrition Association, and the National Alliance for Nutrition and Physical Activity all played leadership roles.

Make sure that you give all credit to the political leaders and to your political champions – we, in public health do not need the credit; we need the behaviour change. We gave all the credit to our political leaders. Let it become their story. Let them go out and talk about the fruit and vegetable snack programme as an example of what they are doing to combat childhood obesity and to create healthier school environments.

One of the things I think is critically important is that we need to deliver results very quickly. Politicians work within a very short timeframe and so we need to deliver those results as quickly as possible. If we are really serious about behaviour change, we need to work on changing the school environment.

Building Political Will and Ownership

- Give credit to political champions
- Let it be their story... "We are improving children's eating habits to combat childhood obesity"
- Deliver results - Political champions need results they can see and talk about –quickly
- Make it easy for political champions to succeed at environmental change
- Translate "creating healthy school environments" into "increasing the availability of F/V in schools"
- Positive results build trust



When politicians see something, they believe it, so when we take them into schools and they see children eating more fruit and vegetables, as far as they are concerned the Fruit and Vegetable Snack programme is working.

An evaluation of the pilot programme was developed as a Report to Congress and the results of this Report have been aggressively marketed.

One of the other critically important things is to continually talk about how environmental changes are more effective, less expensive, less labour intensive and faster than traditional nutrition education.

We got results and positive changes in behaviour very quickly; one could say that at the end of week 1 of the Fruit and Vegetable Snack programme, children's fruit and vegetable consumption has increased!

Where are we going now? We have 9 million dollars in permanent funding, and have 8 states and 3 Indian Tribal Organisations participating. Our immediate policy goal is to secure appropriations from Congress to expand the fruit and vegetable snack programme to all 50 states (25 schools per state). This would cost approximately 42 million dollars. In this way, every legislator in our country will experience the benefits of having a fruit and vegetable programme in their state/district.

In the long term, our policy goal is to expand the programme so that every child in every school in every state will have a fruit and vegetable snack every day at their school. This is estimated to cost 4.5 billion dollars. If we are really concerned about improving children's health this is a small price to pay. Thank you.

Let me quickly introduce a dear colleague, Morten Meyer from the Danish Cancer Society. Morten is in charge of the 6 a Day programme in Denmark, which is based at the Danish Cancer Society. Morten, along with Laurent, is one of the leaders of efforts to increase fruit and vegetable consumption in Europe.

Effective and sustainable worksite-based interventions to promote fruit and vegetable consumption in adults

Morten Strunge MEYER

Danish Cancer Society / 6 A Day, Copenhagen, Denmark

It is a pleasure to be here and learn and network. I am pleased to have this opportunity to explain to you what I believe can be done in the workplace to increase the intake of fruit and vegetables. I am going to talk about 1) what is effective when we want to change people's behaviour in the workplace, 2) criteria for good interventions inspired by a recently published a WHO review, and 3) the Danish Worksite Fruit Programme.

Imagine the ideal intervention. It would be one that stayed in real life after the project period was over (sustainability). It would be nice if it was one that did not need millions of euros to do (cost-effectiveness). It would deliver results immediately – which would make it easy to sell, from a political point of view. From a more scientific point of view it should be possible to document changed behaviour - because that is what we want most.

So, how do we do that? Here is an effective solution: "Offer free and easy access to fruit and vegetables in the worksite". If you put a bowl of fresh fruit close to people and they can take it for free, they will of course take and eat it. In worksites this should be done not just during breaks, but also while employees are working and during informal breaks.

What are the chances of implementing this? It all boils down to one question: How do we get employers to pay for this?

Some of the answers we get from interviewing the employees. We did research to estimate how excited workers are about getting the free fruit. 79% thinks free fruit is a valuable sign of appreciation from the employer. Lots of people think that it is delicious and healthy. The fact that the fruit is free is also a motivation factor, when less health items like candy, sodas and chips are not free. In fact some of the employees like the free fruit because they think it help them eat less candy and salty snacks.

The fruit and vegetable industry is of course also excited about this programme. They see the Worksite Fruit Programme as a new market. In Denmark there are now close to 50 new businesses that make a living from the simple idea and concept of having free fruit in the workplace. So you can count on strong support from the fruit and vegetable industry in running a Worksite Fruit Programme.

The role of Health NGO and government is then to inspire and convince employers to pay for the free fruit programme. How can that be done? To make such new and social norms is not an easy task, but evaluations and subsequent PR can be used to position the fruit as an attractive, modern and for the employer relatively cheap workers' benefit.

We have done a number of evaluations on workers satisfaction, intake and the dissemination of the programme. After each evaluation we go to the media and sell it as a news story and make sure that worksites on the programme are strongly exposed

as a good example in the media. This is a way of effectively introducing new social norms in a society.

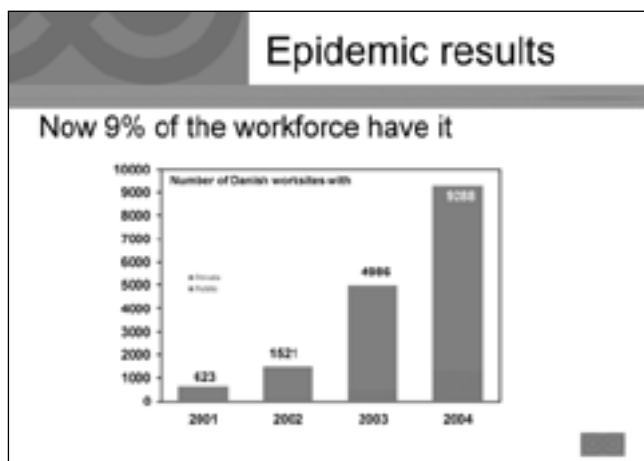
Free Fruit in the Worksites is probably our most successful intervention. In fact, the fruit and vegetable industry has now completely taken over and there is no longer a lot to do for the Danish Cancer Society and the Government. This is truly a self sustainable intervention; today, industry is doing the whole thing.

In the beginning we needed to evaluate if the free fruit is effective from a nutrition point of view. Do people change behaviour when the workplace fruit programme is introduced? Therefore we designed a study and here are the results: The fruit intake went up 0.7 servings per person per day on average. Equally important, the men halved their intake of snacks, cakes, ice-cream, liquorice, and so on.

Our challenge was and still is to influence the employers to pay for the fruit for their employees. So does such a study of increased intake make a big difference to employers? No, they could not care less. They need other kinds of evidence to legitimize this extra cost. We found that the free fruit is not just appreciated by for some of the workers; in fact all of them actually liked and eat the fruit. And eighty per cent expressed that they do not think this money could be spent in a better way and that it would be unimaginable if the fruit was taken away. That is the kind of research that is important to have in relation to convincing the employers.

Also we wanted to measure if the free fruit has an effect on people taking fewer days off sick? But this is almost impossible to measure. We choose to associate the two by letting employers know that what the cost to the company of having somebody stay home an extra day, is directly comparable to the value of providing free fruit for one employee for a whole year. We also argue that free fruit is a very cheap workers' benefit compared to anything else you can give to your staff, considering how well it is appreciated by the employees. So in a workplace where you need to attract staff and retain them, the free fruit proves to be a popular and important instrument. Also, for the employers, it is an important argument to say that this is perceived as a sign of appreciation. That last point is the one that has really been driving the program forward. There are a few other arguments that we have not been able to substantiated, amongst these are that productivity might improve as people do not go 'sugar cold' in the afternoon.

Figure 1 shows the dissemination of the Worksite Fruit Program in Denmark. We measured this in March 2004 and you can see the increase in the number of workplaces that provided fruit in the workplace. I am very pleased. A year ago almost 10 000 workplaces in Denmark provided free fruit to their employees. This is equal to approximately 9% of the Danish workforce. Before we started to promote the Worksite Fruit Program in 2000 this figure was very close to zero.



This programme is unique in the sense that traditionally you need to inform people and build awareness and intention to change behaviour, but in this programme we make an important shortcut. Introducing the Worksite Fruit Program will lead to changed behaviour overnight. Awareness, intentions and changed values you get for free after the behaviour is changed. Employees will start bragging about this new and wonderful programme. Bragging is one of the best kinds of marketing you can get for a programme.

This concludes my talk on the workplace fruit programmes. As one last thing I would like to draw your attention to a new WHO study that was published just two months ago. This is a study that compared the effectiveness of the different fruit and vegetable promotion interventions globally. The researchers found 3 500 different papers that were relevant. Only a little more than 300 were actually designed to increase fruit and vegetables, and

when they took out all studies with a less than perfect design, only 60 studies were left. If you look at these 60 studies, only 34 are actually dealing with adults. As you can see on Figure 2 worksites are one of the relatively well investigated arenas for increasing fruit and vegetable consumption.

34 adult studies

General population	4
Worksite	11
Health care setting	9
Churches	3
Low-income	5
Supermarket	2
Total	34

This research evaluated the many studies according to whether there was a control group, whether there was a long follow-up period etc. From this the researchers concluded that the most successful interventions are those targeted at people that are already at high risk of getting a disease and hence are highly motivated. One-to-one communication is also very effective. Comprehensive and community-wide interventions have also proven effective. But I believe an important aspect is missing in this new research. We must not forget to bring sustainability and cost effectiveness of interventions into the equation when evaluating worksite and all other interventions.

References

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The 5 colours of well-being: opportunities for consumers and producers

Fabrizio MARZANO

UNAPROA, National Union between the Organization of Fruit, Vegetables, Citrus and fruit in shell producers, Rome, Italy

Thank you. The producers of fruit and vegetable of Italy and Europe thank you of choosing Rome for this great event to promote the consumption of fruit and vegetables. I thank you as well as this beautiful city of Rome which, I hope, has welcomed you in the best possible way.

In 2003, on the occasion of the Verona "Fieragricola" fair, UNAPROA (National union of organizations of fruit, vegetable, and nut producers) launched the "The 5 Colours of Well-Being" initiative aiming to increase fruit and vegetable consumption, borrowing from the American "Five a day the color way" experience. With this initiative UNAPROA intended to further extend the invitation to consume fruit and vegetables not only through five servings a day, but five servings of fruits and vegetables of different colours, in order to build the protective shield for our organism, through the presence of phytochemicals: blue/purple, green, white, yellow/orange, and red, "the 5 colours of well-being". The initiative immediately met with great success, so much so that the European Commission approved, the same year, a project presented by UNAPROA for a three-year campaign to promote the consumption of fresh fruit and vegetable products.

"Nourish yourself with the colours of life" is the slogan of the promotional campaign begun in June 2004, whose image – three smiling young faces framed by fruits and vegetables – stresses the connection between the liveliness and freshness of the faces shown and the consumption of fruit and vegetables.

The programme is based on a series of actions for publicizing to consumers the benefits deriving from the consumption of fruit and vegetables, and the messages have received the approval of the Italian Ministry of Health and the AGEA (Agricultural Payments Agency) itself.

The initiative, aiming to promote the consumption of fresh fruit and vegetables, is carried on with the scientific collaboration of the Institute of Food Science of the "La Sapienza" University of Rome, and aims to consolidate the results of the most recent studies and surveys on food consumption. These studies demonstrate the strong tie between diet and health and how people are increasingly aware of and sensitive to their well-being, achieved through a varied diet and active lifestyle.

The objective of the campaign is to reassert the "freshness" and "natural" nature of fruit and vegetables, and to promote their consumption, especially in the young age groups and in families, stressing that fruit and vegetables are indispensable for a healthy and correct diet, to protect our bodies' health.

The UNAPROA campaign envisages, alongside the advertising planning, other actions of communication and information, including:

- the production and distribution of a "Guide to Well-being", containing the nutritional aspects and organoleptic properties of fruits and vegetables, printed in a run of 4.5 million copies and distributed together with periodicals and in school and university cafeterias;

- the **press office** activity for the entire length of the campaign;

- the creation of a **website** with all information on the project, intended for consumers, with an area reserved for youngsters and containing briefings written by nutrition experts;

- the organization and holding of **yearly events** in the squares and streets of the most important cities in Italy, with the aim of raising awareness in citizens with regard to seasonal fruit and vegetable consumption, and of disseminating information on their nutritional principles.

The campaign, promoted by UNAPROA and carried out with the co-financing of the European Community and Italy through the AGEA, envisages a total three-year investment of approximately 5.6 million euro.

The public financing is granted under Council Regulation (EC) no. 2826/00 and Commission Regulation no. 94/02 on information and promotion actions for agricultural products on the European Union internal market.

It is our intention to disseminate as much as possible "The 5 colours of well-being" message across the food supply chain, so that it can be well integrated into consumers' lifestyle. Protecting our health through the consumption of fruit and vegetables improves our quality of life. We must maximise the opportunity for a better quality of life through a suitable diet and well-defined policy decisions.

Moreover, "The 5 colours of well-being" message is an opportunity for the producers themselves and their organizations. The examples reported from other countries around the world which have already, for some time, launched similar promotional campaigns, confirm the positive increases in consumption and the economic results benefiting production. This is all thanks to an effective organization of the commercial relations through to the distribution phase.

During the European Union's Agriculture and Fisheries Council meeting of this past 18 October, the fundamental role played by fruit and vegetables in a healthy diet was stressed once again. This is but one of the latest events confirming internationally accepted theories. Despite widespread international consensus, the commitment of governments in this matter still appears too weak, considering the poor funding allocated to the promotion of fruit and vegetable consumption.

A broader view of the problem would enable us to consider the expenses for encouraging the consumption of fruit and vegetables as a cost effective endeavour in that, by protecting health, fruit and vegetables contribute to reducing health care expenses. Thus, taxation exemption on fruit and vegetables through the various stages leading up to the consumer, as well as harmonization, at least on the Community level – perhaps through a directive on the subject – could be a key element in achieving our objectives.

Discussion

Member of the audience - Alain Perez - Journalist, France

I am a journalist and my question is for Mr Damiens. As a French taxpayer, I do not understand why the state should subsidise the advertising campaign made by the fruit and vegetable industry. I live in the centre of Paris and my experience is that the price of fruit and vegetables has increased by 30% or 40% over the last 2 or 3 years. Why do you not just try to reduce the price of fruit and vegetables instead of asking for state aid?

Laurent DAMIENS

Nobody decides the price of fruit and vegetables. Compared to an industrialised product, where you would have a big company that decides the retail price at which the distributors should sell the product, in the fruit and vegetable economy, which is made up of 120 000 companies, the price of a product is led by the market at different levels – at the production level, the wholesale level, and then at the retail level. It is like a pure economy system where you have supply and demand, and so the market decides the price of the product. The food industry is made up of big capitalistic industries on the one hand, and on the other hand, for fish, meat and fruit and vegetables, we have another economic system where the price cannot be decided.

Regarding price increases over the last 2 or 3 years, the increases in France 2 years ago were mainly due to the fact that demand was quite high and we had problems with the weather: production was not high enough, which led to a difference in supply and demand, so prices increased a little. The economy was different last year because although the supply was alright and the agricultural price level was not very high, the demand was also there, so the supplier could fix the prices fairly high and they decided the price the consumer could bear. It is always a matter of competition: if you have a lot of products and if you have a lot of demand, the price will adjust. So no one can really decide the price.

Of course, politicians can decide the price because of the EU's agricultural policy, which for 40 years has made choices on the price of milk and beef, but which has also chosen not to do anything for the price of fruit and vegetables. Mechanisms do exist for prices but as individuals, no company can decide what the price should be – even the big supermarkets like Carrefour or Auchan have to adjust to the prices of their competitors – so it is a pure market economy for fruit and vegetables.

The question is related to the fact that some people with small budgets cannot afford fruit and vegetables, and I think that is more of a political issue.

Knut Inge KLEPP

To follow up on that, I think there is no doubt that the price of fruit and vegetables is a very important factor. The perception in Norway is that fruit and vegetables are very expensive. It is a correct perception. If you look at the price development, it is clear that over the past few years the increases have been much higher on fruit and vegetables than on other food items. Our policy in the National Council on Nutrition is very clear: the government needs to reduce the price of fruit and vegetables. They have a number of opportunities to do that, at least in Norway. One way would be to take away the sales tax completely on fruits and vegetables and increase it on food products whose consumption we all agree should be reduced, such as soft drinks. Things could also be done on things like import taxation, which could help reduce the cost of the products. We definitely support that kind of economic incentive.

Bill CLAY – Chief of the Nutrition Programme Service, Food and Agricultural Organisation

I would like to thank the speaker; it is really gratifying to see good examples of programmes that work and that can make a difference. I would like to correct one point: Mr Meyer referred to the WHO report that came out of the workshop; it is an FAO WHO report.

One of the things that comes through in each of the presentations is the need for effective partnerships, and one of the key elements in this – certainly from our side – is getting those concerned with health and those involved with the supply and marketing of food to work together. We recognise that it is important to bring these two sectors together and we are working very hard to try to do that. We would like to hear more examples of how we can do that, what we can do to try to get the different partners in these different areas to come together. It is a crucial element, but we are pleased to see that there are some successes we can point to and that we are committed to trying to make more of them.

Lorelei DI SOGRA

I am very happy that you are here because one of our political champions for the Fruit and Vegetable Snack programme for increasing fruit and vegetable consumption will be leading a delegation from the United States to FAO starting on Monday, so I think it would be a good opportunity for you to talk to him about the support from agriculture and how in the United States the Department of Agriculture, the Department of Health, the National Cancer Institute and the Produce for Better Health Foundation all work together in partnership on the Fruit and Vegetable Snack programme and on other efforts to increase fruit and vegetable consumption.

Jean SALES – A French producer of vegetables and President of the Council of the National Office of Fruit and Vegetables (Conseil de direction de l'Office National des Fruits et Légumes)

Fruits and vegetables are products, which, at the nutritional level contribute in nutrients more than a number of industrial foodstuffs. They should indeed be free! This exemption from payment is probably a very interesting scenario to go back to a balanced food. However, the problem of price is a central element if one wishes to promote a continuity of consumption, keeping in mind that the exemption from payment proposed by the public services will not be indefinite in time. However, this essential problem must be dealt with the entire food supply chain, from production to distribution, which implies costs of labour, inputs and transport. The development and implementation of social programs require a thorough thought process. I noticed the difficulty that Laurent DAMIENS had in expressing the variability of the prices of these products, although he did explain it very well. I doubt that the scientists present today and the journalists, who are not specialists, fully understood the nature of the mechanisms which govern prices. I am quite sure that a doubt remains on the manner of determining them. We must fully benefit from work such as yours since it is as important a subject as improving life expectancy and health of the population. From a personal standpoint, I must emphasise

that this work is beautifully done and remarkable. However, one should not forget to make statements about the importance of consumption does not necessarily lead to increased consumption. In the same way, the exemption from payment is probably not an end in itself. It is more necessary to work upstream with the food supply chain in order not to dismantle the national programs aiming at improving the provision of the products, the accessibility and the availability. In addition, if one wishes to 'demedicalise' the recommendations on food, we must work more on taste and on facilitating consumption of these products. As actors in distribution and trade, we put ourselves at the disposal of the scientists. However, do not forget us in the chain of events and in the development of this future which you recommend and to which we adhere. Thank you.

Morten MEYER

If I may make a brief reply, I would say that in the workplace fruit programme in Denmark, we do not see any trends or signs of this slowing down. This is still on a huge increase, so there are really no signs of this not being a sustainable intervention to have. Workplaces pay for this. I can see your concern if we were thinking about government-funded interventions, but this is privately funded and each workplace decides voluntarily to do this programme.

In fact, when you really focus on availability and accessibility issues on a national scale, you can see huge impacts way beyond what Laurent has been able to achieve with just commercial advertising. We have an increase of 38% on the national average intakes of fruits and vegetables, and a substantial part of that is actually due to the fact that we have been focusing on availability issues in schools and workplaces. We are making another strategic move of making it available, for free if possible, and managing the access.

This way is much cheaper and that is my proposal to the next distinguished speakers here. This way, people are actually doing what they want to do themselves and not for any other reasons; people take part purely because they think and believe and know that they can benefit.

These kinds of interventions are sustainable and I think it is very important not to be concerned about needing high prices to sell.

Member of the audience

My impression is that Mr Klepp hinted at what we could do when he talked about the tax on soft drinks in relation to the cost of the campaign on fruit and vegetables. We have another model in the fight against tobacco, where price increases have proved to be very successful. If on one hand we have foods that are beneficial for health (everybody agrees on fruits and vegetables and we could probably list others), and on the other hand foods that everyone could agree are detrimental (those containing above a certain level of fats, sugars, saturated fats, trans-fats, etc.), that could help the politicians to tax those health-detrimental products to help promote the health-beneficial products. We would then have a lowering of the consumption of bad products and at the same time an increase in the promotion of the goods ones. I think this could be acceptable. Of course, it would not be very pleasant for some industries, but that could encourage them to improve the quality of their own products if they did not want to fall into that taxation system.

Member of the audience

On the same point, we have heard about fiscal approaches on taxation and de-taxation, which seem to be naively good. In the particular context of the European Union, I wonder whether that would not hit straight into the wall of altering the competition, which is one of the EU's sacred principles.

Tobacco is different because it is just one product, but if you start to put taxes on food item A and de-tax item B, I suppose that is not feasible. I would like some illumination on that point.

Knut Inge KLEPP

I think there are a lot of sacred principles we have to challenge if we want to promote public health. In terms of taxes, all sorts of criteria are used all the time. In Norway, when the sales tax was reduced on food, food was defined as everything you put into your mouth except tobacco, alcohol and medication. I think you could easily come up with a clear set of other criteria that could then be used to promote the kind of food that we, from a public health point of view, want to increase and to reduce the others.

It is clearly a big challenge but I think we may have to make it clear what the different options are, what the health consequences are, and just keep pushing it. Use examples like the one I tried to use with soft drinks to visualise the amount of money that is being moved around in the public sector, and that this clearly has health consequences, even though the health concerns are not used when it is put in place in the first place.

Member of the audience - Ivan DRAGONI, Responsible of the school canteens of Milan

This is more a small contribution than a question.

I wanted to ask, how come in the program Pro Children, about which the Norwegian reporter told us, Italy has not been contemplated between the tested countries when the trend that there is in Italy is absolutely contrary to what is verified in the other countries. My name is Ivan Dragoni and I am responsible of the school canteens of Milan, where we produce eighty thousand meals per day for the children in primary schools and day nursery, therefore from the age of one year until fourteen. The school canteens in Italy are an obligatory service that is financed by the public institution and therefore by townships and in part paid by the parents, proportionally to their income. The menu must obligatorily involve vegetables and a fruit per day and not only a snack in the afternoon. The problem that we find is exactly the opposite: the offer is not free, but we observe a waste that for the fruits and vegetables approaches 70 to 80 % in the sense that when we distribute eighty thousand apples, normally seventy thousand come back refused and so do the vegetables to an even greater extent. This has led us to think that, all in all, merely offering fruit and vegetables is not enough, especially with the smaller children. There is also a need for actions to promote consumption, through classes at school, and also through the parents, and well-known speakers. Therefore we are studying a program of appraisal of cooking activity. It will actually start next week. Rather than tasting the flavour of several fruit and vegetables with appropriate cards, the children will come to school to be gathered around a table in order to peel a fruit, to prepare a fruit salad, to grate carrots and, even, to prepare small festivities for their parents. We believe that unfortunately the mere offer does not constitute, at least in our territory, a sufficient contribution to the change in the dietary habits. It has to be supported by a strong action from the school, towards the families and especially the children, but accompanied by definitely ludic activities.

Serge HERCBERG

Director INSERM and Vice-Chairman of the Strategic Committee in charge of the PNNS
(UMR Inserm/Inra/Cnam), ISTNA/CNAM, Paris, France

First, I would like to thank the Organizing Committee for its kind invitation and for giving me this opportunity to present data on the Nutrition and Health National Program (PNNS) set up in France in 2001.

I will summarize this Program and, according to the topic of the Round Table, I will highlight specific aspects demonstrating the role of politics, and especially of national public health authorities, in the carrying out of such a program.

The Nutrition and Health National Program was implemented in France under the aegis of the Ministry of Health. It is, in fact, the reflection of the French nutritional policy.

Nutritional policy is a concept which should be differentiated from a single specific action. In the first round table, we listened to some very exciting specific actions, proposed by different actors. All of these are perfectly relevant.

But each of them has a single specific objective, for example, to increase the consumption of fruits and vegetable in the overall population or in certain population groups.

A nutritional policy, by definition, implies a public health effect at the nationwide level. For instance, the PNNS (*Nutrition and Health National Program*) has as a general objective, the improvement of the state of health of the entire population, by intervening at the level of one of its major determinants, nutrition.

It is clear that no single action or measure, even if it is carried out under the best conditions, can be considered, in itself, as truly effective in achieving this global objective.

As a veritable public health program, the PNNS (*Nutrition and Health National Program*) includes a combination of synergistic and complementary actions, measures, rules, regulation and laws.

The success of a public health nutritional policy, such as that developed by the PNNS is grounded in a certain number of basic conditions:

1. First, there is the choice of nutritional priority objectives, which can be achieved within a targeted period and which can be measured at the end of that period

Nine nutritional priority goals were initially determined for the 2001-2005 period, which was extended to 2008 within the framework of the French Public Health Law adopted in 2004.

Five of these concern diet (fruits and vegetable, calcium/vitamin D, lipids, carbohydrate/fibers and alcohol); one relates to physical activity (in the daily life) and three concern nutritional markers (cholesterol, blood pressure and obesity).

They are the same as those recommended by scientific authorities throughout the world. But the originality of this program lies in the fact that it provides clear quantification for each objectives defined for the specific period (2001-2008).

- For instance, concerning fruits and vegetable, the objective is to increase consumption of fruits and vegetables in order to reduce the number of 'low consumers' of fruits and vegetables (defined as someone consuming less than four portion of fruit and vegetables per day), by at least 25%;

- For physical activity, the quantifiable objective is to increase by at least 25% the number of people doing the equivalent of at least half an hour of fast walking per day.

9 nutritional priority goals (2001-2008)	
5 objectives concern diet	
fruits and vegetables	25 % number of low consumers of fruits and vegetables
calcium / vitamin D	25% population with Ca intakes <RDA, 25% prevalence vit D deficiency
lipids	total fat intakes < 35% of daily energy intake, with 25 % in the population's consumption saturated fatty acids (< 25% of total fat intakes)
carbohydrates / fibers	> 50% of daily energy intakes, by 25% starchy carbohydrates, 25% simple added sugars and 25% consumption of dietary fibre by 50%.
alcohol	alcohol intakes among consumers < 20g of pure alcohol/d
1 objective concern way of life	
physical activity in the daily life	25% in the number of people doing equivalent of at least 30 min fast walking per day
3 objectives concern nutritional markers	
cholesterol	mean blood cholesterol level in the adult population by 25%
blood pressure	systolic blood pressure in adults by 10 mm of mercury.
obesity	prevalence of overweight and obesity (BMI > 25 kg/m ²) in adults by 25% and to halve the increase in the prevalence of obesity in children

Likewise, all objectives are precisely quantified. Therefore, they are measurable at the end of the targeted period.

These objectives, though ambitious, do not attempt to cover all of the nutritional problems affecting the overall French population. They are simply pragmatic targeted proposals.

These choices represent a politic decision validated by French Authorities based on strong scientific arguments.

Apart from these objectives aimed at the whole population, nine specific nutritional objectives aimed at specific populations (pregnant and lactating women, children and teenagers, the elderly, the underprivileged, etc.) and concerning specific nutrients (iron, calcium, vitamin D, folate,...), have been defined.

9 specific nutritional objectives	
✓	To reduce iron deficiency during pregnancy
✓	To improve the folate status of women of reproductive age, particularly in those planning pregnancy
✓	To promote breastfeeding
✓	To improve iron, calcium and vitamin D status of children and adolescents
✓	To improve calcium and vitamin D status of older people
✓	To prevent, screen for and restrict malnutrition in older people
✓	To reduce the frequency of vitamin and mineral deficiencies and malnutrition among disadvantaged people
✓	To protect people following restrictive diets from vitamin and mineral deficiencies; take care of the nutritional problems of people with eating disorders
✓	To take the problem of food allergies into account

As a global policy, the Nutrition and Health National Program combines different strategies oriented towards communication, information, the nutritional and alimentary environment, food composition and food availability.

Actions are oriented towards different targets: general populations, high-risk groups, health professionals, education professionals, social workers, local and territorial collectivities, associations and economic actors.

The program adheres to some fundamental principles including the notion of pleasure, conviviality and gastronomy; it takes a

positive approach oriented towards promoting protective factors. It is never oriented towards prohibition, and any inherent messages should be adapted to lifestyles. It relies on synergy, complementarity and coherence in all the actions it implements.

To succeed in attaining its goals, the Nutritional and Health policy had first to establish a clear, scientifically recognized, referential setting including:

- a logo (with the official colours of the French flag –blue, white, red- along with a smile as a reminder that health is perfectly compatible with pleasure!), designed to authenticate all action undertaken and managed in conformity with the nutritional objective of the PNNS.

- However, the key point of the national referential setting is the translation of Public Health objectives into practical reference guidelines which provide quantitative and qualitative information for daily food choice available to the general public.

These guidelines provide practical benchmarks for foods as they are purchased and consumed by the population. We are not talking here about nutrients, but we are talking about fruits, vegetables, bread, meat-fish-eggs and sweets. Details are provided for the quantities and types of foods: how many fruits and vegetable per day, which kinds ; how many dairy products and starchy foods, ...How much physical activity, etc...

Of course, it is not enough just to formulate quantitative and qualitative recommendations. It is really important to adapt these recommendations and guidelines to all real life situations, and to show that they are attainable by most of individuals.

This is being done by means of the National Food Guides, which set guidelines available to all types of population. These guides provide advices to individuals whatever their lifestyle, economic levels or cultural background enabling them to adapt their behaviour in line with the recommendations, thereby adhering to protective factors without changing their way of life.

The advices and recommendations take into consideration the notions of pleasure, conviviality and gastronomy in daily food consumption; they are easy to use and never oriented towards forbidding certain foods.

More than three and half million copies of the National General Food guides have been distributed to the general public. Specially adapted versions of the National Food Guide have been developed for parents of children and adolescents and are in preparation for pregnant women and older people.

The messages are always adapted to the lifestyles. For that purpose, the Food Guides present different patterns (models) of consumers, in whom everyone can recognize his or her own situation. Thus, in the space of 2 or 3 pages, readers quickly find practical advice and useful tips on how to follow the recommendations adapted to their own specificities without having to dramatically change their way of life.

As a spin-off of these Guides, several general mass media campaign (using TV, radio, posters, etc.) have been developed which support the different recommendations of the Food Guides including a promotional campaign for fruits and vegetables or physical activities.

These campaigns are highly pragmatic and their messages are adapted to all situations. For example, for fruits and vegetables, the slogan was “at least 5 fruits or vegetable, fresh, canned or frozen, raw or cooked,

nature or prepared”. For physical activities, it was demonstrated how they can be included among daily activities....

In order to reach as large audience as possible, different tools (posters, kits, etc...) have been developed for distribution at various levels (in schools, among caterers, in companies, etc...).

The success of a public health policy lies in the capacity to ensure that all the concerned actors participate in coordination of the program.

This is why the Steering Committee of the Nutrition and Health National Program includes all the stakeholders involved in the field: 7 ministries, several health agencies in charge of communication on prevention, health monitoring, food security, the Social Health system, the Mutualist Federation, the National Committee on foods, the National institute of research, the Association of Food Producers, catering services, food products retailers, consumers organizations and scientific experts.

This coordination facilitates the involvement and cooperation of the different stakeholders. For instance many actions have been developed in coordination with the Ministry of National Education.

- These include:
- * the publication of a Guidance for the Composition of School Meals and for Food Safety, to improve school meals in terms of nutritional quality and food safety.
 - * the project of integration of nutrition into school programmes
 - * the production and distribution of educational tool such a national brochure recently edited for adolescents which will be distributed to teenagers by teachers taking part in teaching programs.
 - * Analysis of whether educational materials produced by the food industry are in conformity with the PNNS.
 - * The traditional, nutritionally inadequate snacks and light meals previously served in the morning in French schools have now been cancelled by an official circular sent to all establishment by Education Authorities.

While the PNNS is not a specific medical program, some of its actions are specifically oriented toward health professionals.

I won't go in details about all of these, but will simply highlight some aspects. Special versions of the national Food Guides for community-based professionals, particularly health professionals, have been produced and largely distributed.

Some actions are particularly oriented toward preventing, detecting and treating nutritional disorders in the health care systems:

- facilitating access to nutrition consultations, both in hospitals and elsewhere in the community, and developing nutritional care in hospitals by appointing dieticians and hospital practitioners,
- Producing adequate tools for nutritional assessment (such as a disk to calculate BMI or a specific disk to assess malnutrition in the elderly, etc...),
- Defining functions and professions in the field of nutrition, and revising the educational curriculum for health professionals,
- Producing recommendations for clinical practice,
- Distributing scientific reviews for helping professionals to introduce the objectives of the PNNS into their practice.

It is not enough to develop actions in the field of nutritional communication when attempting to inform the population on how to improve individual food behavior.

It is also indispensable to develop complementary actions to improve the nutritional quality of foods and the availability of foods which help to achieve the objectives of the PNNS.

The PNNS has urged the food producers to reduce the salt content of foods (especially bread, cheese, meat products and processed foods...) so as to reduce, by 20% in five years the average sodium intake of the general population. Health Authorities first contacted food producers to request their participation in this reduction on a voluntary basis.

A similar strategy is currently under discussion for reducing added simple sugars in food products.

Concerning food advertising, no efficient self-regulation has been possible with food producers. But prompted by French members of Parliament, especially Jean-Marie Le Guen, a specific regulation concerning food advertising was introduced into a Public health Law (promulgated in August, 2004), imposing an official nutritional message in all commercial advertisements for food products (on TV, radio, in the press and in all promotion activities). Food producers can avoid having to include this message by paying a tax to the French Institute of Prevention and Health education, to promote actions in the field of nutrition.

Under that same law, and in order to ensure coherence in nutritional recommendations, an article has imposed a ban on vending machines in primary and high schools.

Currently, debates and discussions are ongoing about providing consumers with clear and meaningful information on food labelling based on nutritional profile of foods. The goal is to promote the intake of certain foods and conversely to avoid excessive consumption of some others, avoiding to condemn specific foods.

