Cancer in the year 2025

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How will cancer look in the year 2025? More than fifty UK cancer care specialists – physicians, scientists, health managers, economists, health service watchers – together with cancer charities and patients spent two days together in late 2003 asking themselves this question. Here is what they came up with.

In 2025 over three million people in the UK will be living with cancer. Like diabetes, heart disease and asthma, cancer will become one of the major chronic diseases that impact on the way people live but do not inexorably lead to death. The model will be prostate cancer, which men tend to live with, rather than die from. Progress will be made in preventing cancers and even greater progress will be made in understanding its myriad causes and in detecting, diagnosing and treating the disease. Refinements of current technologies and techniques – in imaging, radiotherapy and surgery – together with the availability of targeted drugs will make cancer a controllable disease.

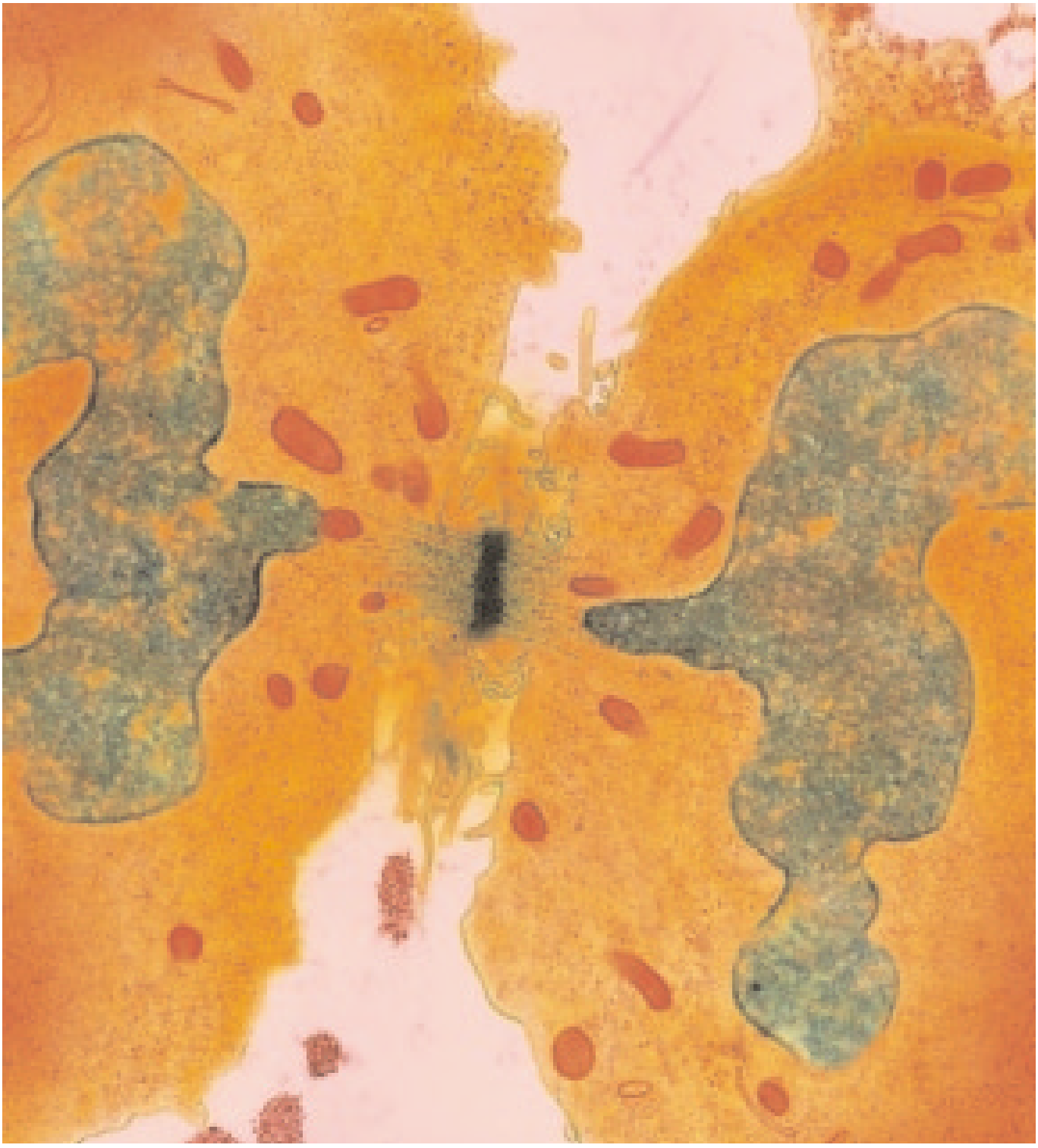
Cure will still be sought, but will not be the only satisfactory outcome. The fear that cancer kills, still prevalent in the early years of the 21st century, will be replaced by an acceptance that many forms of cancer are simply a consequence of old age.

