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Special Paper

European School of Oncology Advisory Report to the European Commission for the "Europe Against Cancer Programme" European Code Against Cancer

P. Boyle, U. Veronesi, M. Tubiana, F.E. Alexander, F. Calais da Silva, L.J. Denis, J.M. Freire, M. Hakama, A. Hirsch, R. Kroes, C. La Vecchia, P. Maisonneuve, J.M. Martin-Moreno, J. Newton-Bishop, J.J. Pindborg, R. Saracci, C. Scully, B. Standaert, H. Storm, S. Blanco, R. Malbois, N. Bleehen, M. Dicato and S. Plesnicar

A European School of Oncology Advisory Group has reviewed the European Code Against Cancer after its initial use over a 6-year period. With minor modifications, the original ten recommendations were found to be adequate, although it was agreed that an Annex was necessary to explain the scientific evidence supporting each point, and is presented herewith. Tobacco smoking clearly remains the most important cause of cancer, and now it can be quantified better than ever before. It is also clear that it is never too late to stop smoking: stopping even in middle age, prior to the onset of serious illness has a beneficial effect on life expectancy. Alcohol drinking is an important cause of cancer, and yet modest consumption levels protect against cardiovascular disease mortality. The optimal strategy seems to be a consumption not exceeding 2–3 drinks per day, although this limit may be lower for women. Increased consumption of fruits and vegetables, reduction in consumption of fatty foods, reduction of obesity and increased physical activity can all be recommended to reduce cancer risk. Exposure to excessive sunlight remains a problem which should be limited. Control of occupational cancer is a three-way partnership: legislation identifies and limits exposure to known carcinogens, employers enact the legislation and workers should respect the measures introduced. There are a number of signs and symptoms which may lead to cancer being diagnosed earlier, and patients with these should be referred to a doctor. For women, participation in organised programmes of cervical cancer and breast cancer (after 50 years of age) should lead to a reduction in mortality from these forms of cancer. The key element is *organised* programmes, where quality control and quality assurance are in force. These revised recommendations are the result of an agreement following advice, review and dialogue with cancer experts throughout Europe. They were approved by the European Community Cancer Experts at their meeting in Bonn on 28–29 November 1994. Their implementation by the European population should greatly reduce cancer incidence and mortality.

Key words: cancer, epidemiology, prevention, screening
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FOREWORD

THE EUROPEAN CODE Against Cancer was originally produced and endorsed by the Committee of Cancer Experts in 1987. The European Commission invited the European School of Oncology to assemble a group of international experts to examine and consider revision of the scientific aspects of the recommendations in the current Code. This occurred and a new version was adopted by the Committee of Cancer Experts at its meeting in November 1994.* The revised Code will be the theme for European Cancer Week 1995.

* *Present members of the Committee*: Prof. Veronesi, Prof. Bleehen, Prof. Boon, Prof. Van Der Schueren, Prof. Diehl, Prof. Overgaard, Prof. Estape, Dr Gonzalez Enriquez, Prof. Kleihues, Prof. Pujol, Prof. Garas, Dr Buttimer, Prof. Dicato, Prof. Kroes, Prof. Conde, Prof. Einhorn and Prof. Holm.

INTRODUCTION

In the European Community in 1990, it is estimated that 1 292 000 incident cases of all forms of cancer, excluding non-melanomatous skin cancers, were diagnosed. This burden was shared almost equally between sexes, with 647 000 new cancers in men and 645 000 incident cancers in women, although the forms of cancer which were the most common differed in men and women. In men, the major forms of cancer were lung cancer (141 500 cases), cancer of the colon and rectum (80 200), cancer of the prostate (76 100) and stomach cancer (46 700). In women, the major forms of cancer incidence were breast cancer (157 000), cancer of the colon and rectum (89 200), lung cancer (33 900) and stomach cancer (33 800). In contrast to stomach cancer, which shows a downward trend in its occurrence, all other cancers are still increasing, although for lung cancer the risk appears to have stabilised in some countries among younger men. Within the European Community considerable geographical differences in cancer occurrence do exist, with a noticeable overall lower risk for all major cancers (except for stomach which is higher) in southern countries, such as Portugal, Spain, Italy and Greece, compared to northern countries.

Against this background of cancer as an important Public Health problem, being the commonest cause of premature and avoidable death in the European Community, the European Code Against Cancer was introduced as a set of recommendations which, if followed, could lead, in many instances, to a reduction in cancer incidence and also to reductions in cancer mortality. The European Code Against Cancer was used throughout Europe for 6 years before being revised by a group of European cancer experts. This revised version also took into account the advice, observations and recommendations of a large number of individuals and groups who had experience with using the original European Code Against Cancer. Below, the scientific rationale for each recommended point of the European Code Against Cancer is outlined.

CERTAIN CANCERS MAY BE AVOIDED AND GENERAL HEALTH IMPROVED IF YOU ADOPT A HEALTHIER LIFESTYLE

Any recommendation made to reduce cancer occurrence should not be one which could lead to an increased risk of other diseases. The ten recommendations which comprise the revised European Code Against Cancer (Table 1) should, if followed, also lead to improvements in other aspects of general health. It is also important to recognise from the outset that each individual has choices to make about their lifestyle, some of which could lead to a reduction in their risk of developing cancer. These choices, and the rationale underlying their recommendation, are presented below.

Table 1. Revised European Code Against Cancer

EUROPEAN CODE AGAINST CANCER

Certain cancers may be avoided and general health improved if you adopt a healthier lifestyle.

1. Do not smoke. Smokers, stop as quickly as possible and do not smoke in the presence of others. If you do not smoke, do not experiment with tobacco.
2. If you drink alcohol, whether beer, wine or spirits, moderate your consumption.
3. Increase your daily intake of vegetables and fresh fruits. Eat cereals with a high fibre content frequently.
4. Avoid becoming overweight, increase physical activity and limit intake of fatty foods.
5. Avoid excessive exposure to the sun and avoid sunburn especially in childhood.
6. Apply strictly regulations aimed at preventing any exposure to known cancer-causing substances. Follow all health and safety instructions on substances which may cause cancer.

More cancers may be cured if detected early.

7. See a doctor if you notice a lump, a sore which does not heal (including in the mouth), a mole which changes in shape, size or colour, or any abnormal bleeding.
8. See a doctor if you have persistent problems, such as a persistent cough, persistent hoarseness, a change in bowel or urinary habits or an unexplained weight loss.

For women

9. Have a cervical smear regularly. Participate in organised screening programmes for cervical cancer.
10. Check your breasts regularly. Participate in organised mammographic screening programmes if you are over 50.

