

**Report of the  
Cancer Research UK Population and Behavioural Sciences Committee  
Expert Meeting on Prevention Research,**

**held on Monday 31 March 2003,  
at 10 Cambridge Terrace, Regents Park, London NW1**

**1. Introduction**

The aim of the meeting was to identify the most promising areas for developing cancer prevention programmes and the associated research needs. Recommendations from the meeting will inform strategy and research priorities within Cancer Research UK and the wider cancer prevention community via the National Cancer Research Institute. A list of participants is at **Appendix 1**.

Brief presentations from the meeting are summarised below, addressing the issues of: smoking; diet, lifestyle and obesity; screening; genetic predisposition; hormones and cancer risk; and infections. The main points arising in discussion and the key recommendations agreed by participants are also summarised.

**2. Funding for research into cancer prevention in the UK: *Dr Liam O'Toole, National Cancer Research Institute, London***  
(PowerPoint presentation is at **Appendix 2**)

Using the Common Scientific Outline classification of prevention (defined as research into prevention interventions), current UK spend in this area is only 2.4% (which equates to £6.3 million) as compared to 9% in the USA. However, a broader definition of prevention which also covers risk, elements of aetiology, behavioural studies and health communication gives a spend of 7.2% (£18.6m). The National Cancer Research Institute, which brings together the 15 major funders of UK cancer research, has set up a Strategic Planning Group on Prevention and Risk Strategy. This involves representation from the major funders and the aim is to ensure that NCRI Partners develop a coherent national approach to funding in the area.

**3. Tobacco: *Professor Robert West, Department of Psychology, St George's Hospital Medical School, London***  
(PowerPoint presentation is at **Appendix 3**)

Reducing the harm from tobacco use involves two key strategies: reducing smoking prevalence (by reducing uptake and increasing cessation); and harm reduction (reducing smoke intake and increasing the use of less harmful products). While all approaches have potential, and studies must continue into the nature and development of cigarette dependence, research into how to encourage and help smokers to stop is likely to bear the greatest fruit in the short to medium term. Preventing teenagers taking up smoking is important, but research into achieving this has so far yielded few promising lines of enquiry; in addition, once a successful strategy is found this will only begin to impact on mortality some 30 years in the future. A simple model of factors influencing smoking cessation rates in the UK was presented which shows that cessation aids (e.g. nicotine replacement therapies, behavioural support) are probably contributing about 0.6% of the approximate 2.2% adult smoking cessation rate. Smoking cessation treatment is now supposed to be

an integral part of NHS provision. Currently about 2% of smokers use this treatment. For these smokers the treatment represents exceptional value for money as a life-preserving intervention, but the numbers taking advantage of it will need to increase many fold for this to noticeably affect smoking prevalence. In fact about 30% of smokers make an attempt to stop in a given year, and only about one quarter of these use any effective form of assistance. Therefore, a key research priority is to find ways to increase the frequency of quit attempts and the use of effective aids to cessation such as the NHS treatment services. Under realistic assumptions about what might be achieved (40% of smokers making a quit attempt in a given year and 50% of these using some form of effective cessation aid), this research could contribute to saving many thousands of lives in the short to medium term.

Now that quite effective treatments are available it will prove more difficult with randomised controlled trials to test improved treatments because of the sample sizes required. More use needs to be made of the existing treatment services by ensuring that data on participants, methods and treatment outcomes are recorded rigorously, accurately and according to common standards.

#### **Key potential area for prevention and associated research needs**

Studies on improved behavioural support methods, more effective pharmacological aids, and studies into effectively preventing uptake should continue. However, in the medium term, the greatest health gain will be achieved through increased numbers of quit attempts and greater use of effective methods.

A national “toolkit” is needed to be able to estimate the effects of different cessation approaches, as well as the impact of supportive policies, such as the introduction of smoke-free workplaces. A cohort of around 40,000 smokers would allow for analysis by socio-economic and other target groups. Setting up a new cohort need not be overly expensive, especially if done through General Practices. Using existing cohorts would not allow for the range of issues which need investigating, such as nicotine addiction, product changes and genetic factors. Collaboration with existing MRC initiatives should be explored.