With the increase in demand for treatment, the cost of cancer care is expected to soar, creating immense challenges for health services. While in 2025 more patients will benefit from better diagnosis and new treatments, technology will also bring greater inequality to the health sector. It is unrealistic to assume that the best care possible will be offered to all patients irrespective of their socio-economic circumstances. Well-informed patients, with adequate funds, will ensure that they have rapid access to the newest and best treatments. Many of these will take place close to patients' homes using mechanisms devised by innovative service providers.

Clinicians in Europe will continue to be dependent on technologies primarily designed for the world's major health market – the United States – which, with 5% of the world's population, consumes nearly 55% of cancer medication. Targeted niche drugs will be less appealing to industry as the costs of bringing each new generation of drugs to the market will not match the returns from current blockbusters. Intraprofessional boundaries will blur – doctors from traditionally quite distinct specialties may find themselves doing the same job. And clinical responsibilities will be assumed by health professionals without medical qualifications. All professionals are likely to find challenges to their territory hard to accept. But new ways of working need to be developed soon, as the leaders of the health professions of 2025 – doctors, nurses, pharmacists and their support staff – are already in training.

Prevention and screening

At the beginning of the 21st century, 10 million people in the world developed



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Coloured transmission electron micrograph (TEM) of a section through a cancer cell undergoing mitotic cell division

WHAT DO YOU THINK?

Will fear and anxiety be mitigated?

Will the focus be increasingly on control, not cure? Should it?

Will we have a generation of elderly living with chronic cancer, treated as outpatients and supported by ever-dwindling numbers of carers?

Will patients rely on other patients to guide them through treatment options?

Are we training for specialisms that have no future in their current form?

Will the cost of drugs bring national health systems to their knees?

Send your comments to Kathy Redmond, Editor, Cancer World, at magazine@esoncology.org or fax them to +39 02 43359640

cancer each year. The cause of these cancers was known in roughly 75% of cases: 3 million were tobacco related; 3 million were a result of diet; and 1.5 million were caused by infection. Anti-smoking initiatives were considered to be successful – although it took 50 years from the time the association between smoking and cancer was first identified. In the UK, 80% of the population smoked in the 1960s; in 2003 the figure fell to 30%, but masked real health inequality (the percentage of smokers in the higher socio-economic bracket fell to single figures, while remaining around 50% in the lower socio-economic bracket). Banning smoking in public places will lead to a further drop of about 4%.

Lessons from anti-smoking initiatives will be instructive for prevention in the future. Although the link between poor diet, obesity, lack of exercise and cancer has not yet been confirmed, there is sufficient circumstantial evidence to suggest that strong associations will be found. Long before 2025 there will be bans on advertising for crisps, sweets and soft drinks on television.

A health tax on these products will be introduced and sponsorship of public events by manufacturers of these products will be banned. By 2010, obesity among the middle classes will be socially unacceptable, but will remain common among the economically disadvantaged.

The future prevention picture will be coloured by post-genomic research. In 2003, it was accepted that about 100 genes were associated with the development of a whole range of cancers. Carrying a changed version of a particular gene – or combination of changed genes – will not necessarily lead to the development of that cancer but will increase the risk. By 2025 most people will be genetically mapped. The information – gained from a simple blood test – will be easily stored on a smart-card. Legislation will be required to prevent this information being used to determine an individual's future health status for mortgage, insurance and employment purposes. However, the process of mapping and screening will reveal a predisposition to certain diseases and people will have to learn to live with risk.

