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UK public 'needs confidence' in science

Dialogue between the public, the science community and policy makers needs to be enhanced, says the UK Government. Society should have confidence and increased awareness in scientific research and its innovative applications.

This aim is stated in a 10 year framework (2004–2014) for investment in science and innovation. 'The public needs to have confidence in the ethical and regulatory framework within which scientific advances are made,' the report states. It also stresses a determination to protect legitimate research activities from animal rights extremists (*see Eurofile, overleaf*).

The main thrust of the report is to examine the contribution of science and innovation to economic growth and public services, its attributes and the funding arrangements. The Government's long term objective is to increase the total spent on research and development from 1.9% to 2.5% of GDP by 2015.

The report acknowledges the need to increase participation in science within higher education and asks the Higher Education Funding Council for England (HEFCE) to support universities, industry and scientific societies in outreach activities to schools and colleges. HEFCE will also examine the implications of falling science provision for student access and may provide additional funding to university departments if falling provision in a particular region would hinder student access to disciplines considered important.

Universities are urged to adopt a responsive approach to remuneration in order to recruit and retain high quality staff. The PhD stipend is to be increased in line with inflation between 2005 and 2008, and the funding for 'golden hellos' for new teaching staff maintained beyond 2005/6.

HEFCE welcomed the 10 year framework, saying it, along with the extra funding announced, will help put higher education on to a more sustainable footing. Rama Thirunamachandran, HEFCE's Director of Research and Knowledge Transfer, said the strategy is 'a significant step forward', and that, 'We particularly welcome the government's continuing support for the dual support system of public funding for research – by the higher education funding councils and the research councils – as well as the central role which the Government expects HEFCE to play in the delivery of the strategy'.

(*See www.hm_treasury.gov.uk/spending_review/spend_sr04/associated documents/spending_sr04_science.cfm*)

Clinical trials 'must be registered'

Registration of clinical trials before patients are enrolled will reduce selective reporting, say journal editors. Selective reporting distorts the body of evidence available for clinical decision-making (*Lancet* 2004, **364**, 911–912).

The International Committee of Medical Journal Editors (ICMJE) has issued a statement insisting that, for studies to be considered for publication, they must have been entered in a public trials registry before patients were enrolled. It applies to any clinical trial stating enrolment after July 1, 2005. Trials that began enrolment before this date will have to be registered before September 13th, 2005.

Acceptable registries need to meet certain criteria, such as being accessible to the public at no charge. They must be open to all prospective registrants and managed by a not-for-profit organisation.

The ICMJE says that researchers and editors are generally more interested in publishing positive than negative trials. They are unenthusiastic about inconclusive trials. This is particularly important, where the interventions being researched could enter mainstream clinical practice since unpublished data cannot influence the thinking of experts writing guidelines.

'If all trials are registered in a public repository at their inception, every trial's existence is part of the public record and the many stakeholders in clinical research can explore the full range of clinical evidence,' they write.

The policy currently applies only to members of ICMJE, which are general medical journals, such as *The Lancet*, and *JAMA*. ICMJE acknowledges that there will be objections, such as from research sponsors unwilling to allow competitors full access to their research plans. It argues that enhanced public confidence in research will compensate.

'Patients who volunteer to participate in clinical trials deserve to know that their contribution to improving human health will be available to inform health-care decisions. The knowledge made possible by their collective altruism must be accessible to everyone. Required trial registration will advance this goal,' the statement concludes.

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Lung cancer among non-smokers

Around one-third of women with proven primary lung cancer have never smoked, say French researchers (*Lung Cancer* 2004, **45**, 279–228).

They studied 904 women (mean age 64 years) with histologically or cytologically proven primary lung cancer. All were diagnosed in the year 2000 in pneumology departments across France.

Overall, 32.3% of the women had never smoked. Of those with adenocarcinomas, which were the most frequently diagnosed of the non-small cell lung cancers (NSCLCs), 43.4% of the women were never-smokers. Multivariate analysis found that adenocarcinoma was related to less smoking and younger age.

The findings are in accord with a meta-analysis which found that adenocarcinomas appear to be more frequently observed in never-smoking women (49–74% of cases of lung cancer) than in women who were smokers (33–43%).