Correspondence to P. Boyle.
P. Boyle, U. Veronesi and P. Maisonneuve are at the European Institute of Oncology, Via Ripamonti 435, 20141 Milano, Italy; M. Tubiana is at the Centre Antoine Beclere, Faculté de Médécine, 45, rue des Saints-Pères 75006 Paris, France; F.E. Alexander is at the Department of Public Health Sciences, University of Edinburgh, Teviot Place, Edinburgh EH8 9AG, U.K.; F. Calais da Silva is at Av. Oscar Monteiro Torres 8-4 Esq., 1000 Lisboa, Portugal; L.J. Denis is at Algemeen Ziekenhuis, Middelheim, Lindendreef, 1 2020 Antwerp, Belgium; J.M. Freire is Director-General, Escuela National de Sanidad, Ministerio de Sanidad y Consumo, Calle Sinesio Delgado 10, 28029 Madrid, Spain; M. Hakama is at the University of Tampere, Department of Public Health, Box 607, SF-33101 Tampere, Finland; A. Hirsch is at Service de Pneumologie, Hopital Saint-Louis, 1, Av. Claude Vellefaux, 75475 Paris Cedex 10, France; R. Kroes is Director of Rijksinstuut Voor Volksgezondheid en Milieuhygiene, 9, Antoine Van Leeuwenhoeklaan, 3720 BA Bilthoven, The Netherlands; C. La Vecchia is at Istituto di Ricerca Farmacologica 'Mario Negri', Via Eritrea, 62, 20157 Milano, Italy; J.M. Martin-Moreno is at the Department of Epidemiology and Biostatistics, Escuela Nacional de Sanidad, Calle Sinesio Delgado, 8 28029 Madrid, Spain; J. Newton-Bishop is Senior Lecturer in Dermatology, The Royal London Hospital, Whitechapel, London E1 1BB, U.K.; J.J. Pindborg is at the School of Dentistry, Health Science Faculty, University of Copenhagen, Norre Alle 20, 2200 Copenhagen, Denmark; R. Saracci is at the International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372 Lyon Cedex 08, France; C. Scully is Dean and Director of Studies, Eastman Dental Institute for Oral and Dental Healthcare Sciences, University of London, 256 Gray's Inn Road, London WC1X 8LD, U.K.; B. Standaert is Directeur, Provincie Antwerpen, Provinciaal Institut voor Hygiene Kronenburgstraat 45, 2000 Antwerpen 1, Belgium; H. Storm is at the Danish Cancer Society, Section for Cancer Epidemiology, Department of Cancer Registration, Strandboulevarden 45, P.O. Box 839, DK-2100 Copenhagen, Denmark; S. Blanco is Head of Sector, "Europe Against Cancer" Programme, Commission of the European Communities, Bat. J. Monnet Plateau du Kirchberg, 2920 Luxembourg; R. Malbois is part of the "Europe Against Cancer" Programme, Commission of the European Communities, 200, rue de la Loi, 1049 Brussels, Belgium; N. Bleehen is Director, Medical Research Council, Clinical Oncology and Radiotherapeutics Unit Addenbrooks Hospital, Cambridge CB2 2QQ, U.K.; M. Dicato is at the Service d'hemato-cancerologie, Centre Hospitalier de Luxembourg, 4, rue Barble, 1210 Luxembourg; and S. Plesnicar is at the Chair of Oncology and Radiotherapy, Faculty of Medicine, Vrazov trg No. 2, 6100 Ljubljana, Slovenia.
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1. Do not smoke. Smokers, stop as quickly as possible and do not smoke in the presence of others. If you do not smoke, do not experiment with tobacco

It is estimated that between 25 and 30% of all cancers in developed countries are tobacco-related. From the results of studies conducted in Europe, Japan and North America, between 83 and 92% of lung cancers in men, and between 57 and 80% of lung cancers in women, are attributable to cigarette smoking. Between 80 and 90% of cancers arising in the oesophagus, larynx and oral cavity are related to the effect of tobacco, both acting singly and jointly with alcohol consumption. Cancers of the bladder, pancreas, kidney, stomach and cervix are causally related to tobacco smoking, and there have been suggestions of an association with cigarette smoking and an increased risk of leukaemia and colorectal cancer, although the casual nature of these latter associations has not been accepted. Because of the length of the latency period, tobacco-related cancers observed today are related to the cigarette smoking patterns of the two previous decades. Consequently, following any decrease in smoking prevalence, there will be a period of time which will elapse before any decrease in the incidence of tobacco-related cancers becomes apparent.

There is now strong evidence of the adverse health consequences of Environmental Tobacco Smoking (ETS) sometimes referred to as passive smoking. On the basis of the available epidemiological data, the United States Environmental Protection Agency declared in 1992 that ETS was a proven lung carcinogen in humans. The risk of lung cancer is increased in non-smoking women who have husbands who smoke tobacco. There also appears to be an increased risk of myocardial infarction due to exposure to ETS, and the adverse health consequences in children whose parents smoke include an increase in the frequency and severity of asthma and of upper and lower respiratory tract infections.

Use of tobacco can result in a variety of diseases, many of which can lead to death, including lung cancer and other forms of cancer, heart disease, strokes and chronic bronchitis and other respiratory diseases. The death rate of smokers in middle age (between the ages of 35 and 69 years) is 3-fold that of non-smokers, and approximately 50% of regular cigarette smokers will eventually die from their habit. Many of these will not be particularly heavy smokers, but can be characterised by starting smoking in their teenage years. Half of the deaths from tobacco will take place in middle age (35–69 years), and each will lose approximately 20–25 years of non-smokers life expectancy: the remaining half of the deaths will take place after the age of 70. However, there is clear and consistent evidence that stopping smoking before cancer or some other serious disease develops avoids most of the later risk of death from tobacco, even if cessation of smoking occurs in middle age (Table 2).

Worldwide, it is estimated that smoking kills three million people each year: the second half of the Twentieth century is notable in that it is estimated that there will be 60 million deaths caused by tobacco. In most countries, the worst consequences of the "Tobacco Epidemic" are yet to emerge, particularly among women in developed countries and in populations of developing countries, since by the time the young smokers of today reach middle or old age, there will be approximately ten million deaths each year from tobacco. Approximately 500 million of the world's population today can expect to be killed by tobacco, 250 million of these deaths being premature and occurring in middle age.

The situation in Europe is particularly worrying. The European Community is the second largest producer of cigarettes (694 billion in 1993) after China (1675 billion) and the major exporter of cigarettes (218 billion). In Central and Eastern Europe, there is a continual increase in the smoking habit. Of the six World Health Organisation (WHO) regions, Europe has the highest per capita consumption levels of manufactured cigarettes, and faces an immediate and major challenge in meeting the WHO target for a minimum of 80% of the population to be non-smoking. Currently (Spring, 1994) in the European Community, 42% of men and 28% of women are regular smokers. The smoking prevalence in women is artificially lowered by the low rates reported in southern Europe, where there is evidence that these rates are rising and seem set to continue to rise over the next decade. In addition, smoking prevalence in the age range 25–39 years is high (55% in men and 40% in women) and can be expected to have a profound influence on the future incidence of cancer. It is particularly disturbing that the smoking prevalence among General Practitioners, who should have an exemplary lifestyle in terms of health, remains high in many parts of Europe. This should be a target for immediate action.

It has been demonstrated that changes in cigarette consumption are affected mainly at a sociological level rather than by actions targeting individuals (for example, individual smoking cessation programmes). Actions such as advertising bans and increases in the price of cigarettes influence cigarette sales particularly among adolescents. Therefore, a "Tobacco Policy" is necessary to reduce the health consequences of tobacco, and experience shows that this should be aimed at stopping young people from starting smoking and helping smokers to stop. To be efficient and successful, a tobacco policy has to be comprehensive and maintained over a long time period. Increased taxes on tobacco, total bans on direct and indirect advertising, smoke-free enclosed public areas, education, effective health warning labels on tobacco products, a policy of low maximum tar and nicotine levels in cigarettes, encouragement of stopping smoking and individual health interventions have to be implemented.

