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Cancer causes and prevention: A condensed appraisal in Europe in 2008

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ABSTRACT

The rising cancer burden in Europe, mainly due to a rapidly ageing population, demands a clear and coordinated response from researchers, oncologists and other physicians, public health professionals and policy-makers. Primary and secondary prevention is the front line in the complex battle against cancer in Europe.

To formulate the best strategies in this fight, the major determinants of cancer are summarised in the order of their relative importance in Europe, including tobacco smoking, alcohol, diet, physical activity, occupational factors, environmental factors, infectious agents and genetic and hormonal factors.

Furthermore, this paper offers explicit recommendations on individual behaviour modification and possible public policies. It also details the numerous examples of European policies and programmes already in effect which aim to reduce the impact of these risk factors on cancer. Although there are still pending questions, which need further epidemiologic research, it is also true that we have more operational knowledge for cancer prevention than ever before. The prompt implementation of prevention programmes such as those detailed here should be applied with determination to maximise the prevention results.

1. Introduction

Because cancer is one of the leading causes of death in our society,[1] because its cure is uncertain, costly and painful, because its burden will only increase with time, an integrated approach to cancer control is essential.[2,3] Within this approach, prevention is potentially our best hope to limit its impact. To optimise our efforts, it is necessary to take stock of the evidence on what we know, what we can do and what needs to be done. This paper aims to comprehensively assess the known risk factors from an epidemiological viewpoint and address possible intervention and policy-making for primary and secondary preventions, using the action plan in the *European Code Against Cancer* as a framework.[4]

The underlying idea behind cancer prevention is to explore the causes (determinants) of the disease upon which we may act or that we can control. Primary disease prevention requires that we identify those causes of disease that can be modified through public health actions, especially actions related to the environment and to the lifestyle habits. Secondary prevention deals with early detection (screening), and its goal is to detect cancer in its earliest stage, increasing the probability for successful treatment.

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2. Key lifestyle risks and prevention policies

Lifestyle factors play an important role in the causation of cancer. This is strongly supported by several facts including international variation in cancer, changes in incidence over time and change of risk in migrants.[5] Thus, there is a strong justification for cancer prevention activities focused on reversing behavioural patterns linked to tobacco smoking, alcohol drinking, unhealthy diet and physical inactivity. Tackling these risk factors has the potential to address the underlying causes of many other major diseases besides cancer, including cardiovascular disease and diabetes.[6]

2.1. *Tobacco smoking*

As an acquired behaviour pattern, tobacco smoking is the largest single avoidable cause of premature death in our society.[7] In Europe, studies have shown that 87–91% of lung cancers in men and 57–86% of lung cancers in women are attributable to cigarette smoking.[8,9] Further, for both sexes, 43–60% of cancers in the oesophagus, larynx and oral cavity are attributable to the effect of tobacco, either alone or in combination with alcohol consumption. In addition, a significant proportion of cancers of the urinary bladder and pancreas, and a smaller proportion of cancers of the kidney, stomach, cervix and nose, as well as myeloid leukaemia, are also causally related to tobacco smoking.[4,7] In total, it is estimated that 29–38% of all cancers in men in Europe are directly linked to smoking (Tables 1a and 1b).

Since the early 1990s, there has been a decrease in mortality rates from cancers related to smoking in the male population, reflecting the decrease of smoking prevalence amongst males as a result of anti-smoking efforts implemented in many European countries since the early 1980s. However, progress is uneven. According to the European Tobacco Control Report 2007,[10] smoking prevalence in Europe is about 40% for men and 18% for women, but whilst smoking amongst men in most countries has stabilised or is falling, there is a slight upward trend amongst women, especially in Eastern Europe (Fig. 1). The mortality from cancers related to smoking also reflects this, showing an increase in tobacco-related cancers amongst women.

Other vulnerable population pockets remain as well. Worldwide, the rates of premature mortality due to tobacco smoking, particularly amongst males, are inversely related to education and/or income.[11] Thus, smoking has been identified as a major contributing factor to the gap in mortality and healthy life expectancy between the least and the most disadvantaged in society. In the United Kingdom (UK), for instance, premature deaths from lung cancer are five times higher amongst blue-collar workers than amongst those in professional work.[12]

Fortunately, these dire risks are not irreversible. On quitting or reducing smoking, the increased cancer risk induced by smoking rapidly decreases or even ceases. The benefit of smoking cessation is clear within five years and is progressively more noticeable with the passage of time.[7]

2.1.1. *Preventive intervention and policy-making: smoking*

Individual and/or group intervention approaches such as group behavioural therapy and smoking cessation using the available therapies (Table 2a) have been shown effective to aid individuals in quitting smoking.[13] However, policy changes have proven to have the greatest impact on the rate of smoking in a population (Table 2b).

Vigorous advocacy is needed to create and sustain effective tobacco-control programmes. To be efficient and successful, a tobacco policy must be comprehensive and must be of long term. The importance of implementing effective interventions can be shown by their impact on the rates of lung cancer. In Nordic countries, which have adopted integrated policies and programmes against smoking and maintained them since the early 1970s, lung cancer rates are now low. In the UK, tobacco smoking has declined by 46% since 1970; consequently, lung cancer mortality amongst men has been decreasing since 1980, although the rate still remains high. In France, between 1993 and 1998, there was an 11% reduction in tobacco consumption following the implementation of anti-tobacco measures.[4,7]

For the first time in the history of the World Health Organisation (WHO), a legally binding international treaty amongst its Member States has been implemented.[14] The Framework Convention on Tobacco Control (FCTC) is a unique public health tool that will facilitate international cooperation through protocols,[15] aiming at the necessary systematic

Table 1a – Proportion of cancer incidence attributable to different avoidable factors in Europe[8,4,16,29,63,69–72]

Factors	Men (%)	Women (%)
Smoking	29–38	2–10
Alcohol	5–9	2–4
Overweight	3	6
Physical activity	2[a]	
Diet	30[b]	
Fruit and vegetable	5–12[c]	
Infection	8	
Sunlight	8–10[d]	
Environmental and occupational exposure	5	

a Based on mortality for colorectum and breast cancer, for incidence it might be higher because these cancers have a much higher incidence rate.
b Also includes other nutritional factors such as fat intake.
c Worldwide estimate, may vary with regions.
d Estimates based on Western populations.

