

Strategic Analysis 2002

An overview of Cancer Research in the UK directly funded by the NCRI Partner Organisations

Partners in Cancer Research

NCRI

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October 2002

Partners in Cancer Research



Association for International Cancer Research (AICR)



Marie Curie Cancer Care (Marie Curie)



Biotechnology and Biological Sciences Research Council (BBSRC)



Medical Research Council (MRC)



Breakthrough Breast Cancer (Breakthrough)



Northern Ireland Health & Personal Social Services Research & Development Office (N. Ireland)



Cancer Research UK (CR-UK)



Scottish Executive Health Department (Scotland)



Department of Health (DOH)



Tenovus The Cancer Charity (Tenovus)



Leukaemia Research Fund (LRF)



Wales Office of Research & **Development for Health & Social** Care The National Assembly for Wales (Wales)



Ludwig Institute for Cancer Research (Ludwig)





Yorkshire Cancer Research (YCR)



Macmillan Cancer Relief (Macmillan)

Work on the development of the NCRI Cancer Research Database, analysis of the combined research portfolio and drafting of this report was carried out by the NCRI Secretariat. Thanks go to all the staff of Member organisations who invested a considerable amount of time and effort in providing their portfolios for inclusion on the database and for commenting on the draft report. The coding of portfolios on the CRD was carried out and overseen by Dr Lynne Davies (CR-UK), Dr Janet Valentine (NCRI), Dr Graham Cadwallader (MRC), Dr Helen Campbell (DOH), Dr Anna Smith and Dr Mark Matfield (AICR). We are grateful to Dr Steve Harris (NTRAC), Ms Angela Hinkley (FMI) and Ms Dominique Capostagno for providing invaluable technical assistance during the database development. The NCRI wish to acknowledge the assistance and support of the CSO Partnership, and in particular would like to thank Ms Cherie Nichols, Ms Anne Tatem and Ms Brenda Underwood from the US National Cancer Institute. All activities of the NCRI are overseen by the NCRI Board, details of the Board Membership are given below.

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Dr Liam O'Toole (Administrative Director) Dr Helen Campbell Dr Lynne Davies Mrs Samia Majid Dr Magdalena Sara Dr Janet Valentine Mr Martin Waller

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Cancer research in the UK is funded by an estimated 250 charities, numerous Government bodies and the Pharmaceutical Industry. The National Cancer Research Institute (NCRI) is a new partnership between the major funding bodies from Government, charitable and private sectors. NCRI Members include the following fifteen organisations from Government and charity:

The Association for International Cancer Research, Biotechnology and Biological Sciences Research Council, Breakthrough Breast Cancer, Cancer Research UK, Department of Health, Leukaemia Research Fund, Ludwig Institute for Cancer Research, Macmillan Cancer Relief, Marie Curie Cancer Care, Medical Research Council, Northern Ireland HPSS R&D, Scottish Executive Health Department, Tenovus, Wales Office of R&D, Yorkshire Cancer Research.

The NCRI was established on 1 April 2001 with the aim of accelerating progress in cancer research in the UK for the benefit of cancer patients. This initiative was stimulated by a new way of thinking within the cancer research community and a desire for greater coherence and more efficiency.

The role of the NCRI is to:

- Take a strategic oversight of cancer research in the UK
- Identify gaps and opportunities in current research
- Facilitate collaboration between funding bodies
- Monitor progress

The central aim of the NCRI is to add value by providing an independent forum to facilitate joint strategic planning and develop national resources that are of benefit to the whole UK cancer research community.

There are no accurate data for the total spend on cancer research in the UK, however, industry spend alone in 2000 is thought to be in the region of £134 million per annum. Combining this figure with estimates of funding from all the Government agencies and all the research charities, the total UK spend on cancer research can be estimated at between £450-500 million per annum. The NCRI brings together the fifteen largest funders of cancer research from the Government and charity sectors with a collective spend of greater than £335 million per annum. Cancer research funding is made up of a number of different components including the direct spend on programmes of research, infrastructure, support services and laboratories. The first of these, direct support for research, is of most value for co-ordination and strategy setting. This Report presents an analysis of the direct spend component of cancer research (£257 million per annum) funded by these fifteen leading UK cancer research organisations.

In the past, strategic planning of cancer research on a national level has not been possible due to a lack of reliable and comparable data on the current activities of the major research funders. In order to overcome these issues the NCRI have established The Cancer Research Database (CRD) which is designed to contain accurate information on the directly supported cancer research currently funded by Member organisations. The CRD is a powerful tool for carrying out comprehensive and detailed analysis of the cancer research activities of the NCRI Partners. These analyses will provide a baseline against which research funders can individually and collectively strategically plan for the future.

Information on the CRD is in the form of a common data-set that includes details of the Principal Investigator(s), an abstract of the research conducted and details of funding awarded. In order to interrogate the database in a meaningful and reproducible way, every research project has been coded using three internationally recognised classification systems: the Common Scientific Outline (CSO) – a classification system of cancer-related research terminology that categorises research activities into specific areas (e.g. Biology, Aetiology, Treatment etc.); Disease Site codes; and Medical Subheadings (MeSH). The use of these standardised coding systems will, for the first time, allow reliable comparisons between portfolios of national and international cancer research organisations. The NCRI CRD will be updated and will eventually be made available on the Internet as a resource for scientists planning their future research and identifying collaborators, and also a source of information for the wider community interested in cancer research.

This NCRI Report is the first analysis of the portfolios of the fifteen NCRI Member organisations held on the CRD. It provides, for the first time, an accurate overview of the cancer research activities of the NCRI Partnership that were ongoing on 1 April 2002 and outlines how and where these organisations are spending their money. The Report focuses on the combined portfolio of the NCRI Members, concentrating in particular on the pattern of direct research spend as defined by the CSO and Disease Site classification systems. A broad geographical distribution of research funding in the UK is also presented. This Report seeks to explain some of the patterns and trends emerging from the analysis and highlights areas where there is an opportunity for further strategic co-operation between the Member organisations.

The analysis confirms a healthy picture of a varied and generally well-balanced cancer research base in the UK. Examination of the types of research that the NCRI Members are currently funding shows that the largest proportion of the collective Members' spend is in the field of Biological research, with most organisations funding research within this area. Research in Aetiology and Treatment are also well supported by the Partnership. Two areas where research investment across the majority of funders appears to be relatively low are Prevention Research, and Cancer Control, Survival and Outcomes Research.

Analysis of Disease Site funding shows that the majority (60%) of the cancer research funded by the NCRI Partners is generic and applicable to all cancer sites. Within research that is site specific, the relative proportion of funding spent on particular tumour types generally follows the increasing disease burden, as measured by incidence and mortality, associated with these cancers. This is particularly evident for breast, colon and rectal, and prostate, three of the highest funded cancer sites. In contrast there is relatively little investment in lung cancer research compared with the high incidence and mortality of the disease. Leukaemia research is well supported which may reflect a history of high quality research that is continuing to attract funding from many of the Partner organisations. Further analysis of prostate cancer, as a disease specific case study, illustrates how a more

strategic approach to funding by several NCRI Partners working in collaboration has influenced the pattern of spending in a specific area.

There are two key areas highlighted by this first analysis of the CRD that NCRI Member organisations have agreed would benefit from much closer joint strategic examination; research into cancer risk and prevention and research into supportive and palliative care. These are both cross-cutting areas of research that are important to all cancer types and encompass all NCRI Partner organisations. They both involve a significant patient-based focus and are characterised by being areas of low direct research activity in the UK where there are clear scientific opportunities. The NCRI will set up a 'Strategic Planning Group' in each area, bringing together senior representatives from the relevant NCRI Partner organisations. These Groups will carry out a much more detailed analysis of the research activity in each area, discuss any potential opportunities and barriers and identify any further action necessary.

Following work on these two cross-cutting areas, and taking account of recent US National Cancer Institute strategic reviews, the NCRI will carry out more detailed strategic examination of research activity focused on individual disease sites.

This is the first in a series of ongoing analyses to be carried out by the NCRI. Over time the cancer-relevant portfolios of additional Government and charity bodies of significant size will be added to the database and included in future analyses.

The contents of this Report and the database of information that was used to compile it provide a valuable tool for NCRI Member organisations and other cancer research funders in the UK to plan and prioritise their spending on cancer research. Continued analysis and joint planning will ensure better strategic oversight and better co-ordination of cancer research in the UK.

1 Introduction & Purpose of this Report

There are a large number of organisations that fund cancer research in the UK including an estimated 250 charities, numerous Government bodies and the Pharmaceutical Industry. There are no accurate data on the combined spend of these organisations, however, industry spend alone in 2000 is thought to be in the region of £134 million per annum. Combining this figure with funding from all the Government agencies and all the research charities, the total UK spend on cancer research can be estimated at between **£450-500 million per annum**.

The NCRI brings together the fifteen largest cancer research funders from the Government and charity sectors with a collective spend of greater than £335 million per annum. Funding of cancer research is made up of a number of different components including the direct spend on programmes of research, infrastructure, support services and laboratories. The first of these, direct support for research, is of most value for co-ordination and strategy setting. This Report contains an analysis of the direct spend component of cancer

research **(£257 million per annum)** funded by the fifteen leading cancer research organisations in the UK Government and charity sectors. It provides, for the first time, an accurate overview of the majority of current cancer research activity in the UK and outlines how and where these organisations are spending their money.

The Report describes the present situation, suggests reasons behind the funding patterns observed and highlights areas where there is an opportunity and need for further strategic co-operation between different funders.