The main challenge to the success of the PNNS lies to the capacity of the program to become operational at local actors (associations, municipal and territorial politic authorities, caterers ...). The national level has designed the recognized tools and it is offering a set of reference for the development of actions in the field. National and regional funds are available to enable field actions which will help to achieve the objectives of the National Program.

More than 150 experimental field projects have been granted for municipalities, associations, companies, schools, ...

A national charter was signed between the Ministry of Health and local municipalities (large, medium or small cities) which is committed to developing actions for attaining the objectives of the PNNS.

Finally, the main role of health authorities is to promote, initiate, design, coordinate and assess public health policies at a national level and to act as the guarantor of mutual cooperation, synergy and coherence in the different actions which are undertaken.

No action, measure, or tool alone can be considered as truly effective. It is the role of the steering committee chaired by the Ministry of Health to set up national programs, to coordinate and control this point!

It is also the role of health authorities to organise the evaluation of the program by checking the state of the objectives during and at the end of the program

A Monitoring and Nutritional Epidemiology Unit (Unité de Surveillance et d'Epidémiologie Nutritionnelle) was set up in 2001 with the mission of developing a surveillance system for nutrition at the national level, and especially for monitoring the objectives of the PNNS.

A national study will be carried in 2005 and repeated in 2008 on a representative sample of six thousand subjects, with measurement of food and nutritional status permitting verification of whether or not nutritional objectives have been achieved.

In conclusion, we should point out the difficulties encountered, and limitations inherent in the development of a French Nutritional Policy.

First, in order to develop the tools and referential settings of the Program, more time than expected was necessary; funds were not adequate for communication of the various aspects of the program; the creation of jobs for dietician and hospital practitioners was insufficient; difficulties were encountered when attempting to motivate regional actors; lobbying of the food industries; lack of a Food policy....

Jean-Marie LE GUEN

Deputy and Chairman of the Parliamentary Study Group on Obesity
Assemblée Nationale, Paris, France

Dr. Serge Herberg introduced the policies that were implemented in France some years ago and he defined the main principles of any nutrition policy. As far as I am concerned, I am in charge of obesity-related issues at the French National Assembly. Although both topics are in many ways interlinked, they are not interchangeable. Dealing with the nutrition issue is not only about promoting a balanced diet and a controlled calorie intake. As well, the fight against obesity is not limited to strictly dietary aspects, though these may prove determinant.

My intervention within the French National Assembly has turned into a private bill that has not been discussed yet but that was in part resumed in the document that refers to public health. Actually, two rather strong measures were voted about a month ago. We still need to assess how well they will be implemented.

I felt the need to put together a private bill that, while remaining within the guidelines of the PNNS, the French National Program for Health and Nutrition, would benefit from more ambitious means. It is the role of the Parliament and the National Assembly to provide administrations and experts with the means to conduct the desired policies. Of course, we fully agree with the principles of the PNNS, notably the idea that, as far as nutrition is concerned, recommendations and policies should not aim to make people feel guilty, nor blame or forbid anything, but rather emphasize such aspects as pleasure, conviviality and diversity. We want to stress this core message in order to improve our policies in terms of public health and the fight against obesity.

Nevertheless, the role of public authorities should not be restricted to a mere information supplier. Other orientations must be developed, that go beyond traditional responsibilities of experts and ministries.

More than informing consumers, we must call attention to the education aspect of the issue and we therefore need means that match the challenge our society is facing. Today, because of such phenomena as time fragmentation, loss of values, individualism in France and all industrialized countries, we can no longer rely on the traditional role of the family as a transmitter of dietary education. School remains a significant actor but it cannot teach our children "everything". Its public mandate is already quite demanding. Society as a whole, and particularly the media, thus has an explicit responsibility.

I therefore suggested that we first intervene on commercials that finance children TV programs. In France, a child watches television over two hours a day in average. Among these, at least fifteen to sixteen minutes consist of commercials, which comprise ten to twelve minutes of advertisement for the food industry. As Mr. Damiens explained earlier, those commercials do not advertise for fruit and vegetables, but they promote sodas, burgers, candy bars... Let's picture the case of a two-year old child who would discover the world within a loose, unbalanced family framework – if balanced family frameworks ever existed throughout history – and who would get food education only through television commercials: this child would know only a few types of products. We must respond to this situation: our first idea was to stop such disinformation about nutrition. Yet after

discussing the issue with experts, I tried to invert the process by making use of the funds invested in advertising for information and education purposes. Hence, the idea of encouraging (if not forcing) food industrials to include an informative message on health and nutrition within their advertisements. This proposal has been agreed upon and voted, but it has not been implemented yet. I would be happy to share with you the first results assessment of this new challenge in a few months.

Another way is to modify the environment in which consumers and children live. This means we should intervene on television, advertisement, but also on dietary issues of the whole population, notably the youth, in terms of economy and business; we should also take a closer look at mechanisms that govern today's dietary habits. We would then realize that the burden of direct marketing and availability/accessibility issues add up to regular TV advertising problems: in the US as well as in Europe, finding soda if you are thirsty - or a fast-food restaurant when you are hungry - will prove much easier than getting water – or fruit and vegetables. The whole economic background has to be questioned. The price issue also plays a crucial part: it proves determining, notably among under-privileged populations. From this perspective, bad dietary habits are very much linked with living costs. People who cannot afford fruit and vegetables tend to eat less of these, until they finally leave them out of their eating habits.

For those of you who would want to undertake political responsibilities, do not hesitate to select themes that you identify with, and to provide advice to your relatives and friends because there are great expectations around those themes in the general public. With regards to such expectations, we can be hopeful that a change through political action is indeed possible, at the behavioral as well as economic levels. The French are awaiting extremely dynamic policies as their awareness on major public health stakes is growing. I think that the philosophy of the PNNS matches a real expectation on the side of the French society. If we prove able to offer policies that impose limits on the media, business mechanisms, the food industry. We would certainly get support from the population.

The issue of nutrition raises deeper questions on our society: dealing with obesity means questioning business tracks in our country. In a few weeks, we will debate on hypermarkets and the issue of prices. Our recommendations on public health, in particular the need for nutrition and health education within hypermarkets, will most certainly upset the debate. But this can be done. Many MPs of various movements will probably take part in this initiative.

As we are facing a global issue on obesity and dietary problems, that certainly is linked to globalization, many possible ways of solution still need to be explored. Either we choose the "laissez-faire" and its disastrous consequences in terms of health, economy and society in our countries (including the impact on life expectancy), or we choose to control and improve our lifestyles, which I think we should do. While controlling the future has turned into a major concern among our fellow citizens, the dietary issue brings us at the heart of crucial questions around democracy and citizenship.

Antonia TRICHOPOULOU

Director of the World Health Organization Collaborating Center for Nutrition , University of Athens, Greece

Thank you Mr Chairman. Ladies and Gentlemen, I would like to thank the organisers for giving me the opportunity of being in Rome to attend such an interesting conference.

My presentation refers to how politics are involved and can a national nutrition policy be developed.

In Greece we have a national nutrition policy committee in the Ministry of Health. This committee has set five nutritional priorities in terms of public health.

The first is to reduce childhood obesity. The second is to increase the consumption of pulses and vegetables. The third is to reduce the consumption of meat and increase fish consumption. The fourth is to improve mass catering services with the application of food quality principles. The fifth is to increase consumer awareness on food safety and quality.

National Nutrition Policy Committee*Five objectives – nutritional priorities in terms of public health:*

1. Reduce childhood obesity
2. Increase the consumption of pulses and vegetable
3. Reduce the consumption of meat and increase fish consumption
4. Improve mass catering services, with the application of food quality principles
5. Increase consumers' awareness on food safety and quality.

Established by the Greek Ministry of Health

The plan of action in order for those priorities to be accomplished refers to three axes: training and education, research in the field of human nutrition, and a high level of collaboration between the Ministries of Health, Education, Agriculture and Development.

Plan for action in order to accomplish the priorities:

- A. Training and education
- B. Research in the field of human nutrition
- C. High level collaboration among the Ministries of :

**Health
Education
Agriculture
Development**

I think that these points are well-known to all of you and are similar to those in other countries, following either WHO or European Commission guidelines.

I would like to focus on the rationale of certain decisions that were taken in our nutrition policy committee in Greece and mainly on the one that refers to collaboration with the Ministries of Agriculture and Development.

One of the priorities is the consumption of vegetables and legumes in the Greek population. The domestic production of vegetables and legumes has decreased over the last few years leading to price increases and increasing imports of vegetables and legumes. So the demand is met by imports as domestic production is generally small. An increase in the consumption of vegetables and legumes will require an increase in domestic production, with the corresponding reduction in prices.

You may ask why we recommend to increase vegetable consumption in Greece. Greece is a Mediterranean country and vegetable consumption is among the highest in the EPIC centres and in Europe. Nevertheless, according to the DAFNE data (DAFNE is a databank which contains comparable and harmonised data between countries), the recommended vegetable consumption of 250 g per day is not being met by 50% of the population in Greece – it depends on the age group, the education level and the region. Of course, there are certain persons in Greece who consume 600 g of vegetables a day, but there are others who do not meet the recommendation.

DAFNE - Data Food Networking

Percentage of low consumers

Countries	Fruit < 150 g/p/day	Vegetable < 250 g/p/day
Belgium	68	76
France	59	71
Germany	43	88
Greece	38	50
Hungary	66	76
Italy	34	71
Luxembourg	41	83
Norway	69	93
Poland	81	75
Portugal	55	83
Rep. of Ireland	74	88
Spain	38	77
United Kingdom	70	78

Naska et al. BJN 2000

What about meat? From 1995 to 2001, domestic meat production declined (with the exception of poultry), but meat imports steadily increased – a fact that underlines the national cost of the over-consumption of meat. We do not produce meat. In the past we used lamb, goat, some pork, and we only consumed meat several times a month. The Ministry of Agriculture has calculated that if domestic production remained constant, reducing consumption by half would lead to a reduction of import costs by about 25%. Bear in mind that the money Greece pays to import meat almost equals the amount of money we pay to import fuel. So it is extremely important that a nutritional policy plan takes into consideration the position of the Ministry of Agriculture.

Our approach is to try to relate public health and nutrition intervention with agricultural policy. We are trying also to motivate small enterprises to produce traditional foods, because the Mediterranean diet is based on traditional foods.

Food quality is not limited to safety: it has organoleptic and nutritional characteristics related to food processing and is closely associated with the production area and its cultural dimension. This is very important because when we are promoting local traditional foods, at the same time we enhance the areas where they produce these foods and where people live in small villages in the country. So this issue has important cultural dimensions and quality is linked to specific production areas and cultural traditions.

Local traditional foods have health aspects, cultural aspects, they sustain the environment, because very often the local traditional foods respect the environment, and economic aspects, because they have added value and also because they keep people in their own environment and the countryside is not abandoned.

Talking about traditional food reminds me of what was happening 25 years ago when we started talking about the Mediterranean diet – nobody believed in it. Ten years ago we started talking about traditional food, and suddenly there are important studies. I am quite proud to tell you that in EUROFIR, which is a European Commission Network of Excellence project, there is a work package on traditional foods. In this work package we tried to define the term ‘traditional food’ because there is a lot of commercial interest and it is quiet often misused.

Since I am in this beautiful and historic country, may I make a suggestion? There are 3 715 traditional foods registered according to the Italian definition of traditional food. However, the registration is according to a national definition which surprised me for a country like Italy: they call ‘traditional’ every product which has been on the market for 20 years. I think that

when we call something traditional, we should have to go back at least 50 years – at least for countries like Italy, Greece and Spain.

We hope that our traditional guidelines of the Greek Ministry of Health, which are based on the traditional Mediterranean diet, can be implemented more easily if traditional foods are on the market. That is why we are going to encourage small enterprises to produce them –we will have quality foods, and we will also respect the environment and keep the people in the villages.



So, in our small area of endeavour, is to allow the traditional Mediterranean diet to flourish in spite the wave globalisation. Thank you for your attention.

Finnish experience on national policies and strategies for chronic disease prevention

Pirjo PIETINEN

Head of the Nutrition Unit, National Public Institute, Helsinki, Finland

I want to thank the organisers for inviting me here; it is always a pleasure to be in Rome.

I will give you a very quick overview of what has been going on in our country. I chose to do this because Finland is one of the few countries which have been working in this field, having had food and nutrition policies for chronic disease prevention for many decades. My point will be that it is not a campaign; it is hard work for many decades, it is endless and everybody needs to be involved.

We really started in the 1940s right after the Second World War. For example, we have had a free school lunch in every school in the country since that time – it is one of the cornerstones of children's nutrition in my mind – and we have had fortification programmes since the 1940s and 1950s. To give you an example, we put iodine in salt in the early 1950s.

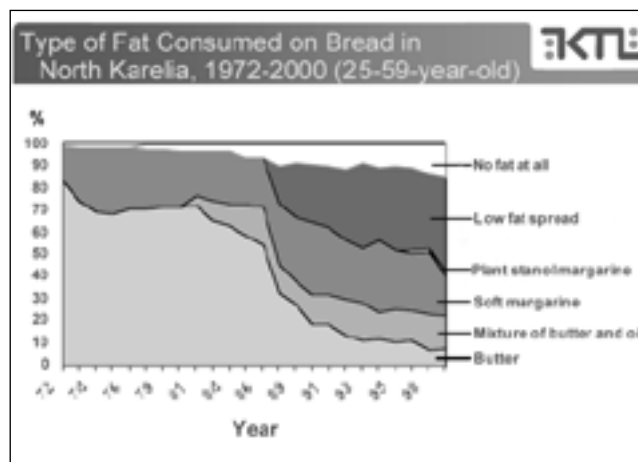
In the 1970s the main emphasis started to be in chronic disease prevention, because we were the leading country in coronary heart disease mortality in the late 1960s and early 1970s, and that was the start of the North Karelia Project. More recently, we have new problems – some of the older problems are gone. Now it is weight control and prevention of diabetes that are among the most important issues to be tackled.

As many of you know, the North Karelia project was one of the first community-based intervention programmes. It started in the early 1970s and was able to show that you can actually change the diet and lifestyle of ordinary people. It has a huge impact on their risk of coronary heart disease especially.

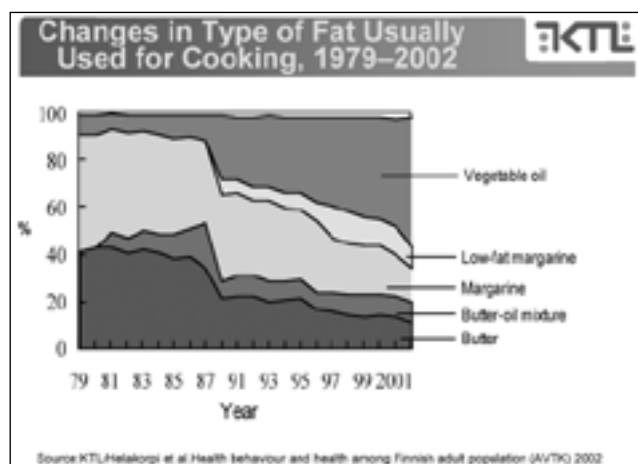
It had several elements, from media activities to training professional workers, environmental changes working, with the food industry and supermarkets, as well as establishing regular monitoring systems.

It is useless to educate an individual and persuade him or her to change his diet or other lifestyles if the environment does not give any help. For example, it is totally useless to talk about using less salt if you do not make a nice variety of low-salt breads and other foods available in the supermarkets. It is totally useless to try to educate teenagers not to use the vending machines in their schools; you have to take the vending machines out and offer something more healthful instead. You cannot put a person in an impossible dilemma time after time – it just will not work.

I will give you some examples of the dramatic changes that have happened over the years. Bread and milk were the main carriers of saturated fats in the old days. The picture has completely changed (Figure 1). Here you see that butter consumption dropped, especially in the mid-1980s. We have on the market a beautiful variety of different kinds of fat spreads which have different oils in them, and the newest are the plant sterol and stanol margarines. So this has completely changed. When people shift from fatty milk to skimmed or low-fat milk, the saturated fat that used to come from milk drops dramatically. Different types of margarine plus oil have come to the market for good.



There has been a dramatic change from fatty milk to skimmed milk and low-fat milk. Rapeseed oil and canola oil, which is now locally produced, has replaced butter in cooking (Figure 2). This has also been very important for the agricultural sector because it gave business to the old dairy farmers.



The sources of saturated fatty acids have changed completely; the number one is now cheese, especially in young women because they avoid other dairy products or use low-fat varieties. There is a drop in serum cholesterol both in men and women, which has levelled off though, but there is concern that new types of sources of saturated fat have become fashionable, especially among the younger generations.

We have a symbol launched by the National Heart Association; it says 'Better Choice' in Finnish and Swedish. Companies can put this logo on their products if the product meets certain criteria: is reduced in salt, high in fibre, its fatty acid profile is good, it is low-fat, etc. This is being increasingly used and helps the consumer tremendously in the supermarket. If you see different kinds of bread and you see this symbol on one loaf, then you automatically know that it must be a healthy choice, and you do not have to look at the label and read the small print.

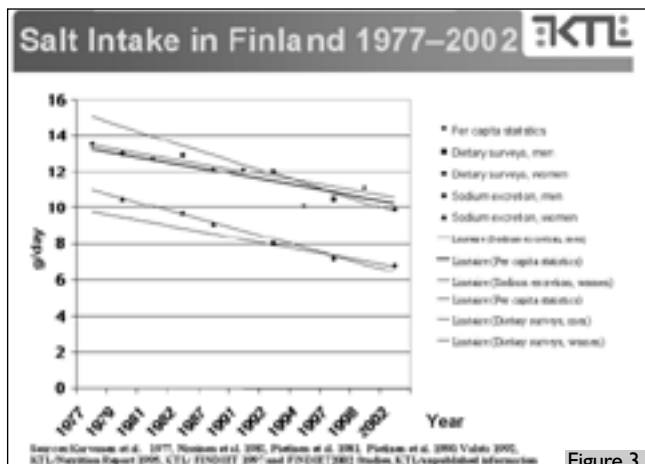


Figure 3

We are one of the very few countries which have documented a decline in salt intake (Figure 3). We started to talk about salt and blood pressure in the late 1970s. Salt intake was sky high and it was a matter of concern. There was a three-year pilot project in North Karelia, called the Salt Project, which demonstrated that if you work with the food industry and educate not just the people but also health-care workers etc., you can make a change. It then escalated to the whole country. What has also been a very important tool – and the EU is a little against this at the moment – is that we have had a national decree since 1985 which enables the food producers to put on the label the mark ‘reduced salt content’ if it meets certain criteria, and which obliges the food producer to label a product as heavily salted if it exceeds a certain limit. I will give you an example. Normally, the salt content of bread is around 1.1% to 1.3% of fresh weight. If it is less than 0.7%, it can be labelled as reduced salt. If it goes beyond 1.3%, it needs to be labelled as heavily salted. Immediately, all the heavily salted products disappeared from the market because nobody wanted to put that label on. The EU does not like national decrees but we have tried to make them understand that these really work.

Changing the diet at the population level requires systematic work. It is not just one campaign and you really have to work with the industry, the people and the health-care sector – you have to get everybody involved. It still takes a lot of time, and if you quit putting your energy into it, it is finished.

The availability of fruit and vegetables improved tremendously starting in the 1970s. You can now go to ski in Lapland and buy avocados and kiwis in any of the little supermarkets there. Simply the availability has improved. We did not have to educate anyone, it just happened. The price levels have also been reasonable in our country.

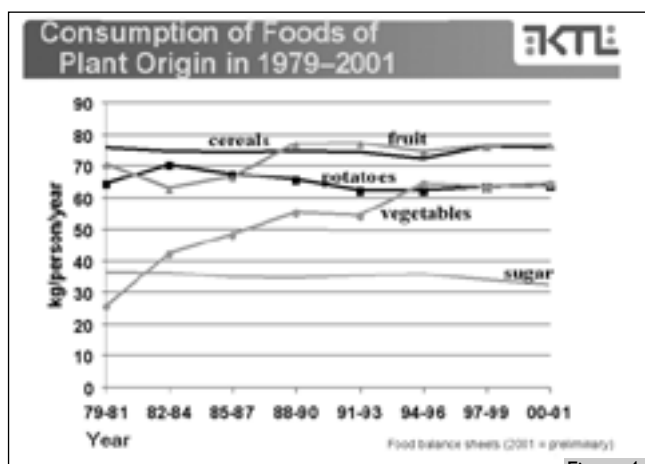


Figure 4

If you look at the fruit and vegetable consumption statistics based on Food Balance Sheets, you can see that we are eating more fruit than

potatoes – and we are a potato-eating country – and in the comparisons with the Nordic countries, we are doing quite well (Figure 4). There has been a threefold increase in vegetable consumption since the 1970s.

What made the vegetable revolution was that in the early 1980s, the trade unions made an agreement to subsidise worksite lunches. It still happens. Most of us have a warm worksite lunch and there is always a free salad bar. Imagine a factory with blue-collar workers and there is a free salad bar. The meal is a package – if you do not take the salad you still pay the same. Of course, everyone tries to get the maximum for their money. This really increased vegetable consumption, especially in men.

Why did the diet change? We have a long history of population studies, epidemiological studies, active researchers, international collaboration, economic development, women’s employment, etc. Improved availability of healthy food has been a key issue. Catering services at worksites with the well-balanced worksite lunch which meets the dietary recommendations set out by the National Nutrition Council has been another key element. We have had many demonstration programmes and public education programmes. People seem to understand the issues concerning the quality of fat. We never had a black and white message ‘all fat is bad’, we always said you should reduce hard fats, but you have to take in oils and other soft fats – they are good for you.

In a little country, it is easy to have political consensus as well as consensus in the medical community. Everybody has been very supportive. Nobody has been against these activities and the food industry has been quite cooperative.

The results are good: a 75% reduction in coronary heart disease mortality since the late 1960s, and an even higher decrease in North Karelia, where they started at a higher level. The decline in coronary heart disease mortality can be explained by the common risk factor level decreases until the mid-1980s, when the observed decline was better than could be predicted and the explanation is better treatment.

We do have a growing concern about overweight and obesity but fortunately, our situation compared to England, for instance, is not as bad. However, this is one of the issues we have to tackle – more in men than in women.

What are the current issues? We want to maintain a good free school lunch – the municipalities are in financial trouble trying to do everything and our concern is that if you really want to maintain a good lunch with vegetables for less than 70 cents, it soon becomes impossible.

We need to get vending machines out of schools. This movement is going on, but not by any governmental decree. It started about two years ago with concern from the Dental Association. The dentists noticed that even though we have a decline in dental decay, it is levelling off. The Dental Association, the Minister of Health and our institute put our efforts together and simply started a discussion. The media loves the issue and has given it good coverage, so now more and more schools are offering a healthier snack for a small sum or encouraging the students to bring a piece of fruit from home and they are simply taking out the vending machines. Legally, if the school system is being paid for by us taxpayers, we have the right to see that there is nothing unhealthy on the school ground.

There is also growing concern on the lack of physical activity among youngsters, so there is more and more organised leisure time physical activity after school hours on the school ground.

We need new ways to increase fruit and vegetable consumption because we know there are still groups in the population where the consumption is not enough. Thank you.

Donato GRECO

Director General of Health Promotion
Ministry of Health, Rome, Italy

I come from Naples, the capital of the Italian Mediterranean diet. I would like to take this opportunity to remind you that within the original campaign origin, one of the most relevant studies ever made on the health effects of the Mediterranean diet was launched, and many scientists from the US and Italy helped in the study.

As I think we are going to be overwhelmed with the 'dietary story' over the next few days, I thought I would use the next five minutes to tell you some other news about what Italy is trying to do.

After 29 years in science, I moved to implementation because I felt strongly about this enormous gap between what we know should be done and what is done.

We have seen that there is a gap in this country, in your country, as everywhere. We have known for a long time that we should eat more fruit, that we should not smoke, and that we should walk for an hour a day, but in fact there is little evidence that the population is moving, rather a lot of evidence that the population is going the other way. So we have to do something about this impact gap. Of course, I do not have a solution – otherwise I would not be here.

We are trying to create a new programme with a new institution to try to get science messages through to the population. This is why our parliament approved through a new law last year the Italian CCM, Il Centro nazionale per la prevenzione e il Controllo delle Malattie [The national centre for prevention and control of diseases]. It is a network between the regions and the many institutions to build our capacity to work together in a network. Our mission is to help attain assessment, surveillance and response in coordination with the regions. Each of the 21 independent health authorities of the country are becoming more and more independent. They have their own ministers, parliament and funds (funds are not managed in Rome anymore, but remain where they are collected.)

So we have training to do, presentation, networking, and information feedback. It is a very heavy mission. To start with, we have been given 6 tasks: infectious diseases, health promotion, environment and climate, vaccines and vaccination, road and domestic accidents, and bio-terrorism. This covers the country's major health problems.

We have a small additional budget on top of our main budget which allows us and the network to function. This fund is granted every year and is protected against any cuts by the government or treasury minister.

The National Plan of Active Prevention (NPAP) :

1. Cardiovascular Risk
2. Diabetes
3. Obesity
4. Cancer Screenings
5. Vaccinations
6. Accidents




We have a national plan for active prevention, the word 'active' being a message we would like each citizen to hear; we want to reach them in their homes.

Of course, when we speak about these diseases, we are speaking about the major causes of disease: 250 000 deaths caused by cardiovascular disease and more than 1 million sick people every year at any given moment. Diabetes is now our great challenge: according to our treasury calculations, our entire health budget in the next ten years will be barely sufficient to pay for diabetes only – let alone the rest!

Our actions must include cancer screening. I have just come from the World Health Assembly in Geneva in which cancer control was one of the items discussed, and again, diet is crucial, as one third of cancers are associated with diet.

What are our main points? Smoking: I am proud and pleased to say that we are now one of the leading countries in the world for combating smoking because we have approved a quite stringent and effective law that forbids smoking in all public places. Believe it or not, despite our 'illegal' attitude – we do not usually like to respect red lights – the Italian population is accepting this law very happily. We have figures showing a minor drop in consumption of cigarette sales of about 10% a month, and out of the many tens of thousands of police inspections of restaurants and bars, less than 3% were fined for irregularities. The population is happy about the restriction of smoking in public places. However, we are not forbidding smoking: this is not a law against smokers; it is a law against passive smoking to protect the non-smokers. Things are going very well.

Physical activity: over the next few days you will hear in different presentations how people are not inclined to move and walk.

Nutrition, of course, is a major issue, as has already been mentioned by other colleagues.

As in many other European countries, alcohol is our problem, but I am pleased to say that our total alcohol consumption over the last ten years has decreased by more than 20%. We are drinking better and drinking less, and we are not much fond of spirits. Although alcohol consumption is going down, Italy, like most countries, do have a huge problem with alcohol and smoking among the young – youngsters love beer and there are many new pubs springing up, even in Rome.

There is good news, however. In general, all programmes are applied to Rome and nothing happens in other regions. However a few months ago the 21 regions signed a pact with the State to engage in this national active prevention plan for three years from 2005 to 2007. (The plan is the one I showed you earlier). What is also important is that 1 320 million euros have been set aside for these five items, including nutrition and physical activity. Historically, this has never happened. This is part of Italy's 90-billion-euro health budget, not an enormous amount, but significant enough so that there is no longer any justification for the 250 local authorities or the 21 regions not to act in accordance with the national guidelines which aggressively address the risk-factors we will be speaking of over the next few days. For once, the money is directed at the target – which sounds very simple, but that never happens in this country! The regions have to start implementing this action next month – otherwise they do not receive the funds.

Finally, there is a mechanism to assist regions as well as a verification mechanism whereby each region has to be periodically certified on the active prevention plan within its own territory to get its quota of money. I am quite hopeful and believe that this mechanism will make it difficult to deny or divert the money to pay for other things.

This is a heavy task and I strongly hope that over the next few days of this meeting, we will go in the direction that Italy is ultimately trying to take to fill the gap between science and the benefits to the citizen.

Thank you.

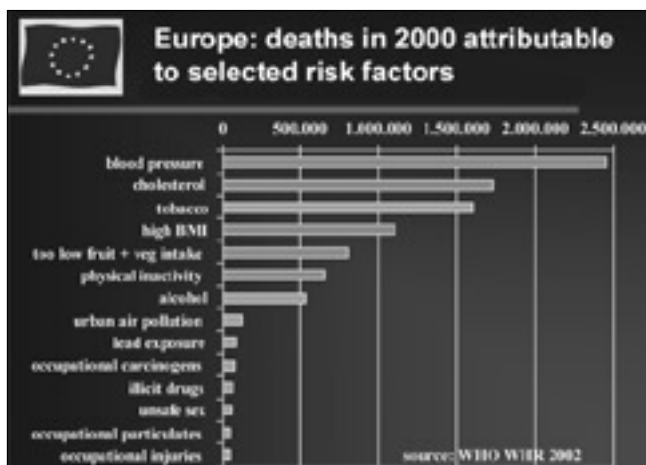
Community action on nutrition and physical activity

Wilfried KAMPHAUSEN

Principal Administrator, European Commission
European Commission, DG SANCO G/3 Health and Consumer Protection, Luxembourg

Good evening, Ladies and Gentlemen. I am very honoured to have been invited to speak at this third edition of the international conference on health and the Mediterranean lifestyle. We have to congratulate the organisers for choosing such beautiful surroundings in Rome for this meeting. Even more so as it is an even greater pleasure these days to go into an Italian café or restaurant because the Italian government has had the courage to ban smoking in public places, for which I think they deserve our congratulations.

In my talk, I would like to evoke the need for action on nutrition and physical activity because of obesity and diabetes. A lot has already been said on this but I would like to add a few elements. I would then like to show how the Community goes about building a strategy in this area.



There are many ways in which you can present the effects which nutrition has on health and on health risks. This is one of the ways I like the best. This graphic gives you a breakdown of premature deaths in Europe by risk factors. One can say that 6 out of the 7 main risk factors for premature death, including alcohol, relate to the way in which we eat, drink and move – the odd one out being tobacco. I think we still have a lot to do when it comes to creating awareness in the media. If you look at the bottom half of this list, there are many elements in there which make people very much afraid, but they are in a totally different order of magnitude. I think you will be glad to see that fruit and vegetable intake is one of these factors where we still have a big margin for improvement and where a lot still needs to be done.

We know that by changing lifestyles it is theoretically possible to avoid up to 80% of CVD cases, up to 90% of type 2 diabetes, and up to one third of cases of cancer. We have heard from a lot of studies here today that the Mediterranean diet can make a great contribution to this.

Information and education is important – it is essential for changing behaviours. We have heard today that you can change behaviours without having to spend too much time and effort on education and information, which I found a very interesting point. We have also heard that changing the environment is also a very important factor if we want to see improvements in this field.

I will say a few words on obesity. These are the figures from a few selected countries. We can see that we have the usual suspects – like the United States – but we can also see that countries like the

United Kingdom come very close to the situation which, in Europe only a couple of years ago, we ridiculed a little – “Yes, the Americans have this obesity problem, how terrible...” We have it in our own countries now.

It is even more worrying if we take a look at trends in obesity. These are some figures for the early 1980s, some for the late 1980s, and some for the 1990s. If we look again at the United Kingdom, we can see that in a period of less than 20 years, obesity has trebled. That is very worrying indeed.

The situation is even more worrying if we look at overweight in children – so this is not obesity, this is overweight with a body mass index of over 25. These figures from the International Obesity Taskforce certainly give the picture and the trends. We see that in the Mediterranean countries, the figures are fairly high. Nutrition is one element of the picture and you can certainly argue how much children in the Mediterranean countries now still benefit from the traditional Mediterranean diet. We have had globalisation all over the world, and certainly children here are as keen “junk food” eaters as they are in other parts of Europe.



Physical activity also plays a part. Here are some statistics for young girls indicating the number of girls, broken down by age group, who meet certain guidelines – the guidelines being that you should have 30 minutes to 1 hour of moderate physical activity a day. You can see that there are very few countries – Ireland, in fact, is the only one – where about half of the girls in the younger age group meet these criteria. You can also see that there are fairly low levels for the Mediterranean countries. When we look at the obesity issue, we must never forget that it depends on ‘energy in and energy out’ and that physical activity also plays a part.

Obesity and diabetes: there are estimations which say that more than half of the European population will suffer from type 2 diabetes during life. We know the risk factors: obesity and central adiposity, physical inactivity, excess calorie intake.

The World Health report estimated that more than 50% of diabetes globally can be attributed to high body mass index. We know that obesity and type 2 diabetes are linked. There are a number of studies to confirm that. One example is the nurses’ cohort study in the United States which established that the risk of diabetes was increased 5 times for individuals with a BMI of over 25, and 93 times for those who were heavily obese with a BMI of over 35. WHO predicts an explosion of diabetes figures worldwide by 2030, and though it is

true that we will see most of this increase in the developing world, the situation in Europe is also very worrying. These are estimates for 2000, and these are projections for 2030. Again, some of the Mediterranean countries – Greece, Italy, Portugal and Spain – are fairly high on this list. Again, it is a question of nutrition and physical activity – amongst other factors, certainly.

If we look at physical activity once more, this is a slide showing how many people stated that they did not have any physical activity in a typical week. The European average here is around 30%, with Portugal, Italy and Greece fairly high above this level.

Life expectancy: we have had a very positive picture over the last 40 years, with an increase both for males and females in the order of 7 to 8 years of life gained in that period. Now, there are scientists who predict that children born today will in fact have a lower life expectancy than their parents, and they say this is due to the obesity epidemic.

WHO and the Federal Agricultural Organisation have very nicely summarised the evidence for obesity risk. There is convincing evidence that obesity risk is increased by a high intake of energy-dense foods and by a lack of physical activity. There is convincing evidence that risk is lowered by a high intake of dietary fibre and of fruits and vegetables, and by regular physical activity. There is probable evidence that risk is increased by sugar-sweetened soft drinks and fruit juices, and by heavy advertising of foods which you would normally consider less healthy. Something that is worrying us very much at a European level is the amount of advertising of energy-dense, nutrient-poor foods to which children are exposed, especially on television. There is also probable evidence that low socio-economic status contributes to obesity risk.



There is probable evidence that the risk is reduced by breast-feeding, and by supportive environments at home and in society in general.

What do we want to do at the Community level about all this? First of all, we have to improve the data we have. Why? All of us know the trends, but if we want politicians to make changes, they will ask us for hard and comparable data. We still have to make some progress in this area.