Table 1b – Recent estimates by the IARC from a sample European country[73]

Factors	Men (%)	Women (%)
Smoking	27	6
Alcohol	11	5
Overweight	1	3
Physical activity	<1	5
Infection	3	4
Sunlight	1	2
Occupational exposure	3	<1
Environmental exposure	<1	<1

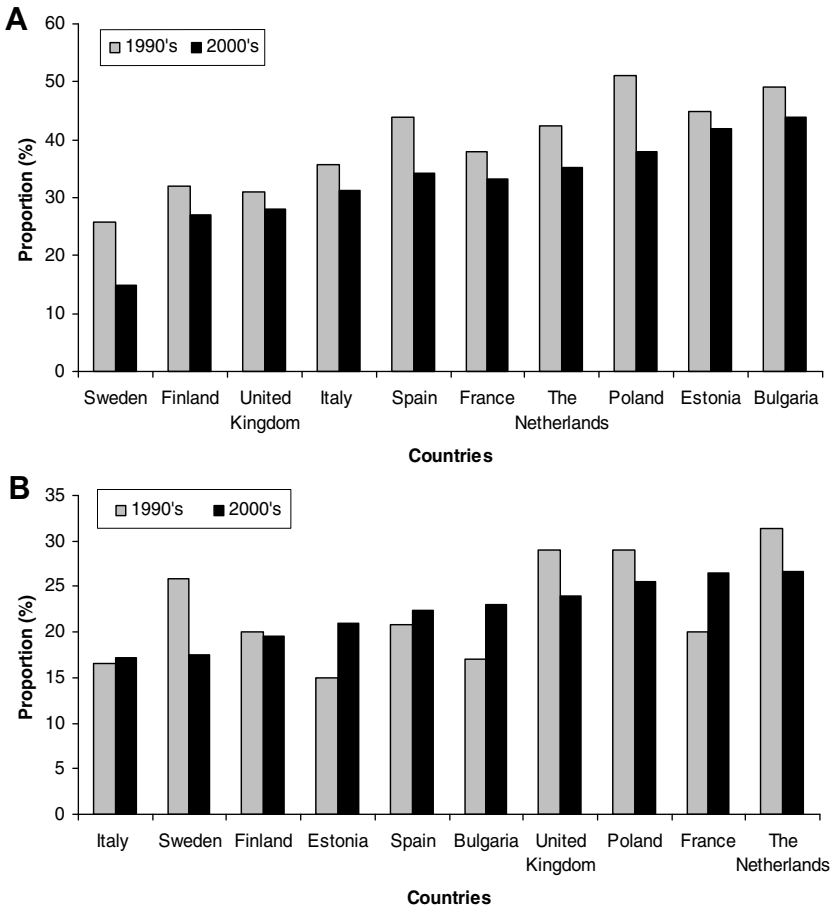

Fig. 1 – Prevalence of daily smokers amongst adults in Europe.[79] Panel A refers to men. Panel B refers to women.

approach to address issues such as pricing and tax measures; protection from exposure to tobacco smoke; regulation of tobacco products; tobacco use cessation; restriction of tobacco advertising, promotion and sponsorship; strengthening the regulations on tobacco product packaging and labelling; controlling illicit trade of tobacco products and banning sales to and by minors. Despite the fact that the above strategies are known, there is still room for improvement: all European Member States should consistently implement the described recommendations, which have been identified as successful in the WHO Framework Convention on Tobacco Control.

2.2. *Alcohol*

Excess alcohol consumption also plays an important role in the causation of several cancers, most notably, in the oral cavity, pharynx, larynx and oesophagus as well as breast, liver and colorectal cancer. Up to 9% of cancer incidence in Europe is attributable to alcohol intake[16] (Tables 1a and 1b). Although there is no clear threshold (a level of alcohol consumption which is safe), the European Code Against Cancer recommends that men limit their alcohol intake to two drinks a day, and women to one. In fact, the very same Code reports in its background references that an increased risk of breast cancer has been consistently reported in epidemiological studies conducted in different populations. The more a person drinks, the higher the risk, a risk which increases exponentially when combined with smoking.[4]

Despite the attempts to combat excess alcohol intake through policy, though, it is clear that the general population underestimates, ignores or is unaware of the risks. Currently, the WHO European Region has the highest alcohol intake per capita of any WHO Region, twice as high as the world average, a figure which also corresponds to the burden of alcohol-related diseases in Europe relative to the rest of the world.[17] Clearly, though, some European populations and countries consume more than others (Fig. 2). Amongst young people, alcohol consumption is the leading risk factor for diseases and other causes of death, including leisure time activities, and in the adult population it is only surpassed by high blood pressure and smoking. In spite of this, an increase in alcohol consumption has been observed in the EU since 2003,[18] obviating the need for public actions such as those in the Nordic countries, which have proven effective in controlling alcohol intake.[19]

2.2.1. *Preventive intervention and policy-making: alcohol*

Sweden is one example of success in reducing alcohol intake at a population level through policy-making. After restricting beer sales based on alcohol content in 1977, consumption decreased by approximately 15%.[20] In 1992, the European Region launched a region-wide action plan on alcohol. Two

Table 2a – Intervention and its impact on five avoidable risk factors of cancer in adults: individual measures

