Overcoming Cancer in the 21st Century

With increased cancer risk awareness and better access to more effective preventive and curative treatments, most cancer deaths before late old age could be eliminated by 2050

Summary

Age standardised cancer death rates have fallen in Britain by over 20 per cent since 1990. Yet nationally and world-wide cancer is in total causing more death and disability than ever before. Globally, about 14 million new cases are diagnosed each year and 8 million cancer deaths are recorded. Current estimates indicate these figures could double by the early 2030s, unless there are further major developments in prevention and treatment.

In the UK 325,000 new cases occur annually, and cancers are in total responsible for 150,000 deaths. Neoplastic diseases affect people of all ages. The annual risk of a person aged 20 or under developing a condition like leukaemia or a solid tumour is 1 in 5,000 (which is equivalent to a 1 in 250 chance of each child or young adult having been diagnosed with cancer by the age of 21) while cure rates can now be as high as 80 per cent or more.

By contrast, amongst people in their 50s the annual incidence of cancer is 1 in 100. Over the age of 65 the yearly risk of developing a cancer is 1 in 30. Just over half of all cancer deaths in Britain are today amongst people aged 75 and over. Population ageing is responsible for the increasing numbers of cancer cases despite improving age standardised outcomes.

Positive progress has stemmed from factors such as tobacco related harm reduction, more effective early diagnosis strategies and better surgical, radiological and drug treatments. Deaths from the 'top four' cancers (breast, lung, bowel and prostate) fell by 30 per cent between 1991/93 and 2010/12.

Further reducing cancer death rates will demand continued advances in primary, secondary and tertiary prevention. Community and hospital pharmacists can contribute to cutting the incidence of cancer and improving cure rates through optimising medicines use in hospitals and in the community and via activities such as supporting smoking cessation and weight management programmes, enhancing access to screening and diagnostic services, and providing better services for people living with cancer and the unwanted effects of current treatments.

Opportunities for primary cancer prevention also include extending male and female access to protective forms of immunisation such as HPV and Hep B vaccination, better screening for 'pre cancers' such as bowel polyps, and using aspirin to prevent bowel and other cancers. Expanding

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testing for genetic vulnerabilities such as being a *BRCA* gene carrier could also permit more effective preventive interventions. In the UK access to such risk testing is in danger of falling behind that enjoyed in some other advanced nations.

Secondary prevention involves identifying early stage cancers and treating them effectively. It has been estimated that 5,000-10,000 lives a year could be saved by raising this country's performance to that of the best in the world. Innovations such as the Macmillan Cancer Decision Support (eCDS) Tool enhance GPs' early diagnosis rates, provided people can overcome their fears of cancer enough to voice their health concerns and are not worried about '*wasting the doctor's time with minor symptoms*'.

Cancer awareness programmes in community pharmacies could play an additional part in improving the prevention of cancers and their early detection. Awareness support should provide opportunities for people to reflect about health risks without becoming needlessly anxious, and to communicate with health professionals about small but potentially important changes they may have observed in themselves or in family members such as their children. Some people find it easier to talk with their pharmacists than with other health professionals.

'Winning the cancer war' in the twenty first century will in part require reforming health care cultures which discourage the reporting of 'minor' symptoms that can be indicative of serious disease. All cancers are most effectively treated at an early stage. But there is also a need for better therapies (including specific cancer typing) and supportive care for people with more advanced and metastatic cancers. In future decades combinations of innovative medicines coupled with enhanced radiological and surgical interventions will, provided research investment levels are maintained, mean that many more individuals with advanced cancers will be cured, or enabled to live with them in a fulfilling manner.

To date there is little evidence that restrictions placed on NHS patient access to relatively expensive cancer medicines have at the population level caused cancer death rates in England to be higher than in countries like America or France, albeit individuals have on occasions been distressed and disadvantaged. But as treatment effectiveness improves the consequences of access limitations may become more serious. Needlessly creating conditions in which people feel they have to beg for the best available care undermines confidence in the NHS, and could in the longer term generate costs rather than savings.

There is currently controversy surrounding the future of the Cancer Drugs Fund in England. The CDF has in recent years funded medicines regarded as non-cost effective by NICE. In Scotland the arrangements surrounding access to anti-cancer drugs and for taking advantage of Pharmaceutical Price Regulation Scheme (PPRS) flexibilities designed to permit full access to innovative treatments within a fixed NHS budget appear to be significantly more patient and public interest centred than those in place 'south of the border'.

There is robust evidence that the changes in public and patient behaviour and in the primary and other care services needed to further reduce the disease burden imposed by cancers will also promote wider gains in areas such as cutting age specific vascular disease, diabetes and dementia incidence and mortality rates. The ongoing development of 'healthy living pharmacies' and allied approaches to modernising pharmaceutical care in the community could have widespread public health impacts in relation to not only cancers but also vascular and neurological diseases.

As service users and health professionals become more confident that established tumours can and will be effectively treated fear levels will decline. This should increase their willingness to be actively involved in cost effective preventive and early stage cancer detection and treatment programmes. Overcoming cancer in the 21st century will require a holistic and empathetic approach to understanding and meeting both individual and community needs.

Introduction

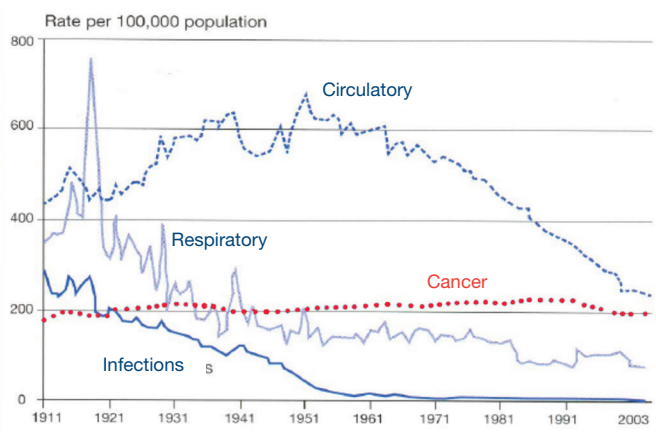
About two and a half thousand years ago Hippocrates and his contemporaries, whose work built on what was then already ancient knowledge about disease and the actions of plant based medicines, first used the words *carcinos* and *carcinoma* (in Greek, crab or crab-like) to describe cancerous growths. This was because the projections that seemed to reach out from tumours looked to them similar to crabs' claws. They observed that even though cancers could not be cured, the suffering they caused could to a degree be curbed.

About 500 years later the Roman physician Celsus translated the word carcinos into cancer. Not long afterwards Galen, who lived soon after the start of the Christian era, employed the term *oncos* (the Greek for swelling) to describe tumours. But these medical pioneers also thought of cancers as incurable. It was not until around 200 years ago and the contributions of early modern era pioneers such as the Scottish renaissance surgeon John Hunter and the German founder of cellular pathology Rudolph Virchow that the concept of being able to cure cancers began to gather force.

Even after the process of understanding tumours in today's scientific terms had commenced, it was only 20 years ago that incrementally more effective prevention strategies and treatment regimens started gradually to reduce the overall age standardised mortality caused by cancers in richer nations like those of North America and the EU. In both the UK and the US the overall death rate from neoplastic illnesses is, when adjusted for population ageing, falling. Because cancer is primarily a disease of later life its absolute incidence and prevalence is higher than at any other time in history. But in age standardised terms cancer mortality is now some 20 per cent below the peak rate recorded at the start of the 1990s – see Figures 1 and 2a and 2b.

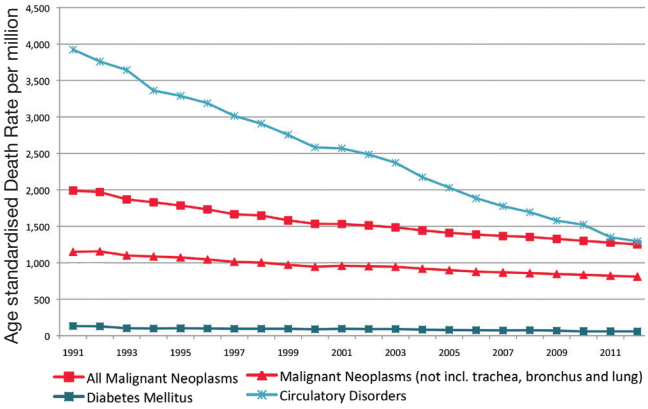
There were some 325,000 new cases of cancer diagnosed in Britain in 2013, and about 150,000 deaths recorded. Approaching a half of those given an initial cancer diagnosis were aged 70 or over, while just over

Figure 1. Age standardised death rates in England and Wales from 1911 to 2003



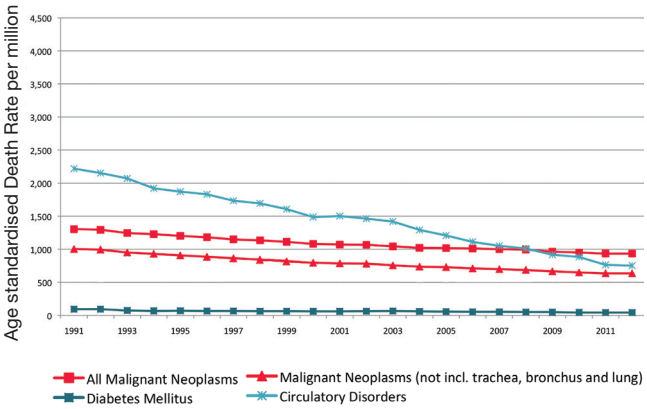
Source: Office of National Statistics

Figure 2a. Age standardised death rates in Males for selected causes in England and Wales 1991-2012



Source: Office of National Statistics

Figure 2b. Age standardised death rates in Females for selected causes in England and Wales 1991-2012



Source: Office of National Statistics

half of the people who died from cancer in that year were aged 75 or more (Moller et al., 2011). In fact, in the population aged 20 or under the annual risk of developing a cancer is only 1 in 5,000, albeit that any chance of children or young adults developing a life threatening illness is a special concern. Between the ages of 50 and 65 the yearly risk of being diagnosed with a cancer rises to 1 in 100. In people aged over 65 it is approaching 1 in 30.

Continuing rapid advances in biomedicine and associated disciplines, including not only molecular biology and human genetics but also health psychology and medical sociology, have led to claims that more has been learned about cancer in the past two decades than in the preceding two thousand years (American Cancer Society, 2014). Yet despite the accelerating progress outlined in Figure 3, cancer remains a major and growing cause of suffering and loss of life throughout the world (Stewart and Wild, 2014).

At the global level the burden of death and disability neoplastic diseases impose will rise markedly in the period

Figure 3. A Cancer Timeline

3000 BC	Oldest description of 'cancer'. The Edwin Smith Papyrus describes eight cases of tumours
400 BC	Hippocrates first used the word carcinos to describe tumours
40 AD	Celsus translated the Greek carcinos (meaning crab) into cancer
1750	Scottish surgeon John Hunter suggested that surgery might cure some cancers
1846	Anaesthesia first used in surgery, broadening possibility of surgery for cancer
1850	German pathologist Rudolf Virchow determined that all cells, including cancer cells, are derived from other cells. He also predicted a link between chronic inflammation/irritation and cancer
1880	William Halstead pioneered radical mastectomies
1903	First use of radiotherapy to treat cancer
1911	Payton Rous discovered the link between viruses and cancers
1949	Nitrogen mustard approved by the FDA for treatment of Hodgkin's Lymphoma. This was the first chemotherapeutic agent
1953	Structure of DNA identified
1954	Doll and Hill reported a link between cancer and smoking building on early German and other British observations
1960	Philadelphia chromosome linked to Chronic Myeloid Leukaemia
1970	Discovery of the first confirmed oncogene
1971	The National Cancer Act was instituted in USA
1981	The FDA approve the first vaccine against Hepatitis B, which can cause liver cancer. This was the first example of an indirect 'anti-cancer vaccine'
1986	Tamoxifen approved as adjuvant therapy for post-menopausal women with breast cancer
1994	BRCA1 and BRCA2 genes, also known as 'breast cancer susceptibility genes', cloned for the first time
1997	FDA approves first monoclonal antibody for cancer – Rituxan (rituximab) for the treatment of B-cell non Hodgkin's lymphoma
2001	Glivec/Gleevec approved by the FDA for use in the treatment of chronic myelogenous leukemia (CML)
2003	Human genome decoded, leading to novel molecular targets for treatment
2006	Herceptin approved as part of adjuvant therapy for women with Her-2 positive breast cancer. FDA approved vaccine against HPV
2010	Initiation of the 1000 Genomes project, which may lead to additional treatment targets. Provenge, the first specific anti-cancer vaccine, approved for use prostate cancer
2014	Kadcyla (trastuzumab emtansine) launches in the USA. It is currently only available in the UK via the Cancer Drugs Fund

to 2050, unless and until the advances now being made in more affluent nations such as America and Britain (as well as by pharmaceutical and other scientists working in emergent economies like China) can be developed and implemented on a universal basis. World-wide there are presently some 8 million deaths a year due to cancer, and 14 million new cases diagnosed annually (International Agency for Research on Cancer, 2012).

Against this background the aim of this UCL School of Pharmacy report is to provide an update on improvements in understanding the causes and consequences of cancer and to discuss critically how most effectively the disease processes involved and the harm they inflict can be prevented, cured or alleviated. It in particular explores how raising public awareness of cancers and their causes and sharing relevant knowledge and promoting personal skills through new community pharmacy based services might reduce the risks of developing neoplastic diseases, and in addition enable their prompt detection when prevention fails. It also considers how to help people affected by cancer recover as fully as possible from their treatments and continue to live on as well as possible. This is increasingly recognised as a key priority (Corner and Wagland, 2014).

Modernised community pharmacy services have an important part to play in England and elsewhere in supporting self-care and in optimising health care delivery (Smith et al., 2014). Enhancing the role of pharmacy as a profession could also prove relevant to recent public debate surrounding fair and affordable access to innovative anti-cancer medicines. This area is important, not least because of the likely benefits of maintaining public trust in the NHS. When individuals are threatened by life endangering illness, fears that they or family members will not be given the best possible treatment can have corrosive effects. The goal of overcoming cancer in the 21st century will not be achieved by life style changes alone. Investing in the development and effective use of better therapies is also a vital priority.

A range of conditions

Policy makers and service users alike should be aware that cancers involve not only many separate body sites and cell types (seen from this perspective, cancer comprises over 200 distinct conditions that fall into half a dozen main categories – see Box 1) but also a wide variety of complex molecular, acquired epigenetic (gene

Box 1. Cancer Types

Historically, cancers were – and often still are – named on the basis of the site in which it was presumed they had first developed, such as the breast, prostate, or lung. More recent classifications have been more precisely based on the type of tissue in which a cancer originates (histological typing). This approach can now be supplemented by details of the specific molecular and/or genetic lesions involved. There are six main histological cancer categories:

- **Carcinomas.** These are of epithelial origin: that is, they are cancers of the internal or external linings of the body, which account for 80-90% of all cases of neoplastic disease. They can be subdivided into adenocarcinomas (which have a glandular origin) and squamous cell carcinomas, which occur in the upper layers of the skin.
- **Sarcomas.** Cancers that originate in supportive and connective tissues like bones (osteosarcomas), cartilage (chondrosarcomas), skeletal muscle (rhabdomyosarcomas) and fat (liposarcomas).
- **Myelomas.** Neoplasms which originate in the plasma cells of bone marrow.
- **Leukaemias.** Cancers of the white blood cells (myelogenous leukaemias) and the lymphoid blood cell series (lymphatic, lymphocytic or lymphoblastic leukaemias).
- **Lymphomas.** These develop in the glands or nodes of the lymphatic system, and are sub classified into Hodgkin lymphoma and non-Hodgkin lymphoma.
- **Mixed Cancers**. Examples include carcinosarcomas and adenosquamous carcinomas.