The importance of adequate intervention is demonstrated by

Table 2. Hazards for the individual cigarette user

BIG RISK, especially among those who start smoking cigarettes regularly in their **TEENAGE** years: if they keep smoking steadily then about **HALF** will eventually be killed by tobacco (approximately one-quarter in old age plus one-quarter in middle age).

—Those killed by tobacco in **MIDDLE** age (35–69 years) lose an average of **20–25 YEARS** of non-smoker life expectancy.

—Throughout the European Union, tobacco is much the greatest cause of death. (In non-smokers, cancer mortality is decreasing slowly and total mortality is decreasing rapidly.)

—Most of those killed by tobacco were not particularly "heavy" smokers (but most did start in their teenage years).

STOPPING SMOKING WORKS: Even in middle age, stopping *before* having cancer or some other serious disease avoids *most* of the later excess risk from tobacco (and benefits of stopping at earlier ages are even greater).

This table has been adapted from the following source: Peto R, Lopez AD, Boreham J, Thun M, Heath C. *Mortality from Smoking in Developed Countries* 1950–2000. Oxford, Oxford Medical Publications, 1994.

the low lung cancer rates in Scandinavian countries which, since the early 1970s, have adopted integrated central and local policies and programmes against smoking. In the U.K., tobacco consumption has declined by 30% since 1970 and lung cancer mortality among men has been decreasing since 1980, although the rate still remains high. In France, between 1991 and 1994, there has been a 7% reduction in tobacco consumption due to the implementation of anti-tobacco measures introduced by the Loi Evin.

Therefore, the first point of the European Code Against Cancer should be:

DO NOT SMOKE. Smoking is the largest single cause of premature death.

SMOKERS: STOP AS QUICKLY AS POSSIBLE. In terms of health improvement, stopping smoking before having cancer or some other serious disease avoids most of the later excess risk of death from tobacco even if you stop smoking in middle age.

DO NOT SMOKE IN THE PRESENCE OF OTHERS. The health consequences of your smoking may affect the health of others around you.

IF YOU DO NOT SMOKE, DO NOT EXPERIMENT WITH TOBACCO. Most who experiment become regular smokers: it is difficult to stop once you have started.

2. If you drink alcohol, whether beer, wine or spirits, moderate your consumption

Alcohol drinking has not been demonstrated to be a carcinogen *per se* in animal experimentation, although there are data indicating that chronic oral ethanol ingestion may have a co-carcinogenic effect on tumours of the oesophagus and possibly of the non-glandular forestomach induced by well-known chemical carcinogens in experimental animals.

In humans, there is convincing epidemiological evidence that the consumption of alcoholic beverages increases the risk of cancers of the oral cavity and pharynx (other than the salivary glands and the nasopharyx) and of the oesophagus, and larynx. The risks are essentially due to the ethanol content of the alcoholic drinks consumed, and appear to be linked to the most commonly used alcoholic beverage in each population. They tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident.

There is evidence that alcohol consumption and cigarette smoking together increase the risk of cancers of the upper digestive and respiratory tract, each factor approximately multiplying the effect of the other. Compared to never-smokers and non alcohol drinkers, the relative risk of these neoplasms is increased between 10- and 100-fold in heavy smokers and heavy drinkers. Indeed, in the absence of drinking and smoking, the risk of oral pharyngeal and laryngeal cancers in developed countries is extremely low.

Alcohol drinking increases the risk of many upper digestive and respiratory tract neoplasms, even in the absence of smoking. This suggests that alcohol may facilitate the carcinogenic effect not only of tobacco, but also of other carcinogenic agents to which the human upper digestive and respiratory tract are exposed, particularly those of dietary origin. Although it has been suggested that alcohol derived from "strong" drinks is more deleterious for cancer risk at these sites, at comparable levels of alcohol intake the evidence is inconclusive. Thus, the total amount or ethanol ingested appears to be the key factor in determining this increased risk, rather than the precise source of that alcohol, and it is total consumption of ethanol ingested which should be reduced.

Alcohol drinking is also strongly associated with the risk of primary liver cancer, although the relationship is more difficult to demonstrate in epidemiological studies, since most alcohol-related liver cancers follow a cirrhotic degeneration, which may itself have been caused by alcohol drinking and whose existence in an individual may well have led to a subsequent reduction of alcohol drinking.

Epidemiologically, alcoholic drinking has also been linked to cancers of the large bowel in both sexes and of the female breast. Although the associations are moderate and hence open to discussion, these are the two most common neoplasms in developed countries after lung cancer, so even a small risk from alcohol drinking may have important public health implications.

The J-shaped or U-shaped pattern for alcohol intake distribution in relation to risk of cardiovascular disease, cardiovascular mortality and total mortality is well-known: this classic pattern is one of decreased risk in light drinkers compared to non-drinkers and then an increasing risk as alcohol consumption increases (Figure 1). Nevertheless, the task of fixing a threshold on daily alcohol intake, below which alcohol drinking is definitely free from cancer risk (or, in other words, identifying the upper limit of completely safe regular alcohol consumption) is not simple. Factors such as sex, age, physiological conditions or dietary intake probably modify any such threshold.

There is some evidence showing that a daily alcohol intake as low as 10 g/day (that is, approximately, one drink per day) may be associated with some increase in breast cancer risk relative to non-drinkers: some studies suggest that this risk may be increased by between 30 and 50% compared to non-drinkers. The lower limit associated with a significant risk of cancer at other sites (such as cancers of the upper digestive and respiratory tracts, liver or colorectum) is probably somewhat higher (approximately 30 g per day), and this appears to be particularly true for men. Furthermore, alcohol drinking is sometimes associated with lower intake of certain potentially beneficial nutrients, such as those arising in fruits and vegetables.

All the above points should be considered to give sensible advice regarding individual recommended limits of alcohol consumption. These limits should not exceed between 20 to 30 g of ethanol per day (i.e. approximately two to three drinks of

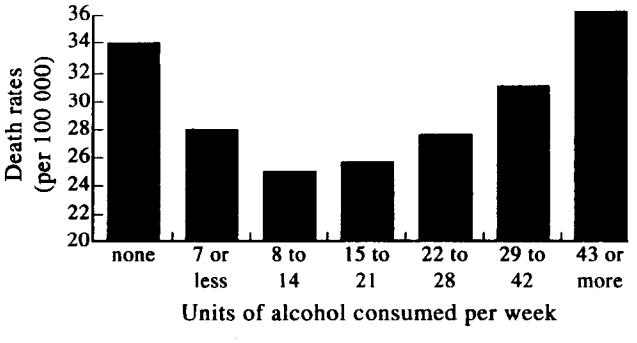

Figure 1. Annual mortality by alcohol consumption for all causes of death in men. Source: Doll R, *et al.* Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. *Br Med J* 1994, 309, 911–918. 1 unit of alcohol (=1 glass of beer, wine or spirits) corresponds to 8–10 g of ethanol.

beer, wine or spirits each day) and may be lower than this for women.

3. Increase your daily intake of vegetables and fresh fruits. Eat cereals with a high fibre content frequently

There exists a large and consistent body of epidemiological evidence indicating a strong protective effect of higher intakes of vegetables and fruit on the risk of a wide variety of cancers, in particular lung, larynx, oropharynx, oesophagus, stomach, colon, rectum and pancreas. Analysis of the type of vegetables and fruits, whether raw or fresh, shows that lettuce, carrots, leafy green and cruciferous vegetables, citrus fruits, broccoli and allium vegetables (garlic, onions, etc) consistently show a preponderant negative association with cancer risk. Pulses, sometimes referred to as legumes, although still showing a negative association, have the least pronounced effect. A higher consumption of vegetables and fruits is consistently associated with a reduced risk of cancer at most sites, the association being most marked for epithelial cancers, in particular those of the alimentary and respiratory tract, although such an association is weak to non-existent for hormone related cancers.