Smoking		Alcohol		Body weight		Physical activity		Fruit and vegetable	
Intervention	Impact (quit rate)[a]	Intervention	Impact (mean difference)	Intervention	Impact (weight change)	Intervention	Impact (mean difference)	Intervention	Impact (serving/day)
Group behavioural therapy	2.17	Brief intervention in general practice or primary care	41 g/week	Lifestyle modification (diet and exercise)	0–5.8 kg	Point of decision prompts	54% increase in stair climbing	Individual intervention (counselling, lectures, phone counselling, printed material)	0–0.44
Bupropion	2.06			Food provision and incentive	6.4 kg	Social support in community including workplace	20% increase in exercise frequency	Combined individual and environmental changes	0.7–0.85
Intensive physician advice	2.04					Lectures (includes reducing TV watching, etc.)	Inconsistent		
Nicotine replacement therapy	1.77								
Individual counselling	1.56								
Telephone counselling	1.56								
Nursing interventions	1.47								
Tailored self-help interventions	1.42								

Refs. [13,34,74–77].

a Likelihood of quitting smoking amongst those who receive interventions compared to those who did not received intervention Weight difference between the intervention versus control group after follow-up.

Table 2b – Intervention and its impact for five avoidable risk factors of cancer in adults: policy measures[13,15,34,76–78]

Smoking		Alcohol[a]		Body weight		Physical activity		Fruit and vegetable	
Intervention	Impact	Intervention		Intervention	Impact	Intervention	Impact	Intervention	Impact (serving/day)
Healthcare financing for quitting	Full versus no coverage: 1%	Alcohol prices		Taxation of foodstuffs, i.e. containing fat[35]	1% price increase = 1% decrease in consumption	Community-wide campaign	4.2% more active	Environmental changes	
Clean indoor laws	Increased quit rate 12–38%	Reduce availability		Environmental changes	Not reported	Enhanced access to physical activity places	48% increase exercise frequency	–Community based activity	Control group: −0.5 Intervention group: 0
Taxation	10% price = 3–5% increase quit rate	Measures against drunk driving						–Social marketing	0.63
Workplace intervention	Decrease in work-day tobacco use (no sizeable effect)	Measures against underage drinking						Interventions at supermarkets (printed documents, nutrition display, incentive) Workplace intervention –Combined individual and environmental	0 0–0.7

a Order is based on strength of impact, best in combination.

consecutive action plans (1992–1999 and 2000–2005) and two ministerial conferences – the European Charter on Alcohol (1995) and the Declaration on Young People and Alcohol (2001) – have all had policy implications and offered paths for the development and implementation of effective measures in European countries. The most recent instrument is the Framework for Alcohol Policy in the WHO European Region.[17] These actions focus on alcohol-free settings within a range of environments: the environment of young people, including sports and leisure; the transport environment, both at land and sea; the workplace, promoting the idea that from a public health point of view, alcohol should not be a part of normal working life; and of course pregnancy. In the absence of demonstrated safe limits, abstinence from alcohol during pregnancy is recommended and actively encouraged.[17,21] Finally, at the European Union (EU) level, a very important policy instrument in Europe to support Member States in reducing alcohol-related harm was communicated in 2006.[22]

2.3. *Diet and nutrition*

It has been estimated that up to one-third of all cancer mortality may be related to what we eat.[23] Most research is still inconclusive about specific dietary items, although this domain is very dynamic, with new reports about diet, nutrition and the risk of cancer appearing almost weekly.[24] In line with the nutritional experts in other fields, however, the ECAC, the WHO and the American Food and Drug Administration (FDA) recommend the "five-a-day" regimen of fruits and vegetables, high-fibre whole-grain cereals, olive oil and fish. Saturated fats, added sugar and salt and *trans*-fatty acids should be avoided (Table 3).

Recent developments in new DNA chip technology and functional proteomics may shed new light on the complex nutrient–gene interactions. This may improve the ability to conduct cancer surveillance and provide new pieces of potentially useful information for the understanding of cancer causation and prevention.[23,25] These advances will become increasingly more important, as nutritional practices are changing rapidly in Central and Eastern European countries towards a more 'westernised' type of diet, with adverse effects on death rates from chronic disease.[26]

Fig. 3 illustrates the fruit and vegetable availability in Europe and its trend during the last two decades. Availability serves as a proxy for consumption. In countries where consumption was high such as in Italy, Greece or Spain, the decrease in fruit and vegetable intake is notable. On the other hand, though increase of fruit and vegetable availability can be observed in Northern European countries, consumption is still much lower than in southern Europe.[27]

2.3.1. *Preventive intervention and policy-making: diet and nutrition*

In healthy adults, primary prevention interventions to increase fruit and vegetable intake increased servings by approximately 0.1–1.4/day (Table 2a). Combining individual with environmental changes seems to work better in changing personal individual diets. A key complementary message is to develop affordable, safe and healthy choices for consumers, and to practise responsible marketing of food products,

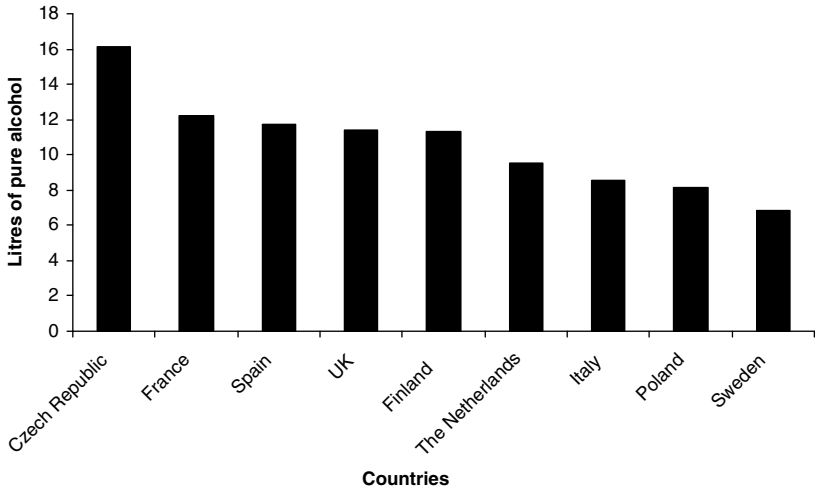

Fig. 2 – Recorded alcohol consumption (in litres of pure alcohol per year) per adult (15+ years) in Europe.[79]

