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Primary and secondary prevention in the reduction of cancer morbidity and mortality

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Abstract

Overall, cancer is a highly preventable disease. Indeed, modifiable external factors, discovered by epidemiological studies during the last 50 years, account for a majority of all cancer deaths. In this review, we discuss briefly these factors and their contribution to the current burden of cancer with an emphasis on the developed countries. Needless to say, tobacco smoking remains the largest contributor to the cancer landscape, whilst the contribution of poor diet and obesity may be equally important, but much more difficult to quantify. Our main goal was to assess what prevention of cancer has accomplished and might accomplish in the next two decades. Based on (necessarily crude) estimates, age-adjusted mortality rates from cancer in year 2000 had been reduced by approximately 13% due to primary prevention and an additional 6% due to the combined effect of early diagnosis and screening (secondary prevention). According to a realistic goal for the year 2020, a further 29% reduction might be achieved by primary, and 4% by secondary prevention. The main contribution to such accomplishments would be a reduction in tobacco smoking, improvements in diet—including reduced alcohol intake—and arrest of the obesity epidemic, in part through increased physical exercise. Rather than being granted, these goals require great effort and major commitment from all those who share responsibility for public health.

Keywords: Epidemiology; Primary prevention; Secondary prevention; Risk factors; Cancer burden; Predictions

1. Introduction

The purpose of this work is to consider, in realistic terms, what prevention of cancer has accomplished and what it is expected to accomplish in the future. The presentation is going to rely on what we currently know. It will not enter futuristic scenarios of how cancer could be prevented by, say, manipulating telomerase, signal transduction, receptor function, apoptosis or other molecular processes. Instead, to be as realistic as possible, the effectiveness of primary and secondary prevention will be considered at three levels: theoretical effectiveness, clinical effectiveness and population effectiveness.

Theoretical effectiveness describes what could be accomplished under optimal, theoretical conditions. Clinical effectiveness expresses what could be accomplished by a group of sophisticated, knowledgeable persons with plentiful resources (who, nevertheless, are still human and thus subject to errors, miscalculations and other inadequacies). Lastly, population effectiveness quantifies realistic expectations, taking into account the fact that a fraction of all people will remain poorly educated, inadequately informed, unable to access adequate health services, careless, or otherwise refractory to the principles of good preventive practices. Our terminology has been borrowed from the field of human contraception, where it has been used successfully for several years.

In a way, population effectiveness reflects what had already been accomplished in some highly developed countries, at the end of the century, whereas clinical effectiveness represents the objective for the future in the absence of major new discoveries. The presentation will rely largely on the experience of economically

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developed countries for which data are more readily available and more reliable, and in the genuine hope that all countries of the world will have become developed by the end of this new century.

2. Primary and secondary prevention

It has been stated that one of the consequences of frenetic scientific writing is that more scientific papers are actually written than read. Nevertheless, all authors have the secret hope that their work will be widely read and we represent no exception. Thus, for the sake of our readers, who may not be familiar with the terms primary and secondary prevention in the field of cancer (as distinct from, say, the meaning of these terms in psychiatry), we provide the necessary information.

Prevention of cancer may be accomplished through primary prevention, secondary prevention, or a combination of these approaches. The objective of primary prevention is to prohibit effective contact of a carcinogenic agent with a susceptible target in the human body, so that the sequence of events that culminates in the occurrence of clinical cancer does not begin or is aborted at the start. Primary prevention is implemented in two ways: (i) by avoidance, interruption or abatement of a carcinogenic exposure as, for example, by never taking up smoking, stopping smoking, or switching from high to low tar cigarettes, respectively, and (ii) by fortifying the body's defences through vaccination (e.g. against hepatitis B virus) or dietary chemoprevention (e.g. by increasing vegetable intake).