Central nervous system specific cancers (of which there are many types, including gliomas, blastomas and medulloblastomas) do not fit easily into the above categories, and are hence sometimes regarded as an additional form of tumour.

expression controlling) and inherited genetic mechanisms. The precise 'mix' of these varies between individuals, and shifts as tumours evolve from one stage to another.

Achieving good cancer outcomes depends on individual, family and community abilities to act appropriately on risk related information. The capacities needed to overcome the shock of receiving a diagnosis of a potentially fatal illness and to cope with the longer term stresses of treatment and survival after life changing events play an essential role in optimising therapeutic results.

Such realities mean that there cannot ever be a single, low cost, 'magic bullet' technical solution to overcoming all the challenges that cancer presents. Likewise, for health professionals concerned with protecting, treating and supporting people experiencing cancer, minimising harm today demands models of practice far removed from traditional paternalistic patterns of care. Simply instructing patients about accepting treatments is no substitute for working with them and respecting each individual's freedom to choose how they should face serious illness and defend their own best interests (Coulter and Collins, 2011).

For some, this conclusion may seem discouraging. A number of observers appear to believe that the costs of improving cancer care are threatening to become unaffordable in richer as well as poorer nations (Chalkidou et al., 2014). It is on occasions implied that the most important task for health care providers in the next few decades will be to limit expenditures, even though this may mean that it will not be possible to provide optimal personal treatment for all.

However, it is worth stressing that even today in the wealthiest parts of Europe and North America outlays on cancer care amount to no more than 6-7 per cent of all health spending (see, for instance, Sullivan et al., 2011). On average, this represents approaching 0.7 per cent of overall national income (GDP). Looking beyond the more affluent communities, some 70 per cent of all cancer deaths now occur in developing countries. Yet poorer nations presently spend significantly less of their total wealth on health than richer ones. In addition they tend to spend less of their limited budgets on cancer care than do more affluent communities.

Within the 'rich world' overall cancer services spending envelope, outlays on anti-cancer medicines are today in the order of 0.1-0.2 per cent of GDP. This is affordable for countries that wish to prioritise improving cancer treatments, particularly given that pharmaceutical spending in many other therapeutic areas is falling. Even within oncology, drug cost increases are being checked by the fact that as widely used drugs become generic and fall in price their higher cost successors are being prescribed to relatively small numbers of people.

Effective cancer prevention requires many of the same measures that are needed to protect against infectious diseases, vascular conditions (including heart attacks and strokes) and some, if not all forms, of dementia. The promotion of healthy and active ageing becomes increasingly vital for the financial and the social wellbeing of nations as the average age of their citizens increases. Minimising the mental and physical harm caused by cancer is integral to this task.

Future value

There is evidence that improving cancer care is at this point in history a special priority for many people living in developed societies (see, for instance, Public Health England, 2014). From a policy perspective it could well prove counter-productive to deny the expressed preferences of health care consumers or to exaggerate the costs of providing better access to better cancer treatments, whether these are surgical, radiological, pharmaceutical or psycho-social in nature. Financial resources are of course finite. But in the improving cancer care context emphasis arguably needs to be placed on the value of removing barriers to continuing scientific and therapeutic innovation and more effective professional service provision.

Enabling the average person to increase their awareness of cancer in ways that help them to avoid it when possible and respond effectively when challenges arise is also emerging as a key 21st century priority. In Britain the NHS may, despite its advantages, have in the past discouraged the sensitivity to 'minor' symptoms and what can sometimes be called 'time wasting' questions vital for optimally successful cancer prevention and treatment. There may also have been a fatalistic acceptance that cancer therapies will always be inconsistently available to those who could benefit from them.

Yet with a growing recognition of such problems, and ongoing investment in both public health and the biomedical sciences central to achieving further therapeutic progress, the view offered here is that by the middle of this current century humanity's *'war against cancer'* that can be dated back to Hippocrates and before could and should have been largely won. It is realistic to expect that by 2050 nearly all cancer related deaths in children and adults aged up to (say) 80 years will have become preventable through life style changes and because of the availability of protective technologies and better pharmaceutical and other therapies.

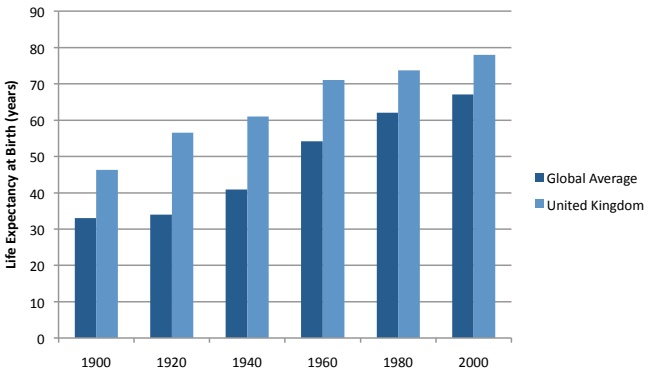
The long term value to humanity of achieving this goal after over two thousand years of conscious fear, pain and premature loss of life cannot be adequately expressed in conventional 'cost effectiveness' or 'value for money' terms. There is a case for believing that the true worth of such a success could well exceed all the health care costs incurred since formal health services were first established in Asia and Europe.

In the final analysis, advances in the biomedical and allied sciences that are being made via modern cancer research will open the way to other fundamental forms of progress, not only in medicine but in areas ranging from food and energy production to environmental protection. A central message of this report is therefore that although economising on pharmaceutical care and other health services may appear a desirable policy option for governments seeking to minimise tax burdens in a time of perceived economic austerity, the long term price of failing to develop better anti-cancer treatments and more effective forms of self-care support would be likely to prove high for patients and policy makers alike. As far as the immediate future is concerned, better use of existing knowledge through innovative service provisions in settings such as community pharmacies could save more lives for little extra expenditure, given sufficient public and professional commitment.

The emergence of cancer as a global challenge

In the modern era economic development – linked to the processes of demographic and epidemiological transition – has transformed the structure, health and size of the world's population. Globally, life expectancy at birth increased by 30 years over the course of the last century (Rosling, 2012 – see Figure 4). Even less advantaged countries such as, for instance, Nigeria,

Figure 4. Global and UK life expectancy in the twentieth century



Source: Gapminder

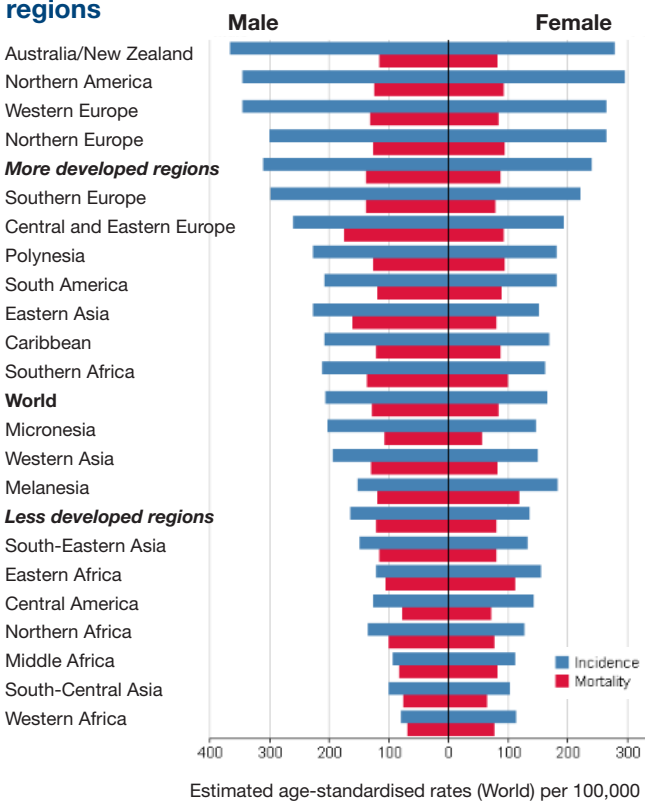
now enjoy survival figures that are significantly better than those recorded in nations such as Britain, France, The Netherlands and Germany in the period leading up to the First World War, when colonialism was at its peak and many of today's poorer nations were not yet established as independent entities.

Initially, death rates due to infections in young adults fell in north-western Europe and subsequently other parts of world, primarily because of better nutrition and improved sanitation. This progress was followed by relatively rapid declines in child and subsequently infant and maternal mortality. Consequent birth rate reductions opened the way to further improvements in mother and child health and, in time, to population ageing. This last is marked by an increase in the average age of communities and a progressive rise in the proportion of people in later life relative to the numbers of children and young adults. In public health terms the main burden of illness in post-transitional communities shifts from infections towards non-communicable diseases, albeit this need not increase the number of years the average person lives with disabilities.

Such trends are accompanied by profound changes in personal and community values and in factors ranging from gender relationships and access to education through to, later in the development cycle, the emergence of universal health care systems. For the purposes of this report key points to highlight about this and the emergence of cancer as a growing global challenge are:

- as the 2014-15 Ebola virus epidemic in West Africa illustrates, it is not yet the case that infection related death and disability burdens have been brought under satisfactory control in areas such as sub-Saharan Africa and other poorer regions. There are still ongoing threats from 'new' diseases and also from drug resistance problems in affluent and less prosperous regions alike. Nevertheless, in most countries infections now only account for a small percentage of the total burden of disease;
- as infections decline, the mortality and morbidity caused by vascular diseases in middle and later life becomes more apparent. In general, the age

Figure 5. Age standardised cancer incidence and mortality rates in developed and less developed regions



Source: International Agency for Research on Cancer – Globocan (2012)

specific levels of illness caused by events such as strokes and heart attacks are lower in richer countries than poorer ones, in part today because of better (although still sub-optimal) access to medicines such as anti-hypertensives and statins. In the UK, despite problems such as obesity and increased numbers of people being diagnosed with type 2 diabetes, age standardised vascular disease death rates now stand at only a third of the level recorded in the 1950s;

- with the enhanced control of vascular disease and continuing population ageing, the absolute and relative numbers of deaths from cancers rise. So too does the overall prevalence of neurological disorders like the dementias. Once again, age standardised incidence rates for many tumours (excluding sex hormone related conditions such as breast and prostate cancers, which are more prevalent in well-fed communities) and conditions such as Alzheimer's Disease are lower in rich countries than poor ones. But high rates of survival into old age can mask this trend.

In countries where illnesses caused by agents such as Hepatitis B and C and the Epstein-Barr and Human Papilloma viruses (which in the UK most commonly cause glandular fever and genital warts) or *helicobacter pylori* (a bacterium which causes gastric ulcers as well as stomach cancers) are prevalent, 20 per cent or more of all neoplastic conditions have an infectious origin. Consequently the average age at which deaths due to cancer occur is relatively young. In better protected settings fewer cancers are caused by viruses and other external carcinogens, with the exception of tobacco.[1] More cancers occur in older people and are linked to variables such as having children late in life, obesity, low levels of exercise and relatively high rates of processed meat and alcohol consumption.

At present, recorded age standardised cancer incidence rates are much higher in high GDP regions than in low GDP areas. Death rates are much less variable – see Figure 5. This is largely indicative of enhanced case finding and outcome recording in well-resourced settings. However, such findings also underline the limited efficacy to date of later stage cancer treatments, and so the value of seeking prevention wherever possible. Despite high rates of diagnosis in the OECD nations, the adjusted cancer mortality levels observed in them are not very much lower than in poorer settings.

Table 1. The percentage of cancer attributable to lifestyle and environmental factors in the UK in 2010

	Men	Women
Tobacco	23	15.6
Diet	11.9	7.2
Overweight	4.1	6.9
Exercise	0.4	1.7
Alcohol	4.6	3.3
Infections	2.5	3.7
Radiation (ionizing)	1.7	2.0
UV light	3.5	3.6
Occupation	4.9	2.4
Breastfeeding + HRT	--	2.8
All	45.3	40.1

Source: Parkin, 2011

Data such as those presented in Table 1 indicate that, again with the notable exception of tobacco smoking (see Box 2), it would be wrong to over-state the extent to which modifications in any one life style factor can protect individuals and/or communities from cancer. Yet in aggregate life style changes, especially when combined with the use of vaccination programmes and pre-cancer and early stage disease detection and treatment services, have the potential to halve current age standardised cancer death rates (Parkin et al., 2011). Achieving complex and multiple life style changes demands society wide cultural and environmental adaptations, linked to enhanced life-long health related educational and awareness raising experiences such as those that can be offered in pharmacies.

The growing challenge of protecting the populations of less economically developed countries against cancer is more daunting than it is in the rich world. This is because human and material resources are more stretched and the rate of epidemiological change is more rapid than that

1 In the most advanced countries smoking rates are now falling. But globally such trends have to date been offset by an increased use of tobacco in middle income/emergent economies.

Box 2. Tobacco and Cancer

Tobacco smoking in Europe dates back to the mid-16th century. But it only became a mass habit involving frequent deep lung inhalation from the beginning of the 20th century. The full health impacts of this did not become apparent in the UK until the 1950s and 60s, in part because smoking typically takes 20-30 years to kill its victims. In the long term use of conventional cigarettes causes the death of about a half of their users, and disables many of the remainder.

Efficient cigarette manufacturing techniques and the impacts of the two World Wars lay at the heart of increased early tobacco use in men. A corresponding rise in women's smoking rates in nations like the US and Great Britain was delayed by several decades. This helps explain why although lung cancer and other smoking related disease death rates are falling in males in this country, female lung cancer mortality is still rising.

Despite the recent overall decline in smoking prevalence in the UK and in most other OECD nations, tobacco use is still the single largest avoidable threat to public health in the industrialised nations and is fast gaining a similar status in the emergent economies. Currently, about 80,000 people die annually as a result of smoking in England alone, where it remains the largest single cause of class related inequalities in health.

Such data underline the importance of the NHS continuing to invest in stop smoking services in pharmacy and other settings. Increased use of e cigarettes and allied nicotine delivery devices as substitutes for conventional tobacco products and – although clear evidence of their efficacy in this context is not as yet available – as a means of facilitating total cessation of nicotine use could help further to reduce tobacco related harm. But this should not divert attention and funding away from the provision of professional support for people who remain at high risk from harm because of their physically and psycho-socially driven addiction to smoking. In the UK there is robust evidence of the cost effectiveness of such community pharmacy centred services.

in the past experienced by those nations that now have life expectancies at birth of 80 years or more. Even so, if the lessons that have already been learned about public health protection in Europe and countries such as, for instance, the US, Canada and Australia – combined with access to the currently costly but in the long term much more affordable pharmaceutical and other therapies now in development – can in future be effectively applied in today's emergent economies, the next few decades will see substantive progress against cancer everywhere on earth. Vaccinating girls and boys against HPV is an example of a technology that has far more to offer the world than it is presently providing, assuming that the need for this form of immunisation is rationally accepted.

