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NEWS...NEWS...NEWS

Intolerable workloads: oncologist's stress

Cancer specialists are suffering increased emotional exhaustion due to the enormous pressures they are being placed under at work, reports a study in *The Lancet* (2005, **366**, 742–744).

The study, led by Cath Taylor from Cancer Research UK London Psychosocial Group at the Institute of Psychiatry, King's College, London, assessed changes in the mental health of UK hospital consultants from five specialties between two surveys – one conducted in 1994 (880 consultants) and the other in 2002 (1308 consultants).

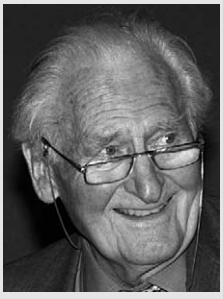
Results show the proportion of consultants suffering from psychiatric morbidity rose from 27% in 1994 to 32% in 2002; and that the prevalence of emotional exhaustion increased from 32% to 41% over the same period. Psychiatric morbidity was estimated with the 12-item General Health Questionnaire (GHQ-12); and emotional exhaustion (the principal component of burnout) with the Maslach Burnout Inventory.

The study shows decline in mental health among hospital consultants is most pronounced for surgical and clinical oncologists. Among surgeons, rates of mental distress rose from 22% to 33% and emotional exhaustion from 27% to 41%; while among clinical oncologists mental distress rose from 28% to 38% and emotional exhaustion from 39% to 52%. Researchers also studied gastroenterologists, radiologists and medical oncologists, among whom significant changes were not found.

Cancer Research UK says between 1994 and 2002 appointments of all types of consultants increased across the board, with, for example, the number of medical oncologists going up by 147%. However, in the same time period the number of surgical oncologists only rose by 45% and the number of clinical oncologists by 33%.

''The increase in numbers of doctors becoming surgical and clinical oncologists is much lower than for other specialties such as gastroenterology, so those currently in post are over-burdened by their work,'' said Professor Amanda Ramirez, director of the Cancer Research UK London Psychosocial Group. ''Engaging consultants more directly in managing their workload and improving their clinical services may increase their job satisfaction. More openings for consultants to teach or carry out research are also likely to boost morale.''

''MORE OPENINGS TO TEACH AND CARRY OUT RESEARCH WOULD BOOST MORALE''



Richard Doll
October 28, 1912–July 24, 2005

Sir Richard Doll, widely hailed as the greatest epidemiologist of our time, has died at the age of 92. Among many achievements in a long career, he will be best remembered as the scientist who showed the conclusive link between tobacco smoking and lung cancer, a finding that has undoubtedly saved millions of lives.

William Richard Shaboe Doll trained at St Thomas's Hospital, London, and undertook wartime service with the Royal Army Medical Corps. In 1948, he joined the Medical Research Council (MRC) and with Austin Bradford Hill investigated the rising number of deaths from lung cancer. Prime suspects had initially been exhaust fumes from cars, and tarring of the roads in response to the expansion of car ownership. But when the team interviewed hundreds of newly admitted patients in 20 London hospitals, they discovered those diagnosed with lung, liver or bowel cancers were more likely to have smoked than those admitted for other reasons. Publication was delayed for a year at the insistence of Sir Harold Himsworth, then MRC Secretary, who felt it important to ensure no special London factors were involved, by conducting a second study of hospitals around the country.

Such scrupulous confirmation of results became the hall mark of Doll's later studies. Sir Richard continued studying the effects of smoking, identifying among other things, the association between smoking and other cancers, heart attacks and emphysema and the dangers posed by passive smoking. He investigated numerous other aspects of health, including the effects of exposure to asbestos, radiation and oral contraception.

In 1969, Doll became Regius Professor of Medicine at Oxford University, where he played a key role in the creation of Green College. He was knighted in 1971. At Oxford University's Clinical Trial Service Unit, in collaboration with Richard Peto, he continued research into carcinogens. The World Health Organization based many of its conclusions on a landmark study conducted at CTSU, which concluded that tobacco, diet and infections accounted for 75% of worldwide cancers.

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Study tailors HPV vaccination

A study of human papillomavirus (HPV) prevalence reveals variations of up to 20-fold in different areas of the world, with additional evidence for significant regional variations in distribution of HPV types, reports *The Lancet* (2005, **366**, 991–998). Investigators from the International Agency for Research on Cancer believe their findings have important implications for both the development of HPV DNA testing as an adjunct to Papanicolaou screening and tailoring the composition of future second generation HPV vaccines to different areas of the world.