Table 3 – Dietary items and their effect on cancer[4,23–25]

✓ Fruit and vegetable	May reduce the risk of various epithelial cancers: oesophagus, stomach, colon, rectum and pancreas
✓ High-fibre and whole grain cereals	May reduce the risk of mainly colorectal cancer
✓ The "Mediterranean diet" (rich in olive oil, fish, vegetables and fruits and low in animal fat)	Incidence and mortality of digestive tract cancers is lower in Southern Europe than in other European regions. More research is necessary to substantiate evidence
X Red and processed meat	Increased colorectal cancer risk
X Salt, fats and sugar (?)	Salt probably increase stomach cancer. Results on fat and sugar and cancer are inconclusive

especially to children. Simple, clear, non-misleading and consistent food labels should be issued to provide the consumer with information on the composition of food.[28]

2.4. *Physical activity, overweight and obesity*

Evidence linking obesity and overweight to the development of cancer, heart disease and diabetes is more concrete,[6] indicating that 3–5% of all cancers in Europe can be attributed to overweight and obesity (Tables 1a and 1b). In Western Europe, approximately 11% of all colon cancers, 9% of breast cancers, 39% of endometrial cancers, 37% of oesophageal adenocarcinomas, 25% of kidney cancer and 24% of gallbladder cancer are attributable to this.[4,29] One of the main causal mechanisms is that the excess weight causes the body to produce and circulate more of the hormones oestrogen and insulin, which can stimulate cancer growth.[30] Body composition may be an indicator of how the body handles calories, and this may be more important for controlling cancer risks than the overall energy intake.[30,31]

There is consistent evidence that regular physical activity is associated with a reduction in the risk of developing colon cancer, and many studies also suggest a reduction in the risk of cancers of the breast, endometrium and prostate. Although this effect seems to be strongly linked to the impact of physical activity on body weight, the preventive effect of regular exercise for some cancers seems to act independently of weight control.[4,32] Exercise habits vary in Europe (Fig. 4). The Dutch seem to have the highest level of physical activity whereas the Swedish have the lowest.[33]

Unfortunately, overweight and obesity in Europe have now become serious public health challenges (Fig. 5). Some 30–80% of adults in the countries of the WHO European Region are affected. Amongst children and adolescents, about 20% are overweight and a third of these are actually obese,[26] 10 times as many as in the 1970s. By 2010, the impact of obesity is expected to affect 150 million adults and 15 million children.

2.4.1. *Preventive intervention and policy-making: physical activity, overweight and obesity*

An important public health message is to recommend some brisk physical activity every day and maintenance of a body mass index (BMI – weight in kilograms divided by the square of height in metres)[4] in the range of 18.5–25 kg/m^2. People who are already overweight or obese should reduce their BMI to below 25 kg/m^2. A lifestyle that incorporates a healthy diet, exercise and weight control reduces both cancer risk and the risk of other chronic diseases.[30]

So far, no population-based scale intervention study on the prevention of overweight has been completed. Reviews suggest that targeting individual and social as well as physical environment would bring the biggest impact on reducing overweight and increasing physical activity.[34] Taxation of food that contains fat may further reduce the consumption of fatty food.[35]

In Europe, the elaboration of a non-binding set of recommendations for health promotion in the form of a Global Strategy on Diet and Physical Activity was adopted by the Member States in 2003.[36] This non-binding approach provides an important template for countries to develop national plans of action and approaches for dealing with this important public health problem.[37]

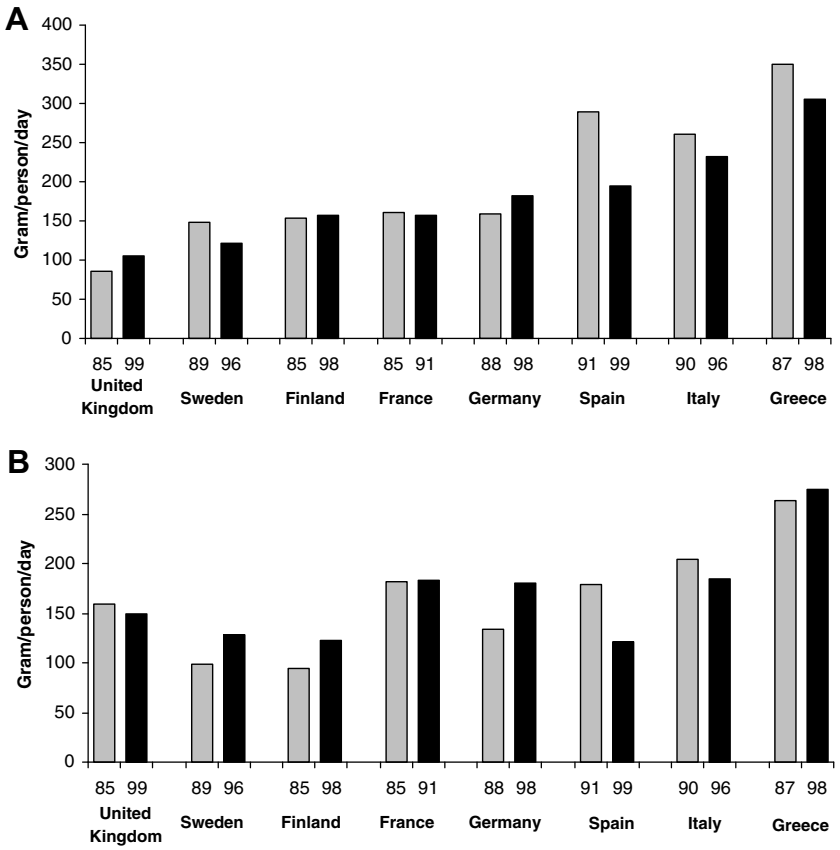

Fig. 3 – Average fruit and vegetable availability in Europe.[27] Panel A indicates fruit availability. Panel B indicates vegetable availability. Please note that years are indicated on the horizontal axis.

