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Education & knowledge through people & facts

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Mike Richards

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Editor
Kathy Redmond
editor@eso.net

Assistant Editor
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Website Liaison
Chatrina Melcher

Art Editor
Jason Harris

Layout Designer
Max Fuller

Production
HarrisDPI
www.harrisdpi.co.uk

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Jason Harris

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Direttore responsabile
Alberto Costa

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All enquiries about Cancer World should be made to:
ESO Editorial Office
Via del Bollo 4
20123 Milan, Italy
e-mail: magazine@eso.net
Fax: +39 02 8546 4545
All correspondence should be sent to the Editor at editor@eso.net

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A question of human dignity

Mary Robinson ■ GUEST EDITOR

Social and economic progress over the course of the last century has helped people in many countries enjoy longer, healthier lives. Public health, by and large, has improved and health interventions are now available to prevent or treat most conditions, including cancer.

Yet cancer continues to kill millions of people worldwide every year and the death toll is projected to rise dramatically. A full 70% of these deaths occur in low- and middle-income countries.

According to the WHO, up to one third of the cancer burden could be cured if detected early and treated adequately, and another third could be reduced through cancer prevention strategies aimed at reducing the exposure to cancer risk. These include changes in tobacco use, immunisation against HPV infection and control of occupational hazards.

Cervical cancer is just one example. Although we have the tools to prevent this terrible disease, it affects an estimated 500,000 women each year and leads to more than 250,000 deaths – the vast majority in developing countries. Most women affected do not have access to local health systems or routine gynaecological care, including regular screening, which plays a critical role in preventing cancer in industrialised countries.

Much more must be done to encourage the international support necessary to make life-saving tools such as HPV vaccines available to those who need them most and to ensure that robust health systems are in place to support their delivery.

The World Cancer Declaration, which will be launched at the UICC World Cancer Congress in Geneva this August, outlines the critical steps needed to build the basis for sustainable delivery of effective cancer prevention, early detection, treatment and palliative care worldwide. The Congress provides a critical forum for health professionals, policy makers and advocates to galvanise the global health community behind the goals of the Declaration.

These and other steps to advance global health are not just matters of moral concern: they are issues of fundamental human rights.

Article 25 of the Universal Declaration of Human Rights declares that "everyone has the right to a standard of living adequate for the health and well-being of himself and his family, including medical care."

As members of The Elders, we have highlighted the right to health as part of the Every Human Has Rights Campaign (www.everyhumanhasrights.org) to mark the 60th anniversary of the Universal Declaration.

The message that health is a fundamental human right must be heard again today. We all have a role to play in moving the cancer control agenda forward.

Mary Robinson, former UN High Commissioner for Human Rights, is the President of Realizing Rights (www.realizingrights.org) and a member of The Elders – a group of public figures noted as elder statesmen, peace activists, and human rights advocates

Mike Richards:

the man with the plan

➜ Marc Beishon

"Congratulations, you are now in charge of sorting out England's failing cancer services, what are your plans and can you start on Monday?" The job offer took Mike Richards by surprise but, mindful of the fickle nature of political support, he accepted the post, got straight down to work, and within six months he not only had a plan, but was ready to put it into action.

There are two ways of looking at the job of a country's cancer 'czar' – the person charged with masterminding a national cancer control plan. Many will see it as an impossible task, trying to keep everyone from politicians to doctors and patient groups in line with a programme that could never be comprehensive and chasing targets that are constantly out of reach, thanks to an ageing population, unhealthy lifestyles and lack of treatment progress, not to mention continual changes in healthcare bureaucracy. Others, however, will point to countries where a cancer plan and its leader have made clear progress despite these odds, and on the international stage arguably the most prominent example is England and its national cancer director, Mike Richards.

England stands out because, when it embarked on its cancer plan in 2000, it was the first large country in recent years to take this step. Denmark started its plan around the same time, but it was not until 2003, with the launch of the French cancer plan, that another large country followed suit. England also stands out as a country that was in desperate need of playing 'catch up' with comparable countries in the West (and this also applied to the other countries in the UK, to which responsibility for health has now been devolved). The NHS Cancer Plan for England as drawn up in 2000 was, as Richards says, a long overdue necessity.

"No country has a perfect system, but ours was far behind many," he says. "When I became national cancer director I visited Sweden and talked to people in charge of service delivery – they told me we were beginning to do the right things but they'd started 20 years earlier, with systems such as regional care networks and service guidelines. The UK had great fragmentation in its cancer workforce and too few people and facilities – we were not looking at cancer in the round, from prevention to screening, diagnosis, treatment and care. It was a system failure."

The plan in 2000 set out to address these shortcomings. It has now been revised as a new reform strategy, targeting in more sophisticated ways areas that are proving most problematic, such as early diagnosis. After several years of spending a lot more on cancer – although still less per head than Germany or France – the emphasis is shifting to effectiveness, and Richards is now looking to establish England's cancer care among the world's best.

For his own part, Richards – who was a professor

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of palliative medicine in his last clinical post – does not preside over an expensive bricks-and-mortar institute to direct the strategy. He has kept his office at St Thomas' hospital, London, with a view over the River Thames to the Houses of Parliament, and has a small team to call on. Networks, and networking, he feels, are far more effective than central diktat.

A snapshot of just a few days in Richards' diary reveals just how varied his own networking is – and provides an insight into what a cancer czar does. "I had meetings and workshops on England's End of Life Care Programme [which Richards leads]; gave a briefing to England's health minister preparing for a European summit; made a presentation on the economics of care at the Berlin breast cancer conference; chaired a meeting with other national clinical directors; attended a meeting on funding hospices; met the chief executive of Cancer Research UK on initiatives for early diagnosis; attended a session on 'e-learning' for oncologists; and attended meetings on initiatives such as the UK's National Cancer Research Institute, radiotherapy standards, laparoscopic surgery and multidisciplinary teamworking."

All this activity points to another key factor in running a national cancer programme – leadership. While a string of health ministers – and now one Prime Minister – have come and gone under Richards' tenure, he has been in post for all eight years of the initial plan, and has every intention of seeing through the latest reform strategy during the next five years. Finding a director for a national plan is no easy task for a government – there are very few senior clinicians in any country who possess the necessary managerial and diplomatic skills, and who are prepared to step away from successful jobs in front-line oncology. But an oncology background is surely a prerequisite for gaining the confidence of a diverse and complex healthcare workforce.

Richards thoroughly enjoyed his time as an oncologist and researcher and had never envisaged becoming a manager. "Fifteen years ago I wouldn't have believed anyone who told me I'd leave my clinical work to take on a role like this.

"I come from a medical family – my father was a GP, and both my sister and brother had gone into medicine – but I hadn't seriously considered it myself until I switched from a natural science degree at the end of my first year at university. I found it combined science with humanity and I've never regretted making the change," he says.

Richards did the usual training in general medicine, and found his way into medical oncology. "It wasn't any one factor – but an influence was meeting Gordon Hamilton-Fairley when I was a student at St Bartholomew's ['Barts'] in London. He was a very charismatic leader in this new field, but was tragically the victim of an IRA bomb. I also got involved with one of the first randomised controlled trials for chemotherapy, in small-cell lung cancer, while working in Nottingham."

At Barts, a specialist centre for haemo-oncology, he gained exposure to lymphoma and leukaemia, and saw the potential of one of the first MRI machines in detecting lymphomas. "That's given me insight into how you evaluate diagnostic technologies, which is not an easy area," he notes.

He then moved to Guy's hospital in London to become a breast cancer specialist, although he'd had little experience with the disease. "I've demonstrated throughout my career that I can take jobs for which I'm not qualified," he says, adding more seriously that oncologists should be prepared to be adventurous in the way their careers evolve. Guy's was (and is, with its merger with St Thomas' hospital) one of the UK's leading teaching hospitals, and Richards was able to practise high-quality breast cancer care with some of the latest equipment and multidisciplinary working. But in the early 1990s he took a seminal phone call from an oncologist in a hospital outside London.

"This colleague was based in a city just 50 miles from London, and he asked my opinion about whether a 32-year-old woman with breast cancer should receive adjuvant chemotherapy. I asked three questions. Has the cancer spread to the axillary lymph nodes? Answer: 'The surgeons here do not

"Oncologists should be prepared to be adventurous in the way their careers evolve"

remove lymph nodes.' Second – what grade is it? 'The pathologists here don't measure the grade.' Finally, I asked how large the tumour was – and was told it was not recorded in that case. I was horrified by this standard of care, and thought then I could either sit in my ivory tower and practise on relatively few patients or try to do things on a wider scale."

Working with colleagues in his regional cancer registry he found that this was not an isolated example, and there were wide variations in care. "That led me to work with the British Breast Group, which comprised researchers from a variety of backgrounds, where we wanted to produce guidance on breast cancer services. We were told it would be impossible to get consensus, but in six months we wrote a document on multidisciplinary teamworking in breast cancer, and that led to national guidance for all sorts of cancers. It was a very influential programme – these were not clinical treatment guidelines, but how services should be organised, as it became apparent that the problem in the UK was more about the system than anything else."

Along with underinvestment in the workforce and facilities, Richards says there was far too much fragmentation among the tiers of the health service – primary, secondary and tertiary – and also among disciplines within the acute sector. "People working in oncology were of high quality, but many were not looking sufficiently broadly at the care pathway."

Some other countries still suffer from very similar fragmentation and underinvestment in their cancer services, so an important question is how such a situation arises and is allowed to continue. Losing several cancer champions, such as Hamilton-Fairley, and in the early 1990s, the pioneering medical oncologist Timothy McElwain, certainly did not help, reckons Richards, but generally cancer did not have a high enough profile in the UK – in the media, among the public or in medicine. "And there was a fatalistic attitude, such that when I was a junior doctor an eminent gastroenterologist told me he couldn't understand why I wanted to be an oncologist. Equally, as a country, we were slow to believe we had fallen behind in care. We had a passionate belief in the NHS and it was hard to think our outcomes were worse than comparable countries."

It was the Eurocare comparative studies of European cancer registries that triggered a change in British thinking, says Richards. Eurocare-1, which included patients diagnosed from 1980 to 1984, came out in 1989, and showed the UK well down the ranking for survival. The subsequent Eurocare-2 and 3 studies showed, he says, "that although outcomes were improving in the UK, the country was not closing the gap with others." While it is easy to dismiss some of the findings – there is for example incomplete cancer registration in Germany and regional bias in Italy – Richards says it became quite clear that data from Norway and Sweden, which have complete registration, were indicative of a higher quality cancer control system.

Eurocare-3 covered survival up to 1999, the year before the NHS Cancer Plan, but Eurocare-4, published last year, covered the early years of the plan and led to press reports that it is failing, as the UK figures were still not good. Richards notes, however, in an article on the Eurocare approach, that the time lag from diagnosis to analysis (from five to seven years) needs to be narrowed, and better information, such as on staging and symptom duration, needs to be added (see *Lancet Oncology*, online 21 August 2007). He is confident that England's cancer mortality and survival rates will show a closing of the gap with other nations.

