The hidden assassin

Cancer in the UK:
a guide for donors and grant-makers

- One in three of us will be diagnosed with cancer in our lifetime – there are more than 270,000 new cases diagnosed annually in the UK, and over a million people living with cancer here.
- One in four will die of it – there are over 150,000 deaths each year in this country.
- Mortality rates are falling, however, by almost 12% during the last 25 years, a period that has seen incidence rise by nearly 24%.
- Increasing incidence is partly the result of an ageing population – cancer primarily a disease of old age. 65% of cancers are diagnosed in people over 65 years of age; as we get older, so cancer risk increases.
- Nonetheless, an increasing number of younger people are also getting cancer, and of those who die before retirement age, more than one in three will die of cancer. The loss of these people to their families will of course be huge; but there is a cost to the overall economy, too, from lost output, of around £600 million each year.
- Cancer arises from a combination of genetic defects, lifestyle factors – such as diet, smoking, drinking and exercise habits – the environment in which we live and, especially in the developing world, pollution and infectious disease – and chance.
- It is a disease where a single cell amongst the body's hundred billion, having suffered genetic damage, begins to divide in an uncontrolled way, invading and destroying healthy tissue around it to become a tumour which, left untreated, will ultimately spread throughout the body.
- The problem is huge, the interventions many. In this report we look at treatment, mainly the preserve of the state, but with a growing number of charities supporting it, providing services from bone marrows to information help-lines; palliative care (also the subject of a separate NPC report), where the state and voluntary sector work together to provide hospices and home care; and research, where a long-established charitable sector is increasingly working with the state to improve cancer prevention, detection and, of course, treatment.
- We estimate that although well over £5 billion is spent on cancer each year in the UK, principally by the state, but also by charities and pharmaceutical companies, the desired outcomes of the various interventions are fairly simple: the improvement of quality of life and/or quantity – prolongation – of life.
- Philanthropists have a long history in this field – from the private founding of hospitals and hospices, through the setting up of the Imperial Cancer Research Fund early last century to the funding of supportive and palliative care in more recent years. Yet future funding opportunities remain many and compelling in treatment, palliative care and research alike.

Written by:
Dinah McKenzie
Justin Alexander
Iona Joy

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Introduction

'*Doctor Thomas sat over his dinner,*
Though his wife was waiting to ring,
Rolling his bread into pellets;
Said, 'Cancer's a funny thing.

Nobody knows what the cause is,
Though some pretend they do;
It's like some hidden assassin
Waiting to strike at you.'

W H Auden, from the poem *Miss Gee* *

Many of us will succumb to cancer at some point during our lives. All of us will know someone living with the disease, and several who have died from it – its ubiquity a stark fact of the modern world. So what, if anything, can philanthropists do to improve the picture? *The hidden assassin: Cancer in the UK* seeks to explore the extent of the disease in Britain, and to look at the various interventions to treat and support cancer patients, present and future, made by the voluntary sector and the state – in the hope of pointing up the places where funders can make a difference.

The purpose of this report

This report aims to be a practical guide for donors interested in funding projects to help those affected by cancer in Britain. Its purpose is to provide the information and analysis required more fully to understand the extent of the issue**,** the types of response offered by the state and by voluntary sector organisations, and the outcomes generated by those various interventions. It is addressed to all donors – from private individuals, who may be relatively new to the subject, through to grant-makers with extensive experience in the area. When we refer to 'donors' we include grant-makers, private individuals, companies or anyone else wishing to donate funds or to provide grants, goods or services.

Funding projects in this field can be far from straightforward, first because there are over a thousand cancer charities in the UK, and then since it is not always apparent where private funding is most appropriate, and which cancer services should be financed by the state. We consider it vital, therefore, that donors be well informed about the field as a whole before making funding decisions, and have aimed to show opportunities for philanthropy across the piece. Detailed reports on specific organisations are available to assist in grant-making and NPC is happy to discuss these, should a funder wish to develop grants.

The scope and content of this report

The report is based on research carried out through extensive meetings with voluntary and state organisations, scientists, doctors, businesses and policy makers. We have made use of primary research, charities' reports and evaluations, and interviews with experts in the field. Owing to the enormous range of work in this field being carried out in the UK, it should be noted that organisations are mentioned as examples, and omission does not imply a negative assessment by NPC, no more than inclusion need imply a recommendation.

The report is divided into sections covering background, interventions and outcomes. Section 1 provides background material on the extent and nature of cancer in Britain. Sections 2, 3 and 4 examine interventions in treatment, palliative care and research respectively, with Section 5 looking at the outcomes from those interventions and Section 6 setting out our conclusions. Appendix 1 lists the charities and institutions that we have visited – a list which is by no means exhaustive, given the multitude of cancer charities in Britain – and those assessments and recommendations we have made on individual charities and projects are contained in supplementary reports. Appendix 2 is a table showing incidence, mortality and survival rates for the UK's greatest cancer 'killers', and Appendix 3 a look at those cancers individually. A glossary, acknowledgements and endnotes follow.

**Collected Poems* by WH Auden, reproduced by kind permission of Faber and Faber Ltd.

Section 1: Background

Cancer arises from a combination of genetic defects; lifestyle factors – such as diet, smoking, drinking and exercise habits; the environment in which we live – and chance. The risk of cancer increases as we get older, so it is no surprise that with an ageing population such as the UK's, incidence has risen almost 24% over the past 25 years.[1] Mortality rates are declining, however, down by nearly 12% over the same period[2], due to better treatments and earlier detection and diagnosis thanks to greater education and improving awareness of the population. Globally, however, mortality rates are rising alongside increasing incidence, especially in developing countries, where there are neither the resources, nor often the political will to provide the levels of treatment and education we experience here.

What is cancer?

Cancer is a disease where the body's cells grow in an uncontrolled way, invading and destroying healthy tissue, and leading in the majority of cases, still, to death.

We look at the biology and progression of cancer on page 16, but to summarize: the human body is made up of many different tissues, forming our organs, skin and bones, which in turn are made up of millions of cells, each one directed by its underlying genes. If a single cell amongst the body's hundred billion begins to behave abnormally, and instead of dividing only when the body needs it – for repair or growth – starts dividing too fast, a mass of cells can be formed – a tumour. Tumours need not always be cancerous – lumps often turn out to be benign – but where they are cancerous, or malignant, if left untreated, the expanding mass of cells invades the healthy tissue around it. Ultimately, the tumour begins to metastasize, or to spread through the body via the lymphatic and blood systems, causing secondary cancers in the various organs.

There are many types of cancer, but they all stem from faulty genes misdirecting a single cell in the body, so that it proliferates to form a tumour.

First recognised as a disease in ancient Greece – from where it gets its name, carcinoma, the crab, of which the Latin form is cancer[3] – cancer arises from a combination of genes, environment and chance. The likelihood of contracting it increases with age, partly because cancer takes many years and sometimes several decades to develop, and partly because medical advances in other areas are keeping us alive for longer than ever before. And so 65% of cancers occur in people over 65 years of age – and one in three of us in the West can expect to receive that diagnosis over the course of our lives. In the UK, one in four of us will eventually die from it, cancer deaths now exceeding those from coronary heart disease.[4*]

There are over 200 distinct types of cancer[5] and many more sub-types, so that cancer can affect every tissue in the body. 95% of cancers are the so-called solid tumours, such as lung, breast, colo-rectal, stomach, liver and prostate.[†] Tumours can originate either in the surface membranes of the body (for example the skin or the gut), in which case they are termed carcinomas – by far the most common type of tumour – or from within the connective tissue (such as bone cartilage or muscle), in which case they are known as sarcomas, or, more rarely, from brain tissue – gliomas. The remaining 5% of cancers are often known as blood cancers, affecting the blood (leukaemia) and the lymph system (lymphomas) – between them these two forms represent over half of child and adolescent cancers.

Cancer is very hard to deal with – adaptable and autonomous, a tumour will always 'fight' to survive any treatment. Great strides have been made in treating some cancers – especially the blood cancers, breast cancer and, to a lesser extent, prostate cancer (improvements in these cancers being the main reason for falling UK mortality rates), but overall, mortality from cancer remains high, with just over half of those diagnosed with the disease here dying within five years.[6]

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[*] In 2001 there were over 150,000 deaths from cancer and over 120,000 from coronary heart disease. All heart and circulatory diseases together led to 245,000 deaths, representing 40% of all UK deaths in 2001, while cancer represented a quarter of all deaths that year.

[†] In order of global incidence.

Incidence, mortality and survival

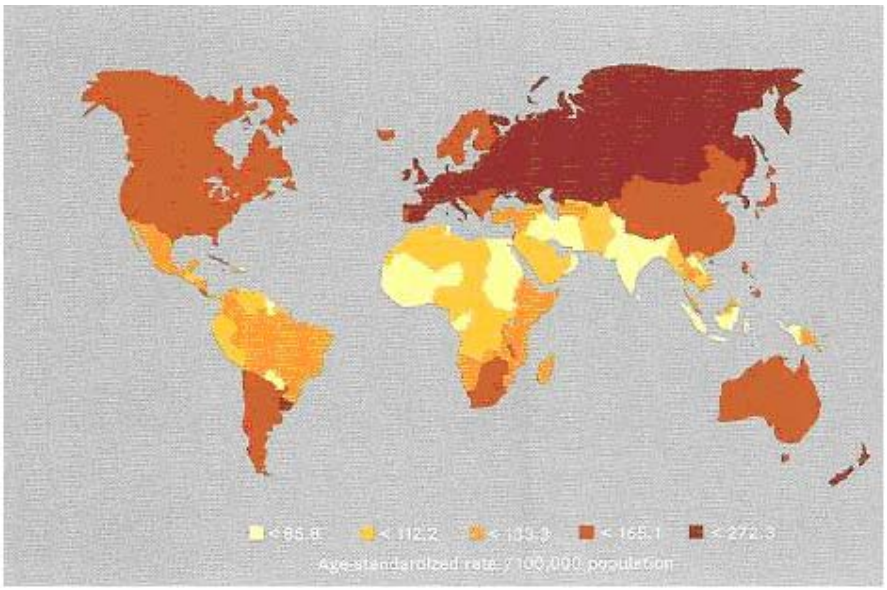
The global picture

According to the World Health Organisation (WHO)'s *World Cancer Report*, published in 2003, there were just over ten million new cancer cases diagnosed in 2000, and around 22 million people living with the disease worldwide. There were over seven million deaths from cancer – accounting for 12.5% of all deaths[7] – making cancer the third most common cause of death worldwide, after cardiovascular and infectious diseases.

Globally, 10 million new cancer cases are diagnosed each year.

These figures are rising – global cancer incidence is up 19% over the decade, with mortality up 18%.[8] Cancer is a growing problem not only in those nations with ageing populations such as ours, but also in the developing world, where mortality rates are currently half as high, but increasing, whereas Western death rates have begun to decline, albeit slowly.

Figure 1: Mortality rates in men for all cancers (excluding non-melanoma skin cancer)



Source: WHO World Cancer Report: The global burden of cancer

If current levels of incidence are extrapolated alongside population growth, the WHO expects to see 15 million new cases annually by 2020.

Increased incidence in developing countries is largely a result of increasing levels of cancer-causing factors as varied as infectious disease, environmental and workplace pollution and, above all, drinking and smoking – the World Bank, for example, predicting in 1999 that the number of smokers globally, then 1.1 billion, would reach 1.6 billion by 2025. Africa, Latin America and the Caribbean, and South East Asia (excluding Japan) all see populations increasingly at risk from cancers associated with these factors, particularly lung, stomach, liver and cervical cancer. Moreover, in those nations where economic growth is beginning to have a Westernising influence on lifestyles, recognisable patterns of the prostate, breast, lung and colo-rectal cancers so prevalent in the West are also developing. But whereas cancer patients in the West have a 50% likelihood of surviving for five years or more, the comparable figure in the developing world is 20%.

At the moment, the most common cancers globally (excluding non-malignant skin cancers) are lung (12.3% of all cancers), breast (10.4%) and colo-rectal (9.4%),[9] although since the latter two are relatively easy to diagnose and treat, the major causes of death from cancer worldwide are lung (17.8%), stomach (10.4%) and liver (8.8%) cancers, all of which have poor prognoses.

If growth in the world population is extrapolated alongside the growth in cancer incidence, the WHO predicts that 2020 will see 15 million new cancer cases, a 50% increase on today's number. This is due in part to the ageing populations and relatively unhealthy lifestyles of Western countries, in part to the prevalence of smoking (especially in less developed nations), and to continued pollution in the developing world, parts of which also suffer high levels of cancer-causing infectious disease.

Much of the global cancer burden could be prevented by increased spending on education and screening – late diagnosis a major cause of high mortality rates in the developing world.

Of these 15 million cases, the WHO argues that one third could be prevented – largely if education on diet and especially on tobacco were successful.* A further third could be successfully treated were there sufficient political and corporate will to provide funding – governments increasing resources not just for treatment but to improve screening and diagnosis, and pharmaceutical companies becoming more generous with cancer drugs, as has happened with AIDS.† As for the remaining third, the WHO argues that those who will not survive the disease could and should enjoy a better quality of life, and death, with pain relief and palliative care – even in very poor nations.

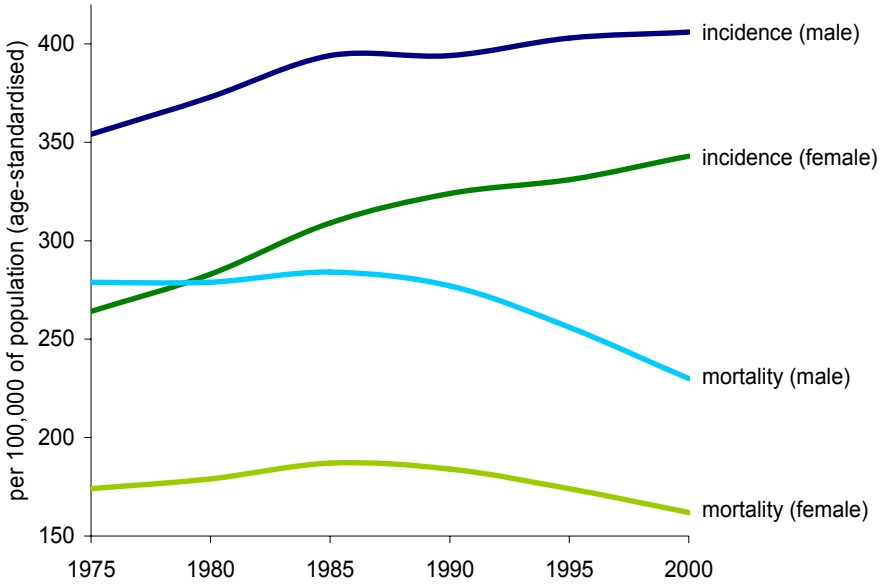
National Cancer Control Programmes, co-ordinated by the WHO, are attempting to turn the tide of increasing cancer incidence. However, many of the countries most in need of systematic cancer programmes have neither the political will nor the health or educational infrastructure so to do. Therefore it seems likely that the current pattern of growing incidence but slowly declining mortality in the West and a steady increase of both incidence and mortality in the developing world may well persist through our lifetimes and into those of our children.

The UK

As in the US and Europe, one in three UK citizens can expect to be diagnosed with cancer over the course of a lifetime, and around one in four to die from it – though mortality rates here do not compare over-favourably with other Western nations.

Cancer incidence is increasing in the UK – inevitably, given our ageing population – but mortality rates have begun to decline.

Figure 2: Cancer incidence and mortality in the UK over the past 25 years‡



Source: Cancer Research UK

As far as the **incidence of cancer** in the UK is concerned, around 270,000 new cases were diagnosed in 2000[10], split between the various types of cancer as shown in Figure 3 below.

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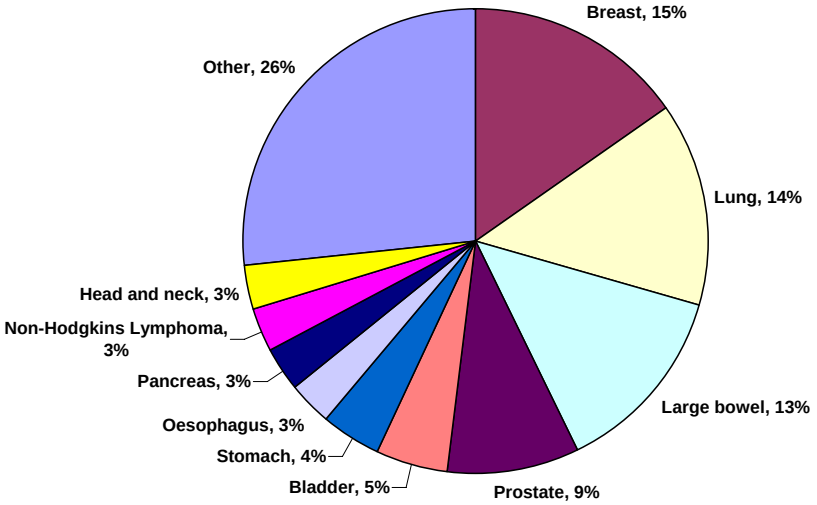
* The WHO is consequently about to adopt the Framework Convention on Tobacco Control in all its member states – we will look at prevention in Section 2.

† Raphael Bengoa, the WHO's Director of Management of Non-Communicable Diseases, is eloquent on the initiative to persuade pharmaceutical companies to improve access of developing nations to cancer drugs.

‡ 'Incidence' excludes non-melanoma skin cancer.

*Figure 3: UK incidence rates (2000)**



Source: Cancer Research UK

Incidence rates of lung cancer have fallen over the past 25 years, but colo-rectal, breast and especially prostate cancer numbers have all risen.

If we compare these figures with those from 25 years ago, the first and most obvious change is the sheer rise in cases over the period, from just over 180,000 new cases in Great Britain in 1975 to 264,000 in 2000 (this excludes Northern Ireland, which had no national cancer registry until 1993). This is an increase of almost 50% in absolute numbers, reflecting a rise in underlying incidence of almost 24%† – partly due to improvements in diagnosis, and to the increased efficiency of cancer registry data collection, but also an indication, were one needed, of our ageing population, one, moreover, where continual medical progress leads to increasingly successful treatment of other disorders.

Secondly, it is interesting to note the shift in the type of cancer diagnosed. In 1975, lung cancer was the most common cancer in men, with over 30,000 cases diagnosed, against 12,000 cases of colo-rectal and 8,000 prostate cancer. Of course these figures are somewhat distorted – the past figures flattered by today's improvement in diagnosis, so that we're more aware these days, and earlier on, too, of when someone has cancer. Nevertheless, following the introduction of the PSA blood test, prostate cancer became for the first time in 1999 the most common cancer in men (24,300 cases, against 23,000 men diagnosed with lung cancer), its incidence rising as that of lung cancer falls following the sustained public health campaign against smoking.‡

Cancer incidence in women has risen by 30% over the past 25 years, against a 15% increase for men – although more men than women still die from cancer each year in the UK.

Sadly, that message appears not to have had the same impact on women, where the decrease in smoking rates has stalled (with rates actually rising in younger women), and lung cancer incidence is increasing, from 23 cases per 100,000 women in 1975 to 36 in 2000. For women overall, however, breast cancer remains by far the most commonly diagnosed cancer, with 40,000 cases in 1999, followed by 16,500 colo-rectal cases and 14,500 lung. And the incidence of breast cancer continues to rise, by around 1% each year, its current rate probably now more than 1 in 9 women, which compares with around 1 in 14 in 1975. This is the primary reason for the growing overall cancer incidence in women, from 264 per 100,000 women in 1975 to 343 per 100,000 in 2000, a 30% increase over the last 25 years. Male incidence, happily, is rising more slowly, from 354 to 406 per 100,000 men over the period, a smaller increase, of 15%.[11]

Incidence of cancer in the UK is rising, then, and given our ageing population we cannot expect that trend to change any time soon, despite considerable efforts being made in prevention – indeed a June 2004 report, *Cancer 2025*,[12] predicted a trebling of the number of people living with cancer in the UK, from one million now to three million by 2025.

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* Again, excluding non-melanoma skin cancer.

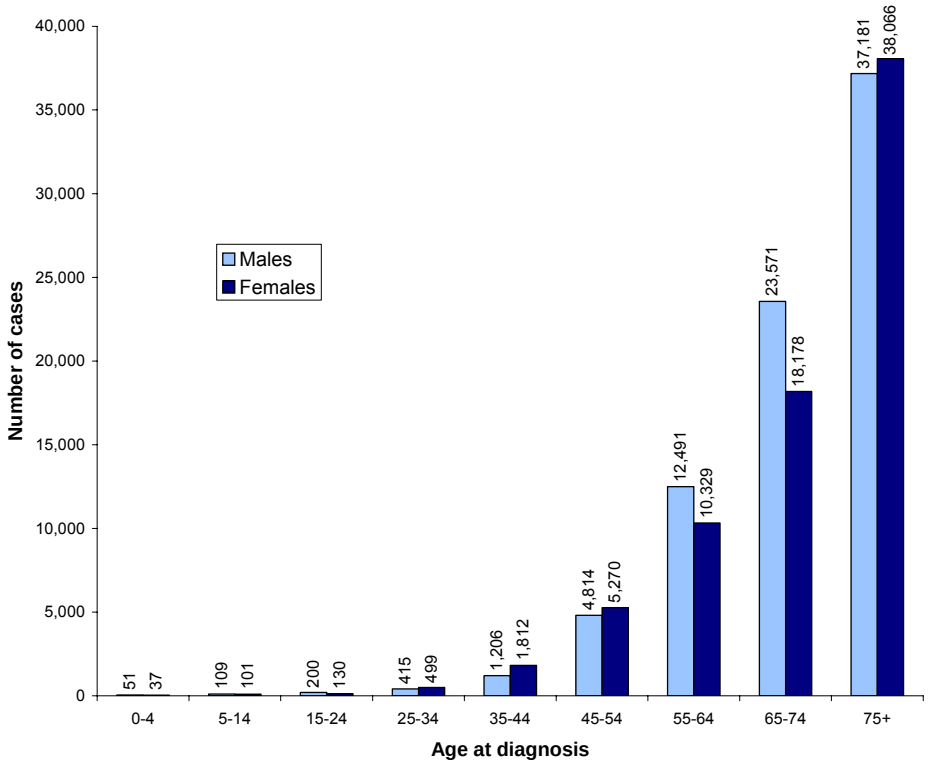
† From 295 per 100,000 of the population in 1975 to over 365 per 100,000 now.

‡ Appendix 1 contains detailed UK incidence and mortality figures for the most common cancers.

Mortality rates, however, are falling, though not as far or as fast as in other Western nations – if we have a one in three chance of being diagnosed with cancer in the UK, we still have a one in four chance of dying from it.

The latest available figures show that 154,460 people died from cancer in the UK in 2001.[13] Three-quarters of those deaths were of people over 65 years of age (and more than half the total deaths – some 75,000 in 2001 – were of people of 75 or over). For the 37,000 people dying each year before retirement age, the proportion of deaths from cancer is relatively high – just over one in three (36%) of this age group dying from cancer. In men, the percentage of 'early' deaths due to cancer is 30% and in women 45% – that is almost one in every two early female deaths is due to cancer, much of this because of breast cancer, where survival rates are improving, but incidence still rising.

Figure 4: Deaths from cancer in the UK, 2001 by age and sex



Source: CR-UK Cancer Stats

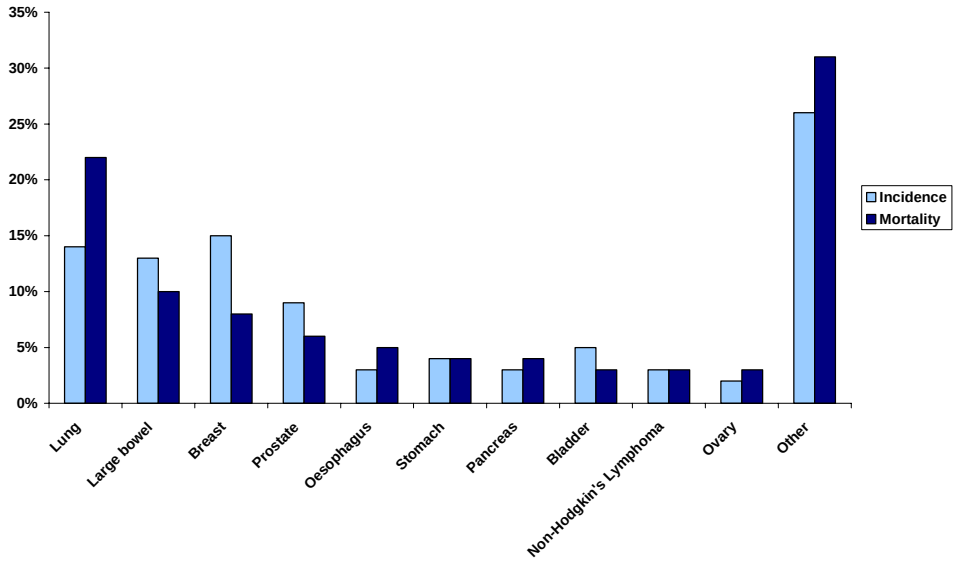
One in four UK deaths is from cancer, but one in three early deaths (i.e. before retirement age) is from the disease, and one in every two childhood deaths is from cancer.

Any death is sad, of course, but these relatively high proportions of 'early' deaths from cancer are particularly so. Not just for the family and friends of the patient – that goes without saying – but also for the nation. Around 500 children and adolescents die from cancer each year – this figure representing half of all childhood deaths – with tens of thousands more dying before retirement age. If we assume that of those 37,000 people, almost all of working age, three quarters would have been working and contributing to the economy, the remaining quarter maybe looking after a family. On an average wage of around £20,000, that represents a loss to the economy, broadly speaking, of around £600 million each year after these deaths in 2001 until retirement was due. Plus a further £600 million for the 37,000 'early' deaths in 2002, and so on.[14]

The four most commonly diagnosed cancers (breast, lung, prostate, colo-rectal) are still the four most common causes of death, though not necessarily in the same order, reflecting the relatively early diagnosis and relative efficiency of treatment for breast and prostate cancers. We look at this more closely in Section 2, and again in the separate pages on each cancer in Appendix 3.

The four most common cancers – lung, breast, colo-rectal and prostate – account for just over half of annual cancer diagnoses in the UK, and just under half of cancer deaths.

Figure 5: UK incidence (2000) and mortality (2002) rates[*†]



Source: Cancer Research UK Cancer Stats[‡]

Lung cancer is still the biggest killer, at 22% of all cancer deaths, although it accounts for 'only' 14%, which points up the difficulty of treatment – even though 22% is lower than at any time in recent history. For decades, the UK had the highest male lung cancer incidence and mortality rates in Europe, and was second only to the US worldwide. Lung cancer deaths in males peaked in the early 1970s – the legacy of the previous 30 or so years – at around 110 per 100,000 men, the rate almost halving since then, given widespread publicity on the link between smoking and the disease. The picture for women is not so rosy, however –- although rates have never been as high as for men, the incidence of lung cancer in women has been rising steadily over the past 25 years, and mortality rates are almost a third higher than in 1975.

Breast cancer, on the other hand, while also seeing a high incidence rate – 15% of all cancers diagnosed in this country, a rate which continues to increase – has a much lower mortality rate, 8% of cancer deaths, thanks to the strides made in education, detection and treatment over the past 20 years. Of course, with over 1,000 breast cancer deaths each month, the problem is far from 'solved', but the dramatic falls in mortality – 20% over the last decade – are significant in a field where progress in other solid tumours is won only slowly.

Mortality rates are falling overall – more quickly for men, where the rate of death from cancer has fallen more than 17% over 25 years, than for women, where the decline is less than 8%.

Colo-rectal or bowel cancer, with an incidence of 13% – a rate increasing in men but static in women – represents 10% of cancer deaths, its mortality rate falling by around a third since 1975. Here too, the improvement is due to improved detection and treatment – an improvement that should continue with the forthcoming introduction of nationwide screening. Similarly, prostate cancer, the fourth biggest 'killer', where incidence is rising rapidly (from 33 per 100,000 men in 1975 to around 80 now), largely as a result of the new and controversial methods of detection discussed in Appendix 3 – but mortality is rising far less quickly (from 20 deaths per 100,000 men in 1975 to 26 per 100,000 now).

Overall, then, although the absolute number of deaths is rising – from 134,000 in 1975 to over 150,000 today – the rate of death has fallen, from 214 per 100,000 then to 189 per 100,000 in 2002, down almost 12%. As with incidence, the picture is rosier for men than for women – cancer mortality rates are still higher in men (230 per 100,000 men against 161 per 100,000 women), but are falling more rapidly (comparable figures in 1975 were 279 and 174). Figure 6 shows how mortality rates in the UK have been declining steadily, albeit slowly, over the past decade.

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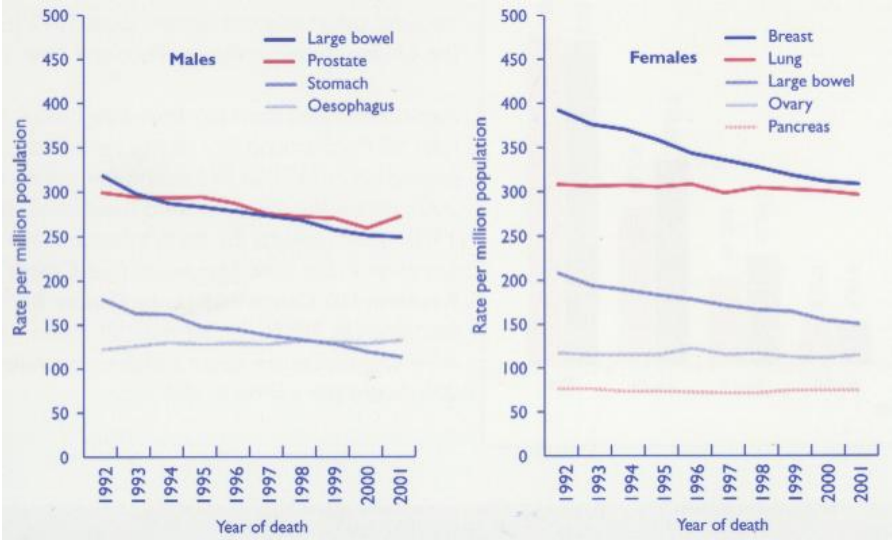
[*] Incidence generally refers to the number of cases diagnosed (see glossary)

[†] Again, excluding non-melanoma skin cancer.

[‡] More than half of these 'other' cancer deaths caused by (in descending order): cancer of the bladder, leukaemia, brain, kidney, head and neck, myeloma, liver and malignant melanoma.

Figure 6: UK mortality rates for some cancers, 1992-2001



Source: Cancer Research UK Cancer Stats

This is an encouraging picture, although **survival** rates here are relatively low in comparison with other Western countries – rates for men are heading towards the average, but those for women still below. And in the more deprived parts of the UK they are lower still – an unskilled worker is believed to be twice as likely to die of cancer as a professional – this partly due to differing regional levels of affluence, diet and, especially, smoking patterns, and partly to wealthier social groups being more knowledgeable about the risks of cancer and the benefits of screening, and more vocal in obtaining early diagnoses and, sometimes, better, quicker treatment in our so-called postcode lottery of care.

Survival trends are also improving, albeit slowly, towards European levels, although not yet to US levels – although the chasm between survival rates for different social groups here still gives much cause for concern.

The 2003 European Cancer Conference, ECCO 12,[15] led to stories in the press that the UK's cancer survival rate was higher only than Denmark's in Europe, at 37.1% of men and 50.8% of women still alive five years after cancer was diagnosed (five years is the traditional yardstick for measurement of cancer 'survival') against comparative European figures of 40.5% and 53.6% respectively. These numbers might be misleading, however. This is partly because the UK is one of the few countries in the world to have complete cancer registration data[*], while many European countries have only partial data – figures for France and Germany, for example, being extrapolated from 3% and 2% of the population respectively[16], and so might not be truly representative. It is important to note, too, that the UK figures might also suffer from the fact that, in the 1990s, we had the highest proportion of over-65s in our population in Europe,[17] as well as the fact that, as many UK cancer specialists argue, since we do not screen for cancers that may well never present in a person's life, but which appear as 'cured' in countries which do (prostate cancer, for example), UK figures suffer by comparison. Whatever the truth behind headlines such as these, they are nevertheless sobering, and prompted the Health Secretary, John Reid, to observe, correctly, that these data stemmed from the period before the 2000 introduction of the Cancer Plan, and to reiterate the government's determination to reach European levels of survival by 2010.

More sobering still are comparative survival figures from the US, where maybe five times as much is spent on cancer treatment per patient, and where the American Cancer Society reports survival rates rising steadily over the past three decades, from 50% of patients diagnosed between 1974 and 1976 and still alive five years later, to 60% of those diagnosed between 1989 and 1996.[18] Again, though, we must be wary of statistics. The US figures are somewhat unrepresentative – first of all this data is not complete, being extrapolated from nine states. Secondly, it is largely based on patients with medical insurance, who tend to enjoy better survival rates[19] – the exigencies of the medical insurance industry mean that its clients are better screened than we are in the UK, which not only brings huge benefits in terms of early diagnosis, but also means that many cases of non-life-threatening prostate cancer, for example, are included in these statistics, which distorts the survival numbers.

Notwithstanding these caveats, it does look as though overall UK survival rates are lower

[*] This information is gathered by the UK Association of Cancer Registries, recording every case of cancer, and is so full that it represented a third of the overall European numbers in the Eurocare survey.

than those in the US and probably still lower than a European average, albeit improving slowly overall (though more slowly in the more deprived groups than less deprived).* The reasons for the UK's relative underperformance are shortcomings in each part of the cancer 'journey'. Traditionally we have been less aware of risks to our health – our lung cancer problem is witness to that, and largely responsible for our relatively high mortality rates – and an over-burdened health service with out of date equipment and too few oncologists has meant that speed of diagnosis and treatment has not always been guaranteed. In simple terms, we present to GPs later than elsewhere, are diagnosed later[20] – later still if we come from less affluent social groups – and as a nation spend a smaller proportion of GDP on health than most comparable countries, as we shall see in Section 2. We will also then discuss the introduction of the Cancer Plan – in which it is freely admitted that cancer patients here have poorer survival prospects than elsewhere in Europe.

Causes of cancer

There is no one single cause of cancer, the disease arising from a combination of our age, lifestyle and environment and the effect of all of these on our genes – and chance.