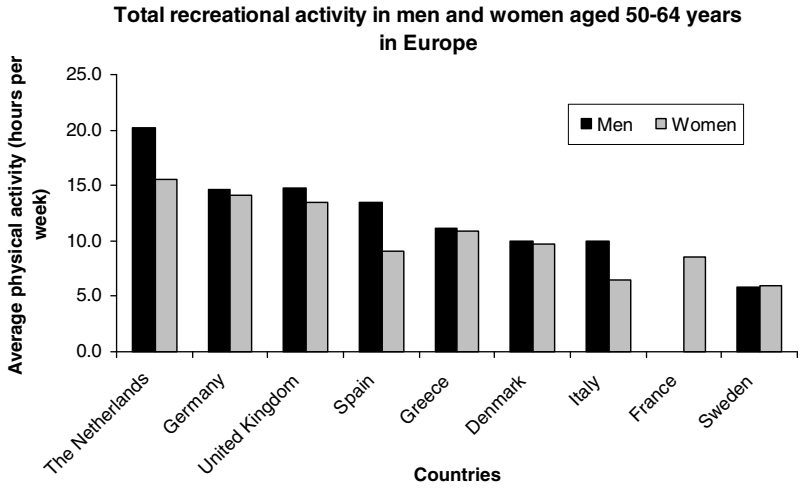

Fig. 4 – Total recreational activity in men and women aged 50–64 years in Europe*.[33] (*Recreational activity comprises cycling, walking, gardening and sports. Male data for France were not available from the study.)

3. Occupational and environmental factors

Occupational and environmental carcinogens are amenable to preventive strategies, hence cancers arising from these causes are highly avoidable.

3.1. *Occupational factors*

Approximately 5% of cancers in Europe have been attributed to work environments, but like most occupational health haz-

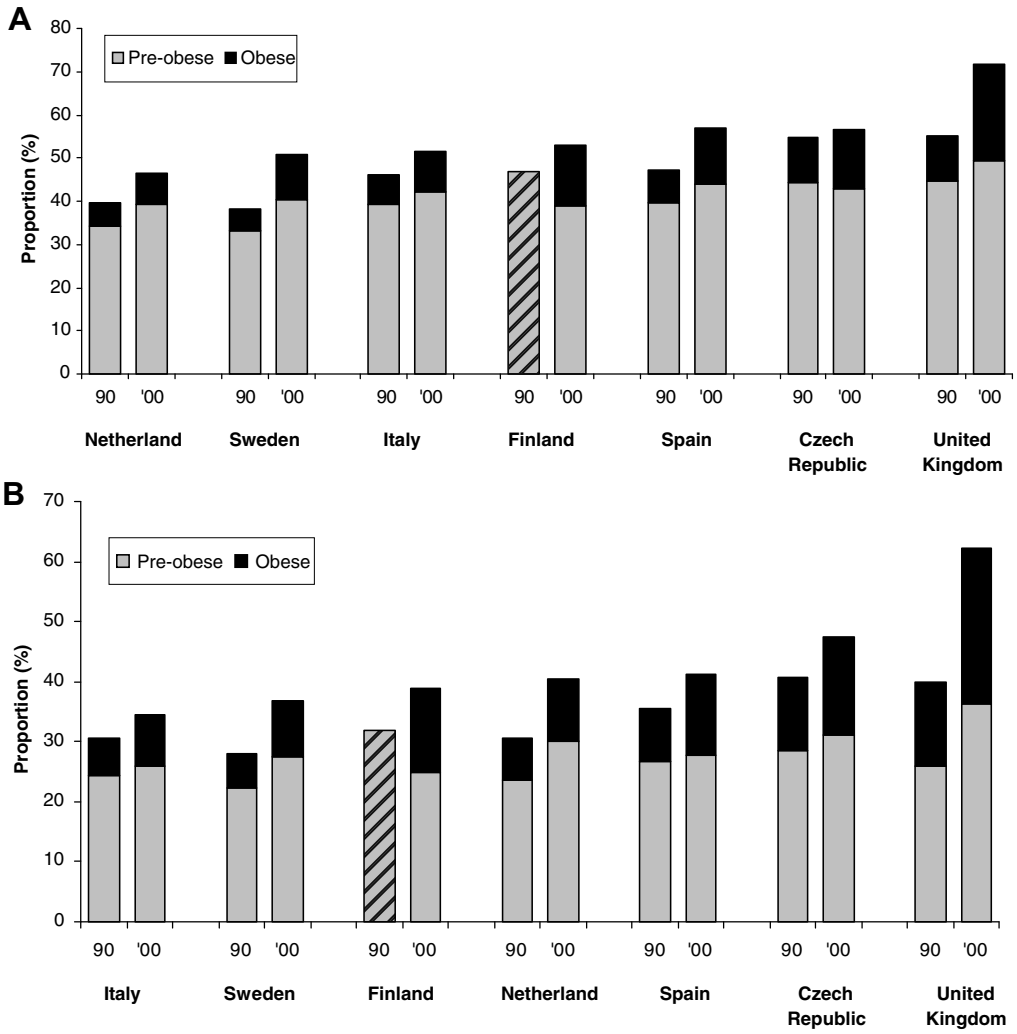

Fig. 5 – Prevalence of overweight and obesity in Europe in 1990 and 2000.[80] Panel A refers to men, Panel B refers to women. Pre-obese was defined as BMI: 25.0–29.9 kg/m^2. Obese was defined as BMI $\geqslant$ 30.0 kg/m^2. Finland has no separate data for pre-obese and obese.

ards, the importance of exposure to carcinogenic risk factors is probably underestimated.[4,38]

Although the situation has improved considerably since the 1990s, when around 23% of those employed in the EU (approximately 32 million workers) were thought to be exposed to carcinogenic agents at levels above the natural background, there are still numerous occupations and substances which present risks[38,39] (Table 4).