Secondary prevention relies on presymptomatic disease detection at an early, and hopefully, more treatable stage before the appearance of the symptoms or signs that usually result in the patient receiving medical attention. Sometimes secondary prevention aims at the detection of precursor lesions—for example, colonic polyps and carcinoma *in situ* of the cervix—rather than early invasive cancer. Secondary prevention may be implemented through individual *check-ups,* or through population *screening*. Prompt recognition of cancer symptoms or signs by means of increased public and professional awareness is not equivalent to *presymptomatic* diagnosis, but serves a similar objective by facilitating the diagnosis of cancer at an earlier stage (*downstaging*); this latter approach might indeed account for much of the improvements in cancer prognoses during the 20th century.

Primary prevention is generally considered to be superior to secondary prevention and treatment (tertiary prevention), even when the three approaches are equally effective in terms of mortality reduction. This is because prevention is not accompanied by the anguish that characterises the diagnosis and treatment of cancer, even presymptomatic cancer, and because failure of primary prevention leaves intact the two other lines of defence. Moreover, the frequently disseminating nature of clinical, or even subclinical, cancer imposes limits to the effectiveness of local cancer treatment. Nevertheless, primary prevention has never been appreciated as much as secondary prevention or treatment, since the results of prevention cannot be individually recognised. In contrast, a successful treatment of cancer in oneself, a friend or family member is a landmark event, and even rare events of cure or remission become widely known. In addition, the results of an effective treatment of cancer become apparent fairly soon, whereas the impact of primary prevention may take several decades to emerge.

3. Preventability of human cancer

The preventability of cancer was recognised when laboratory experiments documented the existence of identifiable causes of several forms of cancer in animals. Further support for the hypothesis that primary prevention of human cancer represents a realistic option came from studies of migrants who tend to adopt the cancer pattern of the host country within a period that can vary from about approximately 10 to 20 years for cancer of the large bowel to a few generations for cancers of the breast, stomach and prostate. Indeed, a first crude approximation of the potential of cancer prevention can be made through the identification of the lower rates for any particular cancer type in any large population of the world with reliable cancer registration data. This approach, however, underestimates the contribution of preventable causes that are common to the compared populations (e.g. tobacco smoking). However, it assumes that unknown causes for the differences in the cancer occurrence patterns observed in these populations can all be identified and modified in due time.

Strategies for minimising cancer risk usually cover a broad population scoop. In some instances, however, the target group may be more limited and better defined. For example, particular individuals have been identified as carriers of highly penetrant mutant genes that dramatically increase the risk of particular cancer types for these people. Likewise, defined occupational risk may also justify job and cancer type-specific preventive measures. In the near future, more targeted interventions may become more motivated as genetic polymorphisms are identified with the potential to affect risk of specific cancer sites when combined with particular environmental exposures.

4. Causes and primary prevention of cancer

Estimation of the theoretical effectiveness of measures of primary prevention requires the calculation of the

fraction of the population incidence rate of a cancer that can be attributed to a particular component cause (population attributable fraction or PAF) [1]. This statement needs to be qualified by indicating that it applies to single causal factors because causal attribution to two or more factors requires consideration of possible interaction between them. Moreover, rate ratio estimates must be unconfounded, unbiased, reasonably precise and ideally corrected for possible non-differential misclassification of the exposure; such misclassification always entails underestimation of the true strength of association with the outcome. Last, the proportion of exposed needs to be validly estimated and consequences of the latency should be accounted for.

Causal factors for various cancers are summarised in Tables 1 (lifestyle factors), 2 (dietary factors), 3 (biological factors) and 4 (occupational factors). Most of the information in Tables 1, 3 and 4 is based on the valuable work done by the International Agency for Research on Cancer (IARC) [2,3], whereas the information in Table 2 is based on major reviews undertaken by the Harvard Center for Cancer Prevention and the World Cancer Research Fund and American Institute for Cancer Research [4,5].