Early detection saves lives

Although some patient groups may question the use of militaristic language the term '*the war against cancer'* was popularised by President Richard Nixon at the start of the 1970s. Against the background of America's unpopular involvement in the Vietnamese conflict of that period, he signed the 1971 National Cancer Act (NCA). This injected considerable amounts of new public money into cancer research. Together with pharmaceutical industry and charitable donations, the United States remains by far the world's largest funder of oncological innovation. Americans carry around half the cost of all public and private cancer research. When expressed as a proportion of GDP only the UK taxpayer invests comparable amounts (Kanavos, 2014), albeit English and other UK outlays on anticancer medicines are significantly lower than those made not just in the US but also by countries such as, for example, France and Spain (Wilking et al., 2009; Wilking and Jönsson, 2011).

However, therapeutic advances proved harder to achieve than was originally anticipated by US and other policy makers. In the late 1960s increasing knowledge about, for instance, the role of viruses in human oncogenesis[2] had led to hopes that near universal anti-cancer vaccines might be rapidly developed. Yet this did not prove to be the case, and as a result some commentators have judged the NCA a failure.

But in scientific terms the progress made in the last half century in understanding at a fundamental level the nature of cancers and the mechanisms underpinning their development has been profound. For example, the term oncogene (which in essence refers to a cancer causing or promoting gene mutation) was first used at the end of the 1960s. Since then a relatively comprehensive although not yet complete understanding of how genetic variations are involved in human carcinogenesis has emerged. The appreciation of how epigenetic changes (including alterations in the extent to which gene expression controls permit protective 'anti-oncogenes' to function) has been an even more recent development.

Hanahan and Weinberg (2000, 2011) have summarised today's insights into how cancers evolve as involving the 10 interlinked stages outlined in Box 3. The gradual accumulation of detailed knowledge about how each of these steps towards potentially lethal malignancies takes place means that cancer researchers are better placed than ever before to develop treatments that will impede tumerogenesis and/or offer new curative opportunities.

The treatment of more advanced solid cancers is moving towards a tipping point. Haematological cancers have a more established record of successful treatment. Yet this should not obscure the importance of prevention and of maximising the chances of early (ideally pre-cancerous) disease diagnosis. Figure 6 illustrates this in relation to the four most common causes of cancer related death

2 Understandings that avian cancers can be caused by infectious agents date back to the decade before World War 1. However, it was not until the mid-1960s that human oncoviruses were first identified.

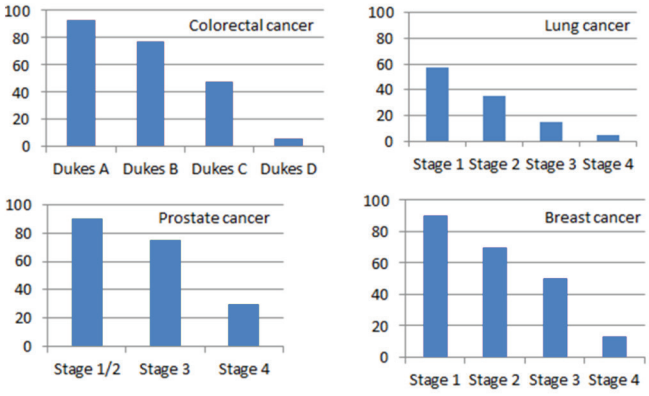
Box 3. Cancer's Hallmarks

Tumours are complex tissue aggregates composed of multiple types of cells that interact with each other and surrounding normal body components in order to permit their unrestricted collective proliferation. Understanding the processes involved in the transition from normal to neoplastic cells has been a central aim of much cancer research. In 2000, Hanahan and Weinberg outlined six key hallmarks of cancer (Hanahan and Weinberg, 2000). They followed this eleven years later with a further analysis of the essential characteristics of cancers (Hanahan and Weinberg, 2011). These can be characterised as:

- **Self-sufficiency in growth signals.** Normal cells control the production and release of signals that promote tissue growth. Cancer cells effectively deregulate the latter's availability. This can involve an overproduction of growth factor ligands (binding agents) or receptors, along with the additional production of altered receptors that are no longer ligand-dependant.
- **Insensitivity to anti-growth signals**. Normal cell proliferation is controlled by growth inhibitors that interrupt cell division. Cancers become resistant to growth-preventing signals.
- **Limitless replicative potential.** Healthy mammalian cells typically have a limit of around 60-70 replications before reaching senescence, when they no longer divide. But tumour cells often display an increased production of telomerase, the enzyme that maintains the length of the telomeres that govern cell multiplication.
- **Evasion of programmed cell death (apoptosis).** Programmed cell death normally causes cells to die if they become abnormal. Cancer cells are able to overcome this, most importantly by evading *TP53* which elicits apoptosis in response to DNA damage. The tumour suppressor gene *TP53* is mutated in more than half of all cancers in ways that facilitate increased cell growth.
- **Sustained angiogenesis (new blood vessel growth).** Cancers can trigger new blood vessel formation to provide a blood supply sufficient for their ongoing growth.
- **Tissue invasion and metastasis.** Cancers have the ability to invade surrounding tissues or distant body parts. Metastatic cancers achieve this via cell-cell adhesion molecule (CAM) based mechanisms.
- **Deregulated 'cellular energetics'.** The uncontrolled cell proliferation characteristic of neoplastic diseases requires adjustments to cellular metabolism in order to fuel cell growth and division. Cancer cells often, for instance, employ aerobic glycolysis. In normal cells glycolysis generally occurs in anaerobic conditions.
- **Genome instability leading to enhanced mutation rates.** In cancer cells the surveillance systems that normally monitor genetic integrity and force genetically damaged cells into programmed cell death or senescence become compromised. Mutability can also be achieved through increased sensitivity to mutagenic agents.
- **Avoiding immune destruction**. In cancers immune-editing results in neoplastic cells being able to evade immune surveillance.
- **Tumour-promoting inflammation**. Cancerous lesions contain infiltrations of cells from both the innate and adaptive immune systems. Inflammation is an enabling characteristic of cancers because it facilitates the supply of bioactive molecules such as growth and pro-angiogenic factors and extracellular matrix-modifying enzymes in the tumour microenvironment. Inflammatory cells may also release mutagenic chemicals that accelerate evolution toward heightened states of malignancy.

In addition to Hanahan and Weinberg's cancer hallmarks it is from a clinical perspective important to note that following treatment and a period of apparent recovery dormant cancer cells can in some cases reactivate and cause recurrent disease which may be resistant to treatment.

Figure 6. Five year survival by stage



Data from Cancer Research UK
Graph from Wardle, 2014

in the UK. Together, breast, lung, colorectal and prostate cancers account for over 50 per cent of all cancer diagnoses and a similar proportion of deaths in England (Figure 7).

Cancer Research UK has recently highlighted the fact that in the UK between 1991/93 and 2010/12 the age adjusted mortality from the 'top four' cancers fell by about 30 per cent (Cancer Research UK, 2014b). In the case of breast cancer the death rate declined by almost 40 per cent – see Table 2. These are encouraging rates of progress, linked to advances made in areas ranging from smoking cessation support to radiotherapy, surgery and drug treatment.

Some critics of cancer screening and case finding programmes argue that early diagnosis can, if statistics are incorrectly interpreted, make it look as if survival is being extended when in fact only the period of living with a fatal diagnosis has been lengthened. If and when this is the case, and particularly where there are allied risks of 'over-diagnosis' and 'over-treatment', then the mental distress and other harms associated with such interventions may well outweigh their benefits.

But against this there can be no doubt that the age standardised mortality data available reflect real trends. The present task for countries like the UK is to build on existing successes by further improving staged

Table 2. Change in UK age standardised mortality rate for the four most common cancers between 1991 and 2010.

	Mortality rate per 100,000 (age standardised)	
	1991-1993	2010-2012
Top 4 combined	145.5	102.4
Lung	52.2	38.1
Breast (female)	38.9	24.3
Bowel	24.5	16.3
Prostate (male)	29.8	23.6

Source: Cancer Research UK 2014b

cancer survival rates, while at the same time enhancing preventive interventions and the support available to people living with cancer and/or the after-effects of its treatments. As already noted, hospital and community pharmacists could and arguably should play extended roles in all these areas.

Cancer care in the UK

The evidence available confirms that the care provided to people with diagnosed cancers by the NHS is normally amongst the best in the world. However, detailed analyses show that survival in this country has tended to lag behind the highest European standards (De Angelis et al., 2014; Murray et al., 2013). Data relating to the first years of this century suggest that if UK outcomes could be raised to the best level recorded in other EU Member States, in the order of 10 thousand deaths a year would be averted (Abdel-Rahman et al., 2009).

In some instances treatment quality in NHS hospitals could doubtless be improved. Recent reports suggest that English health service restructuring combined with budgetary restraints put secondary and tertiary services under new pressures in 2013/14 (Cancer research UK, 2014c). But even so such findings are consistent with the view that late presentation and linked problems in the community are key areas for improvement. Similar conclusions have also been drawn in Denmark, which has a GP centred primary care system similar to that in England and the other UK countries.

Core problems range from the apparent inability of a proportion of people and/or their medical, pharmacy and other professional advisors to recognise what may be early stage cancer signs (Figure 8) to an unwillingness of service users to report what they fear may be 'time wasting' minor symptoms to doctors or other health professionals. Delays in patient referrals for diagnostic testing compound such barriers to excellent performance (Macleod et al., 2009). The latter may be due to a desire for cost saving, or on occasions unwarranted assumptions that the experiences reported by service users are due to 'trivial' psychological as opposed to 'serious' physical causes (see also Whitaker et al., 2014).

The research available also indicates that British patients, and particularly women, from South Asian and other minority backgrounds are at raised risk of delayed cancer diagnoses (Waller et al., 2009). In the white British population individuals from less educated and otherwise less advantaged backgrounds can likewise have difficulties in communicating with and being heard by their doctors, and do not use screening services

Figure 7. Cancer deaths as a proportion of new cases in the UK for 20 most common cancers (2010)

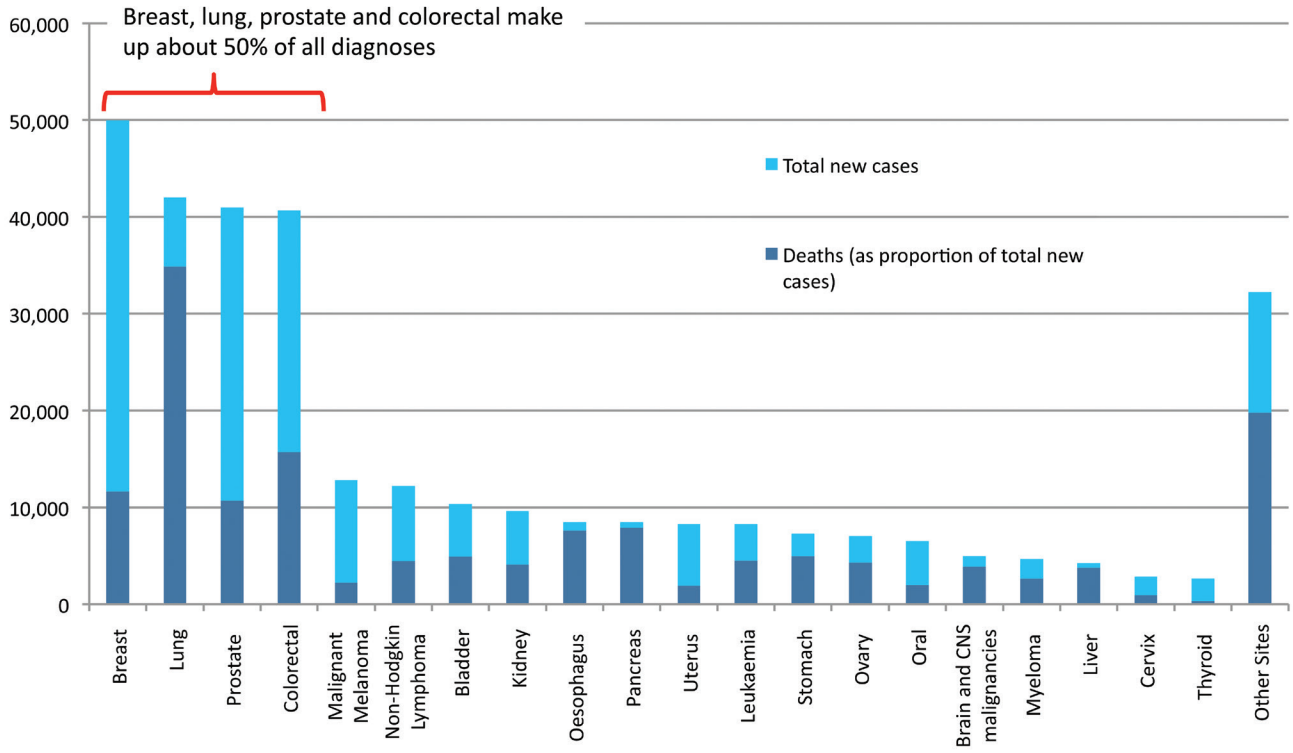
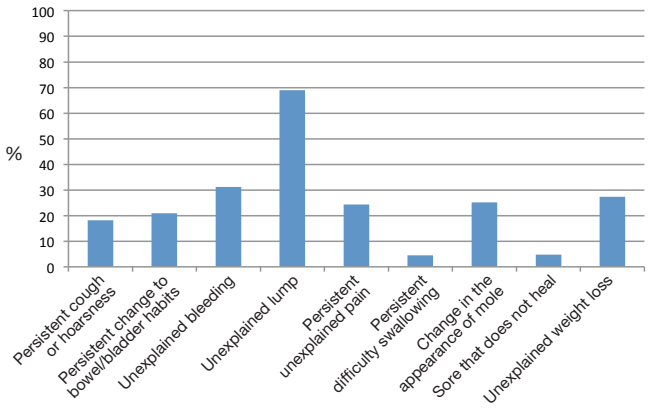


Figure 8. Proportion of people able to recall cancer symptoms in UK (2010)



Source: Data from Wardle, 2014

as extensively as better educated and often socially more confident peer group members. Nevertheless, inappropriate generalisations should be avoided. The extent to which traditional class and/or ethnicity categorisations explain variations in early stage cancer detection rates can be overstated. Within any community a sympathetic appreciation of personal experiences, knowledge, beliefs, preferences and cognitions is needed to explain individual health behaviours.

National policies

There have been a series of NHS and government initiatives designed to enhance cancer care in the UK. In the 1990s the most important of these was the popularly termed 'Calman Hine report', which was formally entitled *A Policy Framework for Commissioning Cancer Services* (Department of Health, 1995). Although mostly concerned with 'purchasing' hospital services, it opened the way to addressing cancer service provision in a more comprehensive and holistic manner than had previously been attempted. It was followed (shortly after Professor – now Sir – Mike Richards was appointed as national clinical director for cancer[3]) by the publication of a 10 year National Cancer Plan (Department of Health, 2000).

This aimed to establish England as a world leader in cancer prevention and early disease treatment, as well as in advanced stage care provision. Perhaps most notably, it led to the establishment of 28 cancer networks, designed to improve hospital care provision as well as to support GP and other community service developments. Since then similar documents have been published in the other UK nations. Additional English policy statements and national initiatives included the launch in 2008 of the National Awareness and Early Diagnosis Initiative (NAEDI – Cancer Research UK and Department of Health, 2008) and the publication in 2011 of *Improving Outcomes: A Strategy for Cancer* (Department of Health, 2011).

3 Sean Duffy succeeded Professor Richards as NHS England's National Clinical Director for Cancer in April 2013. Professor Richards is now the Care Quality Commission's Chief Inspector of Hospitals.