Consistent lower rates of many forms of cancer reported in southern European countries have been linked to the "Mediterranean Diet": this is typically lower in total fat, particularly in fats from animal sources, and meats, and higher in fish, olive oil, vegetables and fruits, fibre and grains. While a link is strongly suspected, this has not yet been proved satisfactorily.

The association with reduced risk of cancer exists for a wide variety of vegetables and fruits, in particular raw forms. There also exists increasing evidence that consumption of higher levels is also beneficial for other chronic diseases. Vegetables and fruits contain a large number of potentially anticarcinogenic agents, with complementary and overlapping mechanisms of action. The preventable proportion for some major cancers is considerable, although the exact molecule(s) in vegetables and fruits which confers this protection is unknown and the exact mechanism of action is unknown. Insight into the mechanisms of action is only incomplete, but this is not required for public health recommendations, although it is not possible to recommend dietary supplementation with vitamins and minerals to reduce cancer risk based on the evidence currently available.

Currently, it is difficult to be precise about the quantity of fruits and vegetables necessary to confer this protection. Fruits and vegetables should be taken with each meal whenever possible. The National Cancer Institute in the United States has advocated a Five Servings per Day programme. According to this advice, a serving refers to either consumption of salad as part of a meal or eating an apple as a snack. Similar actions in Europe could lead to a reduction in cancer risk.

4. Avoid becoming overweight, increase physical activity and limit intake of fatty foods

Within this point there are two distinct potential risk factors: obesity (or overweight) and high fat intake. These factors are not completely correlated, because population differences in weight are not explained primary by fat intake. For this reason, we need to explain the evidence for both statements independently.

Obesity has been shown to be an important cause of morbidity and mortality in general, but it has to be kept in mind that different determinants of body weight, such as physical activity and total energy intake, may also be associated with the risk of the development of certain disorders, including cancer. Moreover, there is some evidence to show that tobacco use strongly confounds epidemiological studies analysing the relationship between relative weight and cancer and other disorders. In addition, excessive alcohol consumption has been associated with both cancer risk and higher relative weight. These comments are made to emphasise the methodological difficulties and the importance of controlling for confounding factors in order to isolate the real and precise effect of relative body weight or the fact of "becoming overweight" on the risk of cancer. Other points that should be considered are the heritable component of obesity, and the highly significant correlation between Body Mass Index values in childhood and adulthood or, in other words, the likely existence of critical periods in childhood for the development of obesity. A practical message on avoiding obesity could best be tailored to children or adolescents, focusing preventive efforts on these developmental stages.

There have been some systematic attempts to describe the pattern of cancer incidence and mortality in overweight individuals. The American Cancer Society followed a cohort of 1 million people, and analysed the data arising from 750 000 volunteers who completed a detailed four page questionnaire including questions on height and weight. In this study, an excess mortality associated with overweight was found from cancers of the colon and rectum, prostate, uterine corpus, uterine cervix, gallbladder and the female breast. Overall, individuals who were 40% or more overweight had a mortality ratio for cancer of 1.33 and 1.55 for men and women, respectively. The second cohort study was carried out in Denmark, and included almost 44 000 obese persons whose cancer incidence was compared with that in the general Danish population. Overall, the incidence was increased by 16% in the cohort of overweight individuals, and the main cancer sites affected included uterine corpus, pancreas, prostate, colon, oesophagus, liver, and breast among women above the age of 70. In younger women, a decreased incidence of breast cancer was observed. Some of the mechanisms which could explain the effect of being overweight are possibly related to hormonal profiles (for breast and endometrial cancer), alcohol consumption (for cancer of the oesphagus and liver in the Danish study), and dietary habits (for cancer sites such as colon or pancreas).

There are also data which provide some evidence that a total fat intake of over 40% calories may act as a risk factor for cancer of the colon, and prostate, and possibly for cancer of the pancreas, ovary, and endometrium. However, a previous postulate which apparently supported the message of dietary fat reduction, mainly the hypothesis that greater fat intake increases breast cancer risk, has not yet been proven in the main cohort and case–control studies. Moreover, various types of fat (saturated, polyunsaturated, monounsaturated, or partially hydrogenated vegetable fats) may have different effects on the risk of cancer. Interestingly, there are some metabolic data, as well as the experience in Mediterranean countries within Europe, which suggest that the intake of a considerable proportion of energy as monounsaturated fat would not be harmful and might be, in some cases, beneficial.

In summary, the available evidence implies that a reduction in dietary fat intake over the ranges currently recommended is not likely to have a tangible and sustained effect on body fatness, without an overall reduction in total energy intake, whereas the recommendation to reduce dietary fat intake is likely to have a small but noticeable effect on cancer incidence, cancer mortality and total mortality. As for the preliminary evidence suggesting an inverse association between the level of monounsaturated fat

in the diet and risk of cancer, further research is necessary. Nevertheless, the underlying message on the benefits of avoiding becoming overweight addressed to the general population should be supported. An awareness of the connection between smoking and relative body weight is essential for clinical and public health practitioners attempting to modify unhealthy behaviour, and this seems to be particularly important in the smoking cessation efforts. Clues to healthy strategies of maintaining body weight without resorting to smoking should be unambiguously formulated. It should also be emphasised that body weight reduction and fat intake limits, especially the saturated fat component, will not only help prevent cancer, but would have beneficial effects on cardiovascular disease.

5. Avoid excessive exposure to the sun and avoid sunburn especially in childhood

The incidence of skin cancer has increased dramatically this century particularly in Northern Europe. The most reliable statistics pertain to melanoma, the incidence of which has doubled every 10 years in many countries. Indeed, the rate of increase has exceeded that of any cancer except lung cancer in women, although there is some evidence from the United States and Australia that the rate of increase may be slowing or has ended in younger cohorts. The annual incidence of malignant melanoma in the United Kingdom and Germany is now, for example 10 per 100000 person years giving an approximate lifetime risk of 1 in 200.

Evidence has accumulated that the major aetiological factor for melanoma is excessive exposure to sunlight. Firstly, melanoma is essentially a disease of caucasians (fair skin being more susceptible to the ill effects of sunlight): as a contrast to the aforementioned risk of 1 : 200 in the U.K., the annual incidence of melanoma in Japan is only 0.2 per 100 000 person-years. Furthermore, although the incidence of melanoma has increased annually in caucasians in Europe, the United States, Canada, Australia etc., there has been very little increase in incidence amongst pigmented peoples of African or Asian origin.

Secondly, there is a relationship between latitude and incidence of melanoma in caucasians. The incidence of melanoma, for example, is highest in countries such as Australia (50 per 100 000 per annum) and in hotter regions of the United States, such as Southern Arizona. Furthermore, there is a relationship between the length of time that an individual has lived at lower latitudes and risk of melanoma, presumably representing lifetime accumulated excessive exposure to the sun.

Thirdly, case–control studies within Europe have identified recreational, intermittent exposure to the sun (such as occurs during outdoor recreation) as a risk factor for melanoma. Several studies have, for example, identified high social class, indoor occupation, sunburn and sunbathing holidays as risk factors for melanoma; thus, the relationship between risk of melanoma and sun exposure may not be simply cumulative.