We need to increase the overall awareness of the understanding of diet and physical activity for health, and increase the awareness of the potential which healthy lifestyles can have to reduce health risks. We need to do that among the general population, among the politicians, and also – and very importantly – among the media. We need to make sure that best practice is disseminated. We need to promote the healthy choices and physical activity. We also need, very importantly, to orient other Community policies towards public health and nutrition objectives into account. There are some things we can do within the health policy at Community level, but there are many more things which can be done by, for instance, the Common Agricultural Policy, education policies, sport policies, and also by policies linked to town planning, buildings design and many other things.

In order to develop a strategy on this issue, we have created a European network on nutrition and physical activity, with participants from various backgrounds appointed by Member States. The objective of this network is to advise the Commission on the establishment of a Community strategy on nutrition and physical activity.

In parallel, we have looked very intensively over the last year into ways and means of getting industry and the economic operators on board in the fight against obesity. There were 3 questions asked to the food industry. Will they publicly commit to devoting more resources to fighting obesity? Will they accept that other bodies will control what they are doing in this field? Will they accept to draw up benchmarks and verifiable objectives in the field?

In the meetings, we had the impression that such an approach was at least worth trying, and therefore we established in March this year the European Platform for Action for Diet, Physical Activity and Health, which brings together European-level umbrella organisations of the food industry and also of the consumer and health NGOs. We also have the advertising industry in there and the broadcasting associations, and also the scientists and international organisations to advise us.

The objective is to sit down with the Platform members to establish first of all a base line, which establishes what they have been doing so far in this field. Once we have agreed on that, we want them to commit publicly to what more they will be doing in this field over the next year. These commitments can be of a very different nature. For instance, there can be commitments to withdraw vending machines from schools or to change the content of the vending machines – putting fruit instead of chocolate, mineral water instead of soft drinks – and there can also be restrictions on advertising to children.

We also want this forum to help us to better identify best practice in this area. We also want it to better integrate the contributions which other EU policies can make to the issue. We want to see achievements come out of this also in the field of self-regulation as regards certain forms of advertising, and my Commissioner has made it very clear that if this does not happen, then we will have to consider regulatory means.

The platform development will be continued and evaluated for the first time in the middle of next year. We will have a debate on obesity in the Health Council on 3 June; the Commissioner has prepared an issues paper for this purpose and the Council has prepared Council conclusions, which will become public very soon. The Commission then intends to prepare a Green Paper on nutrition and physical activity, which will be available towards the end of this year and which will launch a very broad consultation. We expect replies from all kinds of players in society to the basic alleys which will be portrayed in this Green Paper. We will analyse them very carefully, and we will then come forward with a Commission communication on nutrition, physical activity and obesity by the end of next year.

We all know that diet and physical activity are very strong determinants for a number of very serious diseases. Obesity depends on what we eat on the one hand, and on the energy we expend on the other hand. The food industry is no scapegoat, but the food industry certainly is part of the problem and so therefore should also be part of the solution.

We know there is a lot more that needs to be done in order to enable consumers to make the healthy choices. For instance, fruit and vegetables need to become more available, affordable and accessible. We know that advertising and marketing of certain food products to children is a very critical issue.

We hope the platform will show results by the middle of next year, and we are very convinced that the Mediterranean diet can make a significant contribution to healthier lifestyles.

You can find more information on our website and I would like to thank you very much for your attention.

Conclusion

Antonios TRAKATELLIS

Vice-President of the European Parliament and member of the Commission of the Parliament dealing with the environment and public health, European Parliament, Brussels

Thank you very much. Firstly, I would like to thank the organisers for inviting me to such an important meeting. I must say that the contributions were great and I think this has been an extremely important meeting.

There is no doubt that the accumulated scientific evidence clearly shows that there is a very close relationship between nutrition and state of health. Good nutritional, and consequently healthy diets can not only prevent diseases, as we have heard from many contributors today – cardiovascular diseases, certain cancers, obesity, diabetes – but can also significantly contribute to a higher life expectancy. Needless to say, good nutrition is a great contributor for a good quality of life in aged people.

Taking all this scientific proof into account, it is now important to turn it into actions, measures and programmes, not only at the national level but also at the European level. I have to remind you that this is an obligation at the European level which is even in the treaties – in the old ones and even in the new treaty now under discussion in the various States. The political will is there and it is increasing. The citizens of Europe are very interested in all these subjects for many reasons – the nutritional crises we have had in the past, people have lost confidence, consumers are very interested, NGOs are following this subject very closely – therefore there is pressure from the public and the political will is growing. We therefore have to consider what we can do in this area at the national level as well as at the EU level.

We have done many things already. For example, we have a programme (which I introduced as the rapporteur) for public health which runs from 2003 to 2008. It is very innovative because it is basically a programme of collecting and analysing data – all kinds of technical data and also data on lifestyle, nutrition and other factors. This is very important because by collecting and analysing this data, you can really come to understand what the health determinants are – the important factors today which make a person to go from a state of health to a state of disease. I will read you this definition: 'Health determinants can be categorised as personal behaviour and lifestyles, influences within communities which can sustain or damage health, living and working conditions and access to health services, and general, social, economic, cultural and environmental conditions.' It is very important that this part of the programme is called Positive Health, Nutrition and Physical Activity. We should continue to collect the relevant data.

We now have a new programme which we will be discussed in the Parliament. The proposal is from the Commission and it will be the new public health programme. The previous programme is still in progress and will run until 2008, and the new programme will run from 2007 to 2013. The new programme will focus on public health issues, as does the previous one, and it will continue with the same ideas of collecting data and analysing health, but it will also address certain consumer-interest issues. In other words, it will be a combined programme. To show you how we are advancing in this area, I can tell you that the previous programme now running has been invested with around 400 million euros, and the new programme will be invested with 1.4 billion euros – about 4 times as much. We therefore have a political interest and a political strategy for doing more for public health in Europe.

First, we have to act – and we are acting. Secondly, we can

continue research in this area – research in nutrition is very important. We are going to put this topic in the seventh research framework programme which is now under discussion. This is important because when we have the data then it can be used to strengthen public interest and consequently the political will.

The third thing we can do has to do with the education process. It is very important to introduce this subject into schools. As a subject, nutrition is not like history, which can be understood and taught using regular teaching tools; nutrition has to do with acquiring taste and learning and following new habits – in other words, by eating fruits and vegetables. You cannot learn nutrition by reading a book; you have to acquire a taste that you can follow in your life.

We also have to make sure that governments and the EU spend money on these types of programmes that provide fruit and vegetables. We have to convince them with data collected from this programme. You could apply for a project using certain parameters obtained from schools in these pilot programmes to compare children with a population of children that do not have this opportunity of having vegetables – you are sure to find very important data there. This is very important because you then have something very powerful to push governments towards this particular programme. Therefore, teaching, education, teaching nutrition, acquiring taste, and having the data to prove the importance of these programmes are some of the things that have to be done.

Fourthly, the information campaign is also very important. An information campaign is something we can do at the EU level. We already have an information campaign on cancer – we could have an information campaign on nutrition. Why? Firstly, because people are getting more and more information – people know more about cholesterol today than they knew 50 years ago and they try much more to select what they eat based on the knowledge they have. It is also important for another reason: if you have a business, then you try to go with the trend. Do you remember having a vegetarian dinner on an aeroplane 15 years ago? No – but you do today. If you have a restaurant, it is good for business to offer vegetarian meals to vegetarians, and it is good to offer something tasty. There is a misconception that healthy food is not tasty and it is not true. So industry can do quite a lot to improve and present 'healthier' products for children or adults. Therefore, an information campaign increases public awareness over what we choose to eat, and also increases industry awareness of what they should do in the new environment, which is different from before.

The fifth point will be covered by coming European legislation and has to do with labelling – what goes on the label for all products. I think we can improve quite a lot on this because I do not think labels satisfy the consumer today. Why? Take a bottle of water. What do you see on the label? You see a number of constituents – for example, sodium is 3 mg per litre. If you are a consumer, what does that mean to you? Do you know if the sodium level is high or low? It is useless information for the ordinary consumer. Labels have to be meaningful to the consumer. The consumer should be aware that this food has more cholesterol than it should, for example. This is something that really informs the public and also pushes the industry to promote healthier products, so labelling is very important. I know that the Commission is studying various kinds of labelling. We are

introducing it for certain kinds of foods, but we have to do it in a meaningful way for the consumer. I think this will also have an influence in the calculation of good nutritional habits.

The sixth point is something we have already done in part and is to do with special diets and traditional foods. What are special diets? These are diets for athletes or bodybuilders – there are all sorts of special diets. These will come under several kinds of EU legislation within 1 or 2 years and we have to agree with Council what this particular legislation will include. The same is true for traditional foods, some (not all) of which are very important in conserving healthy habits – olive oil, for example. These special kinds of foods and traditional foods are very important and merit our attention for coming EU legislation.

I have a seventh point which is a little controversial. It has to do with using financial tools. This is the most difficult part and will meet the most resistance, but let us discuss it. It is taxes – lower taxes or higher taxes. This will meet the most resistance because people will say that it is against competition in a free market. However, you have to remember that we also have other priorities in the European Union, and public health is a priority. If you think about how much money is spent by national governments on health services – we spend billions of euros –

then you will appreciate the need to use all sorts of tools to really get rid of this high bill for providing services to people who suffer from cardiovascular disease, cancer and many other things. If we make an effort, we can succeed in doing something in this area by using financial tools for promoting good traditional habits in order to alleviate or prevent diseases. An important part of these financial tools would be cheaper advertisements in the media for these kinds of issues, because advertising is very expensive today. If the media agreed to promote these kinds of advertisements for healthy food, healthy habits or information campaigns, that will also be great.

These are tools we can use in the future. We have the coming EU legislation and I am sure many things can be done at the national level. National governments can do a lot of things, especially in schools, by promoting these nutritional habits and behaviour in children very early. We will do our share at the European level regarding data-collecting data programmes, promoting research in the field, or even using some financial tools in order to make sure that Europe changes nutritional habits. That will be a great contribution to public health because if we can change and introduce healthier habits to the citizens of Europe, we will definitely have a fantastic effect on public health and on the prevention of many diseases. Thank you very much.

Discussion

Member of the audience – *President of the Society of Journalists, France*

I am pleased to hear that there is going to be much more money and political strength behind the health policy. I am now President of the Society of Journalists in France, but I started 25 years ago as a doctor. Money is given to the doctor as a drug distributor. Our teachers and hospital heads were given money by the pharmaceutical industry. The doctor's role is not even being thought of. The social security system in France does not recognise prevention consultation and the doctor is supposed to give therapeutics. At present, prevention is not a recognised medical act reimbursed by the social security, so there is a very important economic background if you want doctors to be involved in this programme.

I was appointed to train their managers in marketing advice in a big distribution system called Auchan 15 years ago. I explained what we explain today: lower the sugar, salt, saturated fat, change the fat, push omega-3. We did a nice campaign on salmon, but in the background there was an enormous amount of money being put into the promotion of fats, sweets and salted products. Again, 15 years later, I have been appointed by Auchan to re-do the same training, and they are much more open this time. They say it is fantastic, you are right, but when we promote these fruits and vegetables and bio-products (and they even tried Max Avalor), nobody buys them.

I think that if we want the industry, the distributing networks and the doctors to be involved, they need some economic incentive. I think the industry can make money with good products; I think the doctor can make money with prevention, but this also has to be economically rewarded. It is David against Goliath at the moment, and that is what I have been experiencing for 25 years. We have been sending good messages but there have been no means behind. That is why I am so pleased to hear that Finland has done it and that Europe is going to do it.

Jean SALES - *A French producer of vegetables and President of the Council of the National Office of Fruit and Vegetables (Conseil de direction de l'Office National des Fruits et Légumes)*

I wish to intervene again on the problem of price. Before this round table, one of the eminent speakers expressed to me the irritation of the scientific community regarding the problem of the price. This question also concerns me. If a better accessibility can be obtained by a reduced price and makes it possible for all to consume fruit and vegetables, in abundance, daily, under all the social and economic conditions, we will all be very happy. However, in their great majority, the speakers tackled this problem by implying that the price of the fruit and vegetables was too high. The weight of the moral and scientific authority of the scientific community is such that it is important to be prudent in such statements. I propose to you, before the next EGEA, that a study be carried out by independent experts, agronomists, lawyers and economists, in order to determine whether, according to qualitative conditions which you state, fruit and vegetables are more expensive than other food. Mr Kamphausen said at the beginning of his intervention: "I was tempted to choose an ice-cream at the corner of the street because they are splendid and good". I imagine that this ice-cream would have cost approximately 3 euros. If in the cone he found pieces of kiwi instead of ice cream, at the price of 3 euros, wouldn't he have found that it was actually very expensive? Thank you.

Jacques VANOYE – *President of Apple Marketing Commission, France (Président de la Commission Marketing Pommes, France)*

My question is mainly for Professor Trakatellis and the political authorities. How do you explain that while almost everybody at the scientific and political levels agree with the fact that we have to change our nutritional habits, at the same time the EU has reduced the budget dedicated to the promotion of fresh fruit and vegetables?

Elio RIBOLI

That is a specific question. Are there any other comments?

Member of the audience

I have two questions for Antonia Trichopoulou. You mentioned that over the last few years in Greece, vegetable production has decreased. Why was that? Was it because the crops were bad, or was it for deeper reasons, that the producers leave agriculture and there are no young workers to replace them, for example?

What do you think is the main problem in the Mediterranean countries for maintaining the traditional Mediterranean diet? Is it that the consumption patterns are changing from a traditional diet to a less healthy diet because of globalisation? Or is it that the producers of traditional products in general are finding difficulties because they must compete to keep their production levels or even the quality of their traditional products? If that is the case, maybe we should think of specific supply policies and of new ways to promote these traditional products, both in our country and abroad.

Elio RIBOLI

Are there any other specific questions or comments?

Member of the audience – the Netherlands

I have a question for Professor Pietinen. I was very interested in the food-labelling system you have now in Finland for 'Better Choice.' We are thinking of this ourselves in the Netherlands but we are struggling with what is best, so I was curious about your experience in Finland about how to arrive at this healthy stamp.

Elio RIBOLI

We have three specific questions. One is about why the European Union has reduced the budget to support the promotion of fruit and vegetables. Who would like to answer?

Wilfried KAMPHAUSEN

I would suggest that for the next edition of this conference, you invite colleagues from the Commission's General Directorate for agriculture. I am speaking here for the General Directorate for health and it is a known fact that we do not always agree with what

our colleagues do in the agricultural policy. The most prominent example of this is the fight we had for many years on the tobacco subsidies, where we, as the health DG, were campaigning against smoking, whereas our colleagues in the agriculture DG subsidised very heavily in a totally different order of magnitude, with about 1 000 times the amount, the production of tobacco in Europe.

Changing things in the agricultural policy takes time, but it is also possible. The Commission is officially committed now to phasing out the tobacco subsidies, and now that is over, I think we have to look into other issues. Certainly, the possible imbalance between promoting meat products, cereal products and full fat milk products, and the promotion of fruit and vegetables, is something we will have to look into. These are things which are going on at the Commission level between the Commission services. However, I cannot defend here things which are decided in the agriculture DG, so I would suggest that for the next edition, you invite a colleague from DG Agriculture. These are very interesting questions and I think they need to be debated.

Antonios TRAKATELLIS

I would like to say that the European Union's agricultural policy is a very important of the European Union. I have to remind you that a great part of our budget, maybe 40%, goes into this area – and rightly so, because we have many people employed in this sector. Having said that, I would agree with Mr Kamphausen from the Commission that it would be a good idea to invite somebody from that important sector of the Community to contribute his point of view.

However, I will also say that overall, we have increased expenditure in the area contributing to better nutrition. I have to remind you that we have the public health programme and we are occupied with many kinds of legislation in the European Union, especially in the area of nutrition. Therefore, European Union interest, according to my estimation, is increasing. Why? Because public interest is increasing and the political will is there. I think we have to continue pushing in that direction and we are probably going to have changes in the agricultural policy in the near future.

Elio RIBOLI

Thank you for this comment. It is certainly very reassuring from my point of view to see the major improvement in the balance of the allocation of funds from what was the case 6 years ago when the Europe Against Cancer programme was allocated 12 million euros to fight against cancer, and the growth in tobacco production was allocated 1 100 million euros the same year. Obviously, that created some uneasiness for those who were fighting to prevent cancer. We are very pleased to see that things have substantially improved now at the European Commission and European Union levels.

There was a specific question for Antonia about why there is a decrease in the production of fruit and vegetables, and a decrease in consumption.

Antonia TRICHOPOULOU

The decrease in production is related to the fact that it is not economically rewarding for those working in fruit and vegetable production. They usually prefer to work in big hotels or in big cities. That is why our nutrition policy will focus on traditional foods which are very often of high quality – thus having an added value, they might attract people to go back to producing them.

As for maintaining the Mediterranean diet, you might know that there are several actions. One started in Spain with the Society for the Advancement of the Mediterranean Diet. Another was initiated in Calabria and is now moving to the university in Rome. It is not limited to the EU Mediterranean countries but also includes the North African and Middle Eastern Mediterranean countries. There is also a movement in Greece. We collaborate with all three networks and our first task is to agree on a definition of the traditional Mediterranean diet and the definition of traditional foods, because I think they are related to health, culture and the economy.

Elio RIBOLI

Thank you, Antonia. There is now a question for Dr Pietinen about the food-labelling system in Finland.

Pirjo PIETINEN

You are referring to the 'Heart Health' symbol launched by the National Heart Association. It required a lot of work to set up the criteria and they are food-specific. I have not personally been in that group, but if you send me an e-mail, I will find out about the present criteria for you. I think it is good to know the available criteria that could possibly be modified for the Netherlands and you would have an idea on what we ended up using.

Elio RIBOLI

I think this is an extremely delicate issue. I have been involved in discussions at different levels about the meaning of labelling what is healthy and what is not. I think it may be important for future occasions to have a specific discussion on what evidence there is that this kind of labelling would improve consumer choice. There probably is evidence, but there is also a lot of concern raised by the food and distribution industry about what it would mean having red, orange and green, for example, labels – what is bad, very bad, may be bad, very good – put on different foods. I think it is a very important issue.

Pirjo PIETINEN

This label only means that it is a super-healthy product – bread with low salt content, reduced salt content and high fibre content – there are no greens or yellows. It is a sort of guarantee that if you choose one of these products, it is a good one.

Elio RIBOLI

This is very important because it is one of the options. Is there any last comment?

Member of the audience

I am from Freshfel, the fruit and vegetable industry body representing the industry. You spoke about the 6 million euros being cutback to 4 million euros and I would hate the questioner to go away with the opinion that the industry is doing nothing about that. I happen

to assist as Vice-President of the consultative body for the Commission. We have been writing to the Commission about this cutback and making representation at various meetings of the consultancy with the Commission about this, because to us, it is incomprehensible as to why it should go from 6 to 4 million euros, especially when you consider that the European Union has been increased by another 10 countries. I would just like to say that we are doing everything we can to DG agriculture to try and get an increase.

Elio RIBOLI

Thank you for your comment. I will give the last word to Professor Trakatellis.

Antonios TRAKATELLIS

I will just make a comment about globalisation. It is true that globalisation may have adverse affects in this area, but at the same time we have an increase in public awareness. I was very interested in following the story in the United States that some people are starting to show big chains like McDonald's that they are fat harbingers to which they attribute the obesity of children. As a result, McDonald's is thinking of offering some different products to the public. I know in Greece, we have a chain similar to McDonald's which offers vegetarian sandwiches and certain choices. I think globalisation has its effect, but there are counter effects today and people are very much aware. That is why I think we are at a turning point and that industry is starting to take into account the new era in the area of nutrition. This could be good, because industry is there to make money and will therefore have to change, and if this can be combined with good public health in Europe, that is even better. I think this is what we are going to see in the future

Elio RIBOLI

Thank you. We can close on this positive note that there is good hope of finding a solution that would accommodate everybody's needs.

Introduction

Adam DREWNOWSKI

University of Washington, School of Public Health and Community Medicine, Seattle, Washington, USA

This session is devoted to the topic of snacks

The first presenter is Dr Didier Chapelot. He will talk about the metabolic responses to snacks, and deal with the physiology of leptin, ghrelin and insulin. Following his presentation, Dr Jane Wardle from London will talk about children's preferences for vegetables and fruit. Following that, we will have a presentation from Dr Susan Jebb on snacking and obesity. I will close the session by introducing a new way of assessing nutritional density of foods presenting some of the joint work done by myself and Nicole Darmon from Paris. We looked at nutrient to calories ratio and the nutrient to price ratio.

So the theme of the conference will go all the way from metabolic aspects of snacking to public health to communication. I suspect we will come to the inevitable conclusion that where snacking is concerned, only vegetables and fruit are the naturally nutrient-rich snacks. We will build up in terms of science, starting with metabolism and physiology.

It is my great pleasure to introduce Dr Didier Chapelot from Paris who will talk about the metabolic responses to snacks: leptin, ghrelin and insulin.

Metabolic response to snacks: leptin, ghrelin and insulin

Didier CHAPELOT

Physiologie du Comportement Alimentaire, Université Paris 13, UFR Santé Médecine et Biologie Humaine, Bobigny, France

The title of this presentation is “Metabolic responses to snacks: leptin, ghrelin and insulin”. Paradoxically, today there is no standard definition of what is a snack. It is quite a problem because the relation of these three hormones with this eating occasion will depend on the definition of “snack”. So I will try here to examine the question of this definition.

Apparently, the situation is quite simple. To trigger the eating behaviour, the organism produces a sensation which is hunger. Then, of course, animals (and we are animals) eat when they are hungry..., or when they are not, since observation strongly suggests that sometimes eating can occur without any previous hunger cue. We can summarise this in the following sentence: all hunger signals lead to eating, but eating does not always seem to be motivated by hunger.

One of the best known examples is the cafeteria rat. When rats are provided with only chow or with a wide variety of highly palatable food items, there is a striking difference in energy intake and body weight gain. As you can imagine, the cafeteria rats become heavier than the control rats. The question is: is the rat on a cafeteria diet hungry before eating?

In a classic study, Rogers and Blundell provided rats with only bread and chocolate. They observed that food intake dramatically increased as early as the first day, and remained elevated throughout the month. As expected, there was too a very strong increase in body weight. Cafeteria rats became twofold heavier than the control groups.

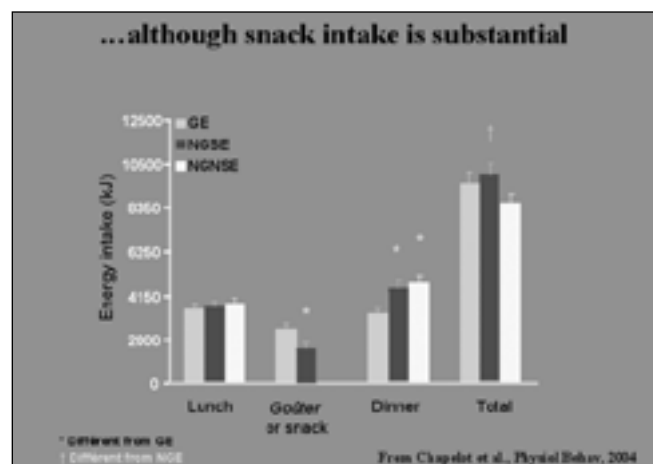
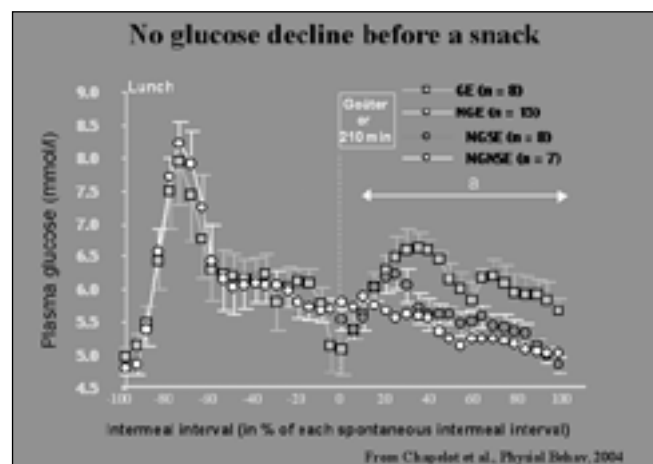
When we look at the evolution of meal size and meal frequency, we see that both become very elevated as early as the first day, suggesting that in the cafeteria rat, eating can be re-initiated during the usual satiety period. So rats may not always be hungry when they eat.

There is another very important point to be made in this study. Three months later, meal frequency became lower in the cafeteria groups than in the control group. This suggests that this supplementary eating occasion is sensitive to metabolic control. One hypothesis is that fat deposition will lead to an action on satiety, as we will see later. So in the presence of cafeteria food, eating is re-initiated during a usual satiety period. This suggests that these eating occasions are not meals and could be called snacks.

The questions are: do we really need to take into consideration whether the animal is hungry or not hungry before eating? Is this relevant to human eating behaviour?

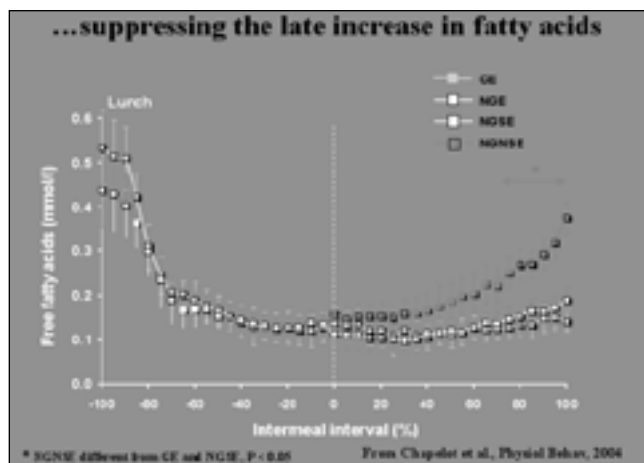
Some years ago, we showed that if biological parameters could help to discriminate between eating in a hungry state and eating in a non-hungry state, this would strongly argue for a distinctive mechanism between these two eating occasions. In particular, biology might help to assess whether the mechanisms leading to snacking are similar to usual meal eating, and whether consuming foods as a snack or as part of a meal have different consequences on further metabolism.

In 1980, Jeanine Louis-Sylvestre published a very important paper showing that before a meal there is a blood glucose decline. This profile was considered as driving hunger leading to meal intake, the meal being interrupted by satiation which relies mainly, as shown by David Booth, on sensory cues. Then you have satiety, which is determined firstly by metabolism. The causal relation between the blood glucose decline and the meal onset has received much support in humans, such as in a study by the team of Margriett Westerterp-Plantenga. On a stable baseline, a 5% decline in blood-glucose for 15-20 minutes preceded meal requests by subjects who could ask to eat whenever they wanted. So if meals are eating occasions preceded by a blood glucose decline, we have some concern about the fact that snacks can be considered as meals for some reasons. First, Campfield showed that in rats, this profile is not observed before the conception of a new highly palatable food that we can call snacks. Then, we found recently that in humans, this profile is not observed before the consumption of food during a usual satiety period.



In a study recently published, we selected two groups. One group of subjects who always eat something in the afternoon between 4 p.m. and 5.30 p.m., an eating occasion called in France the *goûter*. Another group consisted of subjects who never eat anything between lunch and dinner. In half of this second group, we presented highly palatable food that they could eat, entirely, in part or not. You will not be surprised to learn that they all ate something. This food was presented 210 minutes after lunch, the usual delay observed between lunch and *goûter* in the *goûter* eaters. We found that only usual *goûter* eaters had a blood glucose decline before this eating occasion. At lunch, energy intake was similar between groups. Then at the *goûter* period, non-*goûter* eaters ate a substantial amount of energy, but less than the *goûter* eaters. The opposite was true at dinner intake, non *goûter* eaters ate more than *goûter*-eaters. On the whole, the snack increased energy intake during the experiment. Moreover, the snack leads to only a slight rise of plasma glucose until dinner, but a dramatic insulin increase. The main consequence of this high insulin level was to suppress the usual increase in free fatty acid that we all have when we have not eaten for 6, 7 or 8 hours. Therefore, the snackers did not display any increase in free fatty acids.

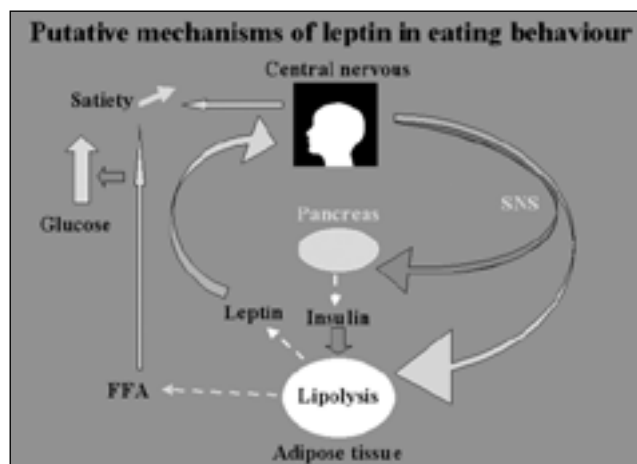
You could say that *goûter*-eaters did not show either this increase in free fatty acids, but there are arguments suggesting that when you have higher meal frequency, the metabolism relies less on fat stores. This was found in a study where the snack was mandatory and energy fixed about 1 h after lunch. We observed that the snack led to high insulin secretion and also to a reduction in free fatty acids. It is important because free fatty acids in the late part of the interval between two meals contribute to satiety in sparing glucose, and therefore in delaying the next blood-glucose decline, meaning a later meal request. Interestingly, after eating



the snack, there was no difference in the delay of dinner request. Furthermore, intake was similar in the two conditions. It was of course important to demonstrate that these free fatty acids were oxidised, and we did that some years ago. The high insulin secretion after the snack was associated with a higher respiratory quotient, which means that a smaller amount of free fatty acids was oxidised at the end of the interval.

Now, did the other blood parameters provide interesting data for understanding snacks? Not really. Thus, plasma leptin was not very different between snack-eaters and non-*goûter* eaters, except maybe that the level remained a little bit elevated until dinner. Nevertheless, there was no change in leptin levels before the *goûter* or the snack. However, leptin provided interesting information about other topics.

I will first briefly present leptin. Leptin is a hormone secreted by the adipose tissue and when the adipose tissue becomes larger, leptin is more secreted. Leptin is also considered as a satiety factor. Most of other studies cite the behavioral-mediated effect of leptin, which means that the brain leads to increased satiety. But people often forget that leptin can act in a peripheral way, firstly via the sympathetic nervous system in stimulating lipolysis, and also enhancing this effect by inhibiting insulin secretion. This leads to the release of free fatty acids by adipocytes. These free fatty acids can contribute to spare glucose via the glucose-fatty acids cycle, and therefore help to enhance satiety.



I personally think that leptin is not so much involved in satiety than in satiation. In a first study published in 2000, we found that there was an inverse relation between plasma leptin at the onset of the meal and energy intake at this meal, at lunch or dinner. This was observed in a between-subject study. In this study, we found again an inverse relation between leptin levels and consumption or energy intake at this afternoon eating occasion, whether this was a snack or a *goûter*.

Now we move to ghrelin. Ghrelin has received less support than leptin for its action in eating behaviour. However ghrelin can increase energy intake and ghrelin increases before meals. We have recently undertaken a study with David Cummings in which we observed a decrease in ghrelin after the meal and then, after 50% of the examined interval, an increase sustained until the dinner request. There was a great overlap of the hunger curve, this overlap being actually found in every subject. However, we found that some subjects did not have this late increase in ghrelin, and this is quite a problem. In the *goûter* study, there was actually an increase in ghrelin before the *goûter*. This increase was rather small but significant. In most subjects, however, ghrelin did not increase before dinner.

What is the explanation? The main explanation for this seems to be insulin. Why? Because ghrelin and leptin do not modify the model according to which insulin is the pivotal step between metabolism and eating behaviour. It is well known now that insulin and leptin are positively correlated, and we have shown with others that the relation of ghrelin to insulin is inverse. In the second study, we will publish the same inverse relation: the more insulin you have, the less ghrelin you have. And the insulin in *goûter*-eaters does not return to the baseline level before dinner.

To conclude, what can we say about leptin and ghrelin in relation to snacking? For leptin, there is no difference in the preprandial level profile between a meal and a snack, but there is a tendency

of a sustained elevation after a snack. To date, there are no studies on ghrelin and we hope to do some in the near future. This would help to answer to two questions. Do preprandial

ghrelin increases observed before the goûter occur before a snack, and does the snack-induced insulin increase lead to a decrease in ghrelin?

Questions

Adam DREWNOWSKI

My question is whether or not the metabolic impact of snacks is driven by calories alone, or does the energy density of the snack play a contributory role? On the one hand you have potato chips or a chocolate bar, for example, on the other hand you have fruit – caloric value may be the same, but the energy density would be very different. What would you say would be the metabolic consequences?

Didier CHAPELOT

Where ghrelin is concerned, the important thing is the foods and the nutrients. There is no decline in ghrelin after protein, but there is a small decline with fat and a very sizeable decline with carbohydrates. However, you cannot say that this is a good way of measuring satiety because protein provides rather high satiety, and there is nothing dealing with the relationship between snacks and ghrelin published to date. For leptin, the more carbohydrate and the more insulin you have, the more leptin you will have. The main problem with leptin that everybody should be aware of is that leptin is the "illustration" of fat mass, but during the day the profile of leptin is the illustration of what we eat. We should articulate these two phenomena and not confuse them.

Member of the audience

Do you get the same release of leptin when you get carbohydrate from fructose and glucose, or is it different?

Didier CHAPELOT

We did not perform this study, but it is clear that glucose will secrete more insulin and that you should have more leptin with glucose. I do not think the study was done. It was quite a surprise because leptin was considered as being linked to fat storage, and to see that carbohydrates are the main determinants of leptin was quite apparently paradoxical, but you should always consider insulin as doing a job.

Member of the audience

You say that snacking leads to an increase in insulin. If I remember rightly, some years ago it was shown that dividing the daily food intake into several meals, but with good compositions, leads, on the contrary, to a decrease in global insulin secretion, so the energy density in the fibre of snacks changes. Have you any comment about that?