NAEDI has from its inception been jointly led by Cancer Research UK and the Department of Health, and has incorporated as one of its key elements the *Be Clear On Cancer* campaign. This is encouraging people to consult GPs about symptoms that, like a persistent cough or difficulty with swallowing food, may prove harmless but might alternatively be indicative of an early stage cancer. At the same time GPs have also been provided with support aimed at improving their awareness of the possibility of cancers, and their ability to recognise combinations of warning signals.

For example, Macmillan Cancer Support is – with government and various partners, including BMJ Informatica – currently in the process of supplying to GPs a new computerised 'tool' for enabling individuals with a more than 2 per cent chance of having developed a condition such as, say, cancer of the oesophagus or the pancreas to be identified rapidly via their primary health care records. This resource (which has recently been complemented by new NICE guidelines) has already been piloted in 550 practices. The process of rolling this programme out nationally should be completed during 2015.

Cancer Research UK and Macmillan Cancer Support have, along with bodies such as NHS England, Public Health England and district level NHS and Local Authority agencies been additionally involved in a wide variety of other initiatives. Collectively, these are helping to improve the nation's record in cancer detection and care, and in promoting healthy ageing more generally. Some are involving community pharmacies like Boots and its high street competitors.

The publication in 2013 of *Living Well for Longer: a Call to Action on Avoidable Premature Mortality* (Department of Health, 2013) illustrates the growing political and wider social acceptance of the importance of avoiding conditions like cancer wherever possible, and of identifying them and treating them rapidly whenever necessary. As the availability of effective treatments has increased, so there is emerging evidence that the general public's willingness and ability to maintain a realistic and effectively protective 'front of mind' awareness of the manageable threat from neoplastic disease is also rising.

In the past, counter-productive fears and anxieties – together with risk denial and sub-optimal access to screening and diagnostic testing and specialist expertise – have been barriers to improving outcomes. There is reason to hope that this problem is now in the process of being overcome. In future the availability of innovative services online and in NHS pharmacy and other community settings will not only help people already receiving cancer treatments to use them to best effect, but also to further enable primary prevention and earlier diagnosis.

Yet there is still more to be done in terms of promoting constructive cancer awareness, especially – but by no means exclusively – in the context of less advantaged community groups. The next main part of this document highlights the opportunities that exist for achieving further progress. However, the remainder of this section briefly discusses issues relating to the pricing of new anti-cancer medicines and the actions already being taken to improve care for people with commonly occurring tumours.

Anti-cancer medicines access

Cancer medicines pricing and access is important not only because of its immediate consequences for NHS and other patients seeking effective care, but also because of indirect impacts that public debate about whether or not treatments are affordable can have on confidence and trust in the health service. In general, NHS users can be assured that once they have presented for treatment and have been correctly diagnosed they will often receive world class cancer treatment. Yet as recent disputes over access to, for instance, the prostate cancer medicines abiraterone (Zytiga) and enzalutamide (Xtandi) illustrate, drawn out disputes about the circumstances in which innovative medicines may or may not be used can harm trust and confidence. Public discussions about the future of the Cancer Drugs Fund (CDF) could have similar effects. Health professionals such as pharmacists should be in a position to understand this, and help others manage relevant concerns.

In this context Prostate Cancer UK was in 2014 sharply critical of the situation in England, describing it as a *'fiasco'*. The charity argued that the National Institute for Health and Clinical Excellence (NICE) evaluation process was *'not fit for purpose'*. Its chief executive has also subsequently noted concerns that the existence of the CDF may have given pharmaceutical companies (and indeed NICE itself) a 'perverse incentive' not to negotiate price agreements.

It would be outside the scope of this report to attempt to examine all the issues surrounding how the cost

Box 4. NICE and Cancer Treatments

The National Institute for Health and Care Excellence uses a cost per incremental QALY (quality adjusted life year) based methodology for assessing whether or not medicines are affordable for the treatment of NHS patients. Taking into account provisions made for end-of-life care and factors such as whether or not a medicine is used to treat an 'orphan' (rare) indication, a ceiling ICER (incremental cost effectiveness ratio) cost of between £30,000 and £50,000 per additional QALY appears to have been in place in recent years.

If NICE does not recommend an anti-cancer or other relatively costly medicine it is unlikely in England or Wales to be purchased via normal NHS mechanisms. But in England the Cancer Drug Fund (the CDF) has since 2010 been available for funding some therapies not judged cost effective by NICE. The CDF currently spends approaching £300 million out of a total of some £1.3 billion devoted by the English NHS to anti-cancer medicines purchasing. This represents a per capita outlay below that of western European countries such as Sweden, France, Germany and Spain, but above central and eastern European anti-cancer spending levels.

Drug treatments now typically represent up to 20 per cent of all cancer care costs in economically developed nations. The latter in turn represent between 5 and 10 per cent of all health care expenditures. Such figures mean that anticancer medicines are not in reality a major item of public expenditure. Nevertheless, considerable controversy has surrounded the pricing and perceived affordability of such drugs in the UK. Health service linked sources and some patients have accused companies of over-pricing innovative cancer treatments. (See, for instance, Hirshler, 2014.) Other patient groups and most pharmaceutical companies argue that prices are reasonable given the continuing need to attract risk capital funding into cancer research and treatment development, and that some NICE decisions have been perverse.

There are legitimate although sometimes conflicting public interests in both limiting cancer care costs and devoting more resources to developing better medicines and other therapies. For the purposes of this report points worth emphasis include:

- Britain has historically played an important part in biomedical innovation, and has continuing economic interests in research based industry and publicly funded institutions such as Universities. Compared with countries such as the US, Switzerland and China its position is not as strong as it was in the 1960s and 1970s. Without robust policies aimed at supporting scientific innovation and industrial investment the UK may in future be unable to provide 'cutting edge' welfare services;
- Pharmaceuticals have relatively high fixed costs of development, regardless of whether or not they can benefit large or small numbers of patients. Yet once they have been fully tested and licensed they normally have relatively low marginal costs of production. This makes their pricing during periods of exclusive supply controversial. 'Low' prices reduce future investment in high risk research. 'High prices' can in the absence of adequately funded universal health care systems cause patients to go untreated, albeit that some 80 per cent of cancer care costs are non-pharmaceutical.
- In part because new anticancer medicines are initially given to severely ill people in order to demonstrate statistically significant survival advantages before periods of intellectual property protection expire, their value may initially seem disappointing relative to their costs. Nevertheless, if current investments can be maintained there is good reason to believe that most cancers will be preventable or effectively treatable by or before the middle of this century. The value to humanity of such progress could well be regarded as inestimable; and
- The exploitation of patients during disputes about the prices of medicines and/or the legitimacy of public service rationing strategies in ways that cause avoidable fear and suffering ought not, it is contended here, to be tolerated. To the extent that such abuses are occurring all sides should seek to find ways of improving the situation, and where possible combine universal access to good quality care with sustainable ways of maintaining privately and publicly funded cancer research and treatment innovation.

effectiveness of new medicines is assessed. However, the information in Box 4 provides an explanation as to why the pricing of new medicines is often controversial. A key point to emphasise is that presently the Cancer Drug Fund (the CDF) provides money to purchase anti-cancer treatments for English NHS patients that NICE has either not assessed or judged as being non-cost effective, but which might in individual cases be thought necessary and desirable. The CDF's funding has recently been raised to £280 million a year, although its status after 2016 is uncertain (Hawkes, 2014; Gallagher, 2014)

There have been calls for greater alignment between the criteria used to shape NICE and CDF decisions, and about 40 drugs currently on the CDF list are being re-assessed by NHS England. However, in Scotland the Scottish Medicines Consortium (SMC) has recently introduced a new approach which promotes a much fuller representation of individual experiences and views in the decision making process that determines which expensive treatments are or are not made available to NHS patients than is permitted in the English system (Ryner, 2014). To the extent which health service user empowerment is genuinely thought desirable, this approach might well in time be seen as a valuable example 'south of the border'.

So too may Scotland's establishment of an Innovation Fund which allows local NHS budget holders to access money returned by pharmaceutical companies via the UK Pharmaceutical Price Regulation Scheme (the PPRS) in order to allow NHS patients to access anti-cancer treatments without exceeding an overall limit on health service medicines expenditures. To date the responsible English authorities have seemed unwilling to establish similar arrangements, despite their potentially positive impacts on patient wellbeing and British public interests in ongoing pharmaceutical innovation.

No universal health care system committed to optimising the health of the population it serves can unconditionally guarantee to pay medicine producers whatever they may ask for the products they offer while enjoying intellectual property protection (IPP). However, there are countervailing dangers that organisations such the NHS will exercise excessive monopsony purchasing power. It is also noteworthy that when medicines lose their IPRs (intellectual property rights) their prices typically fall dramatically. This can make them cheaply available for decades or even centuries to come, unless or until they become therapeutically redundant. Such phenomena help explain why, despite the ongoing process of new treatment development, the proportion of total NHS spending allocated to medicines has stayed broadly stable for the last 50 years.

Even within the field of cancer care total anti-cancer medicine costs have risen modestly relative to financial investments in cancer services as a whole in the last few decades, both in the UK and elsewhere in the OECD. As high volume use products have become generically available via community pharmacy or other channels, new higher cost pharmaceuticals are being prescribed for smaller numbers of hospital treated and other patients.

Arguably, one of the problems inherent in the 'cost per QALY' methodology employed by NICE to determine the affordability of pharmaceuticals is that it makes no adequate allowance for order of magnitude variations in the sizes of the patient populations using given therapies, despite the fact that in the UK the NHS Pharmaceutical Price Regulation Scheme now ensures that total medicine costs will not rise above an agreed ceiling. Neither does it address whether or not the overall amount spent on medicines and health is appropriate relative to other economic opportunities. Such limitations could in global public interest terms mean that in aggregate 'too little' is paid for some innovations and 'too much' for others.[4] Over time such distortions might harm the interests of cancer patients and the wider community by slowing progress towards better health outcomes.

Condition and patient specific strategies

It is now known that cancers (and pre-cancers) involve not only a wide range of cell types but also many genetically based molecular mechanisms which come in and out of play as neoplastic growths evolve within the bodies of those affected by them. As with other non-communicable diseases, this complexity means that in future treatments will tend to become increasingly 'personalised'. To be optimally effective they may have to be tailored to fit each case / case type as it progresses.

However, efficiently deliverable approaches to public health improvement and disease management address common pathways wherever possible, and support individuals as members of groups sharing common experiences and opportunities. The analysis below is based on this perspective, and an acceptance of the need to locate personal health care and social requirements within a wider framework of generic social and bio-scientific understandings. Ultimately, medicine has always been about personalising 'general' treatments, even in Hippocrates' day. The challenge for cancer care now is, with the increasing amounts of detailed information available, to be able to apply knowledge and skills in a way which does not fail to take advantage of phenomena which exist at a population level yet at the same time meets individual needs as effectively as possible.

Childhood cancers

Some parents may still fear child cancers such as leukaemia as much as people once did infections like polio. Yet child cancers are relatively rare, and are now in developed countries largely curable. In annual incidence terms less than one per cent of all new cancer cases are diagnosed in children or young adults aged 14 and under. In Britain today the overall chance of a child developing cancer by the time he or she reaches the age of 14 is in the order of 1 in 500.

4 Public and political concerns about the overall profitability of new hepatitis C treatments could be taken to illustrate this point, although the total future savings generated from being able to cure HCV infections is likely to significantly exceed the cost of treatments. When personal welfare benefits are added in to the equation the benefit to cost ratio is further improved.

Nonetheless, some 1,600 children are diagnosed with cancer in the UK each year. Although often initially associated with mild and commonly occurring symptoms their conditions can progress rapidly (Box 5). Prompt action is often best facilitated through parents and responsible carers having a confident idea of what is normal for their children, and being willing to press for a clear professional diagnosis whenever they believe one is needed.

Leukaemia accounts for a third of all childhood cancer diagnoses. Its occurrence peaks around age two to three years. Brain and central nervous system tumours account for a further quarter of all childhood cancers, followed by (Hodgkin and non-Hodgkin) lymphomas. These last are rare before the age of two, and are most commonly diagnosed in boys age 10-14. Retinoblastomas, cancers of the bone, Wilms tumours, neuroblastomas and soft tissue sarcomas provide further examples of childhood cancers which if diagnosed early in well-resourced modern environments are now normally curable (Figure 9).

There is little evidence that life style factors affect a child's risk of getting cancer. This is unlike the situation with adult cancers. It implies that 'inborn' as opposed to post-natally acquired genetic differences often play causative roles. Known genetic disorders such as Fanconi anaemi and Li-Fraumeni syndrome are associated with an increased risk of some types of childhood cancer. But in many instances the fundamental causes remain un-identified. It is likely that in most children who develop a cancer there has been some kind of very early mutational 'head start' which reduces the time needed for cancerous cells to develop. However, this does not necessarily mean that any sort of harmful abnormality was inherited from a parent.

Box 5. Child Cancer Symptoms

Childhood cancers are relatively rare – see main text. However, when they occur they can progress rapidly. It is therefore important to diagnose them as quickly as possible, although as with many adult cancers the majority of early child cancer symptoms coincide with those of relatively benign conditions (Feist, 2005). This adds to the difficulties of diagnosis. The key warning signs can be summarised as:

Continued, unexplained weight loss

Headaches, often with early morning vomiting

Increased swelling or persistent pain in bones, joints, back or legs

Lump or mass, especially in the abdomen, neck, chest, pelvis or armpits

Development of excessive bruising, bleeding or rash

Constant infections

A whitish colour behind the pupil

Nausea which persists, or vomiting without nausea

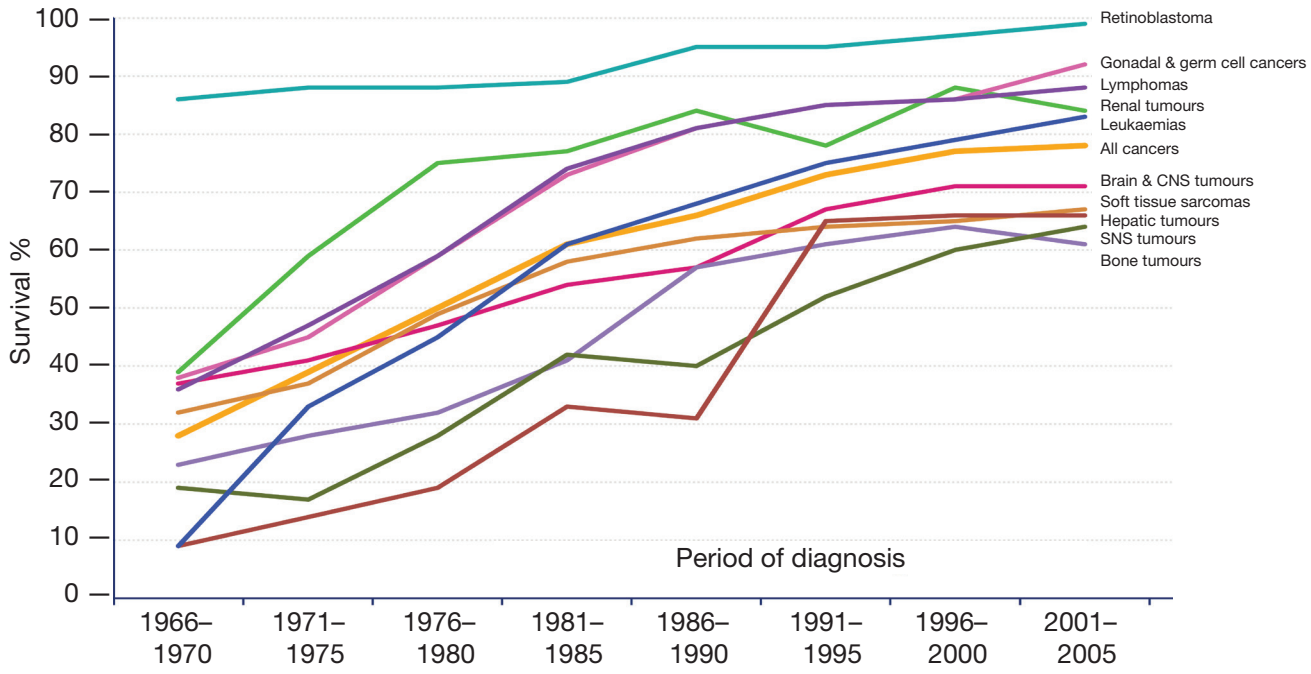
Constant tiredness and/or noticeable paleness

Eye or vision changes which occur suddenly and persist

Recurrent or persistent fevers of unknown origin

If a child suffers from one or more of these potential cancer symptoms for more than a fortnight an investigation should be initiated. Effective safeguarding depends in part on parents knowing what is 'normal' for their children and, if they suspect anything untoward, being able to communicate their concerns effectively to GPs and/or other health care professionals.