In the early years of the 21st century, the average age of diagnosis of cancer was 68. This figure is expected to fall by 2025 as a result of improvements in screening, detection and diagnosis. Predisposition for certain cancers which tend to manifest themselves when the patient is 70 or 80, will be detected in young adult life and corrected successfully when the patient is 30. And while increasing age will remain the strongest risk predictor, the computing power of the future will bring accurate calculation of risk factors, and predictions will take place on an unimaginable scale. Screening programmes will be developed on a national basis and novel providers of risk assessment services are likely to emerge.

Detecting cancer

By 2003 it was established that cancers were fundamentally somatic genetic diseases that result from several causes: physical, viral, radiation and chemical damage. Other processes – chronic inflammatory change, immuno-surveillance and failure of apoptosis, were also implicated. By 2025 cancer will no longer be understood as a single entity – it will be considered to be a cellular process that changes over time. In 2003 most diagnoses of cancer depended on human interpretation of changes in cell structures seen through a microscope. By 2025 microscopes will be superseded by a new generation of scanners that detect molecular changes and can build

THE NEW DIAGNOSTICS

- Radiology and pathology will merge into cancer imaging
- Dynamic imaging will create a changing image of biochemical abnormalities
- Cancer changes will be detected prior to disease spread from primary site
- Greater precision in surgery and radiotherapy will be used for pre-cancer
- Molecular signatures will determine treatment choice

a picture of change over time, imaging cellular activity. We will have the ability to probe molecular events that are markers for early malignant change.

Imaging and diagnosis will be minimally invasive and enable the selection of the best and most effective targeted treatments. Even better imaging will be able to pick up pre-disease phases and deal with them well before they are currently detectable. These techniques will also be crucial to successful follow-up. A patient who has a predisposition to a certain cancer process will be monitored regularly and treatment offered when necessary. Not all cancers will be diagnosed in these early stages – some patients will inevitably fall through the screening net. Nevertheless, there will be opportunities to offer less invasive treatment than at present. Surgery and radiotherapy will continue, but in greatly modified form, as a result of developments in imaging. Most significantly, surgery will become part of integrated care. Removal of tumours or even whole organs will remain necessary on occasion, but the surgeon will be supported by 3-D imaging, radio-labelling techniques to guide incisions and by robotic instruments. And although many of the new treatments made possible by improved imaging will be biologically driven, there will still be a role for radiotherapy – the most potent DNA damaging agent – in treating cancer with great geographical accuracy.

In 2025 most cancer treatments will be able to be performed on an outpatient basis. Minimally invasive treatments will reduce the need for long stays in hospital and the need to provide care close to where patients live will be both desirable and possible. Highly sophisticated scanning equipment and mobile surgical units will be transported to where they are required. Technicians, surgical assistants and nurses will provide the hands-on care, while technical support will be provided by the new breed of clinician – a disease-specific imaging specialist working from a remote site. Cost control will be an essential component of the diagnostic phase.

New treatment approaches

In 2025 eradication of cancer, although still desirable, will no longer be the primary aim of treatment. Cancers will be identified earlier and the disease process regulated in a similar way to chronic diseases such as diabetes. Surgery and radiotherapy will still have a role depending on the type of cancer, the stage at which the disease is identified and the performance of new drugs, but treatment will be less aggressive.

By 2025, cancer treatment will be shaped by the new generation of drugs. What they will look like is not yet apparent and will depend on the success of agents currently in development. Over the next three to five years, we will understand more fully what benefits compounds such as kinase inhibitors are likely to provide. It is estimated that in 2003 around 500 oncology drugs were being tested in clinical trials. Of these, around 300 were against specific molecular targets. This number is set to rise dramatically. Two thousand compounds will be available to enter clinical trials by 2006 and 5,000 by 2010. Many of the drug candidates will be directed at the same molecular targets, and industry is racing to screen those most likely to make it through the development process.

So what will these drug candidates look like? In 2003, small molecules were the main focus of research – most of them designed to target specific gene products that control the biological processes associated with cancer, such as signal transduction, angiogenesis, cell cycle control, apoptosis, inflammation, invasion and differentiation. Treatment strategies involving monoclonal antibodies, cancer vaccines and gene therapy are also being explored. While there is great confidence in the efficacy of these targeted agents, their overall efficacy at prolonging survival is more uncertain. Many could just be expensive palliatives.