5. Screening and secondary prevention of cancer

Among the lay public, cancer prevention is identified with secondary cancer prevention that relies on presymptomatic detection and screening programmes [6]. Screenings, however, are complex undertakings and the evaluation of their effectiveness is particularly difficult. The problem is not made simpler by the fact that scientists who have access to screening data have frequently a vested, perhaps subconscious, interest in the screening being a success. In our view, the collective evidence supports that screening for breast cancer has the theoretical potential to reduce breast cancer mortality by up to 30%; screening for cancer of the cervix by at least 50%; and screening for colorectal cancer for up to 25%. Although it is still hypothetical, screening for cervical cancer might become more effective if cytological testing is combined or substituted with tests for oncogenic human papilloma viruses (HPV) [7]. Likewise, colorectal cancer mortality might be further reduced by periodic colonoscopy, an expensive and resource demanding intervention [8].

In spite of the popularity of screening for prostate-specific antigen (PSA), no reliable data exist about its effectiveness in reducing prostate cancer mortality [9]. Screening for hepatocellular carcinoma, cancer of the urinary bladder, stomach and lung has been reported to be effective in some populations, but this is not universally accepted, nor adequately documented in randomised trials; indeed several trials have failed to show any benefit from lung cancer screening. Lastly, biochemical cancer indices are widely used in medical practice, but their use is limited in monitoring cancer progression and recurrence.

Contrary to measures of primary prevention of cancer, that usually have a high benefit-to-cost and risk ratio, screening requires considerable resources and is not devoid of risks [6]. It has been estimated that regular screening for breast cancer will force more than one half of all women to undertake a breast biopsy [10], and a substantial proportion of men, regularly screened for prostate cancer, will face the consequences of prostatectomy for an occult carcinoma that may never had progressed to a life-threatening condition. Thus, the establishment of an effectiveness to detect cancer is not a sufficient criterion for the widespread adoption of screening.

6. Primary prevention of tobacco and alcohol-related cancers

Effective control of the tobacco smoking epidemic remains, as it should, the principal target of most cancer prevention campaigns, but it has proved to be a very elusive target. The prevalence of smokers has declined in most developed countries, but it is rapidly increasing elsewhere in the world. Small-scale programmes and traditional health education efforts are no match for the addictive power of nicotine and the sociopolitical influence of the tobacco lobby. In a democratic society, three complementary approaches appear most promising: improving general education, taxation and cultivation of an anti-smoking social ethos [11].

Table 1
Lifestyle factors established as human carcinogens

Lifestyle factor	Site(s) of cancer
Tobacco smoking	Lung, bladder, oesophagus, mouth, larynx, kidney, pancreas
Environmental tobacco smoke	Lung
Ethanol	Oesophagus, larynx, mouth, pharynx, liver, breast
Betel chewing	Mouth
Ionising radiation	Bone marrow and probably most other sites
Ultraviolet light	Skin, lip

Table 2
Risk implications for major forms of cancer by consumption of foods in major groups, intake of energy-generating nutrients, intentional dietary exposure to selected non-nutrients, and nutrition-related indicators

	Oral cavity	Nasopharynx	Oesophagus	Stomach	Large bowel	Liver	Pancreas	Larynx	Lung	Breast	Endometrium	Cervix uteri	Prostate	Urinary bladder	Kidney
Major food groups															
Vegetables	reduce		**reduce**	**reduce**	reduce	reduce?	reduce?	**reduce**	**reduce**	reduce	reduce	reduce	reduce?	**reduce**	reduce?
Fruits	**reduce**		**reduce**	**reduce**	reduce	reduce?	reduce?	**reduce**?	reduce	reduce?	reduce?	reduce?	reduce	reduce?	reduce?
Red meat					**increase**		increase?								
Macro-nutrients															
Protein (as animal)					increase?		increase?				increase?				
Fibre					reduce?		reduce?								
Saturated fat (as animal)					(increase)				increase?		(increase?)		increase?		increase?
Mono-unsaturated fat										reduce?					
Non-nutrients															
Alcohol	**increase**		**increase**		increase	**increase**		**increase**		**increase**					
Salt (NaCl)															
Nutritional covariates															
Height					increase?					**increase**					
Obesity					increase					dual[a]	**increase**				**increase**
Physical activity					**reduce**					reduce (?)			reduce?		
Hot drinks			**increase**												

'?' indicates current data are only suggestive. Bold type indicates data are convincing.
[a] Obesity reduces risk among premenopausal and increases risk among postmenopausal women.