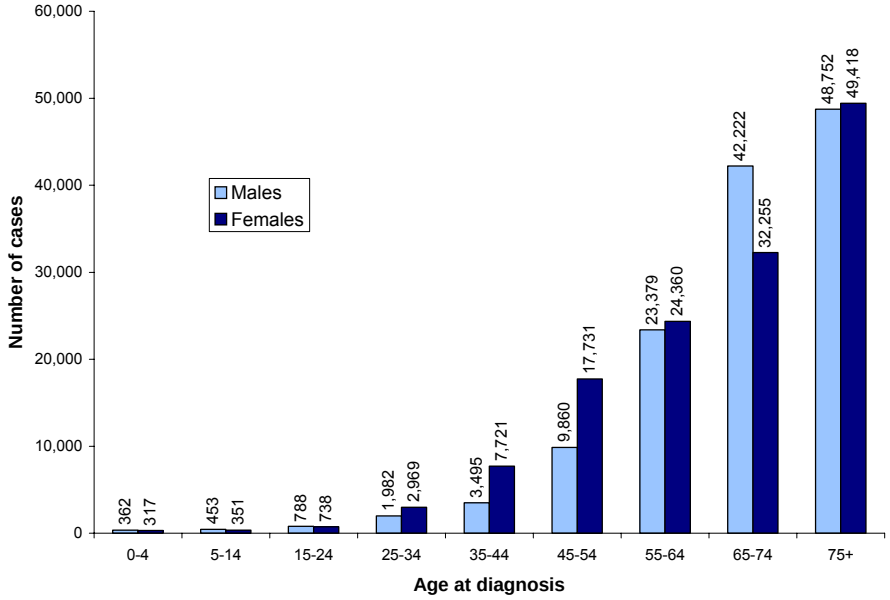
Our genes can cause cancer either alone or in combination with other factors. Lifestyle and environmental factors – those we can control, such as smoking, what we eat, the amount (of alcohol!) that we drink and our exposure to the sun. And those factors which in general we cannot control, or certainly many people cannot – exposure to pollutants at work and in life generally, where air, water or the earth itself may be polluted, or infection rife.

Age

There is no one single cause of cancer – many factors play a part, among them age…

Age is the most common factor when cancer is diagnosed. In the UK, 65% of those diagnosed with cancer, and 75% of those who die from cancer, are over 65,[21] increased cancer risk correlating with increasing age.

Figure 7: New cancer cases in 1999 in the UK, by age and sex



Source: CR-UK Cancer Stats

Why? Partly because more people live until old age in the West than ever before – the strides made in medicine over the past century have diminished the risk of our dying young – and partly because with each passing year there is a greater likelihood that genetic changes in our bodies and/or past exposure to carcinogens will catch up with us, and a lesser likelihood of our DNA repair systems being able to cope.

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* A 2004 study from the London School of Hygiene and Tropical Medicine showed the 'deprivation gap' in survival of many cancers still widening, with survival rates of poorer groups sometimes five years behind those of their richer peers.

Hereditary/Genetic Susceptibility

The WHO estimates that inherited cancer genes may account for around 5% of all cancers. While most cancers occur anew in a person – the damage to his or her genes known as 'somatic' mutations, which are not heritable – our genetic make-up can also influence the risk of our getting cancer. Most cancers can 'run in families' – a fact that has been noted for well over a century but only properly understood much more recently. Scientists are now capable of isolating the genes responsible for a cancer occurring in a family, identifying them and even, in some cases, beginning to screen for them. This may become an especially important screening method because inherited cancers generally occur at an earlier stage in the patient's life than other cancers, and so often cause early death.

The best known of the inherited 'mutant' genes are probably the BRCA1 and BRCA2 genes, responsible primarily for breast and ovarian cancers (5% of all breast cancers, in fact), but occasionally also colon, prostate or pancreatic cancer. Unusual though they are – one in a thousand people may carry the BRCA1 gene – the risk of cancer for those with that mutation can be high. A woman carrying a mutated BRCA1 gene will have a 70% increase in the risk of developing breast or ovarian cancer, compared with a woman without the mutation.[22]

…hereditary susceptibility and our dietary habits – smoking, excessive drinking, too much consumption of meat and animal fats, too little of fruit and vegetables.

Tobacco

Tobacco use is the leading cause of death from cancer globally, accounting for over a million deaths each year.[23] It is identified by the WHO as the major preventable cause of death worldwide, causing not only lung cancer but other respiratory and vascular (heart) diseases, so that one in two regular smokers will probably be killed by the habit, half of these in middle age.[24] Prevention will always be an uphill struggle, however, with world production of tobacco close to seven million tonnes a year, a major industry supplying global demand ranging from an estimated 60% of adult men in China down to 22% of American women. Fewer than 30% of men or women now smoke in the UK, compared with 65% of men and just over 40% of women in 1948.[25] While consumption is declining in the Western world, it continues to rise in developing countries (see Appendix 3 on lung cancer for details), leading the WHO to predict an 'epidemic' of lung cancer in the coming decades.

Of course, most tobacco-related cancer deaths are from lung cancer, although tobacco consumption also causes tumours of the larynx, pancreas, kidney, bladder, and (if plenty of alcohol is also consumed) cancer of the mouth and oesophagus – tobacco smoke containing over 4,000 different chemicals,[26] over 40 of them carcinogenic.[*] Passive smoking – continual exposure of non-smokers to tobacco smoke – can also increase the risk of lung cancer, heart disease and, in children, respiratory diseases, asthma or possibly even cot death.[27]

Diet

Up to 30% of cancers may be related to diet and nutrition, according to the WHO's 2003 *World Cancer Report*, which echoes the concerns of Professors Doll and Peto in their seminal 1991 work, *The Causes of Cancer*.[28] The risks are fundamentally threefold: a Western diet high in protein and animal fat combined with a sedentary lifestyle, too much salt, and not enough fruit and vegetables.

Epidemiological studies[29] show a link between high consumption of meat, particularly red and processed meats, with colo-rectal cancer.[†] Why that should be has not been conclusively determined – some scientists believing that it is because meat and/or fat consumption influences the production of bile, others that carcinogenic compounds form during the cooking of meat. The link between other proteins and fats with cancer is less clear, however. Despite received wisdom, and plenty of studies, the only consistently observed link is between animal fats and colo-rectal cancer – indeed consumption of a vegetable oil such as olive oil may be associated with a reduction in risk. Nor are food additives proven to correlate with increased risk of cancer – and so the primary cancer risk from a 'Western' diet appears to stem from over-consumption of red meat, often combined with a sedentary lifestyle and its concomitant 'energy imbalance', and low intake of fruit and vegetables.

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[*] Tobacco smoke's particulate matter – or tar – contains thousands of compounds, of which nicotine is the most prevalent, at up to 2 mg per cigarette, but there are many others, including benzene and heavy metals.

[†] It is thought that daily consumption of 80g of these may increase the risk of colo-rectal (large bowel) cancer by 25% for red meat, 67% for processed meats.

Of the studies into nutrition, the most consistent results relate to fruit and vegetables. Over 250 epidemiological studies have been carried out in recent decades, around 80% of which[30] have shown a link between consumption of some types of fruit and vegetables and a reduced risk of cancer of the pharynx, larynx, lung, oesophagus, stomach and cervix.[*] How? Probably through the interaction of the constituents of fruit and vegetables – vitamins, minerals and fibre – with the process of carcinogen metabolism and communication between cells. Vitamins C and E, carotenoids and possibly selenium have an antioxidant effect – inadequate intake of vitamin C, for example, is linked to increased risk of cancers of the stomach, mouth, pharynx and oesophagus – low levels of B6 and folic acid probably linked to risk of colo-rectal cancer, low zinc with oesophageal cancer.[31]

Studies into salt intake[32] show an increased risk of arterial hypertension and of stomach cancer. Although salt consumption and therefore the cancer's incidence are declining in the West due to education and new methods of food production – not least the advent of refrigeration – in developing countries, especially in Asia, this is still a problem. Food contamination has also been linked with cancer, although just how many cancers are attributable to this is hard to quantify. In the developing world, some contaminants arise naturally, often due to inadequate storage; in the West we are more concerned with pesticide residues on crops and, increasingly, given our lifestyles, with carcinogenic hydrocarbons sometimes caused by certain cooking methods, notably barbeques.

Alcohol

Around 3% of all cancers (4% in men, 2% in women) are thought to be linked to excessive alcohol intake. Epidemiological studies have established a causal link between drinking alcohol and oral, oesophageal and liver cancers as well as some breast cancers and, possibly, colo-rectal cancer.[33] As with tobacco smoking, the risk of cancer rises with the amount of alcohol consumed.[†] Those countries with relatively high consumption levels – France, where the WHO estimates that an adult drinks almost 15 litres of alcohol (pure ethanol) annually against an estimated global average of four litres, Germany, the US and Russia all see a relatively higher incidence of head and neck cancer. As with smoking, although alcohol consumption seems to be declining in Western countries (though not in the UK, where it is rising towards eight litres annually[34]), it continues to rise in the developing world.

The good news is that, whilst epidemiological studies point up the correlation between excessive drinking and cancer, it does seem increasingly clear that moderate intake of alcohol – usually defined as a single alcoholic drink each day – has a beneficial effect on cholesterol levels and is correlated with a decreased risk of heart disease in the elderly.

Indeed our very lifestyle is suspect – and we see increased cancer incidence in people migrating to the West compared with levels in their countries of origin.

Lifestyle

A **sedentary lifestyle** and/or **obesity** also seem to increase the risk of cancer – Cancer Research UK believes that around 5% of cancers in women and 3% in men could be avoided if people kept to a healthy weight. Studies[35] have shown a correlation between excess body mass[‡] and incidence of such cancers as endometrial cancer in women, and colon and gastric cancer in both sexes. (Interestingly, breast cancer risk appears slightly to lessen in obese women pre-menopause, increasing again afterwards.) Colon and breast cancers seem to be more common in those with a sedentary lifestyle – physical activity linked, for example, with a 50% lower risk of getting colon cancer.[36] The worrying trend in lifestyle choice – whereby we eat ever bigger quantities of ever less nutritious food, while exercising ever less – leads CR-UK to predict that by the middle of the next decade we may see up to one third of cancers caused by obesity, as is already the case in the US.

Along with some other medicines (discussed below), **hormone treatments** may cause some cancers, as may the hormonal patterns of our chosen lifestyles, especially in the West. The risk of breast cancer, for example, is significantly increased by high and prolonged levels of oestrogen in the body – some of these influenced by lifestyle choices not available to previous generations. So, probably more at risk are women who take the contraceptive pill for long periods of time; who either have no children, or late first pregnancies, or, possibly, those who choose not to breast feed once they do have children; women who start to

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[*] See Figure 11 in Section 2

[†] Accelerating rapidly once more than the equivalent of a bottle of wine is drunk in a day, regularly.

[‡] Your body mass index is calculable by dividing body weight in kg by height in metres squared. A result of over 25 indicates overweight, over 30 is obese, and it is estimated that 47% of men and 33% of women are overweight in the UK, with obesity creeping toward the 20% mark in both sexes.

menstruate very early or who reach the menopause late, or, again only possibly, take HRT (hormone replacement therapy) on reaching the menopause.

The huge increase in numbers being diagnosed with malignant melanoma due to **exposure to sunlight** could also be included under lifestyle, and in many cases that may be correct, especially where sunbeds are concerned, but such is scientific concern over increasing levels of ultraviolet light that it will be discussed below, under 'radiation'.

Environmental risks – pollution

The WHO estimates that 1-4% of cancers globally are linked to pollution – of the air, of water and of the soil itself by carcinogenic pollutants such as those in asbestos (dealt with under 'workplace risks', below) or some pesticides (notably DDT)[37], chlorination by-products in water and toxic agents in air. Many cancers are associated with these pollutants – lung cancer the most clearly linked with polluted air, and water and soil pollution primarily with bladder cancer, but also with cancers of lung, liver, colon and kidney.

We are fortunate in this country to have the knowledge, not to mention the wealth to ensure that environmental pollutants such as these are increasingly under control, with the introduction of emission controls and the outlawing of asbestos – although urban areas still have higher incidences of lung cancer than do rural communities.[38] In developing countries increasing amounts of traffic using untreated fuels see rising levels of vehicle emissions, particularly in urban areas, alongside the by-products of electricity production from burning coal, wood and even animal dung. Indoor air pollution is a problem in many parts, too. There are high lung cancer rates in parts of south-east Asia among women who do not smoke but who spend much of the day inside a home – the effect due to smoke from heating or cooking fuels or even, in some parts of China, from heated cooking oils.

There are cancer risks in our environment too – from radiation and carcinogenic pollutants…

– radiation

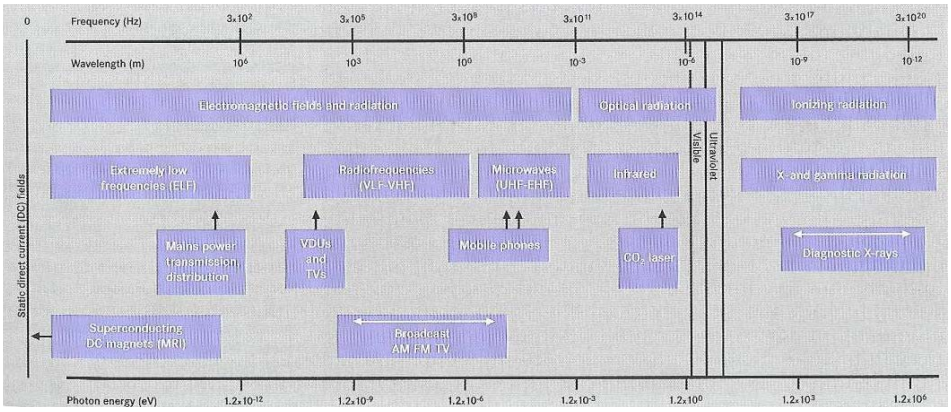
Exposure to radiation from natural, as well as industrial and medical sources can cause cancers such as malignant melanoma, leukaemia, breast and thyroid cancers.

The primary natural source of radiation is of course the sun, 5% of whose radiation is ultraviolet, which can cause malignant melanoma and non-melanocytic skin cancer via damage to the body's cells. Incidence is growing fast, especially in countries with hot climates populated by fair-skinned people – in Australia the incidence is 41 and 32 per 100,000 men and women, respectively, the highest in the world. In the UK, incidence is still around 10 per 100,000 in both sexes, but is seeing the most rapid growth of all the cancers (in England and Wales rates were four times higher for men and three times higher for women in 1997 than in 1971)[39] largely because of the increase in foreign holidays in the latter part of last century. Altogether, malignant melanoma causes around 1% of all cancer deaths in the UK each year – the number of people diagnosed with usually non-fatal non-melanocytic (basal cell and squamous cell carcinomas) skin cancer much greater, over 100,000 annually.

As far as man-made radiation sources are concerned, the greatest risk is from 'ionizing radiation', or X and γ (gamma) rays, where the highest-energy electromagnetic radiation is powerful enough to produce ionization, and thus break chemical bonds. Although present in natural sources, we are most at risk from man-made radiation – X-rays, radiography and radiotherapy, and from nuclear accidents and/or fallout – the most horrific example of which was the dropping of the atomic bombs on Hiroshima and Nagasaki, where those who survived the explosion were exposed primarily to gamma rays, many of them suffering leukaemia, breast and thyroid cancers as a result, some decades after the bombing.

Further down the spectrum, fear is growing about cancer from lower frequency electromagnetic fields, such as those used in mobile telephony. While there is some evidence of increased levels of childhood leukaemia linked with electrical power transmission – enough for the International Agency for Research on Cancer (IARC) to classify extremely low frequency fields as possibly causing cancer in humans – no link has yet been proven between cancer and radiofrequency fields, though research is ongoing.

Figure 8: The spectrum of electromagnetic fields and their use in daily life



Source: WHO World Cancer Report

Workplace risks

…and risks in the workplace, although this is lessening in the West. Of great concern to the World Health Organisation are the growing levels of cancer-causing infectious disease, particularly in the developing world.

Ever since the unusual incidence of scrotal cancer in chimney sweeps was noted some 200 years ago, scientists and doctors have been aware of the possibility of cancer from exposure to carcinogens in the workplace. Carcinogenic chemicals are numerous; IARC recently identified 25 chemicals definitively as human carcinogens and a further 25 as probably so,[40] going on to classify various occupations as definitively, probably or possibly carcinogenic – for example, hairdressing and dry cleaning in the latter two categories and a host of industrial jobs in the former. Those employed in paint manufacture, for example, and painters (some 200,000 workers and several million respectively, worldwide)[41] consistently show unwontedly high levels of lung cancer, which cannot just be explained by smoking, but is due to exposure to the chemicals in paint. Many plastics are suspect, too.

The WHO estimates that cancers resulting from workplace exposure represent 4-5% of global cases, with lung cancer the main threat. As with environmental risk, the risk of workplace exposures is decreasing in the West, particularly following the well-documented findings on asbestos in the middle of the last century, as we learn about the risks and implement employment strategies to deal with them, but still growing in the developing world alongside growth in industrial production, particularly in smaller, unregulated operations.[*]

Infectious disease

Infectious disease is a major cause of cancer – the WHO estimates that it is responsible for 18% of cases globally, the vast majority of these in developing countries. Viruses are the principal agents of cancer here, especially the hepatitis B and C viruses (hepatitis B thought responsible for 60% of primary liver cancer globally, hepatitis C a further 25%),[42] HPV, the human papilloma virus (cancers of the reproductive organs in men and women, especially of the cervix) and Epstein-Barr virus and HIV (lymphomas). As far as bacterial infections are concerned, *Helicobacter pylori* is one of the most prevalent globally, linked with gastric cancer, and, in Egypt, bladder cancer has been linked to contaminated drinking water.

Some medicines

It is worth mentioning, briefly, that, as with radiation treatment, some drugs may, while treating disease, cause cancer – even some cancer drugs, while treating primary tumours, may cause secondary tumours. This is well known by doctors, however, who take care with such doses, as they do when transplanting organs using immunosuppressive drugs – suppression of the immune system being another cancer risk.

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[*] The threat from asbestos, for example, has partly decreased in the West since asbestos production has moved to Brazil, India, Pakistan and Korea where, as the WHO gently puts it, 'health and safety standards may not be so stringent.'

The biology and progression of cancer

We are aware of many of these risks in the UK – yet how does cancer actually happen? And how does it develop? There follows a brief introduction to the progression of cancer, and before that to the molecular and cell biology involved, where our knowledge is growing apace – from the first understanding that cancers are composed of cells in the 1800s, through the work of Crick and Watson on DNA in the 1950s to the sequencing of the human genome in 2000.

The cell is the basic unit of all living things, with the ability to differentiate, from stem cells, into particular types of cells around the body, and also to replicate, by division, for growth and repair. In the centre of each cell is its nucleus, which contains two complete sets of the human genome[*] – one from the mother, one from the father – paired and wound into a double helix, its DNA.[†]

Each strand of DNA contains over 30,000 genes on 24 chromosomes[‡], the individual genes 'encoded'[§] to control the formation of proteins by the cell, by specifying the linkage of a sequence of amino acids. And, since over 100,000 proteins are the basic building blocks of our bodies – from the tough collagen that forms connective tissue and bone, through the fluid haemoglobin that carries oxygen through our bodies, to thousands of enzymes and hormones that drive our body chemistry – the excitement that accompanied the first mapping of the human genome in 2000, its popular name 'the code of life' for once not hyperbole, is easily understood.

Cancer is caused by DNA – our genetic material – that has been damaged either by external carcinogens or internal mutation.

Cancer is characterised by DNA that has been damaged – damage that in maybe 5% of cases is inherited, but which more commonly occurs through genetic mutation either from 'mutagens', the external carcinogens discussed earlier, or during internal replication – and of course, the longer we live, the more likely such damage is to be sustained. Often, mutations may have no detrimental effect on the function of a gene – indeed they may alter its properties for the better, which is how species evolve and adapt over time. Sometimes, however, mutations may cause defective gene function and hence lead to disease – to cancer, in this case, where it is believed that an accumulation of defects in five or six genes is responsible, causing a cell to divide abnormally and to begin to grow out of control.

The great mystery of how cancer can develop and proliferate in an uncontrolled way is largely explicable in the light of our increasing understanding of the two main types of cancer genes that can mutate – oncogenes and tumour suppressor genes. Oncogenes, which encode proteins promoting growth without any external stimulus, are over-active in cancer cells, allowing them autonomy and immortality. Tumour suppressor genes (of which perhaps the best known is p53, implicated in up to half of advanced cancers), on the other hand, are under-active in cancer cells – their normal function, of detecting DNA damage and stopping uncontrolled cell division by inducing cell death lost, so that they are unable to slow the formation of a tumour.

From the malignant transformation of a cell, that cell begins to proliferate to cause a tumour – probably doubling 30 times to form a tumour of one gram, at which point it becomes clinically detectable and is known, medically, as a Stage 0 carcinoma.[43 **]

Nonetheless, a primary tumour such as this can still be non-invasive, as long as it has not moved outside its membrane, shown below, and can be surgically removed. Once the tumour has spread beyond the cell's membrane, however, and become a Stage I and then Stage II cancer, not only does it destroy the healthy tissue surrounding it, but it can and almost always will metastasize,[††] or spread around the body. Cells begin to break off from the tumour and float in tissue fluid, which drains out into the lymphatic channels, which ultimately return the fluid (now called lymph) to the bloodstream – making effective treatment correspondingly now more difficult.

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[*] Except in sperm and egg cells, which have one each, and red blood cells, which have none.

[†] Deoxyribonucleic acid, or more simply, nucleic acid.

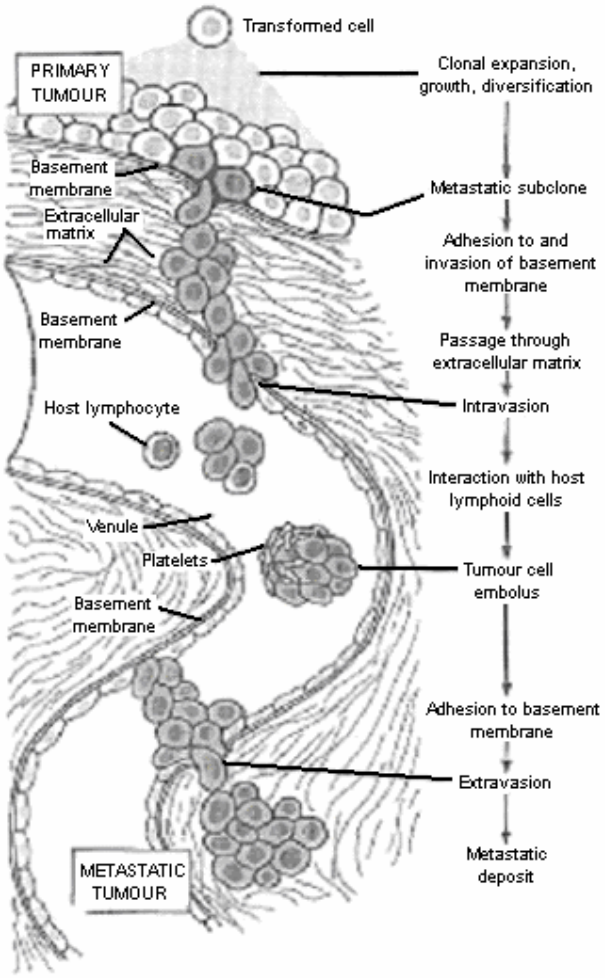
[‡] Numbered 1 to 22, plus the x and y sex chromosomes – males have an X and a Y, females, two Xs.

[§] In different series of four chemical substances, abbreviated to A,T,C and G

[**] From this point, it would only take a further 10 doublings for the tumour to reach a mass of one kilogram.

[††] Except for malignant brain tumours and basal skin carcinoma

Figure 9: The growth and metastasis of a tumour



Source: Robbins Pathologic Basis of Disease, 4th edition

Cancer takes years to develop. During the process many cancer cells apoptose – or self-destruct. But it takes only one to start a tumour, which if unchecked can, and almost always will, metastasize or spread around the body.

On its journey, the lymph passes through glands called lymph nodes, which filter out dead cells and infection. Cancer cells are usually trapped in the lymph nodes nearest to the cancer, where most die – though it takes only one cancer cell to survive to begin to grow in the gland, forming a secondary tumour – Stage III of the cancer. Later, cancer cells move through the lymph nodes to reach the bloodstream, from where they are carried to the body's major organs – though not necessarily the organs nearest to the primary cancer site. It is now understood that surface proteins on cancer cells home in on corresponding cell surface markers or organ 'targets' (prostate cancers tend to metastasize to bone, lung cancers to the brain, and so on). Again, some of these cells will die, others will survive to form further secondary tumours – Stage IV, or metastatic cancer – after which effective treatment becomes very difficult indeed.

And it is the treatment of cancer in the UK we discuss next, examining the roles of both state and voluntary sectors in dealing with such a mammoth problem: 270,000 new cases each year and rising, in tandem with our ageing population.

Section 2: Interventions: Treatment

Having discussed the increasing incidence of cancer in Section 1, we now turn our attention to how the disease is dealt with. Unlike some countries, the medical treatment of cancer in the UK is a virtual state monopoly, but there are nonetheless important roles the voluntary sector can play in supplementing and, especially, supporting the work of government. Charitable donations fund interventions as direct as the provision of additional staff or equipment in NHS hospitals; through many support services, ranging from the provision of bone marrows, to information and counselling, to grants for patient holidays; to education, largely on prevention, and advocacy of patient rights. Thus, charitable interventions are very often enmeshed with state responsibilities, and so to gauge the former we must understand the latter, and immerse ourselves first in the NHS, and the state provision of cancer treatment in the UK.

Structure of the NHS

Founded in 1948 by Attlee's post-War Labour government, the NHS, for the first four decades of its existence, was run by a centralised bureaucracy. In 1990 the Conservative government introduced an internal market in which 'purchasers' (health authorities and some GPs) were given budgets to buy health care from 'providers' (hospitals and care homes, mental health and ambulance services). The New Labour government planned to abolish the internal market in 1997, feeling that competition was damaging the character of the NHS, but in fact took a 'third way' approach of retaining the market but adapting the system to encourage more collaboration.

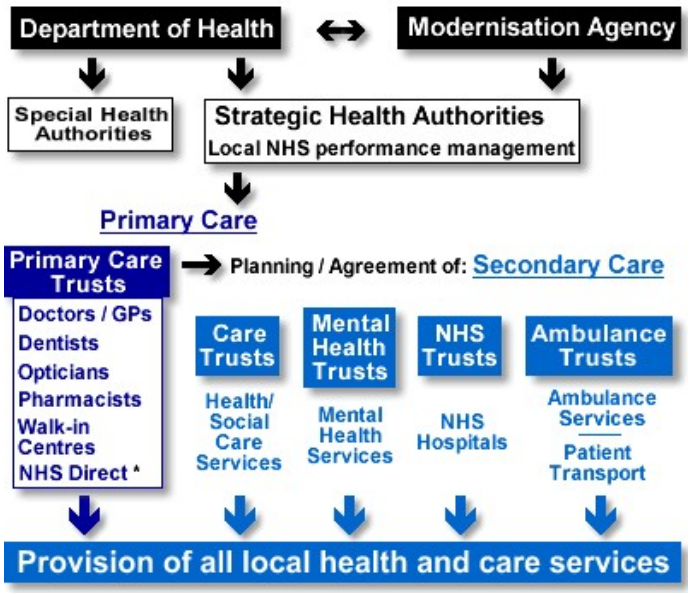
The NHS, restructured at the turn of this century, spends over £74 billion a year – 6.8% of our GDP, proportionally less than most comparable countries.

In 2000 the NHS Plan was published, outlining commitments to increase spending on health significantly and at the same time modernise the system, to be overseen by the new Modernisation Agency. The most radical component of this, thus far, was the *Shifting the Balance of Power* programme in April 2002, which localised decision-making by abolishing the 95 Health Authorities and devolving 75% of the NHS budget to 302 Primary Care Trusts (PCTs), each serving populations varying in size from about 60,000 to 340,000.[44] 28 Strategic Health Authorities (SHAs) were created at the same time, to help co-ordination and to provide a check on the performance of the PCTs. While most of the 'secondary care' purchased by a PCT comes from local NHS hospital trusts, the PCT is free to purchase services from wherever it chooses, including the private sector or NHS hospitals outside of its geographic area. Each PCT is governed by a Board, which is advised by a Professional Executive Committee comprising local health professionals, including GPs, nurses, public health specialists, representatives of the professions allied to medicine, and representatives of the social services department.

Foundation hospitals are the latest development in NHS structures, intended as a third way option between the public and private sectors. They are being set up as public benefit corporations, giving trust managers more freedom over local decision-making – such as an ability to borrow and to vary staff pay, which in theory will stimulate innovation and entrepreneurialism to make health services more efficient, dynamic and responsive to patients. Local people and hospital staff will be able to elect governors, who will choose non-executive directors for the trust hospital. Opponents worry that foundations will create a two-tier system in which elite hospitals get more resources at the expense of failing ones, further widening health inequalities. In particular, they fear that foundation hospitals' freedom to pay more will lead to them 'poaching' staff from other local hospitals, and that by becoming autonomous, hospitals will no longer work together so well.

The NHS budget for 2004 is estimated at £74.3 billion, an increase of 63% in cash terms from 1997 – about 38% in real terms. The share of GDP committed to health has increased over that period from 5.6% to 6.8% (a further 1.1% is spent on private health care and on pharmaceuticals and therapeutic equipment). Despite this increase, the figure is low compared with other Western nations – Germany spends 10.5% of its GDP on health, France 9.6%, Holland 8.6%. Of the major European countries, only Denmark spends a lower proportion, at 6.4%. The US spends double that – almost 13% of its GDP, around $1,700 billion in 2003[45] – a mixture of state and private funding via health insurance.

Figure 10: The structure of the NHS and how it relates to government



Source: www.nhs.uk

Cancer structures in the NHS

As far as cancer treatment is concerned, there is a further set of organisational structures, overseen by Professor Mike Richards, the National Cancer Director (or 'Czar') – a post created in the 2000 Cancer Plan. 34 Cancer Networks – each covering a population of 1-2 million people – facilitate collaboration by bringing together people from the different NHS bodies in a region. It would make organisational sense for the Cancer Networks to be contiguous with the Strategic Health Authorities, but this is not the case since the Networks were introduced earlier than the 2002 creation of the SHAs.

Of that £74 billion, maybe £4 billion is spent on cancer treatment.

Another body introduced as part of the Cancer Plan was the Cancer Services Collaborative, a branch of the Modernisation Agency focusing on redesigning cancer services and spreading best practice around the NHS through the Cancer Networks. The Collaborative has the remit to assess the performance of services, and develop ways of making them more efficient and effective. The NHS is arguably 20 years behind the commercial sector in its application of process techniques such as capacity and demand analysis, and it is hoped that modernisation will rectify this over the next several years.

A perennial concern in cancer treatment has been the 'postcode lottery' whereby patients receive different standards of treatment depending on the policies of the NHS in their area (formerly the policies of the Health Authorities, now those of the PCTs), in particular regarding which chemotherapy drugs are prescribed. To rectify this concern the National Institute for Clinical Excellence (NICE, established in 1999) has been set up partly to recommend drugs for the treatment of particular cancers, drugs which the PCTs are then required to use – a policy increasingly policed by the Cancer Czar.

It is difficult to get hold of precise figures for total government spending on treating cancer. NPC has been told, anecdotally, that it might be around £4 billion a year – equivalent to about 5% of the NHS budget. In the US, we are looking at much larger numbers – maybe 10% of overall health spending, or $170 billion[46], is spent on cancer. Medicare alone will spend almost $20 billion this year (which oncologists complain does not nearly cover the full treatment costs), and Medicare reckoned to represent one patient in three – mostly the poor and elderly. Comparable figures have been hard to track down, and are admittedly imprecise, but do indicate the scale of difference in spending. If the US indeed spends as much as 25 times as the UK on cancer treatment – or, more fairly, around five times as much per citizen – then the difference in survival rates referred to in Section 1 (and tabulated in Appendix 2) can be very readily understood.

The Cancer Plan

In September 2000 the government launched what it claimed to be the world's first comprehensive strategy to tackle cancer, by bringing together prevention, screening, diagnosis, treatment and palliative care. The initiative was motivated by evidence, first properly focused upon in the Calman-Hine report of 1995, that UK survival rates for both men and women with cancer were lower than the European average. Its goals include:

- Improving survival rates: 'By 2010, our five year survival rates will compare with the best in Europe.'[47]
- Reducing inequalities in the quality of treatment across the country – the aim to end the so-called postcode lottery, by operating consistent protocols via the Cancer Networks
- Prevention – e.g. reducing the proportion of the population that smokes from 28% in 1996 to 24% by 2010 and promoting healthier diets
- Early detection – e.g. breast screening is being extended to women up to 70, and improvements and trials are under way for the screening of other cancers (e.g. a colo-rectal pilot for 50-69 year olds is currently under way, with another for ovarian cancer to follow)
- Reducing waiting times from urgent referral following diagnosis to treatment to two months by 2005 and to one month by 2010.
- Investing a further £50m into palliative care by 2004
- Training and employing 1,000 extra cancer specialists (oncologists, cancer nurses and especially radiotherapists) by 2006
- Buying 50 new MRI machines and 200 CT* scanners and linear accelerators by 2005
- Establishing the National Cancer Research Institute to co-ordinate scientific research.

These aims are to be achieved by modernisation of cancer services (through the Cancer Services Collaborative), improved co-ordination (through the Cancer Networks) and substantial increases in resources for staff, drugs and equipment (£570 million by 2003/4).

The Cancer Plan was published in 2000 to help co-ordinate and improve cancer treatment across the country, the incoming Labour government concerned by relatively low cancer survival figures here.

The three year progress report, *Maintaining the Momentum*, has recently been published[48], hailing a 10.3% fall in death rates in the under-75s between 1995-97 and 2000-02, although given that the Cancer Plan was initiated only towards the end of this period, it is unclear how significant its contribution has been to the fall. The waiting period target still requires work, as the latest data (November 2002) shows that over a third of patients, 83,000, were waiting longer than two months from GP referral to treatment,[49] though some cancer charities criticise the use of targets in the Cancer Plan, out of concern that efforts to meet targets will result in reduced standards of care in other areas.