The French researchers showed previously that only 2.5% of men with lung cancer were never-smokers and say their current work suggests that women may be more susceptible than men to lung cancer. They point out that while the epidemic of lung cancer is beginning to slow down among men, it is only just beginning in women.

Circulating steroid hormones, in particular the oestrogens, may play a role in the aetiology of lung cancer. Further, some genetic biomarkers (the mutation of detoxification enzymes cytochrome P450 1A1 and glutathione-S transferase M1) are more frequent in women and may be an age- and smoking-independent risk factor for lung cancer. Passive smoking, environmental and occupational risk factors and family history may also play a role.

It has been suggested that fewer cumulative genetic lesions are required for the development of an adenocarcinoma, compared with other lung cancers. The authors say it is also possible that adenocarcinomas were previously under-diagnosed. However, they conclude, 'Even if tobacco is an important cancer risk factor, women could be susceptible to other factors which need to be investigated in further studies.'

Ageism in breast and prostate cancer

Age may be more important than performance status in determining GPs' management of cancer patients, say Belgian researchers (*Clinical Oncology* 2004, **16**, 474–478). 'This is a very common prejudice,' they say.

Each of 546 GPs answered a questionnaire, which included a breast cancer and a prostate cancer history. The histories of cancer were identical but the simulated cases had different patient-related factors such as age, performance status and comorbidity.

Elderly patients were 13 times more likely to be referred for non-curative as curative treatment for prostate cancer; and 17 times more likely in breast cancer. Neither functional status nor medical history affected treatment orientation.

However, the GPs were prepared to seek assistance from oncologists in both cases, irrespective of the patient's age. 'Whether a given patient should receive appropriate care was left to the specialist's discretion,' they said.

New insights into melanoma

Chronic sun exposure may be the most important risk factor for cutaneous melanoma among dark-skinned Caucasians, say Greek researchers in this issue of *EJC* *(see page* 2502). This contrasts with the major risk factors among fair skinned populations: melanocyctic naevi and intermittent sun exposure.

Researchers compared Cretan patients with age- and gender-matched controls. They found that indices of chronic sun exposure (such as solar keratoses and total sun exposure) were the most important risk factors in this relatively dark-skinned Cretan population.

Crete has one of the lowest estimated annual incidence rates for cutaneous melanoma in Europe, but the researchers point out interest in the situation in Mediterranean countries is growing. 'Differences in phenotypic traits might in the near future reveal genotypic particularities. In this way, our current knowledge... may be supplemented and this data could aid in both prevention and treatment strategies,' they say.

Another paper (*EJC, this issue, page* 2355) considers the rise of the disease in fair skinned societies. Mortality rates are levelling o in many populations with high incidence rates (Australia, USA, North-Western Europe), and a levelling off of the incidence is being observed in some countries, it states.

Changing attitudes towards sun exposure and having a tanned skin could decrease the incidence of melanoma, the paper concludes, but warns that without measures to prevent the ozone layer from further breakdown, and without more prudent sunbathing behaviour and clothing styles, 'skin cancer incidence rates will keep increasing rapidly.'

Public health educators should continue to disseminate information on the dangers of UV radiations, and to discourage use of sunbeds, according to a third paper (*EJC, this issue, page* 2367). 'Sunbed manufacturers and operators should no longer be able to claim health benefits of any sort attributable to sunbed use, and to other forms of intentional sun exposure,' it states.

Parotid-sparing radiotherapy

Parotid-sparing radiotherapy should be considered for selected patients with head and neck cancers, according to a group in Belgium (*Radiotherapy and Oncology* 2004, **72**, 119–127).

Patients with lateralised head and neck tumours (excluding nasopharyngeal tumours and those with bilateral or contralateral neck disease) received 3-dimensional conformal intensity modulated radiotherapy (IMRT).

The group of 72 patients were followed for 19 months, and 20 developed a locoregional failure. However, there were no relapses in the spared area. Overall, the 2-year survival rate was 67%.

The technique 'proved to be safe in our hands', they concluded. It is easy to perform and significantly reduces the dose to the contralateral parotid. 'It should be considered for all selected patients,' they concluded.