The organisations have come together as the NCRI in order to address the question 'Are we being as effective as we should be in the way we are funding cancer research?' This Report and the database of information that was used to compile it will provide a vital tool to inform individual and joint strategic planning of NCRI Member organisations and allow better co-ordination of cancer research in the UK.

2 About the National Cancer Research Institute (NCRI)

2.1 WHAT IS THE NATIONAL CANCER RESEARCH INSTITUTE?

The National Cancer Research Institute (NCRI) is a partnership between cancer research funding bodies in the Government, charitable and private sectors. It was established on 1 April 2001 with the purpose of accelerating and advancing cancer research in the UK. The NCRI aims to do this by developing a co-ordinated strategy for cancer research between Member organisations. The NCRI has a Secretariat of five full-time staff that is equally funded by Government and the cancer research charities. Details of NCRI Member organisations from the Government and charity sectors are given at Appendix 1.

2.2 WHAT IS THE ROLE OF THE NCRI?

The NCRI has two main roles: Firstly to gather accurate information on the cancer research that is currently being funded in the UK, and secondly to use this information to plan future research strategies. Where opportunities or barriers to progress are identified, the NCRI Partners will agree how best to work together to ensure that progress is made in key areas. This may involve joint approaches to providing the infrastructure needed to underpin cancer research in the UK.

The role of the NCRI is to accelerate progress in cancer research by:

- \bigcirc Taking a strategic oversight of cancer research in the UK
- Identifying gaps and opportunities in current research
- Planning and co-ordinating approaches between funding bodies
- Monitoring progress

2.3 HOW DID THE NCRI COME ABOUT?

There are a large number of different organisations funding cancer research in the UK. Previously these organisations have collaborated with one another but never before have come together in a single body to map out what they are doing collectively and jointly plan for the future. Over the past few years there has been much debate about cancer research in the UK and many individuals and organisations have been asking the same question, 'Are we being as effective as we could be?'. The recent merger of Britain's two largest cancer research charities into Cancer Research UK is evidence of new thinking within the cancer research community. A Government initiative brought the main funding organisations together at the beginning of 2000 in a 'Cancer Research Funders Forum'. This move was embraced by the research charities and the NCRI was formally established as a key element of the English National Cancer Plan in April 2001, with a remit to encompass all regions of the UK.

2.4 PAST NCRI STRATEGIC ACTIVITY

In Spring 2000 the NCRI Partners carried out a strategic review of prostate cancer research in response to concerns about research capacity. As a result of this review the English Department of Health, Medical Research Council and Cancer Research UK jointly funded two Prostate Cancer Research Collaboratives designed to increase critical mass and encourage collaboration and networking in the research community. A similar NCRI review is currently underway to examine the current situation and future direction of Radiotherapy and Related Radiobiology research in the UK.

3 The NCRI Cancer Research Database (CRD)

3.1 WHAT IS THE NCRI CANCER RESEARCH DATABASE?

The fifteen NCRI Partner organisations fund the vast majority of cancer research undertaken in the UK. The Cancer Research Database (CRD) is a comprehensive database that is designed to accurately represent the cancer research directly funded by these organisations, and contains data that has been reliably and consistently classified. Information included on the CRD is voluntarily submitted by Member organisations in the form of a common data-set that includes the details of the Principal Investigator(s), an abstract of the research conducted and details of funding awarded.

3.2 WHAT WILL THE NCRI CRD BE USED FOR?

In the past, strategic planning of cancer research on a national level has not been possible due to a lack of reliable and comparable data on the current activities of the major research funders. In order to overcome these issues a source of high quality information was required detailing direct research funding by different organisations. The Cancer Research Database is designed to provide that information.

NCRI Member organisations base their funding decisions on the quality of the research, using a peer review system. The CRD will enable funders to consider how new proposals for research fit into their own research portfolios and how they relate to research funded by other organisations.

The database will be updated regularly to allow ongoing accurate analyses of cancer research activity in the UK. These analyses will be of great value for individual and joint planning by NCRI Member organisations, will be a useful tool for monitoring progress in joint objectives, and will ultimately lead to better strategic oversight and co-ordination of cancer research in the UK.

The CRD will eventually be made available on the

Internet and will then become a resource for scientists to plan their future research and to identify collaborators. The CRD will also be a source of information for the wider community interested in cancer research.

3.3 WHAT DATA IS HELD ON THE CRD?

Funders of cancer research in the UK include an estimated 250 charities, numerous Government bodies and the pharmaceutical industry. The NCRI brings together the largest fifteen of these from the Government and charity sectors with a collective spend of greater than £335 million per annum. The different components of cancer research funding include direct spend on programmes of research, infrastructure, support services and laboratories. The first of these, direct support for research, is of most value for coordination and strategy setting. It is this information from NCRI Members that has been drawn together in the NCRI Cancer Research Database.

The database only includes entries where funding can be directly attributed to a set of clearly defined research objectives. Each of the 1864 records on the database includes details of the researcher(s) carrying out the work and an abstract or brief description of the funded research. This means that the CRD only contains information on all direct research funding (project, programme, fellowship, unit and institute) currently financed by an NCRI Member organisation.

Table 1 shows spend by NCRI Member organisations. The first column shows the total reported spend for each organisation for 2000-2001. These data have either been published in the annual reports of each organisation or provided as formal estimates of spend. By and large these figures are a retrospective record of the actual expenditure made by an organisation on all aspects of research funding – including infrastructure, services and buildings (see Appendix 2). The second column includes the figures for funding for each organisation associated with entries on the NCRI CRD.

NCRI PARTNER ORGANISATIONS	TOTAL REPORTED ORGANISATION RESEARCH SPEND (2000-2001)	RESEARCH SPEND ON NCRI CRD (APRIL 2002)
Association for International Cancer Research	£7,614,901	£4,856,313
Biotechnology and Biological Sciences Research Council	£6,300,000	£10,457,511
Breakthrough Breast Cancer	£4,215,000	£3,021,057
Cancer Research UK	£129,716,000	£117,616,399
Department of Health	£83,761,000	£26,912,230
Leukaemia Research Fund	£16,780,000	£14,393,023
Ludwig Institute of Cancer Research	£6,000,000	£3,554,868
Macmillan Cancer Relief	Not Available	£1,376,900
Marie Curie Cancer Care	£3,512,000	£2,722,918
Medical Research Council	£58,000,000	£65,403,957
Northern Ireland HPSS R&D	£1,000,000	£783,767
Scottish Executive Health Department	£8,800,000	£1,195,928
Tenovus The Cancer Charity	£1,616,464	£1,685,026
Wales Office of R&D	£2,854,000	£266,973
Yorkshire Cancer Research	£4,400,194	£3,247,675
Total	> £334,569,559	£257,494,545

Table 1 contains the total research spend of the fifteen NCRI Partners, for 2000-2001 and the spend associated with the NCRI Cancer Research Database (1 April 2002). An accurate figure for total cancer research spend in the UK does not yet exist. For 2000-2001 the estimated total Government spend in cancer research was £190 million. Estimates for the total charity spend range between £180 to £230 million. The Association of the British Pharmaceutical Industry estimate the Pharmaceutical Industry spent an approximate £134 million on cancer research in the UK during this period.

The total resources associated with this combined portfolio of direct research is over £257 million and five organisations, Cancer Research UK (CR-UK), Medical Research Council (MRC), The Department of Health (DOH), Leukaemia Research Fund (LRF) and Biotechnology and Biological Sciences Research Council (BBSRC) make up 90% of the total.

These two sets of figures are different for a number of reasons. Firstly, for the purposes of strategic analysis only the direct component of research funding has been included on the CRD. Secondly, the database has been designed to capture a 'snapshot' of the research that NCRI Partners are currently funding and therefore only includes projects that were ongoing on 1 April 2002. The financial data on the database has been standardised for all Member organisations. This has been done by taking the total grant value and dividing it by the duration to generate an 'annualised award'. Thirdly, this is the first time that several of the NCRI Members whose mission is to fund a wide range of biomedical research have had their portfolios independently examined by the NCRI Coding Panel for research relevant to cancer (see section 3.7). Some of the portfolios submitted by these organisations include research that is only partially relevant to cancer or is underpinning research that supports not only cancer but also all other areas of biomedical research. The NCRI Partners have agreed that funding associated with these projects be apportioned depending on the degree of relevance to cancer and that a percentage of the total funds be apportioned to the CRD.

3.4 WHAT INFORMATION IS NOT INCLUDED ON THE CRD?

The database focuses on the fifteen NCRI Member organisations and should not be regarded as a record of all the cancer research funding provided by the Government or charity sectors. This section highlights some of the key elements of cancer research funding not yet included on the CRD.

The database does not include the funding provided by the Department of Health to the NHS to support other funders' cancer research and 'own account' work by NHS providers (estimated at a total of £73 million per annum). This information is not included at this stage because it cannot be reliably linked to specific research objectives and would not inform the strategic analysis. However, the NHS R&D programme is currently being modernised and it is intended that an increasing amount of research will be added to the database over time.

The database does not include any information on investment in cancer provided by the Higher Education Funding Council for England (HEFCE).

There are a large number of small charities funding cancer research and data from these organisations are not included. Over time the cancer relevant portfolios of additional Government and charity bodies of significant size will be added to the database and included in future analysis. These will include organisations such as the Wellcome Trust, the Engineering and Physical Sciences Research Council (EPSRC) and the Economic and Social Research Council (ESRC).

Additional sources of cancer research funding are provided by charitable trusts held at the major cancer research institutes. The NCRI is currently carrying out a pilot study with the Institute of Cancer Research to assess the extent and detail of the funding information available and explore the possibility of including this type of data on the CRD in the future.