Richards made another career switch that was to prove prescient, given his current leadership role in England's End of Life Care Programme, becoming professor of palliative medicine at Guy's and

Celebrating success. Earlier this year Richards marked 20 years of the NHS breast screening programme together with the Health Minister Alan Johnson (wielding the knife), Maureen Lubert from the charity Breakthrough Breast Cancer and Jeremy Hughes MP from the Parliamentary Group on Breast Cancer. The cancer reform strategy will extend the programme to women aged 47–73

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St Thomas'. "It made a big impact on me," he says. At the same time, he was working with the Department of Health on reducing waiting times and improving standards in the cancer service, but it came as a big surprise when he was selected as the national cancer director in 1999. "The Prime Minister, Tony Blair, had held a cancer summit earlier that year, where about 25 people including myself set out the problems. Later, I was asked to attend what I thought was an interview with the health minister – but she said, 'It is great that you are going to do the job. What are your plans and can you start on Monday?'"

This was the first salaried post of its type in government – not an advisory position but a full-time programme leader. "I then had a meeting with Tony Blair and put forward the idea of a national plan. He asked, 'Is cancer in this country as bad as made out, why is it so, what can you do about it, how long will it take and what will it cost?' The plan came out of that meeting – and it was clear to me that when you have political support you should act fast, and we published it six months later."

Richards worked mainly with a small, informal group of advisers from across the cancer spectrum, as it was clear what the main priorities should be, especially on the treatment side. But he emphasises that a cancer control plan should be a very broad programme, from prevention to screening, treatment and indeed end of life care, informed by existing evidence and new research as needed. "But there won't always be controlled trials that show you how services should be – I cannot envisage doing an RCT on multidisciplinary team working, for example, as it is unthinkable we'd randomise patients to be managed by professionals who don't work closely together. Sometimes you have to work with commonsense and consensus."

Indeed, he says the single biggest change so far has been in creating multidisciplinary teams (more than 1,500 are in place), aligned with reconfiguring services so that complex procedures are carried out in larger centres where there is evidence that this improves outcomes. "We've moved a lot further here than some countries have been able to – such as for oesophageal cancer, where you should be dealing with populations of a million or more, and pancreatic cancers, for 2 million and over. And now the vast majority of men who undergo a prostatectomy are treated at centres with at least 40 procedures. Each year progress is in the right direction." He adds that units that do not measure up have been closed. For example the number of hospitals carrying out major oesophageal/gastric procedures has halved from 160 to about 80. But he is not an advocate of migrating too far in the direction of a few comprehensive cancer centres – England now has regional networks and he is keen to see as much appropriate care as possible located close to home, with involvement from primary care and district hospitals, and increasing use of tools such as videoconferencing.

The earlier service documents for cancer types

that Richards helped to draw up have now evolved into guidance produced by England's National Institute for Health and Clinical Excellence (NICE). "Each report says what the shape of services should be and who is needed in a multidisciplinary team for the relevant cancer type. We also have a system of peer review in place to assess whether services meet the recommended stance." For the most common cancers and also for supporting services such as radiotherapy and pathology, Richards says more than 2,000 reviews by outside colleagues have been conducted so far – these are mainly appraisals of procedures but may include sitting in on team meetings.

A report on the peer review findings is in preparation, and should also be of interest to international colleagues. "We have identified much good practice, but there are still places where the workforce is not sufficient to hold, say, weekly multidisciplinary meetings. They may be missing certain specialists such as pathologists and, in some cases, nurse specialists, who we think are a very important part of the team.

"Administrative support is also a challenge. We have spent ten years building up these teams – now we need to make sure they work effectively."

Prevention has made headway – smoking rates among adults have now dropped to 22%, and should fall further following the recent smoking ban in public places in England. Richards reports "major success" in screening, with women aged 50–70 now screened for breast cancer with two-view mammography, and colorectal cancer screening being rolled out to people in their 60s. Limiting factors, such as the availability of high-quality endoscopy services, are being mitigated by expanding the range of practitioners who can carry them out – including nurse specialists – and insisting that units must improve quality and cut waiting times to be part of the national screening programme.

Probably the parts of the 2000 plan that have been – and continue to be – most controversial, certainly in the public eye, concern waiting times and drug availability. Richards regularly appears in newspaper items on subjects including the wide variability of access to new drugs such as Herceptin, often presented using highly emotive stories about young cancer sufferers. "We have acknowledged that the interval between a drug being licensed by the European Medicines Agency and approval by NICE is too long," he says, adding that there are moves to speed up appraisal and to monitor the variation of provision around the country. It is not a uniquely British problem though. "Variations in the use of drugs and surgical procedures feature in most countries," he notes.

Waiting times from referral by a primary care doctor (GP) to being seen by a specialist are now much shorter – there is a two-week target set by government. But there can still be lengthy delays in accessing treatment such as radiotherapy. Late presentation by patients and late onward referral by GPs have remained tough nuts to crack, and are major planks of the reform strategy. However, a cancer czar can easily find himself at the centre of a dispute which is not of his making. A recent front page newspaper story suggested that Richards had issued a 'warning' to GPs about 'botched diagnoses'. "I was scurrilously misrepresented," says Richards. "I did say it is hard for GPs who see only about eight new cancer cases a year to distinguish these from the hundreds of people they see with similar symptoms. I had not issued a 'warning', nor had I mentioned 'botched diagnoses'. In England we ask GPs to be gatekeepers and we need to equip them with decision-making aids and better access to diagnostic tests like ultrasound. What we don't need are more guidelines – GPs are already flooded with these."

An important point he stresses is that, while many of the issues facing England are common to other countries, what needs to be done has to fit with the existing healthcare system. While he can see some changes, which might include increasing recourse to private medical facilities, the NHS and its primary/acute system is not likely to change radically.

"The NHS has changed over the past eight years. In the year 2000 plans were all about expansion – now it's about driving change through better information and commissioning, and yes, we can now look

"We have spent ten years building up these teams – now we need to make sure they work effectively"

Critical coverage. Richards has had to learn to deal with the British press, where stories on the NHS tend to be driven by a political agenda

to the independent sector if we want."

The cancer reform strategy includes actions to diagnose cancer earlier through extensions to screening and helping primary care, and it also has a new equality initiative to tackle disparities among populations that have worse incidence, access to services and outcomes. "We need to push relentlessly on the smoking agenda – should cigarette displays now be banned in shops, for example – and develop community awareness. We have a number of pilot programmes running in deprived areas that are trying to inform older people about the major cancers – it is partly the media's fault that many think that cancer is a disease of younger people and not primarily of people in their 60s, 70s and 80s. The media always tend to focus on younger cancer patients."

Other elements of the new strategy include increasing the move towards carrying out more complex procedures in major centres, while doing more ambulatory care closer to home. "We need to free up resources: we spend a lot more on inpatient services for cancer than they do in the US," says Richards. Collecting and applying better information is also a major plank of the strategy. "We already have comprehensive cancer registration and extensive information on patients attending NHS hospitals in England, but we are not making the best use of this." A national cancer intelligence network is now being established to provide comparative data on cancer activity and outcomes. "My aim is to have the best cancer information system of any large-population country by 2012."

Until recently, Richards was also the chair of the National Cancer Research Institute (NCRI), the virtual coordination body for research centres and funding bodies in the UK. The cancer plan has triggered much more research, says Richards – and certainly the various networking initiatives now running are among the more visible success stories on the international stage. Among the achievements are the National Cancer Research Network, designed to boost clinical trial rates in NHS hospitals (the enrolment rate has now reached 12%). A recent initiative has been to establish 19 experimental cancer medicine centres to fast-track phase I/II trials.

The NCRI, adds Richards, also maintains the same database structure of ongoing research as the US and Canada. "I would very much like to make this a Europe-wide initiative, so we can better identify gaps in research." Analysis of the database showed low levels of funding on research into prevention and into supportive and palliative care. As a result, new initiatives have been established in both areas.

Richards' involvement with England's End of Life Care Programme goes beyond cancer to all illnesses – as he says, the majority of the 500,000 deaths in England each year are from a chronic condition. But, as with cancer care a decade ago, end of life experience can vary greatly in quality, and

"It is partly the media's fault that many think that cancer is a disease of younger people"

Richards would like to see much more awareness, and even anger, about poor end of life care

Richards would like to see much more awareness – and even anger – about poor care to help drive up quality for a topic that tends not to be talked about. "Doctors need to be trained to initiate discussion with people about their preferences regarding end of life care – much of the problem starts at the beginning of the end of life pathway."

For palliative care, he notes the huge range of professionals who are involved in helping people towards the end of their lives – but relatively few who are specifically trained in the discipline. "We need to skill up the wider professional community and improve coordination, for example, so that people do not end up in hospital unnecessarily." Survivorship care, as more and more people live with after-effects of treatment, also now needs greater attention, he adds.

Richards recognises that there will be continuing controversies, adding to the string of problems that have already landed on his desk, such as shortcomings in radiotherapy and drug availability. On the latter, the NHS is now in the bizarre but understandable situation of not allowing patients to pay for their own drugs and have them administered by the NHS, as this would promote inequalities. Such 'co-payments' are commonplace in many European countries.

One of Richards' biggest critics – and simultaneously one of his friends – is probably the best known British oncologist, Karol Sikora, who is agitating for much more and faster reform, such as a network of dedicated privately-run clinics, to drive efficiency, and wider drug availability. "There are ten cancer drugs you can get in Calais that you can't get in Canterbury," he comments. But Sikora recognises the tightrope that Richards walks, despite labelling him a 'political servant'. As Richards says: "I can't keep everyone happy – the way I work is to keep what's right for the patient clearly in mind in the way I respond, and that does make me unpopular with some groups." No doubt sometimes the politicians feel he is the patients' – or the oncologists' – servant.

LUIGI INNAMORATI

There is little disagreement – apart from the odd map-reading dispute – with Sikora when they are out hill walking, Richards' great passion outside work. "My aim is to climb all the Munros in Scotland – these are mountains over 3,000 feet (914 metres) – there are 284, and I have done 232 so far."

It's an apt analogy with England's cancer control plan – opinions vary but no one can now deny that a concerted ascent of the cancer mountain has been made. "My ambition now is for England to be among the best in Europe and the world in cancer, and recognised as such, and also to be a leader in end of life care. But of course it is still a big challenge."

Walking a tightrope. Richards spoke of the need to maximise the value cancer patients get from a limited health budget at a panel debating the case for rationing expensive drugs that was organised to mark the 25th anniversary of the European School of Oncology last year

The hopes and frustrations of a career in cancer

The next generation speaks out

Anna Wagstaff

Young oncologists want the chance to develop their skills, reach their full potential and give of their best. But a *Cancer World* survey shows many are frustrated by too heavy clinical workloads, too few chances to lead research and get published, and too little recognition for their clinical skills. Are potential leaders of oncology in Europe having their careers derailed?

For young medics setting out on their careers, oncology offers almost unparalleled richness. You can be part of the march of science, working with lab and clinical researchers on an international stage. You can build up expertise in particular cancers, working in a team to apply it to each new patient. You can make a world of difference to the lives of patients and their families.

Science, medicine and humanity: oncology offers all three. In an ideal world, medical students choosing oncology will taste all these aspects, find out where their talents lie, and develop their careers accordingly. Such a world would also be ideal for patients and for medical progress. But how far does it match reality?

A survey conducted by *Cancer World* has revealed a variety of barriers to developing a career as a cancer specialist. Top among them is the weight of the clinical workload – rated the first or second most important barrier in every region of Europe. In western and southern Europe, this is coupled with a strong sense that the quantity and quality of clinical work counts for little when deciding who should be promoted. In central and eastern European (CEE) countries, pay and lack of job openings and training posts are seen as major barriers.

To throw some light on these and other issues, *Cancer World* talked to a number of oncologists in their 30s or early 40s, who have completed their basic training and are building their careers.