To date, around 100 types of HPV have been characterized, with 40 of these known to affect the genital mucosa, and 13 classified as carcinogenic to humans due to a causal association with cervical cancer. Of these, HPV types 16 and 18 have been found to be particularly associated with preneoplastic and neoplastic lesions.

The study set out to compare HPV-type distribution in representative samples of women from 13 areas in 11 countries across sub-Saharan Africa, Asia, South America and Europe. The areas had been specifically selected to represent regions of low, intermediate and high incidence of cervical cancer. In each area, attempts were made to obtain a population-based random sample that included roughly 100 women in each of the following 5 year age groups: 15–24, 25–34, 35–44, 45–54, 55–64, and 65–74 years. All women in the study were randomly selected from the general population, however the final analysis was restricted to women with normal cytological findings.

Results show age-standardized HPV prevalence varied nearly 20 times between populations, from 1.4% in Spain to 25.6% in Nigeria. However, although both overall HPV prevalence and HPV16 prevalence were highest in sub-Saharan Africa, HPV-positive women in Europe were significantly more likely to be infected with HPV16 than those in sub-Saharan Africa (OR 2.64, $p = 0.0002$), and were significantly less likely to be infected with high-risk HPV types other than HPV16 (OR 0.57, $p = 0.004$) and/or low-risk HPV types (OR 0.44, $p = 0.0002$).

''The study gives an idea of the number of extra women who could be picked up in different areas by introducing HPV screening in place of PAP smears and the type distribution of their HPV infections,'' said Dr. Gary Clifford, lead author of the study. ''And while current vaccination only includes HPV16 and HPV18, the study helps define priorities by region for the inclusion of additional HPV vaccines, made possible by second generation vaccines.''

The authors speculate that differences in the relative prevalence of HPV types might be related to the complex geographical and biological interplay between different HPV types and host immune factors.

Prioritising digital mammograms

Digital mammograms are significantly better than conventional film mammography at detecting breast cancer in premenopausal and perimenopausal women, and those with dense breasts, according to a study conducted by the American College of Radiology Imaging Network. The landmark results were reported September 16, 2005, in a special online publication of the *NEJM* and at a meeting of the American College of Radiology Imaging Network (ACRIN) in Pentagon City, VA.

In the study, images from 42,760 asymptomatic women who had undergone both digital and film mammography at 33 sites in the US and Canada, were interpreted independently by two different radiologists. Breast cancer status was determined through biopsy information and follow-up mammograms.

In total, 335 breast cancers were detected. However, digital mammograms proved 15% more accurate than standard film X-rays among the subgroup of women under 50, 15% more accurate among the subgroup of premenopausal and perimenopausal women and 11% more accurate among the subgroup with dense breasts. For all other women, techniques were equivalent. ''These results will give clinicians better guidance and greater choice in deciding which women would benefit most from various forms of mammography,'' said senior author, Dr. Etta Pisano, of University of North Carolina at Chapel Hill.

But with digital systems currently costing 1.5–4 times as much as film systems, cost is likely to impede widespread introduction. Dr. Pisano added that secondary goals measuring the relative cost-effectiveness of both digital and film technologies, and the effect on participant quality of life due to the expected reduction of false positives are still being assessed and will be reported later in the year.

Optimism for young women

The first comprehensive picture of female lung cancer mortality in Europe, shows a promising trend for young women, although rates in most countries are still rising across all age groups. The study, published in the *Annals of Oncology*, offers ''cautious optimism'' that female lung cancer mortality in Europe will not reach the high levels now observed in the US.

The Italian and Swiss study examined trends over the last four decades for 33 countries (including 25 EU states as of May 2004) to provide world standardised rates per 100,000 of the population, both overall and for two overlapping age groups – 20–44 and 35–64. In a separate analysis, each country was considered individually.

Results show that in the 25 EU countries mortality rose by 23.8% between the early 1980s and early 1990s – up from 7.8 to 9.6 per 100,000. From the early 1990s, it rose by a further 16% to reach 11.2 per 100,000 in 2000–2001.

But in several European countries (including Austria, Hungary, Italy, The Netherlands, Poland, Sweden and Switzerland), rates in the last few years declined among the 20–44-year-old age group. Lead author Dr. Cristina Bosetti, an epidemiologist at Istituto di Ricerche Farmacologiche Mario Negri, Milan, commented: ''Trends for young adults are significant since they offer an early indicator of the recent and potential future impact of changes in the prevalence of risk factors.''

Lung cancer mortality in European women: recent trends and perspectives. Annals of Oncology. doi:10.1093/annonc/mdi313.

UK brought into line with Europe

The National Institute for Health and Clinical Excellence (NICE) issued updated guidance to the NHS in England and Wales in August on use of three drugs for people with advanced colorectal cancer.