Primary responsibility for the prevention of occupational cancer rests on the manufacturers and distributors of carcinogenic substances and the companies who use them. In recent decades, extensive preventive measures in the workplace have led to the prevention of many cancers related to workplace exposures.[4] Most recently, the Global Plan of Action on Workers' Health 2008–2017 was endorsed at the 60th World Health Assembly in 2007 as an update to the WHO Global Strategy on Occupational Health for All. The WHO Regional Office for Europe will implement the Global Plan of Action in European countries together with governments, trade unions, employers, professional associations and other stakeholders.[40] In this respect, the excellent Nordic research on occupational risk factors can serve as a model for other countries, given that they maximise the potential of cancer registries, resolving issues of confidentiality and access to data and operating with the full consent of the involved parties.[41]

3.2. *Environmental factors*

Although the area of environmental risk factors is somewhat murkier and promises less spectacular results, the importance of a clean environment is no less vital for the overall health and should be pursued vigorously. Below are the most relevant areas in need of attention from the cancer prevention perspective.

3.2.1. *Air pollution*

- Even at low-level urban exposure, air pollution is associated with a slightly increased risk of lung cancer mortality (relative risk of about 1.35 when compared to populations in non-polluted areas).[42,43]

Table 4 – Occupational-related cancers and occupational carcinogenic agents at workplaces and industrial processes[4,38]

Primary cancers related to occupational exposure	Most common carcinogenic agents in the workplace	Some occupational carcinogenic and industrial processes (IARC)
Lung	Solar radiation	Boot and shoe manufacture and repair
Urinary bladder	Passive smoking	Painter
Nasal cavity	Crystalline silica	Furniture manufacture
Non-melanoma skin cancer	Diesel exhausts	Rubber industry
Oral cavity	Radon	Aluminium production
Oesophagus	Wood dust	Iron and steel founding
Stomach	Benzene	Hematite underground mining
Colon and rectum	Asbestos	Isopropyl alcohol manufacturing
Pancreas	Polycyclic aromatic hydrocarbons	Manufacture of auramine
Breast	Chromium VI	Nickel refining
Testis	Cadmium	
Kidney	Butadiene	
Prostate	Formaldehyde	
Brain	Nickel compounds	
Bone	Coal gasification	
Soft-tissue sarcoma		

- Especially harmful to residents living near industrial point sources.
- Air-borne carcinogens include combustion products such as polycyclic organic matter (POM), particulate matter (PM), radionuclides, 1,3-butadiene and aldehydes, organic fibres (mainly asbestos) and radon.
- Some clear short-term, acute health effects have been observed due to the effects of PM as well as a significant increase in the risk of death from cardiovascular disease and lung cancer.[44]
- Scientists and policy-makers cite the need for more research to guide public health policies.

3.2.2. *Water contaminants*

- There is evidence that drinking water contains a mixture of known or suspected carcinogenic substances,[45] typically found at trace level concentrations such as
  - inorganic arsenic, involved in the causation of non-melanoma skin cancer and cancers of the bladder, lung and kidney;
  - synthetic organic chemicals (especially disinfection by-products), linked with cancers of the urinary bladder and possibly the large bowel;
  - radium, which increases the risk of osteosarcoma;
  - radon, whose airborne levels link it with lung cancer, and nitrate which increases the risk of gastrointestinal and other cancers.
- Evidence is still inconclusive for many widespread exposures (agricultural pesticides, asbestiform fibres, magnesium, calcium and water hardness) although these last three are actually considered to be the protective factors.

Several strategies are available to reduce exposure to chemical factors by the contamination of water, such as

- The reduction of disinfectant by-products through the application of alternate disinfection procedures or the more selective use of existing disinfection methods.
- The removal of organic, inorganic and particulate contaminants through the use of more advanced water-treatment technologies.[45,46]

An initial EU Water Framework Directive (Directive 2000/60/EC of the European Parliament and Council) was adopted in 2000, and is still in the process of being improved.[46] This was followed by a conference in March 2007, where the European Commission and the European Environment Agency, together with 400 contributors, launched the Water Information System for Europe (WISE), which aims to foster a public health view for the appropriate development of public health in this field.[47]

3.2.3. *Ionising radiation*

One per cent of all fatal cancers are attributable to exposure of the population to sources of ionising radiation, which falls into three categories:

- High dose of ionising radiation (X-rays, gamma rays and neutrons). There is comprehensive evidence for the association between high doses of ionising radiation and cancer in humans.[48] The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) estimates the population risk of dying from cancer after an acute dose of 1000 mSv is about 9% for men and 13% for women[4,49]; man-made sources of ionising radiation (nuclear power production). The consequences of nuclear power and possible accidents (e.g. Chernobyl) are well documented and potentially very dangerous for the general population.
- Radiation for diagnostic purposes (e.g. mammograms, computerised tomography (CT) scans). This is a matter of public concern, although conventional wisdom advises that for now, the benefit outweighs the risk.

Statistical models from sources such as the UNSCEAR are now available to precisely gauge the health effects of ionising radiation,[49,50] providing a good tool to estimate population risk of cancer in relation to a given dose. Moreover, the

International Commission on Radiological Protection (ICRP) recommends avoiding unnecessary exposure to radiation.[51] Other regulations by the International Atomic Energy Agency (IAEA), and specific European regulations (such as the Council Directive 96/29/EURATOM), or (the Council Directive 2003/1227EURATOM) warrant strict compliance.[4]

3.2.4. *Solar radiation*

Sunlight exposure is the main environmental cause of skin cancer. People with fair skin and a tendency to burn in the sun[4] are particularly vulnerable to the most common types of skin cancer: squamous cell carcinoma, basal cell carcinoma and melanoma.