The major criticism of the Cancer Plan thus far, however, is that the additional money promised by the government has not filtered down, and thus treatments are still not standardised across the country. The House of Commons Science and Technology Committee's report on cancer funding warned that '…the increase in cancer care funding may not be reaching those who are relying on it to deliver the Cancer Plan. We are seriously concerned at the apparent ease with which trusts can redeploy such funds if they choose…' – the payment of NHS debts and administration mentioned as possible places where funds might have been redeployed.[50] A 2002 survey from the charity CancerBACUP revealed that almost half of the Cancer Networks had shortfalls in promised funds, some up to 25%. 80% of Cancer Networks did not expect to receive their promised allocation of funds in 2003, the majority also believing that they could be more effective if they were given direct control over their finances rather than receiving money through the Strategic Health Authorities.[51] Even when new money has gone to cancer, much of it may have been consumed by new NICE requirements to prescribe particular drugs. Hilary Thomas, Professor of Oncology at the Royal Surrey, has complained, 'It became clear that whatever extra we got could only be spent on NICE drugs. So we're giving £2,000 worth of drugs to somebody to give them six weeks of life with pancreatic cancer, but we can't improve services we need to treat people across the board.'[52]

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* Magnetic resonance imaging and computerised tomography respectively.

In response to these concerns, the government launched a tracking study in January 2003 to establish what happened to the Cancer Plan money.[53] The study concluded that although the additional 2001/2 spending fell £81 million short of the £280 million target, by 2002/3 the spending had caught up with the target of £407 million for that year. NHS restructuring was blamed for some of the confusion over tracking funding flows. The currently pledged funding may well be insufficient, and the Wanless Review recommended that the NHS spend an additional £1.3 billion on cancer services and equipment by 2005/6, in order to 'deliver the standards set out in the Cancer Plan.'[54] Radiotherapy is one field which requires significant capital investment, and the government reports that between April 2000 and January 2003 54 new linear accelerators, 116 new CT scanners and 35 new MRI scanners have been installed, representing between a third and a half of installed capacity in each of these areas.[55] Fair prescription of NICE-recommended drugs also needs work – the National Cancer Director reporting in June 2004 that wide variations in the provision of 16 important drugs persist between the Networks. The solution to this is less likely to be more money, however, than improved monitoring of prescriptions, to which end a system of electronic hospital prescribing will be brought forward by two years to 2006, as well as, possibly, a link between compliance with NICE guidelines and individual NHS performance ratings.

Prevention

A general criticism of Western medicine is that its search for high-tech treatments can lead people to underestimate the importance of healthy lifestyles. The percentage of cancers that are potentially preventable may be higher than the WHO's one-third – one study, comparing the variation in incidence of different cancers around the world, inferred that 80% could be prevented.[56] It is striking, for example, that prostate cancer among the black population of the southern US is 130 times as common as in the Chinese province of Qidong, while conversely liver cancer is 115 times as common in Qidong as in the Netherlands.[57] There are similar variations in incidence for most cancers, as we saw in Section 1, which implies there are causal factors for the difference in incidence rates, which could, in theory, be prevented.

Skin cancer is a good example of a cancer whose incidence can be reduced through preventative strategies – namely avoiding long exposure to direct sunlight. Skin cancer is most prevalent in Australia, because of the large numbers of whites living in an extremely sunny climate. As a result the Cancer Council of Victoria Province launched the 'Slip, slop, slap' campaign in 1980, which urged people to slip on a shirt, slop on some sunblock and slap on a hat. The campaign claims considerable success in changing attitudes and behaviour, with the proportion of Victorians who like to get a suntan decreasing markedly, from 61% in 1988 to 35% in 1998, while sunburn fell 50% over that decade. In Australia as a whole the incidence of melanoma, the most serious form of skin cancer, increased from about 17 per 100,000 of the population for both genders in 1982 to 32 for women and 41 for men more recently. The value of prevention is obvious, given that the direct health care costs of skin cancer in Australia are estimated at A$735 million each year,[58] with a further A$1.4 billion of indirect costs through sick leave and foregone earnings. An investigation of the potential cost-effectiveness of a national prevention programme modelled on Victoria's 'SunSmart' campaign concluded that a 20-year commitment of A$5 million annually would prevent 4,300 deaths at a cost of A$14,360 each[59], and if the cost were offset against reduced health care spending, it would result in a net saving of A$103 million for the government. This provides good evidence that prevention can be cost-effective, as well of course as being the most preferable result in terms of human welfare.

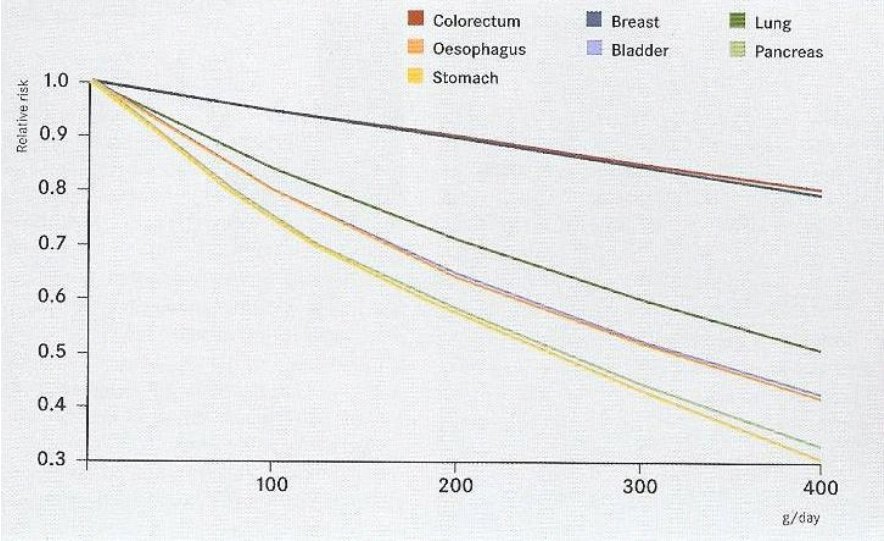
Prevention through education on health is the only way to tackle growing levels of cancer incidence.

Smoking is responsible for a high proportion of cancer deaths because lung cancer is seldom curable. The World Bank makes a chilling calculation that 'if current trends continue, about 500 million people alive today (a twelfth of humanity) will eventually be killed by tobacco, half of them in productive middle age.'[60] In the UK, lung cancer is one of the most prevalent and least treatable cancers – hence prevention is critical, which means reducing smoking. Whilst previous anti-smoking campaigns have been successful – male smoking, for example, peaking at almost 70% in the 1940s – the government would still like to cut current levels of around 27% in both sexes (which have been more or less static for a decade). Hence 1998's White Paper, *Smoking Kills*[61], which allotted £119 million over three years to smoking cessation, with the Cancer Plan later assigning a further £5 million. The aim, to cut smoking rates to 24% by 2010, is equivalent to 1.5 million fewer smokers, which would lead to a significant reduction in lung cancer deaths, albeit after some lag time. The savings are likely to outweigh the costs of the campaign.

Diet and obesity are other significant causal factors for cancer in the UK. The House of Commons Health Select Committee's May 2004 report on obesity[62] an indication that the government is beginning to focus on prevention in this area. Cancer Research UK says that

'changes in our diet could prevent about one in three cancer deaths in the UK.'[63] Red meat, alcohol and some fats can increase the risk of cancer, while regular intake of fresh fruit, vegetables and fish oils do decrease it, which is why, as part of the Cancer Plan, the government introduced the *five-a-day* campaign at the beginning of the decade, stating that 'increasing fruit and vegetable consumption is the second most effective strategy to reduce the risk of cancer, after reducing smoking.'[64] Preliminary results from the European Prospective Investigation into Cancer and Nutrition suggest that eating 500g of fruit and vegetables a day can decrease the incidence of digestive tract cancers by 25%[65], as figure 11 indicates (the chart showing vegetable consumption looks similar).

Figure 11: Correlation of consumption of fruit with reduced risk of cancer



Source: WHO World Cancer Report

Aside from regulating diet, it may be possible to reduce cancer risk by taking certain chemical and nutrient supplements. The evidential base for supplements is currently unproven, but it is thought that aspirin may reduce the risk of colo-rectal and breast cancers, while micronutrients such as β-carotene and α-tocopherol may be among the active agents in fruit and vegetables, though it is unclear whether they are effective when taken in pill form.

The common cancers of gender-specific organs – especially the uterus, breast, ovary and prostate – are influenced to varying extents by levels of sex hormones. Regular use of the contraceptive pill may increase the risk of breast and cervical cancer but also seems to be protective against ovarian and endometrial cancers. There is no clear prevention strategy here, however, since many feel the benefits of the Pill outweigh any small increase in risk.

Since infectious agents such as the viruses HPV (human papilloma virus), EBV (Epstein-Barr virus) and the bacteria *Helicobacter pylori* are causal factors in 18% of cancers globally, tackling these agents through vaccination is an effective prevention strategy in high incidence areas. Hepatitis, for example, causes 85% of liver cancers and can be easily vaccinated for,[66] just as screening for HPV can identify those at risk from cervical cancer.

Detection and diagnosis

Early detection and diagnosis are key to the successful treatment of cancer – hence the increase in screening programmes.

If cancers are detected early on, before they have grown too large or spread beyond the primary tumour, then they are easier to treat. Were every person regularly screened for most of the common cancers, it might be possible almost to eliminate the disease, although of course this would be incredibly costly and disruptive to people's daily lives. There is a case for some level of screening for the most common and easily detected cancers, however, the WHO saying that current knowledge is sufficient to enable 'the early detection and effective treatment of a further one third of cases [on top of the third which are preventable].'[67]

Currently breast cancer screening is available on request to all women over 50 in the UK, with women aged 50-64 (now being extended to 70) reminded by invitation every three years, and most women (20-64) being invited for cervical cancer screening every five years. Preparations are being made to introduce bowel and prostrate screening, and ovarian and lung screening are also being investigated, as is a further extension of the age range of

breast screening. The value of screening depends on the incidence rate of the cancer and the likelihood of successful diagnosis, weighed against the direct cost of the programme and the disruption to the lives of people being screened, which can include health risks, for example colonoscopies can damage the bowel in the search for cancer, or unnecessarily increased anxiety, for example in prostate cancer testing, discussed below.

The Cancer Plan's three-year progress report claims that the cervical screening programme saves around 1,300 lives a year, while the breast screening programme diagnoses about 8,500 cases annually, and has contributed to the 21% fall in deaths since its introduction in 1988.[68] The benefits of screening for other forms of cancer are less clear cut. Prostate cancer is a particularly controversial example – costs aside – as we will see in Appendix 3. There is prostate screening in Germany, France and Belgium, but not here in the UK. In the US, the National Cancer Institute has stated that evidence is insufficient to suggest that screening produces a decrease in mortality, whereas both the American Urological Association and the American Cancer Society have advocated annual screening for men over the age of 50.[69]

While screening can make a significant contribution to reducing cancer mortality, it is inevitably limited by its reach, infrequency or cost. For this reason it is important that the general public, particularly those in groups at risk of particular cancers, are aware of possible symptoms so they know when to consult their GPs – the Cancer Plan seeing this education as something needing work, diagnosis at more advanced stages of cancer generally being one of the reasons behind the UK's relatively poor survival rates.

GPs see on average fewer than nine new cancer patients each year[*] and are likely to see a case of testicular cancer, for example, only once every 20 years. So they refer possible cases to specialist consultants – the aim being that urgent cases are seen within two weeks, using NHS referral guidelines designed to prevent consultants being deluged by a flood of patients with cancer-like symptoms, but not cancer.[70] In a National Audit Office survey of GPs for its March 2004 paper *Tackling Cancer in England,*[71] although half of the GPs who answered found these guidelines useful, the general feeling was that maybe a third of patients ultimately diagnosed with cancer had symptoms vague enough that they were not referred urgently, thus delaying treatment. Again, the Cancer Plan acknowledges that further education is needed here, and is intent too on improving the other major bottlenecks in cancer diagnosis – endoscopy, pathology and especially radiology (scanning) services – by buying more machines for the latter and expanding training in all three.

Once cancer has been confirmed – usually by scan (from X-rays through ultrasound to CT or MRI scans) followed by biopsy – the consultant can plan appropriate treatment, ideally with the specialised multi-disciplinary team (MDT) approach formally recommended by the NHS since the introduction in the mid-1990s of IOG (improving outcomes guidance) reports.

Treatment

Having relied solely on surgery, radiotherapy and chemotherapy for decades, oncologists are beginning to use more recently developed cancer treatment. Surgery remains the treatment with the most encouraging outcomes…

The main cancer treatments are still surgery, chemotherapy and radiotherapy. Other newer treatments include hormone therapy and immunotherapy – both forms of biological targeting, the fruits of relatively recent cancer research. As with detection and diagnosis, it is a key aim to standardise treatment across the UK and tackle the 'postcode lottery' where cancer mortality is lower the more affluent the social group – a divergence particularly apparent in London and the South of England (although this can to some degree also be explained by the concomitant divergence in rates of smoking, and thus of lung cancer, between the different social groups). And so the Cancer Plan seeks to reduce waiting times from diagnosis to treatment to one month by 2010, to ensure that chemotherapy drugs recommended by NICE are consistently administered, and to buy sufficient linear accelerators – and to train more radiotherapists to operate them – to conform by 2005 to good practice delivery times recommended by the Joint Council for Clinical Oncology.

Surgery

The core of cancer treatment is still the oldest medical technique – cutting out the tumour. Given that tumours can appear anywhere, surgery can range from a routine surface removal to an intrusive and dangerous operation deep within the body, and it is standard practice to remove the lymph nodes nearest to the tumour as well, in case the cancer has spread there

[*] Given that there are 270,000 new cancer cases each year, and 30,000 GPs, and that not all diagnoses are made at the GP level.

– thus two common side effects of surgery are pain from regrowing nerves and swelling resulting from the removal of lymph nodes (*lymphoedema*). If, after removing detectable tumours, it is likely that undetectable secondary cancers (*micrometastases*) exist, a doctor may recommend additional (*adjuvant*) treatment to try and kill them before they grow big enough to be detected on a scan. Increasingly, oncologists also recommend neo-adjuvant therapy – radiotherapy or chemotherapy to shrink the tumour ahead of surgery.

Chemotherapy

Cancer chemotherapy is still a relatively recent treatment – used really only for the past 50 years, following studies of the nitrogen mustard gases used during the World Wars. There are now more than 60 cytotoxic (cell-killing) drugs of various types, from the original alkylating agents such as mustard gas to platinum-based drugs, through antimetabolites and anthracyclines, based on fungi, to natural, plant-derived alkaloids such as the taxanes, or yew-based drugs. What these treatments have in common is the propensity to kill cells that are dividing – the action which really defines cancer – but which leads to side-effects, from the relatively bearable (such as hair loss when dividing cells in the follicles are destroyed) to the extremely unpleasant (sickness and loss of immunity as the drugs kill the proliferating cells in the gut and bone marrow, for example). And so drugs are often given in combination – not just with each other, to improve efficacy and overcome the body's resistance – but alongside anti-emetic drugs such as steroids. Newer work, into gene therapy, seeks either to strengthen or to renew the patient's blood cells to increase their resistance to chemotherapy.

Chemotherapy, which is administered in six to eight 'cycles', can sometimes cure cancer – particularly in leukaemias and lymphomas, which is why so many children with cancer now survive when once they would have died. Otherwise it is mostly given to prolong survival, where it is effective in female cancers such as breast and ovarian, as well as in colo-rectal cancer – again, mortality rates for all three are declining. Where chemotherapy is less effective is in other solid tumours – lung, prostate, stomach – where it delivers months rather than years to the patients, and is of no real benefit in liver and pancreatic cancers or in malignant melanoma, where fewer than 20% of patients even respond, and then for far shorter periods.

… and the adjuvant, additional, treatments – chemotherapy and radiotherapy – while as vital as ever, are now sometimes supplemented by hormone therapy…

Radiotherapy

While there has been serious recent complaint about the availability of chemotherapy drugs recommended by NICE in different parts of the UK, it is in radiotherapy that the major treatment bottlenecks occur. Waiting times are often simply too long, due to shortages in both machinery and the staff to operate it – hence the emphasis in the Cancer Plan on investment in this field.

Radiotherapy is the other major cancer therapy – used in around 40% of patients either pre- or post-surgery – its use increasing by 16% in the past five years.[72] Ionizing radiation is delivered to the tumour via machines ranging from enhanced X-ray machines (where the radiation is 100 times more penetrating than a normal diagnostic X-ray), through cobalt machines using gamma rays, to linear accelerators, which can deliver a dose of radiation twice as deep as other machines – to 15cm inside the body – via an electron beam. These latter are radiotherapy's 'gold standard' machines, with minimal side-effects to the surface skin or the tissue around the tumour, costing around $1 million, and surpassed only by particle accelerators, which cost over 20 times as much but have an even deeper dosage capacity. Increasingly, oncologists are using brachytherapy, where the radioactive source is placed directly through or next to the tumour – only really possible where the tumour is fairly close to the body's surface, and so effective in some cervical, tongue, uterine, rectal or breast cancers.

Hormone therapy

Hormone therapy is a way of regulating cancers related to sexual hormones, such as breast and prostate cancer. Tamoxifen has been the big success story here; an anti-oestrogen that starves breast cancer tumours of the female hormones they need to grow, it is given to most patients after breast surgery, appearing to protect them from recurrence for the next five years. Research is going on at once to discover whether taking tamoxifen might actually prevent breast cancer before it occurs, and to refine the drug – Arimidex, for example, shuts down oestrogen production altogether, and seems to have fewer side-effects than its parent (for further information, see Appendix 3: breast cancer). In prostate cancers, male hormones – the over-expression, especially of testosterone, one of the causes of this cancer – can now be suppressed by luteinizing hormone-releasing hormone in preference to surgical orchidectomy (castration).

Immunotherapy

An ideal way of treating cancer would be a vaccine that would stimulate the body's immune system to locate and destroy cancer cells in the same way as it does other 'foreign bodies'. This is the basis of immunotherapy – an idea around since the 1800s, when doctors noticed some tumours shrinking in patients with bacterial infections. Its methodology is still in its infancy, however, although monoclonal antibodies (naturally occurring proteins in the body that bind to target molecules, or antigens) are being developed which could one day mark out cancer cells for destruction by the immune system, or even deliver chemotherapy drugs directly to the cancer. Several vaccines are in Phase III trials.

…with scientists constantly working on more targeted therapies. Of course some cancer patients choose not to receive conventional therapies at all.

New therapies

Targeted therapies such as tamoxifen or monoclonal antibodies point the way in which treatment is expected to develop over the next few years. The recent mapping of the human genome has accelerated the progress of cellular and molecular biologists in finding, or even predicting cancer cells, and designing agents to target their molecular features – in an ideal world, before the cancer begins to develop. We will discuss research into anti-angiogenesis, signal transduction inhibition and gene therapy in Section 4, so suffice it here to note that it is hoped that these newer therapies, when they eventually make it to the clinic, will not only to improve the outcome of treatment – prolonging the patient's life – but are fully expected to improve the quality of that life, their specific targeting reducing the number of side-effects traditionally suffered by cancer patients.

Complementary/Alternative therapies

Some cancer patients choose not to undergo conventional treatment. A high-profile example of this recently was that of Sarah Parkinson, wife of comedian Paul Merton, who died after refusing treatment for her breast cancer. She appears to have done this because the probability of success was low and she preferred to make the most of the final months of her life, rather than spend much of them in hospital, instead employing a variety of complementary medical techniques, largely in palliation. Alternative techniques do seem sometimes to bear fruit, and although many oncologists would dispute this, attributing 'miracles' to an unusual phenomenon whereby a tumour very occasionally shrinks of its own accord, many do increasingly acknowledge their importance, particularly of nutrition. *Living Proof, A Medical Mutiny* is the fascinating account of Michael Gearin-Tosh, an Oxford don who, faced in 1994 with myeloma and maybe a couple of years to live, even with treatment, he decided against chemotherapy and instead embarked upon a time-consuming but thus far successful regime. Based on the Gerson Therapy (a largely vegetarian diet, low in protein, plus coffee enemas for detoxification), Gearin-Tosh also takes many supplements, has acupuncture and does Chinese breathing exercises – and published his book in 2002!

The role of the voluntary sector

As in many areas of society, there are no precise boundaries defining the role of the state in supporting people facing cancer. The NHS provides treatment, but charitable funding can help such treatment, even up to the purchase of hospital equipment or funding of hospital staff, support the patients undergoing treatment or campaign on behalf of patients – current and future. Charities working in this area are necessarily not dogmatic about where the responsibility of the state ends and where that of the voluntary sector begins, and are happy to play a supplementary but rapidly growing role in this area. In some cases (such as support and information) this is because of a lack of resources in the state sector, in others (such as advocacy and education) because an independent voice is useful.

Cancer treatment, while largely the preserve of the state, sees the charitable sector playing a vital supportive role – occasionally providing hospital staff and equipment…

Hospital equipment and staff

Most hospitals have their own appeals offices, plus, usually, several associated charities, often set up by the families and friends of individual patients. In the US some hospitals have huge charitable funding – the oldest and largest of these the Memorial Sloan Kettering Cancer Center in New York, which raises over $250 million each year, via a very well organised fund-raising mechanism offering donors a range of giving options into specific treatment, research or education programmes, or into general funds. In Britain, although cancer treatment is handled by the NHS (and private health care) rather than the voluntary sector, there is some room for charitable involvement. In particular, non-priority equipment, staff and other services can significantly improve the well-being of patients undergoing treatment, but are not likely to be provided for out of the state budget any time soon, or, in some cases, ever.

State-of-the-art equipment is a good example of this – every hospital visited by NPC (see Appendix 1 for details) has a shopping list of hardware it would dearly love to acquire, which would improve patient treatment but for which, given entirely understandable budget constraints, it will have to wait. Consequently much of the work of hospital appeals offices is focused on harnessing local support to raise funds to buy equipment earlier than the hospital would otherwise receive it from the state. One good example, among many, is the current £2.3 million appeal at **The Royal Marsden Hospital** to buy and then house a PET/CT* scanner. These are state-of-the-art machines, using radioactive material to 'label' tissues at once to detect cancer earlier and then to monitor the effectiveness of treatment. Commonplace in the US, where around a million PET/CT scans are made each year, these machines cost £1.6 million and so are still rare in the UK – 5,000 such scans are performed annually here. The Marsden's new machine, bought this year, will bring the total of such scanners in the UK to eight – half as many as in Belgium[73], and although numbers here will increase over the years (the Cancer Czar hoping ultimately to provide one for each of the 34 cancer networks in England and Wales[74]), there is room for the sort of charitable approach that has proved successful at the Marsden.

The other main area focused upon which hospital appeals offices is staff, specifically staff additional to the Trust's NHS budget, but who might make life easier for patient and existing staff alike. An example of this is the specialist leukaemia nurse funded on NPC's recommendation at the **Manchester Royal Infirmary**. We discuss this, the Marsden's scanner and other examples of charitable intervention in detail in Section 5, noting only here that the hospital's Department of Haematology had been hoping to make this appointment for some years, but internal funds were simply unavailable. The nurse's job is an amalgam of some procedures traditionally performed by doctors and a counselling, supportive role. Her appointment has not only created more time for the doctors and nurses in the team, but has highlighted a genuine need in the hospital – which will now take over the post's funding after the initial two years – as a result of which a further two specialist nurses are to be appointed, another funded by the trust, the third by Macmillan Cancer Relief.

Indeed, **Macmillan Cancer Relief** is the major external funder of nurses' positions within hospitals – pump-priming posts with funding for an initial three-year period, its reach across the UK answering concerns some donors have that contributions to individual hospitals may be inequitable, with distribution focused on areas that are either affluent or happen to have enthusiastic fundraisers, rather than being spread across the UK according to need.

Hospital-linked services

As well as appeals for equipment and staff from hospitals themselves, there are many charities providing linked services from national to individual hospital, or even ward level.

… and routinely providing hospital - linked services.

The Anthony Nolan Trust is a register of willing bone marrow donors – bone marrow being needed mainly for leukaemia patients following the intensive chemotherapy that kills many of their white blood cells. The register has almost 350,000 potential donors, around 1% of whom will be called upon each year as a match for a patient – Nolan providing over a quarter of the bone marrow transplants made in the UK each year.

Cancer and Leukaemia in Childhood (CLIC) provides a range of services to make life more bearable for child patients and their families. Its 'Homes from Home' are free, self-catering accommodation allowing parents to be close to children undergoing treatment, while at the same time having a sanctuary away from the hospital, to recharge and receive support from other families in similar situations. CLIC also arranges fun social activities for cancer patients, and makes grants to help poor families forced to make repeated long journeys, give up work or make home alterations to care for a child with cancer – but its major service is the funding of more than 50 cancer specialists, the majority of them nurses, who care for the children both in hospital and at home. Similarly, the work of the **Ellenor Foundation** involves helping clinicians administer chemotherapy to children at home, so that they do not have to go to hospital.

The **Teenage Cancer Trust** has equipped eight hospital wards across the UK with specialist equipment and recreational facilities; its long-term aim is to equip 20 such wards, at a cost of about £750,000 each, in order to support the hundreds of children and adolescents diagnosed with cancer each year. The wards are designed to provide a non-institutional environment where children can feel relaxed and enjoy the company and support of their

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* Positron emission tomography, where radioactive tracers home in on cancer cells, which then fluoresce, overlaid by a computerised tomography scan, which shows the body's soft tissue structures.

peers, and are the Trust's main activity, although it is increasingly involving itself in educational projects for this age-group, and in advocacy. NPC has also visited **Theodora Children's Trust**, a charity sending clowns into children's wards in several hospitals across the UK, and seen games consoles and computers in many of the hospitals we have visited, provided by **Starlight Children's Foundation** and **Express-Link-Up** respectively.

While the charities NPC visits, such as these, tend to work at a national level, there are many others working locally, of which just one example is **Leuka 2000**, which has funded the building and equipping of the Catherine Lewis Centre, where Hammersmith Hospital's leukaemia patients are treated.

Information and support

Hospital-linked services such as these begin to show another dimension to the treatment of cancer: whilst hospital treatment is of course key in arresting the progression of the disease, a patient's response to treatment has a second dimension – how treatment affects physical and emotional well-being. A combination of support, information and palliative care will often be effective in addressing this – helping the patient to 'maximise the benefits of treatment and to live as well as possible with the effects of the disease. It is given equal priority alongside diagnosis and treatment'[75] – indeed sensible information can sometimes inform that treatment through patient choice. The various services offered in the UK include:

Information	Therapies	Courses, Counselling and Support
Information: publications, leaflets, on-line information	**Therapies** to combat the physically demanding side-effects of chemotherapy and radiotherapy	**Courses and coaching** on how to help live with cancer through diet, exercise, relaxation techniques etc.
Telephone help-lines providing information and support to people living with cancer, families and carers	**Complementary therapies** such as massage, aromatherapy, acupuncture	**Counselling and support groups** for patients, families and carers
Patient literacy: training and advocacy for patients in order to obtain the best from the services available	**Psychosocial therapies** such as art, relaxation, spiritual healing	**Places** to go to for support, information, counselling – either 'drop-in' or with an appointment

The voluntary sector provides most of the UK's range of information and support to cancer patients and their families…

Services such as these are provided by a wide range of charities – we estimate that such support organisations spend anything up to £50 million each year. Some are general cancer charities concentrating on a particular service or cluster of services. Others are for sufferers of specific conditions – breast cancer is particularly well served in this regard. Some charities offer 'drop-in' support, while others are residential.

CancerBACUP runs a help-line which offers telephone, e-mail or letter support to 50,000 cancer patients and their families each year. The help-lines are staffed by qualified specialist nurses, supported by a substantial library of clinical publications, and the website visited by over 230,000 each month – informing patients and enabling more informed discussions with their medical practitioners. CancerBACUP also has satellite information centres in some regional hospitals – six so far, with greater coverage planned – and has also developed a project supporting people from ethnic minorities, *Cancer in Your Language*.

Breast Cancer Care provides information on cancer services via help-lines and booklets; volunteer support and support groups; and advice and courses on healthy living. Its website is increasingly the first point of contact for many people, receiving up to 4,000 hits daily, visitors spending an average of 10 minutes on the site, which not only provides all the charity's publications online, but has a noticeboard and its own chatrooms – information and support here merging into the provision of education, as it does with many of the charities working in this field. The charity also provides practical help to cancer patients – advice about appearance and regional clinics on prosthetics after mastectomy. Such post-operational support is key to patients' rehabilitation – mental as well as physical. **Changing Faces** is another charity working here, supporting people with disfigurements, in this case after treatment for head and neck cancer, skin cancer and brain tumours – the charity providing self-help guides and counselling as well as training courses for professionals.

Macmillan Cancer Relief is particularly active in supporting people living with cancer as well as undertaking the clinical activities mentioned above. It has set up 50 Macmillan Cancer Care Centres, which offer a wide range of services, including clinical treatment, as well as other therapies and general support. The set-up costs are funded by local Macmillan appeals, but thereafter the facilities are taken over by the NHS. Macmillan Cancer Relief produces helpful publications, distributes hardship grants (totalling £5 million pa), and is jointly piloting a National Benefits Advice Line, for which it expects the demand to be very high, once it goes public. Macmillan also offers information, training and resources to over 700 cancer support groups, also supporting CancerVOICES, of which more below.

Maggie's Centres (currently three in Scotland, more planned in England) are situated close to hospital oncology units and are ideal for patients needing somewhere before or after hospital appointments to relax, talk to fellow cancer patients, find out information or discuss therapies and symptoms with nursing specialists. **Liverpool Cancer Support Centre** is another local centre offering support groups, advice, a drop-in facility and complementary therapies, though unusually in this field, it is funded from statutory sources, albeit precariously. Most of the people running the centre have been affected themselves, and the emphasis is on self-help: patients are helped in self-advocacy skills. The Centre is part of the Macmillan Cancer Relief CancerVOICES initiative, a network of patients wanting a 'say' in treatment. **The Haven Trust** concentrates on women with breast cancer and their families, with centres in London and Hereford. The centres are 'drop-in', offering counselling, support groups and complementary therapies in a relaxing place – or simply coffee and a chat.

Bristol Cancer Help Centre covers all cancers, and provides appointments or residential courses – on diet, complementary therapies and psychosocial techniques – to help people with cancer in dealing with the disease.

Advocacy and Education

…as it does patient advocacy and, to a lesser extent, education.

Advocacy is one of the most useful roles charities can play in the field of cancer treatment, providing independent advice, commentary and, where appropriate, criticism of the government's delivery of cancer services. Most of the major cancer charities engage in advocacy at some level, by issuing reports and press releases, participating in parliamentary groups and reviews of policy, with formal campaigns and informal lobbying.

Awareness-raising and education are also areas where charities can make a significant contribution. Charities can be very creative and attract the involvement of celebrities who would probably be less interested in participating in campaigns orchestrated by the government. As a result the breast cancer pink ribbon awareness campaign every October[76] has popularised the important technique of self-examination of breasts for potential tumours, although other important symptoms, for less 'fashionable' cancers, remain less well known. Another criticism of awareness-raising campaigns is that the cancer charities have had an undue focus on younger people – **Cancer Research UK** and Help the Aged thus arranged a debate on this issue in October 2003, the same week as the Sunday Telegraph[77] published an article criticising breast cancer charities for using young glamorous women in their awareness raising. A CR-UK survey showed 72% of women over 50 were unaware that they are more at risk of breast cancer than younger women, though the risk is 125 times greater.

CancerBACUP and most large cancer charities produce publications and provide help-lines to educate and support the public. The Cancer Plan talks about improving co-ordination in cancer education and information, delegating the Cancer Czar to 'work with voluntary organisations to review the information available on all the common cancers, and see what more can be done to reach those most at risk.'[78] Hence the Coalition for Cancer Information has been formed to implement this co-ordination, bringing together seven major charities, the Department of Health and the Cancer Services Collaborative. This is a useful first step to recognising and more effectively promoting the 'gold standard' set by charities such as CancerBACUP, and reducing the proliferation of advice on some cancers (breast, bowel, prostate and leukaemia in particular), which can be confusing as well as a waste of resources.

State and voluntary sectors increasingly work together here, as elsewhere then, pointing up once again the difficulty of extricating the contribution to the treatment of cancer made by private funding. As we have discussed, the state through the NHS plays a very considerable role in this field – which might suggest a consequently limited role for charities. While this is true in the area of hospital treatment, where the charitable contribution is small, charities nonetheless play a vital role in supporting those receiving treatment, a role that might well otherwise go unfulfilled.

Section 3: Interventions: Palliative care

Palliative care for cancer patients currently costs over £500 million each year, well over half of which comes from the voluntary sector. The picture of who does what in palliative care is complex, and this section attempts to disentangle that picture. In essence, patients are cared for in a range of settings by hospices (mainly voluntary sector), specialist and general nursing services (some voluntary sector, some NHS), and supported by clinicians (palliative care consultants, oncology units, GPs). There are regional variations as to who does what, and at local level collaboration between service providers is key. At the same time there are important strategic initiatives within both the NHS and the voluntary sector, some of which are being developed jointly.

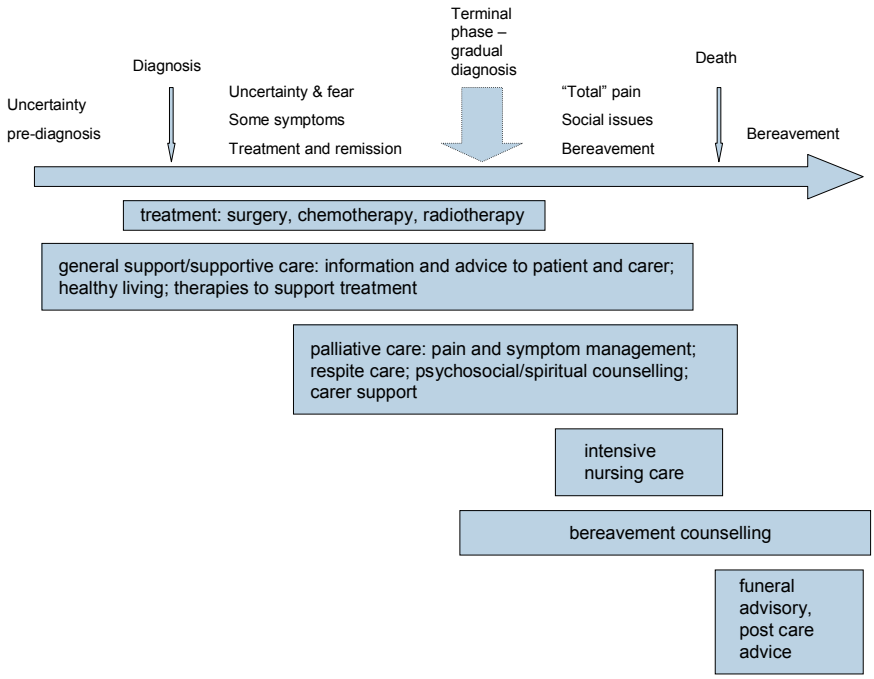
What is palliative care?