For irinotecan and oxaliplatin, the guidance presents slightly different recommendations. Irinotecan should be used in combination with 5-fluorouracil (5-FU) and folinic acid (FA). as a first-line therapy, or on its own in subsequent therapy; while oxaliplatin should be used in combination with 5-FU and FA as both first-line and subsequent therapy. A third drug, raltitrexed, was also assessed but remains 'not recommended', with use limited to studies. The new guidelines will give bowel cancer patients in England and Wales the same opportunities as people across Europe and the USA, where combination chemotherapy is widely accepted as first-line treatment.

Mobile phones in clear?

Mobile phone use does not raise the risk of cancer, at least in the first 10 years of use, concludes a study in the British Journal of Cancer (30 August online). The study by Minouk Shoemaker and colleagues from the Institute of Cancer Research, Sutton, includes data from the UK, Denmark, Finland, Norway and Sweden of 678 people with acoustic neuroma and 3553 controls. The study found no association of risk with duration of use, life time cumulative hours of use, or number of calls for phone use overall, or for analogue or digital phones considered separately. But researchers caution longer follow-up is needed to check health problems do not arise with further years of use.

A meeting ''Cell Phones and Cancer?'' is being organized by the European Cancer Prevention Organization in Blankenberge, Belgium on November 4 and 5, 2005. For registration contact sabjanss@hotmail.com.

Embryo screening approved for retinoblastoma

The UK Human Fertilisation and Embryology Authority (HFEA) has granted a licence to University College Hospital, London, UK, to screen embryos for retinoblastoma. The move broke new ground in the debate over embryo screening as the disorder can be cured in more than 95% of cases, and only 90% of people with the mutation develop the disease. At present, screening for this disease starts shortly after birth. The ruling came just days after the HFEA announced that it would seek the public's views on the appropriateness of screening embryos for disorders hat are not fully penetrant such as hereditary breast and ovarian cancer.

Licensing for preimplantation genetic diagnosis (PGD) in the UK has been confined mostly to serious diseases, such as cystic fibrosis, that develop in every individual with the mutated gene or genes, usually early in life. The public discussion, which is to be held in late autumn, will focus on later onset and lower penetrance disorders. Many people feel that screening should be reserved for incurable conditions. ''Although *BRCA1* and *BRCA2* carriers may be treated for one cancer, there is always the underlying risk of another cancer, like a never-ending cycle'', Siobhan Sengupta (Centre for Preimplantation Genetic Diagnosis, University College London, UK) points out. ''If the mutation is a severe worry to a particular family, I personally don't see any ethical dilemma in screening.'' Muhammed Taranissi (Assisted Reproduction and Gynaecology Centre, London, UK) plans to apply for a licence to screen for the BRCA mutations but insists that the decision is one ''for society as a whole''. He says a rejected embryo ''could give a normal individual who lives for 30 years without disease, and by then we may have a completely different cure''. Josephine Quintavalle (Director, Comment on Reproductive Ethics, London, UK) says the ruling is another step towards selecting embryos in pursuit of ''absolute physical perfection''. She concludes: ''Soon, you'll have to be extremely lucky to be an embryo that gets through PGD''.

Cher Thornhill

This story originally appeared in Lancet Oncol 2005, **6**, *742*

No safe levels for smokers

Smoking just 1–4 cigarettes a day increases the risk of women dying from lung cancer fivefold, and men nearly threefold, report Norwegian researchers in *Tobacco Control* (2005, **14**, 315–20). The study helps quell the notion light smokers escape the serious health problems faced by heavier smokers.

Researchers from the Norwegian Institute of Public Health, Oslo, tracked the health and death rates of 23,521 Norwegian men and 19,201 Norwegian women, aged between 35 and 49 at the start of the study, from the mid 1970s (when they were screened for cardiovascular disease and diabetes) up to 2002. Categories of daily cigarette consumption were recorded for each subject, and mortality followed through national registers of causes of death.

Results show the adjusted relative risks of dying of lung cancer in smokers of 1–4 cigarettes per day, in comparison to non-smokers was 2.79 for men (0.94–8.28) and 5.03 (1.81–13.98) for women. In addition, the study showed the relative risk of dying from ischaemic heart disease was 2.74 in men, and 2.94 in women, with the corresponding rates for all cancer being 1.08 and 1.14, respectively.

''Among light smokers there were 4 lung cancer deaths among men and 5 among women, a difference that could be due to chance,'' said Kjell Bjartveit, one of the authors ''but it's interesting that at 10 years more men had become ex smokers and more women had increased their consumption to 5–9 cigarettes a day.''