Because of the need for confidentiality, no data is currently included on industrial research carried out in the UK. The NCRI is exploring the feasibility of including data from the Pharmaceutical Industry in future analyses. An estimate of the Pharmaceutical Industry investment in cancer research in the UK provided by the Association of British Pharmaceutical Industries is £134 million for 2000.

3.5 HOW WAS THE CRD PUT TOGETHER?

The information contained on the CRD was voluntarily supplied to the NCRI Secretariat by the Partner organisations. These organisations identified and submitted details of all peer reviewed research that was active on 1 April 2002. Information was supplied in the form of a common data-set including details of the Principal Investigator, an abstract of the research and details of the funding awarded. The NCRI Secretariat assisted in gathering all the information

"CSO and Disease Site codes allow accurate and meaningful comparison between national and international cancer research portfolios."

required, and then transferred all records into a uniform and standardised electronic format to ensure high quality clean data that could be used for subsequent CRD analysis.

3.6 CODING AND CLASSIFICATION OF THE CRD

In order to be able to interrogate the database in an accurate and reproducible way, every research project entered on the CRD has been classified using three internationally recognised coding systems, the Common Scientific Outline (CSO), Disease Site codes and Medical Subheadings (MeSH). There are many different classification systems in operation internationally; these three were chosen for the following reasons:

- The CSO is a classification system specific to cancer research
- The CSO is easily understood and used by many organisations internationally
- O CSO and Disease Site codes allow accurate and meaningful comparison between national and international cancer research portfolios including the US National Cancer Institute and other US cancer research organisations (CSO Partners)
- The CSO Partners collaboration provides a framework to ensure consistency and minimise inter-coder variability

 MeSH is an internationally recognised gold standard for classifying biomedical research and will allow published outcomes of research activities to be linked to particular CRD projects over time

The Common Scientific Outline is a classification system of practical and easily applied cancer-related research terminology that has been developed by an international partnership that includes the US National Cancer Institute, other US cancer research funders and the NCRI. Details of the CSO Partners Initiative are given at Appendix 3. Individual projects are classified by Disease Site codes and then into one or more of seven broad cancer research areas defined by the CSO as: Biology; Aetiology; Prevention; Early Detection, Diagnosis and Prognosis; Treatment; Cancer Control, Survival and Outcomes Research; and Scientific Model Systems. Each of these codes is subdivided giving a final figure of 38 individual CSO codes. A copy of the CSO can be found at Appendix 4 and the Disease Specific codes are listed in Appendix 5. The CSO Partners' collaboration provides an internationally regulated framework that ensures comparability, consistency and accuracy of coding.

MeSH is a taxonomy of biomedical research terms that

have been developed over a period of years by the US National Library of Medicine (NLM). The use of MeSH indexing provides an alternative means of searching for specific topics on the CRD. MeSH is also used to classify the vast majority of medical research articles held on the NLM database, Medline. Use of MeSH will enable future analysis of research output trends of projects held on the CRD.

The larger NCRI Partners coded their own research by CSO and Disease Site and the portfolios of organisations without resources to do their own coding were classified by the NCRI Secretariat. Abstracts and titles of all CRD entries were MeSH indexed on commission by the British Library. CSO coders classified proposals using the CSO and Disease Site list as outlined in the NCRI coding guidelines. Up to two CSO codes were applied to each abstract, with additional codes used for large programme grants. An unlimited number of disease sites were allocated per proposal. Following initial CSO and Disease Site coding, each record was independently recoded, all classifications were then cross-checked, and the NCRI Secretariat assigned the final codes.

3.7 HOW HAVE WE ENSURED THAT THE DATA IS TRULY REPRESENTATIVE?

The aim of the CRD is to establish a comprehensive database that accurately represents cancer research in the UK, and that contains data that has been reliably and consistently classified using Disease Site and CSO coding. In order to ensure that this is the case for all fifteen NCRI Member organisations, an independent NCRI Coding Panel with equal Government and charity representation and chaired by the NCRI Secretariat, has been established to oversee the process. The role of the panel is to develop policy and coding guidelines, resolve coding difficulties, adjudicate on issues such as inclusion of research and apportionment of funding, and to liaise with the wider international CSO Partnership on behalf of the UK. In addition, the NCRI will routinely submit a random subset of coded grants to the international CSO Partners for verification and to ensure international coding consistency.

4 Analysis of the NCRI Partners' Cancer Research Portfolio

4.1 WHY CONDUCT AN ANALYSIS OF THE CRD?

The NCRI Partners wish to analyse their current cancer research spending profile to provide a baseline against which they can individually and collectively strategically plan for the future. This CRD analysis is a first step in this joint planning process.

Most research organisations use the peer review system to fund research in response to applications received from the research community. Part of this process may include consideration of how a new research project fits within the organisation's overall portfolio of research. Previously it has not been possible for individual organisations to systematically take into account the financial investment of similar funders. The information from this analysis, and held on the database, will greatly increase individual organisations' abilities to develop their own strategic plans.

4.2 SCOPE OF THE FIRST CRD ANALYSIS

This first NCRI analysis is designed to give an overview of the cancer research activities of the NCRI Partnership. This report focuses on the combined portfolio of the NCRI Member organisations, concentrating in particular on the pattern of direct research spend as defined by the CSO and Disease Site classification systems. A broad geographical distribution of research funding in the UK is also presented. In the future it will be possible to use the CRD to carry out detailed and comprehensive analysis within specific areas but this is beyond the scope of this first NCRI analysis.

4.3 ANALYSIS OF THE TYPE OF RESEARCH THE NCRI PARTNERS ARE FUNDING (Analysis of the CRD using the Common Scientific Outline)

4.3.1 Understanding the CSO

Analysis using the CSO gives an indication of the broad trends in different types of cancer research but should not be taken as an exact measure of the total research activity in any one area. CSO coding should therefore be regarded as a useful indicator of the 'centre of gravity' of a particular piece of research rather than a comprehensive description of all the aims and possible outcomes of that study. In reality the research outputs from any one project can often be applied to understanding many aspects of a disease and may also be relevant to a number of different tumour types. When interpreting the analysis of UK cancer research activity by CSO it is important to recognise that there is no accepted or recommended pattern of spend by CSO category.

4.3.2 Results of the CRD analysis using the CSO

Figure 1 shows the distribution of the collective research portfolio directly funded by the NCRI Partner organisations as classified by the seven major categories of the CSO: Biology; Aetiology; Prevention; Early Detection, Diagnosis and Prognosis; Treatment; Cancer Control and Scientific Model Systems. The largest proportion of funding is concentrated within Biology (41%). There are five subcategories within the CSO Biology section; one relating to normal functioning, three concerning cancer initiation, progression and metastasis, and one dealing with resources and infrastructure related to biology. As can be seen in the breakdown of the Biology category, (Figure 2), greater than half of the proportion of biological research, (61%), is directed at investigating normal biological functioning in cancerrelevant systems.

Understanding normal functioning in complex biological systems is essential to inform research into the mechanisms controlling aberrant processes. The UK has long had an excellent reputation in conducting high quality biological research that has resulted in many major advances in medical science. This type of research is dictated largely by scientific opportunity and tractability and therefore is particularly suited to response mode funding, which arguably requires less strategic direction than other areas of research.



FIGURE 1: PROPORTION OF TOTAL NCRI PARTNERS' SPEND BY CSO

FIGURE 2: SUBDIVISION OF CSO BIOLOGY CATEGORY



Treatment (22%) and Aetiology (16%) proportionately attract the next highest amount of NCRI Partners' funding (see Appendix 6 for the relative breakdown of specific areas within all the CSO categories). Within the Treatment subcategories, research into localised therapies which focuses on radiotherapy and surgery comprises approximately 2% of overall funding. The NCRI is currently carrying out a review on Radiotherapy and Related Radiobiology, and research into surgery may require further examination. In general, research into treatment has benefited and continues to benefit from a more strategic, directed approach from the major funders. CR-UK has long been running a Drug Development Office and new Government investment in the NHS infrastructure for clinical cancer research should help to increase research outputs in all the clinically-related CSO categories, especially Treatment. This new NHS infrastructure, which is under the strategic direction of the NCRI, consists of the National Translational Cancer Research Network (NTRAC) and the National Cancer Research Network (NCRN). NTRAC focuses on translational cancer research and the aim of the NCRN is to double the number of cancer patients in clinical trials.

One of the main issues arising from the CSO analysis of the database is an apparently small investment by NCRI Partners in research into cancer **Prevention (2%)**. However, it is important to bear in mind that the CSO Prevention category only includes research aimed at the direct application of strategies to prevent cancer, and that several other facets of research that inform preventative strategies are covered by other CSO categories (see Appendix 4). Aspects of prevention are dealt with in Aetiology; investigating exogenous factors in the origin and cause of cancer such as tobacco, diet, viral infection etc and their interactions with genes. In addition the CSO Prevention category does not include research aimed at identifying risk factors in specific populations and research into behavioural interventions. and effective education and communication of cancer risk. Much of this fundamental research, which is found in the Cancer Control and Aetiology categories, is needed to inform suitable approaches to possible prevention research and to identify appropriate targets for prevention. Therefore the real investment in research relevant to future cancer prevention strategies is larger than the 2% that falls directly into this category.

The relatively low investment in this area, however, remains an important observation. There is no reluctance on behalf of the research organisations to fund this type of research; indeed this is an area that currently offers some interesting scientific opportunities.

