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Battling cancer and the recession

The US Stimulus Bill gives the National Institutes of Health $10 billion, providing some optimism that funding for American cancer research will be stable in the near future. Signed by President Obama on February 17, 2009, the stimulus package has been created by the incoming administration to try to reverse the trend of global recession.

Sujuan Ba (National Foundation for Cancer Research, Bethesda, MD, USA) welcomes the new investment. 'Without this stimulus, cancer research would be facing a very bleak scenario,' he says. 'After years of cuts in federal investments in cancer research, this may mark a renewed sense of urgency as it relates to cancer and its impact on the health of US citizens.'

Nick Bosanquet (Imperial College, London, UK), says that cancer research and service development has had a special priority in the USA for the last 30 years and predicts that this is likely to continue. However, he views the stimulus package as a short-term boost: 'It is going to be difficult to find funds to pay the revenue consequences; cancer research is about to get a happy hour but serious affordability problems may arise long-term as the 'once for all' public spending boom ends in a debt driven decline.' Lee Blansett of MattsonJack DaVinci (Foster City, CA, USA), a specialist cancer consultancy, takes a different view, pointing out that the USA has recovered well from significant deficit spending in the past. 'My sense is that the new knowledge of genetics and subsequent biomarkers and the advent of personalised medicine will create initiatives that will still attract funding, particularly where they address severe, chronic, or lethal diseases such as cancer,' says Blansett.

'CAPITAL PROJECTS SUCH AS RADIOTHERAPY MODERNISATION WILL BE FIRST HIT, FOLLOWED BY FURTHER RESTRICTIONS ON DRUG BUDGETS'

Europe is also feeling the bite of the recession, but without the warm glow of a stimulus package. 'In Europe there are likely to be informal steps towards rationing access to new treatments as governments seek to contain spending; we are already seeing this in the UK through the restrictions placed on the uptake of expensive drugs by NICE,' comments Bosanquet. The UK and other European systems are likely to be faced over the next 5–7 years with 1% a year of real growth in spending but a 20% increase in demand as a result of population ageing and lifestyle changes, including the effects of rising unemployment, he adds. Alan Maynard (University of York, UK) agrees, pointing out that the Institute of Fiscal Studies in the UK has estimated that NHS funding may give zero real growth for the 3 years after 2010. 'In Europe some will fare better but some will fare worse, notably Ireland and the Baltic republics,' says Maynard.

The pharmaceutical industry in Europe is also under pressure. Cancer research Technology's Phil L'Huillier (London, UK) said that the larger pharmaceutical companies are still cushioned for the time being against a shortage of credit as demand for the drugs they supply remains high. However, as many blockbuster drugs are due to come off patent within the next few years, the larger companies are looking even more keenly for future opportunities and are likely to buy up promising patent rights for products currently in development by the smaller biotechnology companies. 'These highly innovative organisations, which generally rely on credit to finance their investment in drug discovery work for the future, stand to be very hard hit by the recession and it looks as if a proportion will not survive the next few years,' he says.

'EUROPEAN SYSTEMS WILL FACE 1% A YEAR OF REAL GROWTH IN SPENDING, BUT A 20% INCREASE IN DEMAND'

In the UK, although cost decisions made by NICE in response to capped spending budgets may be unpopular, cancer patients will continue to access high-quality treatment and care without health insurance or means testing. But there will be casualties. 'It may take a few more months before we see a real effect, but capital projects such as radiotherapy modernisation and the development of intensity-modulated radiation therapy will be the first hit, closely followed by further restrictions on drug budgets. As we are already the poor man of Europe here, the global recession will have a

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Cancer and the recession

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major impact despite the political wrangling of NICE and their inappropriately labelled 'end-of-life drug strategy',' stresses Karol Sikora, medical director of CancerPartners UK (London, UK).