We are already seeing the emergence of drugs targeted at a molecular level – Herceptin (trastuzumab), directed at the HER2 protein, Glivec (imatinib), which targets the Bcr-Abl tyrosine kinase, and Iressa (gefitinib) and Tarceva (erlotinib), directed at EGFR tyrosine kinase. What will be important in 2025 is whether a cancer has particular biological or genetic characteristics. Traditional categories will continue to be broken down and genetic profiling will enable treatment to be targeted at

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the right patients. Patients will understand that treatment options will depend on their genetic profile and the risks and benefits will be much more predictable than today.

Therapies will emerge through our knowledge of the human genome and the use of sophisticated bio-informatics. Targeted imaging agents will be used to deliver therapy at the screening or diagnostic stage and technology will enable the disease process to be tracked much more closely. Biomarkers will allow clinicians to measure whether a drug is working on its target and, if it is not, an alternative treatment strategy will be sought. Tumour regression will become less important as clinicians look for molecular patterns of disease and its response.

Barriers to the introduction of new treatments

Innovation in cancer treatment is inevitable. However, there are certain prerequisites for the introduction of new therapies. The therapies must be deliverable to the right biological target, and to the right patient, in a way that is acceptable to patients, healthcare professionals and society. Innovation must also be marketed successfully so that professionals, patients and those picking up the cost understand the potential benefits. The explosion of new therapies in cancer care is going to continue and costs will remain high. The cost of cancer drugs in 2003 was estimated to be $21bn globally, of which $14bn was spent in the United States. If effective drugs emerge from the research and development pipeline, the cancer drug market could reach $300bn globally by 2025, with the cost spreading more widely around the world.

But parallel to this explosion in therapies and increase in costs, a number of confounding factors will make markets smaller. Technology will reveal which patients will not respond to therapy, thus making blockbuster drugs history. Doctors will know the precise stage of the disease process at which treatment is necessary. And as cancer transforms into a chronic disease, there will be more co-morbidities and associated drug-drug interactions.

How do we balance this equation? There is a risk that pharmaceutical companies will stop developing drugs for cancer and focus instead on therapeutic areas where there is less individual variation and more scope for profit. Development costs are also rising. Ten years ago, the average cost of developing a new cancer drug was around $400m. In 2003, it was $800m. At this rate of growth, the cost of developing a new drug in 2025 could rise to $2bn. With this in mind, the process of developing drugs needs to be made faster.

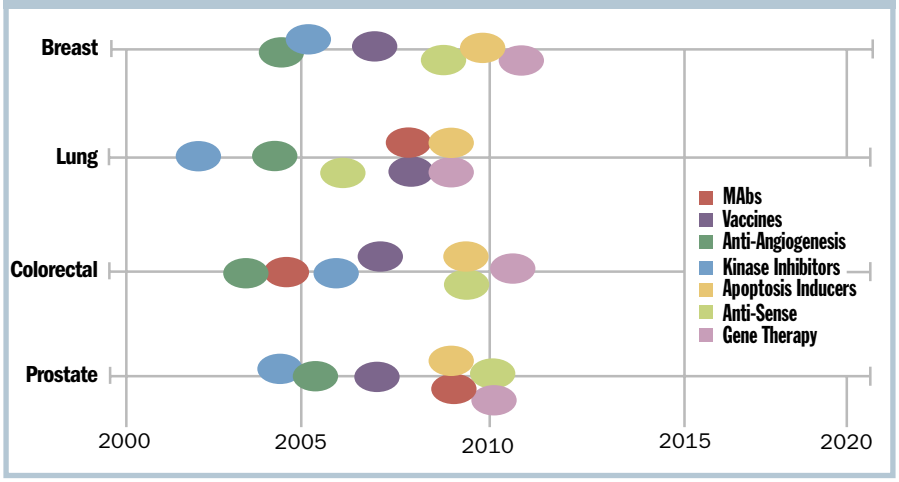
However, instead of research being made simpler, changes in legislation concerned with privacy and prior consent are making it more difficult.