Didier CHAPELOT

Yes. For the past two years I have been working on meal frequency and we submitted a paper that I hope we will publish in the further months, showing that if you decrease meal frequency, this leads to increased fat deposition. So this argues for the role of higher meal frequency being better than lower meal frequency. However, Jenkins had shown what you are saying and actually the pivotal relation between meal frequency and fat deposition is also insulin. I think perhaps that we can say that eating fruit and vegetables is advantageous in that it leads to slight insulin secretion.

Inaudible question

Didier CHAPELOT

That is why I asked the question. Every study on meal frequency confuses the two. So the fact is that we must in the future distinguish between "we eat 5 to 6 meals a day because we are hungry and we have done that for a long time" and "we eat 3 meals a day and we eat foods between these meals and we are not hungry when we eat these foods". This is the reason why we are working on that. As far as the question of whether there are biological distinctive parameters is concerned, I think we have shown that there are. As to whether there are differences in consequence, I think there are many.

Adam DREWNOWSKI

Now, the next presentation has everything to do with public health policy. We heard yesterday from Dr Lorelei Di Sogra that in the United States, we have a programme to distribute fruits and vegetables as snacks in schools to schoolchildren. This is costing 6 million dollars in six states at present, and we are planning to take it nationally at a cost of 42 million dollars for all the states. To take it nationally for every school in every state, the calculation was in the region of 4.5 billion dollars.

A similar programme is underway in the United Kingdom, where children in schools in lower socio-economic areas are being given fruits and vegetables as snacks. However, there was also a question from the audience yesterday from a gentleman from Milan who mentioned that he provides free fruit and vegetables to schoolchildren, but there is a lot of waste and a lot of the food comes back. So we need to know everything there is to know about the preferences of children for vegetables and fruit, because on one hand we are creating supply, but on the other we need to create demand as well, so we have to talk about both axes and the shaping of preferences.

Predictors of fruit and vegetable consumption by children

Jane WARDLE

Cancer Research UK, Health Behaviour Unit, Department of Epidemiology and Public Health, University College London, London, UK

Thank you very much. I am going to talk today about understanding fruit and vegetable intake in children, and I will be talking mostly about individual differences – why one child likes them and eats them more than another.

This picture characterises the modern British child's diet, and I regret to say that many European countries are moving in this kind of direction. If you look at the sorts of things these children are eating, then it becomes apparent in a Mediterranean diet conference, that what is missing is fruit and vegetable intake.

The modern 'children's diet'
(from J Blythman, *The Food our Children Eat*, 1999)

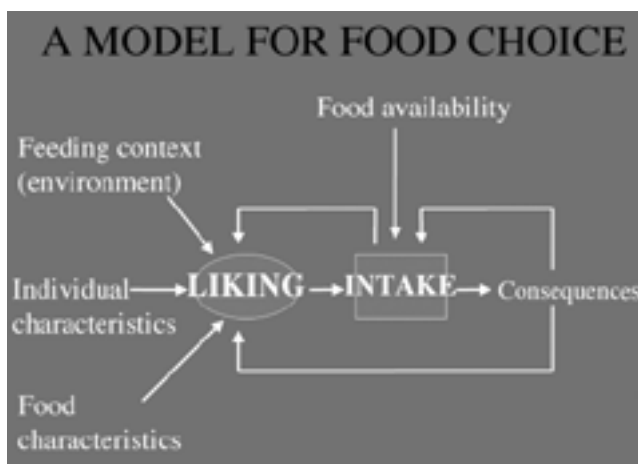
- Sweetened children's cereals (low fibre, added sugar)
- Burgers / sausages (low grade meat and cereal)
- Poultry or fish in breadcrumbs (low grade meat with added fat)
- White bread
- Fries
- Pizza (highly refined dough with processed cheese and sweetened tomato)
- Sweets, biscuits, crisps
- Carbonated and sweetened drinks
- Dairy desserts (fatty and sugary)
- Ice cream (usually blended fats and sugar)

Using the same kind of measure as was mentioned by Knut Inge Klepp and other people, you can see that around a third of British children are eating fruit less than once a day, but encouragingly, you also have around a quarter or a third who are eating it more than once a day. If we could understand something about what puts people in one category rather than another, this might be helpful. The picture is similar for vegetables – again, these are missing from the diet. Around 40% of British children are eating vegetables less than once a day, and only around 15% are eating them more than once a day.

This picture shows the kind of model I have been thinking about when trying to understand children's intake of fruit and vegetables – giving 'liking' something of a priority here – and looking at characteristics of the individual, characteristics of the food, characteristics of the context – which might influence liking. This in turn has an effect on intake – and, of course, there are consequences of intake that might feed back onto some of these variables.

characteristics. These are some data from a sample of 428 four to five-year-old children looking at the proportion of children who say they do not like various kinds of foods. You can see that the outlook is bad for the vegetables. Almost 50% of British children are saying they do not like each of these fairly common vegetables. If you look at the protein foods then 10% to 20% of children – British children say they do not like these kinds of protein foods. If you look at

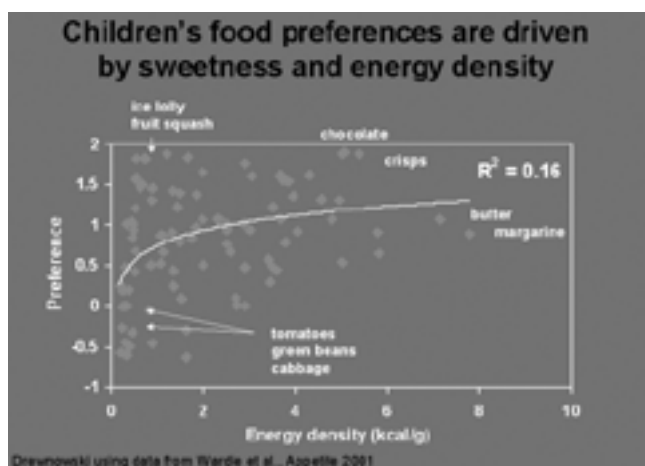
the fruit story, it is a great deal better than the vegetable story, but you still have 10% to 20% of children saying they do not like each of a number of fruits. The only foods that come out well are the starchy, sweet and high fat foods, where you have almost no children disliking the majority of these foods.



What about the characteristics of the food which might influence preferences? One thing that is well established is flavour. Sweet foods tend to be innately more liked, and bitter and sour foods innately more disliked. I used my colleague Leigh Gibson's two-week-old son just to demonstrate children's reactions to sour foods. This is little Thomas Gibson, aged two weeks, who had always been breast fed. Here he is being given his first taste of water, and you can see he looks interested in tasting the water. Here he is being given his first taste of sucrose solution, and he is licking his lips very cheerfully. Here he is being given a taste of lemon juice, and he reflects the two week old child's resistance to this kind of taste.

As Adam mentioned, we have also been interested in energy density as an influence on food liking. Adam himself conducted some analyses on our children's food preferences, looking at the relationship between the energy density of various different kinds of foods and the liking for those different kinds of foods in children. By reanalysing our data, he showed that fruit and vegetable foods, which are relatively low in energy density, come right down here at the low end of the preference scale. Up at the top end of energy density and preference are the high fat, salty, sweet snack foods.

We have done the same analysis specifically within fruits and vegetables and interestingly, you still see the same kind of effect. It is drawn the other way round here, so we have energy density, liking for food and all the fruits and vegetables which were in our analyses represented on here. So at the top are the relatively more energy dense fruits and vegetables which are better liked, and down at the bottom end you have the fruits and vegetables which are lower in energy density. These children typically describe themselves as not liking.



So we could conclude from these results that part of the reason why intake of vegetables is likely to be low is that the low sweetness, low energy density and, for some of them, the higher bitterness, will all tend towards producing lower liking. Intake of fruits may also be low because of relatively low energy density: although some fruits are sweet, not all fruits taste very sweet, so we have relatively low sweetness, especially compared with the sweet snacks that are available and higher sourness leading to lower liking. What is more, fruits and vegetables are frequently offered to children as an alternative to very high fat, very high energy dense foods, and we know from other studies that that a more preferred alternative can influence preferences for the target food.

I will now move on and give you a little data from our studies on looking at the feeding context – the environment that parents provide for children – and looking at how that might influence fruit and vegetable intake. I am looking at three groups of characteristics: availability and modelling in the home, exposure and reward, and health claims which parents might make for the foods they're offering the children in the home.

One of the things that tend to be true within the home is that foods that are in the home are those that parents have chosen to eat. These are foods that are provided there for the children, so that food being available and food being modelled as being eaten by parents tend to go together. This is an analysis from a community sample of 564 3 to 5-year-old (nursery age) children, in which parents completed a questionnaire about their children's fruit and vegetable intake, their own fruit and vegetable intake, and a whole number of other characteristics about the child. However, what you see here and what comes out in study after study is that parental intake is invariably the strongest correlate. These are just univariate correlations but it comes out just as strongly if you use multivariate analyses. So what the parents are doing, which reflects both what they model to their child and availability in the home, is a powerful determinant of what the children are going to eat.

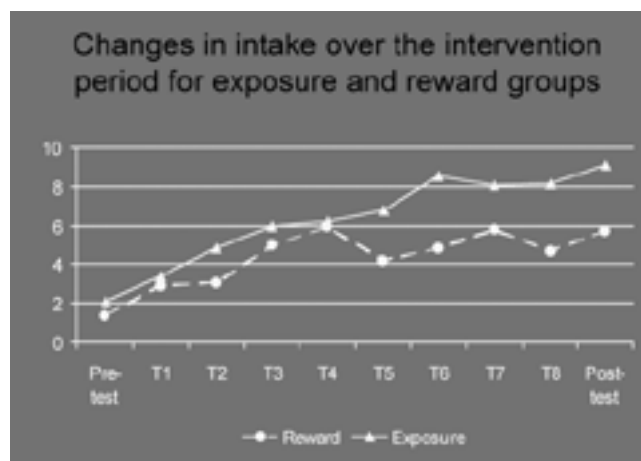
We have also been looking at children being specifically exposed to foods. The first study I did was a small study of children in primary schools, in which I compared getting them to have little tastes of a vegetable they did not like with being given little tastes and promised a reward for these kinds of foods. I looked at the effect over a week, either of daily exposure over eight days (exposure group), daily exposure with a reward over eight days (reward group), or no exposure (control group). We used red pepper. I do lots of studies using red pepper in England because raw red pepper is a convenient food, it is a food that British children do not like very much, do not have very much, and it is

one you can easily cut into little pieces.

Each day the children were asked if they would like a tiny taste of the food and you see a steady increase in intake over the days. Compared with the control group, in the exposure group, you have a dramatic increase in liking for the food over the exposure period. There is a significant increase compared with the control group. The group that has exposure also shows a big increase in the amount of food they are prepared to eat at the end of the exposure period, so we can show that daily exposures both increased intake and liking compared with the no treatment group.

We were also interested in what happened if we said "if you eat this you can have a reward". These were our observations in the reward group. You can see that promise of a reward also increases intake of vegetables over the time period but interestingly, not quite as strongly as in the non-rewarded group. If you look at the change in liking from start to finish, then the reward group comes out intermediate between the exposure group and the control group. The phenomenon is the same for intake: the control group increases a little bit, the reward group increases a little more and the exposure group increases more. To summarise these results, this indicates that this exposure-based intervention can both increase liking and consumption. The finding that the reward group comes in between 'exposure' and 'control' suggests that somehow reward may limit the effectiveness of exposure. The model that we assume is in action here is that the children think "if they have to offer me a reward to do this, then maybe it isn't all it's cracked up to be".

We then wanted to see whether we could get the same kind of effect of an improvement in liking and intake if we asked the parents to do this exposure procedure – after all, it will be the parents that will do this in real life if it is going to be of any use. We explained to the parents that we wanted them to give the children tiny tastes of the food every day for two consecutive weeks, and then we tested the children's intake and liking of the food in the lab before and after they had done this. We did not use a reward condition in this, but we used a control condition in which parents were given a leaflet about healthy eating and encouraged on the importance of getting their children to eat more fruits and vegetables. You can see what happens here as a consequence of the parents doing two weeks of this daily exposure. You get a small increase in liking in the control groups, you get a bigger increase in the children's liking for the vegetable which they had been doing the taste exposure on in the children that had exposure. If you gave the parents a healthy eating leaflet, it actually seemed to make things slightly worse. You get the same kind of pattern of results if you look at changes in intake in our taste test before and after, rather than just changes in liking.



I would like to mention one other thing relating to what parents might do within the home – and anybody who is a parent here will have done this – which is to make a health claim to your child, for example you say “this will be good for you”. Some years ago we conducted a little experiment on the effects of making health claims to children about the food they were being given to eat. These children were presented with a novel drink – this was not a fruit and vegetable study, it was a fruit drink that children were told we were testing for possible marketing. All the children got the same drink, but half of them were told it was just a new drink we were testing out, and the other half were told it was a new health drink that we were testing out. We measured whether they liked the taste of it, whether they wanted their mother to buy it for them, and whether they would suggest to their friends that it was something nice to drink. You can see here that all you need do is tell children that something is good for them and you can diminish their liking for it.

Lastly, I want to move on to individual characteristics, i.e. the features of the individual that might influence behaviour. One of the things we noticed very strongly when we talked to parents is that they will say things such as “one of my children has always liked vegetables a lot but the other doesn’t like them very much”, and there tends to be quite a strong assumption in parents’ heads that these characteristics - liking or affective responses to food - are innate or predetermined and possibly unchangeable. So one of the things that we have been interested in looking at is how much difference there is between individuals in their liking and what kinds of explanations there might be for it.

The first bit of data I am going to talk to you about is the heritability of food preferences. People have been trying to see how heritable food preferences are for rather a long time, but for the most part they used fairly small studies and a rather arbitrary and small selection of foods which they work on. We used twin data from the same data that I showed you earlier. I am sure you are all aware that you can use twin data to assess the heritability of things. If food preferences are heritable, we would expect likes and dislikes to be much more similar in identical twins, who are obviously genetically identical, than in non-identical twins, who only on average share half of their genes.

So these are results from 214 same-sex twin pairs. Half of the twins are MZ pairs and half are DZ pairs. Representing the correlations between the twins are the blue bars for the DZ pairs, the non-identical twins, and the green bars for the identical twins. What you can see is that twins are quite similar, as you often find in the case of siblings. They are all fairly similar in their food preferences, but for all of these food types the MZ twins come out as slightly more similar than the DZ. I should say that what we did was group all of our foods into dessert foods, meat and fish foods, fruit foods and vegetable foods for these analyses, so we are averaging across a lot of food preferences. Then you can use modelling techniques to estimate the heritability. What you see here is some interesting variability between foods, so the liking for these protein foods comes out as significantly more heritable than for any of the other food types. Parents are often quite certain that vegetable liking represents an innate and unchangeable characteristic. But we only have 30% heritability for vegetables. The figure is slightly higher at 50% for fruits, and is very low indeed for dessert foods. So we have evidence for slight heritability but the majority of the variation is environmentally caused variation. Although I do not have the data here to show you, in fact almost all of that is shared environment effect, so these are things that are going on in the home that explain variation.

The other characteristic we have been interested in is child temperament, and particularly the phenomenon of being a picky

eater. Anyone here who has children will know about these picky eaters who say they do not like all sorts of things. We found that about 10% to 20% of parents will describe one of their children as being a picky eater. There are a number of different ways of assessing it, but one that has been most widely used is the measurement of something called neophobia – fear of new food – which typically emerges somewhere between the ages of 18 months and 2 years and manifests itself as avoidance of and reluctance to eat unfamiliar things. It is particularly frustrating for parents when the child says “I won’t try it but I know I don’t like it.” We used Patricia Pliner’s food neophobia scale for these data and this is the same community sample that I showed you before. These results show the relationship between children’s scores on the neophobia scale and the frequency of their consumption of a whole lot of different food types. One thing you see interestingly is that neophobia is much more strongly related to vegetable intake than to any of the other foods, so if you have a child who has this temperamental reluctance to eat new things, one of the things that will come out strongly in this is vegetables. Fruit is also quite strong, meat is relatively strong, but no neophobic child says “thanks, but no thanks, I won’t like this new chocolate; I’m not going to try it.” So when it comes to sweets, which are high energy dense, your neophobic child will just pop it in its mouth and give it a try. It is not the same for a new leaf they have never seen before.

The last bit of data I am going to show you is concerned with looking at the relationship between the children’s school neophobia and what they ate when we gave them a series of test meals at school. The previous data had been based on what parents said about what their kids would like and eat, but we wanted to see if neophobia still predicted what children would eat when we measured what they eat. So the measurements were taken in school and the children each had their lunch in a little dish which had all the different food components in it. We weighed and measured each child’s meal tray before and after. They had protein foods, some fruits and vegetables, some starchy foods, and some fatty and sugary foods. Interestingly, you see the same kind of effect here. In terms of the volume of intake of fruits and vegetables, you saw a strong relationship with the neophobia score, likewise for the protein based foods, but there was no correlation whatever between children’s neophobia and their consumption of these other two kinds of foods.

To sum up what I have been telling you about influences on children’s fruit and vegetable intake, these are the things which I think may be important influences which can make a difference between consumption and refusal, and liking and disliking. Sweetness and energy density of the food is obviously a major determinant, but the food environment and parental intake are also very important. The kinds of strategies that parents use – bribing, arguing and making health claims which are the typical things parents do – are all having adverse effects. Children do have inherited taste preferences and differences in their preferences, some will like fruits and vegetables more than others, and in particular this neophobic characteristic will make a difference.

However, if you want to get your kids to eat their vegetables, these would be my recommendations. First of all, have faith. Humans can learn to like everything that does not actually make them sick. Secondly, create familiarity. Start them young and repeat these novel tastes at least 10 times before you give up. Get good models in the child’s environment. Give them the opportunity to see others eating a wide range of foods – do not have your kids eating on their own separately from parents and others in the home. Be very careful with rewards and equally careful with health claims – do not use this as your major weapons in controlling children’s food intakes.

Questions

Didier CHAPELOT

With regard to the information, do not you think it would be important in the future to separate only the claim 'this is good for you', that 'this is healthy', and to provide a small and easy explanation? Do not you think that a little explanation will help to increase the effect of the information?

Jane WARDLE

I was slightly playing to effect there in terms of the health claims and I do think that once children reach an age of having some intelligence, they are susceptible to getting some kind of health information about food. So I agree with you, I do not think we should regard giving children information as a completely unacceptable way to influence them. In the end, they do need to know these things and they do need to make their own decisions. I think particularly though when children are smaller – we were looking at 3 to 5-year-olds and 5 to 7-year-olds – to start telling the children that the food is good for them may carry this rather specific message. The reason I think that is that the children learn over time that their parents only bring up this 'good for you' story when the child is already not wanting to eat the food, so that it actually becomes paired in the child's experience with something that is not very desirable.

Lorelei DI SOGRA

Jane, thank you for your excellent presentation. In our experience over many years providing fruit and vegetable snacks in schools – not just within the scope of the programme that is going on right now, but with children in the 3rd grade (7 to 8-year-olds), who are older than some of the children in your study – we found that just putting the fruit and vegetables out as a snack without any pressure, without any health messages, putting a wide variety out at snack time and making it fun led to a very high consumption during snack time of many servings. It was a case of the whole social environment being fun and just making them available.

Jane WARDLE

I think that is right, and certainly, other people have already presented data during this meeting showing that children do not see themselves as having very high access to fruit a lot of the time. Also, when fruit is accessible to children, there is often an implicit alternative. I think in some of these school fruit studies, one of the attractions is that you are not having fruit on one table and cookies on the next and asking which they would like, you are just providing them with fruit or vegetables.

Member of the audience

First of all, I am representing the fruit industry. The problem we have always borne in mind is this: when you have a headache you reach for the aspirin, so if you are not feeling well and we have an association with bananas or whatever, it can be very dangerous to make health claims in terms of fruit. This is just a general comment.

My other comment is that in working in Ireland with the food dude scheme and Professor Fergus Lowe, we found that rewards have been very helpful in cracking peer pressure in the playground. Maybe it is the psychology there that, given free access to fruit and vegetables, the kids will eat them and eat them more, but there are always a certain number of cool dudes in the playground who are called rabbits if they eat lettuce. It can be a good idea if they crack, then the rest of the class goes and you have got them on your side.

Jane WARDLE

I think that is absolutely right and Leanne Birch has also shown that same-age peer models would be effective. I think all the social psychology we know would suggest that if the peer models are cool peers and not nerdy peers, then maybe you get an even better result.

Member of the audience

Jane, I cannot thank you enough for your research here. I am so delighted to learn what you have been doing and I think we have been looking for it for a long time. Now I will go back and try to implement some of your wonderful results immediately.

At the end of your presentation, you mentioned that you might also go into limiting access to the bad stuff as part of your strategy. Let me just give you a new hint (I am talking on a personal level here): with my kids, we serve cup of fruits and vegetables, exactly at the moment when they are very hungry in the hours before we eat – they just have fruit lying in front of the television. This way of timing it to when the kids are actually very hungry is a very easy way to control what they are eating. Thank you.

Jane WARDLE

That is a very interesting point about timing and we have actually done a study looking at whether you can improve people's desire for fruit by feeding it to them at a time when they are very hungry compared with a time at which they are less hungry. Because it was based on some other work we had done, we reasoned that given that fruit and vegetables have a relatively low energy density, choosing a time when the person was hungry you would see a more visible change in their energy response to it and that would be a plus. In fact, the results were not very good. One of the things we discovered (and maybe we used a time when they were too hungry) is that if people are very hungry, then they do not want fruit. In fact, fruit seems undesirable and the effect of eating a small bit of apple when you are very hungry is to make you want a biscuit even more than you wanted it before you had eaten the apple. I definitely think this is something to look at a bit more – whether you can position fruit at a time of day in the diet which will maximise the learning of the pleasurable consequences of it.

Member of the audience

First of all, a comment that may be a little facetious. You are saying that rewards do not produce any success, but you tell children not to smoke and not to drink, they pretty soon want to try it out. Perhaps we should be telling them not to eat fruit and vegetables

and make out that they are adult foods, perhaps they would then desire them as part of a cultururation process. That is slightly facetious but there may be some benefit from that.

Jane WARDLE

Interestingly, children do like some of the “treat” fruits, and they seem to like relatively more fruits which they are not allowed freely. In Britain, strawberries are special – you can only have a small number of them and only occasionally – and children tend to rate those relatively more highly.

I think we showed that reward had an intermediate effect between no exposure and exposure. I am not saying that reward is necessarily a bad thing to do but I think it may carry an implicit message which limits the benefit from having repeated exposure towards greater acceptance of the food.

The previous member of the audience

In the North East of Scotland, we have an intervention in primary schools which involves disguising the fruit and vegetables by using energy-dense additions and making fruit smoothies using yoghurt or ice cream, and these are highly acceptable to the children. I wondered if you felt that using the energy dense foods to disguise was a way forward.

Jane WARDLE

Well, it has been studied very little. There was a brief period in which one of the frozen food manufacturers in England, producing chocolate-covered carrots and that sort of thing, which I think did not go down very well. If you look at cookery books and recipes and parent child-feeding books from 50 years or so ago, you see that the dessert was almost always a starch-fruit combination, including fruit pies and fruit desserts of various sorts. Certainly, in the British diet, these were very normal and actually seem to have disappeared from the repertoire. It may be that the effect of mixing low energy dense tastes with some high energy dense tastes could be a beneficial approach, so I think that is a very interesting approach.

Adam DREWNOWSKI

Thank you, Jane. We will move on to the next presentation. I think the question we had about the timing of the snacks and the consumption at various states of hunger leads us perfectly to our next presentation. There has been a great deal of controversy about the satiating value of different foods. People are asking whether or not fast foods have less satiating power than the alternatives, and whether or not we have liquid and beverages as our satiating power. In some of our studies, however, we found that what really makes the difference is not so much the physical nature of the snack, but exactly at what point during the day it is consumed. So the frequency of snacking and the timing of the snack may be the factor that links food consumption to obesity and overweight.

Snacking and obesity

Susan JEBB

MRC Human Nutrition Research, Elsie Widdowson Laboratory, Cambridge, UK

Introduction

This talk will focus on the issue of snacking and obesity and in particular on the kinds of foods and drinks commonly described as snacks. The Mediterranean diet is usually characterised by particular types of foods or certain dietary patterns. It is often forgotten that Mediterranean diet also emphasises food and meals that are freshly prepared and eaten in a very sociable context. That contrasts with an increasing trend in Britain and elsewhere for people to eat individually, perhaps just re-heating food in a microwave, or grazing on snack items. Family eating occasions in Britain are increasingly likely to be centred around the television than the dining table.

Methodological issues

One of the problems of research in this area is to define what is meant by a snack. Most people have a personal view, but it is not easily defined in a standardised methodological framework. Is it a food which is just simple and easy to consume or can be eaten very fast? This would include fruit or chocolate. But it might also include microwavable ready-meals or sandwiches depending on the timing. Are these a snack if they are eaten between regular meals, whereas a meal if they are consumed at lunchtime? Or is the defining characteristic about portion size? At what stage does the size of an item define it as a meal? There is huge confusion. Certain foods, for example, ice cream may be eaten as a dessert at the end of a meal or as a snack in the middle of the afternoon. All of these possible interpretations make it very hard in dietary surveys to define what is a snack and hence to determine its relationship with obesity.

Epidemiology is often the starting point for diet-disease relationships. However, few surveys characterise snacking very precisely and additionally there is the issue of under-reporting. On average dietary surveys fail to capture about 25% of total energy and under-reporting in obese people is more likely to represent 30% or 40% of total energy, immediately introducing a bias into analyses of diet and obesity.

A number of studies have sought to define snacking in terms of eating frequency. Here there may also be post-hoc effects because many obese people may skip meals or eating episodes in an attempt to control their weight. The net effect is that in most cross-sectional analyses, the number of eating episode is inversely related to body mass index or the prevalence of obesity.

The problem with under-reporting is illustrated in data taken from the NHANES (Figure 1) survey which appears to show a positive relationship between eating frequency and BMI. However, in each category of eating episodes there is evidence of significant under-reporting and the degree of under-reporting is related to the number of reported eating episodes. So, epidemiology is a very unreliable ally in these studies of snacking and obesity.

Snacking and energy balance

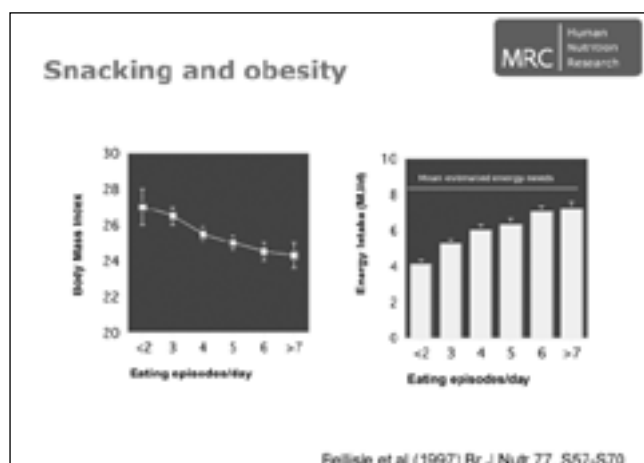
If snacking is linked to body weight regulation, it must be mediated either through energy intake or energy expenditure. Data on energy expenditure in highly controlled experimental studies, usually in whole body calorimeters, shows no effect of eating frequency. Whether you have a small number of eating episodes, perhaps two or three, compared to a very large number, six, seven or even more, there is no difference in net energy expenditure when subjects are fed iso-energetic diets. The effect on intake is more difficult to study. However, preloads which may be considered as a pre-meal snack, show differential effects on subsequent intake depending on the time interval. When consumed very shortly before a meal (30 minutes) there is actually relatively good compensation, while a pre-load or snack consumed 90 minutes or more before a meal results in poor compensation and excess energy intake in total. This suggests that snacks consumed outside traditional meal periods may be associated with an increased risk of over-consumption.

However, the pre-load paradigm usually refers to a single meal or at most intake over a single day. In a longer term study where subjects were given four different kinds of snacks, high or low fat and sweet or savoury, and each was offered for a three-week period, total energy intake was not significantly different across any of the treatments. This suggests that there was good compensation for the imposed snacks.

Concern about snacking has increased in part because there is a secular trend towards a greater proportion of total energy intake being derived from snacks. Data from the CSFII in the USA shows that the increase in the contribution from snacks essentially accounts for the overall increase in energy intake. Between 1977-78 and 1994-96 the number of snacking occasions has increased significantly and the calories per snack have increased, possibly reflecting increases in portion size. There has also been an increase in the energy density of snacks being consumed, reflecting the fact that people are not tending to snack on fruit and vegetables but on much more energy dense items.

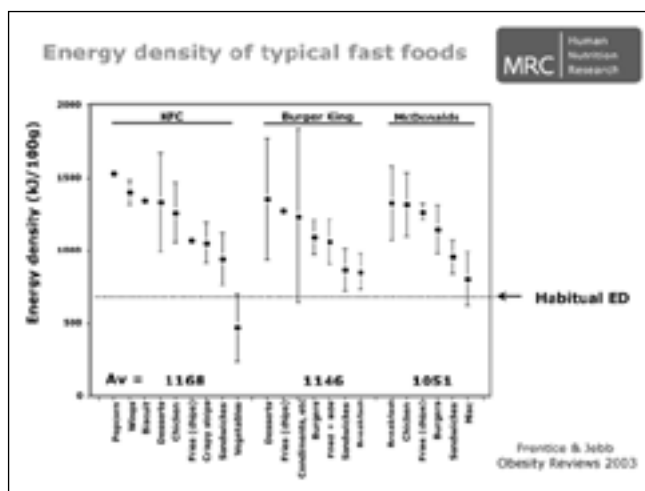
Energy Density

It is now well established that as energy density increases there is an increase in ad libitum energy intake because people fail to down regulate the amount of food they consume to compensate for the increased energy density. A small error in the weight of a low energy dense food consumed has little impact on total energy intake. You can double or halve the portion size for low energy dense food like vegetables with very little consequence for energy intake. In contrast, even a minor error in the assessment of the appropriate portion size for high energy dense food, will have very significant consequences for total energy intakes. Even an extra bite or two of an energy dense food adds a considerable number of calories. Energy dense



foods really do matter in the control of obesity and perhaps one of the most energy dense foods in our diet or groups of food are fast foods.

Fast food may be consumed either as a meal or a snack and has all characteristics of energy dense food: high in fat and/or high in added sugars, low in fruit and vegetables and often very dry foods, or with relatively low water content. We have compared the energy density of the entire menu range as available in fast food outlets in 2002 with the habitual UK diet (Figure 2). This analysis shows that the average energy density of the items available in fast food outlets is much higher than the habitual UK diet, and more than twice the energy density of food habitually consumed by people with a relatively healthy diet (defined as less than 35% energy from fat and more than 400g of fruit and vegetables per day). Traditional fast foods (burgers, fried chicken, pizza etc) have a tremendously high energy density, although it is notable that in recent years we are seeing some diversification in the menu options at many of these restaurants including some options with lower energy density. This variety is to be welcomed but puts a responsibility on the consumer to make the healthier choice.



This high energy density does seem to matter for body weight. Data from a study in adolescents shows that on those days in which they consumed fast food, obese adolescents had a significantly higher energy intake than on those days when they did not consume fast foods. However energy intake was unchanged in the lean subject regardless of whether fast food was consumed. This reinforces the idea that there are some people who appear to have good appetite control systems. We are all living in the same world, yet some people manage to regulate their energy intake and balance their body weight even in the face of fast food restaurants and other eating opportunities. We need to focus much more on the inter-individual variability in response to environmental clues in studies of the aetiology of obesity.

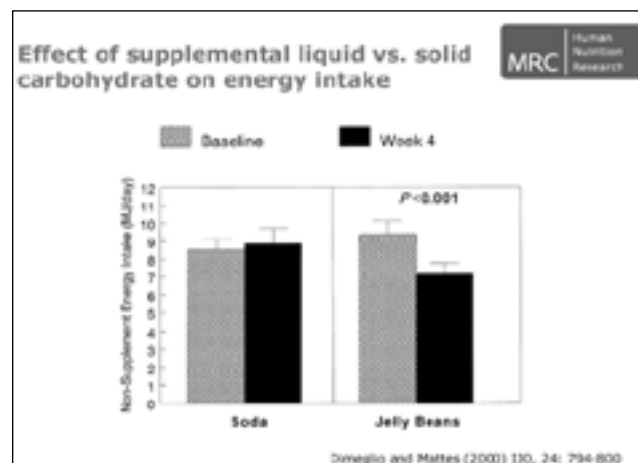
These experimental studies are complemented by a recent large epidemiological analysis which shows links between fast food consumption and obesity. Figure 3 shows data from the CARDIA study which suggests that regular fast food consumption over prolonged periods of time is associated with an increased risk of weight gain and also type 2 diabetes. Together these diverse strands of evidence provide a strong case that fast food, as a particular kind of snack, is linked to an increased risk of obesity.



Soft drinks

When considering energy density, it is very important to exclude beverages from the analysis. Drinks have a very high water content and as a result a rather low energy density. They impact on the body's appetite control system in a quite different way from solid food. There is now growing evidence that the increase in soft drinks, commonly consumed as a snack, may be linked with an increased risk of obesity. It is always very difficult in obesity to find a single clear convincing study which directly associates any one specific food with a particular outcome. However, there is now evidence from ecological studies, looking at secular trends, cross-sectional analyses showing an increased risk of obesity with increases in drink consumption, together with more mechanistic studies which have looked at appetite control in laboratory situations and have shown that drinks have low satiating properties.

Figure 4 illustrates the point why the energy contribution from beverages must be considered quite separately from that for solid foods. People were provided with the same number of calories either as a soda drink or as solid jelly beans. With the jelly bean treatment ad libitum energy intake was significantly decreased, just about sufficient to counter balance the added calories from the sweets. But this was not the case in the soda treatment where energy intake from other foods was unaltered. The additional calories from the drink essentially slipped into the diet apparently unnoticed. This and other studies suggest that sugar-rich drinks tend to supplement, rather than substitute, for other components of the diet.



However the strongest evidence that soft drinks are a risk factor for obesity comes from intervention studies. Astrup's group have shown that over just ten weeks people provided with artificially sweetened versus sugar-rich drinks showed significant

differences in body weight trajectories with modest weight loss in the low sugar group versus weight gain in the sugar-rich group. In the UK a “Ditch The Fizz” study done in schools over the course of one year advised children to decrease their consumption of sugar-rich drinks as part of a more generalised healthy eating message. There was no significant change in the prevalence of overweight in the intervention schools, but this contrasted sharply with a marked increase in the control group schools. This preliminary study points towards an important area for future research.