Based on our current level of knowledge, only certain types of cancers particularly lend themselves to preventative approaches. Further analysis of the CRD CSO Prevention category shows that research in this area relates to a limited number of tumour sites, namely lung, head and neck, colorectal, breast and gynaecological cancers. This reflects those cancers for which aetiological agents have been verified and assessed as suitable targets for preventative strategies. Examples of research currently funded by the NCRI Partners in this category include - aspects of tobacco control, dietary factors in cancer causation and nutritional issues including research into NSAIDS in the chemoprevention of colorectal cancer, breast cancer chemoprevention clinical trials and prevention of cervical cancer by protection against human papilloma virus (HPV).

Cancer Control, Survival and Outcomes Research

currently represents **6%** of the research on the database. This encompasses a wide range of issues from patient care and pain management, surveillance, behaviour and education, supportive and palliative care to cost effective health care delivery. Much of the focus of this research is aimed at understanding and improving those factors that affect a patient's experience of cancer. It is possible that this type of research is generally less expensive to resource than other areas of research. In the future it may be informative to investigate alternative measures of activity, such as the balance between short and long term funding.

In common with many aspects of prevention, investigation into cancer control, survival and outcomes is characterised by challenges in designing, conducting, funding and interpreting high quality experiments. Research is frequently not laboratory based and requires a complex multi-disciplinary approach, often conducted in real-life settings and characterised by endpoints that may need to be measured over long time periods. These factors can



FIGURE 3: COMPARISON OF NCRI (UK) AND NCI (USA) PROPORTIONAL SPEND BY CSO

NATIONAL CANCER RESEARCH INSTITUTE (UK) APRIL 2002

NATIONAL CANCER INSTITUTE (USA) EXTRAMURAL CANCER RESEARCH PORTFOLIO FUNDED IN FISCAL YEAR 2000



make aspects of prevention and cancer control difficult to both carry out and to fund. This is reflected in the breakdown of the CSO Prevention category, where 59% of funding is spent on resources and infrastructure to underpin studies in this area (Appendix 6).

NCRI Partners' spend on research into **Early Detection, Diagnosis and Prognosis** comprises **8%** of the total portfolio. As with many aspects of research, this type of activity is influenced by studies in other areas. Much of the research underpinning the identification of diagnostic and prognostic markers will be found in the CSO categories of Biology and Aetiology. Increasing application of post-genomic technologies such as micro-arrays and pharmacogenomics is likely to increase the number of competitive proposals and augment the funding in the area of diagnosis and prognosis in the future.

One of the advantages of using the CSO classification system is to be able to compare the research activities of different organisations at both a national and international level. Figure 3 compares the distribution of spend by CSO of the UK NCRI Partners with the US National Cancer Institute (NCI) Extramural Cancer Research Portfolio funded in Fiscal Year 2000. Although the NCRI and NCI are two differently structured organisations, where the NCRI represents fifteen cancer funding organisations, the distribution of both profiles shows a broadly similar pattern where the largest amount of funding is dedicated to biological research. In due course as more international data becomes available, comparisons of the NCRI CSO proportional spend will be made with the CSO profiles of other members of the International CSO Partnership (Appendix 3).

The distribution of the combined NCRI Partners' direct



FIGURE 4: PERCENTAGE OF COMBINED NCRI PARTNERS' SPEND BY CSO



FIGURE 5: PERCENTAGE OF EACH NCRI MEMBERS' SPEND BY CSO





FIGURE 6: PROPORTION OF COMBINED NCRI PARTNERS' DISEASE SITE FUNDING

spend by CSO category previously shown in Figure 1, is illustrated in a kite diagram in Figure 4. The total figure for each data point of a kite diagram is the sum of the percentages above and below the line of origin. The CSO proportional spend profiles of the fifteen NCRI Members are displayed in Figure 5. The kite diagram is used here as it is particularly suited to comparing the patterns of CSO activity between different Partners. Each kite diagram represents the individual organisation's CSO distribution calculated as a proportion of that organisation's total research spend. In addition the kites are colour coded to reflect the relative proportion of the combined NCRI portfolio total spend.

The internal funding profiles of the organisations can be loosely grouped into three categories. The Members in the top row, Ludwig, AICR, BBSRC, MRC and Marie Curie focus the vast majority of their research activities in Biology; the Partners in the middle row, Breakthrough, CR-UK, YCR, LRF and Northern Ireland tend to support two main areas of CSO activity; and organisations in the bottom row, Scotland, Tenovus, DOH, Wales and Macmillan form a disparate group with individual funding patterns.

In general most of the NCRI Partners fund predominantly Biology, Aetiology and Treatment research, which is in keeping with the CSO distribution pattern of the combined NCRI Partners' spend. Few organisations focus their research activities in Prevention and Cancer Control. The clear exception to this is Macmillan, which is only active in the area of Cancer Control, Survival and Outcomes Research. The focus on Biology for many of the smaller organisations can be explained in a number of ways. With scientific opportunity and scientific excellence as the main criteria for funding, biological research proposals tend to be numerous and lend themselves to short term project grant funding. This contrasts with the level of financial commitment required to support large clinical trials and epidemiological studies. This is an important consideration for many small organisations with an uncertain long term income.

In general the larger organisations spend proportionally more on Biology, Aetiology and Treatment based research; however, they also support projects that encompass all areas of the CSO. The CSO Treatment category includes both drug discovery programmes that are purely laboratory based, as well as clinical















- Fundamental Research
- Site Specific



FIGURE 7: PERCENTAGE OF DISEASE SITE FUNDING WITHN EACH CSO CATEGORY

trials research, which tend to be long term multi-centre studies that require substantial financial support. While most Member organisations are active in investigating potential cancer treatments, clinical trials which include studies covering Prevention, Detection and Prognosis and Treatment research tend to be funded only by the larger organisations such as MRC, CR-UK and the Department of Health. It can be noted that the funding patterns of the major Government cancer research funding agencies, MRC and the Department of Health, are complementary.

4.4 ANALYSIS OF RESEARCH INTO DIFFERENT CANCERS (Analysis of the CRD using the Disease Site codes)

4.4.1 Understanding disease specific funding Cancer research can be broadly divided into two modes of study; research that is focused on specific tumour types (Site Specific Research) and research that is generic and may be applied to all types of cancer. Generic research can be further subdivided into two groups; research which is pre-clinical and describes mechanistic studies ranging from regulation of basic biological processes, drug synthesis and metabolism, to the design of diagnostic instruments (Fundamental Research); and more 'patient focused' research that is relevant to all cancer types such as cancer education and communication, novel drug delivery systems in clinical trials and studies relating to pain management, and supportive and palliative care (All Sites). Figure 6 shows the distribution of all projects on the CRD amongst the three modes of 'disease type' funding. Interestingly 40% of the combined NCRI Partners' funding is spent investigating specific tumour types, whereas the majority of research currently funded (Fundamental Research plus All Sites) can be applied to all cancer types.

The type of research being conducted will largely dictate whether a Site Specific, Fundamental or All Sites approach is adopted. This is evident when the distribution of disease site funding is broken down within each major CSO category (Figure 7). For example, the vast majority of the CSO Biology section, which forms the largest area of NCRI Partners expenditure (41%), is Fundamental Research, which is potentially relevant to all types of cancer.

Traditionally research into aetiology and diagnosis has been organised in a site specific manner and this is reflected in the greatest proportion of spending on Site Specific research in these CSO codes. Prevention and Cancer Control are equally split between All Sites and Site Specific research with very little Fundamental Research being carried out in these areas. Interestingly, Treatment is evenly apportioned between the three modes of disease site research. This finding reflects the broad nature of this category, which encompasses drug discovery programmes, the development of therapies and delivery systems, and their application in site specific clinical trials.

Classification of cancer research into site specific studies and research that is generic and relevant to all cancer types is a useful analytical tool but also means that care is required when drawing conclusions about levels of funding that are associated with particular disease sites. Research funding that is directly associated with a specific disease site can be misleading if used to indicate the total research investment to combat that tumour type without consideration of the funding that also supports research that is applicable to all cancer types. Similarly, research into certain aspects of specific tumours can produce findings that are relevant to a number of different cancer types.

4.4.2 Results of Disease Site Funding Analyses Fifty different cancer sites are used in the classification of tumour type for the CRD (Appendix 5). Figure 8 shows twenty of these tumour sites, expressed as a percentage of the combined NCRI Partners' spend on disease site specific funding. Breast, leukaemia, colon and rectal, and prostate research currently receive the most site specific funding. It is interesting to note that there are only two NCRI Member organisations dedicated to supporting research on a single tumour type, the Leukaemia Research Fund and Breakthrough Breast Cancer. Research into these areas is also supported by many of the other NCRI Partners, so it is perhaps not surprising that these are the two most highly funded disease sites.

There are a number of factors that dictate the level of research funding into a particular disease site, these include:



FIGURE 8: PERCENTAGE OF TOTAL NCRI PARTNERS' SPEND BY DISEASE SITE

Scientific opportunity – This can be a very important driver. In particular, developments in fundamental research and the introduction of new technologies often stimulate new approaches.

Burden of disease – The incidence and severity of tumour type will influence both researchers and funders.

Researchability – Some tumour types are easier to work on than others but can often provide a model system for other cancers, and many researchers are attracted to areas or diseases where there is real evidence or potential for progress.

Fundraising – Certain tumours may attract more public donations than others.

Quality and size of research workforce – Because of the issues listed above some areas attract more high quality researchers than other areas. This will

undoubtedly affect the number of quality proposals received by funding bodies.

NCRI Partner organisations take these factors into account when making funding decisions. However, the relative importance of each of these in the decision making process varies for each organisation depending on its corporate aims, culture and procedures.