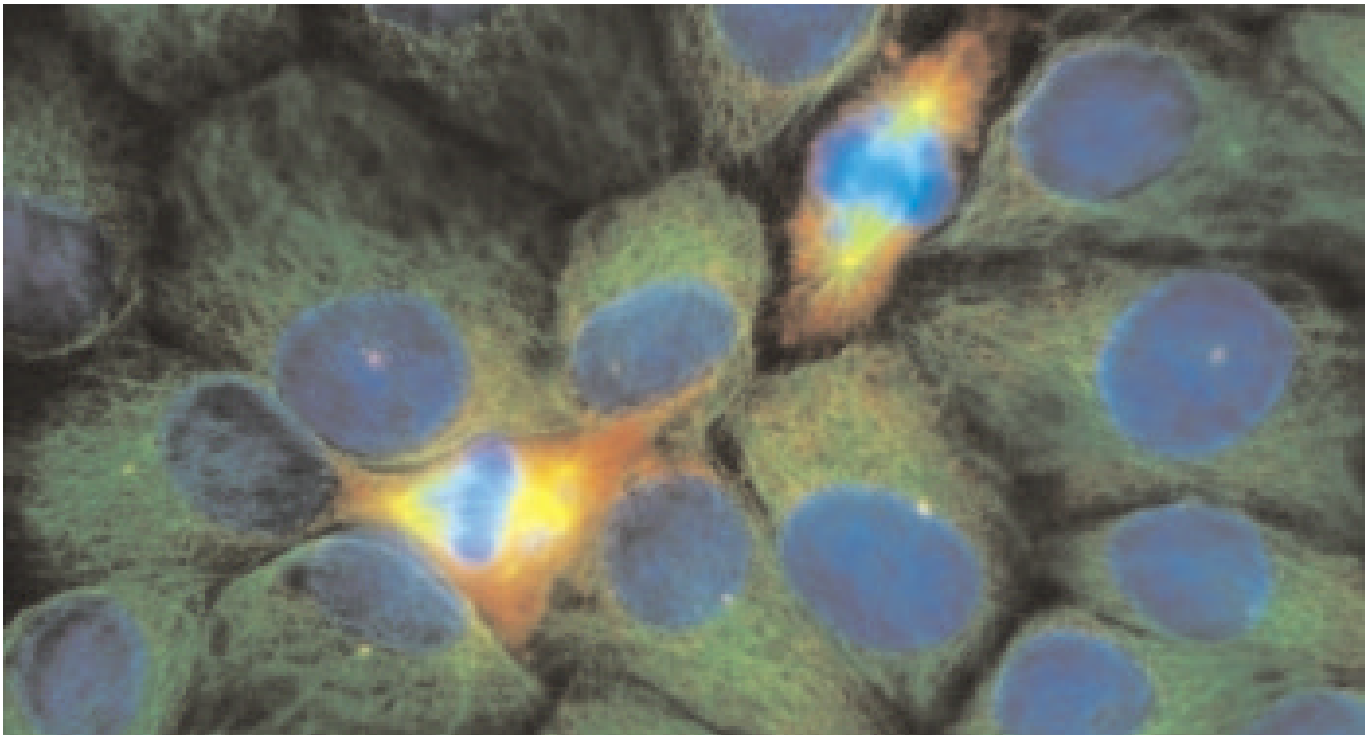
The EU Clinical Trials Directive will make quick hypothesis testing trials impossible. To overcome such constraints regulators will have to start accepting surrogate markers rather than clinical outcomes when approving therapies. Outcome studies may well move to post-registration surveillance of a drug's efficacy similar to cholesterol-lowering agents today. The rise of personalised medicine will mean the temptation to over-treat will disappear. Doctors and patients will know whether a particular treatment is justified. The evidence will be there to support their decisions. As a consequence of this, treatment failure – with all its associated costs – will be less common.

BARRIERS TO INTRODUCING NEW THERAPIES

- The drug industry will continue to compete for investment in a competitive, capitalist environment
- Blockbuster drugs drive profit – niche products are unattractive in today's market
- Personalised therapies are difficult for today's industry machine
- Surrogate endpoints will be essential to register new drugs

PREDICTED NEW DRUG APPROVAL DATES FOR MOLECULAR THERAPIES IN THE USA





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Immunofluorescent Light Micrograph of *squamous carcinoma* cells, cultured from a tumour

At this rate of growth, the cost of developing a new drug in 2025 could rise to $2bn

The patient's experience

Two separate developments will determine the patient's experience of cancer care in 2025 – increased expectations of patients and targeted approaches to diagnosis – both of which will individualise care. Patients will take more responsibility for decisions rather than accepting a paternalistic "doctor knows best" approach. This will partly be fuelled by the Internet and competitive provider systems. With patients having access to a wealth of health information, they will need help in assessing risks and benefits and determining what is best for them. Hence we will have patient brokers who will act as independent advocates guiding patients through treatment options.