Despite ongoing research and improvements in detection and treatment, cancer still proves fatal in more than half of all cases within five years of its diagnosis. For those facing the progression of cancer into a terminal phase, palliative care and support can be critical in improving the quality of life of the patient, supporting the surrounding network of friends and family, and, in many cases, aiming to achieve a 'good' death.

Palliative care affirms life and aims to help patients live as fully and actively as possible until their death.

Palliative care affirms life and aims to help patients live as fully and actively as possible until their death. The approach intends to alleviate the 'total pain' of the dying person, comprising social, psychological and spiritual elements in addition to direct physical symptoms. It provides a support system to family and friends as they adapt to their loved one's deteriorating condition and eventual death. Aspects of palliative care may be applicable at other stages of illness – indeed, there is not always a definitive point where a patient's terminal phase begins.

Figure 12: The cancer patient journey and interventions



The degree of care and support on the patient journey will change as the disease progresses and will vary enormously depending on the patient's condition. The situation is often complicated by the fact that the prognosis cannot always be predicted. Some patients recover completely, some go into remission and lead long and fulfilling lives; others endure a swift and painful deterioration. Thus during the course of the disease, the emphasis of support may shift towards more intensive control of symptoms – palliative care often delivered in the form of surgery and, especially, chemotherapy – and the patient's care

requirements will become more complex, although general support will still have a role. Even for those patients that are given the 'all clear', support may be required to adjust to the emotional repercussions of diagnosis and treatment. Thus palliative care services include:

Physical	Psychosocial	Counselling & Support
Patient	Patient & families/carers	Patient & families/carers
Pain and symptom control (specialist care, intensifying towards the end of life)	**Psychosocial therapies** for patient (e.g. art or writing)	**Bereavement counselling** (this may start before death and continue thereafter, and may be applied to the patient as well as carers and family)
Symptom alleviation (general care; complementary therapies, physiotherapy)	**Psychosocial support** for patients and families, ranging from spiritual guidance and emotional support to hairdressing or practical advice on benefits	**Respite care** for carers (this is particularly important during intensive caring phases)
Practical nursing care (e.g. bathing or use of a commode)		

Palliative care is complex, and generally requires a multi-disciplinary approach. Public services and the voluntary sector are heavily intertwined in service provision, and the question of who does what varies depending on geographical location and the patient's condition. We look here at supportive and palliative care in the context of the patient's journey from cancer diagnosis, through death, to the relatives' experiences in bereavement. Based on a previous NPC report, *Caring about dying: Palliative care and support for the terminally ill*, which covers all terminal diseases in the UK, our comments here omit much, given the complexity of the issues involved, and readers interested in understanding palliative care more fully should refer to the original report.

Benefits of palliative care

As noted in Section 1, there were approximately 270,000 new diagnoses of cancer in the UK in 2000, and 154,460 deaths from cancer in 2001.[79] One in four of us will die from cancer and there are three crucial factors which contribute towards a 'good' death – quality of care, choice in the place of death, and support for carers.

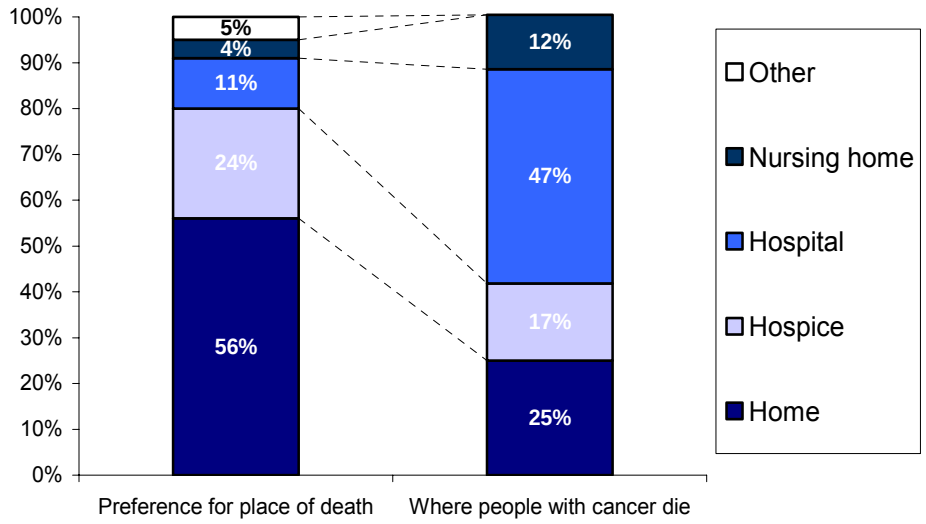
Amongst cancer sufferers, the majority of deaths, 47%[80], occur in hospital, whether NHS or private, though recent studies show that a much smaller proportion (between 4% and 11%) of people would choose to die in hospital[81] – only half of which have specialist palliative care units. Indeed, 56% of people would prefer to die at home, yet only 25% of deaths from cancer happen there.[82] For those who would prefer not to die at home, hospices provide a peaceful and accommodating setting, and 17% of cancer patients die in one of the UK's 208 voluntary sector or 62 NHS hospices each year. Most of the remaining cancer deaths happen either in nursing homes or long-term residential units, neither of which are generally specialised in the delivery of palliative care – elderly people in care homes are often particularly short-changed in comparison with cancer patients in other settings.[83]

Most people would prefer to be cared for at home – lack of time and resources in the NHS and social services often means that this preference is not met.

The gap between practice and desire over the place of death highlights a key failing in the provision of palliative care in the UK. It seems that fewer than half of UK deaths take place in the preferred setting, home deaths particularly difficult to achieve, because of breakdowns in home care leading to emergency hospital admissions.

Choice over place of death reflects anxieties about the other two important factors outlined above that contribute to a 'good' death. There is evidence that quality of palliative care in some settings is poor and that carers may not be considered important. If care and support for patient and carers were improved across all settings, preferences for place of death might be less marked, more would achieve their preference, and the experience would be less distressing for those who for good reasons cannot achieve their preference.

Figure 13: Place of death - preference and reality



Source: Higginson (2003) *Priorities and Preferences for End of Life Care in England, Wales and Scotland*

So more support is needed for people to achieve their preference of dying at home, and for their carers, in order to provide better care and prevent hospital admissions. Improved palliative care in those hospitals without specialist palliative care units, in nursing homes and in residential care homes is needed to provide adequate services to the large numbers of people who do not die at home. Furthermore, there are significant demographic and geographic inequalities in the provision of palliative care across the UK. Providers need to address service accessibility for the most disadvantaged groups, and to ensure that children and adolescents receive specialised palliative care provided by paediatrically-trained professionals.

Who funds palliative care?

Voluntary income plays a crucial role in the delivery of palliative care to cancer patients – providing over half of total annual spending of up to £600 million in this field.

NPC estimates that the cost of providing palliative care services to cancer patients in the UK, last officially calculated in 2000 in the run-up to the Cancer Plan, is over £500 million each year – and set to rise, with new state spending, to maybe £600 million.

The funding of the cancer palliative care sector is complex, drawing on statutory and lottery funding sources, voluntary income, interest, and trading profits from shops and individual charity lotteries. Although funding from statutory and lottery sources is significant, the dominant source of funds is voluntary income, which delivers more than half of all sector funding.

Total income from voluntary sector sources and trading is approximately £350 million each year[*], while charities also provide a significant non-financial contribution (maybe worth £130 million) in the form of volunteers. Marie Curie and Macmillan Cancer Relief dominate the picture, spending around £150 million between them each year on cancer palliative care, with smaller home nursing charities spending maybe £20 million, and the UK's 208 independent hospices a further £261 million – of which around £100 million comes from state and lottery funding. The NHS then spends a further £68 million[84] on in-patient beds for cancer patients in its 62 palliative care units and hospices. Palliative care on hospital wards, and via GPs, District Nursing Services and Social Services, is difficult to quantify and so excluded from the analysis made in our previous report on palliative care[85], but will significantly add to the current £500 million total.

As in other types of intervention into cancer, state and voluntary sectors are increasingly working together here, the National Cancer Research Institute for example, recently announcing a five-year, £5 million plan to bolster research into supportive and palliative care, jointly funded by its state and charity members.

[*] Consisting of £297m pa from voluntary sources and £53m pa from trading in shops, lotteries, etc.

The role of government

State spending (including lottery funding) on palliative care for cancer patients reached maybe £188 million by 2002, [86] since when further state and lottery funding is being channelled into the sector:

- £50 million annually committed by the government under the Cancer Plan from 2003 for palliative care for cancer patients. Funding may go to both voluntary sector and statutory providers of care, and has been set aside for three years, after which the intention is that this funding will be built into main allocations. According to the Department of Health, this represents a 38% increase on government funding, which the Department of Health estimated in 2000 to be £131 million, although it is unclear exactly where this figure comes from, and NPC estimates of government spending are higher.

- The New Opportunities Fund (NOF) was set up in 1998 to distribute lottery money to health, education and environment projects. NOF has allocated a total of £84 million in palliative care for adults (£22 million in England – home care, especially in deprived areas) and children (£48 million – community/home care palliative care teams, hospices, bereavement services) over the last two years.

- In December 2003, the Secretary of State for Health announced an extra £12 million over three years for palliative care education. The funds will concentrate on the Gold Standards Framework and the Liverpool Care Pathway for the Dying Patient (models of best practice developed by partnerships between the NHS and Macmillan Cancer Relief and Marie Curie Cancer Care respectively, and discussed below) and the South Lancashire and Cumbria Cancer Network's Preferred Place of Care scheme.

Improvement in palliative care provision is one of the key aims of the Cancer Plan, now seeing sustained investment by government.

While there are questions over whether £12 million is fully adequate to roll out these programmes nationwide, or whether the other initiatives really represent new money, these moves are welcome. As a result, NPC estimates spending on palliative care will soon be close to £600 million each year, of which almost half will be funded by the state and the lottery.[87]

NHS service delivery and standards

A full discussion of this area is beyond the scope of this report, and is covered in detail in NPC's report *Caring about dying*, although a brief discussion of palliative care standards and the National Institute for Clinical Excellence's recommendations is relevant here.

The National Care Standards Commission is an independent public body, set up under the Care Standards Act 2000, to regulate care services throughout England according to Department of Health standards. Hospices undergo inspections by the Commission, and that there is some anxiety in the voluntary sector over the mandatory costs of compliance -- Marie Curie Cancer Care estimates this initiative will cost it £25 million.

The government has also commissioned NICE to develop evidence-based guidance on supportive and palliative care for adults with cancer. No money is attached to the NICE guidance as yet, and opinions vary on whether additional funding to implement the recommendations will follow – although practitioners are hoping to use the guidelines to encourage the government to put its money where its mouth is. It is also apparent that compliance with guidelines will be necessary when negotiating service agreements with PCTs, and in any case many practitioners view the guidelines as being generally helpful in encapsulating good practice. NICE's recommendations, published in March 2004[88] include:

- Good information provision and communication between patients and professionals involved in their care are both critical.

- Sufficient palliative care services should be provided to meet local needs.

- All patients should undergo needs assessments (physical, psychological, social and spiritual). Identified needs should be met in a timely fashion.

- In-patient care should be delivered by a multi-disciplinary team with links to social, psychological and spiritual support workers.

- Levels of education of generalists and access to specialists should be increased.

- Home care should be available 24 hours a day to all patients with advanced cancer.

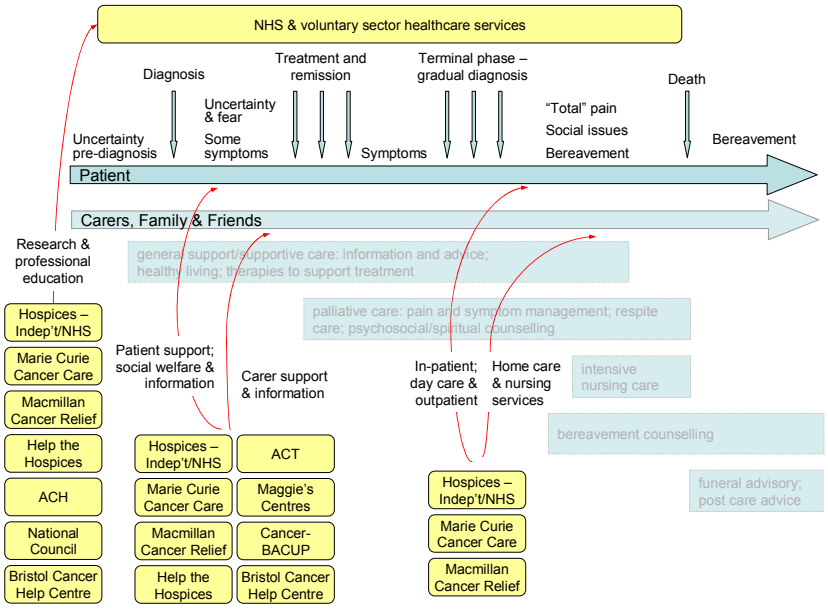
The role of the voluntary sector

The voluntary sector is active in providing palliative care, presenting a collective voice for the terminally ill and their families, and is an innovator of new approaches.

The voluntary sector is active in the following areas, as shown in Figure 14, below:

- Contractual service delivery to government for services which government chooses not to deliver itself but will pay for in part or in full, such as hospices and palliative care nursing.
- Delivery of additional services that the government will not provide or pay for, but which are seen as desirable by non-government stakeholders, such as the provision of information and support for diagnosed patients and their families and carers.
- Research, development and piloting of new services, which may in future become sufficiently mainstream to be taken on by government, including education.
- Providing a voice for patients and their families, and enabling people affected by cancer to have their own voice to influence change.
- Services for children.

Figure 14: Direct service provision in the voluntary sector



It is important to note that voluntary sector service provision is often conducted in close collaboration with the NHS. This chart excludes the very important work of oncology units and nurses in hospitals, and GPs and district nurses from the PCTs in providing care.

Hospices

The hospice movement is a philosophy of care – hospices act as centres from which a range of services can be provided in the local community as well as on site.

Hospices generally provide some or all of the following services: in-patient beds: day care and out-patient facilities, spiritual care, home care services, and services to carers including bereavement care. The modern hospice movement – which began in 1967 with the founding of St Christopher's Hospice in Sydenham by Dame Cicely Saunders – should really be regarded as a philosophy of care more than a series of buildings. Indeed many hospices look after more patients at home than physically on their premises – Dame Cicely recognising the vital interaction between doctor, nurse and social environment in caring for the dying in a co-ordinated way.

The point at which a patient is referred to a hospice varies enormously, dependent upon factors such as provision of other services (such as the District Nursing Service), the relationship between the GP/District Nursing Service and the local hospice, the attitude of the patient and family, and of course the patient's condition. The level of usage of the hospice is likely to intensify as the condition advances, but it is not unusual for a regular

hospice user to die at home rather than in the hospice.

96% of hospice patients in the UK have cancer, and there are 270 hospices here (including 34 children's hospices and 62 NHS palliative care units). Ten hospices are run by **Marie Curie Cancer Care**, six by **Sue Ryder Care** – NPC has visited examples of both, as we have another ten or so in the **independent hospice sector**, all locally funded. Indeed we have seen hospices across the country, some old, some new, and are generally very impressed by the ethos of the hospices and the levels of collaboration with NHS networks, with most hospices having personnel represented on the local cancer network. The average hospice has 15 beds, with an average nurse to patient ratio of around 1.5 to 1 – which explains the average cost of an in-patient over 24 hours at £325.

Charitably-run hospices have around 25% of their costs funded by government, and so have need of other income streams as secure as possible. Some are luckier than others in this, for geographic, historical and even religious reasons, as well as due to varying levels of PCT funding – and indeed demand – across the country.

Independent hospices have not always been collegiate in outlook. However, the revitalisation of the umbrella group **Help the Hospices** since the mid-1990s is resulting in a greater marshalling of common interest. Thus far, this charity has developed a number of services for hospices (on education, training and information) which improve efficiency – also attempting to bring parties together to collaborate across the sector.

Nursing services

With most patients preferring to die at home, nursing services are crucial to the provision of palliative care. Most Primary Care Trusts provide their own nursing services through district nurses, but provision varies widely across the country. The biggest voluntary sector nursing services come from **Marie Curie Cancer Care** and **Macmillan Cancer Relief**, although the charities' roles are very different.

Voluntary sector nursing services liaise closely with the NHS in order to maximise the benefit to patients.

Marie Curie Cancer Care nursing services tend to be 24/7, with around 80% of the work taking place at night towards the latter stages of disease progression.[89] The charity's 2,500 nurses are often deployed during the patient's acute periods and when family carers are unable to cope, and tend to be general rather than specialist palliative care nurses. They undertake the arduous physical nursing required by seriously ill patients, but do not supplant family carers. As some PCTs also provide 24/7 services, the extent of the care provided by Marie Curie Cancer Care will vary accordingly, but adds up to 800,000 hours of nursing each year. Many PCTs contract Marie Curie nurses to provide services, paying 40% of Marie Curie Cancer Care's costs of employing the nurses (arguably the NHS should pay a larger proportion) – indeed 95% of PCTs have Marie Curie nurses in their care plans for patients.

Marie Curie Cancer Care estimates that where a Marie Curie nurse is present, 94% of patients achieve a home death if desired. The charity would like to aim for 100% 24/7 nursing coverage of dying patients in the UK through a combination of the NHS and itself. Continuity of care for patients who are discharged by the NHS is another pressing issue for Marie Curie Cancer Care. There are hidden coverage issues – it may appear that demand for home nursing is being met, but in reality not all patients are being referred. GPs are sometimes a stumbling-block, not readily understanding what Marie Curie nurses do and leaving the District Nursing Service to liaise. A national campaign by Marie Curie Cancer Care to increase patient choice in where they die: *Supporting the choice to die at home* (see below) has the support of the National Cancer Director, and the roll-out of the Gold Standards Framework will help the gap in GP referrals.

Macmillan Cancer Relief nurses have a very different role. With a Macmillan nurse, general care may still rest with the family carer, Macmillan nurses attending during the day for short periods (sometimes as little as once a week, or even once a quarter, depending on patient circumstances), to advise on and apply symptom control. Nurses from Macmillan are more clinically specialised than Marie Curie nurses and so do not undertake general physical care. They are, however, helpful in providing specialist and psychosocial support, particularly regarding diagnosis, especially where a patient may not yet require 24/7 care, but needs advice instead. Macmillan nurses also provide support services to hospital in-patients, the charity 'pump-priming' posts for three years, after which point the post is funded by a third party – the PCT, or the local hospice, or a combination of both – yet the Macmillan title is retained.

Carer support, social welfare and bereavement counselling

Carer support is also crucial, both while the patient is living and, sometimes, after his or her death.

Several organisations, including Macmillan Cancer Relief, Marie Curie Cancer Care and Help the Hospices, have identified carers as a group in particular need of support, and carer breakdown as a principal reason for hospital admissions. Macmillan and other organisations provide help-lines for advice on benefits, and schemes such as **Crossroads** provide emotional and practical support to carers.

Social welfare is also key – the welfare of families who may have lost more than one income of concern to organisations such as Macmillan. Besides its hardship grants, the charity already has a help-line on benefits and is piloting a joint service with the **Citizens Advice Bureau**, to advise those affected on welfare rights and general finance.

Carer support extends to bereavement counselling – if relatives are clearly told that the patient is dying, then they have the opportunity to ask questions, stay with the patient, say their goodbyes, contact relevant people and prepare themselves for the death.[90] Support in the final days is crucial, as loved ones increasingly anticipate and adjust to their loss. Bereavement counselling is not needed by the majority of people, but can help those who are having unusual difficulty in responding to their loss. Nurses are often in a good position to identify those most at risk here – those who have experienced a string of bereavements or those with little social support. There are also counselling charities, such as **Cruse**, and many counsellors believe that short-term interventions around the time of bereavement may help prevent mental health problems later on. For those who manage their grief independently, leaflets on what to expect at various stages may lend some reassurance, and opportunities provided by hospices (such as memorial services at Christmas) may provide a welcome chance to meet and remember sympathetic staff.

Strategic initiatives and bodies

The Gold Standards Framework is a tool to help GPs and others provide more coherent care without the need for significant extra resources.

The palliative care sector is fragmented, characterised by organisations focusing on a particular problem or geographic area. There are now increasing efforts in the public and voluntary sectors to act strategically – current initiatives including:

Macmillan Cancer Relief is supporting the development and roll-out of the **Gold Standards Framework (GSF)**, developed by Dr Keri Thomas, herself an NHS GP with a special interest in palliative care. The aim is to improve the provision of palliative care by GPs and the rest of the Primary Health Care team, the mainstay of care for patients in the community, but often lacking training in palliative care. The GSF provides guidelines for best practice on teamwork with other service providers, continuity of care, planning, symptom control, and support of patients and carers. The key components are identification of patients, assessment of needs, planning, continuity and communication, care of the patient, carer support and sharing of experience and education. All elements should involve as much consultation as possible with patients and carers.

Supported by the Cancer Services Collaborative and NHS Modernisation Agency, GSF is being used by almost 1,000 GP practices. Macmillan Cancer Relief is running a two-year support programme, including a toolkit of resources, workshops and an evaluation by Warwick University. Part of the £12 million recently announced by the Department of Health for palliative care will be applied to the roll-out of GSF, along with the LCP, below.

The Liverpool Care Pathway is a protocol for patients in the last 48 hours of life.

The **Liverpool Care Pathway for the Dying Patient (LCP),** developed by a partnership between the **Marie Curie Cancer Care Centre in Liverpool** and the **Royal Liverpool University Hospital**, ensures best practice in the management of patients in the last days and hours of their life. It provides detailed guidance to practitioners on topics including determination and description of the final dying stage; cessation of non-essential interventions such as feeding; resuscitation and the decision not to resuscitate; diamorphine dosage; patient comfort and anxiety; and recording outcomes.

LCP was awarded Beacon status in the NHS in 2000 and has so far been rolled out to more than 100 centres across the UK. Monitoring and evaluation of benefits and care standards, and dissemination of findings, are key components of the programme. The intention is for LCP to become mainstream practice across the 34 Cancer Networks, via half of the hospitals and PCTs in each network. Many hospices are already adopting practices similar to LCP, and nursing homes are being encouraged to follow, with a target that 30% of hospices and nursing homes will adopt LCP by 2006.

Marie Curie Cancer Care's campaign *Supporting the choice to die at home* was launched in March 2004 with the benefit of economic analysis by Professor David Taylor on the costs of community care compared with hospital care. Costs are estimated at £300 per diem in hospital versus £179 per diem at home over a 14-day episode of terminal care.[91] The campaign makes the case for the NHS taking up the challenge of investment in appropriate community care, thereby enabling patients to choose their place of death and save the NHS resources in the longer term, Marie Curie Cancer Care aiming to lobby the government to double the number of people able to die at home. The NHS would need to spend £100 million each year, although this could free up an extra £200 million annually for hospital services.

Help the Hospices is involved in the co-ordination of education, training and information, as is the **National Council for Hospice and Specialist Palliative Care Services**, which analyses policy, maps needs and works on service provision and standards.

Research and education

Much excellent academic work, practice development and research is taking place in palliative care, some of which we discuss in Section 4. However, there are concerns that dissemination of such work is not as effective as it should be, resulting in an ongoing need for improved education of generalist professionals working in the field. This is compounded by a shortage of palliative care consultants.

There is a need to educate healthcare professionals at all levels, including GPs who may be willing to undertake additional education, but are dissuaded by the cost of locum cover – distance learning can facilitate additional palliative care education. Two examples of initiatives in this area are a web-based learning tool being developed in the Birmingham Palliative Care Network in conjunction with **Birmingham University** and palliative care specialists Dr Keri Thomas (responsible for the development of the GSF) and Dr Max Watson**;** and a distance learning course for healthcare professionals developed by the **Princess Alice Hospice** and Dr Max Watson, **Northern Ireland Training Scheme**.

Services for children

The umbrella bodies representing the users and service providers for children are needed to speak up for the sector and improve strategic direction. They are still small, however, relative to their adult palliative care equivalents.

Although data for children is incomplete, covering only those under the age of 14, recent data from Great Britain's national cancer registration system show that there are over 10,000 children living with cancer, two-thirds of whom are likely to survive for five years.[92] Demand for children's hospices has driven rapid growth in numbers since the first was established in 1982, with 28 in-patient facilities currently in existence, eight more being planned, and six children's hospice-at-home providers. Children's hospices typically provide a similar range of services to their adult counterparts, but tailored specifically to the needs of children Due to the intensive care needs of children, the cost per bed night is £500-700 – considerably more than the typical cost of an adult hospice – of which only 5% is funded by the state.

There are two voluntary sector umbrella bodies for children's services – the **Association of Children's Hospices (ACH),** a small organisation (in income terms) formed by children's hospices. Its work includes raising awareness, facilitating education, research and service development, improving fund-raising, improving communication between stakeholders, and facilitating the development of care standards. The **Association for Children with Life-threatening or Terminal Conditions and their Families (ACT)** is more broadly based, with members including children's hospices, community teams and other organisations, but is also small in terms of income. It is an advocate for children and families, campaigns for co-ordinated care and support networks, promotes best practice and supports families with an information service, also providing education to carers. ACT has published papers on the state of care for children, and will publish a generic care pathway in summer 2004.

The palliative care sector is dynamic, and historically driven by developments and people in the voluntary sector. However, the NHS is increasingly contributing to these developments and taking up its responsibilities – the National Cancer Research Institute, for example, publishing a report on palliative care in conjunction with state and voluntary sector players, containing new initiatives on strategic planning and funding – all of which adds to the sector's dynamism. Cancer is the area where palliative care is most advanced: a side benefit of this is that patients with other diagnoses are starting to benefit from the experience of cancer palliative care developments.

Section 4: Interventions: Research

Many scientists complain that America spends ten times what we do on research into cancer, and that does look broadly right – the UK's roughly £1 billion on research dwarfed by maybe £10 billion equivalent in the US, more than half of that funded by the State, against a quarter here. Nonetheless, the quality of UK research is mostly very good, due partly to an historically excellent and very competitive academia, partly to a rigorous peer review system, dominated by Cancer Research UK, partly to world-class pharmaceutical companies, and to the monopoly of the NHS facilitating clinical trials. And we expect funds, and standards to rise further following the renewal of political will to improve in this area, culminating in the establishment of the National Cancer Research Institute in 2001.

Research funding

Cancer research in the UK sees state and charities increasingly working together, alongside a thriving corporate pharmaceutical sector.

Funding for cancer research in the UK totals over £1 billion each year, taking place in a wide range of institutions, with an even greater number of funders. Within the total the state (around £190 million in 2001) takes second place to the charitable sector (with up to maybe £400 million income last year), with the pharmaceutical industry probably spending around £500 million on research and development (R+D) into cancer treatments (although more than half of this will be on development rather than pure research) – these figures all estimates since exact numbers do not exist.

In the US the reverse is true – the state funding the National Cancer Institute (NCI) to the tune of $6 billion this year, with a further $1 billion being spent by other state organisations, of which the Centers for Disease Control and, interestingly, the Department of Defense are probably the biggest players.[93] Charities trail this slightly – including hospitals such as New York's Memorial Sloan Kettering, they raise and spend around $5 billion annually, the biggest being the American Cancer Society, with income of around $1 billion.[94] The pharmaceutical sector input is also huge – hardly surprising in a nation buying over $10 billion of cancer drugs each year[95] – research and development spending on cancer maybe $3 billion. The state provides the lion's share of cancer research funding, then, and plays an important role as co-ordinator of the nation's research programme, through the NCI. The NCI has been in existence since 1971, when President Nixon famously declared war on cancer – incidentally also proclaiming that America would cure cancer within five years. Despite this early setback, the NCI has been so successful at giving direction to US cancer research that in 2001, as part of the UK government's Cancer Plan, our own overseeing and co-ordinating body, the National Cancer Research Institute, was set up.

The National Cancer Research Institute (NCRI)

Until recently, the funding of cancer research in the UK was fragmented, characterised by large numbers of funding organisations working in isolation and sometimes in competition with one another. In recognition of this, the NCRI was established in 2001, born out of the Cancer Research Funders' Forum (CRFF), itself set up in 1999 to improve collaboration on cancer research between state and voluntary sectors, and involved in the drawing up of the Cancer Plan. Its role, as stated in its 2002 Strategic Analysis, 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 NCRI was established by government in 2001 to co-ordinate and direct the UK's cancer research effort.

In short, the NCRI seeks to co-ordinate and strategically to plan the activities of its 18 members – drawn from state, charitable and pharmaceutical sectors – so that the maximum benefit to current and future patients is made of the limited funding available.

The NCRI is a 'virtual' organisation, consisting of 18 member organisations, drawn from state and voluntary sectors, but which have in common that they spend at least £1 million each year on cancer research and have a system of peer review. Jointly funded by public and private sectors, the NCRI has been led by Dr Liam O'Toole, ex-Medical Research Council (MRC), and meets three times a year, its chair alternating between state and charitable members – currently chaired by Professor Alex Markham, Chief Executive of Cancer Research UK following the initial chairmanship of Sir George Radda of the MRC. Crucially, it has representation from the pharmaceutical industry, which the CRFF did not – the Association of British Pharmaceutical Industries (ABPI) has established a UK Cancer

Group to provide input. The NCRI's board is enthusiastic and supportive, its secretariat equally energetic and effective – the organisation already changing the infrastructure and organisation of cancer research in this country after three short years.

The NCRI does not fund research itself, but acts as an 'independent broker', conducting analyses of current activity and future needs, and ensuring a coherent national approach to cancer research through joint planning. Partnership discussions have thus far resulted in £95 million on joint initiatives, of which £90 million is new government money – its most important achievement to date probably the setting up of the **Cancer Research_Database** (CRD). This, for the first time in this country, has compiled data on all research being carried out by NCRI members*, which represent all state and well over 90% of charitable funding of cancer research in the UK. The ultimate aim is to include data on all current work, from which the NCRI's Strategic Planning Group will be able to spot gaps – such as the current underfunding of prevention and supportive and palliative care – and plan future priorities. This database forms the basis of our examination of UK research work later in this section.

The NHS gives UK researchers a head start – all cancer cases across the UK are registered, and most patients treated within the system, which eases recruitment onto clinical trials considerably.

The NCRI is also beginning to make better use of the infrastructure of the NHS. It has set up the **National Cancer Research Network (NCRN)** – 34 regional networks across England, matching the existing Cancer Networks, with other, though fewer, networks in Scotland, Wales and Northern Ireland – properly to co-ordinate both the subject matter of and patient recruitment onto clinical trials. One advantage the UK does have over the US, where healthcare is not centrally controlled, is this NHS infrastructure, which the NCRN will use to plan and co-ordinate clinical trials. This is something which already happens to some extent – average recruitment onto trials in the NHS is around 8% of new patients, a figure which has doubled since the establishment of the NCRN three years ago, but was already better than the US (which has around 2% participation) – but which the NCRI is keen to foster further.[96]

The NCRI has also established the **National Translational Cancer Research Network (NTRAC),** to co-ordinate clinical trials via 10 leading cancer institutions across the UK, where basic laboratory research can be assessed, then begin to be translated into clinical practice – the aim to enable translational research to be at once better co-ordinated and, to a certain extent, kept 'in-house'. A **National Tissue Resource**, which has been mooted in the past, but not properly realised, such has been the difficulty of co-ordinating the various parties, will establish regional 'banks' of tissues, linked by computer. These tissues are tumours previously often routinely destroyed after surgery, or at best kept for study in individual hospitals, now to become available to all researchers. Finally, the NCRI is also currently attempting to co-ordinate **bio-informatics** (scientific data-handling) across the research community, in the hope that fewer wheels need be reinvented in future research.

Government funding

It is very hard to pin down an exact figure for state funding of cancer research in the UK. The NCRI estimates that in the year to April 2001 (the date of its establishment) the government spent £190 million via its various agencies, as shown by Department of Health figures provided to the Science and Technology Select Committee in March 2002.

The State spends around £200 million each year on cancer research through various bodies…

Figure 15: UK Government funding of cancer research - £190 million in 2000/1:

£83.8m	Department of Health (includes £5.2m NHS R+D)
£58m	Medical Research Council
£26m	Higher Education Funding Council for England (HEFCE)
£12.4m	Regional assemblies (Scotland £8.6m, Wales £2.8m, NI £ 1m)
£6.3m	Biotechnology and Biological Sciences Research Council
£3.5m	Engineering and Physical Sciences Research Council
£0.04m	Economic and Social Research Council

* NCRI founder members were - from the State: the Dept. of Health, the Medical Research Council, the Scottish Executive Health Dept., the Wales Office of R+D for Health and Social Care, the Northern Ireland Health and Personal Social Services R+D office, the Biotechnology and Biological Sciences Research Council; and from the voluntary sector: Cancer Research UK, the Association for International Cancer Research, Marie Curie Cancer Care, Macmillan Cancer Relief, Leukaemia Research Fund, Breakthrough Breast Cancer, Yorkshire Cancer Research, Tenovus and the Ludwig Institute for Cancer Research. These have been joined by the Wellcome Trust, Breast Cancer Campaign, Roy Castle Lung Cancer Foundation and the ABPI, although the NCRI's figures have not yet been reworked to include these new members.

These figures, together with new commitments, via the Cancer Plan and the Joint Infrastructure Fund*, were the basis of the Government's pledge to raise state spending on cancer research to the level of the voluntary sector by 2003. While Sir John Pattison, Director of NHS Research, Analysis and Information, told the Select Committee that, as a result of this, state and voluntary funding would be 'about the same', the same figures were described by the ex-heads of the Cancer Research Campaign and the Imperial Cancer Research Fund, Professor Gordon McVie and Prof Sir Paul Nurse, as 'creative accounting' and 'rebadged' respectively. The Select Committee too was critical of the inadequacy of government funding of cancer research, recommending dedicated funding (i.e. excluding HEFCE and NHS R+D) of £200 million each year – which would effectively be a 25% increase from the current comparative level.

Even though state spending will by now have exceeded £200 million level, however, or even a planned £300 million by 2007/8, this figure will still pale beside annual US state funding of cancer research, where the current NCI budget plan is $6 billion. Research into breast cancer alone attracts up to $750 million annual funding from the NCI, the National Action Plan for Breast Cancer and the Department of Defense, and although of course women across the globe will benefit from any overseas discoveries, it is nevertheless interesting to look at a comparable figure for the UK's breast cancer research effort – the NCRI puts it at around £50 million.[97]

Charitable funding of cancer research

The Association of Medical Research Charities (AMRC) talks of around 350 charitable funders of cancer research – with over 250 registered charities in England and Wales, a further 43 NHS charitable funds and 42 general charities all funding cancer research amongst other projects, plus a number of university or MRC-administered funds.