#### **4. Diet, lifestyle and obesity: *Professor Kay Tee Khaw, Clinical Gerontology Unit, University of Cambridge*** (PowerPoint presentation is at **Appendix 4**)

Huge international variations in cancer incidence point to the role of environmental factors such as diet, which probably contribute as much as smoking to overall cancer rates. Considerable controversy remains regarding the putative protective or harmful effects of specific dietary factors. Bowel cancer is an interesting case in that, while there is a clear association with diet, the anticipated socio-economic gradient does not exist. Intervention/chemoprevention studies have so far proved disappointing.

One main reason for the continuing controversy in this field is the difficulty in measuring diet and the need for long-term follow up. The major European study, EPIC, has shown clearly that a rigorous approach to recording dietary intakes is essential, and that considerable differences are found using food frequency questionnaires (the usual method in most large US studies) and 7 day diaries. EPIC has also stored blood and urine samples which will allow further validation using biomarkers as these become known. Such intermediate outcome measures will greatly facilitate research in this area.

There is growing evidence that physical activity may reduce the risk of certain cancers. However, many issues remain unclear, e.g. whether the exercise needs to

be aerobic, and what duration or frequency of exercise may be important. There is little public awareness at present of the role of obesity in increasing cancer risk, although there is now consistent evidence that among non-smokers it is the largest single risk factor. Dietary interventions to reduce obesity have so far proved disappointing, often due to poor compliance. In one large US study on diabetes, individual behavioural support achieved good results. There is lack of clarity about the role of different dietary factors in obesity, e.g. saturated versus overall fat. Increased waist circumference appears to confer greater risk, while increased hip circumference may be beneficial. The Department of Health systematic reviews on obesity and life course and on interventions will be valuable sources of information. Intermediate markers are needed: they have enabled great advances in cardiovascular disease prevention strategies. A further dimension is the role of “Big Food” in promoting unhealthy diets, especially to young people, and in funding distracting research.

### **Key potential area for prevention and associated research needs**

Obesity is the single largest risk factor for cancer among non-smokers. Targeting obesity could be approached from one of two perspectives: i) specifically for cancer prevention, in which case a better understanding of obesity and cancer endpoints is needed; or ii) as a more general public health issue, in which case the strategy should be to raise public awareness and develop effective interventions. These could focus either on preventing weight gain or enhancing weight loss. Cancer Research UK’s role to advocate for more responsible food marketing should be highlighted. A high level meeting on obesity with the British Heart Foundation would be valuable. Other potential partnerships are with the MRC and the Wellcome Trust, both of whom are in the process of considering priorities for prevention. Other health groups which have also identified obesity as a priority include the Department of Health and Diabetes UK.

Currently, Cancer Research UK has no funding in obesity research. A large, bold initiative should be considered, looking to international experience such as the US Women’s Health Study, which will report shortly. As with smoking cessation, there is a need for acceptable behavioural support programmes, although the message is more difficult as food, unlike tobacco, is a basic human need. Programmes involving small step changes in behaviour should be developed. Much can be learned from the cardiovascular disease experience. The potential for exploring different approaches through cluster randomised trials using Primary Care Trusts should also be considered. While Cancer Research UK should certainly work with other agencies, it should also keep a distinct profile and take a leadership role in promoting the obesity-cancer link, which is a novel one for the public.

### **5. Screening: *Professor Jack Cuzick, The Wolfson Institute of Preventive Medicine, St Bartholomew’s and The London School of Medicine & Dentistry***

(PowerPoint presentation - **Appendix 5** - is only available in hard copy. Please contact the Behavioural Sciences office at [philippa.fiszzon@cancer.org.uk](mailto:philippa.fiszzon@cancer.org.uk))

Screening seeks to prevent cancer mortality through three different approaches: early detection (breast, bowel [using the faecal occult blood test - FOBT]); finding pre-cursor lesions (cervix, bowel [using flexible sigmoidoscopy - FS]); and identifying genetic mutations.