Cancer care will be a two-way street. Patients will coach doctors and other patients. With so many people expected to be living with cancer in 2025, they will have a great deal of knowledge and experience that professionals will need to access. There will be continued interest in complementary medicines covering a wide range of talking, touching and pharmacological therapies operating outside the norms of conventional medical science. Improved regulation of practitioners in this area will enhance the quality of care provided and lead to better organisation of services.

Care in the early stages will be provided near the patient's home. Even the most sophisticated diagnostic machinery or robotic surgeon will be mobile. When cancer centres developed in the mid 20th century, the disease was relatively rare and survival low. In 2025, cancer will be common and when in-patient care will be required, patients will be able to be treated at a 'cancer hotel'. For many, that option will not be necessary as most new drugs will be administered orally, enabling the patients to be treated in their communities. The new

EXPERIENCING CANCER IN 2025

- Patient brokers will guide people with cancer through the system
- Choice will be real and will involve cost decisions
- Patients will make a contribution to their care costs
- Complementary therapies will be widely available and well regulated
- Themed death chosen by patients will be possible

approach, however, will place a huge burden on social services and families, necessitating psychological and physical support systems.

In 2003, 70% of the cancer budget was spent on care associated with the last six months of people lives. Although many recognised that such treatment had more to do with the management of fear rather than the management of cancer, medical professionals had relatively few treatment options available and there was limited awareness of which patients would benefit. There was also an institutional reluctance to destroy patients' hopes that led to confusion between the limits of conventional medicines and a reluctance to face the inevitable – by patients, their families and doctors.

By 2025 much of the fear associated with cancer in the past will be mitigated. Pain relief and the control of other symptoms associated with cancer treatment will be much improved. Demand for treatments with few side-effects or lower toxicity will be high, even if there are only quite modest survival gains. While, previously the transition between active and palliative care was often sudden, in 2025, because patients will be in much greater control of their situation, the change in gear will not be as apparent. More patients will choose where they die and the manner of their death. Euthanasia will be legal, but it will not be a majority choice, because distressing symptoms will be better controlled. Indeed a themed death may be a realistic option. In 1900, 90% of people died at home. By 1950 the figure had dropped to around 50%. In 2003, only a quarter of cancer patients died at home. In 2025 the percentage of people dying at home will climb again. This will be driven by patient choice, better communication between health professionals and increased domiciliary services.

Professional reconfiguration

One of the greatest challenges to providing the best cancer care in 2025 will be having the right people in the right jobs. Henceforth it will be essential not to continue to train people for jobs that no longer exist. In 2025 barriers between health care professions will be broken down in order to enable delivery of the new approaches to cancer care. Intra-professional barriers will disappear. The work of pathologists and radiologists will become one as their traditional skills are augmented by the new generation of diagnostic and treatment devices.

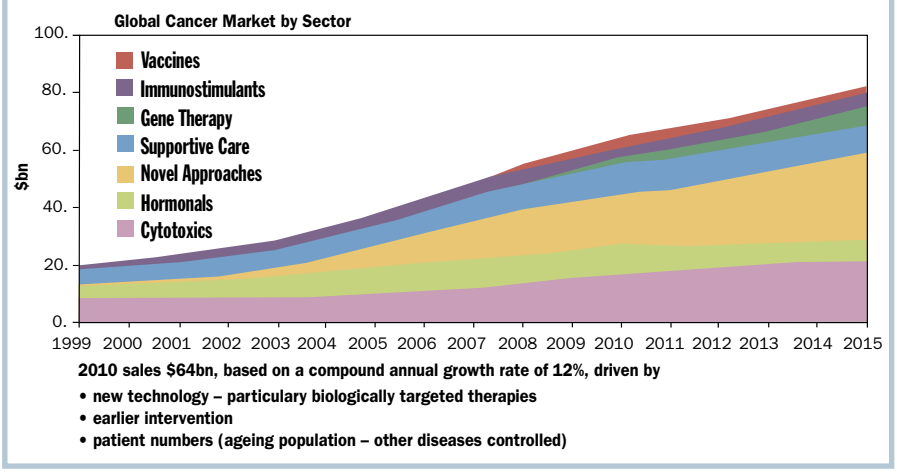
Oncologists will find that many forms of chemotherapy will be delivered with the aid of the new technology, and surgeons will be using robots to enable them to operate. Fewer highly trained specialists will be required, since much of their responsibility will be delegated to specialist technicians and nurses working to protocols, and mobile technology will enable them to work at a number of sites on the same day.