The question of precisely what pattern of sun exposure is most harmful has not been fully answered. The observation that, at least in Northern Europe, indoor workers are more likely to develop melanoma than their outdoor working compatriots, along with the case–control data above, suggest that intermittency is crucial: it is the cycle of being white in the winter, red in the spring and brown in the summer which is harmful. However, there is evidence, particularly from Australia, that the total amount of sunlight is also important. Sun induced non-melanomatous skin lesions, such as basal cell carcinomas and actinic keratoses (which have a simple relationship with cumulative sun exposure) for example, are significant risk factors for melanoma. It is likely then that health education messages should be avoid sunburn and reduce your total cumulative dosage of sun exposure: the latter is another way of saying "don't tan". It is not certain that the use of of sunscreens to reduce sun exposure to the skin will reduce melanoma. While they protect against ultraviolet B they may allow increased exposure to ultraviolet A which may still be harmful.

Although the incidence of melanoma is still not very high in comparison to the more common tumours, a major aetiological factor in its causation has been identified. In Europe, the increase in incidence has been linked with the desire to be suntanned which has been fashionable since the 1930s. It would seem imperative that to reverse the trend in increasing numbers of melanoma patients we have to reverse these attitudes. Use of artificial sources of ultraviolet (U.V.) exposure, such as sunbeds and ultraviolet lamps should also be discouraged. There is increasing evidence that they too increase melanoma risk.

There is some evidence that excessive sun exposure is particularly deleterious in childhood and youth. Studies of migrants to Australia and Israel, do, for example, show a much greater risk of melanoma in people who migrate in childhood than in later life; indeed, migration before about 15 years of age is associated with the same high risk of melanoma as among people born in those countries. Furthermore, some case–control studies linking sunburn to risk of melanoma have suggested that sunburn under the age of 15 years is particularly significant. Finally, there is some evidence from the only prospective study to address the subject, the United States Nurses' Health Study, that early excessive sun exposure was more significant in terms of risk of melanoma than sun in adult life. It is, therefore, necessary that the European Code should specially address the question of sun protection for children of all ages.

6. Apply strict regulations aimed at preventing any exposure to known cancer-causing substances. Follow all health and safety instructions on substances which may cause cancer

The message in this item of the code solicits responsible behaviour from individuals in three respects: (1) from those who have to provide timely and clear instructions, i.e. chiefly legislators, regulators and educators in the public health and occupational health sectors, who are in charge of translating, into sets of instructions in various forms (norms, recommendations, advice), the information on the risk of cancer from substances, or more generally, agents (physical, chemical, biological) in the environment, derivable from research results; (2) from those who should follow these instructions in order to protect the health of others, for instance, managers, hygienists and doctors in industry and in public authorities; (3) from every citizen who, in order to protect his or her own health, ought to pay heed to the presence of carcinogenic pollutants, especially in the working environment, where they may be found more often and in higher concentrations than in the general environment.

The objective of reducing cancer occurrence through the control of environmental carcinogens rests on the fact that a substantial number of carcinogens, natural and man-made, have been—and continue to be—identified. The latest summary (March 1994) of the series "IARC Monographs on the Evaluation of Carcinogenic Risks to Humans" lists, out of 775 evaluated agents, 39 single agents or groups of agents, 11 mixtures of agents, and 13 exposure circumstances (all occupational) for which there is "sufficient evidence" of carcinogenicity in

humans. An additional 41 single agents or groups of agents, 5 mixtures and 4 exposure circumstances (3 of which were occupational) are classified as "probably carcinogenic" to humans, whereas a total of 209 agents, groups of agents or exposure circumstances are classified as "possibly carcinogenic" to humans, largely on the basis of carcinogenicity data from animal experiments. The proportion of all cancers which can be causally attributed to carcinogens in the occupational and general environment, and are therefore wholly or partly avoidable through exposure control, is certainly not negligible, but remains difficult to quantify reliably, depending as it does on the variable prevalence of the exposures by geographical areas and periods of time, as well as on the concurrent prevalence of other dominant cancer causing factors (typically tobacco smoking). An estimated upper limit of 4% of cancers are attributable to the occupational environment, although wide variations are found in this proportion when, for instance, lung cancer in relation to occupational exposures is examined in different geographical areas, pointing to the importance of local concentrations of cases susceptible to preventive control. Alternatively, agents in the general environment to which a large number of subjects are exposed for long periods, such as environmental tobacco smoke (passive smoking), although increasing only modestly the relative risk for certain cancers, may be at the origin of a sizeable number of cases, running into several thousands yearly in the European Community. It is essential that for any activity liable to present a risk of exposure, the nature, degree and duration of such exposure must be determined in order to define what measures need to be taken to prevent or reduce the exposure.

Among these measures, suitable operating procedures and methods are of the utmost importance. Instructions to be followed may take the form of quantitative control limits of exposure, derived empirically or through formal procedures, which still leave much to be desired. The specification of a quantitative control limit for exposure in the general or occupational environment combines two elements: the quantitative estimate of the risk associated with a given level of exposure and the level of risk regarded as socially "acceptable" (by the parties involved in discussing the limit, e.g. regulators, representatives of the community, etc.), with consideration of the technical feasibility, and human and economic costs of various degrees of control. Evidence is available that limiting the exposures to carcinogens in occupational environments has indeed been followed by a fall in cancer occurrence.

7. See a doctor if you notice a lump, a sore which does not heal (including in the mouth), a mole which changes in shape, size or colour, or abnormal bleeding.

8. See a doctor if you have persistent problems, such as a persistent cough, persistent hoarseness, a change in bowel or urinary habits or an unexplained weight loss

These two points are potentially useful as secondary prevention, and serve as reminders about different visual body signs or symptoms that could easily be observed by anyone and that are possibly related to cancer. It is unequivocally established that cancer survival is better for patients with early, localised disease than for those with the more advanced form of the disease. Thus, the earlier in the disease process a cancer is diagnosed and treated, then the better this is for the patient. The purpose of these two recommendations is to ensure that potential symptoms of cancer are not ignored, but serve as a clear warning for the individual to consult his or her doctor for advice. These two points serve as reminders about different usual body signs or symptoms that could easily be observed by anyone, and that are possibly related to cancer. The signs and symptoms described are not specific for cancer. When any symptom is present, the individual should see a doctor.

Bleeding, sores and lumps

The first sign of certain cancers in an individual can be the occurrence of unexpected bleeding: for example, blood in the stool, blood in urine, blood when vomiting or an unexpected bloody discharge from the vagina which could occur in the postmenopausal women. There are other common reasons why such bleeding could occur, but it is always wise policy to have the reasons for the bleeding determined by a physician. It should be noted that screening for occult blood in faecal material is being evaluated at present as a method of screening for cancers of the colon and rectum, and that cytological examination and the microscopic search for blood in the urine is commonly employed among certain groups of workers in the chemical industry.

Continuous or abnormal external bleeding from the nose, ears or sores, does not always immediately suggest a cancer process at first glance. However, when those symptoms appear, an early process of cancer development should be considered.