The economic downturn is also likely to have a major effect on the provision of cancer support and the funding for cancer research that depends on the major UK cancer charities. 'As we see the capacity of government to fund research being reduced, we will also see a stemming of the flow of funds to charities,' says Maynard. He believes that higher unemployment will reduce personal giving and firms will also slash their donations as sales and profits fall. 'The Lottery Fund will also be unable to fill in gaps because it will be exhausted by Olympic overruns; cut backs will be inevitable,' he says. 'The legacies that make up over 60% of the revenue of the major cancer charities will be certainly much lower in value,' agrees Sikora. Harpal Kumar, chief executive of Cancer Research UK (London, UK), agrees that the outlook for the economic climate is very challenging. 'At present, we are projecting that Cancer Research UK's net income from fundraising in 2009 is likely to be between 4 and 5% less than last year,' he says.

'SMALLER BIOTECHNOLOGY COMPANIES WHICH RELY ON CREDIT TO FINANCE DRUG DISCOVERY WILL BE HARD HIT'

Despite this, Kumar is defiant: 'We are still well placed to deliver our strategy and we are constantly vigilant of any risks going forward; we will not allow the economic recession to deter us from achieving our long-term vision of beating cancer,' he concludes.

Kathryn Senior

The full version of this article appeared in Lancet Oncol 2009;10:212–3

Ovarian screening 'is feasible'

Screening for ovarian cancer 'is feasible on a large scale', say UK researchers. The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)'s prevalence screen suggested that either a CA125-based, or an ultrasound-based strategy, could be used (*Lancet Oncol 2009. doi:10.1016/S1470-2045(09)70026-9*).

Between 2001 and 2005, 202,638 post-menopausal women aged 50 to 74 were randomly assigned to either annual CA125 screening with transvaginal ultrasound scan as a second-line test (multimodal screening MMS); annual screening with transvaginal ultrasound (USS); or to control. Women with abnormal screens had repeat tests; those with persistent abnormality underwent clinical evaluation and, where appropriate, surgery.

Ovarian or tubal malignancies were detected in 87 women overall: 42 (of the 50,078 women) in the MMS group and 45 (of the 48,230 women) in the USS group had cancer. Almost half of those detected were in stage I/II, and there was no significant difference between the groups in the number of stage III borderline cancers found.

Specificity was higher in the MMS than in the USS group, resulting in fewer repeat tests and almost 9 times fewer operations per cancer detected. More borderline epithelial ovarian neoplasms were found in the USS than in the MMS group.

The report did not include data on cancers in the control group, because the overseeing committee felt that the release of this information when screening was ongoing would compromise the overall outcome of the trial. The data will be available soon after screening is completed in 2011.

The results of ongoing screening will be needed before a conclusion can be drawn on the effect of screening and mortality, the researchers say. Analysis of the psychosocial effect and cost-effectiveness of the two strategies is also underway.

However, the group concludes that both have encouraging performance characteristics: 'Both screening strategies are feasible,' they write.

Fertility drugs 'do not increase risk of ovarian cancer'

A large Danish population based study has provided reassuring evidence that there is no strong association between the use of fertility drugs and ovarian cancer. A small increase in risk cannot yet be excluded (*BMJ 2009;338:b249*).

Concerns were first raised by two small epidemiological studies which found increased risks associated with fertility drugs. Subsequent studies were largely reassuring but many had limitations such as small size, incomplete follow-up or lack of control for potential confounders.

The Danish study included 54,362 women referred to all Danish fertility clinics between 1963 and 1998. It found no increased risk of ovarian cancer after use of gonadotrophins, clomifene, human chorionic gonadotrophin or gonadotrophin releasing hormone. No associations were found between all 4 groups of fertility drugs and number of cycles, length of follow-up, or parity.

The results 'provide reassuring evidence for the absence of a strong association between use of fertility drugs and risk of ovarian cancer' but the authors add that they will continue to monitor the risk since many of the women have not yet reached the usual peak age for ovarian cancer.

An accompanying editorial (doi:10.1136/bmj.a3075) said, 'This study is important because it included 156 women with ovarian cancer, more than 3 times as many as any previous cohort study, and it compared infertile women who had used fertility drugs with infertile women who had not used fertility drugs.'

The researchers conclude that any small risk 'should be balanced against the physical and psychological benefits of a pregnancy made possible only by the use of these drugs.'