Quality of teaching

One interesting finding is the variety of experiences. In a profession that relies heavily on 'learning by doing', the quality of the teaching and mentoring is critical. But even hospitals with a good general reputation for training can turn out to be poor when it comes to oncology.

There were comments about very good practice: "I said to [my supervisor] that I wanted to do something in the lab, and he found me funds to do it. I said I was keen to gain some more experience in breast, and he found me somewhere to train in breast. I said I had just heard about the Flims course [on methods in clinical research] and asked, 'Would you help me to go there?', and yes he did."

And comments about very bad practice: "They use their students as menial workers, getting them to write down patients' clinical records, prepare their charts and fetch the films from radiology. But they never give them the chance to discuss that film for 15 minutes with a senior specialist in radiology."

Frustration at being denied oppor-

tunities to assume greater responsibility seems widespread. One interviewee described how even good people can get trapped. "One of my colleagues, a brilliant radiotherapist, suffered for almost 10 years under a boss who wouldn't let him move and didn't give him freedom to develop."

The problem seems to get worse as you reach the end of your residency and try to break into the higher ranks. "Those who are still in training have many more opportunities than a few years ago. The problem is when you are in the middle," said one senior oncologist. "People who have been in a backstage position for a long time and who have learned how to do it should be given the opportunity to lead projects."

Often a head of department seems to protect their own patch. "Maybe they know we are the generation who are going to replace them. There are very few people who say: 'I am going to prepare things for when I leave.' I guess it's only human."

Another commented, "There are places where you feel a ceiling, not even a glass ceiling, just one centimetre above your head and you can't move. Actually they are trying to push the ceiling down."

Big differences in the quality and evaluation of training programmes is also an issue. In Germany, where responsibility for training lies with each of the 52 *länder*, there is no national accreditation of training programmes for any specialty. Some of the German respondents to the *Cancer World* survey are calling for a national curriculum – consistently taught and rigorously evaluated.

Moves towards devolving healthcare to the regions in Spain are prompting similar calls.

ILLUSTRATION: FRED VAN DEELEN, WWW.ORGANISART.CO.UK

Research barriers

The *Cancer World* survey revealed that many young oncologists are finding it hard to build up experience in research – with few opportunities to do lab work, design protocols or lead trials, and many obstacles to getting published. This is a particular problem in countries or institutions with a low commitment to medical research (for a comparison of per capita spending on cancer research across Europe, see figure 6 of the *Second Cancer Research Funding Survey*, ECRM 2007, www.ecrmforum.org).

A survey respondent from Austria called for 'our own national cancer institute'. Comments from Spain and Turkey called for 'collaborative research groups'; from Ukraine, 'good labs with high-tech facilities'; and from Bulgaria, the Czech Republic, Italy, Turkey and Romania, 'more research grants', 'more sponsors to run trials', and 'greater emphasis on research and giving it time'.

But good translational research requires more than just the right facilities. A strong working relationship between lab scientists and clinicians is essential, yet this seems more of an ideal than a reality. "The people in the lab are not really interested in care and the people in the clinic don't have interaction with people in the lab. It is so difficult that in the end people do just straightforward clinical research – not the translational stuff."

Clinical research is itself highly

demanding. It takes money, time and an immense amount of administrative and clerical work. Unless a centre has well-oiled procedures, clinical trial nurses, admin staff, software and other back-up, the burden on the trial leaders can be enormous. Sofia Braga, a young Portuguese oncologist, worked for a year at the Jules Bordet in Brussels and is now back in Lisbon, at one of Portugal's three large oncology institutes, fighting for the chance to lead a trial of sunitinib as a neoadjuvant in breast cancer. She contrasts the two settings: "They get protected time. And they don't have to fill in CRFs [case report forms]. I spend my day filling in these forms. It's desperate – it's a humungous amount of work."

Even when an oncologist overcomes these barriers, it is difficult to get published in a prestigious journal. Braga comments, "My institution has not broken into that kind of group, where your name is known. We're still in a place where some of us have had international experience and we'd love to publish more, but it's very hard. We don't have a Baselga, a Piccart or an Armand."

She feels that many European journals are biased against places like Portugal, even though her centre treats more breast cancers than, for instance, the Jules Bordet. "I published an original article, but it was only the American journals who were interested. Europe is extremely prejudiced. They feel southern Europe is the end of the world. I always tell my fellows to send papers to American meetings and journals, because they respect us."

THE CHANCE TO TRAVEL

Travel is one answer – it is notable how many specialists who make the cover of *Cancer World* mention an opportunity to spend time in a different country as key to their subsequent careers. Many professional and educational organisations offer fellowships where people can get experience in research in different environments (see box).

However, demand is always greater than supply, and while some supervisors encourage their trainees to seek experience abroad, others resent losing an extra pair of hands. Language is a barrier to travel from countries which don't have a tradition of English as a second language. It is also harder to move when you have a young family, or a partner tied to a job. Women are at a particular disadvantage here (indeed, Braga cut short her term at the Bordet and returned to Portugal because of childcare problems).

ESMO (the European Society for Medical Oncology) now offers research fellowships that can be carried out at the fellow's own institution of origin, because of the difficulty some people find in travelling. Martine Piccart, head of the medical oncology department at the Jules Bordet institute in Brussels, who sits on ESMO's fellowships and awards committee says, "That's good I think, but this model should not be favoured too much. I really believe that the most productive

WANT CAREER – MUST TRAVEL

ESSO, the society for surgical oncology in Europe (www.esso-surgeonline.org), offers fellowships to give young surgeons the chance to expand their experience and learn new techniques. They also support surgeons who want to attend the Flims course on methods in clinical research.

ESTRO, the society for radiation oncologists (www.estro.be), offers grants and fellowships for courses, and advertises other fellowship and grant opportunities for radiotherapists on its website.

ESMO, the society for medical oncology (www.esmo.org), recently beefed up its fellowship opportunities. Young oncologists can apply for a 'taster visit' to a translational research unit to see how this research is organised. A one-year clinically oriented fellowship offers young oncologists an opportunity to visit an institution, participate in multidisciplinary rounds, and see inpatients and outpatients. A two-year translational research fellowship offers oncologists with some experience in research the chance to work in a lab.

ESMO recently introduced a 'teach the teacher' fellowship, which supports a group of young oncologists from one centre to travel to a host institution for six weeks to learn different ways of organising clinical work and research – the aim is to maintain those links once the group has returned, and support them in sharing what they learned.

ESO, the European School of Oncology (www.eso.net) offers, in addition to its own courses, senior scholarships for young oncologists to visit specialist centres for three months to a year for practical training in a variety of specialties.

Other bodies offering fellowships include the UICC (www.uicc.org), the European Organisation for Research and Treatment of Cancer (www.eortc.be) and many major cancer centres and charities in Europe and the US.

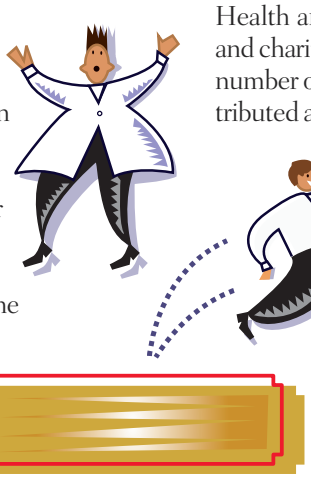
"We'd love to publish more, but it's very hard. We don't have a Baselga, a Piccart or an Armand"

"If it doesn't change, good people won't be recognised as leaders, where they can influence what is going on"

experience for these young people is to go elsewhere for a certain period."

Romanian-born Razvan Popescu, who is now based in Switzerland and also sits on the ESMO awards committee, has led efforts to promote opportunities for young oncologists from CEE countries to visit other institutions to gain experience in research and different models of clinical practice. But he says it is also important to focus on what happens when (and if) they return.

Popescu would like to see greater support for the work of organisations like CECOG, the Central and East European Oncology Group, which are beginning to expand the opportunities for young oncologists to design and conduct clinical trials. He stresses the value such 'home-grown' trials could have for patient care, given that research into the best allocation of resources and optimising treatments that are both good and affordable may be more relevant than some of the research led by the west.



Lack of support for medical research is not just a feature of the less wealthy countries of central and eastern Europe. Miguel Piris, leader of the Lymphoma Group at the prestigious CNIO in Madrid, complains that Spain missed a great opportunity during recent heavy investment in state-of-the-art hospitals. Though there was a significant – and welcome – increase in clinical posts, there was no accompanying agenda to promote research, despite the excellent potential offered by these new centres.

Martine Piccart mentions the UK as a positive example, where a national initiative to promote involvement in clinical trials in 2001 helped boost cancer patient inclusion to 12% and opened up new opportunities for young oncologists. The National Cancer Research Network (www.ncrn.org.uk) is a collaborative effort between clinicians, the Department of Health and funding bodies – both state and charitable – sustained by a significant number of 'clinician researcher' posts distributed across the UK's cancer hospitals.

In France, the National Cancer Plan offers a further positive example. The Plan provided significant funding for research, introduced a regional network of seven 'cancero-poles' (networks) to coordinate and promote research, and provided a back-up team to assist hospitals in building their clinical research capacity. These measures undoubtedly opened new opportunities for young oncologists, though there are growing calls for the decentralisation of research funding – currently concentrated in the hands of the French National Cancer Institute INCa.

Both the UK and France have specific training pathways for 'academic clinicians', which integrate research into the residency programme. This decreases the element of luck about who gets opportunities to develop their research capacity. Indeed, many respondents to the *Cancer World* survey asked for just such training pathways in their own countries. However, there seems to be a feeling among young French and British oncologists that this system forces them to choose between being a clinician or an academic very early, making it harder to change direction as their careers develop.

Lack of opportunity for continuing medical education is also heavily flagged up in the *Cancer World* survey. Though all areas of oncology are heading rapidly towards subspecialisation, there are few opportunities to attend high-quality courses. It is this gap, above all, that the European School of Oncology has sought to fill. It offers a one-week full-immersion masterclass for oncologists in their early 30s to give them a good overview of the field and help them decide which subspecialism to follow. Courses are free, and students continue to receive mentoring from faculty members for several years; however, only 50–60 places are available each year. There is also a pressing need for continuing medical education courses in oncology subspecialties. Currently, ESO is almost the sole non-industry provider, offering short courses in a variety of languages, also free of charge.

Academic–clinical tension

The uneasy relationship between academic and clinical structures seems a major barrier. In France the best treatment and research in solid tumours is done in 20 cancer centres outside the university hospital system. But a young doctor aiming for the prize position of 'professor' has to build a career in one of the university hospitals. "You need to

"When they evaluate you for promotion, what counts is research and publication – not patient care"

clone yourself," said one young oncologist, "It can be very hard to know how to organise your career."

The situation in Italy is not dissimilar. Riccardo Vigneri, who has sat on Italy's national CME accreditation committee for the past 10 years, says that many university hospitals are so poor at treating cancer that they don't have enough patients to be able to teach, and have to farm students out to other hospitals for their clinical training. There they tend to be taught by the head or assistant head of oncology, who is not trained to teach and gets nothing back for teaching. "They often use the trainee oncologists as menial workers. If they do research, it is second class, doing protocols directed by the industry. Their critical faculties are not being engaged to really understand what is going on."

Italy has some excellent cancer centres which offer superb training opportunities for the minority of students who are lucky enough to be recruited. But a doctor who wants to build an academic career must stay at the university, often going from one short-term contract to the next, hoping to be chosen as successor to the incumbent professor.