These studies highlight that it is the type of food or drink that is chosen as a snack which makes the difference to weight. There is no evidence that people snacking on the light or diet versions of these drinks are at an increased risk, but there is growing evidence that the sugar-rich varieties may be detrimental to body weight.

Summary

There are no simple or straightforward answers to the question “does snacking lead to obesity?”. We need to perhaps consider if this is the most useful question to ask. Is snacking itself the root of the problem or is it just a manifestation of a whole cluster of other behaviours. Is snacking acting as a marker of an overall

lifestyle? Is snacking, particularly in children, a measure of a broader family environment (the microenvironment) in which these children live? Physical activity is also an important confounder and we need far more research on the interactions between dietary habits and physical activity. We have done some very preliminary work in this area using the UK National Dietary Surveys and we can see that those children who spend the most time in sedentary activities are also those who consume the greatest quantity of savoury snacks and the least fruit.

In conclusion, at present there is actually no consistent evidence that there is any link between eating frequency per se and obesity. However, many of the analyses are confounded by reporting errors and have not adequately considered the impact of things such as physical activity. Nevertheless there is good evidence that the type of food or drink that people often choose to consume as a snack is very important and may be a marker of broader cultural or social or individual habits, which link to obesity.

I am left to conclude that meal eating may be an aspect of the Mediterranean diet that warrants greater attention. We are perhaps focusing too much on the nutrients or foods rather than the context in which that food is consumed when considering the impact on health.

Questions

Didier CHAPELOT

As you imagine, I do not agree with some points. The first point is energy density. I am sorry to say that I do not really believe the importance of energy density. Can you show that you must eliminate soft beverages to describe the effect of energy density? You know that soft beverages lower the energy density. You know that populations in the past had a very high energy density diet but did not show any obesity. The main characteristic is that when you have high energy density because you have high fat content, you have low carbohydrate and low insulin. Here in our occidental countries we do not have very high energy density; we have carbohydrate and fat and rather high energy density.

I do not agree at all with you about the meal frequency. The studies of the last 30 years are not valid because they do not discriminate between snacks and meals. They say they do not discriminate and they conclude that there are no data in favour of meal frequency, but that there is lower adiposity with higher meal frequency. There was a very important study conducted by Fabry in the 1960s. In intervention studies in three schools it was clearly demonstrated that the school with the lower meal frequency had a higher adiposity at the end of the year, and the school with the higher meal frequency had lower adiposity. In the study we carried out two years ago, we found that with a decrease in meal frequency. So I cannot really say that I can conclude that meal frequency has no link with obesity.

Susan JEBB

Let me take your last point first. I was not concluding that meal frequency does not impact on obesity, I was concluding that the data was very inconsistent and that if we rely just on epidemiology, I do not think we can draw a clear conclusion. You are absolutely right, there are some studies which do show an effect, but many others which do not. I think the methodological issues I referred to including the poor definition of a snack and under-reporting are hard to get around, so I do not think we are going to resolve this just through epidemiology.

We have heard a lot about energy density in this meeting and I do not want to start unpacking the whole argument about whether this is, or is not, a useful way of describing the risk of obesity with certain foods. I think it is methodologically unfortunate that we have to take soft drinks or beverages out of it; it makes for an untidy analysis. However, I think there is now a wealth of experimental data which tells us that the energy density of the solid food component of the meal is a very important determinant of total energy intake. It is not the only determinant, it just happens to be one which explains, I believe, quite a significant proportion of the variability in ad libitum consumption.

Didier CHAPELOT

The difference is between epidemiological studies and intervention studies, that is what Fabry's study was based on.

Barbara ROLLS

I agree with Susan that there is no single explanation of the regulation of food intake. We know protein probably is more satiating than the other macro-nutrients. However, having spent many years working on human food intake, the effects of energy density are absolutely the most robust and convincing, apart from perhaps portion size effects; you just cannot fail to find effects of energy density of foods on food intake.

Susan JEBB

I think the other point to rise is that I have very purposely kept off the issues of meal frequency and the impact on hormones, on insulin, leptin and so on. One can make a case that more frequent meals may have some beneficial effects. When we are considering advice to the public, I think we have to take a much more holistic view rather than just focusing on obesity per se, because at the end of the day, what we want to do is to reduce metabolic risk. Obesity is part of that, but it is not the whole story, and that I think is another reason why it becomes very difficult to make concrete conclusions and advise people about what they should do in terms of eating frequency. I firmly believe that it is the type and total amount of food that people are consuming whether this is all at those episodes, be those episodes 2, 3, 6 or 7 episodes.

Barbara ROLLS

I wanted to just comment on what is happening in the fast food industry in the States. Adam and I have heard a lot from fast food companies recently at the FTA mandated meeting. Interestingly, McDonald's, for the first time ever, presented a scientific poster at Experimental Biology, our biggest biological meeting in the States. Looking at the energy density of their menus, overall from the 1970s to current times, the energy density of their menu has gone down, primarily because of the introduction of the salads and the apple slices, and they have some fruit parfaits now. I am not convinced they looked optimally at energy density – they did not really tweak it the way we would have done – but nevertheless, they are encouraged now to keep introducing fruit and vegetables into their menus. They told us about the barriers that they face: they are now the biggest purchasers of apples because of the apple slices on their menus. If they decide to introduce anything on their menu, even one additional lettuce leaf to a burger, they have to start planning years in advance to grow the lettuce or whatever, so they are trying. I am not defending them; I am just saying what they are doing. It is going to take a long time; they know what they need to be doing and the great thing is that people are buying the fruits and vegetables.

Susan JEBB

The same is happening in Europe and I have had very similar discussions. I think we have to recognise that then puts a huge responsibility on the consumer to make the right choice. Whilst we would all argue that more choice is generally a good thing, choice without the understanding of the implications of that choice is a very significant responsibility, and I think that makes fast food a high risk choice for many consumers who are at risk of obesity.

Nutrient density as a tool for health promotion: Introducing the Naturally Nutrient Rich (NNR) Index

Adam DREWNOWSKI

University of Washington, School of Public Health and Community Medicine, Seattle, Washington, USA

In my presentation I will attempt a synthesis of what has gone on before and take you in a different direction. In this particular session, we started by talking about metabolic responses to snacks; then we went on to discuss food preferences and lifestyles and right now, we are moving on to discuss public policy implications of communicating nutritional knowledge to the consumer.

I am going to be talking about nutrient density as a tool for health promotion. I am going to be introducing the naturally nutrient rich index. I will also describe the thinking behind what are 'naturally nutrient rich foods' and what are 'naturally nutrient rich snacks'.

**Obesity and the food environment:
Science has many answers**

Eating too much	Walking too little
Fat	Sugar or starch
Sucrose	High fructose corn syrup
Sugar	Noncaloric sweeteners
Liquid beverages	Energy dense (solid) foods
Eating in restaurants	Eating at home
Large meals	Between-meal snacks
Fast foods	Vending machines
Gluttony	Sloth

Let us take a little detour here into obesity literature. For the past two days we have been hearing about the various reasons for the obesity epidemic. Science, as usual, has many answers. It is never a single answer. We have papers in the scientific literature saying it is the fat, the sugar, the soft drinks, the fast foods, it is eating in restaurants, eating at home, it is all of those things. So I put together a slide giving various types of reasons for the obesity epidemic. One reason, of course, is eating too much. Another is walking too little. People have blamed fat content of the diet, but they have also blamed sugar and starch. Sucrose has come under scrutiny, but so has high fructose corn syrup. Although we are blaming sugar, there is a paper in literature saying that it is intense sweeteners that actually lead to obesity. We have heard about liquid beverages, but also about energy dense solid foods. Eating in restaurants and, of course, eating at home. Large meals, in-between meal snacks, fast foods and vending machines have all been blamed. There is also the classic paper by Susan Jebb blaming gluttony and my favourite, sloth.

So we have all those various dietary possibilities. The new theme I want to introduce is the following: the unwelcome truth is that for many people, obesity is the social cost of global economic policies. And as a result the exhortations to change individual behaviour are not really going to work, especially for the most disadvantaged groups. We need to have a coherent set of government or international policies with which we structure our diet from both the standpoint of behaviour and also food accessibility and affordability. The point about energy dense foods is they are cheap. When it comes to competing for

consumer attention in terms of calories per dollar or in terms of calories per euro, nothing really competes with sugar. The cost of producing 1 pound of sugar in Brazil is as little as 4 cents per pound, which means that you are getting close to 50 000 calories for one dollar. Nothing comes close.

So the question is, why will people not eat better diets? The unfortunate answer is that in many cases, healthier diets cost more. So although we have been talking about the food industry – the fast foods, the snacks, the chocolate, the soft drinks – there is one other possible answer that we should be keeping in mind: it is not necessarily the junk foods, it may be the junk wages.

The question becomes: Is it low metabolism or is it low incomes? The issue of 'précarités,' the French word for disadvantaged groups, is something that comes to mind when we talk about the obesity epidemic. The one reason why energy-dense snacks are competing with fresh vegetables and fruit is because these snacks provide maximum amount of energy for the amount spent. The question is this: is there an inverse relationship between energy density and nutrient density? Is it true that energy dense snacks are in fact nutrient poor, so that reducing the energy density of the diet would have the automatic effect of increasing the nutrient content of the diet? Are the two in fact reciprocally linked?

The same question has been asked about the American diet: is it energy rich and nutrient poor? We know from data presented by the United States Department of Agriculture that the consumer is eating too many foods from the bottom and the top of the food guide pyramid – the top is the added sugars and fats and the bottom is both refined and whole grains. On the other hand, the consumption of fruit and vegetables is much less than the recommended amount. One question is the issue of cost. I have the same slide that Susan presented and I want to show it to you again for two reasons: to emphasise that what is happening is that when it comes to snacks. One key issue is: portion size – the number of calories per snack is increasing. The other issue is energy density – snacks are very often more energy dense than meals and other foods. Again, we have these twin themes here which have been raised during this meeting several times – portion size and energy density. Both are in fact extremely important in determining total energy intakes.

Significant Increase in Young Adults' Snacking between 1977–1978 and 1994–1996 Represents a Cause for Concern!
Cheryl Zeman, B.S., M.S., Anne Marie Stage III, B.S., Ph.D., and Barry M. Popkin, Ph.D.
Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-8007
Published online February 26, 2003

Variable	1977-78	1989-91	1994-96
Snacking occasions	1.70	1.69	1.92
Calories per snack	247	265	313
Snack ED (kcal/g)	1.05	1.30	1.32
Meal ED (kcal/g)	1.13	1.13	1.11

The third component I want to bring up here is the notion of nutrient density, and I do want to pose the question whether energy dense foods are in fact nutrient poor. I will take you through a few slides to illustrate what energy density is. We have not seen it presented in exactly this way. What I have done is to plot energy density of different types of foods against their water content, because energy dense foods are those that are dry and energy dilute foods are those that have a high water content. On this slide you see the relationship between energy density and the water content of food. Energy density is plotted on a vertical axis. The range of energy density pretty much goes between water and oil. Those are the two extremes of the range: 0 calories per gram for water and 9 calories per gram for oil. Sugar is right in the middle with 4 calories per gram.

What you see here on the horizontal axis is water content. It goes all the way from oil to soft drinks. Contrary to popular belief, soft drinks are not energy dense, they are in fact energy dilute because of their water content. On the other hand, many snacks over here are energy dense. When you put in other foods, for example dairy products, you see that milk is energy dilute, but cheese and yoghurt are more energy dense, though not nearly as energy dense as dry candy and dry cereals. Meat is in the middle of the range because of hydration, so it is not necessarily a very energy dense product. Of course most vegetables and fruit are going to be on the right, having the highest water content. On the left you see grains which have a high energy density. Vegetables and fruit will come up in the next slide.

When it comes to snacks, the popular snacks are generally energy dense, with the exception of soft drinks, which are energy dilute. So the question becomes whether or not the energy dense snacks are nutrient poor. Are vegetables and fruit, which are energy dilute, in fact nutrient rich per calorie? This is where the nutrient density index comes in. Fruits and vegetables are both energy dilute and contain a number of interesting nutrients, vitamins and minerals. Here, for example, you see vitamin C levels for various food groups. Note that many natural foods do not contain any vitamin C. On the other hand, fruits and vegetables are very rich sources and some, such as raw peppers, go right off the scale. So we have started working on new ways of measuring nutrient density per calorie.

This is not a new idea. Looking at the ratio of the nutrients in foods relative to the energy they provide has been tried before. Back in the 1970s and 1980s there were a number of studies looking at the nutrient quality index, nutrient to calories ratio, and so on. However, this research was abandoned because we were told that there were no good foods and there were no bad foods. There were only good or bad diets, and so all the foods were exactly the same. The consumer will not buy this message any more. However the consumer can be convinced that there are good foods and there are better foods. We need to have a system to assess the nutritional profile of individual foods.

There are different ways of doing that. You can have nutrients per calorie ratio, or you can have a calories per nutrient ratio. You can express this either in terms of nutrients per 100g or you can express this in terms of nutrients per serving. Or you can have nutrient to nutrient ratio, based on the good nutrients relative to the bad or problematic nutrients – the problematic nutrients being added sugar, added fat, cholesterol and salt. Here we have an interesting conceptual issue because in the United States, and I suspect elsewhere as well, healthy foods are generally defined by the absence of problematic nutrients. Foods are considered healthy if they do not contain sugar, fat, cholesterol or salt. In fact, in the United States, health claims are only permitted if the food is virtually sugar free, fat free, cholesterol free and so on. No-one pays much attention to the beneficial nutrients that the foods actually do contain. Our approach is very different from

what has gone on before because instead of saying “warning, red light! This food contains sugar”, we are saying that this food has a number of beneficial nutrients in the right proportion to the calories it contains. In such a calculation, energy density is a factor. So we are looking now at positive nutrients and for the positive nutrient content in a variety of foods.

We introduced this notion last year at a meeting in Washington, which was the Naturally Nutrient Rich Symposium Putting More Power on Americans’ Plates. At the time, I made some statements about helping consumers choose naturally nutrient rich foods first and then the less nutrient dense foods as caloric needs allow. Somewhat to our surprise, because you say things in Washington and nobody listens, some of the same language turned up in dietary guidelines for Americans and more recently in the food guide pyramid. The statement in the dietary guidelines was “consume a variety of nutrient dense foods and beverages within a number of food groups, and then consume the discretionary calories as caloric needs allow”. The idea here is to prioritise the nutrient dense foods and then consume the discretionary calories with fewer nutrients in proportion to energy needs.

A preliminary NNR score for the US

- Based on 14 key nutrients
- Based on *mean* %DVs ($\sum \%DV_{1-14}/14$)
- Percent DVs based on 2,000 kcal of food
- Influenced by energy density of foods
- DVs truncated at 2000%DV for the NNR (T) score (we also used a log scale)
- No penalty for “bad” sugar or fat
- No adjustment for bioavailability
- No adjustment for rare nutrients

We have created a preliminary naturally nutrient rich score for the United States. This is a project conducted by myself and by Nicole Darmon. I will show you both the French and the American scores. The American score was based on 14 key nutrients. We based it on the mean percent daily values calculated based on 2 000 calories’ worth of food. Of course, such a score is influenced by energy density because 2 000 calories of red peppers is going to be a huge amount – about 20-30kg. As a result the amount of vitamin C, vitamin A, and so on in 2 000 kcal is going to be enormous. We truncated percent daily values at 2 000 calories so that the foods which contained large amounts of one nutrient did not appear balanced because of their high scores, when in reality their score was driven by a single nutrient. To avoid controversy, we opted not to have a penalty for the good or bad nutrients, so there was no removing of points for fat or sugar content. We did not adjust for bio-availability and we did not weight the nutrients depending on their importance as perceived by us. The idea was to introduce this score as a work in progress.

The key component nutrients were selected on the basis of the nutrients listed on food labels, those that were part of the United States Department of Agriculture definition of good nutrition, and also we looked at the list of nutrients of public health interest as defined by the Food and Agriculture Organisation of the United Nations. On the left, you see the nutrients we took for the American naturally nutrient rich score, and on the right, you see the nutrients that Nicole selected for the French nutrient density score. The percent data values were based on slightly different

recommendations. The French and the American recommendations for the same nutrients are slightly different but this does not really make too much of a difference to the final score.

US	DV	France	DV
Protein (g)	65	Protein (g)	60
MUFA (g)	30	Fiber (g)	25
Calcium (mg)	1,300	Calcium (mg)	900
Iron (mg)	18	Iron (mg)	12.5
Zinc (mg)	11	Magnesium (mg)	390
Thiamin (mg)	1.2	Thiamin (mg)	1.2
Riboflavin (mg)	1.3	Riboflavin (mg)	1.55
		Niacin (mg)	12.5
		Vitamin B6 (mg)	1.48
		Vitamin B5 (mg)	5
B ₁₂ (1g)	2.4	B ₁₂ (1g)	2.4
Retinol (IU)	5,000 IU	Retinol (1g)	700
Vitamin E (IU)	22 IU (15mg)	Vitamin E (IU)	19 IU (12mg)
Vitamin D (IU)	400 IU (10.1g)	Vitamin D (IU)	200 IU (5.1g)
Vitamin C	75	Vitamin C	110
Folate (1g)	400	Folate (1g)	315
Potassium (mg)	3,500		

So to answer the previous question: yes, energy dense foods tend to be nutrient poor. Although we talk about energy dense foods as being nutrient poor, until now, as Nicole pointed out, there really has not been a mathematical calculation to prove that this is, in fact, the case. What you do see here is the negative relationship with energy density. This is our naturally nutrient rich score. Note that vegetables and fruit have a very low energy density and a fairly high naturally nutrient rich score. As you go higher into energy density towards the grains and the sugars and the oils and the fats the naturally nutrient rich score drops. So yes, there is a reciprocal relationship between nutrient density and energy density. By reducing the energy density of the diet (Barbara Rolls's strategy) you increase the nutrient content of the diet (my strategy). Conversely, increasing nutrient content of foods will reduce energy density, so these are reciprocal concepts.

Now, let me show you how these concepts can be applied to consumer communication. This is the old style food guide pyramid from 2003. Note how all the foods are arranged over here. The base is grains, including whole grains, vegetables, fruit, dairy products, milk and meat and beans and nuts, and those little dots are the added fats and sugars to be consumed sparingly. The new pyramid, released just two weeks ago, is what has been called the radiant pyramid. Actually it looks as though there were an earthquake in Washington and all the food fell off the shelves. The earlier versions of the pyramid had a sequence of foods going all the way from whole grains into the doughnuts, snacks and so on. For many reasons, however, no one wanted to prioritise those foods in sequence, so notice here that the foods are arranged in no particular order. Here we have sweet potatoes, broccoli, beans, tomatoes, lettuce, carrots, corn and spinach. For the milk products we start off with cheese, then 1% milk, then yoghurt and so on. Here we have steak and chicken, and then fish. The idea was to have the nutrient dense foods up front to be consumed first, and then the less nutrient dense foods towards the top of the pyramid to be consumed more sparingly. This message has become lost and those foods are down around the base of the pyramid and seemingly in no particular order. The naturally nutrient rich score actually brings the order back into the pyramid. I can show you how it can be used to prioritise foods within the pyramid categories. I will focus here on vegetables and fruit and show you how they are arranged in sequence using the naturally nutrient rich score, from the most nutrient dense to the least nutrient dense.

Let us examine this in more detail. The naturally nutrient rich score for vegetables and fruit is on the logarithmic scale, and this

is energy density. Note that in terms of nutrients per calorie, we have spinach and romaine lettuce, broccoli, tomatoes, cantaloupe, mango, tangerines, strawberries, grapefruit, kiwi, orange juice, avocados, blueberries, and potatoes – which are a high source of potassium. Then, as we move to the left, we have the more energy dense foods such as raisins, French fries and potato chips. On the extreme left we have apple sauce, grape juice, canned peaches and canned berries in syrup, because added sugar, although not a part of the formal score, dilutes nutrient density by adding calories. So this is a way of prioritising the foods from the most nutrient dense to the least nutrient dense per calorie.

The same thing applies for meats. When it comes to nutrient density per calorie, liver is one of the super foods. On the right we have clams and oysters, beef, beef chuck, and ground beef going from the leanest to the least lean and then bacon, turkey, fried chicken, and fried meats on the left. However, there are a couple of more issues. They have to do with palatability and cost: a food may be nutrient dense but children do not like it, for example, liver, or a food can be nutrient dense but is very expensive, such as raw oysters. So you need to think in terms of balancing nutrient density with palatability, pleasure and cost – and this is exactly what we have been hearing in this symposium and over the past couple of days.

These are the scores for dairy products. Again you notice that they go all the way from skimmed milk and non-fat yoghurt with most nutrients per calorie to 1% milk, 2% milk, whole milk, cheese, ice cream and frozen yoghurt. As you move to the left, nutrient density is diluted by sugar content. These are the grains: again we have whole grains on the right, some fortified grains also on the right and then things like crackers, popcorn and so on. Here we have the fats: olive oil, which is most nutritious per calorie, versus other oils or other fats, which have less nutrients per calorie. So actually you can quite successfully assign a nutrient density score to foods within each category. To my mind, that is a more useful approach than engaging in discussions about which is more nutritious, avocado or shrimp. The useful comparisons are those within the category as opposed to across categories, but we can do that as well.

Nicole has been working on this topic in France, looking at two measures of nutrient density. One is a nutrient adequacy score, which is based on 100g of food, and the other is a nutrient density score, which is based on nutrient density per 2 000 calories. Nutrient density is the nutrient adequacy score divided by energy density. We have taken this idea one step further. In addition to talking about nutrients per calorie, we also started looking at the issue of nutrients per unit cost. When you think about it, vegetables and fruit are expensive sources of calories. They cannot compete with raw sugar in terms of sheer calories. However, the sugar is going to be just calories with no nutrients. When it comes to nutrients per unit cost, the question is whether or not vegetables and fruit come out on top. Here we are not talking so much about calories per euro but about nutrients per euro.

This is the inverse relationship between energy density and nutrient density, which you have just seen. We have an energy density graph plotted over here. This is a nutrient density score using Nicole's French data. It is very similar. Vegetables and fruit are on the right since they are very low in energy density and very high in nutrient density. The main point about food costs is that the energy dense foods cost less per calorie. The first point I want to make here is that when it comes to nutrient to energy ratio, vegetables and fruit come right at the very top. Notice here that the vegetables and fruit are low in energy density. So are sweetened beverages but their nutrient content is low as well. Candy has an energy density of 4 calories per gram and low

nutrient content. Oil has a very high energy density, but nutrient content can range from olive oil at the top to other fats and oils at the bottom. The favorable nutrients to calorie ratio is provided by the regression line. So you can start looking at the foods above and below this regression line. Over here there are more nutrients than calories, down here there are more calories than nutrients. So red meat, beef, dairy products, yoghurts are all above the line. Vegetables, fruit, dairy products, yoghurt, meat, nuts, and actually, come to think of it, the key elements of the Mediterranean diet.

The problem is that the energy dense foods actually do cost less. What you have here is energy density represented again in the same curve, and here you have energy cost in terms of euros per 100g. That is the problem: high energy dense foods are nutrient poor but energy dense foods also cost less. This means that the nutrient dense foods are going to cost more. This is the conclusion Nicole drew from her studies plotting nutrient adequacy scores against food price. Yes, it is true that the more nutrient dense foods cost more per 100g and the more nutrient dense foods cost more per 1 000 calories. But some of those foods give you adequate nutrients at a reasonable cost. Perhaps in promoting this notion to the consumer we should be focusing first of all on the positive nutrients that the foods do contain and stop obsessing about the fat, the cholesterol, the saturated fat. Then we can convey the message that fruits and vegetables are really very good value when it comes to nutrient package per unit cost. The best value foods – and again this is drawn from Nicole's work – are fruits and vegetables, then meats, especially organ meats. Well below on the nutrient to price ratio range are the fats and the oils and the sweets and the snacks. So this is a new metric that allows you to start looking at those three

concepts: energy density, nutrient density and both energy and nutrient cost. Fruits and vegetables have a very favourable nutrient to price ratio. Perhaps this is the way of conveying this information to the consumer.

There are a number of issues that need still to be resolved. We need to decide whether or not to base the score on 2 000 calories, 100g, or on food servings. This is a "naturally nutrient rich" score which means that fortified foods are not yet included. We have not devised a score for fortified foods but we may devise a new score for those later on. Right now, there is no punitive score for fat, sugar, cholesterol and salt. We have not addressed the issue of bio-availability. We recognise that spinach is not the most bio-available source of calcium or iron. The calcium in dairy products is more bio-available, haeme iron in meat is also much more bio-available. We are looking at those issues. We have not included phytochemicals and antioxidants in our calculations and we do not have a weighting scheme to favour the hard-to-get nutrients in the food supply. So this is an evolving work. I think that this is a new and interesting approach to assessing nutrient density.

To conclude, the naturally nutrient rich approach is based on the nutrient to calorie ratio. It is intended to help consumers select naturally nutrient rich foods, instead of just counting calories. What we want to do is make each calorie count more, for each calorie to contain some nutrients in the typical diet. The idea is that the nutrient dense options can then be balanced with discretionary calories as caloric needs allow. So we think that this is a nice way of looking at diet quality. We would like to link our index to other measures of diet quality and so help the consumers in their choices.

Questions

Susan JEBB

I have been working on the UK nutrient profiling system so it is very interesting in comparison. You have gone for a within category system and I just wonder whether you think it really helps us if we start prioritising one fruit or vegetable over and above another, when in actual fact what we really want to say to people is choose fruit and vegetables rather than biscuits and confectionery.

Adam DREWNOWSKI

Yes, and this is very interesting because in the past the Federal Trade Commission did not allow cross-category comparisons. Manufacturers were not allowed to say "choose this banana over snacks". However, this is changing. We may be able to do that, but in order to be able to do that we have to have some kind of a metric to say why that is. Also I feel that the demonstration of this inverse reciprocal relationship between nutrient density and energy density is actually very interesting. We knew about it instinctively but it has not really been demonstrated until now. So we have both ways of saying "select foods from this category to begin with, but once you are within this category there are still better choices to be made." This does not apply so much to vegetables and fruit as to grain products or to meat or dairy products; there is a huge difference between fried chicken and lean ground beef. The idea was to prioritise foods within other categories.

I would like to say a few closing remarks about this meeting in general. I think we have heard an extraordinary variety of presentations dealing with all aspects of science, from molecular biology all the way to public policy. In these two and a half days we have had a number of presentations, 61 very high quality posters, not to mention some nice lunches and dinners.

This is my conclusion. There is really no doubt any more that the Mediterranean diet and vegetables and fruit contribute to better health. The evidence suggesting this with respect to cancer, cardiovascular disease, obesity and body weight control is overwhelming. We now need to move from science towards policy and political action. The issue now is how to make those foods accessible and affordable to everybody. Then we can advertise and promote and market the various foods in such a way that they are accessible to the average consumer. So I would say that the scientific work is not entirely over but it is convincing. Where we need to go now is towards more policy and political action, marketing, and changes in some of our agricultural policies.

Conference Conclusion

Luciano TRENTINI
AREFLH President

I would like to thank you for the chance you gave me to conclude the works for this very important congress in which fruit and vegetable products have an important role in promoting consumers' health.

First of all I would like to explain what this meeting of European Regions (AREFLH) is.

AREFLH was established in Aquitania in 1999, with many French Regions, on the will of Guy San Martin, Regional assistant chief. Its aim is to improve the fruits and vegetables system. Other Regions from Spain, Portugal, Italy entered in AREFLH that is constituted today by 23 Regions which represent more than 30% of the European fruits and vegetables system as production value.

In these years AREFLH achieved important results, first of all a better application of 2200/96 Regulation that concerns the common organisation for the market of fresh fruits and vegetables.

AREFLH worked to promote the establishment of a group of more than 30 members of the European Parliament who are interested in this important field. AREFLH has an active part in meetings of this group. Its tasks include secretary's office and technical support. Public Institutions and a Producers Committee (directed by "Catalonia Qualità" - an association of producer's organisations of the Spanish Region) associated in AREFLH.

In this Association there are many branches that deal with different activities: the reform of the common organisation of the market (O.C.M), technical matters such as research and experimentation, in particular integrated production system that is productive methods which reduce negative effects on environment and health. These methods consider reliability of productions as an instrument to warrant the quality of fruits and vegetables.

A special thanks for the organisation that arranged this congress giving the scientific community the opportunity to know the fruits and vegetables productive system organised by AREFLH.

In these days we have understood the importance of fruits and vegetables consumption for consumers' health. Eating little quantity of fruit and vegetables increases the risk of many chronic diseases. We know that in many developed countries political programs concerning nutritional matters wants to increase the use of fruit and vegetables to reach at the least the result of 500g per head a day.

Both every day press and specialized periodicals on agriculture talk about problems regarding the fruits and vegetables system such as overproduction, destruction or distillation of fruit, overprice, orchards removal.

On the square I didn't expect to talk about prices in this occasion too. I think it is important to mention a matter of fact. In Italy every citizen spends 16-18% of his income to buy food. Only 2-3% of this expense is used to buy fruits and vegetables. It is a quite low value.

I would like to make another example: the rate of consumption of processed tomato products is about 22 kg per head. In this case the value of the raw material is just about 10%. If you consider the cost of fresh tomato, this value per year is equal to the cost of 2 or 3 cups of coffee.

So we can say that the price of fruits and vegetables is high but if we compare it to the cost of others goods like coffee or mineral water, we can realize that their value is not too high if we consider benefits that come from consumption of these products.

Despite that, the most worrying fact is the steady drop off of consumption. This reduction is about 10% in the last five years. In a worldwide market we can observe a decrease of consumption, a real reduction of the number of farms and of the amount of their income.

So in the future we have to consider that availability of fruits and vegetables coming from European Countries may reduce more and more, all to the good of products coming from non European Countries, maybe less safe and reliable than ours for quality but less expensive.

We know that many Countries are making projects such as "five times a day or ten times a day" or "the five colors of health". I think that all these ideas should be promoted in a better way maybe with the common effort of different European Countries. This common effort should take into account the value of food as a nutrient, the benefits for human health, his "nutraceutical" value that is a value which concerns nourishment and pharmaceutical aspects.

In these days we talk a lot about industry supporting health system. Today we would like to say that primary raw products too can and have to benefit by their distinctive features or particular productive techniques; these particular features make these products different from common agricultural products.

We could plan together what, how and when cultivate bearing in mind that the different kinds of fruit and vegetables contain elements which protect health. Many farming in Europe cultivate products rich in anthocyanin, carotenoids, lycopene, (cabbages, carrots, pumpkins, apricots, kiwi and pears). As a consequence, it is necessary to join forces to improve contact with consumers.

By increasing the consumption of fruit and vegetables we could protect health in the best way that is choosing natural foods without spending too much.

AREFLH has an important role in communication. In fact we are planning a project in order to make students aware of the value of our productions (Interreg III C with the partnership of Italy, France and Spain). This project concerns educational farms that are farms which can have a main role in alimentary education.

I hope that the AREFLH activities, for the next EGEA congresses, can support more and more your scientific research.

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The first five posters have been selected by EGEA Scientific Committee for an oral presentation on Saturday, May 21st, 2005

Dietary and life-style determinants of mammographic breast density: a prospective study in a Mediterranean population

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Background: High mammographic breast density (MBD) has been associated with increased breast cancer (BC) risk even after adjustment for established BC risk factors. Fewer studies have examined the influence of diet and other life style factors that, overall, might play a role in BC and could be more easily modifiable than factors as reproductive history.

Methodology: In the frame of a prospective study in Florence we identified 2,000 women with a mammographic examination (ME) taken five years after enrollment, when information on diet, life-style habits and anthropometry was collected. Available MEs were identified and retrieved (1,668/2000; 83%) and MBD has been assessed by two experienced readers according to Wolfe's classification and a semi-quantitative scale. Updated information on reproductive history and Hormone Replacement Therapy (HRT) has been collected to take in account short time changes in MBD. A case-control analysis has been carried out comparing women with high-MBD (P2+DY according to Wolfe's classification) and women with low-MBD (N1+P1).

Results: As expected high-MBD was inversely associated with increasing BMI, number of children and length of breast feeding, while it was directly associated with high educational level and pre-menopausal status. A multivariate analysis, adjusted for non dietary factors, showed that high-MBD was inversely associated with increasing consumption of vegetables (p for trend=0.005) and olive oil (p for trend=0.04), and with increasing intakes of beta-carotene (p for trend=0.02) and vitamin C (p for trend=0.05). A positive association was evident for increasing consumption of wine (p for trend=0.01). These results were confirmed also in analyses taking into account HRT at the date of ME.

Conclusions: This prospective study, the first carried out in Mediterranean women, suggests that specific dietary components as vegetables and olive oil are associated with low-risk mammographic patterns, thus providing useful clues for planning preventive actions.

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Consumption of vegetables and fruit in a sample of European children from 9 countries: The Pro Children cross-sectional survey

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As a part of the Pro Children research project, funded by EC DG RESEARCH, a validated instrument was developed for assessment of vegetable and fruit intakes of 11-year old children. A cross-sectional survey took place in all participating countries in 2003. The survey was performed in 9 European countries and included more than 13.000 children. It used nationally, and sometimes regionally representative samples of schools and classes. The instrument included a 24-hour recall component and a food frequency part and was completed in the class room. The number of compliers with the WHO population goal of 400 grams per day was determined, by ranking the subjects within each country according to intake level and identifying a cut-off level by taking subjects off from the lower end until the mean reached 400 grams. The subjects over the cut-off were identified as compliers. The first results show highly diverse intakes of vegetables and fruit in the participating countries. Boys generally consumed less vegetables and fruit than girls did in all countries, vegetable intake was lower than fruit intake. The highest intake was found in Portugal, the lowest in Iceland. Surprisingly low intakes of vegetables were found in Spain. Children's intakes were far from reaching the WHO population goal of 400 grams per day. The number of compliers ranged between countries from 20 to 56 % of the population of 11-year old children. Even though the WHO population goal does not explicitly outline how to estimate intakes for sub-groups of the population such as these 11-year old children, the same results were seen compared to national food-based dietary guidelines especially designed for children. There seems to be a need for targeted promotion programmes in all the participating countries. The Pro Children project will further elucidate determinants of intake in order to make promotion efforts more effective.