… whilst charities spend maybe double that – the sector dominated by Cancer Research UK, whose 2003 income was £306 million.

The sector is dominated by **Cancer Research UK (CR-UK)**, formed in 2002 by the merger of the Imperial Cancer Research Fund and the Cancer Research Campaign, of which the former was founded by Edward VII, the latter splitting away a couple of decades later. Funding cancer research via its own institutes – in the old Imperial laboratories in London as well as at the Beatson and Paterson Institutes in Glasgow and Manchester respectively – as well as via programme grants to other major UK institutes, CR-UK raised and spent over £300 million in the year to March 2003, its size not just a legacy of its history but of the general affection in which it is held in the UK. This allows the charity huge reach and influence, not just on a project by project basis, vital though that is, but in terms of strategic thinking and planning. CR-UK expects to surpass the £300 million figure this year – its income is six times that of the next biggest cancer research charity, The Institute of Cancer Research (of whose £55 million income over £10 million comes from CR-UK grants).

If we look at the Caritas database list of cancer research charities' incomes, and remove, as best we can, the doubly-counted research monies from grant-makers and public bodies (such as that hefty CR-UK funding of The Institute of Cancer Research, which also receives some £20 million each year in government grants via the Medical Research Council and Higher Education Funding Council), and then attempt to split out research spending in those charities where research is only a part of their activities†, we get a figure for charitable funding of cancer research in the UK approaching £400 million. It is harder still to arrive at an estimate of pure research expenditure by UK charities. Here, a best guess might be £275 million – that is, the £191 million spent on science at CR-UK plus say 80% of the expenditure of the other charities in the sector, assuming an average of 20% spent on central costs.

The NCRI admits the difficulty of finding an accurate total for funding – state or charitable. In its 2002 Strategic Analysis, the NCRI states that estimates for charitable funding of cancer research range from £180 million to £230 million, though its director, Dr Liam O'Toole, notes that these figures will have risen considerably since the first numbers were drawn from 2000 and 2001 charity accounts. How far they will have risen he is unwilling to guess, but there will be an updated estimate of members' spending in the NCRI's third-year review, due in October – indeed one of the many benefits to be expected from the formation of this organisation will be increased clarity on who is funding what, and by how much.

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* 'Joint', that is, with the Wellcome Trust.

† Marie Curie Cancer Care, for example, which raised over £80 million last year, of which maybe 5% went to its Research Institute, or The Anthony Nolan Trust, which spends up to 10% of its £13 million income on research.

The peer review system and progression of research

Although many charities have been set up over the years to support specific research institutions, others are grant-makers. CR-UK is a combination of the two – its London laboratories a legacy of the Imperial Cancer Research Fund, with other institutes around the UK historically supported by the Cancer Research Campaign. Common to both sorts of charities, however, and a requirement of any cancer research charity wishing to become a member of the NCRI, is the system of peer review, which submits a scientist's ideas to the scrutiny of his or her peers, and determines which research projects will be funded, and for how long.

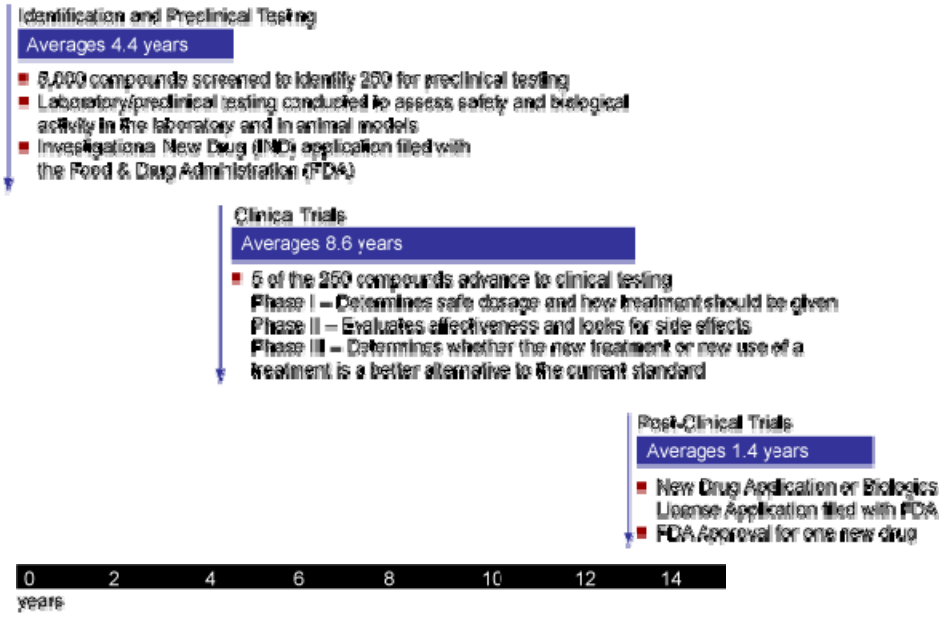
Scientific research is a protracted process, rigorously overseen in the UK by a tried and tested peer review system.

Research teams, usually comprising a team leader and four or five research assistants and technicians, make an application to a funder, either for a project (three-year) or programme (five-year) grant, backed by a referee from an external institution and, for big projects, often one from overseas. CR-UK estimates that it receives over 200 applications each year to its various committees[*], one in four of which will be successful. Grants are made after they have been first assessed externally by up to four separate reviewers, then internally, by committee, which awards the project a score.[†] Successful applicants will be reviewed annually, with a formal review at the end of the grant period.

Traditionally, most charity (and most state) funders have worked in 'response-mode', funding researcher-led applications presented by different teams – funding decisions generally based on scientific excellence rather than the potential impact of the research, necessarily. Increasingly, charities are developing a more strategic approach, aimed at maximising impact and avoiding unnecessary duplication – this is a cultural change, partly due to the establishment of the NCRI, partly due to new requirements for strategic planning from the Charity Commission, and partly because modern, post-genomic science requires it.

Whilst most of the cancer researchers NPC has met are working, broadly speaking, on understanding the biology of cancer and thus working towards improvements to cancer treatments, in exploring the research process it is perhaps more illuminating to look at the rarer development of a new drug fully to understand the stages researchers go through.

Figure 16: Timeline for drug discovery and development



Source: US National Cancer Institute, *The nation's investment in cancer research*

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[*] Excluding PhD applications, of which there are very many more.

[†] Grades traditionally moved from A*, which indicates work of an international standard, to Alpha, which is excellent nationally, and should almost always therefore attract funding, through Beta to Gamma, though this is now changing to a system where a project scores up to 10, where above 7 relates to an Alpha score.

Once a grant is awarded, the research team gets to work. The process begins at the lab bench, where the scientist has already identified a molecule that might be interesting, and begins a basic scientific investigation – pre-clinical testing – the team experimenting with samples from patients, cells grown in labs and small animals (usually mice), to check the safety and the biological activity of the compound. If the molecule still looks interesting after this period (which the National Cancer Institute estimates averages over four years), then the translational phase begins.

Clinical trials, in three stages, taking many years to complete, see oncologists introducing the compound to patients, adjusting its dose, evaluating toleration, side-effects, and of course efficacy and therefore potential. This is when commercial funding usually comes in, as we will see in 'pharmaceutical company funding', below. Phase I trials are usually made on a relatively small group of patients (maybe 10-30), often, in cancer research, these patients are in advanced stages of the disease and may well die anyway, and they are often happy to be used as 'guinea pigs' to test the safety of the drug. Oncologists introduce the molecule, adjust its dose, and evaluate toleration, side-effects and so on.

If successful – and many compounds fall at this hurdle – clinical trials move onto Phase II. These trials are a more detailed evaluation of the drug's efficacy than Phase I, on a larger group of patients (maybe 20-40 people), really to design the definitive Phase III trial. This is a huge undertaking, almost always commercially funded – a randomised, multi-centre trial (i.e. even the doctors do not know which patients are being tested and which are controls) on maybe 10,000 patients – providing a comparison of the relative value of the new drug with the current standard treatment.

Where successful, a molecule will be further tested by the pharmaceutical company in post-clinical trials (sometimes called Phase IV), before being submitted for regulatory approval to the EMEA in Europe and/or the FDA in the US.[*] As the chart above shows, America's National Cancer Institute estimates that one compound in 5,000 completes this process, averaging 15 years so to do, at a cost as high as $500 million.

An exception to the rule, however, is the story of Glivec, which like tamoxifen in the 1970s, this was the cancer drug discovery of the late 1980s. A 'signal transduction inhibitor', where a molecule inhibits the sending of an instruction from proteins outside a cell to the inside of that cell, prompting its nucleus to act abnormally, Glivec is successful in that it targets only the 'rogue' protein of the Philadelphia chromosome, common to all patients with chronic myeloid leukaemia. In clinical trials, of the 31 patients in Phase I, 30 went into remission, and so a Phase III trial was never held, partly due to the ethical decision not to put patients into the placebo control group. Glivec was fast-tracked through the FDA in a record three months. The drug costs £20,000 for an annual course, its annual sales of $350 million advancing it towards 'blockbuster' status for Novartis.[98]

Pharmaceutical company funding

Pharmaceutical companies make $20 billion of cancer drug sales globally each year, which explains why the UK pharmaceutical sector probably spends £500 million on research and development of cancer drugs.

With cancer affecting one in three of us at some point in our lives, it is no surprise that this is an area of major interest for the pharmaceutical industry. Cancer drug sales are estimated to be as high as $20 billion globally each year (with well over half of that in America)[99] – a figure expected to have doubled within the decade, partly due to the ageing profile of Western populations, partly due to the introduction of new types of drugs. Spending by pharmaceutical companies on research and development into cancer is estimated at up to $5 billion each year, of which maybe $1 billion (well over £500 million) is spent in the UK,[100] the lion's share by the big companies, maybe 10% by the smaller, newer biotechnology sector.

Pharmaceutical companies tend to come onto the scene at government and charitably funded institutes as a compound reaches clinical trials – whether the compound has been developed by that institute or by the pharmaceutical company in its own labs. It is unusual for a research institute to fund its own clinical trials – except in cases where it is developing improvements to existing treatments, which are not required to undergo Phase III trialling, so lengthy and expensive is the process.[†] Instead, private and public sectors traditionally work together – research institutes and hospitals providing the patients and data collection for the trials, in return for funding, either of research or administrative posts (even up to professorial

[*] Respectively the European Agency for the Evaluation of Medical Products and America's Food and Drug Administration.

[†] Indeed the process is about to become more expensive still, when an EU directive comes into force this year, requiring all clinical trials to be conducted to pharmaceutical industry standards.

chairs) – or for a fee of up to £5,000 per patient*, which is ploughed back into the institution's funds – UK academics generally very straight about this. Staff also move between the two worlds – academic researchers can probably make one and a half times their former salaries in the private sector (the same amount, incidentally, that they would probably make by moving to an academic institution in America), although of course the quid pro quo is a slight loss in prestige, not to mention independence.

The relationship between pharmaceutical and academic sectors is symbiotic, although academics are increasingly hoping for a bigger slice of the pie.

Thus the relationship between corporate and academic sectors is a symbiotic one – pharmaceutical companies gain live patients instead of cell lines on which to experiment, and to progress their drugs towards regulatory approval, and thus sales, and academics gain funding to finance research, posts they might not otherwise have been able to fund, and more information and knowledge for publication in medical journals – the route to success for any scientist. Then, later on, after a new drug has been approved and put on the market, the oncologist becomes a pharmaceutical company client†.

Increasingly, however, there is a trend for researchers to want a bigger slice of the pie, of which the NCRI's NTRAC is the most obvious sign, following the trend started by America's NCI, which jointly develops new drugs with the private sector. Improvements to clinical practice have always been the province of hospitals and research institutes – for the rarer cancers, especially, it is not worth a pharmaceutical company pouring funds into marginal improvements to treatment – but some academics are beginning to look for a greater recognition of their input into the development of new drugs. Partial shares of new drugs patents are not unknown; indeed some scientists now patent their discoveries as they make them, to prevent pre-emption by commercial companies, although the more common route is the joint-venture approach undertaken by some research institutes, especially with the smaller biotechnology companies, many of which are clustered around Oxford and, especially, Cambridge.

Possibly the best model for the way forward here is CR-UK's wholly-owned subsidiary, **Cancer Research Technology (CRT)**. Here, a team of 50 staff patents the intellectual property for CR-UK scientists' new discoveries, and for those at other, smaller charities, of which the biggest is the Leukaemia Research Fund, and then licenses the compound to the pharmaceutical company, which then develops the drug (or, if CRT is dealing, as it increasingly is, with a smaller biotechnology company, it sometimes takes a slice of the equity instead). The further along the research presented to the pharmaceutical company, the more advantageous to CRT the licensing deal, hence CRT has its own lab, further to leverage CR-UK's 'pipeline' – of which some 20 compounds are already licensed to various corporates – and thus to increase its annual contribution to CR-UK.

Current research in the UK

Altogether, then, of the £1 billion spent on cancer research in the UK last year, more than half was spent by the state and charitable sectors combined. Before the setting up of the NCRI, the allocation of these resources was fairly loosely monitored by the UK Co-ordinating Committee for Cancer Research, which despite its name had no real powers to co-ordinate, nor to take a strategic view. The formation of the NCRI and the coming together of the various state and charitable agencies around its table are changing the landscape of cancer research in this country – an indication of this its Strategic Analysis of October 2002, which provided a first cut of the work currently being done in the UK.

One of the first tasks of the NCRI was to map where UK research monies were being spent…

The categorisations are those used by America's NCI – the CSO, or common scientific outline – and the NCRI has subsequently, in partnership with both the NCI and other US funders of cancer research, set up a cancer portfolio website (www.cancerportfolio.org), where the work funded by their members is broken down into the CSO categories. This is an extremely useful site – the sort of thing one can't believe didn't already exist once up and running – fascinating not just for the lay viewer interested in seeing what research is being done, but of course an important tool for scientists. Here, researchers can see who is doing what, where the gaps are, what possible collaborations they might find – and it begins to answer the criticism that scientists might often be re-inventing the wheel, duplicating research done elsewhere. Whilst many scientists say that a degree of duplication is healthy – competition driving excellence – nonetheless this portfolio tool should in time see resources applied more strategically than hitherto.

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* Goldman Sachs estimates $7–10,000 per patient per trial.

† Some critics see this relationship more as collusion than collaboration – the American doctor Sam Epstein, in his *The Politics of Cancer*, pointing out the conflict of interest he sees as inherent in the system.

Figure 17: Percentage of research spending in each field in UK and US

Field	UK (NCRI)	US (NCI)
Biology	41	25
Treatment	22	25
Aetiology	16	17
Early detection, diagnosis and prognosis	8	12
Cancer control, survival and outcomes research	6	9
Scientific model systems	5	3
Prevention	2	9

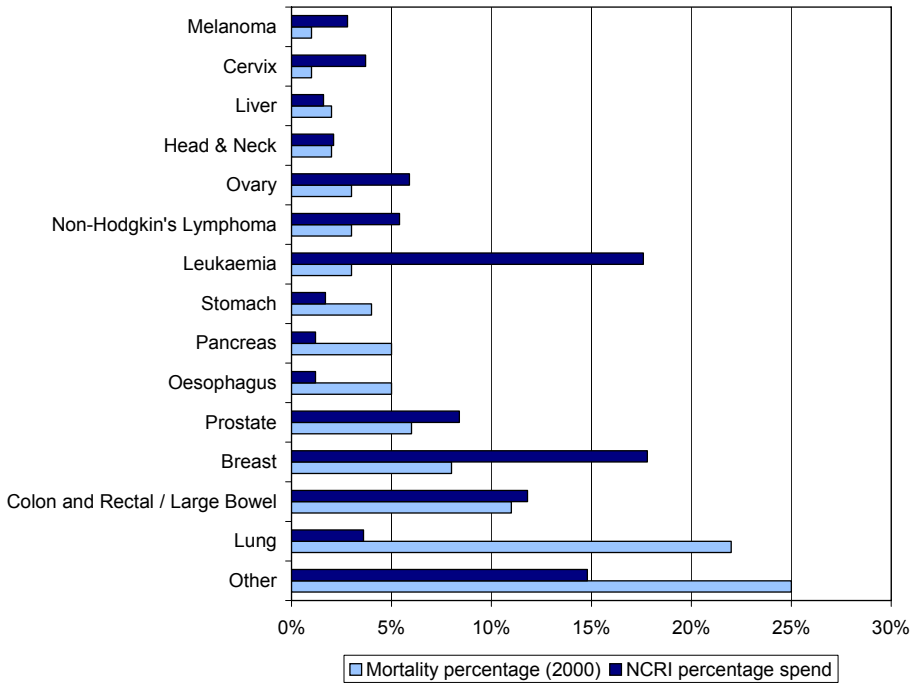
Source: Science and Technology Select Committee

…to discover, as expected, that almost half was being spent on basic biology, the key to understanding cancer…

In its strategic review, the NCRI also shows a different classification of research spending by its members – one not yet formally attempted in the US – fascinating in so far as it shows the amount of money spent on individual cancers as opposed to cancer generically. Thus 60% of NCRI member spending goes on research relevant to all cancer types: 43% funding 'fundamental research' relating basically to lab work on all cancers, 17% on 'all sites' on more patient-focused research – drug delivery systems, education and communication, studies of pain management and supportive and palliative care.

The other 40% of NCRI member spending is 'site-specific', and is dominated by funding for breast cancer and leukaemia, with 18% of the total each (and the only two individual cancers initially to be represented on the NCRI board, with Breakthrough Breast Cancer, shortly to be joined by Breast Cancer Campaign, and the Leukaemia Research Fund, although the Roy Castle Lung Cancer Foundation has also recently joined). Research into colo-rectal cancer accounts for 12% of site-specific spending, prostate 8% and ovarian 6%, but the really interesting statistics are those that show spending levels against rates of incidence and mortality, as follows in figure 18:

Figure 18: NCRI spending compared with mortality



Source: NCRI Strategic Analysis

…and that, of the individual cancers, 'fashionable' causes dominated funding.

This comparison is one of the major reasons for the setting up of the NCRI – identifying gaps between incidence and, especially, mortality rates and funding such as that in the lung cancer field, which will still look anomalous even after the arrival of the Roy Castle Lung Cancer Foundation onto this chart. This puts numbers to what had always been recognised

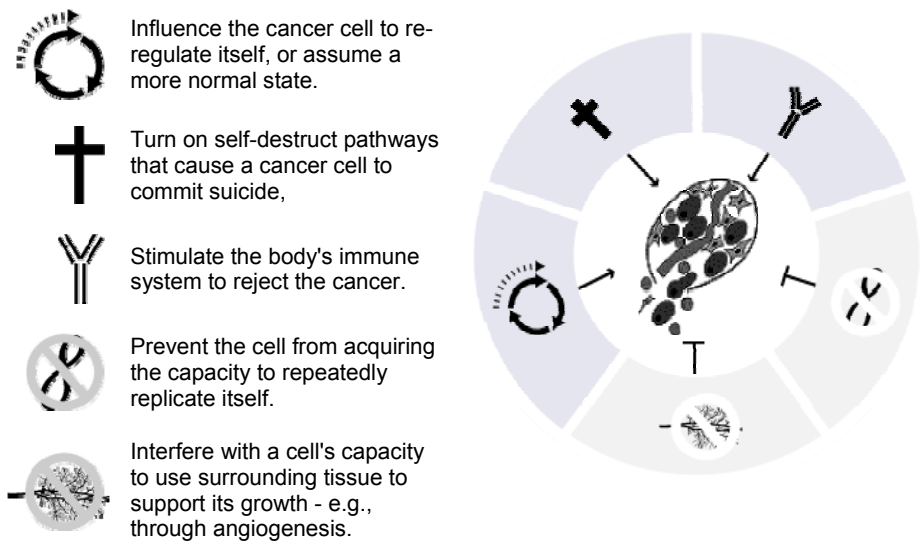
as gaps, but never properly quantified.* Thus while cancers such as leukaemia and breast cancers are well supported in research terms – largely because of the relatively high and very well-publicised proportions of younger patients, with more years of life to lose, than there are with other cancers† – less 'fashionable' causes such as stomach, pancreatic and oesophageal cancers have more difficulty attracting funds.

However, it is to the CSO (common scientific outline of research funding) that we will return to examine the research being carried out in the UK today, reflecting as it does the patient journey – from the biology of cancer, its risk factors (epidemiology) and causes (aetiology), through prevention, detection, diagnosis, treatment, control and, all too often, palliative care.

Biology (41% of NCRI members' spending)

Almost half of UK research funds are spent investigating the biology of cancer – something that informs the rest of cancer research. Of the couple of thousand scientists working in cancer research here, maybe half will be looking at the basic science of the disease – its cellular and molecular biology – and attempting to discover new ways to target it, as shown below:

Figure 19: Research avenues for molecular targeting



Source: National Cancer Institute

Scientists studying the biology of cancer are really all looking at why cancer develops – understanding the genetic basis for the disease the first step toward targeting it.

Of the players in this field – and indeed all the sections of the CSO – **Cancer Research UK** dominates. NPC has visited several of its labs in London – its headquarters in Lincoln's Inn and at The Institute of Cancer Research, Barts and St Mark's, as well as the Beatson and Paterson Institutes in Glasgow and Manchester respectively, and at the Cambridge Cancer Centre – meeting many individual researchers and their teams working on many different projects, some of which we discuss below.

We have also spent many hours with researchers from the **Sanger Centre**, outside Cambridge, funded by the Wellcome Trust to the tune of £300m over five years, where the UK contribution to the sequencing of the human genome was made. Here, **The Institute of Cancer Research**, in partnership with the Wellcome Trust, is running the Cancer Genome Project under Professor Mike Stratton, Head of Cancer Genetics. This massive project, costing £30m over five years, has as its aim the systematic screening of all human genes for the genetic abnormalities associated with cancer, to see what goes wrong, when. With its

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* While we have been unable to find comparable figures for the US, the bias looks similar. For example, we do know that funding for breast cancer research takes around 10% of the NCI's total budget, prostate cancer research around 5%, with work on lung cancer accounts for over 4% of spending there.

† We spell out a person's risk of contracting most types of cancer both before and after the age of 65 in Appendix 2. In the case of leukaemia, the risk at a younger age does not look out of the ordinary on that table – the fact that it accounts for most childhood cancers is not obvious there, so small, relatively speaking, are the actual numbers of children with cancer.

history in cancer genetics – the Institute has been pioneering research in this field since the early 1960s – the team is steadily isolating cancer genes. The latest to be discovered, a gene for bladder cancer, adds to global knowledge of almost 300 cancer genes so far (of which maybe 40 are inherited) – new knowledge such as this increasingly enabling the discovery and development of efficient new methods of prevention, detection and treatment.

At The Institute of Cancer Research's labs on the Royal Marsden campus in Sutton, Surrey, Professor Colin Cooper is working alongside the Sanger Centre team at The Institute's Male Cancer Research Centre, where the most recent discovery is of a gene, E2F3, heavily implicated in prostate cancer. The team's ultimate aim is to identify diagnostic markers to provide an accurate prediction of the aggressiveness of individual prostate cancers – which the current PSA test does not do – thus making it possible to avoid unnecessary over-treatment of the majority of these cancers, and then to find new therapies by creating compounds which inhibit such genetic activity.

At the **Beatson Institute** in Glasgow, Dr Ed Tobias has discovered a tumour suppressor gene on chromosome 7 – TES – that appears to suppress the proliferation of cancer cells. The team has created in its laboratory cell lines of breast, cervical and ovarian cancers, into which it introduces a functional copy of the TES gene, which appears to stop any further cancer growth. Dr Tobias has registered the gene with the European Molecular Biology Labs, and his team is now working on discovering how the gene actually functions, so as to develop a treatment based on increasing the level or the effectiveness of TES. This project is interesting in that it shows private and voluntary sectors working together – Dr Tobias has a funded fellowship from Glaxo-Wellcome, his assistant and the lab is funded by CR-UK, but there is no funding for the third and fourth researchers that would speed up the work – and at present Dr Tobias does not expect to reach Phase I trialling within 10 years.

At the **Weatherall Institute of Molecular Medicine**, Dr Roy Bicknell's team is studying angiogenesis – the supply of blood to cancer cells that allows them to keep growing and ultimately to metastasize. Thus far the team has identified several genes involved in the formation of blood vessels, of which it is furthest along with one called Robo 4 – the idea being that such genes will be targets for therapeutic interventions in cancer. With core funding from CR-UK and the EU, Dr Bicknell is nevertheless, like all the scientists we have seen, constantly seeking new funding for extras to speed up his research.

Aetiology (16% of NCRI members' spending)

Aetiologists examine why and how cancer develops…

Aetiology, the study of the causes of disease, in this case cancer, or the study of its risk factors, represents a large proportion of NCRI spending – although 16% is probably an underestimate, since the lines between cancer biology and aetiology are somewhat fuzzy (as indeed they are between many of the CSO categories).

The **Cambridge Cancer Centre** is planning a new Centre for Genetic Epidemiology. Here, Professor Bruce Ponder hopes to bring together – he thinks uniquely in the world – 170 scientists working on epidemiology, biostatistics and large-scale sample collections with the intention of translating the knowledge they gain into public health.

The **Leukaemia Research Fund**, like CR-UK, funds scientists in institutions around the country, one of whom is Professor Mel Greaves at the LRF Centre for Cell and Molecular Biology at The Institute of Cancer Research. Here, scientists working in conjunction with Professor Hows' cord blood bank at the University of Bristol are attempting to understand how specific blood cells in children yet to be born become leukaemic in the child's infancy.

Breakthrough Breast Cancer is just completing the piloting of a big, 50-year cohort study about to be launched in partnership with the ICR. Over 100,000 women will be recruited over the next couple of years, answering an initial questionnaire on their general health, family history, diet and lifestyle, then to be monitored every two and a half years over the following five years at least. The aim is to pinpoint further the environmental, behavioural, hormonal and genetic causes of breast cancer (and maybe, in due course, of other cancers) by seeing which women in the cohort succumb to cancer, and at what stage in their lives.

Dr Rob Clarke, a Senior Research Fellow at the **Paterson Institute** at the Christie Hospital in Manchester, is looking for funding for a project attempting to identify the genes responsible for the development of breast cancer – crucially, before they mutate. While the BRCA1 and 2 genes are responsible for around 5% of cases, the Paterson team believes that in the remaining 95% of cases multiple genes (maybe 10-20) probably exist, making women more susceptible to the disease – and would like ultimately to be able to screen for them. The team has carried out a pilot study for the project, looking at samples from 30

women (15 with a high risk of breast cancer, 15 not), and has found a couple of genes that look interesting. To further the investigation Dr Clarke has received two years' funding for a research clinician to collect many more samples, and is about to hear from Manchester University's Innovation Unit (which would then hope to patent any genes found) whether a year's funding for a technician has been awarded. Even so, the team has a shortfall in funding for the two staff, given the three years necessary to explore this new avenue fully.

Prevention (2% of NCRI members' spending)

…others, how to prevent that development.

Most cancers could be prevented. This is the stark conclusion drawn by the WHO in its 2003 *World Cancer Report*, which states that the goal of primary prevention is to avoid the development of cancer by reducing or eliminating exposure to cancer-causing factors, and that secondary prevention aims at early detection. Indeed, prevention comes in many guises, from public health guidelines provided by the state, to education provided by charities, to the scientific study of the development of cancer that we talked about above. One of the anomalies thrown up by the NCRI's categorisation of research, however, (notwithstanding work being done on prevention in other categories such as biology and aetiology) was the relatively small amount of resource dedicated to research into interventions to prevent cancer, at 2% of total spending. Small in comparison with US spending, and small in relation to the outcomes to be gained by successful prevention of cancer, in terms both of personal well-being, and of cost – hence the establishment by the NCRI of a joint Strategic Planning Group to address this issue.

Dr Andrew Povey at the Centre for Occupational and Environmental Health at the **University of Manchester** is co-ordinating a couple of studies into prevention. On lung cancer, he is part of a team currently interpreting statistics from the UK part of the EU-wide ESFA (European Smoking Prevention Framework Approach) longitudinal study. 6,000 children from 42 schools in the West Midlands and the North-West took part, 20 of the schools acting as controls, the other 22 trying interventions such as an increase in education on smoking and a clampdown on smoking in the playground, as well as leaflets being sent to the children's parents. The children were followed up over a four-year period and the rates of smoking uptake recorded. The data is currently being examined, and although Dr Povey is doubtful that rates after intervention will have improved much from the norm (1 in 5 boys and 1 in 3 girls of 15 claiming to be 'regular' smokers), he is hopeful that lessons might be learned from other interventions in European countries where rates did improve.

Dr Povey is also part of a joint team with the **Paterson Institute** looking at colo-rectal cancer, where a year's pilot study has been funded by the Food Standards Agency to explore the possibility of a link between processed meats and the disease. Alkylating agents – found in the body but also in tobacco smoke – seem sometimes to become carcinogenic, metabolised possibly by the bacteria in the colon in conjunction with chemicals in processed meats. The pilot study will finish this summer, and if successful, the team will be hoping to fund a three-year project, costing £250,000.

Early detection, diagnosis, prognosis (8% of NCRI members' spending)

Early detection and diagnosis are key to the successful treatment of cancer, scientists in this field often looking at screening for different manifestations of the disease…

Early detection and diagnosis is key to the success of cancer treatment – put simply, a small tumour still in its primary site is much easier to deal with than a larger tumour which is beginning to metastasize into the lymph system, and a body with secondary growths in different organs the hardest of all. Hence the importance of early detection and diagnosis, and the emphasis in the Cancer Plan on screening programmes and waiting times from GP to consultant. Yet, as with research into prevention, work in this area is relatively under-funded, at 8% of UK research spending against 12% in the US.

To take one example, Dr Wendy Atkin at the **CR-UK Colo-rectal Cancer Unit at St Mark's Hospital, Harrow**, is trialling detection methods as part of a Department of Health pilot into nationwide screening for bowel cancer, which sees over 30,000 new cases each year, and up to 15,000 deaths. It is pretty clear that screening will be introduced by the end of the decade here, such has been its success in reducing mortality in the US, so this trial seeks to determine the best (and most cost-effective) method of screening, be it the well-established faecal occult blood test (which detects 'invisible' blood in the stools, but which is not infallible) or flexible sigmoidoscopy (a mini-colonoscopy). Dr Atkin's team is looking at flexible sigmoidoscopy, which not only picks up tiny, pre-cancerous polyps in the lower part of the bowel, but removes them there and then, giving the patient many years of protection. The trial is being carried out on a thousand people aged between 55 and 64 in Harrow, and concurrently in Sheffield, and will take two years to complete, audit and make recommendations. While this trial, costing around £500,000, is almost fully funded by the Department of Health, Dr Atkin is also seeking further funding for research into detecting the

cancer in the part of the colon above the reach of the sigmoidoscope – whether the polyps scientists see there might lead to markers in the patients' stools that would avoid the need for a full colonoscopy, which is expensive, intrusive and can occasionally be hazardous.

Treatment (22% of NCRI members' spending)

… and much effort has always been made constantly to improve treatment once cancer has been diagnosed.

At 22%, spending on research into treatment forms a large chunk of NCRI member spending, but is nevertheless dwarfed by American spending of over $1.5bn annually. One of the big gaps immediately identified in the NCRI's database was here – there is very little work being done on radiotherapy and radiobiology, the science of which has plodded while molecular biology has been racing ahead. Hence the establishment of a working group in this area, to draw together knowledge of this science and plan ahead.

At the **Hammersmith Hospital**, Professor Jane Apperley of Imperial College is hoping to find funds (around £800,000 over five years) to allow UK scientists to join the international 'Spirit' clinical trial for chronic myeloid leukaemia (CML). This is a Phase III trial being jointly run by academics and pharmaceutical companies until 2010, in an attempt to assess the most effective treatment for this type of leukaemia (whether Glivec at a standard or higher dose, or Glivec plus interferon, or plus a new drug, Iressa).

Dr James Brenton, CR-UK-funded at the **Cambridge Cancer Centre** at Addenbrookes Hospital, is leading a study into the treatment of ovarian cancer. By the time most patients are diagnosed with this type of cancer, it is already fairly advanced – 85% of women diagnosed will die within five years of that diagnosis, partly because tumours quickly become resistant to chemotherapy. Dr Brenton is studying 60 ovarian cancer patients to try to establish underlying genetic signals in the different types of disease that should then indicate which chemotherapy regime (taxol or carboplatin) will have the most effect.

Dr Leanne Fleming is part of a team at the **University of Glasgow**, looking at disturbed sleep in cancer patients. Studies have shown that 45% of patients had insomnia, compared with 14% of controls – hardly surprising, since insomnia is common in groups suffering stress, but serious not only for the obvious inconvenience but because insomnia is a primary risk factor for depression. The team, funded by a project grant from CR-UK, is conducting a randomised trial comparing the clinical effectiveness of cognitive behavioural therapy against pharmacological 'treatment as usual', and expects to report improvements in both objectively measured and 'self-reported' sleeping hours in its subjects.

Scientific model systems research (5% of NCRI members' spending)

These are various systems created to mimic cancer in humans and thus to be experimented upon by scientists ahead of Phase I trials on humans: cell lines, yeast, flies, worms, fish and mice – the latter with the most complex system, as close to humans as research can currently get. Controversially, at the time of writing this report, a facility planned for Cambridge where monkeys were to be used for experimentation, especially into neurological diseases, had just been dropped as unworkable in the current climate of hostility towards animal experimentation. However, the most common model systems are 'cell lines', where scientists take a patient's cancer tissue and add growth factors to allow the cancer cells to grow to sufficient numbers to allow experimentation. At **Manchester Royal Infirmary**, Dr Bryson Pottinger is part of a team attempting to create a vaccine against adult myeloid leukaemia (AML), specifically against relapse of older people into AML following chemotherapy. The work is still at an early stage – and we discuss it further in Section 5 – but in order for Dr Pottinger to prove a principle before ultimately commencing clinical trials of the vaccine, he is working on numerous cell lines grown from patient samples.

Cancer control, survival and outcomes (6% of NCRI members' spending)

As with prevention, detection and treatment, this part of the CSO is under-funded by comparison with the US, where some $500 million (9% of the total) is spent. 'Survival' is an American term, relating to anyone who has been diagnosed with cancer and is still alive, so this sub-sector of cancer research is concerned with monitoring cancer cases nationwide, plus what we might term palliative treatment – symptom control, quality of life and psychosocial factors.