Although usually not fatal, treatment for these cancers is a considerable human and financial burden for individuals and the healthcare systems, and skin cancer remains an important challenge for cancer prevention and control.[52,53] The best preventive message would be to avoid excessive sunburn, especially in summer.[4]

On the other hand, recent evidence supports the hypothesis that some exposure to sunlight may actually protect against the development of several major cancers including colorectal, breast and prostate cancer, possibly through the formation of vitamin D.[54] If sunlight has a protective effect against colorectal and prostate cancer, it is important to balance the positive and negative effects of sun exposure in public health messages.

Recently, the incidence rates of melanoma has started to level off or decrease starting amongst young people in the Nordic countries.[55] Within Europe, EUROMELANOMA (www.procms.be/euromelanoma) has been doing campaigns against skin cancer by increasing the awareness on skin melanoma and the risk of excessive sunbathing. Possibly, the efforts of such campaigns are starting to show an effect.

3.2.5. *Electromagnetic fields and other non-ionising radiation*

The link between exposure to non-ionising radiation (such as power lines and electrical equipment) is inconclusive.[56,29] However, the association between childhood leukaemia and high exposure to extremely low frequency (ELF) magnetic fields has been suggested in certain studies.[57] These studies have shown a pattern of a twofold increase in childhood leukaemia associated with the extremely rare existing fields above 0.3–0.4 μT.[4] Nevertheless, the excess may be attributable to patient selection and publication bias, and a plausible biological mechanism is not known.[58]

Despite the lack of conclusive evidence, the International Commission on Non-Ionising Radiation Protection (ICNIRP) has issued preventive guidelines for limiting exposure to non-ionising radiation.[56]

4. Other cancer determinants and related preventive strategies

4.1. *Exogenous hormones*

Oral contraceptives (OC): studies have shown that breast cancer and cervical cancer (for HPV positive women) risk increase up to 20% amongst current or recent OC users compared to non-users. Conversely, the use of OC reduces the risk of ovarian cancer by about 30%.[59]

Hormone replacement therapy (HRT): a combined oestrogen–progestogen HRT is associated with an excess risk of breast cancer in current, long-term users. Unopposed oestrogens are strongly related to an excess risk of cancer of the uterus. HRT has also been reported to be associated positively with the risk of ovarian cancer. Recently, a major decrease in breast cancer incidence in the USA has been attributed to the reduced intake of HRT.[60] However, in European countries where consumption has always been low, such a decrease is not yet apparent.[61]

It should be noted that endogenous hormones determined by the women's reproductive behaviour (e.g. early age at menarche, late age at first birth, low number of children and late age at menopause) strongly affect the risk of breast cancer, the most common cancer in European women. However, opportunities to modify these factors seem to be small.[62]

4.2. *Infectious agents*

Even the most conservative estimates state that at least 8% of human malignancies worldwide are attributable to persistent infections with bacteria, viruses or parasites (Table 1a).[63,64] In the European Union, this is mainly related to cancers of the cervix uteri, liver and stomach and certain haemo-lymphopoietic malignancies. Awareness of the role of infectious agents in cancer has expanded rapidly in the last three decades, leading to the formulation of new strategies, such as vaccines, to control the spread of several cancer-causing infectious agents (Table 5). To reduce their impact, it is important to strengthen surveillance, prevention and control of communicable diseases, and particularly to use safe and effective vaccines when they are available.

4.3. *Immunologic factors, hereditary risk of cancer and genetic modifiers of cancer risk*

Immunodeficiency disorders can be inherited or acquired from immunosuppressive drugs given after an organ transplant or from the spread of HIV infection. The latter have marked effects on incidence of skin cancer, non-Hodgkin lymphoma and Kaposi's sarcoma, whilst the former are rare and linked to lympho-proliferative malignancies.[65]

Hereditary neoplastic syndromes account for a relatively small percentage of new cancer cases. Approximately 5% of all cancer is considered to be strictly hereditary. On the other hand, research in this area has increased the understanding of genetic factors in common cancers.[66] In the last decade, discoveries have shown the genes that underlie these hereditary forms of cancer, offering an approach to more accurate diagnosis, an effective screening tool, and in some cases, enabling diagnosis before the patient has symptoms. The next phase of genetic discovery will be the identification of genetic modifiers that contribute (although not decisively) to the heritable component of the cause of cancer, conferring a mild-to-moderate increase in predisposition to cancer.[67]

The main challenge is to quantify the risk associated with genetic variations in different environmental settings, and to intensify our research on gene–environment interactions in

Table 5 – Infectious agents related to cancer incidence and their preventive measure[64]

Infectious agents	Possible consequences	Preventive measures
Human papilloma virus (HPV) Spread: sexual contact.	HPV is in ±99% of cervical cancer biopsy specimens. HPV 16, 18, 31, 33, 45 account for over 85% of cervical cancer specimens in Europe.	Primary: effective vaccine; efficiency or cost-effectiveness for population-based use is still under study. Secondary: organised screening programmes (with early detection and appropriate treatment)
Hepatitis B and C (HBV and HCV) Spread: sexual contact and blood, respectively.	Chronic infections with the HBV and HCV are associated with an increased risk of liver cancer.	Primary: vaccine for HBV, not for HCV yet. HCV prevention through control of blood infection and avoidance of exposure. No national immunisation programmes in Europe Secondary: early diagnosis and pegylated interferon-2a, with or without ribavirin
Helicobacter pylori (HP)	65% of new cases of stomach cancer in Europe may be attributable to HP	Primary: none yet (vaccines under development) Secondary: early diagnosis and proton-pump inhibitors and antibiotics

relation to cancer risk. Biobanks and large-scale population-based studies will be required to make progress in this field.[68,69]

5. The ECAC and the European fight against cancer

The European Code Against Cancer (ECAC) stands out amongst other initiatives for its clarity and accessibility as a short set of recommendations for the general public. Set up in 1987, the ECAC was formulated by a committee of experts commissioned by the EU. It created a 'code' –a series of cancer prevention messages and guidelines, targeting all EU citizens. The first ECAC was formally approved in 1988, and consisted of 10 recommendations (six addressing cancer prevention and four addressing early diagnosis) to reduce cancer incidence and mortality (see Appendix A).