EUROFILE

UK clampdown on animal rights extremists

The increasingly violent and intimidatory tactics used by animal rights extremists in the UK have forced the British government to take action to protect companies and individuals from harassment. On July 30, 2004, the UK Prime Minister and Home Secretary jointly signed the foreword to a document ''Animal welfare – Human Rights: protecting people from animal rights extremists''. The document sets out measures to outlaw certain types of protest, including demonstrations outside the homes of scientists who experiment on animals and the harassment of anyone associated with their laboratories.

The document is a response to the news that direct action against the main contractor for a new animal laboratory at Oxford University has halted its construction. Earlier in the year, another campaign stopped work on a neuroscience laboratory at Cambridge University.

Scientists have been warning for years that such activities could halt medical research in some fields, but now they have been joined by major players from the pharmaceutical industry. Jean-Pierre Garnier, chief executive of GlaxoSmithKline, was recently reported as calling extremists ''despicable cowards'' and said that his employees were being ''terrorised'' by them.

Furthermore, news that US activist Jerry Vlasak had been invited to an extremists 'training camp' in the UK in September, 2004, made it fairly certain that the government would have to take some action. Vlasak is an advisor to one of the most militant animal rights groups, Stop Huntington Animal Cruelty, and has been quoted as advocating the assassination of biomedical scientists to save animal lives.

The proposed measures will make it an offence to protest outside homes in such a way which causes harassment, alarm or distress to the residents. This will be an arrestable offence, even after the event. At present, once protestors have left the scene, they can not be arrested.

It will also become an offence under the Protection from Harassment Act to harass as few as two people who are connected (e.g., who work in the same laboratory), even if each individual is only harassed on one occasion. Previously workers who had not been harassed themselves had no protection under the law, even if colleagues had been.

Another new offence will forbid those who have been 'moved on' from returning to a house within three months ''for the purpose of representing to or persuading the resident, or anyone else, that he should not do something he is entitled to do, or that he should do something he is not obliged to''.

These three offences will come about through amendments to existing legislation, rather than through the introduction of a stand-alone law to deal with animal rights extremism, as many scientists had wanted. The government has not ruled this out entirely, but says ''it would not be sensible to try to seek a separate bill which, because of pressures of parliamentary time, could not be taken this year''.

Already civil liberties groups are lining up against the proposals, warning that they will criminalise legal protests, and

''CIVIL LIBERTIES GROUPS OBJECT TO THE PROPOSALS''

saying that the amendments could be difficult to make.

The government document takes pains to spell out the medical benefits of animal research to both animals and humans. ''Some of the serious and very unpleasant side effects of cancer treatment have been prevented by the development of new drugs which required the use of animal testing. Without the use of animals, the treatments now being used would not be available and progress towards our understanding of cancer and the development of new treatments and possibly cures would be severely affected''.

Scientists say that the government is giving a clear signal of support for moving the issue up the police agenda. ''This is the strongest statement to date, the most

''THIS IS THE STRONGEST GOVERNMENT STATEMENT TO DATE''

comprehensive statement they have made'', said Mark Matfield of the Research Defence Society. ''They've never put their vision on the line as clearly and firmly as this''.

Universities remain concerned that the government document contains references to how the measures would affect business and industry, and does not specifically mention universities. Only two days prior to publication of the document, the three pharmaceutical companies with the largest research operations in the UK had put up a 4m research fund to pay for animal experiments in academic institutions. ''Being able to do this kind of research is key to our ability to deliver the best care to patients'', said Gill Samuels, executive director of science for Pfizer.

Professor Sir Walter Bodmer, former director general of the UK's largest cancer charity, and Principal of Hertford College, Oxford, welcomed the new moves. ''These long-needed measures will protect those who do medical and veterinary research with animals, and all those involved indirectly in such work, from the appalling activities of a small group of ''animal terrorists''. All the major advances in our understanding and ability to deal with cancer as a disease depend at some point on experiments with animals. Increasingly, modern genetic technology can provide better and better models for human disease and there is now greaterpromise than ever before for new approaches to dealing with major diseases''.

Mary Rice

Brussels

US Food and Drug Administration to set up new oncology office

The US Food and Drug Administration (PDA) has announced plans to establish a new cancer office called the Office of Oncology Drug Products, within the Center for Drug Evaluation and Research (CDER). The new office will be implemented when PDA Oncology relocate to new premises in White Oak, MD, USA, in April, 2005.