Research on palliative care is vital in developing best practice based on evaluated outcomes, but has historically been neglected – this despite more than half of patients dying within five years of diagnosis.[101] Research currently takes place within various organisations, including hospitals, universities and voluntary sector organisations, although it is somewhat

lacking in co-ordination and seems disparate in comparison with the cancer sector as a whole. Hence the current effort by the **NCRI**, which established a strategic planning group with representatives from the Department of Health and the voluntary sector to identify problems and develop responses – this has led to increased funding in the field of £5 million over the next five years. Much more research into palliative care for children and adolescents is also required – **ACH** and **ACT** are active in this area and keen to extend research.

Palliative care research has traditionally been under-funded, but has been prioritised by the NCRI.

The **National Council for Hospice and Specialist Palliative Care** is seeking funding to establish a policy unit on palliative care strategy until 2020, particularly focusing on developing access to palliative care services for all. **Macmillan Cancer Relief** and **Marie Curie Cancer Care**, the most active of charities in the area of cancer palliative care research, carry out their own research and pilot service provision models, and **King's College, London** has a specific palliative care research department, where the **Dame Cicely Saunders Foundation**, currently in development, plans to establish a research institute for palliative care.

Dr Max Watson is co-ordinating a study at the **Northern Ireland Cancer Centre** on reducing nausea and the effects of weight loss in patients with advanced malignancy, using melatonin. Weight loss is one of the major complaints of patients with advanced cancers, and creates a vicious circle in that without gaining weight, patients may not be fit for further treatment. Nausea also makes lives a misery. The protocol for the trial has been approved, but funding of £60,000 is needed to provide nursing support to proceed.

Other examples of current research programmes in palliative care include the **University of Sheffield Palliative Care Services Group** and **North Trent Cancer Research Network**'s work emphasising patient and public involvement, the **Universities of Wales in Cardiff and Swansea**'s palliative care units which include research on paediatric palliative care nursing, and the **University of Bristol**'s active Department of Palliative Medicine.

These are fascinating times to be involved with research into cancer. There are major, ongoing, structural changes in the organisation of cancer research in the UK, changes symbolised by the advent of the NCRI and the increased partnership between the key players in this field – bringing with them the potential for philanthropists to make an impact strategically as well as at the level of the laboratory bench. There, the work of the past few decades on molecular biology is prompting a change in our approach to cancer – from the traditional treatment of surgery followed by cytotoxic drugs or radiation to hopes of a more effective, less toxic approach. Not just by the refinement of chemotherapy drugs, important though that is, but by looking at the underlying faulty genes and finding ways to target them. Voluntary, state and corporate pharmaceutical sectors each have a role to play here, and private funding is key in getting projects off the ground that might otherwise never receive investment – it is a little known, fact, to take a major example, that the human genome was sequenced as soon as it was, and crucially with full publication of the resulting data, only because of sustained, hefty funding from the Wellcome Trust, prompting matching funds from the US administration.

Section 5: Outcomes

The problem of cancer is huge, the interventions many and multi-layered, from public and corporate sectors as well as from charities – yet the desired outcomes are really fairly simple: quantity and/or quality of life. The inputs into the interventions we have looked at are various – ranging from £30 to fund one call to a help-line to over £2 million for a new generation PET/CT scanner. The outputs are equally diverse – one person being helped in the first instance, over a thousand each year for the life of the machine in the second. Yet the aims of the hundred or so people NPC has met in the field are the same: prolongation of life or (sometimes and) improvement in quality of life. And it is the effective intervention which creates such outcomes that the philanthropist should be seeking.

Assessing outcomes involves asking what effect a charitable donation might have on cancer patients – current and future. Will it improve the quantity and/or the quality of their lives?

This is an incredibly difficult area to gauge – there are no simple figures on 'returns', no easily comparable metrics, huge uncertainty and, as everywhere in healthcare in the UK, private funding becomes enmeshed to a degree with statutory responsibilities. Moreover, quality of life especially is a notoriously difficult concept to pin down – particularly, as is so often the case in the cancer field, in the face of death. Gauging the outcome of that call to the help-line, the researcher working on palliative chemotherapy or the nursing service that allows a person to die at home is difficult to articulate, and nigh on impossible to measure – a factor to be borne in mind by philanthropists wanting to donate to these types of interventions. Quantity, or the prolongation of life (to either complete survival or more disease-free months or years), is happily rather easier to assess for many of the interventions we have discussed – there is plenty of research on the clinical effectiveness of cancer interventions. The difficulty comes in trying to unravel the various inputs into a process that takes many years – sometimes, in the case of new drugs, decades – to come to fruition.

Nevertheless, it is important to grapple with the subject of outcomes to identify some of the funding opportunities for philanthropists in the cancer field, and we attempt to do so below, always bearing in mind, however, that the measurable outcome is not always the better outcome. Certainly those outcomes which can be identified and measured should be, but many outcomes representing real benefits to cancer sufferers and their families are not amenable to straightforward measurement, and should not be devalued because of this. We will look at outcomes of treatment, palliative care and research separately below, and end this section with a table showing, as best we can, indicative outputs and outcomes for an input – donation – of £100,000 into various types of intervention.

Treatment

The public sector

There are two main ways to reduce deaths from cancer – prevention and better treatment – and a huge amount of research has been done on the clinical effectiveness of cancer interventions, a sizeable part of which has also considered the issue of cost effectiveness. This contrasts with many of the sectors that NPC researches, where there has been little, if any, quantitative costing of outcomes. There is in fact an overload of information, because there are so many different forms of cancer and interventions, in particular many types and combinations of chemotherapy drugs. Research studies, which may be based on real or modelled data, tend to focus on very specific decisions, such as what combination of drugs to use to treat a certain stage of a particular cancer. A typical study title might be 'Clinical and cost-effectiveness of capecitabine and tegafur with uracil for the treatment of metastatic colo-rectal cancer', and the conclusions of such studies tend to be very dependent on factors such as drug prices, which are liable to change. This makes it difficult to compare recent studies against older ones, moreover foreign studies may be difficult to apply to the UK, as the pricing of inputs such as doctors' salaries and hospital bed costs will differ significantly.

The standard outcome measures used are cost per life year (LY) saved or per quality-adjusted life year (QALY) saved, a multiple of the number of life years and the experiential quality of each year – an attempt to tackle the morally difficult but intuitively sensible notion that a period of healthy life is worth more to an individual (let alone to society) than one beset with discomfort and disability. Consideration of pure LYs might, for example, favour routine mastectomy for breast cancer, whereas a QALYs approach might reveal that alternative treatments that produce fewer LYs are actually favourable because of the enhanced quality of those fewer number of years.

QALYS can be further refined for elderly patients by basing calculations on active life expectancy – a measure of the number of disability-free years a person can expect to live. All these measures allow the negative risks and side-effects of treatments, such as possible incontinence and impotence from prostatectomy, to be factored into calculations. An additional complication for outcome measurement is that many cancer patients receive surgery, radiotherapy and chemotherapy, so it is difficult to attribute the effects of the individual treatments. Therefore progression-free survival, the period of time in which the cancer remains under control after a particular treatment, is sometimes used in calculations to isolate the cost-effectiveness of each treatment. A final issue is the discount rate used for life years, counting a life year saved in the future as less valuable than one today, which of course can make a vast amount of difference – for example, the cost per LY of population screening for the *Helicobacter pylori* bacteria (which influences gastric cancer) is £5,866 for 40-year-olds at a 6% discount rate, but only £1,027 if discounted at 1.5%. While discounting makes good sense for money, it is less clear why it should be applied to life – although if we had a choice between saving a life today, or a hundred years in the future, we naturally prefer the more immediate option, giving some intuitive support for the notion.

Outcomes from different types of treatment are measured by the state in terms of the cost per QALY – quality-adjusted life years.

We have been surprised not to have found any attempt, in the UK or overseas, to draw together the vast field of cancer health economics to produce an overview which would enable a comparison between cancer types, treatments and indeed between interventions relating to prevention or detection against treatment. The closest to this are literature reviews, such as those produced as part of the NHS's excellent Health Technology Assessment Programme or by the Cochrane Collaboration, but these are all very tightly focused on specific cancer treatments. It would be fascinating to see a full overview prepared for the Department of Health, not least to inform budgetary decision-making – but in the absence of this, NPC has tabulated many recent UK studies, plus a few interesting US and Australian studies. Based on the data shown in figure 20, opposite, some initial conclusions can be drawn.

The cost effectiveness of **prevention** comes across very clearly, with the proposed Australian skin cancer campaign (rolling out Victoria state's Slip, Slap, Slop nationwide) expected to cost the government just over A$1,000 per life year gained (although this is in part because individuals pay for their own sun cream) – but effectively to save the government considerable amounts when medical cost offsets are taken into account. Action to remove radon gas (which can cause lung cancer) seems cost-effective in Northamptonshire, an area of high radon density, but a more widespread programme in the US could cost up to half a million dollars per life year saved, obviously prohibitively expensive. What is not so clear is why public education seems so often not to deliver. Campaigns such as Australia's on skin cancer and that in the UK against smoking have had dramatic results in terms of malignant melanoma and lung cancer incidence respectively, yet there are still many people (especially men, it seems) who ignore them, continuing in bad habits, such as smoking, when the risks have been well publicised. Many of the oncologists to whom we have spoken are frustrated by this, and feel the need for more research by behavioural scientists into this area – certainly something NPC has yet to come across.

Detection can also be a very cost-effective strategy. The current UK breast screening programme costs just £2,522 per life year saved, and a study this year on cervical cancer from the London School of Hygiene and Tropical Medicine concluded that nationwide screening is saving around 5,000 lives annually, at a cost of £36,000 per life saved – probably thus below £2,000 per QALY. Familial screening is important too, not least because inherited cancers often occur earlier in life than somatic cancers, and so often lead to early deaths.

As far as **treatment** is concerned, chemotherapy usually seems to cost in the region of £15,000 per life year saved, although in the cases given here (such as lung, pancreatic and breast cancer) less than half a year of life is saved for each patient. In the case of advanced breast cancer, tamoxifen hormonal therapy appears to be marginally more expensive than letrozole – however, since it saves almost three months more on average, this would easily justify paying the slightly higher cost. Surgery can be quite cost-effective, with resection for oesophageal cancer costing only £5,484 per life year, while a process of detection to ensure surgery is used only when prostrate cancer is sufficiently advanced to require it can save QALYs at a cost of £12,068 each by limiting unnecessary prostatectomy, which could cause incontinence and impotence. And, obvious though it seems, specialist surgeons have much better outcomes than general surgeons – part of the reasoning behind the Cancer Plan's accelerated training programme.

Figure 20: Some outcomes from governmental cancer interventions

Cancer	Intervention	LY gained per patient	Cost/LY	Date
Breast, advanced[102]	Hormonal therapy (tamoxifen)	0.81	£5,917	2003
Breast, advanced[103]	Hormonal therapy (letrozole)	0.58	£5,873	2003
Breast[104]	Screening (current programme)	N/A	£2,522	1998
Breast[105]	Screening (to age 69)	N/A	£2,611	1998
Breast[106]	Chemotherapy for the elderly	0.21-0.46	$14,910 - $24,400	1993
Colo-rectal[107]	Chemotherapy	?	£14,794	2002
Colo-rectal[108]	Detection	1.8	$10,983	2002
Colo-rectal[109]	Prevention – aspirin	N/A	$47,249	2002
Gastric[110]	Population screening for H. pylori	?	£5,866	2003
Hodgkins[111]	Chemotherapy (new drugs)	+0.8-1.1	£12,800 - £17,600	2000
Lung[112]	Chemotherapy	+0.2	£14,620	2002
Lung[113]	Chemotherapy	+0.4	£12,104	2002
Lung[114]	Radon remediation (Northants)	N/A	£13,250	1997
Lung[115]	Radon remediation (US)	N/A	$80,000 - $480,000	1999
Oesophageal[116]	Surgery (resection)	?	£5,484	1998
Ovarian[117]	Hormonal	0.83-0.96	£6,500- £10,000	2000
Pancreatic[118]	Chemotherapy	0.19	£16, 543	2001
Prostate[119]	Detection	?	£20,000 (estimate)	2003
Skin[120]	Prevention – proposed Australian national campaign	N/A	Aus$1,360	1999

In the voluntary sector we also look at the quality and/or the quantity (i.e. the prolongation) of life given by various interventions.

Vital though it is for the state to find a balance between the most cost-effective treatments giving the greatest possible number of QALYs, we do not claim that such treatments will 'save' state money in the long term. After all, we all have to die of something, and a person saved from cancer may ultimately die a death more costly to the state, especially if he or she has spent many years in a care home in the interim. It is only really the 37,000 people below retirement age dying each year from cancer who, if their treatment is successful, should then be able to contribute financially to society. So our focus, whilst acknowledging the importance of cost-effectiveness, is not primarily a financial one, but firmly upon whether treatment improves the life of any cancer patient – young, or, much more commonly, old.

So, given that the state plays the crucial role in cancer treatment, where does the voluntary sector come in?

The voluntary sector

Hospital equipment and staff

The outcomes from funding either new machinery or staff for hospitals are twofold: first the improvement to patient well-being in terms of quality and sometimes quantity of life from the speeding-up of a decision that would have been taken by the state later on – hospitals seldom ask for anything the state would not provide, were funds available. Secondly, external funding of a post, or of new equipment, often works as 'pump-priming' – demonstrating a real need at the hospital and thus stimulating subsequent public funding.

A good example of both is the PET/CT scanner, costing £1.6 million, that the **Royal Marsden Hospital** has recently bought from charitable donations – which is now beginning to perform up to four scans a day. This will ultimately give 1,200 patients a year more accurate diagnoses from which oncologists will work – and around 30% of patients will have their treatment regime changed as a result of a PET/CT scan.[121] In lung cancer, for example, where very intrusive surgery is often unsuccessful because of the advanced stage of the cancer, information revealed by PET scans can identify people who would not benefit from surgery and hence reduce by 51% the number of patients who receive futile surgery.[122] So, ignoring for the moment the machine's key detection and monitoring functions, and concentrating on improved treatment regimes alone: 30% of the probable 10,000 scans the machine will generate over the next 10 years should result in a change in patient treatment, for 3,000 people, all of whom should experience better quality and (hopefully) quantity of life as a result for around £3,000 per patient. And, if each then gains, say, three extra years of life, that amounts to £1,000 per QALY.[123] Moreover, the donations that funded this purchase can also be said to have leveraged state spending, in that the NHS will pay the £750,000 it takes to operate the machine each year.[124]

The charitable provision of hospital equipment or staff will always improve quality of life for cancer patients, and often quantity of life, too.

All the hospitals NPC visits have 'shopping lists' of equipment, ranging from substantial sums like this down to £1,400 donated for a syringe driver, part of an NPC-recommended £150,000 grant to help fund critical care equipment in the Adult Leukaemia Unit at **The Christie Hospital**, which would otherwise, along with the rest of that equipment, have had to wait.

The outcomes are similar for philanthropic funding of hospital staff. First of all, of course, is the actual filling of a gap in ward staff – one NPC client, for example, funding two years' salary and costs to allow the **Manchester Royal Infirmary**'s Department of Haematology to add a specialist nurse to its team. A donation of £65,000 enabled the recruitment of this senior nurse, whose role splits fairly evenly between patient support and counselling, and the performance of some procedures traditionally done by doctors – thus at once improving the patients' experience and freeing up doctor time (which costs around twice as much as that of a nurse). The second, and arguably greater, outcome of such a donation, is the so-called 'pump-priming' effect. The fact that a position has been created and funded for a couple of years often makes the hospital trust aware of the gap and convinced of the benefit of an additional member of staff, in a way that constant written applications might not. This has certainly been the case at the Manchester Royal Infirmary, where the Trust has not only agreed to take over funding of this post at the end of the NPC-recommended grant, but has also employed another specialist nurse, so beneficial has been the arrival of the first.

As with hospital equipment, there is a fairly unanswerable argument that such funding – if really necessary – should, and will, eventually, be provided by the state, which the philanthropist might thus be regarded as subsidising. Equally convincing, however, is the counter-argument that for philanthropists to step in meantime cannot but improve the quality and often the quantity of the lives of current patients. NPC's view is that charitable funding of what, at first glance, seems an obvious role for the state should not be dismissed if such funding is the route to proving the need for a service, after which the state will often step in to continue funding. And so pragmatism offers donors the only sensible basis on which to make decisions here. If there is a clear near-term NHS commitment to a specific service, then it does not make sense for private funding to pick up the tab. Otherwise it is not really possible to prescribe clear rules – any private funding will probably pay for services that sit side by side with NHS services and, quite possibly, piggy-back on NHS resources to gain greater effect. Key questions to be asked thus include:

- Is there a clear NHS commitment to fund this service?
- Will my funding help existing NHS resources be more effectively applied?
- Will my funding gain greater impact from working alongside NHS resources?
- Will my funding help pump-prime future NHS funding?
- Are there clear and valuable outcomes to be gained from my funding?

It is this last question that is most important – will my funding make a difference to the quantity or quality of people's lives? If yes, then funding should be recommended. If this goes hand in hand with a positive answer to the first question, a funder might also consider funding some advocacy – putting pressure on the government to live up to its commitment. Depending on the sums available, advocacy could go hand in hand with a donation to provide the service to ensure current needs are met.

Despite fuzzy dividing lines such as these, there are a wide range of areas where charities have managed to carve out valuable roles which rely on the generosity and support of individuals and grant-making trusts and foundations. These activities offer real and tangible outcomes to funders, and we discuss many of them below.

Hospital-linked services

Hospital-linked services are primarily focused on enhancing quality of life, but in some cases will also lead to increased survival rates.

As well as appeals for equipment and staff from the hospitals themselves, there are many other charities providing linked services.

The **Anthony Nolan Trust**, providing donor bone marrows for mainly leukaemia patients, costs around £13 million each year to run. Nolan expects this year to provide 450 marrows (including imports) for transplant, of which maybe 60% will be successful and save the patient's life. So, crudely speaking, the outcome from an input of £30,000 will be a bone marrow for transplant – what the Trust calls a 'chance for life' – or, more crudely still, for an input of £50,000, a marrow that will save a life. Moreover, given that bone marrow transplants are normally carried out on patients who are relatively young, if £50,000 saves a life, prolonging it for, say, 10 years, that implies an outcome of £5,000 per QALY (or £12,000 per QALY once the costs of the NHS transplant operation – another £70,000 – are included). Quantity of life increases, then, as does its quality – not just for the patients, but for loved ones too.

Similar calculations – crude but compelling – can be made with other charities focused on one main intervention. The **Teenage Cancer Trust**, for example, spends £1 million on equipping a ward for adolescent cancer patients, typically with 10 beds at around £100,000 per bed – though it is harder to make such calculations where a charity has many activities. **CLIC**, for example, funds nurses, 'Homes from Home', grants, holidays and clubs for children with cancer and leukaemia and their families; so a donation of (say) £100,000, unless restricted to a particular project (such as paying for a CLIC nurse for three years), would, again crudely, given the charity's annual spending of £8 million, see an output of just under a week's running costs for the charity, supporting its various activities – all of them directed to the outcome of improving quality of life for patients and their families.

Information and support

Information and support are key to the well-being of a patient diagnosed with cancer…

As an example of support available to cancer patients, **Maggie's Centres** provide very welcoming environments situated close to the oncology units of hospitals – three thus far opened in Scotland, with more in the pipeline. Here patients can browse information, chat over a cup of tea, discuss their diagnosis and treatment with an oncological nurse (with no time limit), prepare for appointments with consultants, even see a psychotherapist. Courses on a range of topics, such as nutrition, are also available. The centres cost £3 million each to set up, and about £350,000 to run each year. The centre in Edinburgh welcomed 1,500 patients last year, so the annual running cost per patient is £233 (after set-up costs – if we include capital costs and assume 10 years pass before more money is required for repairs, then the cost per patient helped would be £433). Knowledge is a good antidote to fear of the unknown: the benefit to patients and carers is that by having somewhere where they can inform themselves and discuss their conditions in a more relaxed manner, they are better able to discuss treatment choices with medical practitioners and to come to terms with how their disease may progress – and thus quality of life is enhanced at a very difficult time.

The outcome of information provision by **CancerBACUP** (through help-line, email and booklets) is that patients and carers understand the disease and its implications much better – knowledge can improve patients' sense of control and improve their confidence in being part of the care discussions. The costs of such interventions represent reasonable value, ranging from £50,000 to fund the running costs of a CancerBACUP local centre, to £30 for a call to its help-line, or, to take a different example, £250 per beneficiary supported for a year by a small information and support centre such as **Liverpool Cancer Support Centre**.[125] **Bristol Cancer Help Centre** takes this a step further by offering full courses (£1,000 for a two-day residential course, shared between patient and Centre) to enable patients to improve their quality of life through diet, relaxation techniques, spiritual practices – then getting patients to feed back their experiences to try to get a feel for outcomes.

…and advocacy and education are aimed at improving survival statistics in the long run.

Advocacy and Education

There is evidence that charities can influence policy through their advocacy. In the US, where cancer advocacy really began, it appears to have helped stimulate a dramatic increase in cancer research funding. Since the National Breast Cancer Coalition launched in 1991, federal funding for breast cancer research has risen almost eightfold, to more than $800 million in 2002.[126] The Coalition gathered 2.6 million signatures in 1993 to demand a National Action Plan on Breast Cancer, which President Clinton subsequently enacted. One concern here, however, is that strong campaigns on specific cancers might cannibalise funding from other types, rather than stimulating additional funding, although this is hard to prove.

In the UK, advocacy charities are gaining momentum. **CancerBACUP** – a major player whose main role is nonetheless information and support – undertook a survey in October 2003[127] to find that 61% of women with breast cancer in the South West had access to the groundbreaking drug Herceptin, but only 14% could get it in the Midlands. CancerBACUP estimated that a thousand women were missing out on the drug because of this 'postcode lottery', even though NICE had recommended it for all women with advanced breast cancer – prompting Health Secretary John Reid to demand that the health authorities explain why they were not prescribing the NICE-recommended drugs.[128]

CancerBACUP probably spends around £100,000 each year on advocacy, **Breakthrough Breast Cancer**, the other major player (especially after its recent merger with the UK Breast Cancer Coalition) a further £350,000. The output may be ten people altogether working full time on advocacy. The outcome is harder to quantify – it is impossible to say that 'x' spent here will always have result 'y' there – but advocacy does increasingly contribute to policy decisions, charities as small as the **Genetic Interest Group** sitting on relevant government committees, and comparisons with the US effort are compelling.

The outcomes of charities' educational activities are still harder to quantify, although we have seen some of the impressive outcomes from improved prevention and detection that come about through awareness-raising, much of which is done by the state in conjunction with the major charities, from CR-UK on down. **Breast Cancer Care** tells us that its 'Healthy Living Days' cost around £5,000 each, including all the associated office costs, and help around 15 women each time to learn how best to keep healthy while living with cancer, at a total cost of just over £300 per woman.

Palliative care

There are broadly two levels of outcome from palliative care interventions: first of course the direct impact of services currently being provided and how they affect individuals at this most difficult time in their lives. Secondly, and key in the medium and long term, is the strategic impact of new services that might be piloted and subsequently rolled out, generating direct outcomes in the future.

The qualitative outcomes of palliative care interventions are complex and diverse, and are explained in detail in NPC's earlier report, *Caring about dying*. While many of the outcomes cannot be subjected to direct quantitative analysis, it is possible to derive indicative costings of interventions for quantified outputs, the scope of their impact and consequent outcomes.

As we saw with the charitable provision of hospital staff and equipment, it is possible to engage in philosophical discussions about what the state should provide in the palliative care area, and what should be left to philanthropy. If anything, the boundaries are yet more blurred here, there being no document setting out the government's mandatory obligations – and the reality, here as elsewhere, is PCTs with finite funds with too many calls upon them. The state currently funds around half the UK's palliative care provision, and although some donors may feel uncomfortable funding services that should arguably be left to the NHS, focusing then more on strategic initiatives or umbrella bodies rather than day-to-day funding of a specific hospice, say, it should be remembered that without the latter kind of private support, the sector would collapse.

Hospices

Hospices are a vital component of palliative care service delivery. On average it costs £325 for each in-patient over 24 hours, slightly less for home nursing, and much less for day care at the hospice – which seems a small price to pay for the benefits conferred on the patient. The decision whether to opt for in-patient, home or day care is generally driven by the patient's condition and circumstances, not cost, and it is likely that a mixture of services

Hospices need continued funding. A bed-night costs around £325 and the average length of stay is 13 days.

would be deployed during the patient's 'journey'. The outcome of hospice care is that patients are more likely to be cared for in an environment (be it home or hospice) of their choice, and in a manner appropriate to the terminal phase of life. Hospital admission is more likely to be avoided – hospitals, as discussed earlier, are less than ideal places of death. And there are also benefits to the carers and bereaved: if the death is a 'good' death, the experience is less traumatic for all, moreover hospices are crucial in providing respite to carers, often alleviating some hidden costs of caring, such as ill-health and depression.

26,000 cancer patients die each year as in-patients in hospices, with possibly as many again benefiting from hospice services at some point, so while donors have a huge role in funding individual hospices, the work of the umbrella body, **Help the Hospices**, in co-ordinating the sharing of best practice, education, service development is also vital.

Nursing services

The familiar surroundings of home can be a huge comfort to the dying, and at under £200 a night is cheaper than being cared for in either hospital or hospice.

Arguably, place of care is less important than quality of care. Thus the nursing services provided by the voluntary sector are a vital component of palliative care, enabling patients to remain in non-clinical settings (at home, for example, or in some cases within their care home) as well as improving care, such as symptom and pain control, within many settings. Outcomes vary depending on the type of service – for example, the outcomes of **Macmillan Cancer Relief** funding a specialist palliative care nursing post for three years are two-fold. In the first instance cancer patients and their carers (professional and non-professional) will receive specialist advice on symptom control and other issues, and secondly the post, once created, becomes part of the NHS infrastructure and the Macmillan funding subsequently passes to a new post – in this way expertise is gradually rolled out across regions and settings. The outcome of **Marie Curie Cancer Care** providing its full-time nursing services is different – its night-sitting service, crucially, allows patients to remain at home, properly cared for, and provides invaluable respite to anxious carers. The cost of this service is estimated by Marie Curie Cancer Care to be £179 per 24 hours, in contrast to £300 or more for a hospice stay – so not only are better personal outcomes achieved, resources are saved too.[129] In either case, quality of life for patients and carers is greatly enhanced.

Carer support and social welfare

Support for carers can have a significant effect on their experience, particularly in bereavement. Simple recognition of what they are going through is often much appreciated, and reassurance is commonly needed by carers, who may need to hear that what they are feeling – be it anger, guilt or depression – is normal and nothing to be ashamed of. Admission of the patient to hospital or the take-up of home support is a crucial time for carers – if their contribution is valued and they are included in patient care, then the guilt they may feel can be somewhat assuaged, and quality of life improved. Carer support can have the added benefit of preventing hospital admissions, where a common reason is 'carer breakdown' – where a carer is too exhausted or overwhelmed to continue care at home[130]. The outcome here is not just improved quality of life for carer and patient, but fewer hospital beds taken up, and thus reduced cost to the state.

People affected by serious illness can suffer financially, too – many do not claim the welfare benefits to which they are entitled. People can enquire about specific benefits, but there is no central agency assessing eligibility for the full range of help – hence charities providing advice on benefits (such as **Macmillan Cancer Relief**, shortly to initiate a nationwide service with the **Citizens Advice Bureau**) or indeed grants for those in need (such as **CLIC**) often lift a significant burden for patients and their families.

Strategic funding

A peaceful and dignified death lessens the distress not only of patients, but of their loved ones, too.

Both **Marie Curie Cancer Care** and **Macmillan Cancer Relief** have contributed to the development of important protocols – Liverpool Care Pathway and the Gold Standards Framework respectively – which, when rolled out, will have sizeable impacts on people's experience of dying. Such strategic initiatives continue the long tradition of the voluntary sector in encouraging change and introducing innovation – innovations often then taken up and funded by the state. In the meantime, it is important to stress that although some interventions (such as education for GPs as part of the GSF roll-out) are inexpensive, the intervention in question may not be successful without existing infrastructure and service provision. For example, GPs will be able to apply their newly informed recommendations for patients only if they have tools – a 24/7 nursing service or local hospice – available to them.

Although it is too early to say if it will be successful, the Marie Curie Cancer Care campaign *Supporting the choice to die at home,* by identifying the economic benefits of dying at home, may result in more effective allocation of state resources. This was the case earlier when the National Council of Hospice and Specialist Palliative Care drew attention to inequalities of provision, helping persuade government to fund £50 million more to specialist palliative care.

Services for children

It is striking how often parents refer to respite care in a children's hospice or at home as a 'lifeline'.

The effects of sensitive care and communication over the illness and sometimes the death of a child are similar to those for adult patients, except that it is even more important to set that child within the family context. **Acorns** children's hospice in Birmingham was set up in response to several families at a specialist school not coping after their children's deaths, with some family members committing suicide. Acorns hopes its work will prevent such tragedies recurring – helping a family member adapt to the child's illness and possible death has an impact on all family members, particularly since the reaction of the parents is thought to be crucial for the remaining children.[131]

As far as the child patient's time in a hospice is concerned, it is striking how often parents refer to it as a 'lifeline' – not just in alleviating the physical burden of care for the child, but in providing a welcoming, supportive environment for the whole family. The crude cost of providing hospice care for children is £500-700 per 24-hour period, depending on facilities, staffing ratios and the age and condition of the child. This may seem expensive – about twice the cost of an adult hospice place – but if one includes the parents and siblings as additional beneficiaries of such services, then the cost per beneficiary falls.

The umbrella bodies in this area, **ACH** and **ACT** – not yet as mature as Help the Hospices – would also benefit from funding to help them develop, particularly as they are about to undertake the mapping of children's palliative care services across England and Wales.

Research

Most researchers are not keen to undertake research unless a 10% improvement in the survival rate is foreseen.

The research process is so protracted, with so many different inputs, from the first investigations of a molecule to the final regulatory approval of a new drug or change in clinical practice some five, ten or even fifteen years later, that it is very hard to quantify outcomes properly. The discovery of the cure for TB is pertinent here – Robert Koch discovering the germ causing TB in the 1880s, yet the first effective treatment for the illness coming some sixty years later.

That said, most of the academics NPC has talked to seem to agree that to carry out research – so expensive, so lengthy – without the expectation of at least a 10% increase in survival rate at the end of it would not be contemplated. The question then is how properly to monitor this. Pharmaceutical companies, of course, can measure outcomes, crudely speaking, in terms of the net present value of a drug's future sales, and the profit margin on those sales after taking R+D, manufacturing, marketing and central costs into account. Public and voluntary sector scientists, however, must look for other methods of gauging whether their work has contributed to increased survival rates – whether through improved prevention, detection, diagnosis or treatment – and by how much.

The process of assessing the future outcome of a piece of research begins with the peer review system. Here, as we described in Section 4, the scientist's idea is scrutinised by his or her peers, the work graded not just for the viability of the idea – crucial though this is – but for the timescale by which the scientist hopes to reach the objective. Only proposals graded at Alpha equivalent or above are likely to receive funding – the 75% who fail at this hurdle must either go back to the drawing board or find other funding to get some preliminary results before re-submission to peer review. Once research has begun, projects are subject to annual review, the following year's grant dependent on success at that review, ending with final reviews where funders assess whether the initial objectives have been met.

Scientists also assess achievement by success at peer review and by publication.

The other major way that scientists regulate themselves is by publication. The scientific world and, here, specifically, the medical world has spawned a vast publishing industry, ranging from prestigious global publications such as the US-published *Science*, *Cell* and *New England Journal of Medicine*, and *Nature*, published here, through to specific international journals for specific diseases (*Blood* for haematology, for example), to national publications – the *British Annals of Oncology*, for example, or the broader-based *British Medical Journal* or *The Lancet*. At the same time, scientists do the rounds of academic conferences – again specific to disease type. As PhD and sometimes undergraduate students they attend conferences, going on later to present their work on posters, huge pieces of paper over a meter square showing the project the scientist is engaged upon, with

the scientist standing in front of it to discuss the work with other delegates. The ultimate acceptance of worth, of course, is to address the conference. An example of this: Bryson Pottinger, a PhD student whose sponsorship was recommended by NPC, who is investigating a potential vaccine against acute myeloid leukaemia at Manchester Royal Infirmary, has had a relatively rapid journey through these stages. The preliminary findings of his research were published in *Blood* in 2001, with posters of his work being displayed at both the British and the American Society of Haematology meetings last year. Finally, at the European Association of Haematology meeting at Lyons, Bryson had a slot on the conference platform.

Bad science becomes fairly obvious, then, given the sheer competition for funding regulated by these really quite rigorous filters. But how can we measure the practical outcome of good science, science that will eventually improve the quantity and/or the quality of patients' lives?

Outcomes from research into the biology and aetiology of cancer, and thence the development of new drugs and treatments

Measuring outcomes is not as simple as, for example, counting the number of new compounds to have emerged from The Institute of Cancer Research over the past five years and dividing that into the total expenditure of that Institute over the past ten years to get a crude 'cost per drug'. Even the number of patents to come out of an institution and the proportion of those subsequently developed commercially – although both are indications of a thriving research team – is not necessarily the right metric. The input of most scientists to the creation of new drugs is not as straightforward as that – pharmaceutical companies almost always take over the process at some point, and although very often the drug would not have been conceived of without the charitably-funded research team, the cost of that team is dwarfed by the funding needed to pursue the clinical trials necessary for its approval.

Research is a very lengthy process, especially where new drugs or treatments are concerned, with no guarantees of success – 14 out of 15 drugs are abandoned during clinical trials. The role of the philanthropist here is often to kick-start a project that may run for many years.

The role of the philanthropist here, then, boils down to kick-starting research that might ultimately end in a new drug, by donating to the research team's funds either through a funding charity such as CR-UK – by a long way the largest and thus able to invest strategically as well as project by project – or The Institute of Cancer Research, Leukaemia Research Fund or Breakthrough Breast Cancer – the list is long and, certainly for charities that are members of the NCRI, prestigious. Or the philanthropist can fund part of a team directly, through its institution – almost all serious research teams will have managed to attract peer-reviewed funding, and this, almost always, is a guarantee of quality, but in many cases, an extra research fellow or a piece of equipment might subsequently be needed, but unfunded. NPC has visited many teams, as well as the big funding charities, and our overriding observation is that philanthropists should avoid funding teams that are either unpublished or not peer-reviewed – there is usually a reason for this.