The system is unfair and deeply unpopular, as many of the Italian respondents to the *Cancer World* survey indicated. Vigneri says, "If it doesn't change, good people won't be recognised as leaders, they won't get into positions of power where they can influence what is going on around them."

The tension between the clinical and academic sides, common to all medical fields, is exacerbated by the way oncology is often fragmented across departments. This is a particular problem for cancer surgeons, who not only have to split their training across a number of units – neurology, gastro-intestinal, pneumonology – but also have to compete with non-cancer surgeons for senior departmental posts.

Financial pressures are now prompting many governments to demand greater value for money, and they are introducing performance-based incentives and penalties. Funding for both hospitals and universities is increasingly based on evaluation and competition.

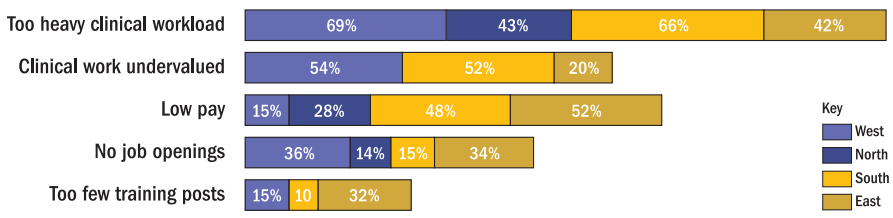
The plus side is that it forces poor institutions to raise their game, and reduces the abuse of personal power and lack of accountability in 'Mandarin' type systems, by introducing transparent and objective measures of quality and merit. Some people, however, think the competition has gone a bit too far. Michael Baumann, professor of radiation oncology and head of the Cancer Centre at the Carl Gustav Carus University Hospital in Dresden, comments, "Sometimes you would simply love some time off from writing grant applications and doing research – at the moment it is too competitive and too little money." He would like to see basic personnel and lab resources guaranteed, with additional grant money available on a competitive basis, more along the lines operating in the UK. "A good mixture of the two would be perfect. At the moment, at least in the poorer places, you have to really fight for grants or you have nothing."

Devaluing clinical work

This heavy emphasis on competition is a growing trend across Europe, and seems to be adding a new dysfunctional twist to the relation between academic and medical worlds. Being an excellent doctor, who keeps abreast of developments, spends time with patients, works well in a multidisciplinary team and enters patients into clinical trials may no longer be enough.

This is one of the key messages of the *Cancer World* survey, in which the second most mentioned barrier to an oncology career was the lack of value attributed to

TOP BARRIERS TO CAREERS IN ONCOLOGY ACROSS EUROPE



Respondents were asked to rate the top three barriers to progressing their careers out of a possible 10 options. The chart shows the top five barriers, with the proportion of respondents from each region who identified each barrier among their top three.
Source: *Cancer World* survey. For further details see www.cancerworld.org/magazine

clinical work when deciding on promotion. Since the number one issue is that the clinical workload leaves no time for research, these two barriers create a vicious spiral.

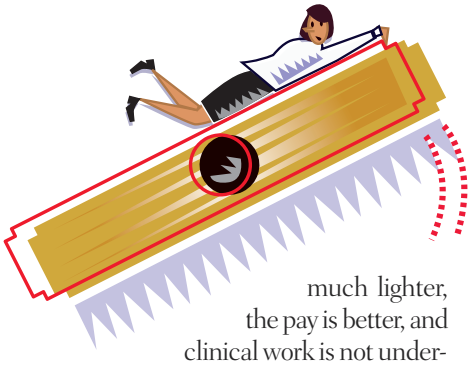
Fatima Cardoso is a senior oncologist at the Jules Bordet institute in Brussels. She has always enjoyed being involved in research, and used to coordinate the translational research unit at the Bordet. But she ended up pulling out of the latter role because she feels very committed to caring for her patients and was finding it impossible to do both.

She warns, however, that choosing to concentrate on patient care is a bad career move for any doctor, and for oncologists in particular. "When they evaluate you for promotion, what counts is your CV – research and publication – nothing to do with patient care. I can understand that if you are applying for a research post, but if you are applying for a position in a hospital, I don't understand why people don't rate your value as a clinician."

Fine ideas about 'translational researchers' in academic posts which allow both clinical care and research work are simply not reflected in reality, says Cardoso. "We are completely overstretched by our full-time work in the clinic. We are going back to having to do the research in our free time."

Cardoso says her generation, now in their early 40s, is suffering because the next generation are not choosing careers in oncology. "They look at my generation, and the way we work, and they tell us: 'I don't want to live the life you lead'. They value their quality of life, so they don't choose this specialty."

At the same time, experienced and committed oncologists are leaving – often to the private sector where the workload is much lighter, the pay is better, and clinical work is not undervalued. "We have lost three senior oncologists in the last two years," says Cardoso, "The workload increases and the workforce decreases."



Andrew Wardley, consultant medical oncologist at the Christie Hospital NHS Trust in Manchester, UK, agrees there is a problem with clinicians being treated as second class within university hospitals. "University hierarchies are only interested in science. In the past few years there has been a big culling of academic clinicians from senior lecturer posts in top UK universities. A lot of people feel the effort to keep up their RAE [research rating based on publications and grants] is not worth it, and they'd rather stay with the NHS."

National policies

At the Jules Bordet institute, Martine Piccart is very aware of the tensions between the clinical and research roles in an academic hospital. "It is the responsibility of the director to recognise the value of very good clinical work," she says, "You cannot function with a team of doctors that do only research, nor with a team that do no research at all. To find this balance is not easy, and to avoid frustrations and jealousies is quite a challenge."

She tries to meet each oncologist individually to agree on their mission. "They may be 100% clinical, 70/30 clinical/research, or 20/80 clinical/research. Once their profile is agreed, we evaluate them yearly in accordance with that profile, because you won't expect someone fully involved in the clinic to publish three papers a year, but you will expect that from someone doing research 80%."

There is a limit, however, to what heads of departments can do in the absence of a joined up approach to healthcare and medical research. Piccart deplores the short-sighted lack of interest shown by many European governments in supporting medical research, and singles out the UK's National Cancer Research Network, for praise. "This is something I consider very impressive."

There is also a limit, she says, as to how much departmental heads can do within a climate that increasingly devalues doctors, and health structures that hugely underestimate the skill and effort required in oncology.

"Governments need to re-evaluate how they support oncology clinics. When I see the time we need as oncologists to explain to patients their diagnosis, what is going to be done, the different treatment options, the side-effects of the treatment… You can easily spend one hour. And when you look at what the hospital gets for that, it is peanuts." The same applies to surgical oncology: "These people often do operations that last hours, and there is a ridiculously small amount of money in place for that kind of surgery."

Even the battle to get recognition for medical oncology as a specialty has not yet been won in many countries. "That's the first step and we are not there yet. How can you be attracted to a profession that is not even recognised, and where the things you do are permanently underpaid?

"How can you be attracted to a profession where the things you do are permanently underpaid?"

Personalised medicine: the dream and the reality

Marc Beishon

Recent years have seen a scramble to identify the genetic variance that predisposes or protects against certain cancers and the tumour gene signatures that could indicate which therapies will work and which won't. A picture is now emerging of an infinitely complex field that is unlikely ever to live up to the high hopes of some scientists, but is certainly confounding the sceptics.

The lay public must be a bit confused about the term 'personalised medicine', which has become one of the hottest health topics at present, judging by the sheer number of mentions it is getting in the mass media. On face value, it seems to imply that we have arrived at a promised land of individual treatment, certainly where the genetic make-up of people and disease is concerned. After all, the one concept that everyone knows is that we are all – bar identical twins – genetically different from each other. But in fact we are far away from applying many different, individual treatment regimens based on genetic characteristics.

What personalised medicine currently means in practice is treatments or procedures that apply to groups of people, although those groups could be quite small parts of the population. In general medicine, a transfusion of a certain blood type is a 'personalised' approach. In cancer there are many that can be mentioned, such as the Herceptin (trastuzumab) monoclonal antibody for Her2-positive tumours and screening for the BRCA1 and 2 breast cancer genes. A recent technique showing promise allows personalised levels of chemotherapy dosing for colorectal cancer patients based on a blood test, rather than the 'gold standard' of calculating drug dose by body surface area.

It is genomics – and all the other molecular sciences such as proteomics – that are making the running in the personalised medicine debate. One person's tumour is as different from another's as a fingerprint or iris, so it is no wonder that cancer is a prime target for personalisation. There is now a massive body of published papers – more than 50,000 alone on molecular signatures for cancer, for example.

Interest and publications are also growing fast in complex genetic variance that may confer risk (or protection) – hardly surprising as the human genome has now been sequenced. Luminaries such as Craig Venter and James Watson have had their own DNA analysed (in Venter's case this showed he had no known indication for skin cancer – and yet he did develop melanoma).

There has been a lot of hype about the value of both genetic variance and tumour profiling. Helping to bring us down to Earth is a professor who is expert in research methodologies with a special interest in genomics and cancer, and is helping to navigate what is becoming an exponentially complicated field. John Ioannidis, head of the department of hygiene and epidemiology at the University of Ioannina, Greece, made waves with a paper, 'Why most published research findings are false' (*PLoS Medicine*, 2005). He suggested that the hottest scientific fields – with many research teams involved – are less likely to come up with true findings, and there is 'ping pong' between extreme positive and negative results – and no topic illustrates this better than molecular genetics.

Markers of risk

Bearing this 'reality check' in mind, Ioannidis is by no means pessimistic about progress, and has an overview of where we currently are in both genetic