''Establishment of a new oncology office shows our continuing commitment to finding new and better ways to get safe and effective treatments to cancer patients'', says Lester Crawford, Acting PDA Commissioner. ''We expect this new office to provide an even stronger and more consistent approach to the regulation of new drugs for the prevention, diagnosis, and treatment of cancer''. The new office will also regulate cancer therapeutics (including monoclonal antibodies and recombinant therapeutic proteins) and imaging products.

''It is the beginning of a very serious cancer programme at the PDA'', says Ellen Siegel (Chief Executive Officer, Friends of Cancer Research, Washington, DC, USA). ''With priority setting for cancer, it should open up opportunities for prevention and for people to invest in this area, which is desperately needed.'' Others feel the timely organisational changes will address concerns about the number of new drugs emerging for cancer, and will help the promising, but complex, research on molecular therapies.

''IT IS THE BEGINNING OF A SERIOUS CANCER PROGRAMME''

The Office of Oncology Drug Products will be a consolidation of three existing divisions within the CDER (Oncology Drug Products, Therapeutic Biology Oncology Products, and Monoclonal Antibodies), which are currently spread over 16 locations in Washington, DC. The new office will have three review divisions, details of which will be announced in the next few months.

A search is taking place to appoint a director for the new office, who will control approval of new molecular agents and new indications for doses and safety. Importantly, the director will also influence review policies for cancer drugs, which ''will make the position more attractive to the sort of highly qualified individual necessary to make the office a success'', points out David Johnson, President, American Society of Clinical Oncology (ASCO).

An office to regulate all products for cancer was first proposed several years ago by advocates for patients with cancer through the US Cancer Leadership Council, who initiated hearings in the US Congress. But after several structural changes within the PDA, advocates, including well-known clinical and translational researchers, heads of cancer centres and cooperative research groups, and industry repre- Maiyland: new pastures for US cancer care. sentatives, still felt that more could be done to consolidate the review process for cancer products. Over the past few months the PDA formalised plans for an oncology office. Crucial stakeholder input secured the decision for the office to have both a review and policy function.

''The FDA really listened and worked with the cancer community in the development of [the new] approach'', explains Margaret Foti, Chair of the American Association for Cancer Research. The PDA consulted with advocate groups, academic organisations (such as ASCO), and the US National Cancer Institute (NCI). ''We were very heartened by that [process]'', says Foti, ''we feel that that is, in a sense, a new beginning''.

Collaboration between the PDA and the wider cancer community is set to continue, with the simultaneous announcement that an Oncology Program will be launched alongside, and coordinated from, the new office. The Oncology Program will coordinate technical consultation on cancer products between other parts of the PDA (e.g., the Center for Biologies Evaluation and Research [CBER], the Center for Devices and Radiological Health, and the Center for Food Safety and Applied Nutrition). Furthermore, the Oncology Program will facilitate wider interaction with professional societies and stakeholders by providing a forum for discussion of regulatory policy and by initiating training and educational activities.

With the establishment in 2003 of the NCI's 2015 Initiative to eliminate suffering and death from cancer by 2015, and in March, 2004, the launch of the PDA's Critical Path to analyse the development of new medical products, the Office of Oncology Drug Products adds to the growing list of practices to improve coordination within the US federal government for research and development of cancer products.

''[Although the new office] is a very good first step, it's only the beginning of a process'', says Siegel. ''It clearly needs to go further'', she adds, echoing the view the oncology community. The decision to leave the regulation of cancer vaccines, cell therapy, and gene therapy within the CBER has been met with disapproval. ''We were disappointed that the PDA chose to leave those products in CBER'', says Johnson. ''While these product categories currently have more potential than practical application, they represent the best hope for certain types of cancer [and] will be used in conjunction with traditional chemotherapy drugs in most cases'', adds Margaret Tempero (2003–04 ASCO President).

There are further concerns about funding for the PDA, to ensure that the new office has adequate logistic support and can attract the most suitable individuals. ''The PDA is a very under-resourced agency. The [cancer] community needs to make sure [the PDA] has the resources needed to integrate the science'', says Siegel, highlighting how important the two-way interaction through the Oncology Program will be. ''There needs to be directed education to decision-makers – the government – about how important resources are going to be to the PDA'', Siegel concludes.