Eurocourse: a welcome boost for cancer registries

Eurocourse, a 3-year ERA-Net project funded under the EU's Framework-7 programme, is aiming to spread best practice among cancer registries across Europe, and to prepare them for future challenges in oncology and public health. Key aims of 'Eurocourse' are to improve collaboration between cancer registries, and to expand the role of the network of registries towards quality control of screening programmes, involvement in clinical epidemiological research and research with biobanks in trans-national projects.

Professor Henrik Møller (King's College, London, UK), who was instrumental in putting together the appli cation, said that several working groups will analyse trends, pull out examples of good practice, refine them in discussions with the committee and use them to inform practice elsewhere. He said that the project will bring new opportunities to every kind of cancer organisation. 'There may be new cancer registry services in places where there have been insufficient resources to develop one. But even well-established registries will have the opportunity to develop within Eurocourse. There will be something in this project for all cancer registries, even those which already perform well,' he said.

The UK has well-established collaboration between cancer registries and quality assurance for screening programmes; this is the sort of example of good practice which could be spread to other parts of Europe, Professor Møller said.

'COUNTRY BY COUNTRY COMPARISONS FORM THE BASIS FOR NATIONAL CANCER PLANS. THE DATA MUST BE GOOD'

Professor Jan-Willem Coebergh (Erasmus Medical Center, Rotterdam, the Netherlands), who took over as Eurocourse coordinator late in 2008, described the project as the 'cement' in the building of cancer control and cancer research in Europe. 'Collaboration between different registries is essential for generating comparative data. It's not only the frequency of cancers, and survival, but country by country comparisons are very useful for cancer control strategies and form the basis for national cancer plans. In these circumstances, the data must be good, analyses have to be accurate, biases need to be addressed, and so on. The weaker registries should have incentives to improve.'

He stressed the importance of registries in conducting population-based research: registries include unselected patients and have an important and increasing role to play in the evaluation of expensive new treatments, of quality of life, and of the effectiveness of chemotherapy for example in the increasing number of elderly cancer patients.

'The proportion of patients over 70 years is increasing so rapidly in many countries that there is a need to distinguish many more subgroups: those with a particular cancer and also diabetes or cardiovascular disease, or both. Clinical research usually involves selected populations whereas registries are sampling forums and enable you to study the whole spectrum of disease.'

Registries are inexpensive compared to the general spend on cancer, Professor Coebergh said. 'A cancer registry costs roughly half a Euro per inhabitant, per year. Even if you divide the cost between those who have, and who have ever had cancer, it still only comes to about 15 Euros per patient per year. It is a very small amount of money compared to the amount spent on cancer care.'

Part of Eurocourse's aims will be to stimulate registries to become more productive, in particular, by improving their partnerships with clinical staff and academic epidemiology. 'This is already best practice, but clinicians need to know the registries are there to support them. Proper use of the registries will improve clinical studies, but those in registries and clinics need to collaborate closely if we are to derive maximum benefit from the data.'

A perennial problem faced by some registries is the legislation governing privacy and data protection which can create barriers to the collection and linkage of data from various sources. Dr. Hans Storm (Danish Cancer Registry, Copenhagen, Denmark) was involved in drawing up the Eurocourse proposal and will be heading up the Working Party examining privacy. He said the situation varies widely across Europe.

'The interpretation of the European Directive on Privacy (95/46) is very heterogeneous. In some countries they have almost completely closed down data linkage by insisting on informed consent, which is not always possible. In Estonia, cancer registries have no access to death certificates for cancer patients, which is a very important measure of quality in cancer registration. It makes comparison between some countries virtually impossible.'

'A CANCER REGISTRY COSTS ROUGHLY HALF A EURO PER INHABITANT, PER YEAR'

'It comes down to the difference in legal framework. There is popular support for cancer registries; in Denmark, almost 95% are in favour of health data being made accessible to public health for cancer control. But it depends how you ask the question. If it's explained thoroughly that research is population-based and it is not possible to identify individuals, almost everyone agrees to having their data included.'

'Of course in principle, it is possible that confidential information could be disclosed if researchers are not careful. But in the 30 years I have been involved with cancer registries – most of these before the European directive came into force – this research has never given rise to a breach of confidentiality.'