Comparison of oxidative stress status and carotenoid status in volunteers from five European countries

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Exposure to a high fruit and vegetable diet increases antioxidant concentrations in blood and body tissues and potentially protects against oxidative damage to cells and tissues. Within Europe there are differences in cardiovascular disease risk between countries and this might be related to dietary habits. As part of a European multicentre project, several studies were undertaken with the aim of testing whether the consumption of food rich in carotenoids reduces plasma oxidative damage. In the present study, we described the intake and status in carotenoid and the oxidative plasma parameters (SH, SOD, GPx, oxidative resistance of LDL) at baseline from five European regions with different fruit and vegetable intakes and reported rates of C.V.D. Eighty volunteers (forty males, forty females per center), age range 25-45 years, were recruited from France (FR), United Kingdom (UK), republic of Ireland (IR), the Netherlands (NL) and Spain (SP) and their oxidative status compared. The total carotenoid intake was not different between male and female in each centre, but it was significantly higher (18mg/d) in FR and significantly lower (10,5mg) in Spain than others participating countries. The main sources of β -carotene were carrots in the diets of the volunteers in all countries except Spain were spinach was of slightly greater importance. A large number of foods (n=25) contribute to dietary lutein intake in these European countries. The main dietary sources of lutein for UK and IR were peas (36% and 19%), broccoli (8%, 16%) and eggs (8%, 10%) respectively. The main source of lycopene and β -cryptoxanthin was tomatoes and oranges respectively in all participating countries. Serum concentration of β -carotene was highest in the French volunteers whereas the carotenoids status in SP was one of the lowest from the participating countries. Lutein and zeaxanthin are highest in France and Spain. Mean female plasma ascorbic acid was higher in female than male counterparts but there were no significant differences between either male or female means between centres. Mean plasma thiol was lower in SP than either FR or UK but was similar to all others centres. The GSSG as a product of oxidized GSH was lower in SP and GPx activity was higher in SP than FR, suggesting difference in oxidative stress maybe in relation with carotenoids status. This result is in agreement with the mean urinary MDA/creatinine ratio which was lower in FR than SP. In turn the others countries were similar from FR (GB) or SP (IR & NL). In contrary the differences in carotenoids intake or status could not be related to ex vivo resistance of LDL (lag phase) or to red cells SOD cu-Zn, suggesting that carotenoids could play an important role in protection of SH groups. In conclusion, these data on oxidative stress parameters may be considered as 'reference values' in serum of healthy, middle-aged subjects from five European countries. Considering our results, a protective effects of the Mediterranean-like diet from carotenoids status could be explained by a protective effects of carotenoids on SH groups, but not on LDL oxidizability. SP is a less consumer of total carotenoids among the European participating country, even if the lutein intake is higher with FR than others countries.

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Meal patterns and obesity

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Swedish Nutrition Recommendations include guidelines for temporal distribution of energy intake over the day as well as eating frequency. However, the current evidence for health effects of meal patterns is sparse. The objective of this study was to describe the association between habitual meal pattern and obesity.

The study is based on data from the research programme INTERGENE. The study population consists of randomly selected women and men, aged 25-74 years, living in the Västra Götaland Region in Sweden. A total of 3602 participated. Participants with measured BMI \geq 30 were compared with other participants with respect to questionnaire data on habitual meal patterns (breakfast, lunch, night meal, meals outside home, cooked meals, meal frequency and portion size). Odds ratio (OR) with 95% confidence intervals was adjusted for age, sex and physical activity in logistic regression models.

Being obese was significantly associated with omitting breakfast, OR 1.49 (1.12-1.98), omitting lunch OR 1.30 (1.03-1.64) and eating at night OR 1.69 (1.16-2.47). Obesity was also related with larger self-reported portion sizes, with a 11% increased risk of being obese per unit increase in portion size on a scale of one to nine. Moreover, women who reported eating meals outside home were less likely to be obese compared to other women, although no corresponding relationship were observed for men. No significant associations were observed between obesity and meal frequency or consumption of cooked meals.

In summary, obese and non-obese individuals do not differ in their self-reported frequencies of consumed meals or cooked meals. However, the results indicate that obese men and women have a meal pattern shifted to later in the day as well as consuming significantly larger portions than the non-obese.

Association of diet quality with lifestyle variables, energy density, and macronutrient intake at population level

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Objective: The Mediterranean diet score (MDS) and the Healthy Eating Index (HEI) are two measurement tools of diet quality, based on different concepts. The objective of the present study was to analyze the association of these diet quality indices with lifestyle, energy density, and macronutrient intake at population level.

Methodology: The subjects were Spanish men (n=1547) and women (n=1615) aged 25-74 years who were examined in 1999–2000, in a population-based cross-sectional survey in the north-east of Spain (Girona). Dietary intake was assessed using a food frequency questionnaire. A Mediterranean diet score, including foods considered to be characteristic components of the traditional Mediterranean diet and, the HEI (based on a 10 component system of five food groups, four nutrients, and a measure of dietary variety of food intake) were created. Detailed information of leisure-time physical activity, smoking and alcohol drinking habits was recorded.

Results: Generally, a higher diet quality was found with increasing age. Hence, all further associations were adjusted for this confounder. Increasing diet quality, characterized through the MDS and HEI, was inversely associated ($p < 0.05$) with smoking and sedentary lifestyle in both genders. Elevated alcohol consumption was more frequent in men with a low rather than a high diet quality level.

Both diet quality indices showed a similar association, according to direction and magnitude, with macronutrient intake expressed in percentage of energy intake and energy density (calculated by three different methods). Diet quality was directly associated with intakes of carbohydrates and inversely related to total fat, saturated fat, and protein ($p < 0.01$). In contrast, the intakes of mono and polyunsaturated fat were inversely associated with the HEI ($p < 0.01$), but showed no significant relationship with the MDS. Low energy density was associated ($p < 0.01$) with higher diet quality, independent of the measurement tool used.

Conclusion: In general, the MDS and HEI showed a great similarity according to their associations with lifestyle variables, macronutrient intake, and energy density in both genders. High adherence to a good quality diet was associated with a healthier lifestyle, higher consumption of carbohydrates and lesser intake of total fat, saturated fat, and protein in men and women. Most importantly, regarding energy balance, high quality diet is inversely related to energy density.

Relationship between folate status and the healthy eating index in a group of schoolchildren

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The Healthy Eating Index (HEI) is a tool that allows us evaluate the quality of a diet of a population. Even though global diet deserves a special attention, folate acid deficiency may be relatively frequent in developed populations and this may have strong sanitary and functional repercussions.

Objective: To study the relationship between the HEI scoring and folate status in schoolchildren.

Methods: It has been studied a group of 128 schoolchildren from 7 to 10 years from Madrid (Spain). The dietetic study was carried out by a food record for three days and the "precise individual weighing" for meals carried out in the school's dining. Food was transformed in energy and nutrients, subsequently we can value if the diet is adequate to the RDI of folate. We also calculated the HEI. Blood samples were obtained for serum folic levels evaluation.

Results: The score obtained for the HEI was 64.7 ± 9.9 , only 43.8% of the population covered the folate RDI. However, as diet's quality increased it did also the contribution of folate intake to the covering of the RDI ($r=0.39$, $p<0.001$). Besides, it was observed a positive association between the HEI and the serum folic levels ($r=0.18$, $p<0.05$).

Conclusions: Even though more studies are needed in this field, the fact that the intake of folic acid increases together with the HEI supports the using of this index to evaluate the status of folate.

	Poor Diet (score <50)	Needs improvement (score 50-80)	Good diet (score >80)
Children	11	109	8
Folate intake ($\mu\text{g}/\text{d}$)	201.6 ± 43.0 b*	245.2 ± 66.2	284.8 ± 64.2 b*
Coverage of RDI (%)	80.7 ± 17.2 b*	97.9 ± 26.5	113.9 ± 25.7 b*
Folate density ($\mu\text{g}/1000$ kcal)	87.7 ± 9.6 a** b*	116.7 ± 30.1 a**	126.9 ± 21.8 b*
Serum folic levels (ng/mL)	8.4 ± 3.7 b*	10.1 ± 5.6 c*	12.1 ± 7.2 b*c*

Equal letters mean significant difference between the groups. ** $p<0.01$, * $p<0.05$.

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Only a minority of Spanish adolescents consumes an adequately-composed breakfast- Regional results from the AVENA* Study

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Introduction: An adequately composed breakfast can essentially contribute to cover daily nutrient needs, especially during childhood and adolescence¹.

Objective: Assessment of breakfast habits of Spanish adolescents.

Methods: Breakfast habits of 1282 adolescents (13-18.5 years; 572 males) from Santander, Zaragoza, Granada enrolled in the AVENA study² (a randomised, cross-sectional multi-center study carried out in Spain) were assessed using a validated food frequency questionnaire. For the evaluation of the nutritional quality, the food pattern consumed was compared with a predefined "optimal" breakfast consisting of one portion of milk (pure or cacao) for calcium needs, one portion of carbohydrate-rich food (toast, granola, cereals) for delivery of energy and dietary fibre and one portion of fruit or their juices (for vitamins and minerals). Age, gender as well as regional differences were analysed by Chi-square test (level of significance $p<0.05$).

Results: 13.2% of the adolescents consumed an adequately composed breakfast with significant geographical differences (Santander: 19.4%, Zaragoza: 9.4%, Granada: 10.5%; $p<0.001$). Gender differences were only found in Zaragoza (boys: 14.1%, girls: 5.9%, $p<0.001$). Most of the students did not choose fruit or juice. Six point three percent of all students did not consume breakfast at all; the number of "non-consumers" being influenced by gender (girls: 8.6%, boys: 3.5%; $p<0.001$). The percentage of girls skipping breakfast increased continuously with age (13 years: 1.7%; 17-18.5 years: 13.5%; $p<0.001$).

Conclusion: Only a minority of adolescents in three urban Spanish Areas consumed an adequately-composed breakfast, because they omitted fruits. Since breakfast can essentially contribute to an adequate daily nutrient intake, this is an obvious risk for a generally too low provision of certain nutrients like vitamins and minerals.

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Food habits in Spanish institutionalized elderly group. Adherence to the Mediterranean Diet

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Objective: Mediterranean Diet (MD) has been described as a model from a nutritional and sanitary point of view due to the proportion in which all the food groups are included. Nevertheless, in the last years, changes in the reduction of calories consumption and expenditure, the incorporation of low nutrient dense foods, and food processing methods have contributed to increased the risk of deficiencies intakes, in particular among certain population groups, as the elders. Knowing the extent of this reality is the reason why the aim of this study was to evaluate the food habits in a group of institutionalized elders.

Methodology: The analysis included 54 males and 98 females aged ≥ 65 y who were living in 3 geriatric residents in the Community of Madrid (Spain). Dietary intake was assessed using a "Precise individual Weighing" during 7 days. Daily serving of each group of foods was compared with the recommended for the MD established by Ortega et al. (1998).

Results: Results are shown in Table 1.

Conclusion: Our results provide evidence supporting the progressive withdrawal from traditional MD even in elders. Introduction of corrective policies or a initiate campaigns to inform the consumer about the necessary changes in the diet and about characteristics of the MD, which are being lost and should be restored.

	DRS FOR MD	DAILY SERVING INTAKE		DAILY SERVING INTAKE		COV
		TOTAL SAMPLE		MEN	WOMEN	
Cereals and pulses	6 - 10	3.27 \pm 0.94	***	3.78 \pm 0.76	2.99 \pm 0.92	***
Fruits	2 - 4	1.20 \pm 0.70	***	1.01 \pm 0.41	1.30 \pm 0.80	**
Vegetables	3 - 5	1.75 \pm 0.54	***	1.88 \pm 0.60	1.68 \pm 0.51	-
Dairy Products	2 - 3	2.10 \pm 0.64	*	2.04 \pm 0.64	2.13 \pm 0.65	*
Meat, fish and eggs	2 - 3	1.43 \pm 2.2	***	1.59 \pm 0.40	1.34 \pm 0.38	*

COV: (Covariance analysis adjusted by discrepancy energy intake/expenditure);
* p<0.05, **p<0.01, *** p<0.001.

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Adequacy of food intake compared with the Mediterranean diet in a group of young women depending on smoking habits

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Objective: To analyze the consumption of different groups of aliments in a group of smokers, passive smokers and non-smokers women, compared with the Mediterranean diet profile.

Materials and Methods: The study subjects were a group of 319 women aged 18-35 y (112 smokers, 100 passive smokers and 107 non-smokers), all of them living in the Community of Madrid. A prospective method using a three day food record was followed for three consecutive days including a Sunday, reporting the portion size of each meal in order to obtain the grams per day consumed.

Results: The consumption of cereals after adjusting for energy intake, is higher in non-smokers (159.3 \pm 76.0 g/day) than in smokers (145.6 \pm 69.1 g/day) and passive smokers (141.2 \pm 60.0 g/day) (p<0.05), being in all cases this consumption lower than the recommended. Besides, smokers, both actives and passives, consume less vegetables (235.8 \pm 122.0 g/day in actives and 231.1 \pm 108.4 g/day in passives) than non-smokers (272.1 \pm 124.1 g/day) (p<0.05). It is verified in the three groups a discrepancy between real and recommended consumption related with cereals and vegetables, being this discrepancy more accused in smokers women. On the other hand, smokers have a lower consumption of olive oil (24.2 \pm 12.0 g/day) than non-smokers (27.9 \pm 13.7 g/day) and passive smokers (28.1 \pm 13.7 g/day) (p<0.05).

Conclusions: Smokers, both actives and passives, consume a lower amount of the characteristic foods of a Mediterranean diet such as cereals, vegetables and olive oil. Therefore, added to the danger due to tobacco exposure, which is a major risk factor of a great number of diseases, keeping a more incorrect diet could get worse the negative effects of smoking on health.

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Differences between of the habitual consumption with regard to what consider an adequate diet in a collective of physically active young

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Objective: To know the food habits of physically active young people and to evaluate the differences among the habitual consumption compared to the one considered correct, to determine if there exists a need of improvement (in practice and /or in theoretical level).

Method: There was studied a group of 111 physically active individuals (77 males and 34 women) from 20 to 35 years that carried out an average of 7.8 ± 4.8 hours/week of physical activity which have as main motivation the improvement of health, aesthetics and weight control.

For the dietetic study there was applied a "Food frequency questionnaire". Besides, the individuals were asked about the frequency they believed that the different food should be consumed.

Results: The studied individuals think that they should consume more portions of pasta/rice, cereals, vegetables, fruits and fish compared to what they take actually. Both the habitual consumption and the one considered suitable are away from the guides marked for sportsmen (sportswomen), especially in relation with the cereals and with the vegetables (1).

Conclusion: The lack of knowledge on the characteristics of a diet adapted for physically active people is emphasised, as well as away among the real habits compared to the ideal theoretical one. These results emphasized the need of campaigns of nutritional education in groups of active young people.

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Table 1. Consumption habitual and considered advisable by the studied individuals (Rations / day)

Food group	Habitual Consumption	Think that they must consume
Pasta/rice	$1.0 \pm 0.6^{***}$	$1.3 \pm 0.3^{***}$
Cereals	$2.8 \pm 1.6^{***}$	$4.0 \pm 2.6^{***}$
Vegetables	$1.0 \pm 0.7^{***}$	$2.0 \pm 1.0^{***}$
Fruits	$1.3 \pm 1.0^{***}$	$2.1 \pm 1.3^{***}$
Lacteal	3.0 ± 2.5	3.4 ± 1.8
Meats	0.7 ± 0.4	1.0 ± 0.5
Fish	$0.4 \pm 0.3^{***}$	$1.0 \pm 0.4^{***}$
Egg	0.5 ± 0.5	1.0 ± 0.7
Meats, fish, egg	$1.6 \pm 0.9^{**}$	$2.0 \pm 1.8^{**}$

Consumption of aliments in a group of diabetic and non-diabetic elderly Spanish people

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Objective: To evaluate the consumption of aliments in a group of diabetic and non-diabetic elderly people, in respect to the recommended intake according to a Mediterranean diet.

Materials and Methods: This study was made in a population of 183 institutionalized elderly individuals of the Region of Madrid, aged 63 or more, 50 of them had type 2 diabetes. A seven days weighed food record (including a weekend) was kept in order to monitor food intake, expressing the results in servings/day according the standard size servings and comparing with the recommended in "The correct nutrition in elderly people" (Requejo & Ortega, 1995).

Results: The group of diabetic elderly people have a higher consumption of cereals comparing with non-diabetic ($p < 0.05$), mainly due to the consumption of bread ($p < 0.05$), while diabetics have a lower intake of simple sugars ($p < 0.001$). The consumption of dairy products, specifically of yoghurt, is superior in the diabetic group ($p < 0.05$) as well as the consumption of eggs ($p < 0.05$).

	Consumption of aliments (servings/day) depending on diabetes ($X \pm DS$).				ANOVA2 DIABETES
	NON-DIABETIC		DIABETIC		
	MEN	WOMEN	MEN	WOMEN	
Cereals	3.26 ± 0.77	2.89 ± 0.86	3.67 ± 0.86	2.58 ± 0.90	*
Bread	1.56 ± 0.64	*	1.90 ± 0.89	***	*
Simple sugars	1.31 ± 0.47	1.39 ± 0.54	0.83 ± 0.55	1.58 ± 0.70	***
		1.29 ± 0.52		0.60 ± 0.53	
Vegetables and fruits	2.78 ± 1.06	3.07 ± 1.30	3.35 ± 2.08	2.96 ± 1.30	NS
Dairy products	2.01 ± 0.64	2.07 ± 0.61	2.28 ± 0.65	2.29 ± 0.77	NS
Yoghurt	0.44 ± 0.38	0.42 ± 0.33	0.56 ± 0.37	0.61 ± 0.47	*
Eggs	0.30 ± 0.19	0.29 ± 0.16	0.45 ± 0.37	0.30 ± 0.17	*

*** $p < 0.001$; * $p < 0.05$; NS Non significative

Conclusions: The group of elderly studied have a food intake not adjusted completely to a Mediterranean diet, due to the consumption of cereals and dairy products lower than the recommended, although the diabetic group have a closer adequacy because of the higher consumption of these groups of aliments comparing with the non-diabetic group.

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Mediterranean diet scoring: theory and application to the portfolio eating plan

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Introduction: Assessing the relationship of health with overall diet rather than with single nutrients or foods has intuitive appeal. Traditional Mediterranean dietary patterns have

been linked to less chronic disease and longer life expectancies, the Mediterranean diet score (MDS) is a study specific gradient of adherence to the traditional Greek-Mediterranean dietary pattern. MDS has been used to compare diets of elderly Danes, Greek and Anglo- Australians, and Chinese in four geographic regions – Hong Kong, rural China, Sydney Australia, and San Francisco. In this study MDS was applied to the portfolio eating plan (PEP), a plant food based diet that combines numerous heart healthy components and results in cholesterol and C-reactive protein lowering of up to 30%. Clinical trials have shown that this portfolio diet strategy enhanced the cholesterol lowering effect of a low saturated fat/cholesterol diet, equal to a starting dose of first generation statin drugs (1,2).

Methods: The PEP dietary score was calculated by comparing the daily intake records from 43 hyperlipidemic subjects to the mean intake used as cut-off criteria for respective food categories of the Mediterranean diet. The PEP diet is high in plant sterols, vegetable proteins, almonds, oats, barley, psyllium and vegetables like okra and eggplant.

Results: Scoring of the PEP (vegan, lacto-vegetarian and non-vegetarian formats) against the Mediterranean diet results in a score of 6 out of a possible score of 8.

Conclusions: Quantifying the Portfolio Eating Plan with MDS provides another confirmation of the health benefits of a predominantly plant based foods dietary strategy.

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High-fat, high fruit and vegetable diets: associations with dietary energy density and weight status

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The Mediterranean diet is characterized, in part, by the consumption of health-promoting fats and fruits and vegetables (F&Vs). High-fat foods generally have a high energy density (ED, kcal/g), which may contribute to obesity. Conversely, F&Vs generally have a low ED. This study investigated relationships between a high-fat, high F&V diet, ED and weight status in a representative US sample (1994-96 CSFII). Adults (>19y) with two diet recalls who were not pregnant/lactating or dieting (n=7500) were included in the analyses. ED values excluded beverages. Individuals were stratified on fat intake ($\leq 30\%$ and $>30\%$ calories), then further stratified on F&V intake (<5 , 5-9, >9 servings/d), excluding fried and dried F&Vs and juices. Within each fat category, higher intakes of F&Vs were associated with lower ED values. While the ED of the high-fat, high F&V diet (1.41 kcal/g) was greater than the ED of the low-fat, high F&V diet (1.29 kcal/g); it was less than the ED of most other diet patterns. The prevalence of obesity (BMI ≥ 30) within the high-fat, high F&V diet pattern (9%) was lower than the prevalence within the high-fat, medium F&V pattern (17%, $p<.0019$) and within the high-fat, low F&V pattern (18%, $p<.0003$); but was not statistically lower than the prevalence within the low-fat patterns. Diets characterized by a high fat and a high fruit and vegetable content do not necessarily have a high energy density. A high intake of F&Vs can lower the ED of higher fat diets.

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A nutrient density standard for vegetables and fruit: Nutrients per calorie and nutrients per unit cost

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Objectives: To develop a nutrient density standard for vegetables and fruit, defined as a ratio of the nutrient content of foods in relation to the energy they provide.

Design and procedures: Nutrient adequacy and nutrient density scores for individual foods were based on the foods' content of 16 key nutrients. We used a French national food composition database for 637 foods, including 129 vegetables and fruit, and mean national retail prices obtained from government sources and supermarket websites.

Methods: Relationships between nutrient adequacy (NAS) and nutrient density scores (NDS) for vegetables and fruit, their energy density (ED), and the nutrient to price ratio (NPR) were tested using linear regression.

Results: NAS values were calculated as the mean of percent daily values for 16 nutrients, based on 100g of food. The nutrient density score (NDS) was obtained by dividing the NAS by ED. The nutrient-to-price ratio (NPR) was obtained by dividing NAS by food price per 100g, edible portion. Energy density and nutrient density were inversely linked, confirming the popular belief that energy-dense foods tend to be nutrient-poor. In contrast, fruit and vegetables were nutrient-dense in relation to their low energy content. Although fresh produce can be an expensive source of energy, high NPR values showed that fruit and vegetables provided nutrients (as opposed to calories) at a reasonable cost.

Conclusions: The 2005 Dietary Guidelines recommended that consumer food choices be guided by a nutrient density standard. The desirable foods are those with a high nutrient-to-energy ratio. The present NDS approach permits the examination of the nutrient value of foods not only with respect to the energy they provide, but also with respect to their cost.

Trends and intake structure of calcium from dairy products in the population of youth aged 13-18

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Aim: Analysis of trends and intake structure of calcium from dairy products in the population of youth aged 13-18.

Materials and methods: The research was carried out in the year 2004 among 896 people (405 boys and 491 girls) inhabiting three different environments: country, town and city. The eating habits of 13 dairy products were assessed on the basis of the food intake frequency method, using the ADOS-Ca questionnaire. On the basis of the determined dairy products quantity and eating frequency during a week and also nutrient value tables the calcium intake in mg/day was calculated and compared to recommended daily intake (RDI). The differentiation of calcium intake in sex groups according to age was held using the variation method and features distribution was compared using the chi2 test with p<0.05.

Results: The analyzed boys, in the age groups from 13 to 18 years old, consumed similar amounts of calcium, i.e. about 1044mg (128% of the RDI). Among 38% of boys potential risk of calcium deficiencies i.e. <66.7% of the RDI was revealed. The main calcium sources, regardless of the boys' age groups, were such products as: milk (37% of calcium), yogurts (21% of calcium), hard cheese (18% of calcium) and ice-cream (9% of calcium). The mean calcium intake in girls' population amounted to 721mg (89% of the RDI). The calcium deficiencies risk (<66.7% of the RDI) was stated among 54% of girls. The highest RDI realization was revealed among girls aged 14 (175% of the RDI) and 13 (96% of the RDI), and the lowest among girls aged 18 (66% of the RDI) and 17 (77% of the RDI). The main calcium sources, similarly like in boys' group were: milk (33% of calcium), hard cheese (21% of calcium), yogurts (20% of calcium) and ice-cream (10% of calcium).

Summary: Among about the half of girls and boys the potential risk of calcium deficiencies was revealed, despite satisfactory mean intake. In the boys' group amount and intake structure were not connected with age. Girls consumed less calcium while getting older. In both age groups regardless of age the main calcium sources were: milk, hard cheese, yogurts and ice-creams.

Nutritional profil and hematological parameters in Tunisian children

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Objectives: Iron deficiency in children is a clinical problem caused by inadequate intake of one or more nutritional elements and remains as one of the most important health problem in developing countries. The aim of this study is to determine the relationship between alimentary diet, body mass index (BMI) and haematological parameters in iron deficient children.

Design and methods: Among the children who came to the Polyclinic (CNSS) of Sfax for consultation, we studied twelve diagnosed with iron deficiency (average \pm standard deviation = 17 ± 8 months) and twelve other of the same average were taken as controls. Body mass index (BMI) was estimated by the formula (body weight/ height x height (m²)). Alimentary diet composition of the subjects was rated by their mothers. Blood samples were obtained from a forearm vein with needle technique for routine tests such as iron serum levels and haematological parameters. Red blood Cells (RBC), leukocytes (Leu), Hemoglobin (Hb), hematocrit (Ht), platelets (Pl) were determined.

Results: The results of the nutritional inquiry revealed that children have received an unbalanced alimentary diet quantitatively (irregular food intake) as well as qualitatively (the diet is based on the cow dairy products, cakes, and few vegetables and fruits). In fact, we have obtained in the iron deficient group lower serum iron levels than the control ones (34 ± 17 Vs 95 ± 30 $\mu\text{g}/100\text{ml}$). In iron deficient children, body mass index (BMI) was significantly correlated with serum iron levels ($r = 0,604$) and haematological parameters particularly hemoglobin.

Conclusion: Unbalanced alimentary diet affects iron serum levels and haematological parameters in Tunisian children.

Evaluation of the phenolic content of olive oil at various stages of the milling process

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Olive oil, the end product of the milling process of mature olives is known to contain substantial amounts of phenolic antioxidant compounds. These may contribute to the health promoting effects of the Mediterranean diet. However, the methods used to produce olive oil likely give rise to substantial losses of these substances. To evaluate the extent of this, a site visit to an olive mill in the south of France (Villeneuve-lez-Avignon; Proprieter- Gerard Bertaud) was arranged. Representative samples from all stages of the milling process were collected for analyses of the phenolic antioxidant content. Samples (10 g) from each of the milling steps were extracted with organic solvents using a Soxhlet apparatus. The extracts were fractionated by flash column chromatography on silica gel with increasing concentrations of dichloromethane in methanol. Major components in the fractions were purified by semi-preparative HPLC and subjected to a range of spectroscopic analyses (HPLC, LC-ESI-MS, GC-MS and NMR) to identify and quantitate the phenolic compounds. Major compounds identified and quantited include hydroxytyrosol, tyrosol, caffeic acid, p-coumaric acid, aglycone of ligstroside, aglycone of oleuropein glucoside, dialdehydic form of ligstroside aglycone lacking a carboxymethyl group, dialdehydic form of oleuropein glucoside aglycone lacking a carboxymethyl group, (+)-pinoselinol, (-)-epi-pinoselinol, (+)-1-acetoxypinoselinol, acteoside and luteolin plus the triterpenoids oleanolic acid and maslinic acid. Mature olives contain abundant amounts of phenolic compounds with antioxidant potential. However during the milling proces, due to their inherent water solubility a large proportion (> 50 %) are lost to the vegetation water. Considering the health promoting properties of olive oil, efforts are justified to improve the partition of these to the oil during the milling process.

Dietary diversity and school age child nutrition in North Western Morocco

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Dietary diversity is used alternatively for the assessment of diet quality and food security. Morocco is undergoing nutrition transition while still suffering from a heavy burden of many micronutrient deficiencies and stunting.

Objective: The aim of this work is to assess dietary diversity and its relationship with anaemia and stunting in school-age children in the province of Kenitra.

Subjects: Overall 263 pupils were administered a food frequency questionnaire (FFQ).

Settings: A health team evaluated the anthropometric status and blood haemoglobin levels. Dietary diversity was estimated by two indexes: a dietary diversity score (DDS) based on the number of food categories consumed over a week, and a weekly frequency index (WFI) which expresses the whole frequency of food intake.

Results: Both indices are significantly associated with stunting but not with anaemia. The risk of stunting is greater in rural areas when undesirables' foods (sweetsies.) are excluded from the SDA index. Parent education level is associated to fruits with vegetables and dairy products frequency intakes. It seems that WFI express diversity more than DDS especially in rural areas.

Conclusion: Much more work is needed in this area to elaborate appropriate dietary guides. Nutrition programmes must be integrated in the school health programmes.

Key words: Dietary diversity, anaemia, Stunting and wasting, school age, Morocco

Evaluation of vitamin D insufficiency and its influencing factors in reproductive age women in Tabriz

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Numerous studies in different countries have shown the high prevalence of vitamin D deficiency in Asian countries. The aim of this study was to evaluate the prevalence of vitamin D deficiency and its influencing factors in reproductive age women in Tabriz city. 252 reproductive age, 15-49 years, women of Tabriz city were randomly selected. Weight and height was measured and body mass index was calculated based on weight and height results. Serum levels of vitamin D, calcium, phosphor, and alkaline phosphatase were measured by commercially available kits. Prevalence of severe, moderate and mild Vitamin D deficiency was 15.1%, 15.5% and 33.7% respectively. 3.7% were underweight and 59.8% had different stage of obesity. Only 37.5% had BMI in normal range. There was a significant correlation between serum level of vitamin D and weight ($p < 0.05$). Alkaline phosphatase was increased in 1.6%. There was a decreased level of calcium and phosphor 8.7% and 3.7% respectively. It was not considered any significant correlation between vitamin D status and calcium, phosphor and alkaline phosphatase. In conclusion, vitamin D deficiency is common in women of Tabriz city. Therefore, it is suggested that intervention food fortification, education and sun exposure are recommended for women's health promotion.

Weight gain over ten years in over 6,000 adults from a Mediterranean population. The EPIC Florence study

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Background: Obesity is an important cause of morbidity and mortality. An increased prevalence of overweight and obesity has been reported in most developed countries.

Objective: An update of life-style information, weight and other anthropometric variables is in progress among 12,772 EPIC-Florence volunteers who were alive and not diagnosed with cancer at 31/12/2003, in order to evaluate temporal changes in weight and its correlates in healthy adults.

Methodology: Volunteers were asked to report their weight and to provide a waist and hip measure using a paper meter enclosed with the mail questionnaire. A random sample of the cohort have been invited to the EPIC office to be measured by trained personnel following the standard protocol adopted at enrolment to compare self-reported with measured data in a validation study. Self-reported measures at follow-up have been calibrated according to the validation study results, applying calibration regression models by gender.

Results: Calibrated anthropometric measurements are currently available for 6,425 volunteers (50.3%; mean age at enrolment: 51 years); 365 randomly sampled volunteers have been measured. After a mean follow-up of 9.9 years (range 5.7-12.1) the average age-adjusted weight gain was 2.4 kg (95% CI 2.1-2.7) among men and 2.7 (95%CI 2.6-2.9) among women. The prevalence of overweight (BMI 25.1-30.0) and obesity (BMI>30.0) increased respectively from 50.1% to 55.3% and from 10.3% to 14.7% in males and from 31.2% to 37.1 % and from 9.1% to 14.9% among females. Weight gain was larger among younger subjects (<50 years at enrolment) and among normal-weight subjects, in both genders. No differences were evident according to level of education.

Conclusions: The prevalence of overweight and obesity increased among this large sample of Italian healthy adults in a ten-year period. Dietary and life-style determinants of weight gain will be investigated in the frame of DiOGenes, a collaborative European FP6 project.

Intake of different food groups according to the presence of overweight/obesity in a group of schoolchildren from Madrid (Spain)

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Objective: To investigate the differences between food consumption habits and compliance with Mediterranean Diet, between normal weight (NW) and overweight/obesity (OW/O) schoolchildren of Madrid (Spain).

Methods: It has been studied a collective of 128 schoolchildren (7 to 10 years of age). Height and weight were measured and used to calculate BMI that let us classify the children in OW/O and NW using Cole's criteria (1). The dietetic study was carried using a prospective 'food record questionnaire' over 3 consecutive days and "precise individual weighing" for the meals carried out in the school dining. Differences in dietary data between OW/O and NW subjects were confirmed by analysis of covariance, adjusting for the degree of under- or overestimation (2) of caloric intake.

Results: In both groups of this collective we observed a withdrawal from the recommended food portions for this age group. NW children had a lower daily consumption of meats ($p<0.05$) pre-cooked foods ($P<0.01$), and soft drinks ($P<0.05$) in comparison with OW/O (in g/day). The NW group consumed more servings/day of green-dark and yellow-orange vegetables ($P<0.05$).

Conclusion: In general we observed a withdrawal of the dietetic guidelines. However, the OW/O group presents a worse dietary profile, so this group should deserve mayor surveillance in their diet composition in order to try to make them healthier.

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Evidence for gene-nutrient interaction at the PPAR γ locus in the regulation of BMI and triglycerides

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Introduction: The understanding of the aetiology of complex diseases will require exploration of gene – environment interaction. We present evidence for a diet – gene interaction influencing BMI and triglycerides.

Methods: 201 unrelated patients with type 2 diabetes (118 men and 83 women), aged 35-70 years were consecutively seen at the outpatient clinic of a health district of the province of Naples. Among others anthropometry and plasma lipids were measured. Habitual diet was assessed using a standardized, semi-quantitative, food frequency questionnaire. Participants were genotyped for Pro12Ala polymorphism: 180 patients (89.5%) were Pro/Pro, 20 (10%) were Pro/Ala and 1 (0.5%) was Ala/Ala. All analyses were performed comparing Pro homozygotes with Ala carriers (Pro/Ala + Ala/Ala).