Figure 9. Five-year survival by cancer type in children 0-14



Source: Cancer Research UK

Childhood cancer treatment has improved dramatically in the past fifty years. Today more than three-quarters of the individuals affected survive to adulthood and can be considered cured, although of the 30,000 plus former child cancer patients presently alive in the UK a proportion suffer from long-term or late effects of their initial treatment. Issues such as infertility, an increased risk of further cancers and cognitive and/or growth impairments need to be managed with care, compassion and expertise. As biomedical, social and psychological knowledge continues to increase, so outcomes will further improve.

Events such as those recently surrounding the five year old Ashya King's treatment for a form of brain cancer known as a medulloblastoma (also termed a PNET) in the late summer of 2014 (BBC News, 2014) highlight the value of good communication and trust between parents and health professionals. They illustrate the fundamental importance of avoiding situations in which it may rightly or wrongly be thought that optimal treatments are being denied public or private service patients for undisclosed financial reasons.

Breast cancer

Breast cancer is the most commonly occurring major tumour type in the UK. Over 50,000 diagnoses are made annually, indicating a lifetime risk of one in every eight women (less than 1 per cent of breast cancers affect men). In total there are now over 500,000 people in this country who are either living with breast cancer or have been cured of it. This represents about one woman in every 30 who reaches middle life or beyond.

Recorded age standardised breast cancer incidence rates are presently stable. But they have risen by almost 70 per cent since the end of the 1970s in the UK, largely because of increased rates of diagnosis associated with the introduction of screening programmes. Other possibly relevant factors include earlier sexual maturation, increasing obesity and alcohol consumption rates, the use of oral contraceptives and hormone replacement therapies, and reductions in physical activity rates. Increases in the age at which the average woman has her first baby and in the total time spent breast feeding can also influence the occurrence of this cancer. Scotland in particular has amongst the highest breast cancer incidence rates in the world, as it does for a number of other neoplastic disorders.

Nevertheless, UK breast cancer death rates have fallen by 40 per cent since the start of the 1980s (Cancer Research UK, 2014b). This has probably been partly due to the introduction of screening programmes (although this is disputed by some – see below) together with improved surgical, radiological and medical treatments. Building on the initial use of the oestrogen antagonist (blocker) tamoxifen (which was not proven to have curative benefits until well after a decade after it was launched) drugs such as Herceptin (trastuzumab) have also improved survival, albeit that controversies initially surrounded its costs. More recent innovations such as Kadcyla (trastuzumab emtansine) have attracted similar concerns, despite their potential therapeutic value (Triggle, 2014).

In England NHS patients currently – as has already been described – rely on the CDF to access medicines not judged cost effective by NICE. How long this will continue to be the case after the 2015 general election is presently uncertain – the current extension to the life of the fund is due to expire in March 2016. Patients already receiving treatment have been assured by NHS England that they will not have their medication withdrawn, although for people at risk of developing metastatic and earlier stage cancers the possibility of new limits on the supply of better treatments may well be disturbing.[5] However, from a 'pure' public health perspective early diagnosis is currently a much more important long term survival determinant than access to later stage disease treatments.

More than 90 per cent of women diagnosed at the earliest stage of breast cancer live for at least five more years, compared with (in the period up to the end of the first decade of this century) 15 per cent of those diagnosed at the most advanced stage. The NHS breast cancer screening programme offers women aged 50 to 70 years (47 to 73 in some localities) diagnostic imaging every three years. The density of younger women's breast tissue limits screening opportunities in those under 45. Although only 10 per cent of new breast cancer cases are diagnosed in females aged under 45 there is obviously a greater loss of overall life potential in that group as opposed to older cohorts. Mid-life deaths may also have profound impacts on third parties such as children that current evaluation frameworks often fail to quantify.

Research published in 2010 concluded that the benefits of mammography based screening in terms of the number of lives saved is greater than the harm caused by 'over-diagnosis' and allied concerns (Duffy et al., 2010). An expert independent review commissioned by the Department of Health has also found that there is a 20 per cent relative reduction in mortality from breast cancer in women invited to screening (The Independent UK Panel on Breast Cancer Screening, 2012).

However, a subsequent review by Mukhtar et al (2013) reported that while individual women may gain from breast cancer screening, population based mortality statistics for England do not to date show a benefit from such programmes. Other researchers have since published similar findings. The conclusion offered here is that people wishing to prevent avoidable cancer related harm of all types should be advised to take up all the NHS screening and case finding opportunities on offer, provided they feel able to cope with the stresses that may accompany events such as 'false alarms'.

5 In the past women using the NHS reported feeling isolated and deserted at the time of their initial breast cancer diagnosis. Now outcomes and patient support services have improved this is less likely to be the case. But in the UK and Europe more widely there is evidence that the second shock of receiving a later diagnosis of metastatic disease can still be accompanied by similar experiences, even though breast cancer nursing in Britain is arguably better developed than anywhere else in Europe.

Population screening services of all types are most likely to be of optimum value when combined with high quality personal care aimed at minimising the risks of 'over-treatment' and avoidable anxiety and depression.

There is mounting evidence of multiple genetic influences on breast cancer development and subsequent treatment responsiveness. Women with a mother, sister or daughter diagnosed with breast cancer have almost double the risk of being diagnosed themselves, although this may in part be due to shared life styles. Future applications of new genetic and phenotypic[6] knowledge may well create new opportunities for risk testing in community pharmacy and other settings, as well as in specialist care environments. If delivered as part of well-structured cancer awareness raising strategies such services could in future help further enhance the efficacy of screening and case finding.

Presently most interest has focused on identifying *BRCA 1* and *2* carriers. Although these two abnormal genes – each of which can take various forms – only account for about three per cent of breast cancers in the UK (and a higher proportion in the Jewish population) they are important because the linkage between them and not only breast cancer but also conditions such as prostate cancer in men is relatively strong. In addition, about 10 per cent of all ovarian cancers occur in women carrying *BRCA 1* or *2*. Women carrying such genes have an up to 80 per cent chance of developing an associated cancer

Angelina Jolie's much publicised decision to have a double mastectomy as a protective measure has raised awareness of this issue. So too has the controversy surrounding the intellectual property rights (and associated data) held by a company called Myriad Genetics relating to testing for *BRCA 1* and *2*. From a health policy perspective a key point to stress is that it would be wrong for members of the public to assume that even if there is no known history of breast cancer in their family they are necessarily free of abnormal *BRCA* genes. The available epidemiological findings indicate that in the general community there some 70,000 *BRCA 1* and *2* carriers of both sexes in the UK alone. It may well be that at any one time about half of these individuals are unaware of their raised risks and the actions that could be taken to mitigate them.

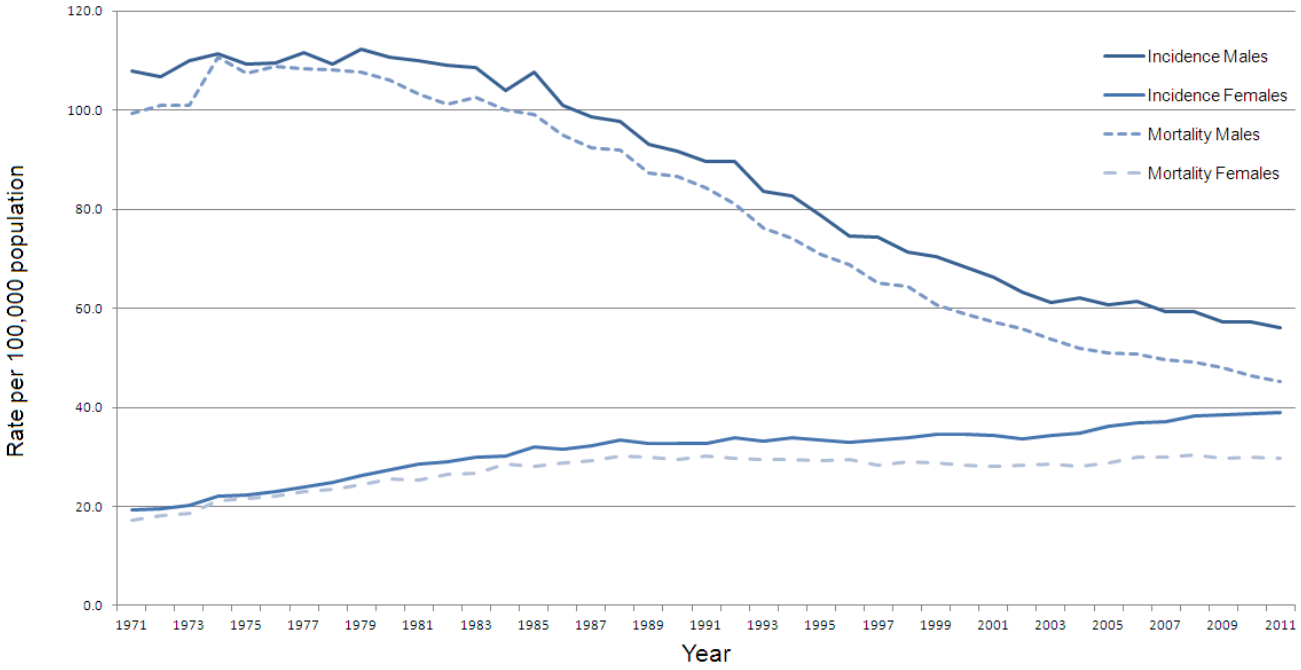
It is already arguable that although the genetics of cancers and other complex NCDs are still far from fully understood, an appreciable level of additional benefit could be derived from extending access to *BRCA1* and *2* and other genes that have been shown to strongly linked to oncogenesis (Box 6). In the eyes of some experts the NHS may now be starting to lag behind the standards that can reasonably be expected of leading health care providers in the developed world (King, 2014).

Lung cancer

In the years leading up to the start of the 1914 conflict in Europe there were still less than 400 cases of lung cancer reported in the entire world literature (Proctor, 2001; Proctor, 2012). Yet in the century since then lung cancer and associated conditions have on a global basis killed more men than the First and Second World Wars combined. Even with recent reductions in tobacco use – smoking causes at least 80-90 per cent of lung tumours in the UK – it remains the second most commonly diagnosed cancer in this country. Every day in England alone about 100 individuals are newly found to have the condition (Cancer Research UK, 2013). As Figure 10 shows, incidence rates in men have passed their peak. Yet female lung cancer incidence is still increasing.

6 An individual's phenotype is the observable result of the cumulative interactions between her or his inherited genotype and the external environment.

Figure 10. Lung cancer incidence and mortality rates, England 1971-2011



Source: Office of National Statistics

Box 6. Cancer Genetics

Cancer is a 'genetic disease' in that it stems primarily from mutations in genes controlling cell division. Some of these can be inherited. However, the majority occur by chance or are acquired via life style and environmentally linked exposures to factors such as cigarette smoke, radiation and UV light. Such mutations are not present in every cell of the body and are not unless they occur in reproductive 'germ-line' cells passed on to offspring.

Changes are normally required in a variety of genes for a cancer to develop. Hence in most solid tumours some 30-60 genes are likely to be mutated and in some skin and lung tumours there can be as many as 200 mutations. Because the number of mutations increases with age the incidence of cancer also increases with age. Specific examples of genes observed to be mutated in cancer include oncogenes such as the *MYC* gene first identified in people with Burkitt's Lymphoma and tumour suppressor genes like *TP53*.

Mutations can happen spontaneously in germ cells. If one of these is inherited it will be present in every cell of the son or daughter affected. Being born with a relevant germ-line mutation does not necessarily mean that a cancer will develop. Yet it can significantly increase the risk. As in all cancer cases a number of somatic mutations will also be required. If a person starts life with a relevant mutation it follows that it will be easier for additional ones to build up to the level of DNA change required for a neoplasm to evolve.

Germ-line mutations are the root cause of hereditary cancer syndromes. Reports on gene mutations such as *BRCA1* and *BRCA2* have stimulated interest in such phenomena. Yet they are actually responsible for only five per cent or so of cancer diagnoses. More often cancers appear to 'run in families' due to the presences of shared risk factors such as smoking. Around 50 clearly inheritable forms of cancer have so far been identified. The Table below provides information on some of the better known of them.

In England and Wales NICE recommendations govern who can be referred for NHS testing to determine if they have a mutation that might cause a hereditary cancer. In the US organisations such as the University of Washington provide relatively comprehensive testing options that can be privately accessed, but at a high cost. The NHS funding available for such investigations is limited. In the case of breast cancer, for instance, women can only be referred for free testing if they have:

- One first degree female relative with breast cancer at <40 years of age
- One first degree male relative with breast cancer at any age
- One first degree relative with bilateral breast cancer where the first primary was diagnosed at <50 years of age
- Two first degree relatives on the same side of the family, or one first degree plus one second degree relative, with breast cancer at any age
- One first degree or second degree relative with breast cancer at any age plus on the same family side one first degree or second degree relative with ovarian cancer at any age (one of these should be a first degree relative)
- Three first degree or second degree relatives on the same family side with breast cancer at any age

At present the benefits for consumers of seeking privately funded genetic testing to assess cancer related risks appear limited compared with the costs involved. But as both genetic knowledge and psycho-social methods for supporting behavioural change continue to improve pressures for enhanced access to quality assured testing are likely to increase.

Syndrome	Cancers	Genes Involved
Hereditary Breast and Ovarian Cancer Syndrome	Breast (female and male) Ovarian Prostate Pancreatic	*BRCA1* *BRCA2*
Cowden Syndrome	Breast Uterine Thyroid	*PTEN*
Li-Fraumeni Syndrome	Soft tissue sarcoma Breast Leukaemia Lung	*TP53*
Hereditary Non-Polyposis Colorectal Cancer Syndrome	Colorectal Uterine	*MSH2* *MLH1* *EPCAM* *PMS2*
Familial Adenomatous Polyposis	Colorectal	*APC*

Lung cancer currently has one of the poorest survival outcomes of any cancer. Less than ten per cent of people diagnosed with it live on for five or more years. Over two-thirds of patients are diagnosed at a late stage, when curative treatment is no longer a viable option. Even when observable symptoms are present early, signs and signals like a persistent cough, hoarseness and shortness of breath may be thought innocuous, and are sometimes seen as a 'normal result of smoking' rather than as cancer indicators. Fear, fatalism and embarrassment can stop people consulting with a GP or other health care professional until relatively late. There is also evidence that NHS doctors on occasions fail to follow up adequately on service users' reported concerns. This may be one factor underlying apparent differences in performance between the French and British health care systems, although there are presently no adequate data to support this conjecture.