The authors conclude smoking control policy makers and health educators need to emphasize more strongly that light smoking endangers health.

High dose radiation in prostate cancer?

High-dose radiation can cut prostate cancer recurrence by half in clinically localized cases, but it has no impact on survival, reports a study in *JAMA* (2005, **294**, 1233–1239).

Anthony Zietman, of Harvard Medical School, Boston, and colleagues set out to determine whether tumour control could be improved in patients with prostate cancer, including those with low-risk disease, by using higher radiation doses.

The study included 393 patients with stage T1b through T2b prostate cancer and prostate-specific antigen (PSA) levels less than 15 ng/mL, randomized between January 1996 and December 1999. The median value for PSA levels was 6.3 ng/mL, and the median follow-up 5.5 years. Patients received either external beam radiation to a total dose of either 70.2 Gy (radiation dose unit; conventional dose) or 79.2 Gy (high dose), delivered using a combination of conformal photon and proton beams. Proton beam therapy is currently only available in a few centers in the US.

Researchers found the proportions of men free from biochemical failure (increasing PSA level) at 5 years were 61.4% for conventional-dose and 80.4% for high-dose therapy, a 49% reduction in the risk of failure. An advantage for high-dose therapy was observed in both the low-risk and the higher-risk subgroups (risk reduction, 51% and 44%, respectively). But there were no significant differences in overall survival rates between the treatment groups ($p = 0.80$).

The lack of difference in survival , said Dr. Zietman, may be due to the fact that prostate cancer is a slow-growing cancer, and the new study only looked at 5 years of data.

In an accompanying editorial, Theodore L. DeWeese, M.D., and Danny Y. Song, M.D., of Johns Hopkins University School of Medicine, Baltimore, comment: ''Whether this increase in PSA control will necessarily translate into improvement in clinically meaningful end points such as longer survival is not yet known.

''WHETHER PATIENTS SHOULD ACCEPT THE MODEST BUT REAL INCREMENTAL RISK OF HIGHER RADIATION DOSES FOR THE UNCERTAIN ULTIMATE BENEFIT DERIVED''

As such, this study has not answered the important question of whether patients should accept the modest but real incremental risk of higher radiation doses for the uncertain ultimate benefit derived.''

They add that additional questions remain including whether higher radiation doses beyond 79 Gy would provide even greater benefit, and the optimal radiation method of dose escalation. ''Given that the addition of androgen suppression to radiotherapy has recently been shown to improve survival in some patients, is dose escalation even the best way to improve radiotherapeutic outcomes in this disease?'' they write.

Aromatase inhibitor update

The St Gallen 2005 guidelines have recommended for the first time use of an aromatase inhibitor (AI) following 2–3 years of adjuvant tamoxifen therapy. The guidelines, published in *Annals of Oncology* (2005, **16,** 1569–83), recommend using exemestane in the adjuvant setting for the treatment of oestrogen receptor positive early breast cancer in postmenopausal women at intermediate and high risk of recurrence.

The guidelines arise from the Intergroup Exemestane Study (IES), published last year in the *N Engl J Med* (2004, **350**, 1081–92), which found switching to exemestane after 2–3 years of tamoxifen, compared to continuing treatment with tamoxifen improved disease free survival by 27%, and reduced the risk of breast cancer recurrence by 30%.

''The apparent support for switching to an aromatase inhibitor after tamoxifen underscores a widely held belief that this optimises treatment for improving disease free survival whilst minimising the risk of tamoxifen-associated long-term adverse events,'' said Mr. Robert Carpenter, a Surgical Oncologist, St Bartholomew's Hospital, London. ''The switch strategy appears to meet the requirement for both clinical and cost effectiveness.''

Erlotinib approved in Europe

In September, the European Commission approved erlotinib HCl tablets (as monotherapy) for locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen.

The approval was based on results of a multi-centre, randomized, phase 3 trial in 731 patients, which showed that patients who received erlotinib survived an average of 6.7 months, while patients on placebo survived an average of 4.7 months, a 42.5% improvement. The study published in *NEJM* (2005, **353,** 123–32), showed that of the patients receiving erlotinib, 31% were alive after one year, compared to only 22% of patients receiving placebo. Erlotinib was generally well-tolerated, with the most common adverse reactions being rash and diarrhea.

Erlotinib is thought to exert its action through the inhibition of epidermal growth factor receptor (EGFR)-associated tyrosine kinase, thereby blocking its stimulation of cancer cell growth.

Erlotinib tablets have already been approved for this indication by Health Canada in July 2005, the Swiss Health Authority Swissmedic in March 2005, and the U.S. Food and Drug Administration in November 2004.