The **cervical screening** programme has been very effective, saving 1,000 lives pa. Human Papilloma Virus (HPV) testing is far more sensitive than cytology, but less specific. A large European trial of HPV testing versus cytology is planned, although

funding is not yet secure. If HPV is found to be an effective screening tool, the best strategy would be to test for HPV first and restrict cytology to the 8% of women testing positive. Given that many HPV infections are transient, it might be preferable to call some women back after one year before any further investigations.

**Breast cancer screening** has also been effective in 50-70 year old women, with a possible smaller benefit to 40-50 year olds. Service screening needs to be evaluated. Breast density is the best predictor of cancer risk, and age-specific measures of density are needed. These could also be useful markers for prevention studies looking at, e.g. physical activity, obesity, soya products etc. Mammograms should be archived electronically on a large scale (this is being done in IBIS II) for future research purposes.

**Bowel cancer** presents an interesting dilemma in that trials of FOBT have shown a 15-20% mortality advantage, while case-control studies of sigmoidoscopy show very large benefits (more than 50%) with one test only. However, compliance needs to reach at least 70% of the target population for effective screening. The ongoing FS trial will elucidate the true benefits of this approach. In the longer term, an ideal test might use radiology and involve no bowel preparation. Meanwhile, both the FOBT and FS options should be kept open.

**Prostate cancer screening** presents many challenges including a lack of understanding of the natural history, with 40% of 80 year old men found on autopsy to have the disease. Trials of Prostate Specific Antigen (PSA) testing for screening are ongoing in Europe and the USA. Given the risks of over-diagnosis and the considerable risks of harm from current treatments, the treatment trial ProtecT should yield valuable insights. While it is too late to do a randomised trial of PSA testing in the UK, it could be evaluated by case-control methods.

In **screening for lung cancer**, Spiral Computerised Tomography (CT) appears to offer a screening tool, but no randomised trials have yet been conducted. It could offer an incentive to smokers trying to quit. However, it could be expensive and remains controversial from a public health perspective, in that it could signal to smokers that they need not quit until tested positive.

For **ovarian** and **stomach cancers**, there is no current evidence for screening, but trials are ongoing. The future for screening for many cancers lies in detecting abnormal proteins in the blood.

#### **Key potential area for prevention and associated research needs**

Bowel cancer is the second cause of cancer death in the UK. There is currently a gap between research findings and implementation, and the government faces the dilemma of whether to introduce FOBT or FS as the screening modality. FS presents further issues, for example: if the chosen age for a single test is 60, would all those 61 years and above be passed over or would all those up to the age of 70, say, be invited for the test? It would be useful to evaluate both approaches, although this could be seen as inequitable. The opportunity therefore exists to test implementation of the two modalities (FOBT and FS), as well as different age groups for FS. A sensible approach might be to introduce FS where sufficient resources and interest exist. A cluster randomised implementation study would be the ideal. Training remains an important concern as, even if/where FOBT is used, follow-up will involve endoscopy.

**6. Genetic susceptibility: *Professor Tim Bishop, Division of Genetic Epidemiology, Cancer Research UK Clinical Centre, University of Leeds, St James's University Hospital***

(PowerPoint presentation is at **Appendix 6**)

Cancer genetics clinics are already very stretched with routine clinical work: a modest financial input could facilitate their research role.

There are currently numerous studies of high penetrance genes in breast and ovarian cancer, bowel and melanoma, including observational, early detection and chemoprevention approaches. The genetics are becoming clearer for stomach, pancreas and prostate cancers.

Research problems include small numbers seen in multiple centres using different approaches to processing high risk families. Opportunities exist to explore behavioural change in high risk families (some individuals being highly motivated, others preferring avoidance). There is also need to better understand modifiers of risk, such as other genes, components of lifestyle etc, and studies are looking at these.