Since then, it has been updated twice by specialists in public health and oncology, cancer associations and cancer prevention units of European Ministries of Health. A key message, which emerged from the last process in 2003, was an assertive emphasis on individual behaviour and healthy lifestyle habits.[4]

The establishment and maintenance of an effective scientific collaboration at the European level will assure that the maximum benefit is delivered to citizens, preventing cancer as much as possible. Appendix B outlines a few key sources to facilitate the assessment of progress against cancer in Europe.

6. Conclusions

There is a large body of knowledge about the causes of cancer and strategies to prevent it. A set of life-style and environmental factors involved in the causation of cancer has already been well defined, including tobacco smoking, alcohol consumption, dietary and nutritional factors, lack of physical activity, occupational and other environmental risk factors and infectious agents.

Preventive interventions operating on many of these factors will also contribute to a decrease in some other non-communicable diseases, such as diabetes mellitus, cardio-vascular disease and chronic obstructive pulmonary disease, therefore having a tremendous positive impact on population health.

The European Code Against Cancer provides a practical framework for health promotion and cancer prevention in Europe, as well as alternative strategies to target the main causes of cancer, which have proven effective when properly implemented.

To achieve truly successful prevention, though, additional steps are necessary:

- Involve stakeholders from many sectors of society and create an integrated response to cancer prevention.
- Target all dimensions responsible in increasing the burden of cancer, including social and economic dimensions.
- Generate commitment to policy change at a governmental and industry level.
- Reinforce advocacy.
- Create a broader European frame of reference for lifestyle-related chronic diseases, i.e. bring together the European Code Against Cancer, the Framework Convention on Tobacco Control and the Global Strategy on Diet and Physical Activity.

We are aware of the complexity to implement all these proposals, at least in the short term. But we should try to move the field forward, and follow up the necessary steps. Of course, actions speak louder than words, and we should passionately advocate effective preventive actions for a successful cancer control.

Conflict of interest statement

None declared.

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Appendix A. The European Code Against Cancer[4]

Many aspects of general health can be improved, and certain cancers avoided, if you adopt a healthier lifestyle:

(1) Do not smoke; if you do smoke, stop doing so as soon as possible.
If you cannot stop smoking, never smoke in the presence of non-smokers.

(2) Avoid obesity.
Obesity is defined as a Body Mass Index equal to or more than 30 kg/m^2.

(3) Do brisk but moderate physical exercise every day.
It is advisable to do 30 min physical exercise a day, at least three times a week. More vigorous activities may offer additional benefits regarding cancer prevention.

(4) Increase your daily intake and variety of fruits and vegetables: eat at least 5 servings a day. Cut back on eating foods containing animal fats.
WHO advocates the "5-a-day" plan as the recommended daily amount to reduce the risk of developing cancer. Ideally, this plan consists of eating two fruit portions and three vegetables a day.

(5) If you drink alcohol, be it wine, beer or spirits, drink in moderation, a maximum of two drinks a day for men, and one for women is recommended.
Smoking and drinking alcohol simultaneously multiplies the effect of the other and is strongly discouraged. No safe limits are recommended for alcohol consumption in minors. Women should not drink at all whilst pregnant.

(6) Care must be taken to avoid excessive sun exposure. It is particularly important to protect children and adolescents. Those people who are prone to sunburn must take precautions when sunbathing throughout life.
People should moderate their sun exposure to reduce their total life-time sun exposure and particularly avoid sun-burn.

(7) Strictly apply the legislation designed to prevent any exposure to carcinogenic substances. Follow all health and safety instructions about the use of such substances. Follow the radiation protection regulations.
This message not only addresses all those in charge of laws and who guarantee that they are observed, but also to citizens so that they can protect their own health. The use of individual protection systems in the workplace is essential where hazardous substances exceed natural levels. Knowledge about carcinogenic substances and how to reduce exposures to them is vital.
Public health programmes to prevent the development of cancer.
Great efforts have been made in the organisation of screening programmes and in the search for new diagnostic methods to enable early diagnoses (mainly secondary prevention). Moreover, there are preventive public health programmes which belong to the primary prevention dimension (particularly through vaccination programmes). For detailed data on the efficacy of screening programs and secondary prevention, please see Hakama and colleagues' analysis "Cancer screening: evidence and practice in Europe 2008" in this issue.

(8) Women over 25 should participate in cervical screening programmes.

(9) Women over 50 should participate in breast screening programmes.

(10) Men and women over 50 should participate in colon cancer screening programmes.

(11) Participate in vaccination programmes against Hepatitis B.

Appendix B. Selected sources to assess progress against cancer in Europe

- The Seventh Framework Programme for Research (FP7) 2007–2013: coordinates some EU funding on cancer research. http://cordis.europa.eu/fp7/cooperation/health_en.html.
- The International Agency for Research on Cancer (IARC): funds numerous projects, such as the European Cancer Network, Eurocan Plus and WELAS (Women in Europe Against Lung Cancer and Smoking) www.iarc.fr/.
- EUROCHIP: monitors cancer incidence to reduce inequalities.www.tumori.net/eurochip/.
- European Network of Cancer Registries (ENCR): improves quality and access to cancer incidence data. Contact Lydia Voti: votil@iarc.fr.
- Eurostat: controls mortality data (including cancer) for the EU Member States. http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/ATLAS/EN/ATLAS-EN.HTM.
- EU Health Portal on cancer: web page provides a single access point for EU wide range of information and data on cancer-related issues and activities at both European and Member States.http://ec.europa.eu/healtheu/health_problems/cancer/index_en.htm.

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