Innovations such as the Macmillan Cancer Decision Support (eCDS) Tool for improving clinical decision-making can enhance diagnosis rates, at least when contact has been made with health care providers who are able to contribute to patients' medical records. Lung cancer is one of the five cancers specifically targeted by this instrument, in addition to colorectal, pancreatic, ovarian and oesophago-gastric cancers. The main aim is to help GPs make more robust decisions about whether or not to refer people for further diagnostic investigations, via evidence based interpretations of patients' reported symptoms combined with information on their long term medical/health history and relevant demographic and epidemiological data.

Pilot investigations have shown that a fifth of those referred for testing would not have been identified as being at risk without the use of the new tool (Macmillan Cancer Support, 2014). However, by themselves advances of this type cannot overcome problems like failing to consult with a GP in good time. Addressing the latter depends on raising public awareness and promoting appropriate actions. It is also possible that making similar instruments available for the support of community pharmacy 'public health' consultations could in future help direct people to timely GP care.

At present no proven non-invasive 'near patient' tests for early stage (or pre) lung cancer are available. Yet in time early diagnosis may be assisted by strategies such as looking for biomarkers indicative of cancer in blood samples and/or lung exhalate (that is, a person's breath). If and when early stage diagnostic technologies suitable for supply directly to the public as home tests or for use in GP's surgeries and community pharmacies are developed, this will open the way to more effective cancer (and other disease) treatment patterns. To optimise outcomes, professionals such as pharmacists (as well as patients themselves) ought it is now widely accepted to be able to amend health records to incorporate observations made outside medically controlled environments. Current NHS plans suggest that this may be possible by 2020 (NHS, 2014a).

Colorectal cancer

New diagnoses of colorectal (or bowel) cancer are made in just over 40,000 people per year in the UK. Five year survival has more than doubled over the last 40 years. This is due to enhanced treatment options and introduction of the NHS FOBT (faecal occult blood test) screening service for the population aged between 60 and 69 years. Because FOBT helps identify early cases of cancer its introduction alone can reduce colorectal cancer mortality rates by over 10 per cent in countries where its use is well established (Wardle, 2014). But it cannot reduce the incidence of bowel cancer by finding (and so permitting the removal of) pre-cancerous growths. For the latter internal examinations are needed.

Conditions such as Hereditary Non-polyposis Colorectal Cancer Syndrome (HNPCC) and Familial Adenomatous Polyposis (FAP) significantly increase risk of colorectal cancer. However, over and above known and unknown inherited genetic variables, a variety of life style linked factors (including obesity, low physical activity levels, high alcohol use, smoking and a diet low in fruits and vegetables but high in processed and preserved meats like bacon and – less certainly – fresh red meats) raise the chance of colorectal cancers occurring. Once a tumour has developed early diagnosis is key to enhanced survival. This again highlights the importance of using screening services.

Recent research has highlighted the positive effects of aspirin use in terms of colorectal cancer harm reduction (Cuzick et al., 2014b). There is now 'overwhelming' evidence that both the incidence and the mortality due to colorectal cancer is reduced with regular use of aspirin in mid-life. Study findings indicate that in populations aged 40 and above whose members have taken aspirin for more than five years the incidence of colorectal cancer is lowered by approaching 40 per cent. Even more significantly, the mortality rate is cut by more than half. Notwithstanding the negatives associated with side effects such as major bleeding events, such data provide strong support for the prophylactic use of aspirin by individuals seeking to avoid bowel cancer.

Novel screening methods are also being employed in order to reduce colorectal cancer incidence. A programme involving flexible sigmoidoscopy (bowel scope) examinations undertaken (once) at around the time of an individual's 55th birthday is currently being piloted in six regions in England. Although it does not obviate the need for FOBT (which can detect cancers occurring higher in the gastro-intestinal tract than sigmoidoscopes reach) this identifies polyps (pre-cancerous lesions) in the lower bowel. Evaluations undertaken to date are indicative of high levels of public acceptability of this service and a fall of almost a third in colorectal cancer incidence amongst those attending screening (Wardle, 2014). There is therefore good reason to hope that although in the past Britain/the NHS has lagged behind the US and some other EU Member States with regard to bowel cancer prevention and cure rates, national performance will in future be improved.

Prostate cancer

Prostate cancer is the most common neoplasm in males in the UK and all other OECD nations. In 2010 41,000 men were diagnosed with the condition. It is more likely to affect black males than members of other ethnic groups for reasons which are presently being researched. It is likely that in settings such as the UK and the US both genetic and social factors have been involved.

There are about 11,000 prostate cancer deaths a year in the UK. About 1,500 are in men aged under 65, and 5,500 are in men aged 65-84 years. Prostate cancers and their treatments also cause significant levels of physical disability and psychiatric disorders such as depression, although the available evidence suggests that in overall terms the mental distress generated is not as severe as that caused by other major cancers (Waller et al., 2009; Varmus and Kumar, 2013; Beeken et al., 2011). This is perhaps because the perceived risk of premature death is relatively low.

Recorded UK prostate cancer incidence rates have tripled over the last 40 years. This is in large part due to improved detection. Survival rates from the time of diagnosis have also increased significantly, albeit age standardised death rates have fallen much more modestly. The proportion of British men living for five or more years after a diagnosis of prostate cancer is 80 per cent, compared with a European average of 83 per cent (De Angelis et al., 2014). For comparison, the reported five year survival rate in Austria was 90 per cent.

In the UK men are able to request Prostate Specific Antigen (PSA) tests from their GPs, although these are not recommended by all doctors. PSA testing has to date been controversial, primarily because of the high risk of false positive results and consequent 'over-treatment'. A large European study recently reported a 20 per cent reduction in mortality in men ten years after receiving PSA testing and treatment as opposed to controls. But its authors nevertheless argued against mass screening using PSA testing (Schröder et al., 2014). This view is supported by many other expert commentators and groups, including the US Preventive Services Task Force (USPSTF, 2012). It implies that although PSA testing conducted as part of a carefully managed personal care programme can be lifesaving, crude population-wide testing may in itself cause needless distress and costs and achieve little or no overall aggregated benefit.

However, other evidence suggests this precautionary view may now need revising. For example, Vickers et al (2013) have on the basis of an analysis of extensive Swedish data reported that measurements in early mid-life that identify the 10 per cent of men with the highest PSA levels serve with a high degree of reliability to identify those men who as a group are at the highest risk of metastatic prostate cancer later in life. If they are followed and treated with special care this could improve outcomes in a relatively economic manner.[7]

In addition, the full potential value of PSA testing may well be higher than that reported above. For instance, Law (2009) has suggested that because prostate cancers are slow growing the mortality reduction gained may be as high as 30 per cent 15 years after PSA testing and subsequent treatment. At the same time research in University College London (UCL) and University College London Hospital (UCLH) has highlighted the fact that past problems with interpreting PSA data may have been in part a function of the biopsy techniques employed (Emberton, 2013).

The effective use of MRI scanning before physically intrusive biopsies, coupled in appropriate instances with novel surgical interventions such as the targeted use of ultra-sound to eliminate cancer cells, promises to deliver improved outcomes. Urine tests aimed at finding 'new' biomarkers like the PCA3 protein (that is, the product of prostate cancer gene 3) could further raise the viability of mass screening approaches, as well as contributing to the individual care of people able to access such technologies on a privately or publicly funded personal care basis.

In the UK the fact that prostate cancer most frequently kills men who are well past retirement age may have been a reason why its detection and treatment has tended to attract less priority than conditions such as breast and colon cancer. Such concerns have underpinned debates about whether and in what circumstances pharmaceuticals such as sipuleucel-T (Provenge)[8] and abiraterone (Zytiga) are affordable in the NHS environment.

As previously noted, no universal health service can be expected to pay unlimited amounts for any product or service. Yet if it is genuinely the case that the public purse in Britain cannot fund more effective ways of identifying and treating hazardous prostate cancers, there may in time be increasing demands for access to 'paid for' services offered via easy to access channels such as community pharmacies. Provided this demand can be met in ways that genuinely advantage individuals and do not further disadvantage (absolutely or relatively) vulnerable groups, this could enhance welfare without increasing politically unpopular taxation levels.

Leukaemias and lymphomas

Blood (haematological) cancers affect the blood, bone marrow and the lymphatic system. The leukaemias, which are mainly characterised by abnormal white blood cell production, account for a little over one case of cancer in every 50. There are four main types:

- acute myeloid leukaemia (AML), which occurs most frequently in people over the age of 65;

7 Men with a close blood relative such as brother, father or uncle with prostate cancer are also at a 2 to 3 times greater relative risk of this cancer. Like black males they could benefit from an initial PSA test in their early 40s, followed as appropriate by enhanced monitoring.

8 The FDA approved the vaccine like product Provenge (sipuleucel-T) for treating metastatic hormone refractory (castration resistant) prostate cancers in 2010. It boosts the immune system's ability to attack cancerous cells within the body, and may be the herald of similar 'immunising' cancer treatments in the future. However, it has in effect to be tailor made and costs in the order of $100,000 per patient (a course involves three doses). This together with its limited capacity to improve survival duration constrained its commercial viability. Related immunological technologies are now being developed for the treatment of B cell leukaemias.

- acute lymphoblastic leukaemia (ALL). This is the most common type of cancer in children, although it also affects young adults age 15-25;
- chronic myeloid leukaemia (CML) can affect people of any age, but is most common in individuals over 60 years and is extremely rare in children. This is the form of leukaemia treated by the pioneering medicine imatinib mesylate (Glivec) and related innovations; and
- chronic lymphocytic leukaemia (CLL). This occurs in various forms, and also typically affects older adults. It accounts for about a third of all cases of leukaemia and a fifth of leukaemia deaths.

Although survival rates have increased significantly, about 4,500 people a year still die from leukaemias of all types in the UK. In aggregate their incidence is increasing. This may in part be because relevant risk factors include past exposures to radiotherapy and chemotherapy. As more people are successfully treated for other cancers their risk of developing a leukaemia later in life rises. Such observations underline the importance of monitoring and caring for cancer survivors effectively, and so minimising the harm caused by iatrogenic diseases.

Chronic Myeloid Leukaemia is characterised by the 'Philadelphia chromosome', which was first identified in the US city of that name at the start of the 1960s. It was this discovery that after 40 years further research led to the marketing of imatinib mesylate. When taken as intended this (oral) medicine can provide many years of protection, although poor quality pharmaceutical and medical care leading to inadequate medicines taking undermines its effectiveness. Promoting and supporting appropriate medicines use is another key role for modern pharmacists in the context of cancer treatment.

Hodgkin and non-Hodgkin Lymphomas affected over 14,000 people in the UK in 2010. About one in every ten cases is a Hodgkin lymphoma, although for the purposes of this analysis the most salient point to note is that both conditions are today often treated with good outcomes. A number of infections have been linked with the lymphomas. Exposures to Epstein Barr virus, *H. pylori*, HTLV1 and Hepatitis C all increase lymphoma occurrence risks in Britain as well as (more frequently) in less economically developed countries.

Skin cancers

There are two main groups of skin cancers: malignant melanomas and non-melanoma skin growths. The most common of the latter are basal cell carcinomas. Non-melanoma skin cancers are frequent (there are over 100,000 new cases a year in the year in the UK) and are today more than 90 per cent curable. But if neglected some spread and on rare occasions prove lethal. It is therefore important to report skin abnormalities of all types. Those most likely to be ignored tend to occur on people's backs, which are difficult to self-check.

Malignant melanomas are more hazardous, although for many people they can in their early stages be very difficult to differentiate from other skin cancers or abnormalities. There are about 13,000 new cases a year diagnosed in this country and 2,000 deaths annually. Malignant melanomas are relatively common in young adults in their 30s.

The incidence of skin cancers of all types is increasing in the UK. The main extrinsic (external) risk factor is sun burn. Those with a genetic predisposition towards having a very pale skin, red hair and freckles have a higher intrinsic risk than the average 'white' skinned individual, while individuals with 'black' skins are at a considerably reduced risk. Modern sun tan creams with factor ratings of 30 and above have robust protective effects, but even so naked skin exposures to very strong sunlight levels should be avoided.

The need to synthesise adequate amounts of vitamin D has been a key evolutionary driver in the context of skin colour. But as foreign travel has increased and populations have become more mixed this relationship can be masked. Health risk awareness messages need to take sensitive account of such trends, and of the importance of achieving appropriate behavioural balances throughout life. In Australia, for example, sun protection campaigns appear to have been successful in reducing melanoma incidence, but at the reported cost of a quarter of the population now suffering from Vitamin D deficiency (Australian Bureau of Statistics, 2014). In the UK children and younger adults with naturally dark skins are likely to benefit from vitamin D supplementation, as are people aged 60 or over from all backgrounds.

Looking beyond primary prevention, early diagnosis is – as with other cancers – key to curing malignant melanoma. About 90 per cent of those diagnosed in stage 1A (where the melanoma is only in the outer layer of the skin, and is less than 1mm thick) survive for more than ten years. But it is normally said that only 20 per cent or so of those diagnosed in stage 4 (when the cancer has metastasised to other areas of the body) live for five or more years, albeit that this may today be an under-estimate.

Recent therapeutic advances are now improving even late stage disease outcomes. For instance, the 'biological' medicine ipilimumab (Yervoy) can, especially when used along with other innovative drugs normally referred to as PD-1 blockers,[9] extend survival by enabling enhanced immune responses (Robert et al., 2014). Such 'paradigm shift' treatments are indicators of the fact that combinations of enhanced preventive approaches and modern biopharmaceutical science based treatments mean that it is genuinely the case that humanity is 'winning' its ancient struggle against cancer.

9 An example of which is pembrolizumab (Keytruda). Blocking the action of programmed cell death protein 1 (PD-1) enables the immune system to attack melanoma cells more effectively. Other drugs in development also inhibit PD-1 or target other molecular mechanisms known to be involved in this form of cancer.

Other neoplastic disorders

Rarer cancers other than the 'big four' and skin cancers account in total for about 50 per cent of all cancer related mortality in Great Britain. The advances now being made in virtually all the 200 or so site-defined and the growing number of molecular mechanism defined cancers cannot be explored in detail here. However, the point to stress is that progress is occurring on many fronts. Although when viewed in a fragmented manner many innovations may currently seem to be of relatively minor value in the context of late stage cancer survival, present oncology treatment developments will cumulatively make much more significant impacts on overall cancer mortality and morbidity in the next few decades.

Current technology evaluation methods do not reflect this wider picture. Towards the 'high science' end of the spectrum recent research in areas such as ovarian and pancreatic cancer care promises, for instance, to open up further opportunities for earlier detection via the extended use of biomarker based screening and/or other case finding techniques employing ultrasound and other imaging methods. The reason why pancreatic cancer presently has lower five year survival rates than any other major oncological disease is that as with lung cancer it has often reached an advanced stage before it is found. (It is possible that the targeted use of CT scanning or alternative technologies amongst smokers in and around later middle life, perhaps supported by targeted genetic testing, will in the coming decade improve early lung cancer detection rates.)