'Burden of disease' is often seen as an attractive benchmark against which to measure funding in different diseases. The major problem here is that there are a number of different ways of measuring 'burden of disease' and many of these suffer from insufficient and low quality data on which to base calculations. Different measures of disease burden include incidence, mortality, morbidity, long-standing illness and disability, hospital in and out patient expenditure, life years lost and disability-adjusted life years lost. As cancers vary significantly in the type of health burden they impose, it is important to stress there is no single measure of the importance of any particular tumour type to the Nation's health.

Given this, the only reliable figures currently available relating to the health burden of different cancers in the UK are those for incidence and mortality, and therefore, these statistics have been compared to the relative percentage of NCRI Partners' spend on specific disease sites in Figures 9 & 10.

The results of this analysis show that the relative proportion of funding spent on different disease sites generally follows the increasing disease burden associated with these cancers. This is particularly evident for breast, colon and rectal, and prostate, three of the highest funded cancer sites. However, there are some diseases where the relative spend is higher than the pattern of disease burden, (e.g. leukaemia, ovarian and cervical cancer) and some where the spending is significantly lower (e.g. lung, pancreas, stomach, oesophagus and bladder).

One of the most striking features of these two graphs is the clear discrepancy between the level of funding of lung cancer specific research compared with the high incidence and mortality of this disease. Traditionally, approaches to the management of lung cancer have concentrated on smoking prevention and tobacco control and the primary focus of lung cancer research on the CRD is in these areas. However, lung cancer is not a particularly researchable or tractable disease to study and it may be for these reasons that lung cancer research is unattractive to many investigators. Although this analysis focuses on the combined portfolio of the NCRI Partner organisations, there is at least one dedicated lung cancer research charity active in the UK, The Roy Castle Lung Cancer Foundation (annual research spend estimated at £1.6 million), whose research is not included in this study. However, even if the entire research budget of this organisation was added to the total NCRI Partners' spend on lung cancer there would still be a significant difference between the relative level of research funding compared with the high incidence and mortality associated with this disease.

Leukaemia research receives the second highest level of funding from the NCRI Partners whereas the disease

accounts for 3% of total cancer incidence and mortality. The UK has traditionally had a very strong leukaemia research focus and has provided an international lead in research into this area. This has resulted in marked improvements in disease survival over the past 30 years, particularly in childhood leukaemias. The emotive nature of childhood leukaemia and demonstration of clear progress in research outcomes in this area may have had a beneficial effect on funding. In addition, leukaemia is a good example of a disease that provides an attractive and malleable model for basic researchers to study. Given this background, the high quality leukaemia research community has continued to attract research funding from many of the NCRI Member organisations. This is demonstrated by the fact that ten of the fifteen NCRI Member organisations support leukaemia research, and between them the LRF and MRC account for over 80% of this total funding.

4.5 WHERE ARE THE NCRI PARTNERS FUNDING THIS RESEARCH? (Mapping Analysis of the CRD)

High quality information on the overall level of investment in cancer research at the various research institutes and Higher Education Institutes (HEIs) across the UK will provide an important tool to help in devising long term research strategies. This will be valuable not only for those organisations conducting cancer research but will also aid NCRI Members in planning strategy and infrastructure provision. The CRD provides the opportunity to conduct this type of analyses and Figure 11 shows the distribution of cancer research funded by the NCRI Member organisations across the UK. In generating this figure, any cities that have less than 1% of the total NCRI Partners' research spend were omitted (31 locations).

NCRI Partners' cancer research funding follows the general pattern of research funding for UK universities as reported in the recent RAE exercise (source: HEFCE, www.hefce.ac.uk/pi, table R1, QR funding from funding councils 1999-2000). The top four universities as listed by HEFCE (London, Cambridge, Oxford, Manchester) are within the cities that have the highest level of NCRI Partners' funding, and institutions ranking low on the HEFCE cancer spend table also tend to be located in cities where the research funding on the CRD is lower.



FIGURE 9: PERCENTAGE OF COMBINED NCRI PARTNERS' SPEND COMPARED WITH INCIDENCE (1998)

FIGURE 10: PERCENTAGE OF COMBINED NCRI PARTNERS' SPEND COMPARED WITH MORTALITY (2000)





London contains 39% of the total NCRI Partners' research spend. This relatively high percentage could be predicted given that all of the large funders have significant investment in the city's research institutions, and a number of the smaller organisations also fund research within London. Further analysis of the distribution of funding within London (defined as research institutions located within the M25), is shown in Figure 12; there is significant variation in investment between the different institutions receiving NCRI Partner funding. The highest proportion (20%) is accounted for in a single research site funded by CR-UK. The combined spend at the two CR-UK funded institutions at Lincoln's Inn Fields and Clare Hall equals the joint spend of the Institute for Cancer Research & Royal Marsden NHS Trust at the central London and Sutton sites. These two groups account for almost 50% of the total research funding in London. High levels of funding and research activity are concentrated at the Royal Free/UCL and Imperial College campuses that are located at several sites across the city. This finding is expected given that both UCL and Imperial College are

amongst the top five generators of research income in the UK (source: HEFCE, www.hefce.ac.uk/pi, table R1, QR funding from funding councils 1999-2000).

4.6 PROSTATE CANCER – AN EXAMPLE OF A DISEASE SPECIFIC CASE STUDY

In 2000 the NCRI carried out a review of prostate cancer research in the UK and as a result the DOH, MRC and CR-UK funded two NCRI Prostate Cancer Collaboratives. Figure 13 shows current distribution of funding for prostate cancer research by NCRI Partners mapped across the UK. Eighteen cities fund prostate cancer disease site specific research of which Sheffield has the highest proportion (31.9%). The high proportion of spend in Sheffield is largely accounted for by two large grants funding the NCRI Northern (& Bristol) Prostate Cancer Collaborative and The ProtecT Trial (evaluating the effectiveness of treatment for clinically localised prostate cancer). In this analysis there are five cities (Belfast, Exeter, Aberdeen, Colchester, York) that were not featured in Figure 11 as they have less than 1% of the overall NCRI Partners' cancer spend reported in the CRD.

FIGURE 12: PERCENTAGE OF NCRI PARTNERS' SPEND IN LONDON INSTITUTIONS

Other Brunel University, University of London School of Pharmacy, University of London London School of Hygiene & Tropical Medicine MRC Clinical Research, Harrow St Mark's Hospital St George's Hospital Queen Mary & Westfield MRC Clinical Trials Head Office St Bartholomew's & The Royal London Guy's, King's & St Thomas' Gray Cancer Institute & Mount Vernon CR-UK, LRI (Clare Hall) NIMR, Mill Hill Imperial College School of Medicine Royal Free & UCL & Medical Schools ICR, London ICR & Royal Marsden, Sutton CR-UK, LRI (Lincoln's Inn Fields)



FIGURE 13: DISTRIBUTION OF TOTAL NCRI PARTNERS' RESEARCH SPEND ON PROSTATE CANCER IN THE UK



Figure 14 shows the CSO breakdown of all prostate cancer grants on the CRD. Comparison of this figure with the total NCRI Partners' spend by CSO (Figure 1), reveals that the patterns of funding of Biology and Treatment are reversed with approximately 45% and 21% of prostate cancer funding spent in Treatment and Biology respectively, compared with 22% and 41% for the total portfolio. The relative proportions of the other CSO categories remain the same for both charts. This focus on Treatment may be explained by the emphasis on translational research by the NCRI Prostate Cancer Collaboratives, and also by the funding of the large ProtecT prostate clinical treatment trial. Interestingly, if funding associated with these proposals was not included on the CRD, the CSO pattern would resemble that of the total NCRI portfolio.

Prostate cancer provides a good example of how a more strategic approach to funding by several NCRI Partners working in collaboration has influenced the proportion of spend and pattern of research activity in a specific area. It is anticipated that in the future the type of disease specific analysis and geographical mapping exercise described here will become an important management tool for research funders and will also facilitate strategic interactions between the NCRI Partner organisations.

4.7 WHAT CONCLUSIONS CAN BE DRAWN FROM THIS ANALYSIS?

The analysis confirms a healthy picture of a vibrant and generally well-balanced cancer research base in the UK. The data shows that the largest proportion of the collective NCRI Partners' spend is in the field of biological research, with nine of the fifteen Member organisations spending the highest proportion of their funding in this area. There are two areas where research investment across the majority of NCRI Partners appears to be relatively low – Prevention Research and Cancer Control, Survival and Outcomes Research.

The majority of the cancer research funded by the NCRI Partners is generic and applicable to all tumour types. Within research that is site specific, the relative proportion of funding follows the increasing disease burden, as measured by incidence and mortality, with a number of exceptions. The analysis shows that funding in lung cancer research is low in relation to its high incidence and mortality. Leukaemia research is well supported which may reflect a history of high quality research that is continuing to attract funding from a large number of the Partner organisations.

The contents of this first published analysis of the CRD will provide a useful basis for NCRI Member organisations and other cancer research funders in the UK to plan and prioritise their spending on cancer research. Indeed the discussions leading up to the production of this Report have already stimulated dialogue on future strategic development between NCRI Partner organisations.



FIGURE 14: PROPORTION OF TOTAL NCRI PARTNERS' SPEND ON PROSTATE CANCER BY CSO

5 Further Action Arising from this First Analysis

5.1 FURTHER EXAMINATION OF CROSS-CUTTING ISSUES

There are two key areas highlighted by this first analysis that NCRI Member organisations have agreed would benefit from much closer joint strategic examination; research into cancer risk and prevention and research into supportive and palliative care. These are both cross-cutting areas of research that are important to all cancer types and encompass all NCRI Partner organisations. They both involve a significant patientbased focus where there are clear scientific opportunities. They are also both characterised by low direct research activity by the NCRI Partnership. The NCRI will set up a 'Strategic Planning Group' in each area, bringing together senior representatives from the relevant NCRI Partner organisations. These Groups will carry out a much more detailed analysis of the research activity, discuss any potential opportunities and barriers and identify any further action necessary.