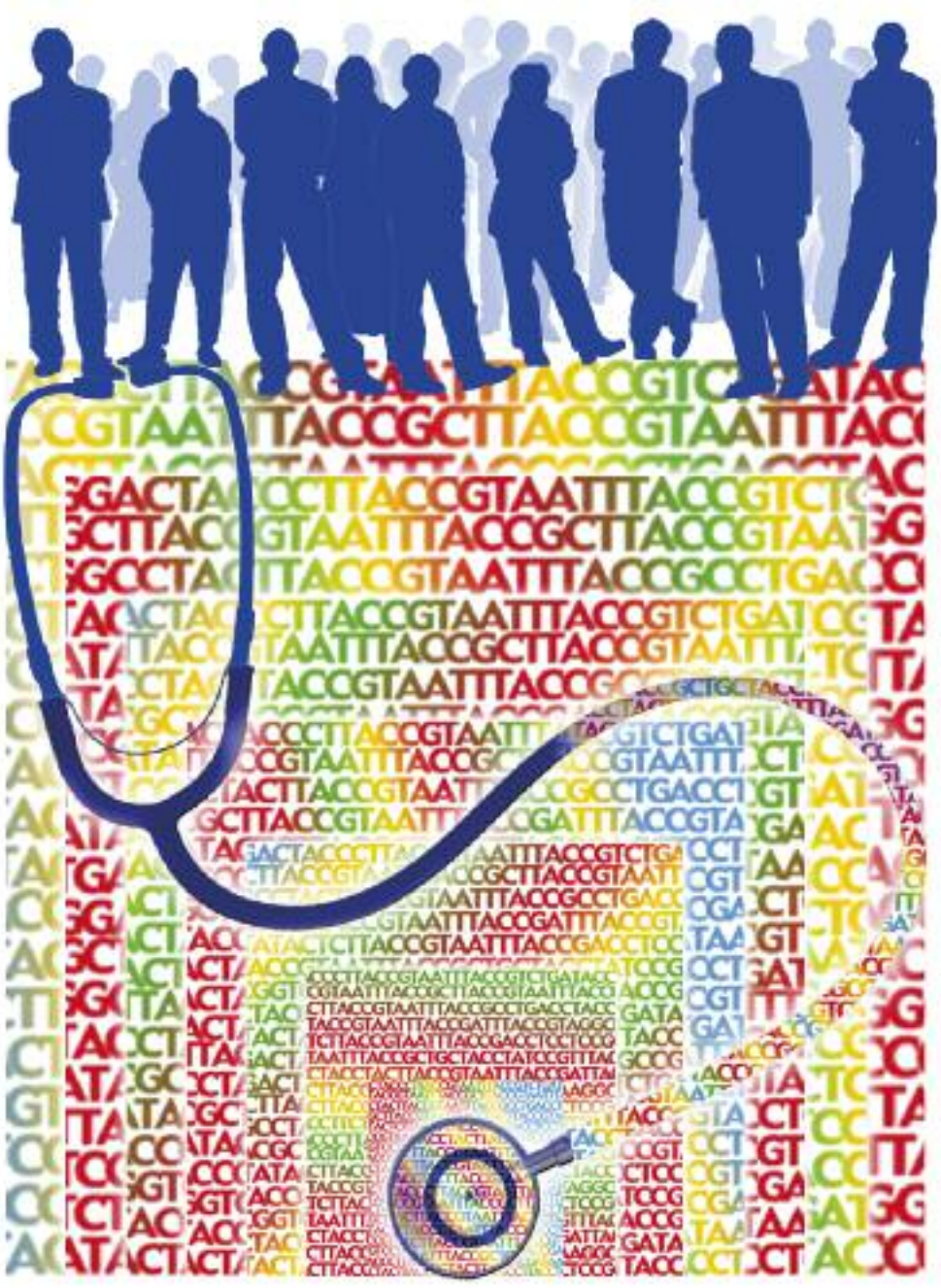


ILLUSTRATION: JANE ADES, NHGRI

variance and tumour profiling. "For genetic variance that confers risk or protects people from cancer, we have now seen identifiable progress for the first time in long while," he says. "Until recently, we had only found syndromes with a high penetrance – meaning there are few genetic factors that could contribute an enormous level of risk, but were very uncommon – but they do not explain why most people get cancer." Well-known syndromes include hereditary non-polyposis colorectal cancer, Li-Fraumeni syndrome, the BRCA1 and BRCA2 genes and so on.

Now, he adds, there are more reproducible findings about genetic variance carried by 10%–30% of people that increase or decrease risk of specific cancers. "We have had most luck with breast and prostate cancer, and found half a dozen common variants, each of which increase or decrease the relative risk of getting these cancers by about a fifth, e.g. from 5% to 6% or 4% in terms of absolute life-time risk." The variants, he says, are single nucleotide polymorphisms (SNPs, also known as 'snips'). "Someone has, say, an A instead of a T in a sequence – but we don't know whether these are the real culprits and are directly increasing risk. They could be mirroring some other genetic site they are linked to. All we really know is we have found markers for some genes – and that's about it." SNPs are found in both coding regions for genes (and so could alter proteins) and non-coding regions (where proximity to a gene can act as a marker). There can be millions of SNPs in each human genome.

"We have found half a dozen common variants, each of which could alter your relative risk by about one fifth"

"We may never be able to answer how bad exactly it is to have two bad variants that interact"

With this level of information, not much individualisation can be done – and the human genome has been screened 'pretty efficiently' now. "At best, we can explain maybe 5%–10% of the variance of the genetic risk of people getting these cancers – just a small amount of the total variability. But other tests – such as the PSA test for prostate cancer carried out on healthy men – are crude measures with low predictive ability, so we may be doing as well and a bit better than before."

Ioannidis says that going beyond identified variants that contribute to single individual risk means looking at many common variants, some of which may contribute an amazingly small increase in risk. "And that is extremely difficult to pick up, even with very large epidemiological studies." Identifying combinations is a daunting task – testing pairs of say a million each is 10^{12} interactions – testing for three is 10^{18}, and pushes even our fastest computers beyond their capability. "We may never be able to answer well the question of how bad exactly it is to have two bad variants that interact."

What the results do offer are opportunities to pursue biological studies. "If we have gene variants with *P*-values of 10^{-20} – and sometimes we are getting to that high level of probability now – we can search for the genes related to the variant and try and understand what goes wrong. There is the possibility they reflect biological pathways and machinery we do not really know about, and maybe we can develop new treatments based on the research – but it is just a promise."

Turning to molecular studies on tumours, it is striking, says Ioannidis, that despite the immense literature built up over the last 10 years, which is more advanced than that on genetic variance, the findings are modest.

For a start, an objective of improving survival by applying molecular signatures has been tempered with more modest aims such as learning how to use chemotherapy more effectively and to minimise unnecessary treatment for those who would not benefit. "We are looking to improve the accuracy of classification for predicting what would happen to patients – where of course the classic application is in breast cancer."

So far, there has been a small gain in predictability, says Ioannidis. "We could classify 65 out of 100 people correctly in the past. Now it is about 70. The number depends on the participation of different subgroups of tumours you have in your sample, so this is a simplified statement, but the gain is modest." That so much emphasis has been placed on the 'hot results' of gene profiling is understandable, he adds, in such a rapidly blossoming field, but there must now be a concerted effort to develop more rigorous methodologies.

"In particular, we must start much larger studies to improve the accuracy of molecular signatures and to reduce the 'noise' level, and it would certainly help if we have more robust validation and replication plans. Until now, most are small studies on a few dozen or maybe a few hundred samples, and validation procedures have sometimes been very shaky."

At least half of papers, in his estimation, have serious methodological problems that could exaggerate their validation performance, especially for cross-validation (i.e. when not using new data). "Many are very complex studies that require a lot of effort in design, analysis and reporting, and are very rich in data. Even minor divergences can produce huge biases."

Markers of response

Two very well known studies that include large sample numbers are the European-based MINDACT trial (Microarray in Node Negative Disease may Avoid ChemoTherapy – see also *Cancer World* 7, July–August 2005), and, in the US, TAILORx (Trial Assigning IndividuaLized Options for Treatment), both of which are looking at molecular signatures in node-negative breast cancer to avoid unnecessary treatment and which are aiming for patient numbers of 6,000 and 10,000 respectively. "They are trying to validate the clinical performance of molecular signatures and I am quite happy if, as a result, we can just improve quality of life and minimise toxic side-effects," says Ioannidis.

A good review article of the progress and practical limitations of this technique, 'Enabling personalized cancer medicine through analysis of gene-expression patterns', has recently been published in *Nature* (3 April 2008) by Laura van 't Veer and René Bernards, pioneers of gene expression profiling who developed the MINDACT signature (see also *Cancer World* 12, May–June 2006).

A feature of the molecular signatures that puzzles many outside the field is that there is little or no commonality between the signatures of identified genes for a particular disease such as breast cancer. As Ioannidis explains, this is probably because there are several genes that have the same effect on the cell cycle, carcinogenesis and the spread of the tumour. Most of these genes are proliferation genes, he says. But having more commonality in the signatures and larger sample sizes should improve accuracy (and also reduce the majority of genes that are just 'noise' in most of the signatures currently used).

So with this 'proof of concept' and with large studies, Ioannidis' guess is that we will be able to increase correct patient classification to about 80–85 out of 100. The gene expression and microarray techniques used in trials such as TAILORx are not the only biological profiles that could show promise, he adds: "Microarrays and gene expression is one level, and other levels include proteomics, metabolomics, epigenetics, nutrigenomics, and instead of measuring messenger RNAs measuring micro RNAs. They can all offer complex biological pictures we can look at, but again there are only pilot studies on very small numbers at present. We need to investigate which techniques are best to take further."

As with genetic variance, his take on what we are likely to see is a small, incremental contribution from adding various techniques – again pointing to the need for large-scale studies of even greater complexity. "Each is a snapshot that may not be independent from another. They should all be pursued."

The TAILORx and MINDACT trials do show that where there is backing from funders, widespread collaboration on large sample sizes for molecular signatures has no barriers. But as Ioannidis also points out, there is irony at present in the way that most of the studies are carried out when compared with work on genetic variance. "The paradigm of molecular signature studies is for one or two centres to do research with a low number of samples, but often investigating a few dozen or maybe several hundred gene expressions. But the genetic variance studies are now screening huge numbers of people for just a single gene variant, or maybe a few."

The genetic variance research did start with relatively few participants, but now there is work on populations of 100,000 or more. "People will not be able to publish in major journals in this field unless they use massive platforms for genetic measurement, and that means massive sample sizes." Consortiums are now looking at variance and susceptibility for diseases such as type 2 diabetes, breast cancer and osteoporosis, with as many as 50,000–150,000 participants, notes Ioannidis, while smaller numbers – but still over ten thousand – are involved in the search for variants for Parkinson's disease.

The good news, he adds, is that researchers are now looking at combining data on molecular signatures, public availability of data is now greatly improved (most databases were not open to researchers only two to three years ago), and there are papers reporting convincing evidence that different labs can achieve similar results when carrying out gene expression profiling.

That may help to create greater consensus about exactly what results we are seeing from studies. Ioannidis has an amusing example of one paper that could be interpreted as very positive to rather negative, and at several points in between – and which one you prefer depends on your expectations. He concludes: "Overall, the best we can currently do is create stratification of risk for certain subgroups – full individualisation is far away."

10,000 HUMAN GENOME PROJECTS

The National Cancer Institute and National Human Genome Research Institute (NHGRI) in the US has started to build The Cancer Genome Atlas, a hugely ambitious project to map genomic changes linked to cancer. Its pilot phase is examining three tumour types, glioblastoma, lung cancer and ovarian cancer. The scale of the challenge is noted in a *Scientific American* article (18 February 2007) by Francis Collins (director of the NHGRI) and Anne Barker: for the 50 most common cancers the effort would be equivalent to 10,000 Human Genome Projects in the volume of DNA to sequence.

"Where there is backing from funders, widespread collaboration on large sample sizes has no barriers"

A scientist without borders

Janet Fricker

A biostatistician with medical training, **Hélène Sancho-Garnier** helped drive the shift towards evidence-based clinical practice in the '60s and '70s. Stepping nimbly over traditional boundaries, she went on to apply this approach to cancer registries, screening, and now prevention and the ultimate challenge of how to communicate health messages to stroppy teenagers.

In addition to her many achievements in the fields of oncology, biostatistics and public health, Hélène Sancho-Garnier has the distinction of being born on September 3rd 1939 – the day World War Two broke out. Her career has spanned the initiation of clinical trials in France, the launch of cancer registries and the development of screening programmes. Throughout this disparate work runs a common theme – the need to introduce evidence-based practices into all aspects of medicine. Today the full force of her fighting spirit is focussed on Epidaure, the education centre for cancer prevention in Montpellier, where she is taking on the challenge of finding strategies for communicating to France's young people, and for evaluating the proposed strategies.

Having grown up on the left bank of the Seine, Sancho-Garnier remains at heart a Parisian, but with an Iberian twist from her marriage to Spaniard Isabelo Sancho-Lopez. Early years were inevitably dominated by the war. Just three days after Hélène's birth, her father, the proprietor of a bespoke shirt making business in the Boulevard St Germain, went to the front. He would be away from his young family for three years after being taken prisoner. Two uncles fought for the French resistance – one was shot and the other died in the gas chambers. Her mother was taken for questioning by the Gestapo after a search revealed a typewriter on the shop's premises. Happily it was broken and they were unable to prove that she had used it to forge resistance documents.