Take the example above of the philanthropically-funded addition of a PhD student to the **Manchester Royal Infirmary** team researching a new treatment, a vaccine for acute myeloid leukaemia – total cost £150,000 for three years' salary and consumables. The outcome, eventually, might be an immunotherapeutic vaccine that prevents relapse in AML patients, of whom there are 1,500 new cases in the UK each year, largely in elderly people. Of these, 50% relapse from remission following chemotherapy, only 10% – around 75 people a year – currently then surviving beyond five years. With the vaccine, the team hopes to improve this survival rate towards 50% – an additional 300 people annually in the UK alone. The team, charitably funded, had already been working on this for a couple of years, before the appointment of Bryson Pottinger, and does not expect to go to clinical trials for a further three years – at which point the vaccine might be taken up and developed either in conjunction with the Medical Research Council or even by a pharmaceutical company for several further years of Phase II and III trials before becoming part of clinical practice. Possibly. A number of imponderables, then, so whilst we cannot say that the outcome of the provision of that team member will be a ground-breaking treatment, we can state that this provision has underwritten a promising project, and one too far 'upstream' for a pharmaceutical company to have wanted to sponsor as yet.

Research fellowships for bright PhD students 'cost' around £30,000 each year, including salary, on-costs and consumables, and perhaps £40,000 for post-doctoral researchers or £50,000 for team leaders (a London allowance is usually less than an additional £5,000). Equipment ranges from a year's research consumables – about £10,000 – to a high-tech machine that the lab might be unable to afford – a DNA sequencer, for example, costing around £100,000, or a flow cytometry sorter, which sorts and analyses cells according to their surface markers, and costs around £200,000.

Outcomes from research into the improvement of existing cancer treatments

The divide between those scientists investigating possible new drugs or treatments and those seeking to improve existing treatments is fuzzy – the only real distinction being that the lead time is rather shorter for the latter than the former, often not requiring the final intervention of a pharmaceutical firm, and thus might be more attractive to philanthropists.

Research into improving existing treatments is a slightly less lengthy and expensive process.

The outcomes are largely the same – prolongation of life and/or improvement in the quality of life for patients – and the mechanisms and unit costs the same – teams usually wanting extra members of staff and/or equipment unfunded by their existing grants. Yet lead times are usually shorter – such improvements need 'only' pass Phase I clinical trials to pass into clinical practice – and overall costs are therefore more predictable, and outcomes easier to gauge. Many of the research teams NPC has met in this field are studying relatively small cohorts of patients – small, that is, relative to the numbers needed for new drug development – in a relatively limited geographic area, and for a relatively short period of time.

To take one example, the ovarian cancer study at the **Cambridge Cancer Centre** mentioned earlier; this trial is expected to take around three years, at a cost of around £300,000 (of which staff will cost just over £200,000, with just under £100,000 for consumables, of which £50,000 is still unfunded). Although its findings, once published, would need further validation before passing into clinical practice, ultimately this work might help the 5,000 or so women diagnosed with ovarian cancer each year in the UK (not to mention those overseas) in terms probably of quality and possibly of quantity of life. Assuming the research is valid, and that it will then take around five years before a scientist comes up with a better way of determining optimal chemotherapeutic regimes for ovarian cancer, that is £300,000 potentially to help at least 25,000 women over those five years – the cost of kick-starting this research just over £10 per woman.

Outcomes from research into the prevention, detection and diagnosis of cancer

As we saw when looking earlier at public sector interventions, the outcomes for preventative and screening strategies – weighing the one-off cost of the research into prevention or screening for a type of cancer, plus the resultant campaign, against the continuing health, not to mention psychosocial costs of those contracting that cancer – are often compelling.

To take the example of the work of the **CR-UK colo-rectal cancer unit** at St Mark's – Dr Atkin's team, while trialling the flexible sigmoidoscope in a study funded by the DoH, is also hoping to fund a connected project to train new nurse-endoscopists to operate the machine. The team has completed a feasibility study, which proved the efficiency of nurse-endoscopists and their popularity amongst patients, and is now looking for £200,000 to undertake the full project. This would fund a team member researching a PhD on the training and development of a nationwide workforce of 300 nurse-endoscopists, by meeting each of the current workforce of 140 twice, and developing with them a programme whereby each existing nurse trains another, thus doubling their numbers. The outcome here would be similar to that seen with the specialist nurse at the Manchester Royal Infirmary, whereby patients should be seen more quickly and certainly more cheaply than they would by a doctor – so speeding up detection, diagnosis and treatment in many of the UK's 33,000 new colo-rectal cancer patients each year, ultimately improving both quality and quantity of life.

Outcomes from research into cancer control and survival

Concentrating here on palliative care, research and evaluation of new approaches is crucial on at least two levels – demonstrating efficacy is important in order to get other practitioners to consider implementing new strategies or setting up new programmes, and will also convince funders, including government, of the value of a new initiative. Thus funding for the mapping of need – not so much at a national level, where the need is well known, but at local levels, where there are large variations in coverage – or for research into new approaches to palliative care, or for the dissemination of the research result, will probably all ultimately shape the provision of services at local or maybe national level.

Dr Watson's trial (costing £60,000) at the **Northern Ireland Cancer Centre** on melatonin to reduce nausea and weight loss in cancer patients could, if successful, result in a drug that helps to manage some of the most distressing effects of cancer, and thus, after further trials, possibly benefit many cancer patients across the UK.

Comparison of interventions – costs, outputs, outcomes:

While it is difficult to make meaningful comparisons between charities that are so many and so various, we have attempted to draw together a representative cost per 'unit' of output for each of the types of intervention in the cancer field. We then look at what a donation of £100,000 might 'buy', and what the outcomes of that donation might be – bearing in mind that however disparate the charities, all are aiming to improve either quality or 'quantity' of life.

Treatment

Intervention	Quality of life	'Quantity' of life	Cost per unit	£100,000 funds:
Purchase of hospital equipment	Usually	Often	Anything from £1,000 to well over £1 million	One big machine (e.g. an echo-cardiograph); part of a bigger one (e.g. a contribution towards a PET/CT scanner); or several smaller ones (e.g. equipping a critical care unit at the Christie)
Funding hospital staff	Yes	Sometimes	Specialist nurse total cost may be £35,000 annually	Specialist nurse for up to three years
Funding hospital-linked services, e.g. Anthony Nolan	Usually	Hopefully, yes	Getting a bone marrow for transplant 'costs' Nolan £30,000	Three bone marrows for transplantation at the patient's hospital (NHS operation costs a further £70,000)
Funding hospital-linked services, e.g. CLIC	Yes	Possibly, where nurses are involved	CLIC nurse costs £30,000 annually, all up; the new Home from Home at the Middlesex will cost £5 million	Three years' funding for a nurse
Advocacy	Ultimately, yes	Ultimately, yes	Probably £40,000 per staff member, e.g. at Breakthrough Breast Cancer	Two-year staff contract, including on-costs
Education	Maybe	Possibly, especially with education on prevention	£40,000 per staff member, including on costs £5,000 would cover the costs of one of Breast Cancer Care's Healthy Living Days	Twenty 'Healthy Living Day' conferences for 300 women
Information	Yes	Possibly	Around £20,000 to sponsor a CancerBACUP booklet, or £50,000 for a year's running costs for one of its local centres	Sponsorship of five publications, or of two years' running costs for one of CancerBACUP's centres (six in existence, more planned across the UK)
Information help-line	Yes	Possibly	£30 per enquiry	More than 3,000 enquiries answered

Palliative care

The purpose of palliative care is not to extend life, but to enhance the quality of life of someone approaching the terminal phase of disease. Although on occasion good care may help to 'buy more time' (perhaps a few days), in most instances this will not be the primary objective. Therefore outcomes should not be measured not in terms of additional 'quantity' of life but in terms of quality of life of the patient, and impact on surrounding family and carers.

Intervention	Quality of life	'Quantity' of life	Cost per unit	£100,000 funds:
In-patient care in a hospice	Yes	n/a	£325 per 24 hours	24 'episodes' of care averaging 13 days each
Nursing services	Yes	n/a	£179 per 24 hours for Marie Curie nurse	Over 500 patient nights, benefiting say 50 patients and families
Day care, usually at a hospice	Yes	n/a	£40 per patient per day	2,500 patient-days, so maybe 200 patients annually – invaluable respite to carers
Carer support	Yes	n/a	n/k, unlikely to be large	n/k, but may avoid emergency hospital admissions
Gold Standards Framework	Yes	n/a	£1.3 million per 1,000 GP practices	80 GP practices brought into scheme, covering 3,200 patients – hospital admissions avoided
Liverpool Care Pathway	Yes	n/a	n/k	n/k
Education for generalists	Yes	n/a	£100,000 annual running cost for a proposed learning centre (once set up)	50-100 generalists each year – if GPs, 500-1,000 patients may benefit
Research	Yes	Possibly	£60,000 to run a trial on melatonin on cancer patients suffering from nausea and weight loss	The trial with change to spare – if successful, thousands of patients may ultimately benefit from use of the drug
Umbrella bodies	Indirectly	n/a	£40,000 to map children's services in Wales[132]	Mapping of 2,000 life-limited children's needs in Wales and part of England[133]
Children's services	Yes	n/a	£500-700 per 24 hours for an in-patient at a children's hospice	150–200 days of care

Research

Intervention	Quality of life	'Quantity' of life	Cost per unit	£100,000 funds:
Staff for research team	Probably	Hopefully	Total cost, including consumables, of PhD student c£30,000 pa; post-doctoral researcher c£40,000 pa senior post-doc/ team leader c.£50,000 pa	PhD student for three years More senior researchers, probably for two
Equipment for research team	Probably	Hopefully	Anything from £10,000 for a year's consumables to £200,000 for a flow cytometry sorter, and beyond	DNA sequencer

Section 6: Conclusions

All the areas we've looked at – treatment, palliative care, research – need more money. Prioritising between them is impossible – the very nature of cancer requires a broad range of interventions, all essential, and donors will have a natural bent to one or more of them. NPC can, however, draw some tentative conclusions within each broad area of intervention – we certainly have views on different charities operating in similar fields, and are separately publishing a series of individual charity reports. We would also make the general point that where philanthropists are interested in the charities NPC has analysed, we would in most cases recommend making an unrestricted donation, advising restricted grants mainly for donations direct to hospitals or university departments, to be made through the institution's endowment office.

Treatment

Treatment covers a wide range of different interventions into patient care, most of those from the state, and whilst some will always say that philanthropists should concentrate on charities providing the vital hospital-linked services that have always been the preserve of the voluntary sector, leaving the NHS to fund hospital equipment and staff, others are more interested in providing the resources hospital patients need sooner rather than later, regardless of whether they are thus 'subsidising' the state. Our view is that both are valid – we have seen the difference that a privately-funded member of staff or piece of equipment makes to an NHS ward, and seen too the vital support work done by charities with hospital-linked services as different as Anthony Nolan and CLIC – all of which seek to improve quality and hopefully quantity of life.

Equally vital is the work being done in information and support, education and advocacy, particularly the first three, while not denigrating cancer advocacy, which has a major role in pointing up inequalities especially of treatment. Education of the public is truly vital to help prevent cancer and, if not, to accelerate its detection – an early diagnosis having an enormous impact on the success of treatment. Although much of this is done through state-led public health programmes, such as anti-smoking and five-a-day (fruit and vegetables) campaigns, the voluntary sector also has an important role to play in trying to change the public's behaviour – Breast Awareness Month each October probably its most successful contribution, CR-UK more recently launching the SunSmart campaign in conjunction with the Department of Health. Information, almost totally the preserve of the voluntary sector, is vital too – if the GP is busy, and maybe too broad-based anyway, and the consultant rushed, then most oncology departments will have information pamphlets provided by charities and often a Macmillan nurse available, and most help-lines, certainly at CancerBACUP and Breast Cancer Care, have long hours and, increasingly, foreign language speakers, with most promising to ring back if a caller is unable to get through. Websites, of course, are always open. Crucially, these organisations have the time that a doctor often lacks, and so can provide support as well as information to patients, or their families, who of course are often shocked and distressed. And voluntary sector organisations – as diverse as Macmillan Cancer Relief, the Bristol Cancer Help Centre and Maggie's Centres – continue to provide support and counselling throughout the patient journey, from detection through diagnosis, treatment and, sometimes, to death.

Palliative care

There is no absolute point in time where a patient's needs switch from supportive care described above to the palliative care which will help him or her on their journey to the end – they will overlap and complement each other for much of the journey. But with over 150,000 cancer patients dying each year, the importance of good end of life care cannot be overstated, since it not only affects the patient but also those around the patient. Fortunately for cancer patients, palliative care is most developed in the cancer sector – indeed it is where palliative care was pioneered in this country.

The voluntary sector has been crucial in the development of palliative care – not just in terms of providing and funding over half of the service provision, but also in its contribution to the development of best practice and strategic initiatives to disseminate it throughout state and voluntary sector services alike. However, everyone in the sector would agree that there is still some distance to go: research is still under-funded, as are pain and symptom alleviation, psychosocial services (particularly for carers), development of services for children, adolescents and young adults – all of these need more funding. There is also a shortage of specialist and general palliative care professionals, and NPC believes, further,

that there needs to be greater transfer of knowledge from specialists to generalists, and on down the chain to informal carers, and that there are opportunities for funding such initiatives. In the meantime there is a substantial human and capital infrastructure which still relies heavily on voluntary sector funding – and in the case of hospices will often have a local flavour which might appeal to donors, particularly in areas of the UK where fundraising is difficult.

Research

As far as research is concerned, these are fascinating times to be involved. Recent work on molecular biology is prompting the beginnings of a change in approach to cancer: from the traditional treatment of surgery followed by heavy doses of cytotoxic drugs or radiation to hopes of a more effective, less toxic approach – not just by the continuous refinement of chemotherapy drugs, important though that is, but by looking at the underlying faulty genes causing cancer and finding ways to target them. It is very unlikely that there will ever be a cure for cancer – the disease is inevitable given, in the West, ageing populations leading modern lives with all the lifestyle choices that implies, and, in the developing world, some populations exposed to environmental and workplace hazards as well as to infectious disease, plus a general trend to increased smoking and drinking. But with more resources spent on education and prevention, earlier detection, quicker diagnosis and improved, increasingly tailored treatment, it is certainly possible to manage the disease better than we currently do.

NPC has met UK researchers working in all of these areas, as well as on the specific sub-types of cancer, and, as with treatment and palliative care, it would be foolish to single out one above the other – all are key to the effort of improving quantity and quality of life, and all relatively under-funded by comparison with US counterparts. Suffice it here to mention again, then, those areas receiving a smaller share of the UK research funding 'cake' than their importance might warrant: research into prevention, detection and diagnosis, treatment and palliative care, as well as into the less 'fashionable' cancers. Work on any type of research can be supported either directly, with restricted grants made to university or hospital departments, or via the big funding charities – CR-UK dominant in the field, followed by the equally impressive, though smaller, Institute of Cancer Research, Leukaemia Research Fund, Breakthrough Breast Cancer, Marie Curie Research Institute and the other NCRI members not yet met by New Philanthropy Capital.

Inevitable and intractable as cancer might seem, and despite the dominant role of the state in treatment, there are many ways in which the voluntary sector intervenes effectively in this field to improve quality and sometimes quantity of life. There is huge scope for philanthropists, too, as there has always been, certainly for the past century since the setting up of the Imperial Cancer Research Fund, now merged into CR-UK, by Edward VII, not to mention philanthropically-founded hospices or hospitals such as Trinity Hospice, the Christie or the Royal Marsden before the advent of the NHS. Whether enabling scientific research, supporting hospital projects or, more recently, funding supportive and palliative care, private funders have a long and impressive history in this field – yet future funding opportunities remain many and exciting, their outcomes compelling. In an ageing population such as ours, especially, cancer is never going to go away, but by constantly improving treatment, palliative care and research we can certainly manage it more effectively, and just maybe begin to take away some of the fear and uncertainty surrounding this most hidden of assassins.

Appendix 1: Examples of delivery visited by NPC

Treatment

Organisation	Description/project	Annual income (£m)
Royal Marsden Hospital	Cancer hospital in London and Sutton: we visited wards at both locations, the nuclear medicine department and the new drug development ward	n/a
The Christie Hospital	Cancer hospital in Manchester: we visited its Adult Leukaemia Unit in particular	n/a
Middlesex Hospital	General hospital, linked with UCL: we visited the Teenage Cancer Trust wards and the ACROBOT orthopaedic project	n/a
Bristol Children's Hospital	New children's hospital: we saw CLIC's 'Sam's Place' unit	n/a
Manchester Royal Infirmary	General hospital: visited its Department of Haematology	n/a
Hammersmith Hospital	London hospital: we visited its leukaemia unit – the Catherine Lewis Centre	n/a
Addenbrookes Hospital	General hospital in Cambridge with big cancer unit	n/a
John Radcliffe Hospital	General hospital in Oxford with big cancer unit	n/a
The Anthony Nolan Trust	Charity that provides bone marrows for transplantation	13
CLIC (Cancer and Leukaemia in Children)	Support and information, provision of nurses, accommodation for parents with children undergoing treatment, social/financial support	7.9
CancerBACUP	Advocacy, education, information, help-line and support for all cancers	3.8
Breast Cancer Care	Education, information, help-lines and support for breast cancer patients and their families	5.6
Maggie's Centres	Support centres in Edinburgh, Glasgow and Dundee, with centres planned UK-wide.	1.9
The Haven Trust	Support centres for breast cancer patients in London and Hereford	1.2
Bristol Cancer Help Centre	Centre offering courses for cancer patients, including complementary therapies and emotional/spiritual support	1.9
Teenage Cancer Trust	Equips hospital wards for use by teenage patients	2.6
Liverpool Cancer Support Centre	Support centre with 'self-advocacy' approach	0.05
Ellenor Foundation	Home-based care	2.2
Theodora	Provides clowns for child patients in hospitals	0.2
Changing Faces	Post-operative physical and psychological rehab	0.9
Genetic Interest Group	Research and advocacy of genetic diseases	0.3

Palliative care

Organisation	Description/project	Annual income (£m)
Marie Curie Cancer Care	Runs 10 adult hospices and nursing services across the UK. Developed the Liverpool Care Pathway for the dying patient.	82.5
Macmillan Cancer Relief	'Pump-primes' palliative care nurses and other healthcare professionals. Makes welfare grants to patients. Funds peer-to-peer palliative care training for GPs. Developed the Gold Standards Framework.	77.4
Sue Ryder Care	Runs six adult hospices and 10 neurological care centres. Some hospices also provide a home care service. Some cancer patients.	46
Help the Hospices	Umbrella body for the independent hospices. Educational and information sharing role. Has programmes related to specific areas of need to distribute funds from grant-making trusts.	2.6
National Council for Hospice and Specialist Palliative Care Services	Research-focused, moving towards a think tank role.	0.5
Cancer Black Care	Cancer support centres based in London, Manchester and Birmingham, targeted at black and ethnic minorities.	0.5
Association for Children with life-threatening or Terminal conditions and their families (ACT)	Umbrella body of children's hospices, community nursing teams and condition-specific groups. Publishes guidance in children's palliative care, campaigns for professionals and voices views of children with life-limiting conditions and their families on what service provision should be. Runs and provides a helpline for affected families.	0.2
Association of Children's Hospices	Umbrella body for children's hospices. Key concerns are the planning of future children's hospices, lack of appropriate trained staff/training and lack of knowledge about services available to life-limited children.	0.3
Dept. of Palliative Care & Policy, King's College, London	A major and well regarded academic department.	n/a
Dame Cicely Saunders Foundation	Proposed multidisciplinary research centre, to be first research institute in the world for care of the dying.	n/a
The King's Fund	Supports research, education and policy development in health, particularly in London area.	n/a

Adult independent hospices and children's hospices

There are over 250 hospices in the UK. NPC visited, communicated with or researched 12 in total for sampling purposes. We are not listing those visited here, as it would be inappropriate to single them out. Hospices offering specialist services have been mentioned in the text.

Research

Organisation	Description/project	Annual income (£m)
Cancer Research UK: Lincoln's Inn Fields	Headquarters of CR-UK, and home of its Cancer Research Technology subsidiary	306
CR-UK: Beatson Institute, Glasgow	Various research teams, including Dr Tobias's research into TES tumour suppressor gene, plus sleep disturbance trial at Glasgow University	
CR-UK: Paterson Institute, Manchester	Various teams, including Breast Biology Group	
CR-UK: Cambridge Cancer Centre	Various teams, including Dr Brenton's ovarian group at the Cancer Genomics Program	
CR-UK: St Mark's Hospital, Harrow	Colo-rectal Cancer Unit	
CR-UK: Translational Oncology Labs, Barts and Queen Mary's School of Medicine	Centre of the Cell project Professor Balkwill's project on the role of anti-inflammatory drugs in cancer treatment	
The Wellcome Sanger Centre, Cambridge	Cancer genome project	n/a
The Institute of Cancer Research, London	Various teams, including the Male Urological Cancer Research Centre and lung, ovarian, melanoma and paediatric cancer teams	55.9
Breakthrough Breast Cancer	Breakthrough Toby Robins Breast Cancer Research Centre at The Institute of Cancer Research	6.7
Leukaemia Research Fund	Research into leukaemia and the lymphomas	16.6
Marie Curie Research Institute	Various, including molecular motors team	3.5
Hammersmith Hospital (Imperial College)	'Spirit' trial into leukaemia treatment	n/a
Weatherall Institute of Molecular Medicine, Oxford	Various, including haematology department and molecular angiogenesis group	n/a
University of Manchester	Cancer Genetics studies	n/a
Manchester Royal Infirmary	Department of Haematology	n/a
UCLH	Department of Haematology	n/a
Children with Leukaemia	Cord blood project at the Lifeline Centre, Southmead Hospital, Bristol University	4.7
Against Breast Cancer	Small cohort study on breast cancer risk	0.4
Genesis	Small Manchester research and support project into hereditary breast cancer	

Appendix 2: UK incidence, mortality and survival rates of the most common cancers

Blue=men Black=women	Incidence per 100,000 (age standardised, GB)		Cumulative risk of developing cancer over a lifetime (England and Wales)			Mortality per 100,000 (age standardised, UK)		Five-year survival rate (1996-99, England and Wales)	
	1975	2000	% by 65	% in life	which is	1975	2000	% UK	% US
Lung	113	69	1.7	8	1 in 13	109	61	6	14
Lung	23	36	1	4.3	1 in 23	22	30	6	15
Breast	74	114	5.6	10.9	1 in 9	39	31	77	87
Colo-rectal	46	57	1.4	5.7	1 in 18	33	25	47	55
Colo-rectal	36	36	1.1	4.9	1 in 20	26	15	48	60
Prostate	33	80	0.9	7.3	1 in 14	20	26	65	98
Oesophageal	9	14	0.4	1.3	1in 75	8	13	7	13
Oesophageal	5	6	0.2	1.1	1 in 95	4	5	8	13
Pancreatic	12	11	0.3	1	1 in 96	13	10	2	4
Pancreatic	7	8	0.2	1.1	1 in 95	8	7	3	4
Stomach	31	18	0.5	2.3	1 in 44	30	12	13	18
Stomach	15	7	0.2	1.2	1 in 86	14	5	15	25
Leukaemia	10	12	0.4	1	1 in 95	8	7	36	46
Leukaemia	6	7	0.3	0.8	1 in 127	5	4	35	46
Non-H lymphoma	7	15	0.6	1.4	1 in 69	4	7	47	56
Non-H lymphoma	5	11	0.4	1.2	1 in 83	3	5	52	56
Hodgkin's disease	4	3	-	-	-	2	0.5	-	84
Hodgkin's disease	2	2	0.4	1.2	-	1	0.3	-	84
Ovarian	15	18	0.9	2.1	1 in 48	12	11	36	53
Malignant Melanoma	3	10	0.4	0.7	1 in 147	1	3	77	98
Malignant Melanoma	4	11	0.5	0.9	1 in 117	1	2	87	98

Source: Cancer Research UK and the American Cancer Society

Appendix 3: Notes on some common cancers

Lung cancer

Incidence and mortality: In this country, one man in 13 and one woman in 23 will be diagnosed with lung cancer over the course of their lifetimes. CR-UK says that one person receives that diagnosis every quarter of an hour here, lung cancer representing 14% of all cancers diagnosed. While overall incidence has declined significantly since the 1970s, when Britain was bearing the legacy of extraordinarily high tobacco consumption levels mid-century (over 65% of men in the 1940s), doctors are concerned that while incidence in men continues to decline, the trend in women has stopped falling. Incidence is more prevalent and mortality higher in less affluent groups, although in all diagnosed cases only 6% of patients will still be alive five years later – lung cancer presents late and is very hard to treat, so it remains the UK's biggest cancer 'killer', representing 22% of cancer deaths. Globally, the WHO refers to lung cancer as an epidemic, now causing over a million deaths each year, a figure that is rising as tobacco consumption in the developing world continues to increase – the WHO forecasting accumulated deaths by 2050 at the 150 million level.

Causes, risk and prevention: In over 80% of lung cancer cases, tobacco smoking is the cause – the relative risk of developing lung cancer twenty times higher for regular smokers than for non-smokers (although passive smokers also run a higher risk of contracting the disease than other non-smokers). The more regularly one smokes, the higher the risk, although the risk diminishes once the smoker, even a long-term smoker, quits. Other risk factors are exposure to industrial carcinogens such as asbestos, some metals and radon – especially where a person also smokes. It is believed that air pollution may also be partly to blame in some cases, since incidence rates are consistently higher in towns than in the countryside.

Biology: Tobacco smoke contains 5,000 different chemicals, 40 or more of them carcinogenic, of which nicotine – also highly addictive – is the most prevalent, at up to 2mg per cigarette. It is believed that enzymes (present especially in the lung) metabolise these carcinogens, binding them to the DNA, the beginning of a complex process involving the loss or gain in function in tumour suppressor genes and oncogenes respectively (including p53 and k-ras) over many, at least twenty, years. There are two main types of lung cancer – the more common non-small cell lung cancer (NSCLC), variations of which affect around 80% of patients, and small cell lung cancer (SCLC), which arise as a mass in one of the lung's airways, spreading via the lymph system usually to bone, brain or liver.

Detection and diagnosis: Because its symptoms – coughing, difficulty in breathing, chest pain, or recurrent, inexplicable bronchitis or pneumonia – present fairly late on in lung cancer's progression, especially in NSCLC, most patients (around 60%) are diagnosed with Stage IV, or metastatic cancer, for which curative treatment is not really possible.

Progression and treatment: In 20-30% of cases, and especially in SCLC, diagnosis is early enough that radical surgery can be carried out, and this has a relatively good prognosis – up to 50% of these patients survive for more than five years. Otherwise, radiotherapy and often chemotherapy are administered: platinum-based drugs (cisplatin) the first line of treatment, followed if necessary by yew-based drugs (docetaxel) and then finally by a new AstraZeneca drug, Iressa (gefitinib) that inhibits the epidermal growth factor (EGF) receptor implicated in several cancers, and has improved survival times in almost half of patients. Trials are also going on in new drugs such as Avastin (Genentech), although it is true to say that in lung cancer, such treatments are often largely palliative, to ease symptoms and pain, since three-quarters of people diagnosed with lung cancer die within the year, and more than 90% are dead within five years.

Lung cancer charities: There are few charities concentrating on lung cancer, the Roy Castle Lung Cancer Foundation the only sizeable one, which explains why, in the NCRI strategic analysis (shown on page 43), there is such a disconnection between the size of the problem and the amount of money spent researching it. However, CR-UK points out the best way to stop people dying of lung cancer is to get them to stop smoking, mentioning the work of the campaigning charity Action on Smoking and Health (ASH), which it supports.

Breast cancer

Incidence and mortality: Breast cancer is the most commonly diagnosed women's cancer (although over 250 men are also diagnosed with this cancer each year). Around one in nine women are now expected to receive the diagnosis during their lives – the vast majority of them (80%) when they are over 50 – with breast cancer accounting for one in three cancers diagnosed in women in the UK. While early detection and the discovery of the anti-oestrogen drug tamoxifen have radically improved survival rates – from 50% of patients still living after five years in the 1970s to 77% now – breast cancer is still the single most common cause of death in middle-aged women in this country.

Causes, risk and prevention: It is believed that hereditary factors account for up to 10% of cases (hence Breakthrough Breast Cancer's recently launched genetic information website), and hormonal factors for many more. It has been shown over the past 50 years that high and prolonged levels of oestrogen in the body significantly increase the risk of breast cancer, and thus the century's dramatic increase in incidence is thought to be linked to more years of ovulatory cycles in today's Western woman than was historically the case. So, probably more at risk than others are women who take the Pill for long periods of time; who either have no children, or late first pregnancies, or, possibly, those who choose not to breast feed once they have had children; women who menstruate early or reach the menopause late, or (again only possibly) take HRT on reaching the menopause. Other factors are thought to come into play: diet, exercise and the environment in which we live. Although scientists cannot be sure of the precise correlation between our industrialised environment and breast cancer incidence, nor of the exact extent to which our alcohol intake or increasingly processed diet makes us more vulnerable, or the extent to which exercise lessens that vulnerability, it does seem clear that our 'lifestyle choices' can put us at risk. Breast cancer incidence is, unsurprisingly, lower in the developing world than in the West – but when Asian women, with a low-risk profile, settle here, their breast cancer incidence rises to Western levels. In the UK, since 1988, breast screening has been offered every three years to women between 50 and 64; the age range is currently being extended by five years to 70, and its frequency also increased; this should further improve survival rates. A recent American study recommends that a daily aspirin seems to reduce risk.

Biology: 85% of breast cancers originate in the epithelium (surface tissue) lining the milk ducts, 15% in breast lobules. While up to 10% of patients will have a family history of the cancer (one or more first degree relatives – mother or sisters – affected), where faulty BRCA1 or BRCA2 genes are often implicated, most cases are 'sporadic', with damage sustained over the woman's lifetime in a number of different genes. Many of these have been identified, including p53, the tumour suppressor gene that is deficient, and the Her2/neu growth factor gene, often over-expressed in this type of cancer.

Detection and diagnosis: A lump is often found in the breast or armpit by the patient herself, and confirmed by the oncologist, using a mammogram (simply a breast X-ray), followed by biopsy.

Progression and treatment: Once the breast lump is confirmed as malignant, it (and often the lymph nodes in the armpit) should be removed within a month. Some women are recommended (or opt) to have a mastectomy (total removal of the breast), the standard, radical treatment for 2,000 years until relatively recent times. Surgery is followed by adjuvant (additional) therapy, usually chemotherapy (anthracyclines) and often, later, radiotherapy to destroy any cancer cells that may have metastasized. If the cancer has metastasized, and the Her2/neu oncogene is over-expressing, then Genentech's Herceptin, a monoclonal antibody, can be prescribed. Hormone therapy (usually tamoxifen) is then also administered in most cases over the following five years – and it is tamoxifen that has largely been responsible for the dramatic reduction in mortality rates since the 1980s. An anti-oestrogen that starves the tumour of the female hormone it needs to grow, tamoxifen was developed by ICI in the 1970s originally as a 'morning-after' Pill. While constantly being refined (its use slightly increases the risk of uterine cancer, so AstraZeneca has developed Arimidex, which shuts down oestrogen production altogether, as does Novartis' letrozole, or Femara, for post-menopausal women), it is still given to most patients after surgery, appearing to protect them for the next five years. Vaccines are also being trialled against breast cancer, as is a drug called Avastin, also from Genentech, which prevents angiogenesis, or extra blood supply to the tumour.

Breast cancer charities: Breast cancer charities are the most numerous of all charities specific to cancer types; the big three are Breakthrough Breast Cancer, Breast Cancer Care and Breast Cancer Campaign, with the Haven Trust growing quickly too.

Colo-rectal cancer (bowel cancer)

Incidence and mortality: 13% of cancers diagnosed in this country are colo-rectal – one in 18 men and one in 20 women developing the disease over the course of a lifetime, the vast majority of those in old age. Incidence is, generally speaking, increasing in the West, although the trend has been reversed recently in America, partly as a result of screening programmes, possibly because of changing dietary patterns. Improving treatment is also leading to increasing survival rates – now over 50% are survivors at five years here (and well over that in the US). Colo-rectal cancer accounts for 10% of UK cancer deaths, with our mortality rate 25% lower than 20 years ago.

Causes, risk and prevention: A disease that is quite common in the Western world but still relatively rare in the developing world, colo-rectal cancer stems from our diet and, to a lesser extent, our lifestyles. Patients tend to have a diet rich in animal protein, fat and refined carbohydrates, sometimes combined with low physical activity, leading the WHO to estimate that up to 70% of cases could be prevented with relatively easy changes to daily routines. Studies suggest that risk can be reduced by decreasing consumption of red meat (especially processed meats) and increasing intake of fruit and vegetables, fish and in this case fibre, which helps flush the system through, and by cutting down on tobacco and alcohol. Since obesity is also associated with increased risk, physical activity is probably also protective, and some studies suggest that either aspirin or HRT in post-menopausal women might also reduce risk.

Biology: The large bowel stretches from the appendix to the anus; around 60% of colo-rectal cancers develop in the colon, 40% in the rectum. While up to 5% of cases stem from familial genetic faults, the majority of cases see the cancer developing over many years from somatic changes in the normal behaviour of tumour suppressor and oncogenes – first usually the tumour suppressor gene APC, allowing the development of early polyps, followed by mutations in the oncogene k-ras, leading to pre-malignant adenomas, then progressed by a final mutation in the tumour suppressor gene p53.

Detection and diagnosis: The symptoms of colo-rectal cancer present quite early in the disease, but are relatively non-specific, including abdominal pain in colon cancer and bleeding in rectal cancer, as well as diarrhoea or (oddly) constipation. And since the average UK GP sees only one colo-rectal cancer patient each year, the disease is often diagnosed later than necessary – hence the efficiency of screening, which in America has been largely responsible for the increase in survival rates in recent years. Screening is most commonly done by a faecal occult blood test (FOBT) – where suspicious, doctors follow up with either a barium enema, or more definitively a colonoscopy. Increasingly, researchers recommend a flexible sigmoidoscopy, where the rectum and lower colon are examined for pre-cancerous polyps that can be removed during the procedure – this another reason for decreasing levels of incidence in the US. Trials are currently being carried out on both methods of detection for the Department of Health in the expectation of an introduction of screening here before the decade is out.

Progression and treatment: Surgery is the main form of treatment, curative if the disease is still at Stage I or II – 80% of patients will undergo an operation, although the cancer will recur in half of them within two years. So surgery is usually followed by chemotherapy (5-FU, an anti-metabolite, one of the oldest cancer drugs), especially if the cancer has invaded the lymph nodes, for the next six months – with a higher success rate in colon than rectal cancer. Advanced cancer in the rectum usually requires a course of radiotherapy, which improves median survival by anything up to a year. Much research is being carried out into different chemotherapies – several new drugs (including irinotecan and oxaliplatin) being tested in clinical trials – and increasingly researchers are looking into new treatments. Possibilities include methods attempting to stimulate the immune system, since colo-rectal tumours are poor at evoking their own response. Vaccination is one idea, or the introduction of genetically-modified viruses; another is Avastin, an anti-angiogenesis compound, plus work is continuing on monoclonal antibodies such as AstraZeneca's Iressa or ImClone's IMC-C225, both of which target the EGF receptor mentioned under lung cancer, which is often present in colo-rectal cancer too.