''THERE ARE CONCERNS ABOUT FUNDING FOR THE FDA''

Claire Tilstone

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PODIUM

New impetus to palliative medicine research

Dr. Max Watson (City Hospital and Queens University, Belfast, Northern Ireland) is an Orthobiotech palliative medicine research fellow. He has just completed specialist training in palliative medicine and is currently conducting a randomised controlled trial (RCT) in patients with advanced malignancy and cachexia.

Dr. Max Watson

How much research is carried out within palliative care?

Not enough! In the UK, the National Cancer Research Institute (NCRI) reported in 2002 that only 4.3% of the total oncology research budget is spent on palliative care. Research into patients' needs has been quite strong, but less has been published on how to meet those needs. Only 10% of the workforce involved in palliative care research in the UK are doctor specialists in palliative medicine. The situation is similar in Europe and the USA.

Why is palliative care research given such a low priority?

Partly because it is difficult with existing models of scientific research. Culturally in the West, we live in a death-denying society, where people frequently reach their 4th decade before someone in their family dies. This denial can make research projects within palliative care less appealing to funders than research aimed at ''cure'' – even if that ''cure'' is only at a cellular level. Palliative medicine involves holistic care, and the field extends from qualitative psychosocial research through to quantitative molecular studies. It therefore lacks a natural 'home', with qualitative research often conducted in nursing or social science settings; and molecular work or RCTs in tandem with oncology colleagues.

Is it just a lack of funds?

No. Cancer research develops rapidly where centres house a critical mass of researchers working together. In palliative medicine we do not yet have such centres, in part because the scarcity of palliative medicine doctors means patient's immediate clinical needs take priority over research. Producing a steady volume of quality valuable research is difficult for isolated, or even small groups of, clinicians.

In addition, we need reliable well-recognised tools to assess objectively palliative medicine endpoints. Such endpoints may range from cytokine levels to what patients or their families feel about an intervention and are desperately needed to set the baseline levels in palliative medicine research

Is it possible to develop reliable tools?

Innovative work is being done. But many of the endpoints have been arrived at using qualitative methodologies and can be difficult to translate into the types of research with which other branches of medicine are more familiar.

Presumably survival is not the most important endpoint?

You learn not to generalise. A man may want to live until his daughter's wedding, and survival until that date may be more important than quality of life. Others may be more concerned with comfort. Some endpoints are particular to individual patients, which can make comparisons difficult.

Is there any place for traditional methods of research?

We need both qualitative and quantitative approaches. I have been involved in qualitative assessment of palliative medicine education and am now setting up a double blind RCT in patients with cancer cachexia. RCTs in palliative medicine are not common and we are anticipating complications due to high patient drop out rates, and difficulties in recruitment. However, patients with palliative needs must not be excluded from the benefits which RCTs have brought to others with cancer. A broad research base needs to be strengthened, the tools to demonstrate effectiveness of interventions proven, interdisciplinary research encouraged and research centres funded.

Has the Clinical Trials Directive made any difference?

Research will become almost impossible within the voluntary sector where many of our patients are managed. Busy hospices with pressing financial needs will find the Directive's requirements for research governance and adequate insurance a major deterrent. The new ethical committees are still finding their feet and there may be particular difficulties in having palliative medicine trials approved. The rigour of research ethics must be maintained within palliative medicine but the risks and benefits of palliative interventions are particularly difficult to assess, and require a distinctive – not a ''one size fits all'' – approach from ethical committees.

Given the obstacles, is progress possible?

The NCRI report is a step forward, highlighting the need for research and outlining a way forward within the UK. One recommendation is for multi-centre trials in the UK to provide objective evidence for basic questions such as the management of constipation, pain and nausea. These studies, which should be funded centrally, will require the recruitment of large patient numbers, and will provide an evidence base for best practice. Dedicated palliative medicine researchers need to work in larger groups with statistical and laboratory support. The NCRI report is welcome but it is written from a cancer perspective and palliative care research must also embrace challenges relating to non-malignant conditions.

Will this happen?

It must. Without a solid evidence base to palliative medicine interventions, and without the improvements that only come with well-organised and funded research, patient care at this crucial time of life will fail to address the huge needs of our patients.