Lumps

The presence of a lump on one site or organ could indicate cancer development. A first approach could be an age-, organ- and site-specific orientated search for lumps related to cancer. The testes, thyroid gland, the neck, armpit and groin are organs and sites where lymph nodes are present and their enlargement could indicate the possibility of a process compatible with that of a lymphoma, a cancer of the soft tissue or of a metastatic process. Among lymphomas, the appearance of nodules are not always observed as a first symptom of this cancer, rather a broad spectrum of non-specific symptoms can occur. The detection of a lump in the breast of a woman should be sufficient for referral to a doctor: methods of detection of such lumps are discussed in section 10 below.

Moles that change in size, shape or colour

Most melanomas are detected by the patient and self examination has the potential, at least, for early detection, not requiring expensive screening techniques. There is, furthermore, a considerable survival advantage in the early detection of melanomas. The prognosis of melanoma is strongly linked to the so-called Breslow thickness, which is a measurement made by the pathologist on the resected tumour sample, and correlates with the tumour volume. It is determined histologically (the depth in mm from the most superficial cellular layer of the skin to the deepest part of the tumour). When this is less than 1.5 mm, then the 5 year survival is 92%, but the 5-year survival falls to only 36% for a Breslow thickness greater than 3.5 mm.

It is desirable, therefore, that both General Practitioners and the general population should be aware of what an early melanoma looks like, and that such tumours should be seen early by specialist medical personnel.

Most melanomas (55% approximately in caucasian European populations) are superficial spreading melanomas, which commonly arise from moles (probably around 60–70%). These lesions have a relatively slow growth rate, and have frequently been developing for many months if not years by the time they present to the doctor. There is, therefore, at any one time a significant percentage of the general population with such lesions

who would benefit from health education directed at early detection. Superficial spreading melanomas are usually larger in diameter than most moles (greater than 5 mm), with an irregular edge and variable colour. In order to facilitate the recognition of such lesions, the general public should be advised to see their doctor if a mole changes in shape, colour or size.

The less common nodular melanomas have a much more rapid growth rate and may have the appearance of a red or pigmented lump which can bleed. It is much more difficult to give readily understandable advice about such lesions to the public which would enable them to distinguish between benign and malignant. The advice to see a doctor if they notice a new lump, especially if it is pigmented or bleeding, seems appropriate but of little help in distinguishing, for example, Campbell de Morgan spots (Cherry angiomas or angiokeratomas) from melanomas.

9. Have a cervical smear regularly. Participate in organised screening programmes for cervical cancer

In many developing countries, the uterine cervix is one of the most prevalent sites for cancer, comprising approximately 25% of all female cancers. In industrialised populations, the disease is less common. In eastern and central European populations, the annual age-adjusted (using the World Standard Population as referent) incidence rates for invasive disease are 15–25 per 100 000 women. In the Nordic countries, the annual incidence was 15–30 per 100 000 women before the start of large-scale mass screening programmes.

The effectiveness of screening for cervical cancer has never been demonstrated in a randomised trial. There is, however, a great deal of non-experimental evidence, in terms of reduced incidence of invasive disease. Screening for cervical cancer reduces the incidence of invasive disease and is applicable as public health policy, but a wide variation is seen, from highly effective programmes to relatively poor ones.

The effectiveness of screening for cervical cancer has been evaluated on the basis of several non-experimental studies—case–control and cohort studies and of time trends and geographical differences. The largest of these is the collaborative study co-ordinated by the International Agency for Research on Cancer, which showed that eradication of the disease is an unrealistic goal, and that maximal protection after a negative smear is approximately 90%, which remains roughly the same for several years after the test. This conclusion is in agreement with the results of studies on the natural history of the disease, which have shown that most pre-invasive lesions progress to frankly invasive cancer over several years.

The effects are somewhat smaller at a population level. In some of the Nordic countries, the reduction was approximately 80% in women in the age groups exposed most intensively to screening. In the mid-1980s, after several years of organised screening, the overall incidence was 5–15 per 100 000 woman years. Because the incidence was decreasing before the screening programmes were begun, the trends probably indicate a minimal effect of the Nordic programmes.

An organised programme consists of several essential elements, including high attendance rates, quality control of the cervical smears and referral of confirmed cases for adequate treatment. These elements allow quality control, monitoring of the process and evaluation of outcome. Experience from the Nordic countries shows that such programmes are effective and consume less resources than programmes based on spontaneous participation. High attendance is a prerequisite for effective screening. If the population to be screened is defined and the women within it are identified, personal invitations can be sent. Personal invitation is probably the single most important means of attaining high attendance, especially when it is combined with effective information through the mass media. A free service has also been shown to improve attendance. Quality assurance of all steps of the process, monitoring and constant evaluation of the proportion of cancer detected, false positives and false negative readings, are mandatory.

In conclusion, near maximal effectiveness is achieved by an organised programme with high coverage, in which screening is initiated at the age of 25 and is repeated at 3- or 5-year intervals up to the age of 60. Extension of this approach should be considered only if maximal coverage has been attained, the resources are available, and the marginal cost-effectiveness of the recommended changes has been evaluated.

10. Check your breasts regularly. Participate in organised mammographic screening programmes if you are over 50

Primary prevention of breast cancer through reduction of exposure to risk factors is not feasible at present; known risk factors are associated with small relative risks (generally less than 2) and are frequently not amenable to modification. The role of diet is currently not well understood, and further research is required; no specific dietary advice is available. Chemoprevention, by the use of dietary supplementation or tamoxifen, is being evaluated in large randomised trials in several countries. Until results from these trials are available, no recommendations can be made for application to the general population.

To reduce the burden of breast cancer mortality in the European Community, attention must therefore focus on secondary prevention through early detection. The general aim of early detection is to identify breast cancers when they are smaller and at an earlier stage and with other favourable prognostic characteristics. There are several strands of evidence indicating that this will reduce breast cancer mortality. Long-term studies of survival show a strong association between poor survival and increasing size and stage of the primary tumour. Trials of breast cancer screening have shown that cumulative rates of "stage II+" cancers in both the screened and the unscreened arms of the trials are highly predictive of subsequent breast cancer mortality. Stage II+ as defined by Tabar includes small node-positive tumours, and it is clear that detection should aim to be sufficiently early to avoid node positivity even in small tumours.

Further indirect evidence of the importance of early presentation comes from comparison of international patterns of incidence and mortality rates; there is poor correlation between these. Mortality rates are rising in many countries including most of the European Community, but they are falling by birth cohort in the United States, Canada, Australia, the U.K., Switzerland and the Nordic countries. The reductions can be attributed, in part, to population changes in known risk factors and, in particular, ages at which families are begun. It is considered that increased breast awareness and screening are responsible for much of the reduction.

Effect of following the advice

There is now good evidence available from randomised trials conducted in the United States, Sweden, and Scotland, and involving over 250 000 women, that regular mammographic screening examinations of women aged between 50 and 70 years will reduce their breast cancer mortality. The best estimates are that the size of the reduction may be around 30% if take-up of

screening in the population is good and quality control standards high. An overview of the Swedish trials reported relative risks of death of 0.71 in the group randomised to an offer of screening with 95% confidence interval 0.57–0.89 for women aged 50–59 at entry. Results for women aged 60–69 were almost identical. There is, as yet, no clear evidence that screening benefits older women, and it is certain that they are less willing to attend for screening.

More importantly, results for younger women (younger than 50) are ambiguous, with no trials having large enough statistical power to analyse these women separately. There are no statistically significant results for this age group reported, but point estimates include both reductions and increase in breast mortality in women offered mammographic screening whilst aged under 50 years.