Sancho-Garnier has few memories of occupied Paris – the knowledge came later when her mother told the teenage Hélène and her older brother Gérard and younger sister Michèle the story of her war. She recalls a happy, carefree childhood. "They called me Papillon because I danced along the boulevards, jumping over the stones. I was a *garçon manqué*, spending my time ice skating, swimming and playing tennis."

Academic studies came easily to her. "The decision to study medicine was greatly influenced by the area of Paris in which we lived. Doctors came to the shop and my school friends had fathers who were doctors, so it seemed the natural thing to do. I longed for adventure and had romantic visions of working in Africa."

In 1959 Sancho-Garnier enrolled in medical school. Student days were dominated by politics, organising demonstrations against the brutal suppression of the Algerian independence movement. She is clearly a woman who does nothing by halves. Politics was so all-consuming that it threatened to

sabotage her medical career, as she could not find the time to sit the examinations (*internat*) required for French doctors to work as clinicians in hospitals.

Pathology was one option she was qualified to take that would enable her to work in a hospital, so she decided to move to the Gustave Roussy Institute, the biggest cancer centre in Paris, to complete her studies. Here she buckled down, sitting her hospital examinations, and becoming interested in skin cancer. She divided her time between seeing patients in the morning and working in the lab in the afternoon.

A career defining moment was a meeting with Evelyne Eschwege, a young scientist organising the first ever clinical trial in France, randomising babies with angiomas to receive radiotherapy or no treatment. When Eschwege went on maternity leave she asked Sancho-Garnier to mind her project. The study, which showed angiomas resolved just four months faster with treatment than without, led to the publication of Sancho-Garnier's first paper, and brought her to the attention of Daniel Schwartz, who was in the process of setting up the first medical biostatistics school in France, and was head of a research unit at INSERM (France's National Institute of Health and Medical Research). In 1964, Schwartz recruited her to his research unit. Part of the

attraction of the career change was her competitive relationship with her brother Gérard, now a professor of physics, who had always ribbed her about medicine requiring no more than good memory skills. "I wanted to prove to him that I was perfectly capable of doing some kind of maths," she says.

In her new role, Sancho-Garnier divided her time between clinical work in cancer dermatology at the Gustave Roussy and providing biostatistical support to a growing number of oncology trials and clinical research projects, driven by Robert Flamant, Schwartz's first medical *élève* and head of the first biostatistical unit at the Gustave Roussy. She also developed an interest in prognostic evaluation – looking at how best to adapt treatments to the individual characteristics of patients and their tumours – and in epidemiological studies of the causes of cancer.

It was an extraordinarily productive period. She inevitably appeared as second author on a great many papers, and also wrote her own papers taking an overview of the concept of clinical trials. She reviewed issues such as knowledge acquisition from randomised trials and their role in establishing treatment policies. Sancho-Garnier can take some credit for placing the concept of clinical trials on the medical agenda. "Being medically trained, it was easier for me to ask the clinicians to introduce good methodology into their clinical trials. I understood the clinical perspective and ethical difficulties."

At the same time as launching her career, Sancho-Garnier was juggling further training (taking degrees in both biostatistics and head and neck cancer) and raising three children. In 1963 she had married Isabelo Sancho-Lopez, a Spaniard working for the Organisation for Economic Co-operation and Development in Paris. The couple had met on a blind date organised by her sister, who thought she was overworking and needed a bit of light relief. Sancho-Lopez's family came from Toledo, but had been forced into exile in France and Brazil after fighting Franco in the Civil War. The couple soon had three children – Marie Christine born 1964, Isabel born 1967 and Xavier born 1969. Sancho-Garnier acknowledges the unswerving support of her maternal grandmother, Marie, then a vigorous 80-year-old, who kept the household going during this busy period.

She and her husband divorced in 1976, but she still thinks that, overall, marriage was a positive experience. "We had three wonderful children together and he taught me the Spanish language and culture." Sancho-Garnier never remarried. "With three children it would have been difficult to find someone, and I wasn't looking," she says, adding with Gallic candour that life has not been without its *divertissements*.

A career woman

With the marriage over, she threw herself wholeheartedly into her career. "I have a big capacity for work. Early on I learnt that for women to have successful careers they can't afford to spread themselves too thin. Many women prefer to have all sorts of other things than work in their lives, then it's to be expected that they are overtaken by male colleagues."

Designed to inspire. Sancho-Garnier with her team at the Epidaure cancer prevention centre in Montpellier (photomontage). The bold architecture provides a stimulating setting for the school children who visit Epidaure's interactive health education centre

Sancho-Garnier can take some credit for placing the concept of clinical trials on the medical agenda

An internationalist. Sancho-Garnier has always sought to extend her contribution beyond the borders of France. She is pictured (right) at an oncology congress in Cairo in the mid-1970s, while she was still based at the Gustave Roussy Institute. The picture below was taken in 2007 at a screening training session at the National Cancer Institute of Uruguay, which she helped organise in her role as the UICC strategic lead for prevention and screening

The hard work paid off in 1988 when she was appointed head of the biostatistical department of the Gustave Roussy, after Flamant was promoted to director of the Institute. With success came opportunities to play a role on France's national oncology stage. Highlights included involvement in the National Commission for Cancer, with Yves Cachin as chairman, which recognised for the first time the importance of population-based cancer registries.

"Cancer registries are vitally important to measure the burden of different cancers. They help resource planning, flagging up where we need to do epidemiological research, and can be a way of evaluating prevention initiatives."

The commission proved a challenge, as it would have been hugely expensive to produce a national registry. "We've solved this problem by having coverage of 10%–15% of the territory with separate registries, which can be used to estimate what's happening in the rest of the country."

Screening became an area of expertise. After landmark trials from Sweden showed that breast screening results in 30% fewer deaths, Sancho-Garnier was recruited to a healthcare commission, headed by Maurice Tubiana, set up to organise the first large-scale breast screening programmes in France. The commission discovered that a majority of the mammography machines in use were obsolete and set about lobbying the Department of Health to lay down mandatory minimum standards and quality control. This was probably the biggest benefit to come out of organising these large-scale programmes, as opportunistic screening was already being used by 40% of the population.

Quality assurance is essential, she says, to keep false-positives and false-negatives to a minimum. As mammography uses ionising radiation, it is also important to ensure the equipment is working correctly, the proper techniques are used and regular testing doesn't start too early and isn't done too frequently. She is uneasy about the screening that is being undertaken in younger women with genetic susceptibilities to breast cancer "The gland tissue is more sensitive to ionising radiation and, because of the density of the breast, mammography is less sensible as it leads to more false-negatives," she says.

Particular issues arise in developing countries, where mammography machines are of dubious quality and inadequate treatment infrastructure is in place. "If you don't have good structures for diagnosis and care, you're doing more harm than good," she says. "Where the extent and quality of the

infrastructure are insufficient, it is important to implement adequate structures and professional training before organising any screening programme."

From screening to prevention

It was Sancho-Garnier's expertise in screening that helped her to make the career transition from biostatistics to public health. In 1991 she was appointed head of INSERM's cancer epidemiological research unit, where she managed a department of more than 40 people in addition to her work at the Gustave Roussy. To her disappointment, the atmosphere was not particularly easy, and she tired of the internecine fighting between her staff. With her children having left home, she felt weary and ready for a change.

A chance remark at a dinner to Henri Pujol, creator of the Epidaure cancer prevention centre, about how much she liked the city of Montpellier, eventually resulted in a job offer to head the Epidaure (part of the regional cancer centre), together with a chair in Public Health at the University of Montpellier. "I loved Montpellier's architecture and climate, and I felt its proximity to the Spanish border combined my French and acquired Spanish culture," she says.

Today she remains based at the Epidaure, an education and training centre housed in an innovative building resembling a space shuttle. "The building was designed to inspire the imagination and show children there are no limits," she says.

Each day parties of school children visit to increase their understanding of health prevention and hopefully change their behaviour. One of the highlights of the two-hour tour is a smoking machine that graphically illustrates how tar accumulates in the lungs. There is also an interactive film where you can change the lives of actors according to the interventions they take. While the activities are principally for children in the Languedoc-Roussillon region, the centre has produced tool kits and training to enable teachers across France to introduce health education messages throughout the French national curriculum. Help is on hand for subjects as diverse as History, Maths, Science, Physical Education, French and English. "Hearing the same messages across all their lessons helps to consolidate the children's health behaviour," she explains.

Teenagers pose particular challenges for the unit. "They're always argumentative. If you say it's red, they'll say no it's black. They live for the moment, and don't care in the least about future health risks." With such formidable challenges, might it not be easier to just leave them well alone until they grow up and become more receptive to messages?

This, says Sancho-Garnier, would be totally irresponsible. "It's a particularly dangerous time, when young people are at risk from alcohol damage and becoming addicted to tobacco and other drugs. They're starting their sexual lives and risk

Kids! Marie-Christine, Isabel and Xavier, demonstrating the teenage capacity to live for the moment. Sancho-Garnier brings a mother's experience to the task of developing strategies for communicating health messages to this difficult age-group

"Teenagers live for the moment, and don't care in the least about future health risks"

"I want to teach my grandchildren the importance of being critical... I want them to ask for the evidence"

exposure to HPV and HIV. You have to try and convince them to take the best possible care of themselves."

The best strategy for getting through to teenagers that Epidaure has used is the peer mentor technique, where younger teenagers are paired with older teenagers who help show them appropriate behaviour. They are also developing tools to show teenagers how they are manipulated by various publicity techniques, particularly from the tobacco, food and alcohol industries.

Critical young minds. Subjected to all the usual manipulative messages from the tobacco, food and drinks industries, Sancho-Garnier's grandchildren are valuable and willing guinea pigs for testing prevention strategies

Coming from her background in biostatistics, Sancho-Garnier took time to appreciate the full dimensions of education. Her current ambition is to incorporate scientific methods into prevention.

"In medicine I was one of the first people to introduce an evidence base for clinicians. Now I'm working with educators I want to incorporate the same scientific rigour and introduce ways of properly evaluating the effectiveness of prevention and the full impact of our contact with children," she says.

Still an internationalist

Since 1998, Sancho-Garnier has served as the French representative at the International Union Against Cancer (UICC). It is a venture that is particularly close to her heart, as she is keen to improve the situation of people with cancer in developing countries, focussing on French- and Spanish-speaking regions.

In 2002 she became the UICC's strategic leader for prevention and early detection. Among her many achievements is the publication of a handbook reviewing the evidence for different cancer prevention strategies, with editions for Europe, Latin America and South Asia. "The idea is to help governments to prioritise the interventions that are important, and the situation varies in different areas," she says, adding that they are currently preparing a handbook for the Mediterranean region.

Like most successful women, Sancho-Garnier's career has not been without sacrifices. "My children now tell me that I wasn't home enough when they were young. I have no big regrets. To function as a mother I needed to feel fulfilled in my career."

The children, one senses, rebelled by not following traditional academic paths. Marie Christine was an airhostess before giving up work to care for her family, Isabel works as a marketing manager in Madrid, while Xavier works in the construction industry. Her six grandchildren offer the opportunity for reinvention and the healing of past differences. Ranging in age between one and 13, they also provide willing guinea pigs to road-test her health education messages. "Above all I want to teach my grandchildren the importance of being critical, and not just accepting the things they are told. I want them to ask for the evidence," she says.