Existing and new vaccines against infections such as HPV and *Helicobacter pylori* also have the potential to generate new health gains, nationally and internationally. It is arguably short-sighted, for instance, that at present the NHS does not provide immunisation for boys as well as girls against HPV infections, given the role of the latter in not only cervical, penile and anal tumours but also in oral and oesophageal cancer formation.

In addition there have also been interesting developments in areas such as the use of BCG vaccine (which is primarily employed for protection against tuberculosis) to reduce the risk of bladder cancer metastasis through generalised immuno-stimulation effects. Raising awareness of the fact that smoking cessation remains the most important way of reducing bladder cancer incidence is vital. Yet it is worth re-emphasising there is evidence that to be optimally effective public health programmes aimed at promoting life style changes need to be complemented by better late stage treatments. Knowledge of the latter should, when good access is assured, reduce fears about what will happen if prevention fails and so encourage greater willingness to engage in all stages of cancer harm prevention.

Future cancer prevention and treatment opportunities

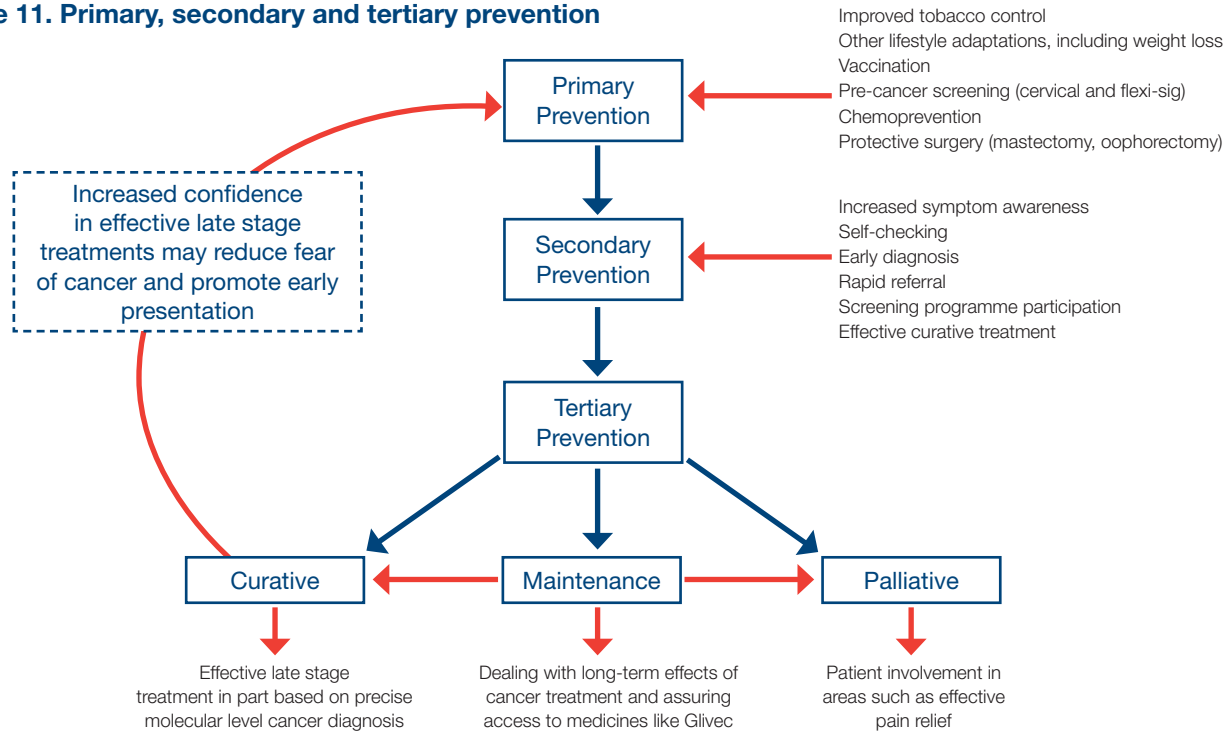
Globally, the absolute burden of disease caused by cancers is currently projected to double in the two decades from 2010 to 2030. Observers estimate that there will be 26 million or more new cases a year by 2030, and some 17 million cancer deaths annually (Thun et al., 2010). However, this anticipated trend is primarily driven by the ageing of populations such as that of China. It is also a function of continued population increases in areas where people are not as well protected from external carcinogens as are most citizens of the wealthier OECD nations, or as able to access screening and treatment services. A large proportion of the population of India falls into this category. The same can also be said of sub-Saharan Africa, although cancer death rates there will probably take longer to peak.

If investment in better treatment and care is continued, the data and findings presented in this UCL School of Pharmacy report suggest that in countries like the UK the age standardised cancer death rate will have fallen significantly by 2030. If established trends continue it will in fact be 40 per cent down on the 1990 figure. If a modest acceleration is achieved the cancer related mortality burden will have reduced by more than a half in the developed world. If in addition the anti-cancer technologies and the social 'know how' created in settings like the US and the UK can effectively be transferred to less advantaged communities, global progress towards radically reducing cancer related death and disability rates should be well on the way by 2050.

As NHS England's October 2014 *'Five Year Forward View'* (NHS, 2014b) highlights, from a strategic perspective achieving improved cancer outcomes will depend on both widening and deepening cancer prevention, detection and treatment. 'Widening' in this context means involving every member of the population more effectively in their own protection and care, and when appropriate in that of others close to them. One route towards this lies in creating opportunities for people to make reflective spaces in their lives for considering information about cancer and allied health issues that they already may know in theory, but have lacked a chance to think about and apply to their personal situations in a non-threatening context. Increased cancer awareness defined in these terms might in part be achieved by offering services like personal health history reviews in 'bricks and mortar' settings such as local pharmacies, coupled with access to 'state of the art' online support resources.

Widening also implies ensuring that more people receive the best possible treatments available at any one time. Relevant illustrations range from making it easier to find safer ways of using nicotine as and when people do not wish to quit its use altogether, through to when beneficial offering proton beam therapies and other sophisticated radiological treatments in a more timely manner than is presently possible (Cancer Research UK, 2014a). It will also involve providing the most effective medicines for conditions such as advanced breast cancer, as well

Figure 11. Primary, secondary and tertiary prevention



Source: The Authors

as increasing the use of services such as bowel cancer screening.

Deepening, by contrast, means adding new knowledge and developing fundamentally new ways of achieving better clinical results in fields ranging from, for instance, obesity rate reductions through to, say, finding and categorising prostate disease or treating more early stage lung and pancreatic cancers. On occasions the actions needed to meet patient and public needs for widening and deepening cancer care may conflict. This is most apparently so, for example, in disputes about balancing community interests in limiting spending on innovative therapies on the one hand and increasing research investments on the other, and also in political reluctance to raise taxes on foods and beverages known to be 'unhealthy'. But in the long term widening and deepening could and should complement each other.

At the same time there are three main levels at which advances relating to cancer outcomes can take place – see Figure 11. The first of these is primary prevention, which entails cutting disease incidence rates and avoiding cancer related problems altogether. The second is that of secondary prevention, which centres on early detection as a preliminary to curative intervention. The third is tertiary prevention.

This last encompasses treating and eliminating advanced disease where possible, ensuring that as far as is possible harm caused by past treatments is minimised, and when necessary dying with cancer with as much dignity and self-fulfilment as possible. The remainder of this section briefly reviews some key points linked to these interlinked care improvement areas, with special reference to service user and patient 'empowerment' and the potential for community pharmacy based services to help promote better health outcomes.

Primary Prevention

The primary prevention of cancers is often taken to be an ideal goal, even though in practice seeking to avoid disease at any cost is not always a rational way forward. When the risks of unwanted events are low and/or treatments are affordable and effective, other harm reducing approaches can be of greater value. In addition it may not be economic to spend scarce resources on, for example, seeking to persuade moderate drinkers to cut their alcohol consumption (albeit there is some evidence that community pharmacy services could be effective in this context – Davies et al., 2013) as compared to investing in alternative measures like improving the diets of people in very vulnerable sections of the community.[10] But it should be noted that there is probably no unequivocally safe level of alcohol intake in contexts such as breast and oesophageal cancer prevention, and that alcohol use often promotes obesity.

There can also be important dynamic links between curative and late stage treatment provision and primary prevention. To the extent that the belief that a condition is curable, or at least manageable in the long term, helps to reduce fear and fatalism and open the way to rational risk awareness, communicating positive messages about later stage treatment outcomes will foster states of mind

10 Alcohol is currently responsible for about 1 cancer in every 25 in the UK. Individual alcohol users might reasonably elect to continue drinking and accept a degree of associated hazard. There are however strong public health reasons for seeking to limit intakes of over, say, 50-100 units a week. Minimum unit pricing – MUP – policies for alcoholic beverages primarily address the latter. The welfare based case relating to cancer prevention via cutting alcohol use is less powerful in well-nourished non-smokers with moderate alcohol use habits. However, this is not to ignore population wide drinking costs and dis-benefits. In financial terms alone, for instance, over four times more is spent on alcoholic beverages in the UK every year than is spent on all medicines combined.

in which hazards are freely perceived and responded to without generating counter-productive anxieties.

The prevention of cancer involves the pursuit of public health objectives of many types, from maintaining the integrity of the ozone layer and reducing levels of diesel derived particulate in urban atmospheres through to assuring food purity and promoting exercise opportunities like 'safe' cycling. But for the purposes of this analysis the five most important elements of cancer incidence reduction to which community pharmacy based services could in future do more to contribute are:

- Optimising immunisation rates.
- Supporting tobacco use cessation and nicotine addiction related harm reduction.
- Promoting other forms of life style related cancer risk reduction, including obesity management and skin protection.
- Encouraging the use of services which identify 'pre-cancers' and genetically linked risks, and so either facilitate disease avoidance or allow individuals to benefit from earlier disease treatment.
- Medicines use optimisation, including chemo-prevention with drugs like, for example, aspirin, tamoxifen and anastrozole.

Examples of how vaccination based cancer prevention could be further improved range from – as mentioned above – enabling boys to have affordable access to HPV vaccination (this end is already being pursued in parts of the US and Australia) to (along with using antiviral medicines to cure hepatitis C) providing more people in the UK with protection from Hepatitis B. The chance of contracting the latter is lower in Britain than it is in nations such as Turkey or regions such as the Far East. Yet it is nevertheless an appreciable threat. In Taiwan, where the first universal HBV vaccination programme was introduced over twenty years ago, all infants are vaccinated shortly after birth. Liver cancer incidence in children aged 6 to 14 years has fallen from 0.5 per 100,000 to 0.2 per 100,000 (Chang, 2009). The long term impacts on adult liver cancer rates are still to be fully determined.

There is good evidence from areas such as influenza immunisation that pharmacy based services can successfully enhance access to vaccination rates (Warner et al., 2013). New products may in time be developed for vaccinating against not only disorders such as Hepatitis C (HCV – although in this case the variability of the virus's outer coat makes immunological targeting difficult, so favouring drug based public health strategies involving pharmacy based or other case finding and treatment programmes) and Epstein-Barr virus (EBV, or human herpesvirus 4) infections but also some bacterial and parasitic diseases, including schistosomiasis. This aquatic snail born condition is still prevalent in countries as close to Europe as Egypt, where it is a common cause of bladder cancer because of its ability to induce chronic urinary tract inflammation.

E-cigarettes and the future role of Nicotine Replacement Therapies (NRT)

Tobacco use is responsible for some 20 per cent of all cancer deaths world-wide. Approaching a fifth of the British population continues to smoke, and it is the single most important driver of social class related health inequalities in this country. Giving up smoking does not significantly reduce an individual's chance of developing a neoplastic disease for at least a decade. But it takes people off the escalator of increasing cancer risk, and confers more immediate vascular disease related benefits. A smoker's excess chance of suffering a heart attack drops by about 50 per cent in the first year after stopping.

Pharmacists can play valuable parts at the clinical care end of the public health activities spectrum by supplying and promoting the use of NRT and other stop smoking medicines and products, as well as professional guidance and psychological support. However, issues relating to e-cigarette supply and the possibility that licensed pharmaceutical products containing nicotine might in future be presented as fashionable leisure goods suitable for long term use are controversial.

From a physical health perspective many commentators believe that 'clean' nicotine is not in itself unacceptably hazardous (especially when absorbed via the buccal cavity rather than through the lung alveoli) and argue that individuals can safely self-calibrate the doses they take (Bates, 2014). There are valid questions about the extent to which allowing the long term sale of an addictive drug in any format intended to promote its leisure use should be accepted as desirable in pharmacies or elsewhere. But from a cancer prevention and treatment perspective it is important to stress that tobacco smoking cessation remains a critically important public health objective. As such, all future community pharmacy and other health linked activities should be consistent with the goal of eliminating it. Seeking to free people of nicotine addiction altogether may also be thought desirable, although it is not as a public health priority as important as stopping tobacco smoking.

Facilitating wider life style changes

As already described, raised cancer incidence rates are associated with obesity and a range of other life style linked factors, from alcohol use to a lack of exercise and avoidable failures to protect against strong sunlight. Although there is clear evidence that most members of the UK public now know the relationship between smoking and health, understanding of other life style and cancer linkages is not as strong. Awareness, in the sense of being in a rational state of readiness to reduce risk, is often weaker still.

For example, there is research indicating that more effort could usefully be put into communicating why having multiple sexual partners is a risk factor for cervical cancer (Keeney et al., 2011). It is also of note that in the UK young female members of black and ethnic minority

groups are currently less likely than young white women to have received HPV vaccinations.

The extent to which personal health care providers can by their own interventions alone facilitate complex life style changes at a population level is limited. Effectively addressing the causes of complex multi-faceted problems such as obesity and excessive alcohol use is much more difficult than supporting smoking cessation (Kelly, 2014). Nevertheless, 'healthy living' and other pharmacy based services can help to reinforce the impacts of wider health promotion programmes involving interventions such as increasing taxes on 'unhealthy' goods and the projection of health messages via mass advertising.

Evidence based approaches to individual health behaviour change aimed at cancer prevention should therefore over time improve outcomes, especially when health promotion can be linked to the supply of protective medicines and other self-care items like sun protection products. As and when, for instance, safer and more effective medicines suitable for pharmacy use in obesity prevention become available this might well open up new opportunities for pharmacist supported self-care in general and cancer prevention in particular. Similar points can be made in relation to alcohol use moderation.

Promoting screening for preventive purposes

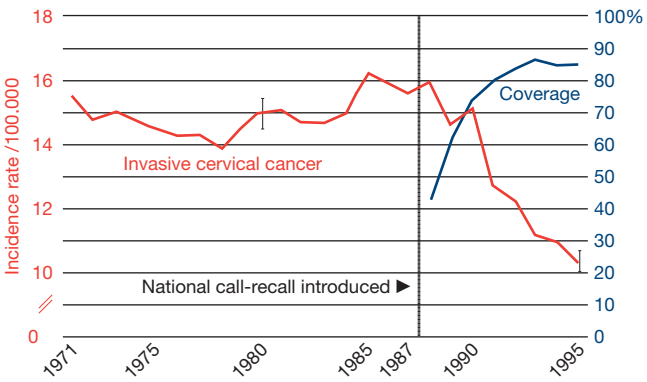
Screening and case finding programmes contribute to primary prevention in two main ways. The first is via identifying pre-cancerous growths such as GI tract polyps or skin abnormalities before they become malignant, so opening the way to their removal. Figure 12 and Box 7 provide data relating to cervical screening, which can identify cervical cell pathologies before cancers are established.