Likely scope of strategic examination of prevention research

Prevention research covers not only the activities listed in the CSO Prevention category but also includes aspects of Aetiology and topics in the CSO Cancer Control category. An extension of prevention research is the investigation of genetic risk. With the wealth of information that is being generated by the Human and Cancer Genome Projects and associated genetic profiling, this is an expanding area of research with increasing scientific opportunity. Genetic risk research covers the identification and characterisation of genes responsible for familial cancer syndromes. It also includes the investigation of genes, in particular specific polymorphisms, in their role in cancer initiation. Additional factors in risk research cover genetic epidemiology, genetic counselling and broad aspects of risk surveillance. The further strategic examination of prevention research is likely to encompass the above areas.

Likely scope of strategic examination of supportive and palliative care research

Supportive and palliative care research falls into the CSO category of Cancer Control, Survival and Outcomes research. The scope for further strategic examination of this area will cover most of this CSO category. In particular, we will examine patient care and survival issues, psychological impacts of cancer survival, long term morbidity, symptom management, psychological or educational interventions, end of life care and

complementary and alternative approaches for supportive care of patients and survivors.

5.2 STRATEGIC APPROACH TO DISEASE SPECIFIC RESEARCH

The NCRI Partners believe it is important to examine the work they fund that is focused on different diseases and consider whether they are utilising their resources as effectively as possible. However, there are over 200 different types of cancer, grouped into 50 categories in this analysis, and detailed strategic review of a particular tumour type is resource intensive and can be divisive.

The US National Cancer Institute (NCI) has recently undertaken a series of Progress Reviews Groups (PRGs) focusing on individual major disease sites. The PRGs have carried out detailed reviews of the current state of research into ten cancer disease sites and have made recommendations to address key scientific opportunities and obstacles for the future. The PRG reports have been published and are available on the NCI Website (http://prg.nci.nih.gov/ prgschedule.html). The NCI is currently responding to these reviews and planning its future strategic investment across these areas.

The majority of the recommendations that result from the NCI PRGs are directly relevant to the situation in the UK research community. The NCRI Partners have decided rather than replicate these reviews it would be of greater benefit to carry out a further strategic examination of disease sites in the light of the NCI response to the PRGs. As a result of this, the NCRI Partners can investigate how UK investment can make the best contribution to the international research effort in different cancers. This might be done by detailed examination of the NCI PRG Reports together with the NCI response (implementation plans) and answering three key questions: a) Is there anything that differs from a UK perspective? b) How does the UK activity map onto the US priority areas and implementation plans? c) What should be the focus of UK activity? As part of the NCRI's commitment to collaboration both within the UK and the wider international cancer research community, the NCI will be invited to take part in this process.

It is important that we carry out this exercise rigorously and effectively. In light of the findings emerging from the analysis of the CRD, NCRI Member organisations have agreed that we should begin this process with lung cancer research.

Association for International

Cancer Research (AICR) Madras House St Andrews Fife KY16 9EH

Biotechnology and Biological Sciences

Research Council (BBSRC) Polaris House North Star Avenue Swindon SN2 1UH

Breakthrough Breast Cancer (Breakthrough)

6th Floor, Kingsway House 103 Kingsway London WC2B 6QB

Cancer Research UK (CR-UK)

PO Box 123 Lincoln's Inn Fields London WC2A 3PX

Department of Health (DOH)

Richmond House 79 Whitehall London SW1A 2NS

Leukaemia Research Fund (LRF)

43 Great Ormond Street London WC1N 3JJ

Ludwig Institute for Cancer Research (Ludwig)

Horatio House 5th Floor South 77-85 Fulham Palace Road London W6 8JC

Macmillan Cancer Relief (Macmillan) 89 Albert Embankment London SE1 7UQ

Marie Curie Cancer Care

89 Albert Embankment London SE1 7TP

Medical Research Council (MRC) 20 Park Crescent London W1B 1AL

Northern Ireland Health and Personal Social Services Research and Development Office (Northern Ireland) 12-22 Linenhall Street Belfast BT2 8BS

Scottish Executive Health Department (Scotland) St Andrews House Regent Road Edinburgh EH1 3DG

Tenovus The Cancer Charity (Tenovus) 43 The Parade Cardiff CF24 3AB

Wales Office of Research and Development for Health and Social Care The National Assembly for Wales (Wales) Cathays Park Cardiff CF10 3NQ

Yorkshire Cancer Research (YCR)

39 East Parade Harrogate North Yorkshire HG1 5LQ Detailed below are additional comments that were supplied by the Member organisations.

AICR

In the year 2000-2001 AICR spent £7,614,901 on cancer research and education. The vast majority of our research funding is in the form of three year grants. Because a certain number of AICR grants start and end on 1 April each year some of these do not appear in the CRD annualised spend figures for 2002.

BBSRC

The actual BBSRC spend on cancer research in the financial year 2000-2001 is £4.7 million. This figure was reached through a rigorous process of project and grant selection, for inclusion in the NCRI database, by both BBSRC and NCRI. With the establishment of NCRI, there is now a greater appreciation of the extent to which our basic cell biology research portfolio underpins cancer. Working to the more focused NCRI definition of cancer research, the figure of £4.7 million reported here is therefore less than the estimate guoted in the S&T report. The figure of £4.7 million contrasts somewhat from the NCRI Annualised spend as a result of the method of calculation. For BBSRC Institute projects, annual spend is reported each financial year. However, for research grants, BBSRC routinely calculates the annual spend as (No. of months grant is current in a given financial year)*(Total value of grant)/(Total duration of grant in months), to give a more accurate reflection of research spend.

CANCER RESEARCH UK

The NCRI Cancer Research Database includes much of Cancer Research UK direct research spend active on 1 April 2002. However, due to variation in the funding cycle, some direct research spend that is planned for allocation in 2002-03 is not yet included. Vital expenditure on research services, some clinical trials spend and infrastructure to support Cancer Research UK's activities has also not yet been included, but it will appear in the next NCRI Report. In total, expenditure on research in 2002-03 will exceed £170 million.

DEPARTMENT OF HEALTH

The 'Total Reported Organisation Research Spend' for the Department of Health shown in Table 1 includes DH indirect spend (R&D Support for NHS Providers), the management of which is devolved to NHS organisations and details are not held centrally. The figure for 2000/01 is estimated to be £73,213,000. However, the NHS R&D programme is currently being modernised and it is intended that an increasing amount of research will be added to the database over time. Other reasons for the difference between the figures are detailed in Section 3.3 and 3.4 of the report.

LUDWIG INSTITUTE FOR CANCER RESEARCH

In 2001, LICR spent £6 million on research in the UK. This figure includes direct research spend plus indirect costs at the two London research branches, support for a research project at University of Oxford and the cost the London office that runs intellectual property matters for the Institute worldwide.

MACMILLAN CANCER RELIEF

Macmillan commissions its research activities through a number of University departments and therefore does not carry any additional infrastructure or overheads costs.

MARIE CURIE CANCER CARE

Marie Curie Cancer Care's total charitable expenditure in the year ended March 2001 was £40.3 million of which £3.5 million related to scientific and palliative care research and the balance was spent on the provision of cancer care through its hospices and nationwide nursing service, and on education and training.

SCOTLAND EXECUTIVE HEALTH DEPARTMENT

Organisation	Chief Scientist Office, Scotland	
Direct Annualised Spend (1st April 2002)	£2,050,814*	
Indirect Funding – to support cancer research in		
NHS in Scotland (2000-01)	£7,100,000	
Scottish Cancer Therapy network (2000-01)	£300,000	

 * Of the 41 cancer research projects that were ongoing at 1/4/02, only 23 were submitted to the NCRI for coding, equivalent to an expenditure of £1,195,928

YORKSHIRE CANCER RESEARCH

The figure of £4,400,194 taken from the 2000-2001 YCR Annual Report relates to direct research spend plus building costs for the YCR Laboratory of Drug Design at the University of Bradford. The CSO and Disease Site classification systems for cancer-related research grants were developed initially by the National Cancer Institute, tested by the US Department of Defence and then further developed and refined in partnership with other organisations. The aim is to create a truly international system for the classification and strategic comparison of cancer research.

ORGANISATIONS CURRENTLY INVOLVED ('CSO PARTNERS')

National Cancer Institute	(NCI)
US Department of Defence	(DoD)
National Cancer Research Institute	(NCRI)
Medical Research Council	(MRC)
Cancer Research UK	(CR-UK)
Oncology Nursing Society of America	(ONS)
Susan B. Komen Breast Cancer Foundation	(Komen)
California Breast Cancer Care Program	(CBCCP)
CapCURE	(CapC)
California Cancer Research Program	(CCRP)
American Cancer Society	(ACS)

The CSO Partners meet or teleconference every three months to discuss all issues pertaining to use of their classification systems. Typically these include resolving difficult coding problems and agreeing any changes or additions of explanatory notes to the classifications.