'Population-based research is not widely understood. If the research community had been better at communicating both the basis of the research – we do not need to present what happens to each individual but rather, we are looking at the group effect – and the importance of its outcomes in influencing cancer priorities, we may never have run into problems with privacy laws. People may want to protect data on themselves, but they also want their children to have the best possible care and they need to understand that this research will help the coming generations.'

The Working Party on privacy will conduct a survey of the state of cancer

Continued over

Recognition for research in public health

The Charles Rodolphe Brupbacher Prize for Cancer Research, 2009, has been awarded to scientists whose work has strong implications for public health. Dr. Nubia Muñoz, of Columbia was chosen for her work on the importance of infections in cervical cancer; and Sir Richard Peto (University of Oxford, UK) for the role of tobacco smoking in premature death.

Dr. Muñoz, a chief scientist at the International Agency for Research on Cancer (IARC), led a major international programme of research there, which showed that infection with certain HPV types is once of the strongest cancer risk factors ever found. Subsequent work defined the HPV genotypes that had to be targeted for prevention. Types 16 and 18 were classified as carcinogenic to humans in 1995, which led to pharmaceutical companies making huge efforts to develop HPV vaccines.

Dr. Nubia Muñoz and Professor Sir Richard Peto at the awards ceremony. Photo courtesy of the Charles Rodolphe Brupbacher Foundation

Sir Richard received his award for his work establishing the absolute benefits of anti cancer drugs and of tobacco control.

The awards are given by the Charles Rodolphe Brupbacher Foundation whose aim is to foster cancer research in Switzerland and internationally. It is bestowed on scientists for their contributions to basic oncological research.

Eurocourse... (*Continued from page 1097*)

registration and epidemiology across Europe, and this will act as a benchmark. A committee including a legal advisor will be set up to help researchers navigate barriers caused by data protection legislation, and improve the systems in place for dealing with requests for research on the data.

'We need to know what is achievable in prevention,' Dr. Storm said. 'We need accurate data to assess this. We cannot solve the whole problem in the 2 or 3 years of Eurocourse but we can start to build the foundations for a better way in future to help researchers monitor progress in public health.'

Medical lawyer, Evert-Ben van Veen (Medlaw Consult, The Hague, Netherlands) is to be involved in the legal aspects of data collection and data sharing. He stressed that harmonisation of the different legal systems in Europe was not an aim. 'Harmonisation may make the situation similar in different countries but it often means that the system becomes stricter in countries where there has been more freedom, without it becoming any less strict elsewhere. Harmonisation tends to level up the barriers to research and can create problems.'

'We're aiming to exchange best practice and will want to demonstrate that best practice does not consist of erecting huge barriers to the collection of data from various sources.'

'IF WE HAD BEEN BETTER AT COMMUNICATING, WE MAY NEVER HAVE RUN INTO PROBLEMS WITH PRIVACY LAWS'

Privacy has been stressed in recent years, and the debate has not generally been helpful, he said. 'There has been a huge discussion on privacy in Europe, following the war on terror. But the cancer registries are a rather innocent activity; no harm has ever come from this data collection, only good. There is a new awareness of privacy but we hope that constructive discussion will allow the registries not only to collect data, but to combine data from various sources, because this is what makes them so valuable.'

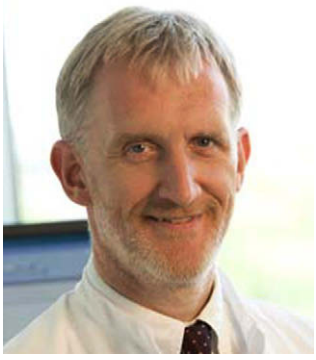
The project will also cover the working and training conditions of the epidemiologists, biostatisticians and other allied health scientists who analyse and interpret the data. Professor Coebergh: 'These people need a wide knowledge of cancer classification, coding and staging, treatments and so on. They need to collaborate actively with clinicians and feed the data back into the clinic. But often, they have no career structure and have to move from project to project. It is not the way to derive maximum benefit from the data.'