Table 3
Biological agents judged by IARC (WHO) as being human carcinogens

Agent	Site(s) of cancer
Aspergillus flavus (aflatoxins)	Liver
Hepatitis B virus	Liver
Hepatitis C virus	Liver
Helicobacter pylori	Stomach
Schistosoma hematobium	Bladder
Opisthorchis viverrini	Cholangiocarcinoma
Clonorchis sinensis	Cholangiocarcinoma
Human papillomaviruses	Cancer of the cervix and anus
Human herpes virus-8	Kaposi's sarcoma
Human immunodeficiency virus-1	Non-Hodgkin's lymphoma, anal cancer, Kaposi's sarcoma
Human T-cell leukaemia virus	Adult T-cell leukaemia
Epstein–Barr virus	Lymphoproliferative diseases, nasopharyngeal carcinoma

WHO, World Health Organization; IARC, International Agency for Research on Cancer.

Table 4
Important occupational agents or work processes considered by IARC (WHO) as being human carcinogens

Substance of process	Site(s) of cancer
Acrylonitrile	Lung
Aluminum production	Lung, bladder
4-Aminobiphenyl	Bladder
Arsenic and certain arsenic compounds	Lung, skin
Asbestos	Gasto-intestinal tract, mesothelioma of pleura and peritoneum, lung, larynx
Auramine manufacture	Bladder
Benzene	Haemopoietic tissue
Benzidine	Bladder
Beryllium and beryllium compounds	Lung
Bis(chloromethyl) ether and chloromethyl methyl ether	Lung
Boot and shoe manufacture and repair	Nasal cavity
1,3-Butadiene	Haemopoietic tissue
Cadmium and cadmium compounds	Lung
Coal gasification	Lung
Coal-tars and pitches	Skin
Coke production	Lung
Chromium and certain chromium compounds	Lung
Diesel exhaust	Lung
Dioxins	Soft-tissue sarcoma, non-Hodgkin's lymphoma
Ethylene oxide	Haemopoietic tissue
Formaldehyde	Nose and nasopharynx
Glass manufacture	Lung
Hairdresser or barber	Bladder
Underground hematite mining	Lung
Iron and steel founding	Lung
Magenta, manufacture of	Bladder
Mineral oils, treated and mildly treated	Skin
Mustard gas	Pharynx, lung
2-Naphthylamine	Bladder
Nickel and nickel compounds	Nose and nasal sinus
Nonarsenical pesticides, spraying of	Lung
Painter	Lung
Petroleum refining, occupational exposure	Skin, haemopoietic tissue
Polychlorinated biphenyls	Liver, skin
Radon	Lung
Rubber industry	Bladder, haemopoietic tissue
Shale-oils	Skin
Silica	Lung
Soots	Skin
Sulphuric acid mist	Nasal cavity, larynx, lung
Talc-containing asbestiform fibres	Lung
Trichloroethylene	Liver, biliary tract
Vinyl chloride	Liver
Wood dust	Nasal cavity

The strong inverse association between general educational achievement and smoking and the trend for better education in most developed countries represent a welcome combination. Increased excise taxation has been shown consistently to reduce tobacco consumption, but the fairness of the measure is questionable, even when it serves such a noble objective. Social disapproval of smoking, combined with compassion and respect for smokers, is a delicate balance that deserves pursuing. A neglected area is risk perception and communication—it is not uncommon to meet heavy smokers who are genuinely concerned about the health effects of radon, air pollution, magnetic fields and xenooestrogens, factors that contribute minimally, if at all, to their cancer risk.