Research will be enhanced by greater sample sizes, achieved through international collaborations. These, however, raise their own problems of funding, communications, ethics and infrastructure. A pilot being run by the British Familial Cancer Record (BFCR) with National Lottery funding, is setting up an anonymised database of individuals who are willing to be re-contacted if future research may impact on their disease.

Low penetrance genes present a particular challenge at the present time; their role in cancer prevention seems limited and the role of gene-environmental interactions is unclear. In the UK, the situation is further complicated by the heterogeneity of the gene pool. Until there is better understanding of the various mutations which are important and of how this knowledge can be translated into benefit to carriers, it is unlikely that any population testing will be of value. Therefore, the priority will be to focus on high penetrance genes which could result in prevention of 2 - 4% of cancers.

**Key potential area for prevention and associated research needs**

The key requirement is to provide the infrastructure to support future research. Currently, there is much information gathering. For high risk genes, recruitment is taking place at a small number of centres, with fairly targeted objectives. Data and samples for genetic analysis should be pooled.

With regard to low penetrance genes, very large studies are needed, but have associated logistical problems – it can take years to set up such collaborations. Central collection of DNA and tissue samples will enable more systematic analysis. There is, at present, a small genotyping (ex-ICRF) facility at Oxford. This service should be expanded, perhaps in 1 - 2 centres. A bigger issue is how to effectively handle the very large number of samples which are being collected. The National Cancer Research Network (NCRN) has recognised that recruitment into clinical trials is poor: there may be scope for UK studies into low penetrance genes to use the NCRN for sample collection and recruiting for follow-up studies.

There is strong support in the research community for a national collection of blood and (later) tumour samples from cancer families. The Cancer Families Study Group already has many ongoing studies, and it would be valuable to scope out what

sample collections already exist in order to pool them. It is difficult to obtain funding for such large infrastructural projects, and Cancer Research UK could take a lead in this by bringing in Department of Health and MRC funds, while itself managing the facility and access to it in a similar way to the national tissue sample collection being set up by the NCRN.

**7. Hormones and Cancer Risk: Professor Tim Key, Cancer Research UK  
Cancer Epidemiology Unit, The Radcliffe Infirmary, Oxford**  
(PowerPoint presentation is at **Appendix 7**)

The main hormone-related cancers are those of the breast, prostate, ovary and endometrium. Of these, the best evidence for a chemoprevention strategy is for breast cancer, either by blocking the effects of oestradiol (by tamoxifen, raloxifene) or by reducing circulating levels of oestradiol (using aromatase inhibitors [in post-menopausal women] and LHRH agonists [in pre-menopausal women]). Other hormones that are linked with an increased risk of breast cancer are insulin-like growth factor (IGF-1) and progesterone (e.g. in Hormone Replacement Therapy). High parity and breastfeeding offer protection.

For prostate cancer, the hormonal association is less straightforward. Blood tests show no difference in blood testosterone levels between men with and without prostate cancer (compared to a 15% difference in oestrogen in women with breast cancer). This may possibly be due to the fact that the form of testosterone found in the prostate (**DHT**) is 100 times more active than that found in the blood. However, there may again be a role for IGF-1, as this is 6% higher in men with prostate cancer. The potential for chemoprevention is being studied in a large US trial of finasteride, which can prevent active testosterone in the prostate. Other strategies might include blocking the androgen receptor and reducing IGF-1. For the latter, a dietary strategy might be considered, although the evidence is restricted to vegan diets, where a 10% difference is seen. This may help to explain the distribution of the disease globally. It would be valuable to collect data on hormone levels and disease outcome, for example within existing studies such as the ProtecT treatment trial.

The evidence for hormonal influence in ovarian cancer is currently unclear, while for endometrial cancer the best preventive strategy lies in reducing obesity.

