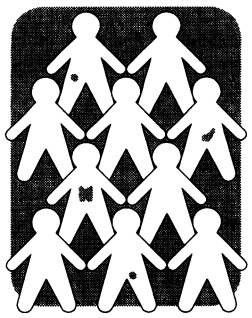
Current trends and some prospects for the future—II

Joan Austoker



This is the concluding part of the last article in this series looking at how cancer can be prevented in general practice. Cancer Prevention in Primary Care will be published as a book in November

Cancer control encompasses the whole spectrum from prevention and early diagnosis to treatment and palliation. The key to the future of cancer control will be to establish multidisciplinary approaches to each type of cancer across this spectrum. For primary prevention this requires some understanding of the causes of each cancer. Although understanding of the aetiology of cancer has greatly improved, prospects for the primary prevention of many common cancers remain remote. Other approaches currently under evaluation include chemoprevention and the use of biomarkers (discussed last week). The identification of predisposing genes for some of the common cancers may have a considerable impact on the ability to recognise those at risk. Overall, however, mortality trends indicate that reduction of smoking remains the main priority for cancer prevention in the United Kingdom. For primary care teams, brief interventions to reduce smoking are likely to achieve the greatest benefit. This should be seen as part of broader policies aimed at achieving change in the whole population. The government must acknowledge its major responsibility to cancer prevention by banning all forms of advertising and promotion of tobacco.

Genetic basis of cancer: prospects for prevention

Cancer is essentially a genetic disease at the cellular level. It is caused by abnormalities in the genetic mechanisms which control cellular growth and proliferation. Most gene alterations associated with cancer are acquired through exposure to environmental carcinogens such as certain chemicals, radiation, infectious organisms, or factors in the diet. Only a small minority are inherited in the germline. Almost all cancers in humans have both sporadic and genetic counterparts. Genetic alterations may indirectly increase the risk of mutations occurring in growth related genes by affecting the metabolism of an environmental carcinogen or DNA repair mechanisms. Genetic predisposition to cancer may also result from inherited mutations in genes that are directly concerned with normal growth and differentiation. Included in this category are oncogenes, which, when activated, promote abnormal growth and proliferation, and tumour suppressor genes, which usually have a role in cellular differentiation and repression of proliferation but which may be lost, damaged, or switched off through mutations. Both tumour suppressor genes and DNA repair defects have been shown to account for inherited predisposition to cancer.

The increased risk of cancer in the close relatives of patients with cancer has been documented for many cancers. This risk of cancer in first degree relatives of index cases may be very high in certain families but is more commonly between two and three times that of the general population. This familial clustering of cancer could be due to environmental factors with a common exposure due to a shared lifestyle (such as diet), genetic factors, or interactions between the two. In population terms genetic factors acting alone or interacting with environmental carcinogens to produce a modest increase in the risk of cancer are potentially more important than the rare inherited disorders which are associated with a high risk of cancer. While such genetic factors could result in the majority of cancers developing in susceptible people, for any given level of exposure to a carcinogen, only a proportion of exposed people will develop cancer. The well recognised variations in susceptibility between people to environmental carcinogens at some stage of the carcinogenic process may therefore be genetically determined. It will be important, therefore, to understand how individual people respond to carcinogenic challenges—that is, how risk relates to individual susceptibility. The implications of identifying markers of carcinogen sensitivity are substantial. Risk assessment is a complex process, which will need to include biological evaluation of the differences between individuals in carcinogenic susceptibility, including measurements of carcinogenic metabolic activation and DNA repair capability. Such susceptibility markers will, in the future, enable us to identify high risk population subgroups that can be targeted for intensive primary and secondary preventive strategies.

GENETIC TESTING FOR PREDISPOSITION TO BREAST AND OVARIAN CANCER

Some people have a very strong genetic predisposition to cancer. Several such inherited cancer syndromes have been identified, characterised by an autosomal dominant mode of inheritance and the high risk of occurrence of specific classes of malignancy, usually at an early age.

Cancer predisposition genes are now known to cause not only the rarer familial cancer syndromes but also a proportion of the common cancers. Although this latter proportion is small, the number of gene carriers could be large and therefore pose a considerable public health problem. This is well illustrated by the example of predisposition to breast and ovarian cancer.