Unless tobacco production ceases, a genuine miracle, smoking cannot be eradicated; few vices ever have been. However, on the basis of past trends, the strong inverse association between education and smoking and the emerging social ethos, it may be reasonable to hope that, within a few decades, tobacco smoking and eventually tobacco-related mortality will be reduced by approximately 2/3 [12]. Admittedly, the inverse association between education and tobacco smoking is consistent in men, while in some settings it is weaker, in others stronger, among women.

Alcoholic beverages are integral components of the communal life of many societies and moderate intake reduces cardiovascular mortality *and* total mortality. Yet, alcohol interacts with tobacco in the causation of cancer in the upper respiratory and gastrointestinal tract, it can cause liver cirrhosis-mediated hepatocellular cancer and also causes other forms of cancer [13]. Strategies that could preserve most of the health benefits of alcohol intake and could reduce the alcohol-related cancer mortality should be time, place and culture-specific. Moderate consumption of wine during meals and a reduction in heavy drinking, particularly binges, may be a way towards the stated objective, and there are indications that this may actually be happening. Nevertheless, it is unlikely that alcohol-related cancer mortality can be reduced by more than a 1/3 [12].

7. Primary prevention of diet-related cancer

It may appear contradictory but it is in fact true that although we know little about the beneficiary or harmful food constituents, we have a good idea of what a prudent diet that reduces cancer *and* total mortality should be [14,15]. This diet should be high in vegetables, fruits, legumes and whole grain cereals; low in red meat, refined cereals, potatoes and salt; and low saturated fat of animal origin. Added fats should be of plant origin and not hydrogenated; among them, olive oil has a safety record of several thousand years.

Obesity should be avoided by all means, but the best way to accomplish this would be by increasing physical activity, which, in itself, can reduce the incidence of colorectal cancer and, perhaps other types of cancer as well. Regular physical activity during childhood and adolescence may also slow down excessive growth and delay menarche. Early age at menarche is a risk factor for breast cancer and excessive growth, as reflected in attained height is positively associated with risk for several cancer types. More research in this complex area is needed, however, before the importance of modifiable factors early in life can be adequately estimated.

Diet, physical activity and obesity are quantitative variables and there usually are in practice no categories of zero exposures. Moreover, absolute measurements are difficult to obtain because most measurements depend on study-specific design, available databases and analytical approach. Usually, individuals are distributed in quintiles, i.e. in 20%-wide categories in the respective frequency distributions. Occasionally, a score is created to integrate the various components of diet [16]. It does not appear unrealistic to expect that individuals in all quintiles except the best ones could be motivated to improve their diets and increase their physical activity so as to move to the adjacent 'better' quintile. If this were to happen, both the diet-related and the sedentary life-related cancer mortality would be reduced by approximately a 1/4 [12]. Reduction of salt intake could, in theory, accelerate the declining incidence of stomach cancer. No other food additive or contaminant has been convincingly linked to cancer.

8. Primary prevention of biological agent-related cancers

Most of the biological agents with established carcinogenic potential are rare in the developed countries. Hepatitis B and C viruses cause a substantial fraction of hepatocellular carcinoma in Mediterranean countries and Japan, but a minority of cases in other developed countries [17]. Moreover, the fraction of viral-related liver cancer is likely to decrease following the availability of an anti-HBV vaccine, improved screening of blood and blood products, and more frequent use of disposable syringes and needles by intravenous drug abusers. Barrier measures directed against the transmission of HIV may contribute to the decline of HPV-related cancer of the cervix [18]. The continuing reduction of mortality from stomach cancer implies a reduction of the carcinogenic potential of the still prevalent *Helicobacter pylori*, probably because of improved sanitation and essential interacting factors are becoming less common [19]. Lastly, there is evidence that the incidence of the AIDS-related Kaposi's sarcoma and non-Hodgkin's lymphoma have already peaked in developed countries. Overall, it appears that in the

absence of a breakdown of measures and policies currently in force, mortality from cancers of infectious origin is likely to decline in the next few decades, probably by approximately 1/5 [12].