Unfortunately, organised programmes of mammographic screening are not currently available to women in all countries of the European Community, although pilot studies have now been established in all Member States without an organised National Mammographic Screening Programme. At present, the use of mammographic screening for premenopausal women remains a topic for research rather than for routine health care. Yet 41% of the years of life lost due to breast cancer diagnosed before the age of 80 years are attributable to cases presenting symptomatically at ages 35–49 years. This emphasises the necessity of conducting the necessary research on this issue.

Breast self-examination (BSE) is a simple method of early detection, which is available for all women. It has, however, been formally evaluated in a single U.K. study and the results were disappointing. Breast cancer mortality was reduced in only one of two English centres where teaching of BSE was introduced; differences in routine management have been proposed as an explanation of these differences. In addition, breast examination practices among the women concerned may not have been enormously influenced by the education they were offered. In the absence of better alternatives, individual breast awareness and breast self-examination should be recommended to European women only when organised mammographic screening programmes are unavailable and, when relevant, between routine mammographic screens.

If this advice is followed, breast cancer incidence will not be reduced and, indeed, is likely to increase. The primary effect will be a reduction in mortality. Subsidiary benefits will include reduction in the absolute incidence (as well as merely the proportional incidence) of larger and higher stage disease, and increase use of lumpectomy and other less mutilating therapies.

ADDITIONAL ITEMS CONSIDERED

The committee discussed a number of other issues in Cancer Epidemiology and Cancer Control, and decided that the situation was not clear enough for any recommendation to be made with a convincing probability of success in reducing cancer risk. It was felt that Screening for Prostate Cancer and Screening for Colorectal Caner with Sigmoidoscopy needed to be evaluated in randomised trials before any recommendations could be made to the general public. At the present time, it is not yet clear whether participation in programmes of either screening for prostate cancer (using any combination of digital rectal examination, prostate specific antigen or trans rectal ultrasound) or colorectal cancer (using either haemocult or sigmoidoscopy) would lead to a reduced risk of death from the disease among participants. Screening for Oral Cancer was also considered, and it was concluded that there was a great deal of further evaluation to be done, including randomised trials, before any conclusion of its efficacy could be made and recommendations considered. It was also recognised that more research work was necessary in breast cancer, particularly with regard to the efficacy of mammographic screening among women under the age of 50.

A number of cancer risk factors were considered, and it was felt that more information was required regarding the magnitude and nature of a number of putative associations, including those between domestic radon levels and lung cancer risk, electromagnetic fields and childhood cancer risk, salt intake and gastric cancer risk and the possible protective effect of dietary vitamin supplementation and cancer risk, before any recommendations could be made to the General Public.

SUGGESTED READING LIST

There are key references proposed for more detailed information and background regarding the points presented above in outlining the rationale behind the recommendations made for the revised European Code Against Cancer. These are presented below separately for each of the points described above.

Foreword:

Doll R, Peto R. *The Causes of Cancer*. Oxford, Oxford University Press, 1982.

Esteve J, Kricker A, Ferlay J, Parkin DM, eds. *Facts and Figures of Cancer in the European Community*, Lyon, IARC, 1993.

Jensen OM, Estève J, Møller H, Renard H. Cancer in the Member States of the European Community in 1980. *Eur J Cancer* 1990, **26**, 1167–1256.

La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends of cancer mortality in Europe, 1955–89. I. Digestive Sites. *Eur J Cancer* 1992, **28**, 132–235.

La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends of cancer mortality in Europe, 1955–89. II. Respiratory tract, bone, connective and soft tissue sarcomas, and skin. *Eur J Cancer* 1992, **28**, 514–599.

La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends of cancer mortality in Europe, 1955–89. III. Breast and genital sites. *Eur J Cancer* 1992, **28**, 927–998.

La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends in cancer mortality in Europe, 1955–89. IV. Urinary tract, eye, brain and nerves, and thyroid. *Eur J Cancer* 1992, **28**, 1210–1281.

La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends in cancer mortality in Europe, 1955–89. V. Lymphohaemopoietic and all cancers. *Eur J Cancer* 1992, **28**, 1509–1581.

Levi F, La Vecchia C, Lucchini F, Boyle P. Cancer incidence and mortality in Europe, 1983–87. *Soz Praventivmed* 1993, Suppl. 3, S155–S229.

Smans M, Boyle P, Muir CS, eds. *Cancer Mortality Atlas of EEC*. IARC Scientific Publication No 107. Lyon, IARC, 1993.

1. Do not smoke. Smokers, stop as quickly as possible and do not smoke in the presence of others. If you do not smoke, do not experiment with tobacco.

Boyle P. The hazards of passive and active smoking. *N Engl J Med* 1993, **328**, 1708–1709.

Bosanquet N. Europe and tobacco. *Br Med J* 1992, **304**, 370–372.

Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observation on male British doctors. *Br Med J* 1994, **309**, 901–911.

IARC (International Agency for Research on Cancer) Monographs

on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoking, Vol 36. Lyon, IARC, 1986.
Joossens L, Naett C, Howie C, Muldoon A. Tobacco and health in the European Union. An overview. European Bureau for Action on Smoking Prevention (BASP), Brussels (1994).
La Vecchia C, Boyle P, Franceschi S, *et al.* Smoking and cancer with emphasis on Europe. *Eur J Cancer* 1991, **27**, 94–104.
Peto R, Lopez AL, Boreman J, Thun M, Health Jr C. Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet* 1992, **339**, 1268–1278.
Peto R, Lopez AL, Boreman J, Thun M, Health Jr C. Mortality from smoking in developed countries 1950–2000. Oxford, Oxford Medical Publications, 1994.
United States Department of Health and Human Services. The health benefits of smoking cessation. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. DHHS Publication No. (CDC) 90-8416, 1990.
U.S. Environmental Protection Agency. Respiratory health effects of passive smoking: lung cancer and other disorders. Office of Health and Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, EPA/600/6-90/006F, December 1992.

2. If you drink alcohol, whether beer, wine or spirits, moderate your consumption.

International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 44. Alcohol Drinking. Lyon, International Agency for Research on Cancer, 1988.
Doll R, Forman D, La Vecchia C, Woutersen R. Alcoholic beverages and cancer of the digestive tract and larynx. In Vershuren PM, ed. *Health Issues Related to Alcohol Consumption*, Washington, ILSI Press, 1993, 126–166.
Doll R, Peto R, Hall E, Wheatley K, Gray R. Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. *Br Med J* 1994, **309**, 911–918.
Marmot M, Brunner E. Alcohol and cardio-vascular disease: the status of the U-shaped curve. *Br Med J* 1991, **303**, 565–568.
Poikolainen K. Alcohol and mortality: a review. *J Clin Epidemiol* 1995, **48**, 455–465.
Rimm EB, Giovannucci EL, Willett WC, *et al.* Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 1991, **338**, 464–468.

3. Increase your daily intake of vegetables and fresh fruits. Eat cereals with a high fibre content frequently.

Block G. Vitamin C and cancer prevention: the epidemiologic evidence. *Am J Clin Nutr* 1991, **53**, 270–282.
Blot WJ, Li J-Y, Taylor P, *et al.* Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 1993, **85**, 1483–1492.
Boyd NF, Martin LJ, Noffel M, Lockwood GA, Tritchler DL. A meta-analysis of studies of dietary fat and breast cancer risk. *Br J Cancer* 1993, **68**, 627–636.
Garland M, Willett WC, Manson JE, Hunter DJ. Antioxidant micronutrients and breast cancer. *J Am Coll Nutr* 1993, **12**, 400–411.
Giovannucci E, Rimm EB, Colditz GA, *et al.* A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst* 1993, **85**, 1571–1579.
La Vecchia C. Cancers associated with high-fat diets. *Monogr Natl Cancer Inst* 1992, **12**, 79–85.
Steinmetz KA, Potter JD. Vegetables, fruits and cancer. *Cancer Causes Control* 1991, **2**, 325–357.