Conference First

The inaugural UK National Cancer Research Conference, designed to unite the UK cancer community, was held in Birmingham (2–5 October, 2005). The meeting, organised by the National Cancer Research Institute (see p 2591), was designed to disseminate research advances in cancer across all disciplines.

''For the first time, the major cancer research funding bodies from the government, charity and industrial sectors have come together to form a true partnership,'' said Professor Alex Markham, chairman of the National Cancer Research Institute. ''Our purpose is to accelerate and advance improvements for the benefit of cancer patients, by engaging the whole UK cancer research community.''

As well as talks from international experts, the meeting placed a particular emphasis on the patient experience. It is planned that the conference will be held annually.

PODIUM

Cancer Czar: A clear focus

Professor Mike Richards was appointed as England's National Cancer Director in 1999. Richards, a medical oncologist and palliative care consultant, is responsible for modernising cancer services and improving survival rates across England.

Professor Mike Richards

Why was a National Cancer Director considered necessary?

At the end of the 1990s, it became apparent England needed a major drive on cancer. The Eurocare study demonstrated both England and Scotland had lower survival rates than comparable Western European countries across a range of different cancers, and there was known to be under investment in cancer, with too few staff, and inadequate facilities. In recognition of this fragmented service, the prime minister made cancer one of the government's top priorities for 1999.

Could you describe your role?

My role is to develop national policy on all aspects of cancer and oversee its implementation. I spent the first year in post developing the National Cancer plan for England, and the last five years implementing it.

What's the National Cancer Plan?

The National Cancer Plan, is a 10-year strategy covering all aspects of cancer care including prevention, screening, diagnosis and research. It sets out four key aims:

- To save lives
- To improve people's experience of care.
- To reduce inequalities, like variations due to geography or social class.
- To build for the future in terms of research, education and the workforce.

In addition, there are commitments on cutting waiting times, making the best treatments available and introducing screening programmes, where there is evidence they save lives.

For organisational purposes, the country has been divided into 34 cancer networks, with the intention of getting hospitals, primary care providers and purchasers working together. Each has a medical, managerial and nurse director to implement national policy.

What type of budget do you have to work with?

By the end of the third year the Government committed to spend 570 million a year on cancer, but the results of our recent tracking exercise show we are now spending 639 million. That means more money is being spent on drugs and equipment.

What are your successes?

Headline figures show the death rate from cancer in people under 75 has fallen by 12% in the last six years. We have extended screening programmes as promised in breast cancer and cut waiting times. We have achieved one of our first pledges that anyone who is referred urgently by their GP is seen within two weeks, and are making progress on broader waiting time targets.

How has the lot of the English cancer patient changed?

Cancer patients now are more likely to be treated by multidisciplinary teams and to get access to the best treatment. Comparing two patient surveys – one conducted by the Department of Health in 2000 and one undertaken by the National Audit Office in 2004, their experience of care has definitely improved. More patients receive written information at the time of diagnosis, report shorter waiting times and get explanations about side effects.

Furthermore, there has been marked improvement in the number of people who feel they are being treated with "**dignity and respect at all times**" — this has risen from 79% to 87%.

Where is there room for improvement?

There is room for improvement in all areas, but we especially need to do more on prevention. I think that the single most important thing we could do here is have a comprehensive ban on smoking in all public areas, as they have done in California, Ireland and Scotland.

We also need to go further on screening, make sure everyone has access to the best treatments, and we need to reorganise services for complex surgery so that operations are only undertaken in larger centres.

What effect has the plan had on research?

As a result of the National Cancer Plan a research institute was established in the UK in April 2001. This is not a bricks and mortar building, but a virtual institute bringing together the main funders of cancer research, with the intention of developing a strategic approach that avoids duplication and identifies gaps. One of the first activities was to establish a database of all ongoing research, which clearly showed we were spending too little on research into prevention, palliative care and lung cancer. As a result we have set up initiatives to enhance research in these areas.

What are your future goals?

Our long-term goal is for cancer outcomes in England to be amongst the best in Europe. We have not got there yet and we have to ensure we maintain the momentum that has been generated over the last five years. Next April we will be implementing a Bowel Screening Programme across the country, after a large-scale pilot showed it works in everyday practice. When the Cancer Plan came out drugs like glivec and herceptin were simply not available. Due to the improved organisation of care we are better prepared to take advantage of this new era of treatment.

Do you have any particular messages for oncology professionals?

The message to my colleagues is one of thanks for all they are doing. I want them to appreciate that if you have a clear focus on cancer and give it the priority it deserves , there is no doubt that it is possible to improve the service and outcomes for patients.