Currently, family history is the only practical way in which inherited predisposition for breast and ovarian cancer can be recognised. The identification of predisposing genes in the near future will have a considerable impact on the ability to recognise those at risk. About 40% of families with several cases of breast cancer, and more than 80% of families with breast and ovarian cancer, are due to predisposition by the BRCA1 gene, which has been mapped to a small region of chromosome 17. BRCA1 may possibly also confer risks of colon and prostatic cancer. Current data suggest that strongly disposing BRCA1 mutations may account for 2-4% of all breast cancer (with a higher proportion at younger ages). The lifetime risk of breast or ovarian cancer for these women will be over 80%, the greater part of the risk falling at ages 30-50, and carriers who have developed one cancer will have a high risk of developing a second breast or ovarian cancer. Prophylactic surgery is a consideration for these women at very high risk.

The cancer risk associated with a BRCA1 germline mutation will need to be determined to offer accurate risk assessment. Different mutant alleles of BRCA1 may confer different lifetime risks for breast or ovarian or other cancers. Weakly predisposing alleles

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of BRCA1 or other genes could in theory be quite common and could account for a greater proportion of the incidence of breast and ovarian cancer than is accounted for by the strong alleles. If this is the case, it would have important public health implications.

There is some indication that when the BRCA1 gene is isolated, interest in genetic testing for cancer susceptibility is likely to be great. There are, however, significant problems associated with the widespread use of genetic testing, and it is premature to consider testing on a population basis. Even restricting testing to women with a strong family history poses considerable problems. There are no guidelines on how best to communicate information about cancer susceptibility to those at high risk or how best to inform women of the potential benefits or limitations of genetic testing. The appropriate management of identified gene carriers, some of whom may be at only moderately increased risk, is uncertain as screening for ovarian cancer and for breast cancer in women under 50 are of unproved efficacy. The role of prophylactic surgery in such women is also unclear. The rapid pace with which molecular genetic research is proceeding and the implications it carries for those at high risk make it a priority to develop and test strategies for communicating information about cancer risk to individuals in the population. Counselling is more likely to be useful if it acknowledges that individuals are already likely to have beliefs about inheritance and their own susceptibility. These need to be explored and understood so that individuals may be assisted in interpreting the information that can be provided from the perspective of clinical genetics. Individuals' priorities may, for example, be expressed in terms of the actions they may take to reduce their own susceptibility; this may be more important to them than precise calculations of their risk.

ROLE OF GENERAL PRACTITIONERS IN GENETIC TESTING OF PEOPLE AT PERCEIVED HIGH RISK OF CANCER

The new potential for precise genetic diagnosis in some families raises important psychological and ethical issues, and adequate counselling will need to precede decisions about whether to request referral for testing. General practitioners will need to understand the issues surrounding testing for mutations and be concerned with providing genetic counselling and management recommendations to those at high risk (box 1). General practitioners could have an important role in informing people at perceived high risk about risk factors and in eliminating misconceptions about personal risk. Appropriate referral will be necessary of those at high risk to family cancer genetic clinics. This will require general practitioners to know what constitutes a high risk. Evidence to date indicates that they have a limited understanding of cancer genetics and often misinterpret its impact on people at high risk. The development of appropriate education and training strategies for general practitioners about genetic screening for cancer should be seen as essential.

Box 1—What general practitioners need to know about genetic testing for cancer

- The risks, benefits, and limitations of genetic testing
- What pretest counselling will be required
- What constitutes a significant family history
- How to assess risk in those at perceived high risk
- How to explain the consequent risks to the individual
- The implications of testing positive
- The implications of testing negative
- The implications for other family members
- Who should be referred for a specialist opinion
- Where patients should be referred—for example, family cancer genetics clinic
- The effectiveness of current methods of screening and surveillance for those at high risk—that is, their limitations
- What post-test counselling will be required
- What advice can be offered to those not requiring referral for testing

Box 2—Cancer services: proposed levels of care[1]

- Primary care—The focus of care, with detailed discussions between general practitioners and the hospital service to clarify patterns of referral and follow up, so ensuring the best outcome for the patient
- Designated cancer units—Should be created in many local hospitals and be sufficiently large to support multidisciplinary clinical teams with the expertise and facilities to manage the more common cancers
- Designated cancer centres—Should provide an extra range of specialised services in support of cancer units and treat less common cancers or provide treatments that are too technically demanding, specialised, or capital intensive for cancer units

Need for improved cancer services

Although the ideal means of controlling cancer is primary prevention, the prospect of preventing the majority of cancers in the near future is remote. Cancer will continue, therefore, to impose a considerable public health burden. Improvements in how patients diagnosed as having cancer are managed must therefore be a priority.