Conclusion

In 2025 cancer will become incidental to day to day life. It will not necessarily be eradicated but it will not cause the same anxiety as previously. Patients in all socio-economic groups will be better informed and have far greater control over their medical destinies. Surgery and chemotherapy will not be rationed on grounds of age since all interventions will be less damaging psychologically as well as physically.

How true this picture will be will depend on whether the technological advances outlined in previous sections

CANCER MARKET SET TO TRIPLE BY 2010



will emerge. The ideal in terms of cancer care will exist for a minority of patients, but the majority may not have access to the full range of services. Old people in 2025, having been relatively poor all their lives, may suffer from cancer and a huge range of co-morbidities that will limit their quality of life. Will there be enough young people to provide the care needed by the old? As with all health issues, the question of access will be determined by cost and political will.

Conservatively, with patients living longer with cancer, rather than dying from it, and with access to new technologies, cancer care costs could increase fivefold (from £20,000 per patient per year in 2003 in the UK to £100,000) and thus absorb a hefty chunk of a country's health care budget. On the plus side, although the technology will be expensive, it will be used more judiciously, as it will be better targeted, and though costs will increase for treating each individual patient, the overall costs will decrease because more care will be delivered at home. At the same time, because people will live longer the life-time costs of cancer care will rise along with co-morbidity costs. Politicians will be faced with a real dilemma: if the prevalence of cancer increases, the cost of delivering care could be massive. Will cancer care need to be rationed in a draconian way?

One dilemma in 2025 will be the political power of old people. Old people will live longer and will wield considerable influence. This educated gerontocracy will have high expectations and will demand high standards of care. Will a tax-based health system be able to fund their expectations? Politicians will have to consider the alignment between patients' requirements and the wishes of taxpayers and voters, for as the population ages the percentage of tax-paying voters will fall. Will the younger taxpayers of 2025 tolerate the expensive wishes of non-taxpayers? The interests of voters may be very different to the interests of taxpayers. It seems likely, therefore, that the days of an exclusively tax-funded health service are numbered. Co-payments and deductibles will be an inevitable part of the new financial vocabulary.

Whatever system is put in place there is the prospect of a major socio-economic division in 2025. A small percentage of the elderly population will have made suitable provision for their retirement, both in terms of health and welfare, but the vast majority will not be properly prepared. Policy-makers need to start planning now. The most productive way forward is to start involving cancer patient and health advocacy groups in the debate, to ensure that difficult decisions are reached by consensus. Societal changes will also leave a greater percentage of old people alone with no psychological crutch to lean on at the onset of serious illness, and there will be a global shortage of carers – the unskilled, low-paid but essential component of any health delivery system. The richer parts of the world are now harnessing this from the poorer, but eventually the supply of this precious human capital will evaporate.

New financial structures will emerge with novel consortia from the pharmaceutical, financial and healthcare sectors, enabling people to buy into the level of care they wish to pay for. Hospitals will become attractive health hotels run by competing private sector providers and global franchises will provide speciality therapies through these structures.

Governments will have long ceased to deliver care. In Britain the NHS, one of the last centralised systems to disappear, will convert to UK Health – a regulator and safety net insurer – already by 2012.

What will be important in 2025 is whether a cancer has particular biological or genetic characteristics

The ability of technology to improve cancer care is assured. But this will come at a price – the direct costs of providing it and the costs of looking after the increasingly elderly population that will result.

We will eventually simply run out of things to die from.

New ethical and moral dilemmas will arise as we seek the holy grail of compressed morbidity. Living long and dying fast will become the mantra of 21st century medicine. Our cancer future will emerge from the interaction of four factors: the success of new technology, society's willingness to pay, future healthcare delivery systems and the financial mechanisms that underpin them.

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