BIOLOGY

1.1 Normal Functioning

- Developmental biology (from conception to adulthood) and the biology of ageing
- Normal functioning of genes, including their identification and expression, and the normal function of gene products, such as hormones and growth factors
- O Normal formation of the extracellular matrix
- Normal cell to cell interactions

1.2 Cancer Initiation: Alterations in Chromosomes

- Abnormal chromosome number
- Aberration in chromosomes and genes (e.g., in CML)
- O Damage to chromosomes and mutation in genes
- Failures in DNA repair
- Aberrant gene expression
- Epigenetics

1.3 Cancer Initiation: Oncogenes and Tumour Suppressor Genes

 Genes and signals involved in growth stimulation or repression, including oncogenes (Ras, etc.), and tumour suppressor genes (p53, etc.) and hormones and growth factors such as estrogens, androgens, TGF-beta, GM-CSF, etc.

1.4 Cancer Progression and Metastasis

- Latency, promotion, and regression
- Expansion of malignant cells
- Interaction of malignant cells with the immune system or extracellular matrix
- Cell detachment
- Cell motility
- \circ Invasion
- Penetration of the vascular system
- Malignant cells in the circulation
- O Extravasation and growth of metastases

1.5 Resources and Infrastructure

- Informatics and informatics networks
- Specimen resources
- Epidemiological resources pertaining to biology
- O Reagents, chemical standards

AETIOLOGY

- 2.1 Exogenous Factors in the origin and cause of cancer Examples of science that would fit:
 - Lifestyle factors such as smoking, chewing tobacco, alcohol consumption, parity, diet, sunbathing, and exercise
 - Environmental and occupational exposures such as radiation, second-hand smoke, radon, asbestos, organic vapours, pesticides, and other chemical or physical agents
 - Infectious agents associated with cancer aetiology, including viruses (Human Papilloma Virus-HPV, etc.) and bacteria (helicobacter pylori, etc.)
 - Viral oncogenes and viral regulatory genes associated with cancer causation

$\ \ 2.2 \ \ {\rm Endogenous \ Factors \ in \ the \ origin \ and \ \ cause \ of \ \ cancer }$

Examples of science that would fit:

- Free radicals such as superoxide and hydroxide radicals
- Genes known to be involved or suspected of being mechanistically involved in familial cancer syndromes, e.g., BRCA1, Ataxia Telangiectasia, and APC
- Genes suspected or known to be involved in "sporadic" cancer events, for example polymorphisms and/or mutations that may affect carcinogen metabolism (e.g., CYP, NAT, glutathione transferase, etc.)

2.3 Interactions of Genes and/or Genetic Polymorphisms with Exogenous and/or Endogenous Factors Examples of science that would fit:

- Gene-environment interactions
- Interactions of genes with lifestyle factors, environmental and/or occupational exposures such as variations in carcinogen metabolism associated with genetic polymorphisms
- Interactions of genes and endogenous factors such as DNA repair deficiencies and endogenous DNA damaging agents such as oxygen radicals or exogenous radiation exposure

2.4 Resources and Infrastructure Related to Aetiology Examples of science that would fit:

- Informatics and informatics networks; for example patient databanks
- Specimen resources (serum, tissue, etc.)
- Reagents and chemical standards
- Epidemiological resources pertaining to aetiology
- Statistical methodology or biostatistical methods
- Centers, consortia, and/or networks
- O Education and training of investigators

PREVENTION

- 3.1 Interventions to Prevent Cancer: Personal Behaviours that Affect Cancer Risk Examples of science that would fit:
 - O Research on determinants of personal behaviours, such as diet, physical activity, sun exposure, and tobacco use, which affect cancer risk
 - O Interventions to change personal behaviours that affect cancer risk

3.2 Nutritional Science in Cancer Prevention

Examples of science that would fit:

- O Quantification of nutrients and micronutrients
- Studies on the effect(s) of nutrients or nutritional status on cancer incidence
- Dietary assessment efforts including dietary questionnaires and surveys
- O Development, characterisation and validation of dietary/nutritional assessment instruments

3.3 Chemoprevention

Examples of science that would fit:

• Chemopreventive agents and their discovery, mechanism of action, development, testing in model systems and clinical testing

3.4 Vaccines

Examples of science that would fit:

O Vaccines for prevention, their discovery, mechanism of action, development, testing in model systems and clinical testing

3.5 Complementary and Alternative **Prevention Approaches**

Examples of science that would fit:

- Discovery, development and testing of complementary/alternative prevention approaches such as diet, herbs, supplements or other interventions which are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses
- O Hypnotherapy, relaxation, transcendental meditation, imagery, spiritual healing, massage, biofeedback, etc., used as a preventive measure
- 3.6 Resources and Infrastructure Related to Prevention

Examples of science that would fit:

- O Informatics and informatics networks; for example patient databanks
- Specimen resources (serum, tissue, etc.)
- Epidemiological resources pertaining to prevention.
- Clinical trials infrastructure
- Statistical methodology or biostatistical methods
- Centers, consortia, and/or networks
- O Education and training of investigators

EARLY DETECTION, DIAGNOSIS AND PROGNOSIS

- 4.1 Technology Development and/or Marker Discovery Examples of science that would fit:
 - O Discovery of markers (e.g., proteins, genes) and/or imaging methods that are potential candidates for use in cancer detection, diagnosis and/or prognosis

4.2 Technology and/or Marker Evaluation with respect to Fundamental Parameters of Method Examples of science that would fit:

- Preliminary evaluation with respect to laboratory sensitivity, laboratory specificity, reproducibility, and accuracy
- 4.3 Technology and/or Marker Testing in a Clinical Setting Examples of science that would fit:
 - Evaluation of clinical sensitivity, clinical specificity and predictive value
 - Quality assurance and quality control
 - Inter and intra-laboratory reproducibility
 - Testing of the method with respect to effects on morbidity and/or mortality
 - Study of screening methods including compliance, acceptability to potential screenees, receiveroperator characteristics

4.4 Resources and Infrastructure Related to Detection, Diagnosis or Prognosis

Examples of science that would fit:

- O Informatics and informatics networks; for example patient databanks
- Specimen resources (serum, tissue, images, etc.)
- O Clinical trials infrastructure
- Epidemiological resources pertaining to risk assessment, detection, diagnosis, or prognosis
- Statistical methodology or biostatistical methods
- O Centers, consortia, and/or networks
- Education and training of investigators

TREATMENT

- 5.1 Localised Therapies Discovery and Development Examples of science that would fit:
 - Discovery and development of treatments administered locally that target the organ and/or neighboring tissue directly, including but not limited to surgical interventions and radiotherapy
 - Therapies with a component administered systemically but that act locally (e.g., photodynamic therapy and radiosensitizers)
 - Development of methods of drug delivery

5.2 Localised Therapies – Clinical Applications Examples of science that would fit:

- Clinical testing and application of treatments administered locally that target the organ and/or neighboring tissue directly, including but not limited to surgical interventions and radiotherapy
- Clinical testing and application of therapies with a component administered systemically but that act locally (e.g., photodynamic therapy and radiosensitizers)
- Phase I, II or III clinical trials of promising therapies that are administered locally

5.3 Systemic Therapies – Discovery and Development Examples of science that would fit:

- Discovery and development of treatments
 - administered systemically such as cytotoxic or hormonal agents, novel systemic therapies such as immunologically directed therapies (vaccines, antibodies), gene therapy, angiogenesis inhibitors, apoptosis inhibitors and differentiating agents
 - $\,\circ\,$ Defining molecular signatures of cancer cells
 - Identifying molecular targets for drug discovery. Includes mechanistic studies of cellular metabolism, combinatorial chemical synthesis, drug screening, development of high throughput assays and testing in model systems
 - O Development of methods of drug delivery
 - Analysis of molecular mechanisms of drug resistance and preclinical evaluation of new therapies to circumvent resistance

5.4 Systemic Therapies – Clinical Applications Examples of science that would fit:

Clinical testing and application of treatments

- administered systemically such as cytotoxic or hormonal agents, novel systemic therapies such as immunologically directed therapies (vaccines, antibodies), gene therapy, angiogenesis inhibitors, apoptosis inhibitors and differentiating agents
- Phase I, II or III clinical trials of promising therapies administered systemically

5.5 Combinations of Localised and Systemic Therapies Examples of science that would fit:

- Development and testing of combined approaches to treatment
- Clinical application of combined approaches to treatment such as systemic cytotoxic therapy and radiation therapy
- 5.6 Complementary and Alternative Treatment Approaches Examples of science that would fit:
 - Discovery, development, and clinical application of complementary/alternative treatment approaches such as diet, herbs, supplements, natural substances or other interventions which are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses

5.7 Resources and Infrastructure Related to Treatment Examples of science that would fit:

- Informatics and informatics networks; for example clinical trial networks and databanks
- Mathematical and computer simulations
- O Specimen resources (serum, tissue, etc.)
- Clinical trial groups
- O Epidemiological resources pertaining to treatment
- O Statistical methodology or biostatistical methods
- Drugs and reagents for distribution and drug screening infrastructures
- O Centers, consortia, and/or networks
- Education and training of investigators

CANCER CONTROL, SURVIVAL AND OUTCOMES RESEARCH

- 6.1 Patient Care and Survival Issues
 - Examples of science that would fit: • Quality of life
 - Pain management
 - O Psychological impacts of cancer survival
 - O Rehabilitation
 - Reproductive issues
 - Long term morbidity
 - Symptom management, including nausea, vomiting, lymphedema, neuropathies, etc.
 - Prevention of treatment related toxicities and sequlae including symptom management, prevention of mucosities, prevention of cardiotoxicities, etc.