Retirement is not a subject she cares to dwell on, although she is amused that for once this is an area where being a mother of three works in her favour. "In France, as a university professor who has had three or more children, you can work for an extra year," she says. "I don't want to retire, there's still lots to achieve and I really do want to get further in providing an evidence base for primary prevention."

Tackling cancer in the Middle East

Euro-Arab School of Oncology contributes a mix of international and local expertise

➜ Jim Boumelha

Cancer is now the fastest growing killer in the Arab world. There is an urgent need to train health professionals on strategies for prevention, screening and appropriate care, and convince governments to act. ESO hopes to contribute to this effort through its Euro-Arab partnership.

For several centuries the Arab world has been viewed by European rulers and power-brokers with a mix of suspicion of its colonial advances in Europe's southern and eastern flanks and curiosity about its cultures and advances in science, in particular medicine. In modern times the New Arab World is slowly emerging from decades of societal and political turbulence to become once again an inevitable partner for Europe. The exchange of ideas and information is flowing again in many fields including medicine and, above all, the fight against cancer. The Euro-Arab School of Oncology (EASO) is one of the most recent manifestations of this.

EASO first emerged as a good idea from discussions between enthusiasts including Mohsen Gadallah, epidemiologist at Cairo's Ain Shams University, Alberto Costa, director of the European School of Oncology (ESO) and Francesco Aloisi, former Italian Ambassador to Egypt, and they nurtured it step by step until it became a reality. "When it was first conceived" said Aloisi, "we had high hopes but little experience."

Gadallah, now co-chair of the organisation, traces the swift progress of EASO to its sound foundation: an agreement signed in 2005 between ESO and the Egyptian Ministry of Health and Population. "We used our first event, Advances in Clinical Oncology, in Cairo in March 2006, to attract practitioners from other Arab countries," says Gadallah, "as well as Egypt, they came from Libya, Lebanon, Yemen, Sudan and Saudi Arabia. We knew then we were handling it right." This was followed by a masterclass in Cairo, an EASO course in Alexandria, and, most recently, an EASO lung cancer course in Damascus, in cooperation with Al Bairouni teaching hospital and the Syrian Oncology Association.

The bureaucracy is, and will probably remain, very light, as EASO is run by an executive committee of three. The emphasis has been on encouraging health ministries in other Arab countries to nominate a country representative as a 'focal point' – the link person with EASO. Eight have so far responded and, as their numbers increase, two or three seats will be added onto the executive, which will be held in rotation. Gadallah expects that when EASO attains a critical mass – hopefully by November – it will be able to move from relying on personal contacts to function through the focal points formally designated by each country. There are plans to raise the issue at the meeting of health ministers of the Arab League, to harness their support and engagement.

At its heart, however, EASO is based closely on the model that has been tried and tested to great effect by ESO over the past 26 years, says Aloisi: bringing together young oncologists, who have completed their formal training, to learn from top international experts, to help reduce the number of diagnoses that are mistaken or too late, and avoid needless suffering from inappropriate treatment.

The Arab world covers 300 million people, with a wide social, economic and cultural diversity and spread across 22 countries. Inevitably, due to environmental, genetic and other factors, the

Euro-Arab School of Oncology

المدرسة الأوروبية العربية للأورام

PETER McINTYRE

Spreading the news. A well-attended press conference at the Damascus masterclass provided an opportunity for local journalists to learn about the scale of the problem and what needs to be done... and to ask questions about how Syria is gearing up to confront its growing cancer problem

incidence of different cancers varies from one society to the next, as do the barriers to effective cancer control. Adapting to local conditions is therefore a core challenge facing EASO. To tune in to the needs of the society concerned, says Gadallah, the first step must always be to consult with the local specialists.

"When we select a country for a symposium, we study the most prevalent cancer in the area and we concentrate our symposium in this area. The country that hosts the programme will benefit from experts coming from Europe to talk about the problem in this country. Of course we cannot cover all problems of all Arab countries, but there are some they have in common – lung cancer for instance."

But EASO is also keen to go beyond specialists at local cancer societies or teaching hospitals, to involve governments, says Gadallah, "We have to be sure that the ministry of health is represented as well as academics. Only then can recommendations for a cancer plan, or for early detection or a new protocol for management, be taken further."

When EASO first started to look for a venue outside Egypt, it contacted several countries. Syria was selected not just because the Syrian group of academics made a serious offer, but also due to the support expressed by the Syrian authorities.

Today the fight against cancer is gaining currency with ministries of health throughout the Middle East, partly because of the increasing work undertaken by the Eastern Mediterranean Regional Office of the World Health Organization (EMRO), but also because of the growing incidence of the disease in the region. EMRO estimates that cancer is currently the fourth highest cause of death in the region, with breast, bladder, lung, mouth and colon being the most common sites. Around 240,000 people die from the disease each year and, alarmingly, this figure is expected to more than double by 2015.

According to Ghada Muhjazi (pictured above, right), from EMRO's Damascus office, while an aging population accounts for some of this projected rise in cancer deaths, "it is changes in lifestyle and behaviour that have become the overwhelming factors." She mentions in particular that people are tending to eat more meat while reducing their fruit and vegetable intake, adding that "40% of cancer cases can be prevented through changing lifestyle and behaviour and others can be treated if diagnosed early."

EASO is determined to play its part in helping the region address this escalating threat from cancer, but it understands that trying to import solutions developed for the European context won't do the trick. "It's not a case of one party imparting knowledge and the other absorbing it," says Gadallah. "Our own experience was also taught at the last three events, and we try to make it an equal exchange of ideas. For example, in Europe they use mammography, but in this region we think that breast examination can be more

effective. We don't use exactly what is used in Europe – we modify it to fit with our culture and our society."

Teaching remains at the core of the mission, but there are many other issues that EASO organisers recognise must be confronted, such as health education and the infrastructure and organisation of cancer services, which involve interacting with authorities and decision makers.

One big challenge is setting up national cancer registries, which do not exist in 50% of Arab countries. For epidemiologists like Gadallah this is a major problem, as they can deal only with estimates, usually extrapolated from a hospital-based study. "These research findings cannot be strong so long as they don't originate from a national cancer registry," he insists. One idea gaining momentum is to set up a single registry to cover all the Arab countries.

Early detection is another major challenge, a key part of which involves setting up appropriate, quality-controlled screening programmes. Cancer tends to be picked up quite late throughout most of the Middle East. In breast cancer, for instance, 65%–75% of cases are picked up at an advanced stage in countries such as Jordan, Syria, Egypt and Sudan. EASO is looking at the possibility of running masterclasses on screening techniques and teaching epidemiologists how to conduct effective national screening programmes.

Involving ministries of health in the activities of EASO clearly makes sense in terms of getting politicians and policy makers to focus on these challenges and work in the same direction. The question, as always, is how to get governments to match their rhetoric with action?

A press conference organised by EASO at the end of its latest symposium in Damascus provided the opportunity for journalists to pose questions not just about the technical and medical aspects of prevention, screening and care, but also about what action the authorities are taking. One journalist wanted to know what had happened with the Syrian cancer registry – he'd heard a great deal of talk since 2000, but had so far seen no evidence of it. Another commented that it is hard to get stories about smoking and the related health problems into newspapers, speculating that cigarette companies are very powerful and have links with the newspaper owners.

Such scepticism is, perhaps, understandable, given the schizophrenic approach many governments have to the tobacco industry. In Damascus, for instance, just as the ministry of health was welcoming the EASO symposium on lung cancer, the deputy minister for economic affairs was splashed all over Syrian TV launching a new cigarette factory as part of a deal with the British-American Tobacco Company. The media, and the public, have good reason to question how this squares with the WHO Framework Convention on Tobacco Control, to which Syria is a signatory.

Tunisian oncologist Farhat Ben Ayad believes that the involvement of civic society is essential to ensure that authorities take action. He cites the work done by his organisation, the Association tunisienne contre le cancer, which has now emerged as the authority on cancer in his country. "We organise international symposia on all aspects of cancer and, at the same time, we feel free to mobilise civic society whenever we need lobbying on major issues," he said. He has been looking for ways to get other countries in the region involved in this work, and hopes to bring in the Tunis-based ALESCO (Arab League Educational Scientific and Cultural Organization). "Any pan-Arab organisation must be supranational, to make it easier for all countries to feel at home."

Though still in the early years of its own pan-Arab mission, EASO is rapidly accumulating valuable experience of working with authorities, bringing together practitioners from different horizons and pressing its own distinct agenda of patient-centred care. With a week-long masterclass on clinical oncology scheduled for Cairo at the end of November, and plans to steadily increase the number of topics addressed and locations used, EASO is quietly building a constructive cooperation between European and Arab oncologists built on a genuine dialogue and shared goals.

Region	% Diagnosed late (breast)
Nile delta, Egypt	70%
Syria	73%
Sudan	78%
Cairo, Egypt	66%
Jordan	69%
Tunis, Tunisia	49% (40% > 5cm)
Iraq	47%
Bahrain	33 % (70% > 2 cm)

In many Arab countries more than 65% of breast cancers are diagnosed at an advanced stage (III or IV)

Source: Cancer in EMRO powerpoint presentation, WHO Syria

The question, as always, is how to get governments to match their rhetoric with action?

Does prophylactic cranial irradiation reduce the incidence of brain metastases in extensive small-cell lung cancer?

Lia Halasz and Noah Choi

A phase III study has shown that prophylactic cranial irradiation decreases the risk of symptomatic brain metastases and may improve overall survival for patients with extensive small-cell lung cancer and response to systemic chemotherapy.

Brain metastasis is a major cause of morbidity and mortality in patients with small-cell lung cancer. Prophylactic cranial irradiation (PCI) is used to treat microscopic or subclinical metastases that are protected from cytotoxic drugs by the blood–brain barrier. Since the 1970s, many trials have evaluated the role of PCI in patients with small-cell lung cancer, but have produced inconclusive results regarding survival benefit.

In 1999, Aupérin et al. conducted a meta-analysis of seven trials that included 987 patients who were in complete remission after chemotherapy for small-cell lung cancer (86% had limited disease), in order to assess the efficacy of PCI.[1] This study showed a 5.4% higher three-year survival rate (20.7 % in the PCI group vs 15.3% in the control group), longer disease-free survival and lower cumulative incidence of brain metastasis in patients treated with PCI compared with controls. According to the analysis of the four total doses (8 Gy, 24–25 Gy, 30 Gy and 36–40 Gy), larger doses of radiation led to greater decreases in the risk of brain metastases.[1]

Slotman and colleagues performed a phase III study to address the role of PCI in patients with extensive small-cell lung cancer who showed any response to 4–6 cycles of systemic chemotherapy (see opposite). The PCI and control groups (each with 143 patients) were well balanced with regard to baseline characteristics. The cumulative risk of brain metastases within one year was 14.6% in the PCI group compared with 40.4% in the control group. PCI was associated with a higher median disease-free survival (14.7 weeks compared with 12.0 weeks in the control group), longer median overall survival from randomisation (6.7 months vs 5.4 months), and a higher one-year survival rate (27.1% vs 13.3%).

In this study, brain imaging was not performed before randomisation unless symptoms indicative of brain metastases were present. Published data indicate, however, that approximately 13% of patients with small-cell lung cancer have asymptomatic brain metastases at the time of diagnosis.[2] Such patients would require a therapeutic dose of radiation (generally 35 Gy in 14 fractions) rather than a lower dose in the range used for PCI.