9. Primary prevention of cancers related to reproductive factors and high penetrance genes

Reproductive factors influence chiefly the risk for cancer of the breast [20] and female reproductive organs. However, the reproductive behaviour of most people has its own dynamics and is not easily altered by external influences. An exception may be created by the growing genetic counselling activities focusing on individuals carrying high penetrance mutant genes, mainly for cancer of reproductive organs and the large bowel [21]. Assuming that the frequency of such new mutations is low, which is likely, and genetic counselling is at least moderately effective, a reduction of inherited cancer mortality by approximately a 1/20 could be possible. However, this is a speculative estimate in a field, which is rapidly changing.

10. Primary prevention of cancers related to radiation, occupational factors and environmental pollution

With respect to ionising radiation and general population exposure to carcinogenic occupational agents, there is little the individual citizen can do, except demand and expect that regulations are enforced. Technological progress, a shift of economic activity away from traditional industrial employment, increasing productivity leading to a reduction in the number of workers in relatively high cancer risk occupations and the phasing out of the asbestos epidemic justify an expectation for reduction of occupational cancer mortality by about approximately 1/4 [12]. Moreover, awareness of the risks associated with prolonged sun exposure and the use of sunscreens could reduce radiation-induced cancer mortality by 1/10 [12].

In developed countries, air pollution has declined over the last 30 years, even though adopted measures were mostly based on short-term health criteria rather than on long-term outcomes, including cancer. Some reduction in pollution-related cancer mortality may occur, but this will be as difficult to document as the existence of the link itself. A token reduction of 1/4 corresponding to the apparent reduction in pollution levels is postulated [12]. This potential reduction might, however, be compensated by a concomitant increase in many developing countries.

Over the last 20 years, no field of epidemiological research has seen so many new hypotheses as that of carcinogenesis from environmental pollution [22]. Candidate agents were as diverse as extremely low frequency magnetic fields, radio frequency range electromagnetic radiation as used in cellular phones, proximity to nuclear plants, toxic dumps, water fluoridation, environmental endocrine disruptors, persistent pesticide residues and unspecified sources responsible for cancer clustering. Few of these hypotheses were plausible, or supported by solid epidemiological evidence, but they all serve an important function: preserving the necessary vigilance in the face of exploding technological developments.

11. Primary prevention of cancers related to medical products and procedures

Several medical products and procedures can cause cancer, but when they are administered to patients suffering from serious diseases, they demonstrate, in stochastic terms, exceedingly favourable benefit-to-risk ratios. The problem is more complicated, however, when pharmaceutical agents or procedures are applied to healthy persons for preventive purposes. This is because the potential benefit is on the average smaller among healthy than among seriously ill persons. Mammography and three categories of pharmaceuticals—oral contraceptives, menopausal oestrogens and tamoxifen for *primary prevention* of breast cancer—have come under special scrutiny.

It is now generally recognised that mammography conveys a negligible risk and a substantial benefit. Oral contraceptives, over and beyond their social benefits, prevent more cancers of the ovary and endometrium than they may cause in the breast and the liver. Menopausal oestrogens can cause cancer of the endometrium and the breast, but the likely protection they convey against coronary heart disease, osteoporosis and perhaps large bowel cancer, probably outweighs their risks in most individuals. However, recent evidence that progestins combined with oestrogens add substantially to risk of breast cancer could alter the balance of risks and benefits. Finally, tamoxifen is likely to protect against breast cancer, but is also likely to increase the risk of endometrial cancer, posing a problem by weighting a considerable possible benefit against a probable, but smaller risk.

Medical products and procedures will continue to cause a small proportion of all cancers, but the substantial benefits, in general, outweigh the risks.