4. Avoid becoming overweight, increase physical activity and limit intake of fatty foods.

Albanes D, Jones Y, Micozzi MS, Mattson ME. Associations between smoking and body weight in the US population: analysis of NHNES II. *Am J Public Health* 1987, **77**, 439–444.
Dietz WH. Critical periods in childhood for the development of obesity. *Am J Clin Nutr* 1994, **59**, 955–959.
Garfinkel L, Stellman SD. Mortality by relative weight and exercise. *Cancer* 1988, **62**, 1844–1850.
Lee IM, Manson JE, Hennekens CH, Paffenbarger RS. Body weight and mortality. *JAMA* 1993, **270**, 2823–2828.
Moller H, Mellemgaard A, Lindving K, Olsen JH. Obesity and cancer risk: a Danish record-linkage study. *Eur J Cancer* 1994, **30A**, 344–350.
Must A, Jacques PF, Dallal GE, Bafema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard growth study of 1922–1935. *N Engl J Med* 1992, **327**, 1350–1355.
Paffenbarger RS, *et al.* The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 1993, **328**, 538–545.
Willett WC. Diet and health: what should we eat? *Science* 1994, **264**, 532–537.

5. Avoid excessive exposure to the sun and avoid sunburn especially in childhood.

Armstrong B. Epidemiology of malignant melanoma: intermittent or total accumulated exposure to the sun? *J Dermatol Surg Oncol* 1988, **14**, 835–849.
Khlat M, Vail A, Parkin M, Green A. Mortality from melanoma in migrants to Australia: variation by age at arrival and duration of stay. *Am J Epidemiol* 1992, **135**, 1103–1113.
Osterlind A, Tucker MA, Stone BJ, Jensen OM. The Danish case–control study of cutaneous melanoma. II. Importance of UV-light exposure. *Int J Cancer* 1988, **42**, 319–324.
Roberts DL. Malignant melanoma in West Glamorgan: increasing incidence and improving prognosis 1986–1988. *Clin Exp Dermatol* 1990, **15**, 406–409.
Scotto J, Pitcher H, Lee JAH. Indications of future decreasing trends in skin melanoma mortality among white males in the United States. *Int J Cancer* 1991, **49**, 490–497.
Vagero S, Swederlow A, Beral V. Occupation and melanoma: cancer registrations in England and Wales and in Sweden. *Br J Indust Med* 1990, **47**, 317–324.

6. Apply strictly regulations aimed at preventing any exposure to known cancer-causing substances. Follow all health and safety instructions on substances which may cause cancer.

Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work.
Council Directive 90/394/EEC of 26 June 1990 on the protection of workers from the risks related to exposure to carcinogens at work.
IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lists of IARC Evaluations (Vols 1–60). Lyon, International Agency for Research on Cancer, 1994.
Simonato L, Vineis P, Fletcher AC. Estimates of the proportion of lung cancer attributable to occupational exposure. *Carcinogenesis* 1988, **2**, 1159–1165.
Swerdlow AJ. Effectiveness of primary prevention of occupational exposures on cancer risk. In Hakama M, Beral V, Cullen JW, Parkin DM, eds. Evaluating Effectiveness of Primary

Prevention of Cancer, IARC Scientific Publication No. 103, Lyon, International Agency for Research on Cancer, 1990, 23–56.

7. See a doctor if you notice a lump, a sore which does not heal (including in the mouth), a mole which changes in shape, size or colour, or abnormal bleeding.

8. See a doctor if you have persistent problems, such as a persistent cough, persistent hoarseness, a change in bowel and urinary habits or an unexplained weight loss.

Britton JP, Dowell AC, Whelan P, Harris CM. A community study of bladder cancer screening by the detection of occult urinary bleeding. *J Urol* 1992, **148**, 788–790.

Dent OF, Goulston KJ, Tennant CC, *et al.* Rectal bleeding. Patient delay in presentation. *Dis Colon Rectum* 1990, **33**, 851–857.

Doherty V, Mackie R. Reasons for poor prognosis in British patients with cutaneous malignant melanoma. *Br Med J* 1986, **292**, 987–989.

Fijten GH, Muris JW, Starmans R, *et al.* The incidence and outcome of rectal bleeding in general practice. *Family Practice* 1993, **10**, 283–287.

Hennrikus D, Girgis A, Redman S, Sanson-Fisher R. A community study of delay in presenting with signs of melanoma to medical practitioners. *Arch Dermatol* 1991, **127**, 356–361.

Marks R, Hill D. Melanoma control: prevention and early detection. *Pub Union* International Contre Le Cancer. 1992 ISBN 0947283234.

9. Have a cervical smear regularly. Participate in organised screening programmes for cervical cancer.

IARC Working Group on Cervical Cancer Screening. In Hakama M, Miller AB, Day NE, eds. *Screening for Cancer of the Uterine Cervix*. IARC Scientific Publications No. 76, Lyon, IARC, 1986, 133–142.

European Guidelines for Cervix Cancer Screening. *Eur J Cancer* 1993, **29** (suppl. 4).

Hakama M, Magnus K, Petterson F, Storm H, Tulinius H. Effect of the organized screening in the Nordic countries on the risk of cervical cancer. In Miller AB, Chamberlain J, Day NE, Hakama M, Prorok P, eds. *Cancer Screening*. Cambridge, Cambridge University Press, 1991.

Wilson J, Jungner G. Principles and Practice of Screening for Disease (WHO Public Health Paper 34). Geneva, World Health Organization, 1968.

10. Check your breasts regularly. Participate in organised mammographic screening programmes if you are over 50 years of age.

Alexander FE, Anderson TJ, Brown HK, *et al.* The Edinburgh randomised Trial of Breast Cancer Screening: results after 10 years of follow-up. *Br J Cancer* 1994, **70**, 542–548.

Ellman R, Moss SM, Coleman D, Chamberlain J. Breast self-examination programs in the Trial of Early Detection of Breast Cancer. *Br J Cancer* 1993, **68**, 208–212.

Fletcher SW, Black W, Harris R, Rimer BK, Shapiro S. Report on the International Workshop on screening for breast cancer. NCI, 1993.

Nystrom L, Rutquist LE, Wall S, *et al.* Breast cancer screening with mammography: overview of Swedish randomised trials. *Lancet* 1993, **341**, 973–979.

Tabar L, Gad A, Holmberg LH, *et al.* Reduction in mortality from breast cancer after mass screening with mammography. *Lancet* 1985, **i**, 829–832.

Wald NJ, Chamberlain J, Hackshaw A, *et al.* Report of the European Society of Mastology (EUSOMA) Breast Cancer Screening Evaluation Committee. *The Breast* 1993, **2**, 209–216.

Tubiana M, Holland R, Kopans DB, *et al.* Commission of the European Communities "Europe Against Cancer" Programme. European School of Oncology Advisory Report. Management of Non-palpable and small lesions found in mass breast screening. *Eur J Cancer* 1994, **30A**, 538–547.