Colo-rectal cancer charities: Beating Bowel Cancer, Colon Cancer Concern, Digestive Diseases Foundation.

Prostate cancer

Incidence and mortality: Prostate cancer has recently become the most commonly diagnosed cancer in men, now accounting for 9% of all UK cancer cases. The rising incidence is a global phenomenon and is controversial. Incidence in the US, for example, is twice that here, and is largely explained by the increase in screening. This has been made easier by the introduction of the simple prostate specific antigen (PSA) blood test, probably now undergone by 70% of US men over 50. However, screening is a vexed issue, since it is estimated that although one man in three over the age of 50 has a small focus of cancer in the prostate gland, this develops into full-blown disease in only around 30% of them, with only one in 25 dying from it – not least because incidence increases dramatically in older men, many of whom will die from some other cause before the prostate cancer has had time to develop. Routine post-mortem examination of the prostate gland in almost any elderly man shows a tiny focus of the cancer, which was clearly best left untreated. Nevertheless, when this cancer does develop, it is not easy to treat; although mortality rates have fallen slightly here since their mid-1990s peak – with survival now over 60% – globally mortality rates continue to rise, albeit slowly, given increasing underlying incidence, to make prostate cancer the third most common cancer in men, after lung and stomach.

Causes, risk and prevention: Up to 10% of cases may be inherited – there is a higher risk for men in families carrying the BRCA2 gene associated with breast cancer – and other risk factors include over-expression of male hormones, especially testosterone, and a high calorific intake, especially of saturated fats, combined with low physical activity. There is a suggestion of higher risk in black populations and a more controversial link being investigated between vasectomy and prostate cancer.

Biology: The prostate gland, situated at the base of the bladder, just in front of the rectum, produces the liquid that combines with semen to make seminal fluid. Prostate cancer is present in a pre-clinical form in many men from the age of around 30, remaining latent for up to 20 years before progressing, in around 30% of cases, to an aggressive, malignant cancer. Its growth is linked to male hormones – androgens and especially testosterone – and to mutations in various oncogenes and tumour suppressor genes (particularly here in GSTPI, a gene involved in carcinogen detoxification).

Detection and diagnosis: Symptoms of prostate cancer range from a difficulty in urinating, or conversely a frequent need to urinate in the relatively early stages of the disease, to pain, often in the back, once the cancer has metastasized to other parts of the body, frequently the bones. A rectal examination is the simplest way to detect abnormalities in the gland; otherwise the PSA test works by measuring levels of a protein consistently elevated in men with the disease. Unfortunately the PSA is sometimes positive in men without the cancer; hence the development in America of a new, more specific protein-profiling test to study nine separate proteins in the blood. Where prostate cancer looks likely, an ultrasound-guided biopsy is performed to confirm diagnosis – oncologists keen not to treat cases that are not aggressive, such are the complexities and side-effects of current treatment.

Treatment: When the cancer is diagnosed at an early stage, still localised in the prostate, the patient can opt either for 'watchful waiting', surgery or radiotherapy. While radical prostatectomies do result in good survival rates, side-effects include incontinence in up to 20% of patients and impotence in up to 80%, with a subsequent inability to produce semen. Radiotherapy (or increasingly brachytherapy, which uses radioactive implants), while also effective, can lead to incontinence in up to 5% of patients and impotence in up to 60%. Hence the increasing popularity of 'watchful waiting', where the cancer is not treated but monitored regularly – the premise being that since the cancer grows slowly the patient may well survive long enough to die of some other condition, without otherwise difficult treatment. However, when a patient presents with advanced cancer, curative treatment is not possible, so palliative treatment is given. This is usually hormone therapy – anti-androgens that lower testosterone, sometimes to castration levels, to achieve some remission – often in conjunction with radiotherapy for localised pain relief. Chemotherapy has little effect on this type of cancer, but where hormone therapy has failed, drugs can palliate the pain. On the other hand, much work is going on in potential vaccines against PSA.

Prostate cancer charities: The Prostate Cancer Charity, The Everyman Male Cancer Research Centre (at the Institute of Cancer Research), Orchid.

Oesophageal cancer

Incidence and mortality: Oesophageal cancer represents 3% of cancer cases and 5% of cancer deaths in the UK, most oesophageal cancers presenting at a fairly advanced stage. Like most cancers, incidence increases with age – it is rare to see a case in someone under 45 – and is diagnosed in more men than women. Incidence in the UK, as globally, is rising at an annual rate of over 5% – the WHO thinks this is partly due to lifestyle factors, especially alcohol consumption, given the wide variation of incidence between regions and ethnic groups.

Causes, risk and prevention: Oesophageal cancer is thought to be linked with excessive drinking and/or smoking, especially in conjunction with a poor diet, and possibly with drinking very hot liquids (oesophageal cancer incidence is high in parts of the Americas where hot maté is drunk, and it is also notably high in Calvados, in France). One form of the cancer, adenocarcinoma, is largely responsible for the current rise in incidence, and is linked to gastric reflux. In the West, according to CR-UK, 30% of adults complain of heartburn at least once a month, 10% of whom will go on to develop pre-malignant lesions (called Barrett's metaplasia), some of which become malignant. In squamous carcinomas, risk factors include excessive smoking and alcohol consumption (over 20 cigarettes and eight units of alcohol daily) – this type of oesophageal cancer, more common in the developing world than here, also linked with nutritional deficiency and the human papilloma virus.

Biology: The oesophagus, or gullet, extends from the back of the mouth to the stomach, and divides into three sections. Around 50% of oesophageal cancers develop in the upper and middle sections, as squamous carcinomas, the rest develop in the lower section of the oesophageal tract, most of these adenocarcinomas. Both types of tumour show many genetic aberrations, including (in most cases) mutations in the p53 gene.

Detection and diagnosis: Most oesophageal cancers present at an advanced stage, when the patient has difficulty in swallowing, with the feeling that food is 'sticking' – other symptoms are weight loss, coughing, vomiting and indigestion. A barium swallow will identify most tumours, followed by scanning to assess the mass and search for metastases.

Progression and treatment: Around a third of patients undergo surgery, the only reliable curative treatment. Chemotherapy can be used pre- or post-operatively or in some advanced cancers, where it can reduce the tumour size and thus improve the patient's quality of life – but it does not really alter the prognosis. Similarly, radiotherapy is often used palliatively, as are stents (flexible tubes), to help patients swallow.

Oesophageal cancer charities: None of significant size

Stomach cancer

Incidence and mortality: Stomach cancer represents 4% of all cancers diagnosed in the UK, and 4% of cancer deaths – a serious problem, yet one much improved since 50 years ago, when stomach cancer was the leading cause of cancer death in the UK. Globally, stomach cancer remains a huge problem – mortality rates worldwide are second only to lung cancer, not just because of high levels of salt in the diet (which have fallen in the West with the advent of refrigeration to preserve food) but because of increasing levels of infection with the *Helicobacter pylori* bacteria. Incidence is falling, although rates are twice as high in areas of greatest deprivation than in areas of least deprivation (as well as in twice as many men as women), but mortality rates remain high. This is a very difficult cancer to treat and fewer than 15% of patients survive beyond five years from diagnosis.

Causes, risk and prevention: This is a cancer that often proceeds from dietary factors. A high salt intake is a prime factor, but high consumption of smoked or cured, pickled or preserved foods also seems to increase the risk (which probably accounts for the relatively high incidence in the Far East, for example) as does an inadequate intake of fruit and vegetables. Conversely, vitamin C appears protective, as does a diet high in cereals, carotenoids and alliums – which probably explains the regional and socioeconomic variation in incidence in the UK as well as globally. Few cancers here appear attributable to infection by *Helicobacter pylori*, but this is a problem in developing countries especially – the bacteria often causing chronic gastritis and sometimes leading to cancer.

Biology: Most stomach cancer cases are gastric carcinomas whose underlying mechanism is as yet unclear. Researchers believe that genetic factors in the patient interact either with the salt or chemicals in foods or with the *Helicobacter pylori* bacteria, where present, causing inflammation, ulceration and, later, damage to the DNA.

Detection and diagnosis: Early symptoms are vague and non-specific – indigestion, tiredness, loss of appetite – so that by the time patients are suffering the nausea, vomiting, weight loss, difficulty in swallowing and gastro-intestinal bleeding that points to a serious problem, the cancer is fairly advanced. In Japan, where incidence rates are high (partly due to high intake of pickled and preserved fish), population screening has been introduced to combat the difficulty of late diagnosis. This has improved survival rates to an (admittedly disputed) 46%. Diagnosis is confirmed by endoscopy and biopsy or by barium X-ray.

Progression and treatment: Early stage cancers can be treated endoscopically, whereas invasive cancers usually require a gastrectomy and lymph node removal. Advanced cancers are often removed too, with pre- or post-operative chemotherapy. All told, up to 80% of patients have surgery, but only around a quarter of these procedures are curative. Radiotherapy is not a standard treatment, since stomach cancer is considered a chemo-sensitive cancer, so most patients receive some sort of chemotherapy, often palliative, which can extend survival by six months. Laser treatment is also increasingly used for palliation, and the Department of Health has recently asked NICE to assess the use of Glivec for this type of cancer.

Stomach cancer charities: None of significant size

Pancreatic cancer

Incidence and mortality: Pancreatic cancer represents 3% of UK cancer cases, but such is the difficulty of early diagnosis and therefore effective treatment that it accounts for 4% of cancer deaths here – around 6,000 each year. Its incidence is higher in the developed world, especially in countries where there are high levels of smoking, but it is growing in the developing world alongside growth in tobacco consumption. Survival levels are very poor – most patients die within a year of diagnosis, and fewer than 5% survive beyond five years.

Causes, risk and prevention: Pancreatic cancer is the most likely of all cancers to have been inherited – maybe as many as 10% of cases. A further 30% or so are attributable to smoking – smokers being two to three times more likely to develop pancreatic cancer than others, with heavy drinkers also at increased risk. Other probable risks include dietary factors such as over-consumption of fats and meats (especially cooked meats) and too little fibre; coffee consumption, once thought a factor, has now been discounted. Diabetics are more likely than others to be affected, and workplace risks also play a part – there is higher incidence of pancreatic cancer among those working with chemicals in mines, metalworks, sawmills and petrochemicals plants.

Biology: The pancreas, in the upper abdomen in front of the spine and lying above the aorta and vena cava (the body's main artery and vein, respectively), is the largest gland in the body. Actually it is two glands in one: an endocrine gland secreting hormones into the blood, of which insulin is the most important, and an exocrine gland that secretes enzyme-containing fluid to break down food into the duodenum, the part of the gut below the stomach. 90% of pancreatic cancers are ductal adenocarcinomas, most of these developing in the head of the pancreas, and seeing overexpression of the oncogene k-ras and mutation of the p53 tumour suppressor gene. The remaining pancreatic cancers are endocrine cancers – both types developing slowly over many years, even decades, but then aggressively once an advanced stage is reached.

Detection and diagnosis: It is difficult to diagnose pancreatic cancer at a sufficiently early stage to deal with it effectively. Symptoms only really appear once the cancer is fairly advanced, and these are non-specific signs such as weight loss, nausea, diarrhoea, weakness, jaundice and upper abdominal and back pain. Diagnosis is confirmed by a CT scan followed by biopsy.

Progression and treatment: Surgery offers the only real hope of a cure (although maybe 15% of patients die as a result of the procedure). Surgeons often carry out a total pancreatectomy, to remove the entire pancreas and duodenum, bile duct, gall bladder, spleen and nearby lymph nodes. Five-year survival chances following this procedure rise to just 10% – the high relapse rate is due to tiny, unseen metastases that escape surgery. This is followed by chemotherapy (5-FU), but not usually radiotherapy, although both therapies are used for palliative treatment of incurable pancreatic cancer. It is believed that gemcitabine (Gemzar, from Eli Lilly) might prolong survival by several months. There is much research into new, targeted therapies for pancreatic cancer, amongst which ImClone's work on EGF receptors plus various vaccines are in clinical trials.

Pancreatic cancer charities: Pancreatic Cancer Research Fund

The lymphomas – non-Hodgkin's lymphoma and Hodgkin's disease

Incidence and mortality: Lymphomas represent around 2.5% of all cancers diagnosed in the UK each year. Cases of non-Hodgkin's lymphoma outnumber those of Hodgkin's disease cases three to one, and together they account for 4% of cancer deaths in the UK**.** Hodgkin's disease is relatively rare, affecting mainly young adults in the West; its mortality rate has halved over the past decade, with up to 90% of Western patients now surviving over five years. However, fewer than 50% survive in the developing world, where the disease tends to affect children and the elderly. Incidence of non-Hodgkin's lymphoma – a range of different diseases sharing common characteristics – has increased by 3-10% annually, affecting mostly older people in the West affecting mostly older people but a wider range of the population in the developing world, associated as it is with infection. Survival rates in the developing world – below 35% of patients living more than five years – are half those for patients in the West.

Causes, risk and prevention: Non-Hodgkin's lymphoma is often associated with infection – hence its increasing incidence in the developing world. Viruses such as HIV, herpes and the Epstein-Barr virus increase the risk of this disease, as do germs such as the *Helicobacter pylori* bacteria. The disease is also associated with immunosuppression – a risk after solid organ transplantation, for example – and chronic diseases such as AIDS and rheumatoid arthritis: hence its skewing to the older part of the population in the West. Genetic susceptibility is rare, and occupational exposure has been pretty much ruled out (it was suggested that exposure to agrochemicals and petrochemicals might increase risk until studies showed that farmers – also exposed to sunlight – had a higher incidence than the workers producing those chemicals). For Hodgkin's disease the risks are less well defined; some types (NSHD – about 50% of cases) associated with the better-off social classes, others (MC and LP HD) with the less well-off, although one unifying factor is the Epstein-Barr virus, present in up to 50% of cases.

Biology: The lymphatic system consists of lymph nodes (or glands), lymphatics (vessels linking the nodes), the spleen and lymphoid cells in other organs (such as the skin, or gut) – the system responsible for returning excess fluid to circulation and for fighting infections, including cancer. Malignant lymphomas are a diverse group of diseases, which have in common that they affect the lymph nodes, or, in a minority of cases, extra-nodal lymphoid tissue. Hodgkin's disease is characterised by the presence of Reed-Sternberg cells, which come from the B-lymphocyte implicated in lymphoid leukaemias, non-Hodgkin's lymphoma is characterised by the presence of either B-cell or T-cell lymphocytes – the former more common, the latter more aggressive.

Detection and diagnosis: The most common symptom for all lymphomas is the enlargement – usually painless – of the lymph nodes, plus, in the more advanced stages, weight loss, unexplained fevers and night sweats. Diagnosis is confirmed by biopsy.

Progression and treatment: Lymphomas progress from a single lymph node to two or more, but still on the same side of the diaphragm. Stage III lymphoma sees the cancer moving below the diaphragm and Stage IV, as with other cancers, metastasis. Treatment for non-Hodgkin's disease tends to be radiotherapy in the early stages (this has a 50% survival rate), with chemotherapy in the later stages, largely to give some remission before the disease recurs. For Hodgkin's disease, treatment with radiotherapy and/or chemotherapy has good long-term survival rates – 70-90% in the West, 30-55% in the developing world – although at a price for young adults; they may later suffer breast cancer as a result of radiotherapy, infertility, leukaemia or even non-Hodgkin's lymphoma following chemotherapy. Increasing attention is being paid to the possibility of treating non-Hodgkin's lymphoma with monoclonal antibodies, several of which are in late-stage trials.

Lymphoma charities: The Lymphoma Association, Leukaemia Research Fund.

Leukaemia

Incidence and mortality: Leukaemia – cancer of the blood – represents 2-3% of all adult cancers diagnosed in the UK each year, and 3% of cancer deaths. It is the most common cancer in young children, its incidence rising again in old age. Most children do survive it – survival rates have improved enormously since the 1960s, from fewer than 10% then to around 75% now – largely because of improvements in chemotherapy. For adults, survival is less likely – overall UK survival at five years is 35%. The most common form of adult leukaemia is chronic lymphoid leukaemia (CLL) – this occurs mainly late in life, is commonly indolent, and patients may survive for many years.

Causes, risk and prevention: In children, leukaemia almost always comes about through infection or, extremely rarely, exposure either to radiation (which is why investigations are being carried out into extremely low frequency magnetic fields), or to anti-cancer drugs or some viruses. It is more common in Downs syndrome children than in others. In adults, its causes are still largely unknown, except in chronic myeloid leukaemia (CML), where almost all patients have in common a specific genetic defect known as the Philadelphia chromosome, although scientists are fairly sure that exposure to high levels of radiation, or some chemicals (e.g. benzene), or tobacco can trigger the disease.

Biology: Leukaemia is the malignant proliferation of blasts, or leucocytes (the precursor to white blood cells), which then accumulate in the bone marrow, and ultimately replace most normal cells there. Its origin is thus the same as that of solid tumours, except that the dividing cancer cell becomes diffused in the bone marrow, or blood, and is thus never visible as a lump. Leukaemia is classified according to the white cell of origin (lymphoid or myeloid) and also according to its clinical course (acute or chronic). In the UK, acute myeloid leukaemia (AML) and chronic lymphoid leukaemia (CLL) are the most common types of the disease, with CML and acute lymphoid leukaemia (ALL) less prevalent, although the latter affects almost all the children to be diagnosed with the disease.

Detection and diagnosis: The symptoms of leukaemia are non-specific, fairly similar to those of anaemia, especially in the myeloid leukaemias – lethargy, pallor, frequent infections and, as the cancer advances, haemorrhaging. In lymphoid leukaemias, the cancer's primary effect is on the immune system, leading to increased susceptibility to infection, and, later, to enlarged lymph nodes and bone pain. Diagnosis depends, in most cases, on detection of abnormal white cells in the circulating blood. Most patients will have a bone marrow sample taken and this will confirm the diagnosis and the type of leukaemia.

Progression and treatment: Rates of progression, as well as treatments, vary with the type of leukaemia. The disease progresses rapidly in the acute types, as the white cells spill out of the marrow into the blood and other tissues. So while survival rates for ALL in children are good, those in adult AML are around 25%. Acute leukaemias are treated with combination chemotherapy and sometimes radiotherapy, occasionally followed by 'rescue' with blood stem cells (either autologous or donated) from bone marrow or the blood itself – this is to stabilise the patient to prevent fatal infections. Younger AML patients will often have a bone marrow transplant, if a match can be found.

The chronic leukaemias progress more slowly, CLL very slowly indeed, often requiring no treatment and, if caught early, CLL has good survival rates. Later in the disease, chemotherapy (alkylating agents), radiotherapy and sometimes steroids are used effectively to control symptoms. CML is different – it progresses more rapidly to an acute phase, where it is highly malignant. Younger, fitter patients, if suitable, can receive donor bone marrow transplants, with a good success rate. However, where most patients were once treated with interferon, the standard treatment is now Glivec, which can produce complete remission, although studies show the body eventually developing resistance. Scientists are also investigating immunotherapeutic approaches to the various types of leukaemia.

Leukaemia charities: There are many – the big two the Leukaemia Research Fund and The Anthony Nolan Trust, which provides donor bone marrow for transplantation, plus the smaller Kay Kendall Leukaemia Fund.

Ovarian cancer

Incidence and mortality: Ovarian cancer represents around 2% of UK cancer cases and 3% of deaths. Mortality is high given the difficulty of detecting this type of cancer in its early stages, so that around 30% of patients survive beyond five years. Ovarian cancer is the most common gynaecological cancer, its risk increasing – as with all cancers – with age, occurring mainly in just pre- or post-menopausal women, especially white women in the more affluent social groups.

Causes, risk and prevention: While familial risk is the single most important factor (in up to 10% of cases), a woman's ovulatory history plays a crucial role. Broadly speaking, it seems that the more times a woman ovulates, the higher the risk of ovarian cancer – risk increasing, for example, where a woman has had no pregnancies, a late menopause or (possibly) hormonal treatment for infertility. Conversely, risk seems to diminish when a woman's ovulation is interrupted by pregnancy, sterilisation, hysterectomy or the Pill – the introduction of the latter thought to be the main reason for declining incidence.

Biology: The ovaries are responsible for producing eggs, and are also the main source of the female hormones (progesterone and oestrogen). In familial ovarian cancer cases (5-10% of the total), 80% are due to mutations in the BRCA1 and BRCA2 genes implicated in breast cancer; elsewhere 50% of cases see mutations in the p53 gene. Researchers are currently attempting to identify protein patterns expressed uniquely in early stage ovarian cancers in order to generate early detection markers.

Detection and diagnosis: Symptoms, when they do appear, are vague: abdominal bleeding and discomfort, excessive vaginal bleeding and gastro-intestinal or urinary tract abnormalities. Given the position of the ovaries deep in the abdomen the cancer will usually be fairly advanced by then – most cases (up to 75%) presenting with advanced cancer that has spread outside the ovaries and even the pelvis. Abdominal or (better) vaginal ultrasound should indicate any tumours, but definite diagnosis comes from laparoscopy and biopsy. Because of the difficulty of detection, CR-UK is leading a trial of vaginal screening of 200,000 women (of whom some 120,000 have been recruited) to determine whether screening is effective in terms of cost as well as earlier intervention and thus better outcome.

Progression and treatment: Most ovarian cancer patients will undergo surgery to remove the ovaries and (usually) the womb and appendix too, although in younger women fertility and the reproductive function can now be saved. Surgery on patients with early stage cancer is often successful – survival rates at five years up to 80%, falling to below 14% for women with Stage IV cancer. Surgery is followed up with radiotherapy for those patients with early stage cancer, chemotherapy for those with more advanced disease – a combination of platinum and yew-based agents, although highly toxic, has the best response rate. However, mortality rates are more or less unchanged over 25 years – hence this type of cancer is much researched, with scientists looking at possible vaccines, monoclonal antibodies and gene therapy targeting the p53 tumour suppressor gene.

Ovarian cancer charities: Helene Harris Memorial Trust

Malignant melanoma

Incidence and mortality: Although not one of the biggest cancer 'killers' in this country – 1% of cancer deaths attributable to it each year – we include malignant melanoma in this survey because of the current increase in worldwide incidence. While up to 100,000 skin cancers are diagnosed each year, what really concerns oncologists is the increase in malignancies. These have more than doubled in 20 years, to currently just over 7,000 per annum in the UK, the vast majority of them melanomas (as opposed to the usually non-malignant basal cell or squamous cell carcinomas). Moreover, many of these are diagnosed in fairly young age groups – malignant melanoma now represents around 9% of all cancer cases in young adults (i.e. aged 15-39), and is now the most common form of cancer in US women in their twenties.

Causes, risk and prevention: 80% of malignant melanomas are caused by (often intense, intermittent) exposure to the sun's ultraviolet (UV) radiation. Countries with hot climates and fair-skinned populations tend to see high incidence rates – in Australia, 40 men in 100,000 and 32 women in 100,000 are thus diagnosed each year, against corresponding rates of 9 and 12 in 100,000 here. UK incidence is rising largely as a result of increasing holidays taken in the sun (from around 4 million in 1971 to 27 million in 1994), however, some scientists are also worried about exposure to the sun at home, the more so because of fears of damage to the ozone layer, allowing more UVC light to penetrate. Indeed CR-UK calculates that if current levels of world emissions remain stable, then there will be 30,000 more malignant melanoma cases each year by 2050, and 5,000 more even if current emissions targets are met. Children are particularly vulnerable – a single dose of radiation to a new-born mouse model can induce a tumour, an adult mouse needing 30 times that – as, almost certainly, are people using sunbeds. Prevention is therefore largely through education – incidence seems to be under control in Australia, following years of SunSmart campaigning, and mortality is also beginning to fall as self-examination catches malignant moles earlier. Education has not been as widespread or long-standing here, however, although CR-UK is now promoting our own SunSmart campaign, but, with a 20-year lead-time, benefits are not expected to flow for many years.

Biology: Malignant melanoma develops from cells known as melanocytes, found between the skin's layers – dermis and epidermis – that produce the pigment, melanin, protecting the skin from the sun's UV light. A suntan is really a sign that the skin has been damaged, and while the transformation of melanocytes into malignant cells is not yet fully understood, it is believed that radiation, especially from UVB light, damages our DNA. This leads in some cases to loss of function of tumour suppressor genes (such as p53, implicated when mutated and thus inoperative in many cancers) and mutation of oncogenes (such as CDK4) – 70% of cases are thought due to mutations in the BRAF gene. Scientists are working on immunotherapeutic approaches to the disease – some melanoma patients are capable of seeing immune responses to their tumours, and possible vaccines are being trialled along these lines.

Detection and diagnosis: More women than men are diagnosed with malignant melanoma here – presenting with moles that have changed shape, size or colour, mostly on their legs, then arms and then the rest of the body. Men's moles are more likely to be on their backs, then chests, then elsewhere. Confirmation is by biopsy.

Progression and treatment: If the melanoma is caught at an early stage, surgery will often be curative, if the lesion is localised and is removed with a margin around and beneath it, with nearby lymph nodes often removed at the same time. However, as the primary mole becomes thicker, the likelihood that it has metastasized grows, and since malignant melanoma is not susceptible to chemotherapy, the prognosis becomes poorer – indeed fewer than 5% of patients survive more than a couple of years. Later stage patients are treated with interleukin-2 – an immunotherapeutic approach stimulating the body's immune response against the cancer' which extends survival for many.

Melanoma charities: None of significant size

Glossary

24/7: 24 hours a day, 7 days a week

Adenoma: type of polyp likely to develop into cancer

Adenocarcinoma: cancerous polyp originating in cells lining some organs

Adjuvant: additional, as in additional therapy

Aetiology: the cause of a disease, or a study of its risk factors

Amino acid: building block of protein

Angiogenesis: the formation of a blood supply

Antibody: blood protein made by the immune system in response to antigens

Antigen: 'foreign body' to our immune system

Apoptosis: 'suicidal' cell death, where a cell shrinks and is rapidly digested by its neighbour

Bone marrow: soft tissue in the centre of bones where blood is made

CT scan: computerised tomography scan

Carcinogenic: cancer-causing

Carcinoma: cancer originating in the surface membranes of the body (such as skin or gut)

Chromosome: part of the cell containing genetic information

Clone: cell (or group of cells) derived from a single ancestor

DNA: deoxyribonucleic acid – the molecules carrying genetic information

Endoscopy: literally 'scope inside' – when a camera enters the affected organ on a probe

Enzyme: a type of protein that speeds up chemical reactions in the body

Epidemiology: study of the incidence and control (and sometimes the causes) of a disease

Epithelium: surface tissue both of the outside of the body and most of its internal structures

Gene: unit of DNA containing information for making protein

Gene therapy: treatment that alters a gene

Genome: the total genetic content (DNA) of an individual

HIV: human immunodeficiency virus

HPV: human papilloma virus – virus causing abnormal tissue growth

Incidence: the number of cases diagnosed (usually expressed as a number per 100,000 of the population, age standardised, per annum)

Inflammation: tissue reaction to injury

MRI scan: magnetic resonance imaging scan

Malignant: where a cancer is life-threatening (as opposed to benign)

Metastasis: the process whereby cancer cells spread from their original site, causing secondary tumours elsewhere in the body

Microarray technology: allows thousands of genes to be monitored simultaneously

Mortality: the number of people who die from cancer, usually expressed as a number per 100,000 of the population, age standardised, per annum

Mutation: a change in the fundamental biology of a cell

Nanoscience: the study of objects and phenomena on an extremely small scale

Oncogene: a mutant gene which stimulates growth of cancerous cells

Oncologist: doctor specialising in the diagnosis, treatment and rehabilitation of cancer patients. (Medical oncologists specialise in chemotherapy, clinical oncologists in radiotherapy too)

PET scan: positron emission tomography scan

Polyp: tumour on the body's tissue surface

Sarcoma: cancer originating in connective tissue such as muscle or bone (osteosarcoma)

Squamous: flat epithelial cells

Stem cell: originator cell of various types of tissue

Survival: the percentage of people diagnosed with cancer still alive 5 years after diagnosis

Tumour suppressor gene: gene that usually stops uninhibited cell division

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Further Reading

Mel Greaves: *Cancer, The Evolutionary Legacy*

Matt Ridley: *Genome*

John Sulston: *The Common Thread*

Sam Epstein: *The Politics of Cancer*

National Audit Office: *Tackling Cancer in England, Saving MoreLives*

John Diamond: *C: Because cowards get cancer too*

Rachel Carson: *Silent Spring*

Michael Gearin-Tosh: *Living Proof, a Medical Mutiny*

World Health Organisation: *World Cancer Report*

Andrew Gitkin, UBS Warburg: *The Cancer Matrix*

ed John Ellershaw and Susie Wilkinson: *Care of the dying – A pathway to excellence*

ed Jeanne Samson Katz and Sheila Peace: *End of life in care homes – A palliative care approach*

ed. Jo Hockley and David Clark: *Facing death – Palliative care for older people in care homes*

Keri Thomas: *Caring for the dying at home – Companions on the journey*

Max Gerson: *A Cancer Therapy*

Michael Lerner: *Choices in Cancer*

Devra Davies: *When Smoke Ran Like Water*

Ruth Picardie: *Before I Say Goodbye*

Deborah Cadbury: *The Feminization of Nature*

and CR-UK's invaluable Cancer Stats pack

Endnotes

[1] CR-UK statistics – UK (excluding Northern Ireland, where cancer registration started in 1993) incidence 295 per 100,000 of the population in 1975, rising to 365 per 100,000 in 2000.
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[98] Novartis website
[99] Datamonitor report*: Cancer Overview*, November 2003
[100] This figure is a guesstimate, derived in two ways. First, *The Economist* newspaper reported on 31 January 2004 that global pharmaceutical industry spending on R+D is around $50 billion each year – $30 billion in the US, $20 billion in Europe. Pharma analysts tell us that cancer R+D represents up to 10% of industry spend – hence $5 billion globally on cancer R+D, of which the UK represents maybe half of European spending, or $1 billion – well over £500 million. Secondly, pharma analysts have helped us extrapolate probable UK spending from the bottom up; if GlaxoSmithKline spends around £150 million annually on cancer research, representing over a quarter of UK pharma spending, that implies an overall total of over £500 million pa. Looking within that total to find the amount spent on 'pure' research requires some estimation; one indication comes from the NCRI which, following a conversation with the ABPI, estimated a total of £134 million on pure research, as opposed to development, for its Strategic Analysis of October 2002.
[101] Eurocare Study early findings, September 2003, published on the BBC News website on 25/9/03. Cancer Research UK website for statistics on incidence.
[102] Ibid; 0.56 QALYs, £8,514 per QALY.
[103] Karnon J, Johnston SR, Jones T, Glendenning A. *A trial-based cost-effectiveness analysis of letrozole followed by tamoxifen versus tamoxifen followed by letrozole for postmenopausal advanced breast cancer.*

Ann Oncol. 2003 Nov;14(11):1629-33. 0.41 QALYs, £8,519 per QALY

[104] Boer R, de Koning H, Threlfall A, Warmderdam P, Street A, Friedman E, Woodman C. *Cost effectiveness of shortening screening interval or extending age range of NHS breast screening programme: computer simulation study.* BMJ. 1998. 317. 376-379. 12,251 LY gained in 27yrs at 6% discount for £30.9m

[105] ibid. 15,161 LY gained in 27yrs at 6% discount for £39.6m

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[109] ibid

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[115] Ford ES, Kelly AE, Teutsch SM, Thacker SB, Garbe PL. *Radon and lung cancer: a cost-effectiveness analysis*. American Journal of Public Health. 1999 Mar;89(3):351-7. US, cost depending on how focused programme is.

[116] Farndon MA, Wayman J, Clague MB, Griffin SM. *Cost-effectiveness in the management of patients with oesophageal cancer.* Br J Surg. 1998 Oct;85(10):1394-8. Compared with £4,104-£13,500 for palliative care.

[117] NICE, *Guidance on the Use of Taxanes for Ovarian Cancer*, May 2000

[118] NICE, *Guidance on the use of gemcitabine for pancreatic cancer*, May 2001. 0.148 QALY gained, so £21,088 per QALY

[119] Calvert NW, Morgan AB, Catto JW, Hamdy FC, Akehurst RL, Mouncey P, Paisley S. *Effectiveness and cost-effectiveness of prognostic markers in prostate cancer.* British Journal of Cancer. 2003 Jan 13;88(1):31-5. £12,068 / QALY, limiting surgery to critical cases.

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[121] Dr. Gary Cook, Head of Nuclear Medicine at the Royal Marsden Hospital

[122] van Tinteren H et al, *Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial.*, 2002, The Lancet. 359(9315):1388-93

[123] Based on an assumption that the PET performs 500 scans in the first year, increasing to a maximum of 1,200 by year five (estimates from Dr. Gary Cook), so around 10,000 scans over 10 years, of which 30% will lead to treatment change. The total cost, including running costs of £750,000 annually, is met by the NHS, and is thus just over £9 million, or £3,000 per patient whose treatment is changed.

[124] NPC meeting with Cancer Czar, January 2004

[125] Information from meetings with CancerBACUP and Liverpool Cancer Support Centre

[126] www.natlbcc.org/bin/index.asp?strid=22&depid=1&btnid=1

[127] www.cancerbacup.org.uk/News/Press/Pressreleasesstatements/2003/1067862661

[128] BBC Online, 28 October 2003

[129] Taylor, D. and Carter,S. January 2004 *Valuing Choice – Dying at home, an economic and social policy opinion commissioned by Marie Curie Cancer Care* p13

[130] Conversation with Dame Gill Oliver, Macmillan Cancer Relief, January 2004

[131] Lowton, K. Higginson, I. (2002) *Early bereavement: What factors influence children's responses to death?* National Council for Hospice and Specialist Palliative Care Services

[132] Dr Ruth Davies, University of Wales College of Medicine, Cardiff

[133] Office of National Statistics 2001: 0–15 year olds in Wales grossed up by 2/15ths to reach 0–17 year olds = 665,000. If £40,000 covers 665,000, then £100,000 would cover approximately 1.6m children – around 2,000 of whom will have life-limiting conditions. (Calculated thus: 11.7m children in England and Wales, of whom ACT estimates 14–20,000 with life-limiting conditions – i.e. around 1,200 children per million).