Recent evidence has shown a clear benefit in survival after 10 years for patients with early stage ovarian cancer treated in teaching hospitals rather than non-teaching hospitals. Multidisciplinary management in a joint clinic and surgery carried out by a gynaecologist were factors leading to improved survival. Evidence from the management of testicular teratoma and colorectal cancer indicates that patients treated at specialist centres have the highest survival rates. Likewise, the results of several comparative studies of childhood cancer suggest that entry into clinical trials and treatment by multidisciplinary teams at specialist centres provide considerable prognostic advantage for the patients concerned. A recent study in south east England showed wide variation in the management of breast cancer. Within the national breast screening programme the diagnosis and management of screen detected breast cancer is carried out by multidisciplinary teams with appropriate expertise and training in managing breast disease.

This multidisciplinary approach should not be restricted to screening programmes and other selected instances but should be the blueprint for cancer services in the United Kingdom in general. A government expert advisory group on cancer has recently reviewed the provision of cancer services. It proposes care at three levels (box 2). The primary care team is seen as a central and continuing element in cancer care for both patients and their families. The advisory group identified the general principles which should be common to all of cancer care (box 3). The key features of the relationship of cancer services with the primary health care team are shown in box 4.

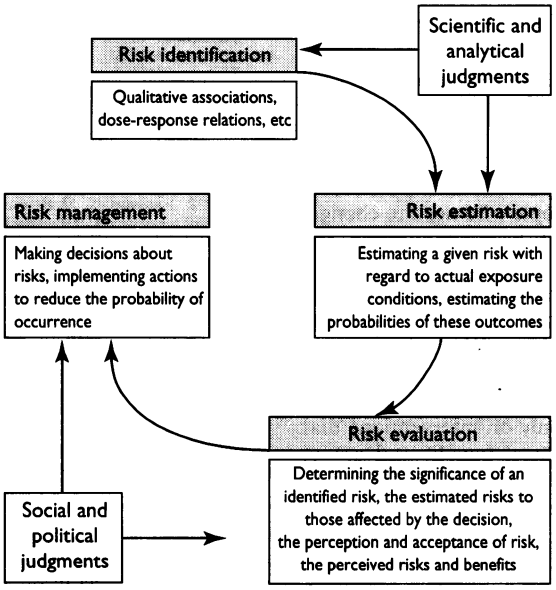
The implementation of the recommendations contained in the consultative document will be essen-

tial if there is to be equity in the management of all patients with cancer, who should have access to a uniformly high quality of care to ensure the maximum possible cure rates and quality of life. This should be seen as part of a comprehensive approach to cancer control, encompassing the whole spectrum from prevention and early diagnosis to treatment and palliation. The key to the future of cancer control will be to establish evidence based, multidisciplinary approaches to each particular cancer across this whole spectrum.

Conclusion: considering a strategy of cancer prevention

CONCEPT OF RISK

Current evidence suggests that a large proportion of the morbidity and mortality caused by cancer is preventable. The aim of cancer prevention is to reduce the risk of cancer. The concept of risk is thus central to cancer prevention. The issues concerned with identifying and assessing risk and the acceptability of risk are generally known as risk management. All aspects of risk management are controversial, entailing a complex interplay of scientific, social, and political considerations. The figure shows a model of the risk management process for cancer prevention. Implementing a strategy in primary care to reduce the risk of cancer or other diseases is not easy. How people perceive their risk varies. Risk perception is a complex phenomenon concerned with people's beliefs, attitudes, judgments, and feelings, as well as the wider social or cultural values and dispositions that people adopt towards potential risks. Attributes that influence risk perception include uncertainties about probabilities or consequences of the risk, fear of the unknown, fear for future generations, and the fact that potential benefits are not highly visible, so that the trade off between perceived risks and potential benefits is hard to assess. There are few definitive studies of how to communicate risk information, and in particular of how effective it is in changing beliefs and behaviour. For cancer prevention in primary care, the strongest evidence of an intervention achieving a change in behaviour relates to smoking cessation.