The second way screening and/or individual 'case finding' contributes to lowering the incidence of cancer is by identifying risk factors that can be mitigated. As the genetic and physiological bases of conditions like, say, irritable bowel syndrome (IBS, which includes both Crohn's Disease and Ulcerative Colitis) become better understood this should pave the way for more effective ameliorative therapies. In the IBS instance these could in turn reduce the incidence of colon cancers.

Health professionals such as community pharmacists can act as 'signposts' to existing NHS screening opportunities. Looking to the future, and to the border line between primary and secondary prevention, pharmacy provided testing for combinations of genetic and phenotypic variations that render those carrying them more liable to developing cancers than the average person (for instance, it is possible that in the coming decade or so a saliva test for prostate cancer vulnerability will become available) could identify individuals likely to benefit from closer than usual monitoring for signs of tumour growth.

As the efficacy of near patient evaluation techniques increases and opportunities for risk checking proliferate, a growing proportion of such testing could take place in, or be accessed via, community pharmacies. This is

Figure 12. Age standardised incidence of invasive cervical cancer and coverage of screening, England 1971-95



Source: Quinn et al, 1999

Box 7. Cervical Cancer Screening

The NHS cervical cancer screening programme began in its current format in the late 1980s. Prior to this local health services were taking and checking cervical smears but coverage was not consistent. The national cervical screening programme has been successful in reducing not just mortality rates but also incidence of invasive cervical cancers. In England this fell from 16 cases per 100,000 in 1987 to 8.7 cases in 2013.

The pre-cancerous stage of cervical disease involves the proliferation of CIN cells (Cervical Intraepithelial Neoplasia). These are abnormal cells which form lesions on the surface of the cervix but do not invade the tissues. Pre-cancerous CIN lesions are normally graded as mild (CIN I), moderate (CIN II) or severe (CIN III). The phrase *carcinoma in situ* (CIS) is also often used to relate to CIN III. Abnormal CIN cells are likely, if left, to develop into cervical cancer. Cervical screening facilitates their removal before this occurs.

In cases where a small number of abnormal cells are identified HPV testing will be offered. If HPV is not found the chance of the abnormal cells proceeding to a cancerous state is minimal and no additional treatment is normally thought necessary. In cases where HPV is present treatment to remove abnormal cells is required.

In cases which have passed beyond the CIN/CIS phase curability depends on the stage at diagnosis, as is the case with all other cancers. Stage 1 cervical tumours are generally localised to the neck of the uterus, with subdivisions made depending on the size of the growth. Stage 2 cervical cancers have spread beyond the neck of the uterus into surrounding tissues, but have not yet grown into any of the muscles or ligaments that line the pelvis. Stage 3 cancers have spread into the surrounding tissues of the pelvis, the lower part of the vagina or towards the kidneys. Finally stage 4 cancers have spread to nearby organs such as the bladder or rectum. Presently quoted cure rates vary from 99% for stage 1A1 to 20% (five-year survival) for stage 4.

a promising prospect. Nevertheless, the current value of much genetic testing should not be exaggerated. It is presently most important in the context of identifying carriers of single genes known, like *BRCA 1* and *BRCA 2*, to have a strong role in cancer causation.

There are already combination test 'chips' available. The use of such products and the linked analytical services needed to employ them productively is currently very limited in the UK. However, their affordability will in time increase. Such trends imply that as the twenty first century unfolds the wider use of family history evaluations and personal preference assessment instruments in the contexts of both professional service supply and self-care delivery could stimulate greater demand for risk testing. This might be met through increased testing in non-medical NHS contracted and/or private health settings, over and above the existing system of limited access to specialist medical clinics counter-balanced by in some instances questionable internet based services.

Chemo-prevention and the timely treatment of established infections

Improved rates of detection and diagnosis of infections such as Hepatitis and *H. Pylori* need to be complemented by optimal medicines use. The appropriate monitoring of patients using drugs known to increase the chance of cancers developing, such as rheumatoid arthritis treatments that block the actions of the naturally occurring protein TNF (Tumour Necrosis Factor), should arguably be seen as one aspect of medicines use optimisation.

With regard to cancer chemo-prevention, the evidence for seeking to reduce the incidence of colorectal and other cancers such as oesophageal carcinomas by 30-40 per cent through aspirin use has, as previously discussed, built rapidly since the start of this century. The role of aspirin in cardiovascular disease prevention has been questioned because its use increases the occurrence of haemorrhagic strokes and other potentially lethal events. Yet as its mode of action, along with that of other medicines employed in cancer prevention, becomes better understood it is probable that demand for protective treatments will grow.

Given the numbers of healthy consumers likely to be involved and the pressures already limiting access to GP care, a wider use of appropriately designed community pharmacy based support and monitoring services could offer a cost effective way of meeting such needs safely. Similar arguments apply in relation to the primary prevention of vascular diseases in middle and later life (Wald and Misselbrook, 2011). There are important potential overlaps between the latter and cancer chemo-prevention, not least with regard to statin use. It is possible although not as yet proven that the anti-inflammatory and allied properties of such medicines could if they are taken at the right stages in a person's life cut the chances of lipid level related cancers developing.

The chemo-prevention of breast cancer via the use of oestrogen opposing medicines is another area where further progress may well take place. Trials have already shown that taking tamoxifen for five years can reduce the incidence of breast cancer by around one third in both pre- and post-menopausal women who are at raised risk of developing the disease (NICE, 2013). An alternative drug, anastrozole, has recently completed clinical trials showing that taking it for five years can reduce or at least delay breast cancer occurrence in high risk post-menopausal women by as much as 50 per cent (Cuzick et al., 2014a).

Secondary prevention

Improving secondary prevention demands expanding opportunities for the detection of cancers in individuals with early stage illness, and providing them with treatments that either cure or block the further development of their conditions.

Key opportunities encompass:

- Increasing self and family awareness of cancer signs and symptoms in ways that encourage greater use of screening programmes and allied resources, and overcome barriers to the reporting of concerns to doctors or other health care providers.
- Enhancing cancer case finding by health professionals, in part by increasing their abilities to communicate empathetically with and respond appropriately to service users from all sections of the UK community.
- Extending access to screening opportunities, including introducing new and redesigned screening programmes when the available evidence supports this would be welfare generating.
- Improving treatment effectiveness, with a view to increasing stage specific cancer cure rates wherever possible.

As already noted, examples of opportunities for improving the secondary prevention of neoplastic disease exist in areas ranging from prostate and breast cancer risk prediction to pancreatic and lung cancer detection. With regard to enhancing treatment there are also emerging opportunities for less damaging forms of intervention, as well as opportunities for using medicines initially introduced as late stage palliative therapies to help cure less advanced disease.

The optimal use of new therapies can paradoxically be delayed by regulations aimed at assuring drug safety and efficacy. It takes less time to demonstrate anti-cancer drug effectiveness in patients who are close to death than it does to show that they have value in early stage illness. From a historical perspective the much discussed Herceptin (trastuzumab) example illustrates this dilemma. But from the viewpoint of this report the most important goals to pursue relate more to increasing public and patient willingness to report symptoms, and enhancing professional abilities to differentiate between transient problems and the initial indications of life threatening disease.

There is evidence that in traditional NHS settings many people, particularly those with limited personal

confidence, may worry excessively about 'bothering' their doctors with 'trivial' matters that might cause them to be given negative labels like 'worried well' (Waller et al., 2009). In modern Britain women and to a lesser extent men from South Asian and other ethnic minority backgrounds can be in special need of targeted support aimed at improving communication quality with health professionals such as GPs (Robb et al., 2009).

The advances made by Macmillan Cancer Support and its partners in relation to using medical record based data more productively provide an example of how UK GP practice performance could be further enhanced in an economically productive manner. As cancer linked knowledge increases and additional risk and diagnostic tests become available the power of such instruments will continue to rise. Similar approaches aimed at empowering patients and the capacity of non-medical health workers such as nurses and 'health champions' – ranging from mobile phone 'apps' to computerised consultation and self-care guides for use either in settings like pharmacies or in people's homes – to offer effective support could provide additional benefits (NHS, 2014a). However, to use such aids to optimum effect all practitioners will need to be able to talk with service users in a flexible manner, rather than being confined to 'tick box' interview protocols.

Tertiary prevention

The tertiary prevention of cancer includes:

- Effectively treating and where possible curing advanced cancers, in part by typing tumours accurately in order to allow targeted medicines to be used to best effect.
- Where necessary managing cancers as chronic conditions, and arresting or at least slowing their ongoing development while at the same time helping individuals to remain in control of their lives and continue with their normal social roles.
- Ensuring that 'cancer survivors' who are living with the unwanted effects of treatments receive appropriate support (Macmillan Cancer Support, 2014).
- When needed, providing effective pain relief and good quality end of life care in service users' homes or when preferred in hospital or in locations such as hospices.

In relation to the delivery of advanced and more 'personalised' treatments the most important pharmacy roles arguably exist in specialised oncology hospital departments. They include the selection and preparation of relevant medicines and when possible the prevention of unwanted side effects and drug interactions associated with both single medicine and complex combination treatments.

However, there can also be key parts for community pharmacists to play in contexts such as long term care involving the home use of anti-cancer medicines, and optimising drug therapy in end of life care. Even reducing the incidence of avoidable problems such as constipation due to opiate taking can be a significant contribution to care quality management.

There is no room for complacency in any of the fields indicated above. The NHS faces challenges in areas ranging from using advanced diagnostics to determine the responsiveness of cancers to alternative treatments through to that of caring well for cancer survivors living with iatrogenic disabilities (Box 8). There is evidence, for instance, that the use of molecular level cancer typing tests in the UK is lagging significantly behind that achieved in countries such as France.

Nevertheless, after diagnoses have been made and care requirements established the UK system (broadly defined to include the specialised nursing that has been pioneered in the UK and 'third sector' hospice and home care providers like, for instance, Marie Curie Cancer Care) is comparatively well equipped to meet the needs of severely ill cancer patients. By contrast, in many (but not all) poorer parts of the world the quality of services such as those for pain relief is often inadequate. Even access to basic medications like morphine can be very

Box 8. Iatrogenic Disabilities in Cancer Survivors

The total number of cancer survivors living in the UK will grow from approaching 2.5 million today to over five million by 2040 (Maddams et al., 2012). Macmillan Cancer Support has played an important part in drawing attention to the social, physical and psychological problems such individuals may face and the actions that should be taken to alleviate them (Macmillan Cancer Support, 2014b; Macmillan Cancer Support, 2014a). About a half of those who are presently living with cancer, or are living disease free after treatment, have one or more moderate or severe unmet need. These can range from bowel or urinary incontinence to chronic fatigue or heart disease, osteoporosis and/or depression resulting from their therapy.

Exacerbating factors can include poor communication between cancer specialists and primary care doctors, and insufficient explanation of treatments and their long term effects or of what patients, families and communities can do to reduce such difficulties to a minimum (Corner and Wagland, 2013). The '*Recovery Package'* provides an illustrative model of after-care developed by the National Cancer Survivorship Initiative in England. It aims to support people who have had cancer, particularly after their treatment has ended.

Patient advocates suggest that all cancer survivors should be systematically followed up during and after their immediate recovery. This may in part be needed to help them regain or build further appropriate personal health expectations and avoid neglecting their overall fitness in the wake of being diagnosed with and receiving treatment for a cancer. Professionals such as community pharmacists should be able to help medicine users understand that the process of successfully coming to terms with a potentially fatal diagnosis can on occasions lead individuals to forget or deny the continuing importance of 'keeping healthy'.

limited, despite the fact that nations such as India are significant producers (Grey and McMikel, 2013).

Palliative and end of life care standards in richer countries like the US can also fall below the standards regarded as acceptable in the UK (Oliver et al., 2004; Clemens et al., 2007). Such problems are especially likely to be found in environments where commercial incentives to provide highly intrusive therapies are not adequately checked by patient oriented professional values and other socially mandated care quality controls.

Conclusion

The treatment of cancer is improving. In future decades there will be an increasing range of safe and effective technologies for detecting and curing early stage disease. There will also be many more medicines and immuno-therapies that, when used either alone or in combination and with complementary radiotherapy and/or surgical interventions, will be able either to cure or to contain the development of even advanced cancers.

The value of such progress against what is in many people's eyes today the most feared remaining killer of children and 'working age' adults in the developed world should not be under-estimated. It is a social and political fact that cancer is in some respects a special case, and is widely seen as '*the emperor of all modern maladies*' (Mukherjee, 2011). Regardless of short term and fragmented attempts at cost effectiveness analysis, the medium to long term benefits of 'winning' humanity's ancient war with neoplastic diseases will in time far outweigh the present costs of cancer treatment, and quite possibly those of health care provision in the round. Applications of the genetic and other fundamental bio-scientific advances linked to today's emerging anti-cancer therapies could also generate future world-wide welfare gains in areas as diverse as food and energy production through to the management of many forms of pollution.

However, important though pharmaceutical and other 'hard science' based developments are likely to prove, overcoming cancer will also require greater understanding of the experiences of people facing the disease and the creation of more opportunities for individuals and societies to develop enhanced competencies relating to (public) health protection. Seen from this perspective, being able to offer progressively more effective psycho-social and practical support for life style changes that help service users to act on the risk related information they possess is as vital for modern health care as continuing to provide safe access to effective medicinal treatments.

Similar observations apply in relation to developing 'healthy communities' which foster and support protective life styles. An important step towards making the NHS *'fit for the twenty first century'* will be to move away from a culture in which people feel inhibited about discussing with health care professionals minor symptoms or subtle changes in their bodies that might seem trivial, but could be indicative of problems like early stage cancers. Against the background of the changes in health service delivery that agencies such as NHS England and Public Health England believe are needed to provide preventive and anticipatory care more effectively, phrases like *'minor symptoms may mean serious illness'* and *'reducing small risks can achieve large gains'* carry important messages about how the burdens imposed by non-communicable diseases that develop over whole-life courses can most effectively be minimised.

Community pharmacy has the potential, along with other contributions (see Smith et al, 2013; Smith et al, 2014), to play a significant part in achieving better cancer prevention and care. This can be achieved via their providing more services directly to the public and through pharmacists working more closely with GPs and other NHS and social care professionals and partners in the private and voluntary sectors to meet service users' requirements without imposing inappropriate judgements as to what needs are legitimate as opposed to being 'trivial wants'. Better pharmaceutical care can also enable medicines and diagnostic products to be used to better effect, and contribute in areas such as further reducing tobacco related cancer rates and improving access to risk testing and disease screening.

Initiatives which cut the age specific incidence of cancers can also reduce vascular disease burdens, along with the occurrence of conditions such as type 2 diabetes and some forms of dementia. Similarly, programmes aimed at enhancing the care of people with disorders like bronchitis (Community Pharmacy Future, 2013) could also prove relevant to, for example, reducing lung cancer mortality.

Major advances in human well-being classically require new technical capabilities, such as the development of steam power in the early nineteenth century and micro-processor based computing in the late twentieth century. Advances in biology and medicine taking place in cancer care and allied fields today offer similar opportunities for coming years. Yet if in the final analysis those who could benefit from scientific innovations are unable or reluctant to use them, or do not or cannot communicate the challenges they face, potential benefits will be lost.

Hence awareness raising, defined as helping people to not only understand the causes of cancer but also to overcome barriers to using their knowledge and the services available to them to avoid illness when possible and access treatment when necessary, will be central to '*winning the cancer war*'. If in future community pharmacists can prove as effective in supporting the behavioural changes needed for self-care and cancer harm prevention as they and their hospital colleagues are in managing medicines, then pharmaceutical care will truly come of age in the twenty first century.

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