Results: BMI, plasma lipid and nutrient intake were not significantly different between Ala carriers and non carriers. Participants were stratified according to sex-specific tertiles of caloric intake and PPAR γ polymorphism status. Four groups were thus identified: Pro homozygotes or Ala carriers with low (1 tertile) or high (2 + 3 tertiles) caloric intake. BMI was significantly lower in Ala carriers as compared to Pro homozygotes in the low caloric intake group, whereas the opposite was seen in the high caloric intake group ($p=0.683$ for the effect of PPAR γ ; $p=0.022$ for the effect of caloric intake, $p=0.039$ for interaction; two way analysis of variance). A similar analysis was conducted stratifying patients for the polyunsaturated to saturated fat (P/S) ratio of the diet (tertile 1 vs tertiles 2+3) and PPAR γ genotype. Triglycerides were significantly higher in Ala carriers as compared to Pro homozygotes in the lower P/S ratio group. This was not the case in the upper tertiles ($p=0.037$ for the effect of PPAR γ ; $p=0.149$ for the effect of P/S ratio, $p=0.023$ for interaction).

Conclusion: This study provides evidence of a diet-gene interaction at the PPAR γ locus for a complex metabolic phenotype resembling the metabolic syndrome (i.e. overweight and hyperlipidemia).

Health Hunters: An intervention to prevent overweight and obesity in young high risk women

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Objective: The prevalence of obesity is increasing dramatically, and prevention is believed to be the only feasible public health strategy for dealing with the growing problem. However, relatively few prevention studies are published. The aim of the study was to develop and implement an obesity and weight gain prevention program targeted to a high risk group.

Method: 18-28 year old women with at least one severely obese parent were randomized to the intervention or control group of the "Health Hunters" program. During one year of follow up, the intervention group received an individualized behavioural program focusing on food choice, physical activity and other lifestyle factors. Anthropometric measures and fitness levels were measured at baseline and after one year. Self-reported changes in obesity-related behaviours were also assessed.

Results: Baseline examinations were conducted in 40 women, of whom 30 completed follow up examinations one year later. Pregnancy was the most common reason for failure to complete the study. Compared to the control group (which gained weight), the intervention group displayed significant improvements in body weight, BMI, waist circumference, waist hip ratio and self-reported physical activity. Further analysis was conducted relating all subjects' weight changes with different diet and fitness factors. Those who did lose weight decreased their energy percent dietary fat (both saturated and unsaturated) and increased their energy percent protein and fiber density while energy percent carbohydrate was unrelated to weight change. Moreover weight loss was significantly associated with an increasing VO₂ max and more time spent on the treadmill.

Conclusion: The Health Hunters obesity prevention program is effective in high-risk young women with familial predisposition for obesity. An analysis of changes in diet and fitness in relation to concurrent weight changes point out energy percent protein and fiber intake and time spent on treadmill as the strongest "protective" associations.

Energy and macronutrients intake differences between overweight and obesity young women

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Objective: Obesity is a priority health problem. The caloric profile imbalance that it is being producing in Spanish diet can contribute to its development. By this reason to evaluate the differences in energy and macronutrients intake based on the suffering of overweight (OW, BMI <27 kg/m²,) or obesity (OB, BMI ≥27 kg/m²) in a group of young women is the aim of this study.

Methodology: 67 women (20-35 years) with BMI between 24-35 kg/m². A "food and drink record" was used to register all intakes (7 days). Energy and nutrient were calculated using Food Composition Tables and the results were compared with the marked nutritional objectives for the Spanish population (1).

Results: OW women had better carbohydrate/lipid ratio than OB women (Table 1). Energy provided by carbohydrates (ETC) were significantly greater in OW women. Furthermore elevated ETC was associated with obesity protection (RR: 0.9 [CI, 0.8 to 0.9]; P<0.05). Finally women with largest weight obtained lower proportions of their energy from carbohydrates (r=-0.2943) and subjects with the largest BMI obtained greater proportions of their energy from lipids (r=0.2923) and lower proportions of their energy from carbohydrates (r=-0.3347). An inverse relationship was also seen between BMI and the carbohydrate/lipid ratio (r=-0.3363).

Table 1 : Energy and macronutrients intake and energy profile

	OW (n=30)	OB (n=38)
Energy (kJ/day)	9465 ± 2287	9414 ± 2257
Carbohydrates/ Lipids	2.11 ± 0.68	1.79 ± 0.39*
Protein (% Energy)	15.1 ± 3.1	16.3 ± 2.8
Lipids (% Energy)	43.4 ± 6.9	45.5 ± 4.8
Carbohydrates (% Energy)	38.8 ± 7.2	35.5 ± 4.5**
*p<0.05, **p<0.01,		

Conclusion: Approximating the diet to the actual recommendations (by increasing the consumption of carbohydrate and diminishing consumption of lipid) could be an effective way to avoid obesity progression.

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Weight gain and other anthropometric measures in relation to incidence of cardiovascular disease, breast and colon cancer in a female Mediterranean population: Findings from the Progetto ATENA

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Women in the European Mediterranean countries are reported not to take full advantage from the declining in frequency rates of cardiovascular disease (CVD), detectable all over European and North-American countries. Moreover, breast and colon cancer have been increasing steadily. In surveys, an increasing trend in their body mass and central fat has been described, suggesting that this condition might be associated with the chronic disease morbidity and mortality rates. This relationship has been explored in the Progetto ATENA, a cohort of 5,062 women, aged 30-69 and recruited between 1993 and 1998, living in the metropolitan area of Naples, Southern Italy. At baseline weight, height and waist circumference (WC) were measured according to a standardised protocol; reported weight at age 20 was also collected. Lifestyle and clinical data were recorded. A total of 110 fatal and non-fatal CVD and colon and breast cancer incident cases were accrued after an average follow-up of 8 years. Adjusting for age, education and physical activity level (PALs) hazard ratios and 95% confidence intervals were: a) for BMI: <25=1.00, >25-29.9 =1.36 (0.84-2.21), >30-34.9=1.50(0.83-2.68), >35=1.69(0.75-3.79); b) for WC (adjusting also for height): <88cm=1.00, >88-99=0.96(0.61-1.52), >100=1.80(1.02-3.18). Using the latter adjustment and a weight gain per year up to 0.5 Kg as reference, we found: weight gain 0.5-0.99 kg per year equal to 1.16(0.73-1.86), weight gain >1 kg per year 2.12(1.05-4.30).

Our results indicate that in a large Mediterranean female cohort weight gain (sustained by central adiposity) from age of 20 plays a major role in determining CVD and breast and colon cancer.

Antioxidant status and diabetes risk in the SU.VI.MAX study - Association with baseline plasma levels and effect of antioxidant supplementation

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The objective of this study was 1) to describe the associations between baseline plasma antioxidant levels and the long-term risk of diabetes and 2) to assess the effect of a supplementation with a combination of antioxidant vitamins and trace elements, at nutritional doses, on this risk.

3,300 adults from the SU.VI.MAX (double-blind randomized primary prevention trial) were included.

Baseline mean fasting blood glucose (FBG) in the supplementation group was not statistically different compared to the placebo group. After 7.5 y of follow-up, mean fasting blood glucose in the supplementation group was not either different compared to the placebo group. Incident cases of diabetes during follow-up (defined as a FBG > 7.1 mmol/l and/or oral antidiabetic treatments) were not significantly different between the supplementation and the placebo groups.

However, compared to the subjects in the 1st tertile, those in the 2nd and 3rd tertiles of serum baseline levels of b-carotene, presented a lower risk of diabetes in age and sex-adjusted analyses: OR [95% CI]= 0.54 [0.32-0.89] and 0.18 [0.08-0.42] (p for trend <0.0001). We also performed multivariate analyses with further adjustment on smoking status, physical activity level, educational level, body mass index and intervention group (placebo/supplementation). Multivariate-adjusted risks were still significant: OR=0.70 [0.42-1.19] and 0.32 [0.14-0.73] (p for trend =0.02). No association could be shown with vitamins E and trace elements plasma levels with the long-term risk of diabetes.

We were unable to demonstrate any overall effect of a low dose antioxidant supplementation on fasting blood glucose levels or on the risk of diabetes after 7.5 years of follow-up. But we found an inverse association between baseline plasma levels of b-carotene and the risk of diabetes.

Varied vegetable intake is associated with improved lipids: A six-month dietary intervention with a Mediterranean-style diet in Type 2 diabetes

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Objectives: To compare an ad libitum Mediterranean-style (MS) diet versus a high carbohydrate low fat (HCLF) diet on weight, glycaemic control and lipids in people with Type 2 diabetes.

Methodology: 8 men and 8 women have completed this on-going 6-month dietary study. Patients were randomised to a HCLF diet (total fat £ 30%E, carbohydrate > 50%E) or a MS diet (total fat £ 40%E, monounsaturated fat £ 20%E) that promoted > 5 serves of vegetables/day eaten with olive oil. Before and after diets, anthropometry, fasting lipids and HbA1c were measured and patients completed a dietary questionnaire.

Results: Patients lost weight on the HCLF diet, otherwise between diet effects did not differ (Table).

Merging groups (n=16), revealed that a greater number of different vegetables eaten per day was associated with change in HDL-cholesterol (r = 0.548, P<0.05).

Conclusion: In this preliminary analysis, little difference was found in the effectiveness of HCLF and MS diets. Nevertheless, higher vegetable intake, a key feature of a Mediterranean-style diet, was associated with improved lipid profile.

	HCLF dieta (n=8)		MS dieta (n=8)	
	0 months	6 months	0 months	6 months
Weight (kg)	83.2 ± 17.3	79.7 ± 15.7 ^b	87.9 ± 13.1	88.5 ± 12.2 ^d
Waist (cm)	105.0 ± 14.0	101.2 ± 12.2 ^b	102.8 ± 5.4	102.4 ± 7.3
HbA1c (%)	6.7 ± 0.9	6.4 ± 1.2	8.6 ± 2.6	7.8 ± 2.8
Cholesterol (mmol/L)	4.9 ± 1.0	4.9 ± 0.9	5.2 ± 1.3	4.7 ± 1.2
HDL chol (mmol/L)	1.3 ± 0.6	1.4 ± 0.5	1.2 ± 0.3	1.3 ± 0.4 ^c
Triglyceride (mmol/L)	2.6 ± 1.9	2.4 ± 1.7	2.3 ± 1.6	1.9 ± 0.9

a Data are mean ± SD;

b P=0.01 within HCLF diet,

c P=0.06 within MS diet (Student's paired t-test);

d P<0.05 between diet effect (Student's unpaired t-test)

Histopathological studies of the hepatic tissue of the sand rat (PSAMMOMYS obesus) during diabetes development

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Introduction: Through the survey of a population of *P. obesus* (Po) we showed that there is a direct relationship between a relatively high caloric diet (HCD), obesity, DS-2 and atherosclerosis. Another current expression of these illnesses is a serious alteration of the hepatocytes that induces a lot of liver diseases.

Objectives: This study is designed to evaluate the histopathology of the hepatic tissue of Po in control (animals fed with the naturally occurring hypocaloric diet; halophile plants), and in animals in HCD.

Material and method: Our study concerned 62 Po of the two sexes, classified into 2 groups, 24 Po were kept as 'witnesses' group and fed on halophile plants, the others and 10 Wistar were on an HCD program. The experimentation lasted 12 months. For the macromolecules and enzymes nine experimental studies have been achieved, 20 enzymatic activities and 5 molecular substances have been compared.

Results: At the obese Po (60%), the glycogenic overcharge increases strongly, the basophily remains normal and the lipids abundant. Among the diabetics (40%), the glycogenesis comes with a steatosis at the NIDDM and by a total glycogenic depletion, a considerable overcharge in lipids and an important decrease in lipoproteins at the IDDM. The enzymatic modifications are deep: the phosphorylase and the UDPG-synthetase, active at the obese and the NIDDM, are absent at the IDDM for which we note a hyperactivity of some lysosomale enzymes.

Conclusion: The Po develop an obesity and a diet-induced diabetes without previous hyperphagy. The liver (central organ in the regulation of carbohydrate metabolism) undergoes deep pathological modifications induced by the HCD. The histochemical reactions found are in perfect correlation with the analytic results and with the histo-enzymological modifications observed. These perturbations of the hepatic tissue are typical of the diabetic state and are similar to those observed in the human diabetes.

Impact of a Mediterranean type diet on the metabolic syndrome

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Background: The metabolic syndrome is an important risk factor for diabetes mellitus and cardiovascular disease and mortality. During the 1990s, its prevalence in the Netherlands ranged from 3% in women of 20-39 years to at least 33% in men >55 years. It is expected that the rates will increase in the near future. Therefore prevention, through e.g. dietary measures, is warranted. In this respect the amount and type of fat in the diet deserves attention. Recently, an intervention study reported that a diet high in mono-unsaturated fatty acids (MUFA) such as from olive oil, increased insulin sensitivity in healthy subjects. However, additional beneficial effects can be expected from the Mediterranean diet as a whole.

Study objectives: Aim of our study is to investigate the impact of the Mediterranean type of diet, and especially the intake of MUFA, on markers of the metabolic syndrome in high-risk subjects.

Methods: We will perform an intervention study comparing the impact of three diets (Mediterranean, high fat in MUFA, high fat in saturated fatty acids) on aspects of the metabolic syndrome (primary outcome: fasting insulin). The intervention, including 60 subjects aged 40-65 years with moderate abdominal obesity, will start in 2007 and will last for a period of 8 weeks. Measurements of serum insulin concentration and other parameters will be carried out at week 2, 6, and 8.

Expected results: Our study will provide information on the role of MUFA and the expected beneficial impact of a Mediterranean type of diet on the metabolic syndrome.

Effects of polysaturated and monosaturated fat diet on insulin action and sensitivity in cultured rat hepatocytes

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Introduction: Insulin resistance is a common phenomenon in obesity and Type 2 diabetes. Increased dietary fat intake will lead to impairment of insulin action. The aim of this study was to find out changing of insulin sensitivity in dependence of fat diet and possible direct action of the diet on the liver.

Methods: Male Wistar rats were fed ad libitum (3 weeks) with standard, high polyunsaturated fat diet (sunflower oil) and monounsaturated fat diet (olive oil). Hepatocytes were isolated by a collagenase perfusion technique and cultured for 24 h in M 199 serum-free medium. The glucose production and α -amino isobutyric acid (AIB) transport was measured.

Results: Hepatocytes isolated from rats on high polyunsaturated fat diet had an increase in basal and glucagon-stimulated glucose production and insulin had no effects. Insulin significantly decreased and normalized basal glucose production in the liver cells from rats on high monounsaturated fat diet. Insulin-stimulated AIB transport was significantly lower in hepatocytes cultured from rats on high polyunsaturated fat diet, but in hepatocytes from rats on high monounsaturated fat diet was significantly higher than in the control.

Conclusion: High polyunsaturated fat diet caused higher glucose production from the liver cells, decrease in insulin action and sensitivity and lead to insulin resistance. High monounsaturated fat diet increased insulin sensitivity in the hepatocytes.

Relationship between ADRB2 and UCP3 variants and risk of type 2 diabetes mellitus in a southern Italy population

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Introduction: Type 2 Diabetes Mellitus (T2DM) is a complex disease with genetic predisposition. Previous studies suggested that T2DM is related through obesity to deregulation of energy homeostasis. We studied DNA polymorphisms in genes encoding peripheral energy expenditure as α -Adrenoceptors (ADRB), Uncoupling proteins (UCP) and regulators of adipocyte growth and differentiation. Genes related to the risk of diabetes could interact in an epistatically way. Epistasis occurs when an allele of one gene influences the phenotypic effects of another gene.

Methods: We conducted an association study in a case-control population. Our population sample is composed by 500 subjects: 200 patients and 300 controls. T2DM group is composed by 82 females/118 males, (age range = 34-79 years, mean 54.6 years, SD 7.33). Controls are composed by 124 females/176 males (age range = 34-77 years, mean 54.2 years, SD 8.35). In this population there are 149 obese and 351 non-obese subjects. The single nucleotide polymorphisms (SNPs) characterized were ADRB1 Gly389Arg, Arg16Gly ADRB2, Gln27Glu ADRB2, G(-866)A UCP2, C(-55)T UCP3, Pro16Ala PPAR α and Gly483Ser PGC1. We genotyped all subjects by SYBR green Realtime PCR. Age, sex and lifestyle (smoking, diet) have been considered in the analysis as influencing environmental factors. We analyzed data by using binary logistic regression (BLR) and multifactor dimensionality reduction (MDR). We stratified the whole population for BMI.

Results: We have found in the whole sample by BLR an association between age class, Arg16Gly ADRB2 and the disease risk ($P = 0.007$). After stratification, in the non-obese group, we found an additional association with UCP3 C (-55)T variant. Also in this case the association seems to be age-dependent. The influence of ADRB2 variant on the disease risk seems to be dependent on the UCP3 polymorphism. Subjects with the UCP3 CC genotype had an evident association between ADRB2 and the disease risk, whereas the UCP3 T-carrier subjects seem to not influence the disease risk.

Conclusion: We found that two genes implicated in the energy expenditure could be involved in the risk of T2DM, interacting in an epistatic way.

Comparison between saturated and monounsaturated fatty acid-enriched diets on oxidative status of patients with type 2 diabetes

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Type 2 diabetes is associated with coronary artery disease (CAD) and elevated levels of oxLDL. Postprandial lipemia, associated to an increased pro-oxidative status, has been recognized as a risk factor for atherosclerosis. On the basis of epidemiological data, the consumption of monounsaturated fatty acid (MUFA)-enriched diets has been related to a lower rate of CAD.

Aim of this study was to compare the effects of a saturated fat (SAFA)-diet and a MUFA-diet on LDL oxidability, TBARS production and LDL vitamin content in type 2 diabetic patients in the fasting and postprandial states. In a balanced, randomized, crossover design, twelve overweight men (53±8 y; BMI 30.2±1.6 Kg/m²) consumed 2 experimental diets for 2 consecutive 3-wk periods. The diets were iso-energetic and similar for macronutrient composition (49% carbohydrates, 35% fats, 16% proteins) but different as regard the type of fatty acids. One was enriched in SAFA (17% SAFA, 3% polyunsaturated fatty acids, 15% MUFA) and the other in MUFA (8% SAFA, 4% polyunsaturated fatty acids, 23% MUFA). In CuSO₄ oxidized LDL, lag-phase values, calculated by monitoring conjugated diene formation, were significantly lower after SAFA diet consumption with respect to MUFA diet, both in fasting (65.0±2.2 vs. 74.7±4.6 min, p<0.05) and postprandial states (60.7±2.2 vs. 70.9±4.0, p<0.05). In postprandial state, TBARS production was significantly higher after SAFA than MUFA consumption (69.3±5.2 vs. 49.8±4.8 nmol/mg of LDL protein, p<0.001). In fasting state, LDL α -Tocopherol value was similar with both the diets. On the contrary, after SAFA diet, the postprandial content was significantly lower respect to the fasting one (1.93±0.10 vs. 1.58±0.11 mg/mmol LDL cholesterol, p<0.05), while no changes were observed with MUFA diet. In conclusion, when a MUFA-enriched diet was consumed, LDL appeared more resistant against oxidation, mainly in postprandial state, probably because of the high α -tocopherol content. Results provide evidence of a protective action exerted by MUFA against the pro-oxidative status associated with postprandial lipemia in type 2 diabetic patients.

Involvement of abdominal obesity, sugar intake and physical inactivity in the occurrence of metabolic syndrome and diabetes in Moroccan women

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Objective: To examine the influences of body weight, physical activity and carbohydrate intake on metabolic syndrome and diabetes in Moroccan adult women.

Methods: Data were obtained on randomised samples of 249 urban women aged 15 and older, non-pregnant, living in Laayoune city of South Morocco and who visited the Public Health Centres during immunization campaign. The following data were collected: Body weight, height, circumferences of waist (WC) and hip, blood pressure, fasting plasma glucose (FPG), triglycerides, dietary intake and physical activity. Body mass index (BMI) and waist to hip ratio (WHR) were calculated.

Results: The overall prevalence of the metabolic syndrome and diabetes were 16.3% and 6.4%, respectively. These values increased with BMI, WC and WHR. Women with diabetes or metabolic syndrome tended to have higher intake of sucrose essentially coming from sweetened beverages. They also spent more time in tea consumption and in afternoon sleeping (sedentarity) and lower time in sport and walking activity.

Conclusion: The results suggest that central obesity, sugar intake and sedentarity are involved in the occurrence of metabolic syndrome and diabetes in Moroccan women. Decreasing sweetened beverage intake, decreasing time spent in tea consumption and in afternoon sleeping, and increasing walking activity might be effective as a step in reducing metabolic syndrome and diabetes.

Dietary patterns and coronary heart disease mortality

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The present study was initiated to study whether major dietary patterns predict coronary heart disease mortality. The study was based on the Finnish Mobile Clinic Health Examination Survey cohort and the study population comprised 5009 men and women, 35-69 years of age and free from heart disease. Dietary intake at baseline was estimated based on a 1-year dietary interview and two major dietary patterns were identified using factor analysis. A pattern labeled 'prudent' was characterized by higher consumption of fruits and vegetables, and a pattern labeled 'conservative' by consumption of butter, potatoes, and whole milk. The participants were followed for 26 years and during that time period a total of 621 participants died from coronary heart disease. Relative risks of coronary heart disease mortality (adjusted for age, sex, serum cholesterol, blood pressure, body mass index, smoking, diabetes, physical exercise, and energy intake) between the extreme quartiles of the pattern scores were 0.81 (95% confidence interval (CI) = 0.63-1.03; P for trend (P) = 0.01) for the prudent pattern, and 1.24 (CI = 0.97-1.58; P = 0.04) for the conservative pattern. The results are thus in line with the hypotheses that conservative dietary pattern is an independent risk factor and prudent dietary pattern a protective factor of coronary heart disease.

Decline of cardiovascular disease mortality in Poland between 1991-2002 – Contribution of changes in dietary habits

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Background: A decrease in mortality due to cardiovascular disease (CVD) has been recently documented in Poland. It is important to identify factors, which caused a reduction in CVD mortality, because the knowledge of this topic suggests further actions.

Aim: To analyse the relationship between changes in dietary habits and reduction in CVD mortality rates in Warsaw population.

Methods: CVD mortality data was obtained from The Central Statistical Office. Standardised CVD mortality rates were calculated for Warsaw population (aged 35-64) in each year from 1984 to 2002.

Individual dietary habits were assessed in 2571, 1397, 1485 and 836 randomly selected men and women from the same Warsaw population in years 1984, 1988, 1993 and 2001. Time-trends for energy and nutrients were calculated.

Results: Reduction in CVD mortality in analysed population commenced in 1991. The CVD mortality rates (age 35-64) decreased by 50% between 1991 and 2002 in both genders.

Over the 17 years of observation significant changes were noticed in the nutrition value of the average diet of Warsaw population. In 2001 in comparison to 1984 a decrease of men energy value by 18%, dietary cholesterol by 35%, animal fats (butter, lard) by 53% in both genders were found. The increase of consumption of vegetable fats (oil and soft margarine) by 330% in men and 250% in women was recorded. The above changes resulted in a significant reduction (25%) of atherogenicity level of diet as expressed by Keys score.

The improvement in dietary habits in Warsaw population resulted in a decrease in CVD mortality. These changes in diet preceded CVD mortality decrease by 5-7 years.

Conclusions: Changes in dietary patterns explain, at least in part, the mentioned reduction in CVD mortality recently observed in Warsaw population.

Dietary habits and cardiovascular risk factors of the Warsaw population in years 1993-2001 – Pol-MONICA Project

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Introduction: Dietary factors are known to contribute to risk of widely prevalent chronic illnesses in Poland such as cardiovascular diseases.

Aim: To evaluate changes in dietary habits and selected cardiovascular risk factors of the Warsaw population in the 8-year period.

Methods: In years 1993 and 2001 dietary habits were assessed in 1485 and 836 randomly selected 35-64 year old men and women.

Results: Over the observation period substantial changes in food consumption pattern were noticed: the percentage of energy from fat decreased from 39,9% to 37,8% ($p < 0,01$) in men and from 38,2% to 35,9% ($p < 0,01$) in women, the percentage of energy from saturated fatty acids decreased from 14,0% to 12,4% ($p < 0,01$) in men and from 13,5% to 11,9% ($p < 0,01$) in women, the percentage from carbohydrates increased from 46,0% to 47,5% ($p < 0,05$) and from 47,5% to 49,6% ($p < 0,01$) and dietary fibre intake from 21,5 g to 22,8 g ($p < 0,05$) and from 15,7 g to 17,5 g ($p < 0,01$) respectively. In 2001 in comparison with 1993 intakes of vitamins C and B2, calcium, magnesium, potassium and iron were significantly ($p < 0,01$) higher in both genders, vitamin B1 in men and E in women. At the same time decrease of population means total cholesterol and LDL-cholesterol (in men 13 mg/dl and respectively 12 mg/dl in women 9 mg/dl and 10 mg/dl) was noted

Conclusion: During the analysed period, changes in nutrient intake were substantial and indicate a change in direction towards the recommended preventive diet.

Effect of Mediterranean vegetable soup ingestion on plasma vitamin C and antioxidant biomarkers in humans

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Consumption of fruits and vegetables is associated with a reduced risk of cardiovascular disease. “Gazpacho” is a Mediterranean vegetable soup constituted of tomato, cucumber, pepper, onion, garlic, olive oil, and wine vinegar.

The objective of this study was to assess the bioavailability and plasma levels of vitamin C from freshly made (FM) vegetable soup –“gazpacho”– and its impact on 8-epiPGF2a (oxidative stress biomarker) and uric acid (cardiovascular risk factor) concentrations in a human population.

For this purpose six subjects consumed 500 mL of FM vegetable soup/day for 14 days. On the first day of the study, the subjects drank the vegetable soup in one dose (dose-response study), and on days 2-14 they consumed 250 mL in the morning and 250 mL in the afternoon (multiple-dose-response study). Blood was collected every hour for 6 h on the first day and again on days 7 and 14. All blood samples were analyzed for vitamin C, 8-epiPGF2a, and uric acid.

The maximum increase in plasma vitamin C occurred 3 h postdose. Vitamin C remained significantly higher ($P \leq 0.05$) on days 7 and 14 of the intervention. Plasma 8-epiPGF2a concentration was significantly lower ($P = 0.05$) at the end of the study. Plasma levels of vitamin C and 8-epiPGF2a were inversely correlated ($r = -0.743$, $P = 0.0004$). In general, across individuals, uric acid concentration was lower when vitamin C was higher.

In conclusion, drinking two servings (500 mL) of FM vegetable soup (“gazpacho”) daily increases plasma vitamin C and significantly decreases 8-epiPGF2a concentrations in healthy humans, which provides new evidence for the healthy benefits of Mediterranean-style diet.

Vitamins C and E suppress stimulated peripheral blood mononuclear cells in vitro

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Several immunologic pathways and inflammation appear to be strongly involved in the development and progression of atherosclerosis. Increased neopterin concentrations and enhanced degradation of tryptophan are found in patients with coronary artery disease and higher concentrations of, e.g., neopterin predict adverse events in patients. Because both these immunobiochemical pathways are induced by interferon- α , the observations support a role of this Th1-type cytokine in atherogenesis. Consumption of food and beverages rich in antioxidants are considered to be able to reduce cardiovascular risk. Earlier we have found that wine, beer and green and black tea suppressed neopterin production and tryptophan degradation in human peripheral blood mononuclear cells (PBMC) stimulated with the mitogens phytohaemagglutinin (PHA) and concanavalin A (Con A) in vitro. In this study, we determined the influence of antioxidant vitamins C and E in the same experimental set-up. Compared to unstimulated cells, PHA and Con A increased production of neopterin and the degradation of tryptophan (all $p < 0.01$). Vitamins C (1–10 μM ascorbic acid) and E (2–20 μM α -tocopherylacetate) were found to counteract these effects in a dose-dependent fashion; significant reduction of neopterin formation as well as tryptophan degradation was observed ($p < 0.01$). Data demonstrate that vitamins C and E are able to slow-down and even to counteract activation cascades in stimulated PBMC as was reflected by reduced production of neopterin and degradation of tryptophan. Data suggest that anti-atherogenic effect of food rich in antioxidants may relate to an immunosuppressive behaviour which is achieved by antioxidant ingredients.

Evaluation of nutritional and metabolic risk factors coexistence taking into consideration cardiovascular diseases

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The increasing global occurrence of obesity and diabetes threatens the health breakdown. These constant trends suggest that obesity and diabetes of the type 2, and also the metabolic syndrome are going to be more and more important etiological factors of cardiovascular diseases. That is why there is a need of undertaking successive research of different types and also effort to define kinds and number of factors responsible for the development of the coronary disease. The research was carried out in the years 2003-2004 among 370 women in the menopause (aged 39-59) from Warmia-Masuria District. Body content of the examined women was characterized on the basis of the carried out anthropometric measurements, i.e. body mass (kg), body height (cm), four skinfolds thickness (mm), waist circumference (cm) and hips circumference (cm) and calculated on their basis indices: the BMI (kg/m^2), fat mass in the body (%FM, %) and the WHR. The evaluation of the eating manner was made using the individual 24-hour recall method, repeated 7 times, and made in irregular terms of time. The consumption of chosen nutrients, anthropometric and biochemic parameters of women were evaluated so as to specify the heart-vessels diseases risk. The main components method with the normalized varimax rotation was used to separate the main factors including those parameters that coexist and characterize the body content and metabolic profile (21 output factors). The correlation coefficient $p \geq 0.5$ was agreed as the boundary value in the analysis. Calculations were made using the Statistica v.6.0 programme. In the analyzed women's group the coexistence of nutritional and biochemic risk factors of the coronary disease was stated. The separated profiles of that coexistence created parameters characterizing body fatness, metabolic profile, and were connected with the amount of eaten nutrients, which allows for an individual interventions dealing, fitted for the analyzed population's needs, to limit the unfavourable trends of vessels diseases.

Mediterranean diet has a beneficial effect on blood lipids in a normal Swedish population – the INTERGENE research program

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Objective: To study adherence to a Mediterranean diet in healthy individuals in a cohort in the west of Sweden, and to study the association to traditional risk factors for coronary heart disease (CHD).

Method: 3602 randomly selected individuals (1903 women and 1699 men), 25-75 years, attended the INTERGENE research program¹ including examination of blood lipids, blood glucose, blood pressure, body composition and ECG. They completed an extensive food-frequency questionnaire. Mediterranean diet was defined as

- Using olive oil in cooking and dressing
- Eating vegetables 2 times/day
- Eating fruit 1 time/day
- Eating fish or fish oil 1-2 times/week
- Fulfilling 3 of the criteria: Eating nuts 1-2 times/week, eating poultry 1-2 times/week, eating legumes 1-2 times/week, drinking wine 1-2 times week.

Results: 15% of the women and 9% of the men fulfilled the criteria for the Mediterranean diet. Women with the Mediterranean diet had lower s-triglycerides (1.10 mmol/L vs. 1.25 mmol/L, $p = 0.01$) and higher s-HDL-cholesterol (1.76 mmol/L vs. 1.71 mmol/L, $p = 0.03$). For the other risk factors for CHD, total s-cholesterol, p-glucose, blood pressure and Body Mass Index there were no significant differences between the groups. There were no corresponding differences among men. Currently smoking was seen in 12% in the Mediterranean diet group and 18% in the remainders.

Conclusion: 9-15% of the participants in the INTERGENE research program fulfilled the criteria for the Mediterranean diet, which seems to have a small but significant effect on two important factors associated with CHD.

¹ www.sahlgrenska.gu.se/intergene

Dietary fiber intake and risk factors for cardiovascular disease in French adults from the SUVIMAX cohort

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Background: increased consumption of dietary fiber is widely recommended to maintain or improve health but knowledge is limited on the relation of dietary fiber sources with cardiovascular disease risk factors.

Objectives: we examined the relationship between intake of dietary fiber types or sources, and cardiovascular risk factors in a cohort of adult men and women.

Design: in a cross-sectional study of 2,532 men and 3,429 women, quintiles of fiber intake were determined for each gender from dietary records. Age- and multivariate controlled logistic models investigated odds ratios of abnormal markers for quintiles 2 to 5 of fiber intake compared with the lowest.

Results: Highest intakes of total dietary fiber and non-soluble dietary fiber were associated with a significant ($p < 0.05$) decreased risk of elevated body mass index (BMI), waist-to-hip ratio, and blood pressure, elevated plasma ApoB, ApoB/ApoA1 ratio, cholesterol, triacylglycerol and homocysteine. Soluble dietary fiber was less effective. Fiber from cereals were associated with a lower BMI, blood pressure and homocysteine level, fiber from vegetables with lower blood pressure and homocysteine and fiber from fruit with lower blood pressure and waist-to-hip ratio. Fiber from dried fruit or nuts and seeds was associated with lower BMI, waist-to-hip ratio, fasting glucose and apoB levels. Fiber from pulses had no specific effect.

Conclusion: dietary fiber intake was inversely correlated in both sexes with several cardiovascular risk factors supporting their protective role on cardiovascular disease and recommendations for increased consumption.

Geographical influences on the association between adherence to the Mediterranean Diet and the prevalence of acute coronary syndromes, in Greece; the CARDIO2000 Study

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Objective: We evaluated the interaction between adherence to the Mediterranean diet and region of Greece on the likelihood of having acute coronary syndromes (ACS).

Methods: During 2000-2001, a random sample of 848 patients (61 ± 10 years) with their first coronary heart disease event, and 1078 frequency matched (by age-sex) controls with no cardiovascular disease in their medical history, from all the country, entered into the study. Among several factors, adherence to the Mediterranean diet was assessed by a diet – score that incorporated the inherent characteristics of this diet.

Results: The multi- adjusted analysis showed that a 10-unit increase in the diet score was associated with a 27% (95% CI 0.66 to 0.89) decrease of the odds of having ACS. Moreover, a highly significant interaction was observed between region and diet score (p < 0.001). The odds ratios varied from roughly 0.5 in Southern to 1.2 or more in Northern Greek regions (p for heterogeneity < 0.05). Differences in food patterns consumed did not explain the previous findings. In addition, when we stratified our analysis by rural and urban areas we found significant differences in the estimated odds ratios (p for interaction between diet score and area = 0.01), since a 10-unit increase in the diet score was associated with 22% (95% CI 0.63 to 0.96) lower odds in urban areas and 31% (95% CI 0.48 to 0.98) lower odds in rural areas.

Conclusion: Our findings underline the importance of the Mediterranean diet on the primary prevention of ACS. Moreover, we revealed a geographical variation in importance of this dietary pattern on coronary risk, independent from the composition of food patterns consumed and the presence of the common cardiovascular risk factors.