Risk management for cancer prevention (adapted from publications of Swedish Cancer Committee[2] and Royal Society[3])

LIFESTYLE ISSUES

The major challenge for cancer prevention is persuading people to adopt healthy lifestyles. This is a complex issue for primary care teams as a substantial amount of what is potentially preventable is linked directly to social and economic factors which provide a setting which can act to enable or constrain health related behaviour. Evidence from a wide variety of sources has shown that patterns of health related behaviour vary greatly by sociodemographic characteristics such as social class, age, sex, and educational background, as well as family circumstances, stress, and the work environment. There is evidence that health is not a priority for most people in the course of their daily lives and only surfaces when health problems emerge. Studies have found little evidence that changes in health related behaviour were a response to formal health messages. There is a clear indication that a strategy of attempting to change individual behaviour by focusing on beliefs about health (or illness) may not be effective, given that many health related behaviours are closely tied to social contexts and circumstances. This has clear implications for preventive strategies based in primary care.

TOWARDS A STRATEGY OF CANCER PREVENTION

Most prevention programmes are designed for a minority of people who are ready to take action on health behaviour problems. The emphasis of research needs to be shifted away from disseminating health promotion programmes to more and more people who are not prepared to use them and towards acquiring a better understanding of what factors cause people to

Box 3—Proposed general principles governing provision of cancer care[1]

- All patients should have access to a uniformly high quality of care in the community or in hospital, wherever they may live, to ensure the maximum possible cure rates and best quality of life
- Public and professional education is vital
- The development of cancer services should be centred on patients
- Patients, families, and carers should be given clear information about treatment options
- The primary care team is a central and continuing element in cancer care
- Communication between sectors must be of a high quality if the best possible care is to be achieved
- Psychosocial aspects of cancer care should be considered at all stages
- Cancer registration and careful monitoring of treatment and outcomes is essential

Box 4—Proposed relationship of cancer services with primary health care teams[1]

- General practitioners will require information about what constitutes best care, both organisationally and for individual cancers
- Local guidelines for identifying and managing symptoms that indicate a high risk of malignancy need to be established for each cancer with reference to nationally agreed, rigorously evaluated standards
- Local referral patterns need to be established in cooperation with primary care
- The primary health care team will act as a link and advocate for the patient with the secondary and tertiary sectors
- The importance of a close relationship and communication between primary care and the specialist services cannot be overestimated
- Each district must have a specialist resource for both primary care and hospital based services, which should allow rapid access to specialised palliative care

Box 5—Cancer prevention in primary care: a framework for action

- Set priorities:
  Consider the relative importance of specific cancers in causing premature death
  Consider the potential benefits that might accrue from implementing specific interventions—for example, smoking cessation
  Undertake only interventions of proved efficacy
- Undergo education and training in health promotion:
  The principles and practice of health promotion are poorly understood in primary care
  Organised training and support locally is essential
- Develop and plan a team approach using the skills of practice nurses and other team members
- Develop a systematic strategy for prevention:
  Set up practice registers
  Identify high risk patients—for example, to stop smoking
  Use a call-recall system
  Plan the intervention and appropriate follow up
- Conduct audit and quality control of interventions:
  Choose criteria
  Set standards
  Measure performance
  Achieve change

change from unhealthy to healthy behaviour. Prevention policies would be more effective if they were not imposed in a paternalistic fashion but were planned carefully to ensure that the unique needs and characteristics of the target population are addressed. This gives greater control to the people who need to change.

In this series of articles I have emphasised the importance of the population approach, which has the greatest potential for reducing morbidity and mortality. The identification of people at high risk and modification of their risk will have only a minor impact on the overall burden of disease. However, the best use of resources in primary care may be to concentrate on those at high risk and focus only on interventions that are likely to achieve the greatest benefit and are of proved efficacy. Primary care teams therefore need to set priorities for their involvement in cancer prevention (box 5). To be most effective, a systematic strategy will be required. The burden of health promotion lies not in collecting data on risk factors (which is, in itself, a meaningless exercise) but in providing subsequent intervention and follow up. Given limited time and resources, brief interventions to reduce smoking should be the highest priority for cancer prevention in primary care.

Ultimately, the involvement of primary care teams in cancer prevention needs to be seen as a part of broader policies aimed at social change in the whole population. A recent study in Finland has shown that a population approach to changing risk factors for ischaemic heart disease was effective in reducing mortality. A reduction in the intake of saturated fats, an increased use of vegetable oils, an increased consumption of fruit and vegetables, and a decline in smoking in men (but an increase in women) were observed. Finland is a small country with a homogeneous population and little socioeconomic variation. Whereas the complexities of a population approach in the United Kingdom are considerable by comparison, this study showed that such an approach to changing behaviour can work. This gives reason for optimism for cancer prevention in the United Kingdom in the future if the many challenges outlined in this series of articles can be overcome.

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A complete list of references is available from the author.