12. An attempt for quantification

There are many uncertainties in the attempt to quantify the effectiveness of cancer prevention measures. For instance, should one evaluate the potential for preven-

Table 5
Cancer mortality reduction, accomplished (year 2000), as well as optimal prospect and realistic goal for year 2020 in developed counties

Factor or group of factors	Accomplished (population effectiveness in developed countries in the 1990s) (%)	Optimal prospect (theoretical effectiveness) (%)	Realistic goal (population effectiveness in developed countries around 2020s) (%)
Tobacco	25	100	60
Alcohol	15	100	30
Diet in adult life, including obesity	10	30	10–20
Perinatal effects and excessive growth	0	0	0
Food additives, including salt	10	20	10
Sedentary life	0	15	5
Biological agents, including viruses	5	30	15
Reproductive factors	0	0	0
Ionising and ultraviolet radiation	5	20	10
Occupational factors	30	60	45
Environmental pollution	20	50	30
Medical products and procedures	5	15	10
High penetrance genes	0	15	5
All causes	≅13	≅49	≅29
Early diagnosis and screening (further reduction)	6	8	4

Percentages in the three columns refer to the cancer deaths linked to the indicated cause (for example 60% of tobacco-related cancers are realistically preventable). In contrast, the per cent associated with all causes refer to mortality rates for all cancers. The dominator for the accomplished reductions is the assumed age-adjusted rate in the absence of any intervention. Prospects for the year 2020 are related to age-adjusted rates prevailing in the year 2000.

tion of lung cancer on the basis of the existing rates of this disease, or on the basis of the rates that would have existed were it not for the curtailment of the tobacco epidemic during the last 20 years? Should social factors be adjusted for, or are they crucial components of the causal complex that increases the risk of several forms of cancer? How could we best account for latency, when exposures change over time? We have chosen to ignore latencies, because addressing them would create insurmountable complications. We also realise that, in order to estimate accomplishments, one would need to know the expected rates of cancer in the absence of any preventive measures, an objective that can only be approximated, but never validated [12].

Table 5 (and Fig. 1) provide guestimates of accomplishments, including those engineered by non-specific socio-economic improvements, and of prospects, with both realistic assumptions and optimal conditions. It should be pointed out that our evaluation relies on age-adjusted mortality, rather than number of deaths, since reduction of mortality rate by, say, 30% is not equivalent to a 30% reduction in cancer deaths. In many, notably Western populations, prevention or postponement of deaths from causes other than cancer will change the age-structure and size of the population due to longer life expectancy. In such populations, the reduction in number of deaths will be smaller than the corresponding reduction in age-adjusted mortality.

Weighting the cause-specific reductions with the attributable fractions by group of causes (Table 6) generates the all-causes estimates shown at the bottom of Table 5. For example, a 60% reduction in the use of tobacco (Table 5), which accounts for an estimated 30% of all cancer deaths (Table 6) would ultimately entail an 18% (0.6×0.3) reduction in cancer mortality. Thus, primary prevention measures are estimated to have prevented about one out of eight fatal cancers, whereas screening may have reduced the residual mortality by a further 6%, notably due to a reduction in cervical cancer. Under optimal conditions, almost half of all fatal cancers could be prevented, whereas mortality for the remaining could be reduced by another 8%. Under more realistic conditions, likely to prevail around 2020, around 30% of today's fatal cancers in the developed countries could be prevented, whereas mortality from the remaining cancers could be reduced by an additional 4%.

Prerequisites for prevention may be substantially different, but not worse in less developed countries. The tobacco epidemic, for example, began in China and elsewhere relatively recently, and its ultimate consequences are predictable. Hence, preventing the young

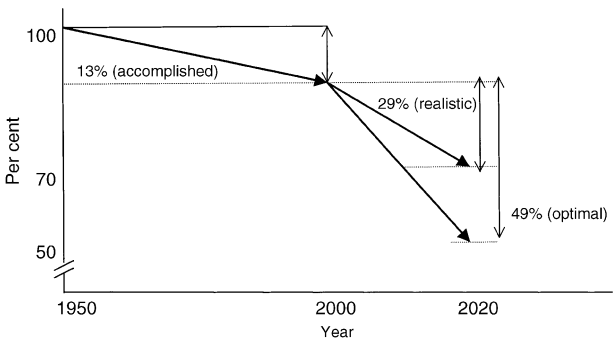

Fig. 1. Accomplished and future, realistic and optimal, reductions of cancer mortality due to primary prevention.