**The priority area for cancer prevention research** lies in understanding the underlying mechanisms of the hormonal influence on breast cancer development. This requires a concerted multidisciplinary effort.

**8. Infections and cancer: Professor Julian Peto, Section of Epidemiology,  
Institute of Cancer Research, Sutton, Surrey**  
(PowerPoint presentation is at **Appendix 8**)

Infections cause about 4% of cancers in the UK, but 20% worldwide. The most important are HPV (cervical), *Helicobacter pylori* (stomach) and Hepatitis B and C (liver cancer).

The current cervical screening programme is actually saving 5,000 lives in the UK per annum (as 4,000 women would have died from cervical cancer had the upward trend prior to the introduction of screening persisted). Vaccines against HPV are in development, and these offer the best strategy for developing countries. Cancer Research UK could play a role in facilitating production of these vaccines cheaply. It may be possible to administer the vaccine orally, although in this form the costs are much greater.

A large scale randomised trial of H *pylori* eradication is currently being carried out by Cancer Research UK and BUPA, involving 56,000 people who will be followed up over 25 years.

**Priorities for cancer prevention research:** In the UK, a vaccine for Hepatitis C would be valuable: there is already antenatal screening for Hepatitis B. It might be possible to vaccinate against H *pylori*, but parental acceptance would be an issue, bearing in mind the resistance to the MMR vaccine.

A more general issue is the need to counter the threat posed by ill thought-out data protection legislation. None of the evidence presented at this meeting would be available without access to individuals' records. A statement expressing the need to protect this access will be modified to remove any ambiguity in the wording. Participants agreed that this statement should then be forwarded with their support to the Patient Information Advisory Group (PIAG).

The statement is as follows (the wording to be modified has been highlighted by italics):

'Consent is not required for access to medical records for non-commercial medical *research that has no effect on the individuals being studied* and has been approved by an accredited research ethics committee.'

**Meeting Attendees:**

**Cancer Research UK Senior Researchers**

Dr Wendy Atkin	Colo-Rectal Unit, St Marks Hospital, Northwick Park, Harrow
Prof. Valerie Beral	Cancer Research UK Cancer Epidemiology Unit, University of Oxford
Prof. Jillian Birch	Cancer Research UK Paediatric and Familial Cancer Research Group, University of Manchester
Prof. Tim Bishop	Division of Genetic Epidemiology, Cancer Research UK Clinical Centre, University of Leeds
Prof. Jack Cuzick	Cancer Research UK Mathematics, Statistics & Epidemiology Laboratory, St Bartholomew's and the Royal London School of Medicine and Dentistry
Dr. Mike Hawkins	Centre for Childhood Cancer Survivor Studies, The University of Birmingham
Prof. Martin Jarvis	Health Behaviour Unit, Department of Epidemiology and Public Health, University College London Medical School
Dr Tim Key	Cancer Research UK Epidemiology Unit, University of Oxford
Prof. Kay-Tee Khaw	Department of Community Medicine, University of Cambridge
Dr Mike Murphy	Cancer Research UK General Practice Research Group, University of Oxford
Prof. Julian Peto	Section of Epidemiology, Institute of Cancer Research
Prof. David Simpson	International Agency on Tobacco and Health, London
Dr Rob Walton	Institute of Health Sciences, University of Oxford
Prof. Jane Wardle	Cancer Research UK Health Behaviour Unit, University College London
Prof. Robert West	Department of Psychology, St George's Hospital Medical School

**Continues overleaf...**

**Cancer Research UK Committee Members****Population and Behavioural Sciences Committee:**

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Prof. KK Cheng	Department of Public Health & Epidemiology, University of Birmingham
Dr Carol Dezateux	Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health
Prof. Eve Roman	Leukaemia Research Fund Centre for Clinical Epidemiology, University of Leeds
Prof. Leslie Walker	Institute of Rehabilitation, University of Hull

**Clinical Trials Advisory and Awards Committee**

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Dr Magdalena Sara	Scientific Programme Manager, National Cancer Research Institute
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