6.2 Surveillance

Examples of science that would fit:

- Epidemiology and End Results Reporting (e.g., SEER)
- Surveillance of cancer risk factors such as diet, body weight, physical activity, sun exposure, tobacco use
- Analysis of variations in risk factor exposure by demographic or other factors
- Registries which track incidence, morbidity and/or mortality related to cancer
- Trends in use of interventional strategies
- O Method development for risk factor surveillance

6.3 Behaviour

Examples of science that would fit:

- O Behaviour medicine research and interventions
- Influence of social factors, such as, community, policy, education, and legislation, on behaviours related to cancer control
- Attitudes and belief systems and their influence on psychological health and on behaviours related to cancer control. For example, how beliefs can alter attempts to seek screening, detection, and treatment
- Interventions to change attitudes and beliefs that affect behaviour related to cancer control and cancer outcomes
- Influences of attitudes and beliefs on compliance to treatment and prevention protocols
- Psychological or educational interventions to promote behaviours that lessen treatment-related morbidity and promote psychological adjustment to the diagnosis of cancer and to treatment effects
- Burdens of cancer on family members/caregivers and psychological/behaviour issues

6.4 Cost Analyses and Health Care Delivery

Examples of science that would fit:

- Analyses of cost effectiveness of methods used in cancer prevention, detection, diagnosis, prognosis, treatment, and survivor care/support
- Studies of providers, such as geographical or caresetting variations in outcomes
- Effect of reimbursement and/or insurance on cancer control, outcomes and survival support
- $\,\circ\,$ Access to care issues

6.5 Education and Communication

Examples of science that would fit:

- Development of communication tools and methods
- Education of patients, health cares providers, at-risk populations, and general population about cancer
- Communication to patients regarding therapeutic options
- Educational interventions to promote self-care and symptom management
- Communicating cancer risk to underserved populations, at-risk populations, and the general public
- Alternative teaching methods to communicate therapeutic options and risk reduction behaviour to patients or the general public
- Communication of lifestyle models that reduce cancer risk, such as communication of nutrition interventions
- Communicating smoking and tobacco cessation interventions
- Special approaches and considerations for underserved and at-risk populations
- Education, information, prevention/screening/assessment systems for the general public or primary care professionals
- Training, predictive cancer models, pain management, and surveillance systems for primary care professionals, telehealth/telemedicine applications
- Communication regarding cancer genetics, managed oncology care, communicating with survivors
- O Barriers to successful health communication

6.6 End of Life Care

Examples of science that would fit:

 End of Life Care issues including palliative care, psychological interventions with families at end of life, hospice care, pain management for terminally ill patients, etc.

- 6.7 Ethics and Confidentiality in Cancer Research Examples of science that would fit:
 - O Informed consent modeling and development
 - Quality of Institutional Review Boards (IRB)
 - Protecting patient confidentiality and privacy
 - $\,\circ\,$ Research ethics
- 6.8 Complementary and Alternative Approaches for Supportive Care of Patients and Survivors Examples of science that would fit:
 - Hypnotherapy, relaxation, transcendental meditation, imagery, spiritual healing, massage, biofeedback, etc., as used for the supportive care of patients and survivors
 - Discovery, development and testing of complementary/alternative approaches such as diet, herbs, supplements or other interventions that are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses
- 6.9 Resources and Infrastructure Related to Cancer Control, Survival and Outcomes Research Examples of science that would fit:
 - Informatics and informatics networks
 - Clinical trial groups related to cancer control, survival, and outcomes research
 - Epidemiological resources pertaining to cancer control, survival, and outcomes research
 - Statistical methodology or biostatistical methods
 - Surveillance infrastructures
 - Centers, consortia, and/or networks
 - Education and training of investigators

SCIENTIFIC MODEL SYSTEMS

- 7.1 Development and Characterisation of Model Systems Examples of science that would fit:
 - Development and characterization of model systems, including but not limited to:
 - Computer simulation model systems and computer software development
 - In vitro models systems
 - Cell culture model systems
 - Organ and tissue model systems
 - Animal model systems such as drosophila and c. elegans, zebra fish, mouse, etc.

7.2 Application of Model Systems

Examples of science that would fit:

- Application of model systems, including but not limited to:
- Computer simulation model systems and computer software development
- In-vitro models systems
- Cell culture model systems
- O Organ and tissue model systems
- Animal model systems such as drosophila and c. elegans, zebra fish, mouse, etc.

7.3 Resources and Infrastructure Related to Scientific Model Systems

Examples of science that would fit:

- Models made available for distribution to the scientific community
- Centers, consortia, and/or networks
- Education and training of investigators.CSO Partners' Disease Specific Codes

SITE SPECIFIC

Adrenocortical Cancer Anal Cancer Bladder Cancer Bone Cancer (includes Osteosarcoma and Malignant Fibrous Histiocytoma) Brain Tumour Breast Cancer Cervical Cancer Chordoma Cancer Colon and Rectal Cancer Endometrial Cancer Eye Cancer, (not including: Retinoblastoma) Gall Bladder Cancer Heart Cancer Hodgkin's Disease Kaposi's Sarcoma Kidney Cancer (including: Wilm's Tumour) Laryngeal Cancer Leukaemia (including: Acute Lymphocytic Leukaemia, Acute Myeloid Leukaemia, Chronic Lymphocytic Leukaemia, Chronic Myeloid Leukaemia and Hairy Cell Leukaemia) Liver Cancer (including: Bile Duct and Hepatocellular Cancer) Lung Cancer (including: Mesothelioma) Melanoma Myeloma (including: Plasma Cell Neoplasm, Waldenstrom's Macroglobulinemia & Multiple Myeloma) Nasal Cavity and Paranasal Sinus Cancer Neuroblastoma Non-Hodgkin's Lymphoma **Oesophageal** Cancer Oral Cavity and Lip Cancer **Ovarian** Cancer Pancreatic Cancer Parathyroid Cancer Penile Cancer Pharyngeal Cancer (including: Hypopharyngeal Cancer & Oropharyngeal Cancer) Pituitary Tumour Prostate Cancer Retinoblastoma Salivary Gland Cancer Sarcoma (including: Chondrosarcoma, Ewing's Sarcoma, Fibrosarcoma, Osteosarcoma, Rhabdomyosarcoma, Soft Tissue Sarcoma & Uterine Sarcoma) Skin Cancer Small Intestine Cancer Stomach Cancer Testicular Cancer Thymoma, Malignant Thyroid Cancer Vaginal Cancer Vulvar Cancer

NOT SITE SPECIFIC

Fundamental Research (includes fluids, secretions, milk, lymph, blood components, cells, cell fractions, tissues, strains, and experimental tumours) All Sites Primary of Unknown Origin

CSO		% OF CSO CATEGORY	% OF TOTAL SPEND		
Biolog					
1.1	Normal Functioning	61.03	25.03		
1.2	Cancer Initiation: Alterations in Chromosomes	9.03	3.70		
1.3	Cancer Initiation: Oncogenes and Tumour Suppressor Genes	11.40	4.67		
1.4	Cancer Progression and Metastasis	7.26	2.98		
1.5	Resources and Infrastructure Related to Biology	11.28	4.63		
Aetiol					
2.1	Exogenous Factors in the Origin and Cause of Cancer	26.20	4.30		
2.2	Endogenous Factors in the Origin and Cause of Cancer	31.27	5.12		
2.3	Interactions of Genes and/or Genetic Polymorphisms with				
	Exogenous and/or Endogenous Factors	23.66	3.88		
2.4	Resources and Infrastructure Related to Aetiology	18.86	3.10		
Preve					
3.1	Interventions to Prevent Cancer: Personal Behaviours that Affect Cancer	Risk 15.26	0.37		
3.2	Nutritional Science in Cancer Prevention	6.52	0.16		
3.3	Chemoprevention	12.14	0.30		
3.4	Vaccines	5.73	0.14		
3.5	Complementary and Alternative Prevention Approaches	1.20	0.03		
3.6	Resources and Infrastructure Related to Prevention	59.14	1.44		
Early					
4.1	Technology Development and/or Marker Discovery	21.31	1.72		
4.2	Technology and/or Marker Evaluation with respect to				
	Fundamental Parameters of Method	8.02	0.65		
4.3	Technology and/or Marker Testing in a Clinical Setting	31.95	2.58		
4.4	Resources and Infrastructure Related to Detection, Diagnosis or Prognosi	s 38.72	3.12		
Treatr	ment (22%)				
5.1	Localised Therapies – Discovery and Development	2.39	0.52		
5.2	Localised Therapies – Clinical Applications	6.73	1.46		
5.3	Systemic Therapies – Discovery and Development	39.38	8.53		
5.4	Systemic Therapies – Clinical Applications	12.65	2.74		
5.5	Combinations of Localised and Systemic Therapies	1.29	0.28		
5.6	Complementary and Alternative Treatment Approaches	0.19	0.04		
5.7	Resources and Infrastructure Related to Treatment	37.38	8.10		
Cance					
6.1	Patient Care and Survival Issues	21.03	1.19		
6.2	Surveillance	8.72	0.49		
6.3	Behaviour Related to Cancer Control	11.63	0.66		
6.4	Cost Analyses and Health Care Delivery	12.55	0.71		
6.5	Education and Communication	15.04	0.85		
6.6	End of Life Care	3.12	0.18		
6.7	Ethics and Confidentiality in Cancer Research	0.00	0.00		
6.8	Complementary and Alternative Approaches for	0100			
2.0	Supportive Care of Patients and Survivors	0.58	0.03		
6.9	Resources and Infrastructure Related to Cancer Control.	2.00			
0.7	Survival and Outcomes Research	27.34	1.54		
Scientific Model Systems (5%)					
7.1	Development and Characterisation of Novel Model Systems	21.01	1.00		
7.2	Application of Novel and Existing Model Systems	75.72	3.60		
7.3	Resources and Infrastructure Related to Scientific Model Systems	3.27	0.16		