Sociodemographic and dietary characteristics of persons with different self-rated health

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The aim of the study was to describe differences in sociodemographic variables, cardiovascular disease risk factors, and dietary variables between persons with poor self-rated health and persons with good self-rated health.

In 2001 information about self-rated health, age, education level, marital status, employment status, smoking habits, anthropometric measures, blood pressure, lipids profile and food intake was determined in a representative sample of 658 men and 671 women aged 20-74 from Warsaw population.

Poor health was more common in women (45%) than in men (38%). In both genders the prevalence of poor health was higher in groups of higher age and lower in groups of higher education levels and physical activity. Men with poor self-rated health had higher triglycerides and glucose level, whereas women had higher body mass index than persons with good self-rated health. In both genders no differences were observed in systolic and diastolic blood pressure, cholesterol and LDL-cholesterol level between persons with poor and good self-rated health.

Men, who rated their health as poor consumed less carbohydrates, magnesium, vitamin B6 and vitamin C than men with good self-rated health. Women with poor self-rated health consumed less energy, protein, fats, calcium, magnesium, vitamin E, and had lower diet atherogenicity in comparison with women with good self-rated health.

Effect of folic acid supplementation on plasma homocysteine levels in patients with coronary artery disease

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Objective: Elevated plasma homocysteine concentrations are recognized as a risk factor for coronary artery disease and are inversely related to plasma folate levels. Therefore, the present study was done to assess the effect of supplementation of the folic acid on homocysteine levels in patients with coronary artery disease (CAD).

Methods: A double-blind, placebo-controlled trial was conducted on 70 male patients aged 45-65 years with documented CAD. Patients were divided randomly into two groups which received respectively 1 mg folic acid or placebo tablets daily for 8 weeks. Before and after intervention period, fasting blood samples were taken for measurement of homocysteine and folate levels. The Student's t and Paired – t tests were used for statistical analysis of data.

Results: After 8 weeks supplementation with folic acid, folate concentration significantly increased in the folic acid group (10/88 ng/ml vs. 5/39 ng/ml) ($P < 0.001$). Increased rate of serum foliate was higher in patients with initial serum folate < 5 ng/ml than other groups (19/44 ng/ml vs. 13/94 ng/ml) ($P < 0.01$).

Although there was no significant change with placebo group, the mean plasma total homocysteine concentration after 8 weeks of supplementation with folic acid significantly decreased (29/50 $\mu\text{mol/L}$ vs. 39/75 $\mu\text{mol/L}$) ($P < 0.001$). Decreased rate of plasma total homocysteine concentration was higher in patients with initial plasma total homocysteine > 30 $\mu\text{mol/L}$ than other groups (15/56 $\mu\text{mol/L}$ vs. 23/21 $\mu\text{mol/L}$) ($P < 0.002$).

Supplementation with folic acid normalized plasma total homocysteine levels ($< 15 \mu\text{mol/L}$) in 50 percent of hyperhomocysteinemic patients.

Conclusion: These findings suggest that daily administration of 1 mg folic acid effectively reduced plasma homocysteine concentration in CAD patients. Therefore, in CAD patients with high homocysteine levels supplementation with folic acid could be recommended.

The effects of medical nutrition therapy (MNT) on the blood lipid levels and nutrients intake in Korean hyperlipidemic patients

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Hyperlipidemia is one of the risk factors for coronary artery disease. The purpose of this study was to investigate medical nutritional therapy (MNT) lead to beneficial outcomes in mildly hyperlipidemic adults. From February to October, 2003, the 43 hyperlipidemic (23 men, 20 women) subjects (total cholesterol > 200 mg/dl or triglyceride > 150 mg/dl) admitted to K medical center were studied. Subjects were randomly divided into 2 groups; with MNT and without MNT for 12 weeks. Anthropometric measurements, blood chemical analysis including lipid levels and dietary assessment were carried out at the beginning and end of experiment. After the 12 weeks of MNT, the subjects had regular and balanced meal pattern. Consumption of foods high in cholesterol and saturated fat, salty foods, fried foods, and instant foods decreased significantly in all groups ($p < 0.05$). Intake of energy and cholesterol also decreased. In conclusion, the MNT improved the dietary habits and moreover the decreased of blood lipid level.

Metabolic syndrome and breast cancer recurrences

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Objective: Several studies showed that hormonal, metabolic, and inflammatory mechanisms may affect cancer progression. We tested if metabolic syndrome could be a prognostic factor for breast cancer recurrences.

Methodology: We analysed, using the Cox proportional hazards model, the prognostic value of the metabolic syndrome in 110 women who participated into a dietary intervention trial aimed at reducing insulin and sex hormone levels in postmenopausal breast cancer patients (Berrino F. et al., Int J Cancer, 2005).

Results: At the beginning of the study 16 patients were affected by metabolic syndrome. They showed significantly higher levels of sex hormones, Insulin, and significantly lower levels of SHBG. The major determinant of prognosis was serum Testosterone. The hazard ratio of recurrence was 2.7 (95% CI 1.2-6.1) for the presence of metabolic syndrome and 7.8 (95% CI 2.7-22.9) for the upper tertile of testosterone distribution (0.5-0.93 ng/ml) compared to the lower tertile (0.16-0.33 ng/ml) after adjustment for disease stage and hormonal receptor status. The adjusted OR of recurrences among women with metabolic syndrome and testosterone levels higher than 0.40 ng/ml (median value) was 9.2 (95% CI 1.84-46.68) compared with women without metabolic syndrome and testosterone levels \leq 0.40 ng/ml.

Conclusions: The results suggest that correcting the metabolic syndrome may favourably influence the prognosis for breast cancer justifying further studies on larger series of patients.

Evidence of protective effect of dietary antioxidant on breast cancer risk in the prospective cohort of ORDET

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Despite the suggestion of a protective role of dietary antioxidant component in breast cancer prevention, the association between total dietary antioxidant capacity and risk of breast cancer has never been investigated. Taking advantage of the recently published database on total antioxidant capacity of Italian foods and beverages (Pellegrini N., 2003), integrated with 50 values for cereal and cereals products, pulses and nuts, the relation between dietary antioxidant capacity and breast cancer was evaluated among women participants to the ORDET prospective cohort study.

From 1987 to 1992, 10786 women volunteers were recruited among residents of Varese Province, Northern Italy, an area covered by a cancer registry. A semi-quantitative self-administered food questionnaire was completed by 9186 participants. Three different assays were used to evaluate the dietary total antioxidant capacity to take into account the wide variety and range of action of antioxidant compounds in actual food: Trolox equivalent antioxidant capacity (TEAC), total radical trapping antioxidant parameter (TRAP) and ferric reducing-antioxidant power (FRAP). After median follow up time of 11.5 yrs, 293 cases of invasive breast cancer were identified. Cox proportional hazards regression was used to adjust for major confounders to determine the effect of TEAC, TRAP and FRAP on breast cancer risk. High dietary levels of the three antioxidant measures were found to have significant protective effect on breast cancer risk: adjusted hazard ratio (HR) for the high versus the low quintile of TEAC was 0.53 [95% confidence interval (CI) = 0.34-0.83]. Figures for TRAP and FRAP were HR = 0.63 (CI = 0.41-0.99) and HR = 0.58 (CI = 0.37-0.90) respectively; interquartile trends were always significant. These findings indicate a consistent inverse association between total antioxidant capacity of diet and risk of breast cancer suggesting that a diet rich in antioxidants might protect against breast cancer.

Differences in food intake and cardiovascular disease risk factors between persons with normal and elevated homocysteine level

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Homocysteine (Hcy) is positively related to atherosclerotic vascular disease, and is of particular interest in the Polish population, where the prevalence of these diseases is relatively high.

In the frame of Pol-MONICA bis Project carried out in 2001, plasma homocysteine, folate and vitamin B12 levels, lipids profile and dietary habits were determined in a representative subsample of 617 men and 657 women aged 20-74 from urban and rural country regions. Food intake was assessed by 24-hour recall method. Mean (geometric) Hcy concentration was 11.0 micro mol/L in men and 9.5 micro mol/L in women. Elevated Hcy levels (Hcy \geq 12 micro mol/L) were seen in 32.6% of men and in 20.3% of women.

Persons with elevated homocysteine level compared to persons with normal Hcy level were older, more often with subjective poor health status and low physical activity, and had significantly lower plasma folate and vitamin B12. No differences were found in body mass index, systolic and diastolic blood pressure, and lipids profile. Men with elevated Hcy level consumed significantly lower amount of grain products, meat and meat products, whereas women with elevated Hcy level consumed lower amount of dairy products, vegetables, fruit, added vegetable fat, and greater amount of alcohol than persons with normal Hcy level.

In multivariable logistic analysis the odds ratio of high Hcy level (Hcy greater than 12 micro mol/L) was modified by age, marital status, physical activity, BMI, plasma folate and vitamin B12 in men. In women it was modified by age, marital status, plasma folate and alcohol intake. Diet did not influence the odds ratio of high Hcy level in both genders.

Reduction of oxidative DNA damage in post-menopausal women by consumption of a high-phenol extra virgin olive oil: a randomized cross-over trial

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Background: Olive oil is the key ingredient of the so called Mediterranean diet. Extra-virgin olive oils, high in phenolic compounds with antioxidant properties, could be partly responsible for the lower mortality and incidence of cardiovascular diseases and, possibly, cancer in the Mediterranean region.

Objective: The present study aimed to measure oxidative DNA damage in healthy women consuming olive oils with different concentrations of natural phenols.

Methods: A randomized cross-over trial of high phenol extra-virgin olive oil (High-EVOO, 592 mg/kg of total phenols), versus low phenol extra-virgin olive oil (Low-EVOO, 147 mg/kg) was conducted in ten post-menopausal women in Florence. Subjects were asked to substitute all types of fat and oils habitually consumed with 50 g/day of the study oil for eight weeks in each period. Oxidative DNA damage was measured by the comet assay in plasma lymphocytes, collected at each of ten visits during the study period. The excretion of the olive oil phenols and selected metabolites in repeat twentyfour-hour urine samples was measured to evaluate compliance.

Results: Extra virgin olive oil is the most commonly consumed fat by the general population in Tuscany, and we observed a quite sustained excretion of hydroxytyrosol at the baseline (682 mg/day). In the intervention trial, urinary excretion of hydroxytyrosol and its metabolite homovanillyl alcohol were significantly increased during the consumption of High-EVOO (p= 0.01). The average of the four measurements of oxidative DNA damage during treatment with High-EVOO was lower than the average during the Low-EVOO treatment, resulting in a 30 % reduction in damage (p= 0.02). Despite the relatively small sample size, this study showed a reduction of DNA damage by consumption of an extra-virgin olive oil rich in phenols, particularly hydroxytyrosol. A larger trial is needed to confirm and expand these results.

Dietary trans-fatty acids and risk of breast cancer: Findings from ORDET Prospective Study

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The relation between dietary trans-fatty acids and breast cancer was evaluated in an Italian prospective study. Dietary trans-fatty acids have been recently reported as having a possible role on the carcinogenesis, although limited data are available testing this hypothesis in humans.

Women volunteers were recruited from residents in Varese Province, northern Italy, an area covered by a cancer registry. Participants completed a semi-quantitative self-administered food questionnaire, and anthropometric and other data were collected systematically. Using published nutritional composition data on trans fatty acids^{1,2,3}, we evaluated the individual daily mean intake of trans-fatty acids. After median follow up time of 11.5 yrs, 293 cases of invasive breast cancer were identified. Multivariate Cox proportional model, with age as the time variable, provided the hazard ratio with 95% confidence intervals. In the ORDET study, dietary intake of trans-fatty acids was directly related with breast cancer risk, also taking into account major risk factors for this cancer site.

These findings suggested an increased risk for breast cancer in women with a diet rich in trans-fatty acids.

	HR (95% CI) for increasing quintiles					P for trend
	I	II	III	IV	V	
Model 1*	1	1.21(0.83-1.77)	1.22(0.82-1.82)	1.56(1.03-2.37)	1.94(1.21-3.12)	0.005
Model 2**	1	1.26(0.86-1.84)	1.31(0.86-1.98)	1.74(1.10-2.74)	2.34(1.32-4.14)	0.004
Model 3***	1	1.25(0.85-1.83)	1.28(0.85-1.92)	1.67(1.09-2.56)	2.16(1.31-3.57)	0.002

* adjusted by age at menarche, menopausal status, weight, height, education, smoking status, energy intake, oral contraceptive use and parity;
 ** adjusted also for intake of saturated fatty acids;
 *** adjusted as model 1 plus dairy products.

¹ USDA Nutrient Database for Standard Reference, 1999.

² Food Standards Agency, 2002 McCance & Widdowson's. The composition of foods, 6th edition.

³ Livelli di ingestione di lipidi e acidi grassi in Italia: I risultati dell'azione concertata CE "Transfair". Pizzoferrato L et al., 1999 La Rivista di Scienza dell'alimentazione: 28(3):259-270.

Raw broccoli increases DNA damage in colonocytes

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Cruciferous vegetables, comprised mainly of brassicas, contribute up to 10% of vegetable intake in Mediterranean countries. The consumption of such vegetables has been associated with a decreased risk of colon cancer (van Poppel et al. 1999). Previously, the consumption of raw broccoli was shown to protect against DNA damage in colonocytes, whereas homogenised and microwaved broccoli had no such effect (Ratcliffe et al. 1999; Ratcliffe et al. 2000). A dietary trial was conducted to compare the effect of raw and blanched/frozen broccoli consumption on DNA damage in colonocytes. Fifteen male Landrace X Large White pigs were divided into five age (79 ± 3 d) and weight (34.7 ± 3.9 kg) matched cohorts, each consisting of siblings to minimise the effect of genetic variation. Within each cohort, siblings were randomly assigned to one of three treatment groups (R, B and C). Each group received a standard, high quality, cereal-based diet (control). This was supplemented with 600 g/d of raw (Group R) or blanched/frozen (Group B) broccoli (var. Marathon). There was a significant increase in the number of DNA strand breaks as measured by the 'comet assay' in pigs consuming raw broccoli, whereas the blanched/frozen broccoli had no effect: Group R 329 (SD 45.6), Group B 289 (SD 56.7), Group C 289 (SD 70.1) (arbitrary units) (P<0.05). This finding was unexpected as previously raw broccoli (variety unknown) had been shown to be protective. A possible explanation is that different varieties of broccoli have different effects. The biological implication of an induction of DNA strand breaks is unclear, but normally reflects genotoxicity rather than chemoprotection. The effects of consuming raw broccoli require further investigation.

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5-methoxypsoralen, a compound found in produce, causes hepatotoxicity

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The psoralens 5-methoxypsoralen (5-MOP) and 8-methoxypsoralen (8-MOP) occur naturally in common fruit and vegetable crops. While lower concentrations of these compounds may have anticarcinogenic effect, levels found in produce are occasionally high enough to cause dermatitis in humans. These compounds are sometimes unknowingly bred into crop plants during programs aimed at selecting for resistance to pests. In addition, although they are carcinogenic, synthetic forms of 5-MOP and 8-MOP are widely used in skin photochemotherapy with UVA (PUVA) to treat disorders such as psoriasis. PUVA has been shown to cause cancer, reproductive toxicity, teratogenicity and even death in some cases. Despite the vast literature on psoralens, studies on their effects on liver cancer and on growth and reproduction in mammals are limited. We report herein on the hepatotoxicity in C57BW mice from daily exposure for four weeks to varying dietary concentrations (0, 50, 250, and 1,000 ppm) of 5-MOP. The livers were removed and fixed by immersion in 10% neutral buffered formalin. Tissue slices were dehydrated in a graded series of ethanols and embedded in paraffin. Tissue sections were cut at 6 μm intervals and stained with hematoxylin and eosin for morphological examination. Exposure to the high doses of 5-MOP caused hypertrophy of centrolobular hepatocytes and increased the amount of amorphous eosinophilic cytoplasm present in livers of treated animals; these are clear signs of morphological liver alterations. Males showed more histological alteration than females. The findings demonstrate the importance of monitoring our dietary intake of psoralens and for determining the potential risk for liver cancer in humans who are exposed to therapeutic, cosmetic, dietary, or occupational psoralens.

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Modulation of telomerase gene expression by zinc in bladder cancer patients

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Telomerase, a critical enzyme responsible for continuous cell growth, is repressed in most somatic cells and activated in approximately 85% of human cancer tissues. It is a useful cancer-cell detecting marker in some types of cancers in which almost all cases show telomerase activity. Role of zinc as a probably interfering microelement in telomerase activity in human bladder cancer is the main subject of this study. This study was a case-control and consisted of 33 voided urine samples. Telomerase activity was measured by TRAP assay. Serum zinc levels of patient and controls were measured by atomic absorption spectrophotometer. 17 (51%) of the 33 cancer patients revealed positive results for cytology, where as using TRAP assay telomerase was positive in all of cancer cases. Only 30% (3 of 10) of the Grade $_$ tumors, 83.3% (5 of 6) of the Grade $_{-}$ tumors and 50% (9 of 18) of the Grade $_{-}$ tumors were diagnosed by cytology. The detection accuracy rates were statistically significant (100% for telomerase vs. 51% for cytology). The difference of RTA (Relative Telomerase Activity) values between Grade $_$, Grade $_{-}$ and $_{-}$ was not statistically significant. The difference of Serum zinc levels between case and control groups were significant ($P=0.04$). Zinc levels in the both affected genders had dominant decreases, besides this shift was mildly more significant ($P=0.04$) in the female patients. There was an inverse significant correlation between the RTA and serum zinc level in the case group ($r=-0.060$, $P=0.48$). In conclusion, it founded that zinc deficiency with increase of telomerase activity has a reverse relationship.

Study of serum levels of Zn, Cu and Cu/Zn ratio in breast cancer patients

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Breast cancer is the most common one in women. In the progression and development of breast tumors combination of internal and external factors including trace elements are involved. The aim of this study was to evaluate and to compare serum levels of Zn, Cu and Cu/Zn ratio in breast cancer patients and controls. This study was a case-control, which composed of 50 women diagnosed with breast cancer and 50 normal individual. The range age of patients and controls was 30-50 yrs. Blood samples were obtained and sera were isolated immediately. The concentration of Zn and Cu were measured using atomic absorption spectroscopy. (AAS)

Mean levels of Zn and Cu in breast cancer patients were 0.015 and 0.023 mmol/L respectively. The mean concentrations of Zn and Cu in normal individual were 0.016 and 0.017 mmol/L, respectively. There was a trend association in patient and control regarding Zn concentration. There was a significant correlation between Cu levels of patient and control ($p<0.001$). In addition, the ration of Cu/Zn in breast cancer patient and controls were 1.52 and 1.12, respectively. This difference was statistically significant ($p<0.001$). In conclusion, it is speculated that changes of trace elements particularly Zn and Cu could have a critical role at the molecular level of the breast tumor cells.

The 'Israeli gender paradox': Higher women risk vs 'cancer shift' to the leading cause of death

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The unexpected Israeli low health status, compared to most Mediterranean countries, in spite of the 'good' diet- low in total and saturated fat, high in P:S fatty acid (FA) ratio, fruits and vegetables, was defined as the 'Israeli Paradox' and attributed to over consumption of n-6FA (12Kcal%). The recent 'Cancer shift' - 23.2%, over heart mortality - 22.3%, emphasizes the growing cancer risk. But Gender analysis reveals that only the women ranked unexpectedly low - 11th of 15 European countries in life expectancy, whereas men rank higher than most of them. This may suggest a 'Gender Paradox' of differential health results on the same diet, especially in cancer: Israeli women cancer death rates are 29% higher than heart deaths (men only by 7% more) and ranked much higher than men, 15thvs 37th in 44 European countries, compared to the rank for Ischemic Heart Disease (IHD), 34thvs 38th, and Cardio Vascular Disease (CVD) 42thvs 44th, respectively.

Arabic population, still holding more of the traditional Mediterranean diet and consume much less n-6 PUFA, have 3.3 times less cancer mortality, but faster growing rates. Their Diabetes and Heart mortality already surpassed the Jewish levels, especially in women. This may suggest that 'Israelization' of the diet, mostly exchanging the traditional olive oil for high n-6 oils and over consuming n-6 FA, affects women health more than men and is associated with cancer becoming the leading cause of death.

This is the first time that a gender is suggested as modulating factor of dietary effects on public health. Research evidences suggest significant Gender effect on Lipid Vs the protective effect of olive oil and low n-6:n-3 FA ratio. Further research may lead to differential approach to gender nutrition, especially as related to cancer epidemiology.

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"5-a-day" in Germany – a small step toward Mediterranean diet and realisation problems in everyday life

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An increased supply of antioxidative vitamins, minerals, trace elements, fibre and secondary plant substances is associated with the Mediterranean diet and thereby a reduction in adipositas, arteriosclerosis, hypertension, hypercholesterolaemia, diabetes mellitus, gout, cancer or a combination of these diseases. Although the health beneficial effects of the Mediterranean diet have been proven, a simple transfer of this diet to countries with so called western diets is nearly impossible. The "5-a-day" campaign launched by the German Society of Nutrition in the year 2000 is a first small step towards adoption in Germany. However in reality, numerous difficulties are encountered in this approach and many of these remain unresolved. Within the framework of the HEILEI study 40 middle aged German women were encouraged to put "5-a-day" into practice over an eight week intervention period. Afterwards the women were asked whether it was generally possible to integrate "5-a-day" into their everyday life. Several problems and barriers of increasing vegetable and fruit consumption were elucidated. Only a few study participants experienced no problems, whereas the majority of the study group had difficulties in realisation of "5-a-day". Barriers indicated by the study participants were: time and other requirements for meal preparations, limited availability of green salad, not overcooked vegetables and fresh fruit when eating out and difficulties in changing personal dietary habits. Encouragement of friends and the better availability of vegetables and fruit during the summer season were stated as helpful aspects to realize "5-a-day" in everyday life. Besides this, some women declared a "feel good factor" in terms of health aspects. Although "5-a-day" could be a first small step toward the Mediterranean diet in Germany, even this step will be hard to realize not only for the whole population but also for people who already have knowledge of healthy diets.

“Chance for the Young Heart” - Polish educational programme of prophylaxis of cardiovascular disorders for children and young people

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Numerous studies indicate that almost 50% of children at the age of 12 have at least one modifiable risk factor for atherosclerosis. Therefore it seems reasonable to undertake prophylactic activities based on the change in lifestyle among young generation of the European Union countries.

In Poland, within the framework of the National Programme for the Prevention and Treatment of Cardiovascular Disorders funded by the Ministry of Health, a pilot multi-centre educational programme for children and young people entitled “Chance for the Young Heart” – acronym: SMS – was implemented. The programme was intended for children in classes 5 – 6 of primary schools and young people in classes 1 and 2 of secondary schools. The objective of the programme was to reduce the incidence of environmental risk factors for cardiovascular disorders with underlying atherosclerosis. The programme is implemented in several layers:

1. through adequate and professional training for trainers – biology and physical education teachers – in cardiovascular physiology, nutrition, and assertiveness,
2. publication of educational materials in the form of 6 thematic brochures (available also in English) for use at work with pupils,
3. implementation of the multimedia programme for teachers as a teaching aid (programme available in English),
4. creation and maintenance of the website as an ongoing source of information for teachers and for the general public, creation of a consultation point for teachers in the form of consultants on phone and e-mail duty.

Preliminary findings showed, for example, that 4400 pupils in classes 5 and 6 of primary schools (on average 96% participation) and 8295 pupils in classes 1 and 2 of secondary schools (on average 56% participation) actively participated in the programme. Participation was assessed by the number of pupils logged in on pages of the www.sms.edu.pl server. As demonstrated by evaluation of the data given by pupils so far, 11% of them permanently take drugs, 9% indicated the presence of cardiovascular disorders in their family, and 32% said one of their parents smoked cigarettes. Further evaluation of young people’s knowledge of cardiovascular risk factors will take place in June after final completion of the programme.

Free participation in the Norwegian School Fruit programme: Increased fruit and vegetable intake gives decreased consumption of unhealthy snacks

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Purpose: It is hypothesised that fruit/vegetables and soda/candy/potato chips are competing snacks. The purpose of the present study is to report the effect of free participation in the Norwegian School Fruit Programme on the consumption of unhealthy snacks.

Method: Nine intervention and 10 control schools were randomly selected within Hedmark County, Norway. All pupils at the intervention schools participated for free in the Norwegian School Fruit programme the whole school year 2001/02, and were thereby given a piece of fruit or a carrot every school-day. A total of 517 6th graders (84%) completed questionnaires in September 2001 (Baseline), May 2002 (Follow-up 1) and May 2003 (Follow-up 2). Unhealthy snacks consumption was measured by three food frequency questions (soda with sugar, candy, potato chips). The effect of the intervention was analysed by mixed model regression on follow-up scores, adjusted for baseline scores and gender.

Results: Significant effects of the intervention were observed at both follow-up surveys. At both surveys, intervention pupils consumed unhealthy snacks 0.7 times/week less than control pupils (adjusted mean values: 6.0 vs. 6.7, $p=0.02$ and 0.01 for follow-up 1 and follow-up 2 respectively). An interaction between parents educational level (college/university education or not) and the intervention was found, indicating that the intervention was effective in decreasing snacks intake of pupils with parents without college/university education only.

Conclusion: Increasing children’s fruit and vegetable intake seem to have a superior bi-effect in decreased consumption of unhealthy snacks. The effect was only significant for pupils with parents without college/university education, contributing to decreasing social inequalities often seen in health and in food habits.

¹ The Norwegian School Fruit Programme, www.skolefrukt.no

The effectiveness of 5-a-day advertisement at the point of sale in Germany

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Introduction: The five-a-day campaign was launched in Germany in May 2000. The German campaign uses different means to communicate the idea of 5-a-day to consumers including advertisement at the point of sale.

Objectives: This study seeks to evaluate the effectiveness of the five-a-day campaign at the point of sale, i.e., in the retail market. We analyze if the recognition of the five-a-day label can be increased on a sustainable basis and if consumers' fruits and vegetables consumption patterns are related to the recognition of the 5-a-day label.

Methods: The five-a-day campaign was heavily advertised in a local supermarket over a two week period in August/September 2004. To evaluate the effectiveness of this campaign, customers were questioned using a closed questionnaire before (N=199), during (N=201) and ten weeks after the campaign (N=152). The collected data were analyzed using ANOVA and multiple regression analysis.

Results: The recognition of the 5-a-day label was increased from 17% before the campaign to 45% during the campaign. Even ten weeks after the campaign the recognition remained high at 33%. We observe a positive relation between label recognition and fruit and vegetable consumption. At the end of the campaign more customers named "a lot or a sufficient amount of fruits and vegetables" as a rule for healthy eating.

Consumers classified as taste-oriented eat more fruits and vegetables than those classified as health-oriented or convenience-oriented. People who consider their consumption of fruits and vegetables as sufficient eat more often fruits and vegetables. Hence consumers who consume too little fruit and vegetables are aware of their insufficient consumption, an important precondition for changing behavior through the five-a-day campaign.

We conclude that advertisement campaigns at the point of sale can be effective in increasing the recognition of the five-a-day label and that this increase will most likely lead to higher fruit and vegetable consumption.

Comparative analysis of national school fruit & vegetable schemes in Denmark, Norway, England, the Netherlands and the United States

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Background: Increasing fruit and vegetable intake is an important public health strategy in preventing Non-communicable diseases. This has led to the implementation of School Fruit and Vegetable Programmes in a number of countries. School Fruit and Vegetable Programmes target increasing Fruit and Vegetable consumption in school food environments by increasing the availability of and access to fruits and vegetables in schools. Such programmes may offer substantial improvements to traditional health education strategies leading to more effective changes in behaviour. Increased fruit and vegetable consumption in children and adolescents can optimize health gains later in life, if food habits are improved early in life.

This study has: systematically reviewed existing literature on interventions focussing on increased accessibility of and access to fruit and vegetables in school settings; described and compared National School Fruit and Vegetable Programmes in terms of ownership, funding, organisation and current policy frameworks; and examined decision making processes that underpin conceptual development and implementation of school fruit and vegetable programmes.

Methodology: Data on relevant intervention studies were gathered by literature search on PUBMED. Descriptive and process evaluations were provided by programme coordinators, and finally semi-structured qualitative interviews with stakeholders provided information on decision making processes in Norway, England and USA.

Results: Interventions that target environmental factors such as availability, access and price seem to be effective and cost-effective compared to multi-component interventions. Preliminary work examining School Fruit and Vegetable Programmes show comparable results. However, few evaluations have examined the School Fruit and Vegetable Programmes impact on long-term dietary habits or outcomes.

A closer look at School FV Programmes reveals interesting differences in delivery systems, ownership and funding that may help inform future programmes or give input to improving current ones. Details are provided in Table 1. School Fruit Vegetable Programmes in the USA and England differ radically from existing school meal policy, because fruit and vegetables are offered universally free of charge regardless of economic status.

Results from qualitative interviews revealed that, it is not always solid evidence that is the driver underpinning School Fruit and Vegetable Programmes. Personal champions, intensive lobby work by industry and anecdotal evidence have played equally important role in expanding programmes. Although there is an increasing amount of evidence that such programmes can be effective in increasing fruit and vegetable intake, other weaker evidence-policy relationships i.e. as an anti-obesity strategy, may be more effective in gaining public acceptance and funding.

Conclusion: Newer notions of public health and food policy demand that policies and programmes are based on good solid evidence, however political expediency and public demands often lead to policy, which is not always based on evidence. School Fruit and Vegetable Programmes can perhaps best be described as programmes with good partial evidence in search of better evidence. More rigorous evaluation of outcomes is needed to create more solid evidence.

Low cost diets: energy-dense, nutrient-poor

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The observed links between poverty and obesity may be explained by the low cost of energy-dense foods. Grains, added sugars and added fats are inexpensive sources of energy. However, energy-dense diets can be nutrient-poor. We examined links between energy density (MJ/kg), energy cost (Euros/10MJ) and nutrient content of both foods and diets in the French SUVIMAX study. To estimate the nutritional quality of foods and diets, a Nutrient Adequacy Score was developed. For foods, it was the sum of the 19 ratios of nutrient content in 100g of each individual food, relative to the daily value (DV) for that nutrient. A Nutrient Density Score was also calculated per 10MJ of each food. For total diets, the Nutrient Adequacy Score was calculated per day, separately for men and women, whereas the Nutrient Density Score was calculated for each diet per 10MJ energy intakes. Energy costs for 851 foods, adjusted for edible portion, were based on mean national food prices. Daily diet costs for 4,981 subjects were estimated by multiplying food prices by portion size and summing over all foods consumed by each person. For both foods and diets, energy density and energy cost were inversely linked, confirming that energy-dense diets cost less. Energy density and nutrient density were also inversely linked, showing that energy-rich foods and diets tended to be nutrient-poor. Finally, higher nutrient adequacy scores were associated with higher costs per 100g food or per day, after adjusting for energy intakes, age, gender, education, and activity in regression models. These analyses show that nutrient-rich foods and higher quality diets were associated with higher costs. Strategies for dietary change ought to include environmental and policy measures to make healthier diets affordable and accessible to all.

Generic campaign in The Netherlands: 'Feel great with fruit and vegetables' 2003-2006

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Fruit and vegetables are an important part of a healthy diet. In the Netherlands there has been a decline of 17% in vegetable consumption and a 16% decline in fruit consumption (since 1987/88). This trend has negative consequences for public health. The slogan '2 + 2' (200 grams of vegetables and 2 times fruit per day) has gained widespread familiarity in recent years. But knowing doesn't automatically mean eating it. The 'Feel great with fruit and vegetables' campaign focuses on the benefits that fruit and vegetables can provide in the short term. This approach appears to have the greatest appeal to young adults (between 20 and 35). TNO Quality of Life provided the scientific support for this campaign. Holland Produce Promotion – communication bureau for the Dutch produce sector - is consignor. The 'Feel great with fruit and vegetables' campaign will continue through 2006; it is funded in part by the EU.

Scientific support: TNO Quality of Life conducted a literature survey on the short-term health benefits of fruit and vegetables consumption. Besides, experts of TNO contributed to the composition of an overview of the state-of-the-art in this field. Nine potential health effects (see frame) and a number of nutrients were selected:

1. Maintenance/enhancement of the immune system
2. Good function/promotion of bowel movement
3. Promotion of satiety/help in keeping a healthy weight
4. Good for the skin
5. Maintenance/improvement of cognition
6. A rapid source of energy in relation to sports
7. Lowering of blood pressure
8. Good for bones
9. Good for vision

On the basis of the composed scientific state-of-the art the relationships of nutrients or vegetables and fruit as such with these nine potential health aspects were classified as: 1.The relationship can be underpinned, 2.The relationship is possible, 3.The relationship is not likely and 4.There is a scarcity of study data justifying a conclusion. On the basis of an evaluation of the strength of scientific evidence for the various relationships and an assessment what vegetable and fruit types are rich sources of the various nutrients, Holland Produce Promotion was able to select in a responsible manner the short-term health benefits that could be claimed in the campaign 'Feel great with fruit and vegetables'. By order of Holland Produce Promotion, an advertising agency made advertising texts on the basis of information collected by TNO Quality of Life. Subsequently, TNO has evaluated these texts on three aspects: compatibility with the state-of-the-art, the absence of misleading information and the absence of medical claims.

Campaign activities: Radio: an effective and efficient medium to reach the target group (young adults between 20 and 35).

Print: magazines are being used to bring the short term benefits to the reader's attention.

Internet: the campaign site is widely published in the media campaign. The functional properties of fruit and vegetables are explained on the website. In addition, the site will focus on simple tips for eating more fruit and vegetables every day.

Direct mail: campaign posters and brochures are sent to intermediaries such as dieticians, doctors, (district) health authorities, hospitals, fitness centres etc.

Evaluation: The first evaluation indicates that the message is taking hold. The target group appreciates the campaign and intends to evaluate their own fruit and vegetable consumption more critically.

The campaign affects the attitude of young adults; they become more critical about their own eating habits, especially with respect to vegetables. Significantly more people realise that they don't always achieve the recommended consumption of 200 grams of vegetables and 2 times of fruit every day. So less people think they eat enough fruit and vegetables. And that is good news, especially because one of the problems in promoting fruit and vegetable consumption is that many people underestimate their own consumption of these products.

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