Eurocourse will emphasise the wide dissemination of results and the project will end with a summit meeting. Professor Møller: 'Training and education are the payback from Eurocourse and why it can actually make a difference. The appointment of a working party of 10 or 12 incredibly smart individuals who know everything about biobanks, for example, won't change a lot if they produce a report: some will read it, some will file it. It will only be actively useful if it the people on the ground learn how to make cancer registries more useful to biobanks. We will be taking practical steps to achieve this.'

Helen Saul

PODIUM

Introducing EJC'S new translational editor!



Professor Christof von Kalle is director of the National Center for Tumor Diseases (NCT), and head of translational oncology at the German Cancer Research Center (DKFZ), Heidelberg, Germany.

His research focuses on gene therapy for human immunodeficiencies, retrovirus-mediated therapy of haematopoietic stem cells, and clinical haematopoietic stem cell transplantation. Professor von Kalle has recently joined EJC's editorial board, in the newly-formed position of Translational Oncology Editor.

How much progress has been made in translational oncology?

Translational oncology is a very exciting area; we are in transition period in the way that cancer therapies are developed and used. Much knowledge to date has been empirical in nature, but in recent years, more targeted therapies are becoming available. The arrival of high throughput sequencing of the human genome will further dramatically change the way cancer is diagnosed and treated. We are beginning to understand cancer as group of molecular lesions in a particular cell that cause it to become cancerous. Our hope is, that as this process progresses, we are going to be able to diagnose and treat several lesions in parallel.

What impact will these discoveries have on resistance to treatment?

A common example of resistance to cancer treatment is the failure of cells to apoptose when treated with chemo- or radiation therapy. An individual's genetic background may determine how quickly resistance develops. Apoptosis resistance is a formidable example of what translational oncology could and should do in future: to take a new understanding at the cellular level and use it to modify treatments according to the genetic background of an individual patient.

What is the focus of your own research?

We are looking at the function and molecular therapy of haematopoietic and other stem cells. This work has extended to include tumour-initiating cells as much as they can be understood as similar to stem cells in solid tumours. Our work on normal blood-forming cells also includes first generation progenitor cells which remain in the body and make progeny for a long time.

Our interests is also in integrating vector systems – modified viruses which carry genetic information into the cell genome – with molecular markers so that we can identify the clonal structure of various stem cell components.

We can establish a transgene in the genome of a cell, which leaves a different molecular marker in every cell. It allows us to distinguish one cell and its progeny from the next. We can modify healthy cells to protect them from the damaging effects of treatment, or, in experimental work, label cells so that we can tell them apart.

This can help us work out whether the tumour developed from a single cell repeatedly dividing or whether all the cells were dividing. The working hypothesis on tumour initiation is that not all cells in the tumour are the same, and that only a minute fraction are capable of moving elsewhere in the body and growing into a tumour.

You are director of a department both at NCT and DKFZ?

Yes and, here in Heidelberg, we are setting up one of the first comprehensive cancer centres in Germany. This is not a well-established concept in our country, because of the way clinical services have been structured and funded.

Heidelberg is in a unique position because we have had the cancer research centre, DKFZ, here for 40 years, with its basic cancer research excellence! Harald zur Hausen carried out his pioneering work on HPV here, and won the Nobel Prize for it in 2008. This is a beautiful role model on how translational can work, under ideal circumstances, but it is also a reminder of how long it takes to get a discovery into practice: 20 years in the case of the HPV vaccine.

Moving research and clinical treatment closer together has happened gradually here, with layers of separation slowly removed. We see about 8000 new patients a year, and will be moving to a new building early next year. It will be half lab, half clinic, and it's in that spirit that we want to go forward. German Cancer Aid has put in a lot of effort to make this possible; people will be watching our progress carefully and that is the way it should be.

What do you hope to achieve at EJC?

I will be as interested in papers on diagnosis and biomarkers as in those trying to develop therapies. Many people think of translational oncology as going in one direction – from bench to bedside – but the opposite direction is just as important for defining effective therapy. I am looking forward to joining the editorial team and building up the content in this very exciting field.

Helen Saul