Table 6
Cancer mortality attributable to specific factors or group of factors in the developed countries

Factor or group of factors	Percentage
Tobacco	30
Alcohol	3
Diet in adult life, including obesity	30
Perinatal effects and excessive growth	5
Food additives, including salt	1
Sedentary life[a]	>3
Biological agents, including viruses	5
Reproductive factors	3
Ionising and ultraviolet radiation	2
Occupational factors	<5
Environmental pollution	2
Medical products and procedures	1
High penetrance genes	2

[a] Does not include contribution to obesity.

generation in such countries from taking up smoking may be the single most important goal in order to achieve a reduced future cancer burden, both locally and globally. Moreover, control of infections with oncogenic bacteria, parasites and viruses—several of them causing the most common cancers in certain settings—will be proportionally more important in developing than in developed countries.

It is obvious that these are approximations and, indeed, crude ones, for both theoretical and practical reasons. Thus, the attributable fractions in Table 6 do not, and should not, add to 100%, so that the weighting process is not accurate. Moreover, some improvements, primary for stomach cancer, have been unintentional and indeed incompletely understood. Latencies and variability of screening effectiveness further complicate the issue. Nevertheless, these estimates are fairly robust and indicate, in broad terms, what has been accomplished so far and what can be expected in the immediate future from preventive oncology in the developed countries.

13. Conclusion

Implementation of primary and secondary prevention takes place slowly and incrementally, rather than through major breakthroughs. Avoidance of tobacco smoke, including environmental tobacco smoke, represents the first priority. With respect to diet, *increased consumption* of vegetables and fruits, reduced *consumption* of refined carbohydrates, salt, red meat and animal fat, and *partial substitution* of some of the remaining animal fat with plant oils (mainly olive oil) are likely to contribute substantially to the primary prevention of cancer. Reduction of excess energy intake in early life, avoidance of obesity in adult life, and increased physical activity throughout life are also desirable. Alcoholic beverages should be consumed only moderately; this applies particularly to smokers because of the established interactive effects of these two exposures, and to women because alcohol intake may be involved in the aetiology of breast cancer, and because coronary heart disease, which is inversely related to alcohol intake, is less frequent among women. Vaccination against hepatitis B virus and control of transmission of hepatitis C virus and some of the human papilloma viruses will have a modest impact on cancer occurrence in developed countries. Avoidance of exposure to ultraviolet radiation, prudent use of potentially carcinogenic medical products and procedures, strict control of occupational exposures, a sound environmental policy and continuous scrutiny of food additives and possible contaminants can also contribute to the avoidance of a small fraction of the cancer burden.

On the basis of existing evidence and exposure trends over time, it has been estimated that primary and secondary prevention have already reduced mortality from cancer by approximately 13%, in comparison to the cancer mortality rates that would have been reached in the absence of these measures. In the next 20 years, a further reduction of cancer mortality by approximately 29% is potentially achievable, mostly on account of measures of primary prevention. Indeed, primary prevention seems to be approximately 7 times more effective than measures of secondary prevention (screening). We want to emphasise, however, that great effort and major commitment will be needed if we are to achieve a 30% reduction. At current levels of prevention, we have only seen a modest decrease over the last 20 years, and without further efforts, primarily related to smoking and obesity, we will not come close to the 30%. However, there is room for further improvement of cancer prevention, but this will require either ideal effectiveness of the preventive measures, which is difficult to accomplish, or new discoveries that could not and have not been accounted for in this paper.

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