Conventional wisdom suggests that PCI would not provide survival benefit in patients who have uncontrolled disease at

Lia Halasz is a resident in the Harvard radiation oncology residency programme at Harvard Medical School, and Noah Choi is professor of radiation oncology at Harvard Medical School, distinguished scholar in thoracic oncology at Massachusetts General Hospital Cancer Center and director of thoracic radiation oncology at Massachusetts General Hospital, Boston, Massachusetts, USA. This article was first published online in *Nature Clinical Practice Oncology* on 22 April 2008, and is reproduced with permission. www.nature.com/clinicalpractice, doi:10.1038/ncponc1125, © 2008 Nature Publishing Group

the primary or distant metastasis sites, or both, because of the likelihood of reseeding to the brain after such treatment. Slotman and co-workers, however, demonstrated survival benefit of PCI in a setting where the majority of patients had persistent disease at the primary (76%) and/or distant (71%) sites.[3]

Consistent with previous trials of PCI,[4] no difference was found in cognitive functioning or global health status among the two study arms after short-term follow-up; however, fatigue and hair loss adverse events were reported significantly more often by patients in the PCI arm.

Most patients received PCI at a dose of 20 Gy in five fractions in order to minimise the length of treatment. To improve the therapeutic ratio of PCI, it is reasonable to use a standard fractional dose of 2 Gy for a total dose of 30–34 Gy in patients with a good performance status and a complete response to systemic chemotherapy.[5]

Overall, this study provides good evidence that PCI is beneficial for patients with extensive small-cell lung cancer and any response to systemic chemotherapy.

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Synopsis

B Slotman, C Faivre-Finn, G Kramer et al. (2007) **Prophylactic cranial irradiation in extensive small-cell lung cancer.** *N Engl J Med 357:664–672*

Background. Brain metastases are common in patients with small-cell lung cancer and indicate a poor prognosis. The role of prophylactic cranial irradiation (PCI) in patients at high risk for symptomatic brain metastases who do not experience a complete response to chemotherapy is unclear.

Objective. To determine whether PCI can reduce the incidence of symptomatic brain metastases in patients with extensive small-cell lung cancer.

Design. In the period February 2001 to March 2006, this randomised, multicentre, phase III trial enrolled 286 patients with histologically or cytologically confirmed extensive small-cell lung cancer. All patients had to have experienced a response to chemotherapy in order to be eligible. Specific inclusion criteria included age between 18 and 75 years, WHO performance status of 0 to 2, response following 4–6 cycles of chemotherapy, no evidence of brain metastases, no previous radiotherapy to the head or neck, and no other cancer.

Intervention. Patients were randomly assigned to undergo PCI (n=143) or to receive no therapy (n=143). Radiation was specified to the midline and delivered on a schedule of 4–5 fractions per week using one of the following schedules: 20 Gy in 5 or 8 fractions; 24 Gy in 12 fractions; 25 Gy in 10 fractions; or 30 Gy in 10 or 12 fractions. Radiotherapy had to commence 4–6 weeks after chemotherapy. When any symptoms indicative of brain metastases were present, CT or MRI was performed.

Outcome measures. The primary outcome was the development of symptomatic brain metastases. Secondary outcomes included survival, toxic effects, quality of life and treatment costs.

Results. Symptomatic brain metastases were observed in 24 patients in the treatment group and in 59 patients in the control group. For the irradiation group, the hazard ratio for symptomatic brain metastases was 0.27 and the cumulative risk of metastases was 4.4% at six months and 14.6% at 12 months. The corresponding cumulative risks in the control group were 32% and 40.4%, respectively. Median survival without disease progression in the irradiation group was significantly longer than that in the control group, (14.7 vs 12 weeks; P=0.02) and median overall survival was significantly longer in the irradiation group than in the control group (6.7 vs 5.4 months; P=0.003). Survival rates at one year were 27.1% and 13.3% in the irradiation and control groups, respectively. Acute reactions associated with irradiation included headache, nausea and vomiting, fatigue and skin reactions.

Conclusion. The incidence of symptomatic brain metastases is reduced after PCI in patients with extensive small-cell lung cancer who have experienced a previous response to chemotherapy.

Acknowledgement: The synopsis was written by Mandy Aujla, Associate Editor, *Nature Clinical Practice.*

Comparison of gemcitabine plus platinum analogue with gemcitabine alone in advanced pancreatic cancer

Eileen O'Reilly and Ghassan Abou-Alfa

A pooled analysis of two randomised trials has shown that gemcitabine in combination with a platinum analogue (cisplatin or oxaliplatin) is a potential front-line treatment option in advanced pancreatic adenocarcinoma.

Treatment for advanced pancreatic adenocarcinoma remains a major therapeutic challenge. In 2008, international standards of care include single-agent gemcitabine, gemcitabine and erlotinib[1] and arguably gemcitabine-based cytotoxic combinations that include a platinum agent or an oral fluoropyrimidine. The pooled analysis performed by Heinemann and colleagues (see opposite) adds to the collective evidence that supports the use of a gemcitabine-based cytotoxic combination in patients with either locally advanced or metastatic pancreatic adenocarcinoma and good performance status.[2]

This pooled analysis combines two important trials conducted in Europe. The French Multidisciplinary Clinical Research Group (GERCOR)/Italian Group for the Study of Gastrointestinal Tract Cancer (GISCAD) study compared single-agent gemcitabine with a gemcitabine and oxaliplatin combination, while the German multicentre trial investigated the use of a gemcitabine and cisplatin regimen. The summation of data from these trials indicated that combining gemcitabine with either oxaliplatin or cisplatin, enhances progression-free survival (HR 0.75, P=0.0030) and overall survival (HR 0.81, P=0.031) when compared with gemcitabine alone. The benefits associated with combination therapy were most pronounced in patients with a good performance status (HR 0.82, P=0.063).

The pooled analysis overcomes some of the limitations of small individual trials – the conclusions of which can be limited by a lack of statistical power – and is strengthened by assessment of individual data points. Furthermore, the results of this pooled analysis support the well-recognised value of performance status in delineating patient outcomes. Notably, the conclusions are similar to those drawn by Sultana and colleagues in a larger meta-analysis.[2] A potential weakness of the pooled analysis is that the experimental arm included both standard 30 min and fixed-dose rate (protracted infusion) gemcitabine schedules in combination with cisplatin or oxaliplatin. Of note, and somewhat contrary to the conclusions by Heinemann and colleagues, are the preliminary results of the ECOG 6201 trial, which did not suggest a benefit of a gemcitabine–oxaliplatin-based combination over single-agent gemcitabine.[3]

Given the recent disappointing results of phase III trials of gemcitabine in combination with the antivascular agent bevacizumab,[4] or the monoclonal antibody cetuximab[5] (wherein no benefit was noted over single-agent gemcitabine in either study), the relative utility of a cytotoxic combination can be appreciated. Themes are consistent for cytotoxic combinations, with improved response rates, time-to-tumour progression and clinical benefit

Eileen O'Reilly is an associate member, and Ghassan Abou-Alfa is a medical oncologist, at Memorial Sloan-Kettering Cancer Center, and Eileen O'Reilly is an associate professor of medicine, and Ghassan Abou-Alfa is an assistant professor of medicine, at Weill Cornell Medical University, New York, USA. This article was first published online in *Nature Clinical Practice Oncology* on 29 April 2008, and is reproduced with permission. www.nature.com/clinicalpractice, doi:10.1038/ncponc1128 , © 2008 Nature Publishing Group

Synopsis

V Heinemann, R Labianca, A Hinke et al. (2007) **Increased survival using platinum analog combined with gemcitabine as compared to single-agent gemcitabine in advanced pancreatic cancer: pooled analysis of two randomized trials, the GERCOR/GISCAD intergroup study and a German multicenter study.** *Ann Oncol 18:1652–1659*

Background. Several randomised trials have demonstrated an improved survival in patients with advanced pancreatic cancer treated with gemcitabine plus a platinum analogue compared with patients treated with single-agent gemcitabine; however, none of these studies has shown a statistically significant survival advantage of combination therapy. It has become clear that trials enrolling larger numbers of patients are needed to prove a statistically significant benefit of therapy with gemcitabine plus a platinum analogue.

Objective. To determine whether treatment with gemcitabine plus platinum results in better overall survival than treatment with single-agent gemcitabine in patients with advanced pancreatic cancer.

Design and intervention. This was a pooled analysis of single-patient data from the French Multidisciplinary Clinical Research Group (GERCOR)/Italian Group for the Study of Gastrointestinal Tract Cancer (GISCAD) intergroup study (n=326), which compared gemcitabine plus oxaliplatin with gemcitabine, and the German multicentre study (n=195), which compared gemcitabine plus cisplatin with gemcitabine. Both trials had similar inclusion and exclusion criteria and both recruited patients with histologically proven, unresectable, metastatic or locally advanced pancreatic cancer.

Outcome measure. The main outcome measure was overall survival (OS).

Results. Data were available for 503 patients, 252 of whom were treated with gemcitabine plus a platinum analogue and 251 of whom were treated with single-agent gemcitabine. Overall response rates were significantly higher in patients receiving gemcitabine plus a platinum analogue than among those receiving single-agent gemcitabine (22% vs 14%; P=0.028). The median progression-free survival (PFS) for the study population as a whole was 18 weeks. Pooled univariate analysis of PFS revealed a hazard ratio (HR) of 0.75 in favour of combination therapy (P=0.0030). Subgroup analysis revealed that the beneficial effect of the combination regimen on PFS was greater in the group of patients with locally advanced disease than in the group of patients with more widespread disease (35 vs 21 weeks; P=0.051). In addition, among patients with a good performance status, those receiving combined chemotherapy experienced a longer median PFS than patients treated with single-agent gemcitabine (33 vs 14 weeks; P=0.013). Median OS for the whole cohort was 33 weeks, OS was significantly greater in patients receiving combination chemotherapy than in patients receiving gemcitabine alone (HR 0.81, P=0.031). The most important predictors of prognosis were stage of disease (P<0.0001) and performance status (P<0.0001). Subgroup comparisons among patients receiving combination therapy revealed significantly longer OS in patients with good performance status (ECOG status 0) than in patients with more aggressive disease (52 vs 36 weeks; P=0.063).

Conclusion. The results of this pooled analysis reveal that, in comparison with single-agent gemcitabine therapy, treatment with the combination of gemcitabine plus a platinum analogue significantly improves OS and PFS in patients with advanced pancreatic cancer. Combination therapy seems particularly beneficial in patients with a good performance status.

Acknowledgement: The synopsis was written by Mandy Aujla, Associate Editor, *Nature Clinical Practice.*

being relatively constant across studies.

The consistency of these results indicates that in patients with good performance status and symptomatic or bulky disease, a cytotoxic-drug-based combination is a justifiable treatment consideration. It is currently unclear whether two-drug combinations or combinations comprising three or more drugs will confer optimum benefit over gemcitabine. In addition, the extra toxicity incurred from multi-drug combinations needs to be balanced against the potential benefits.

Notwithstanding the modest incremental value of the treatment option suggested by the results of the pooled analysis (i.e. a gemcitabine-based combination), much needs to be done to improve the treatment options for all stages of pancreatic adenocarcinoma. The identification of new active drugs against novel pathways integral to tumour growth and survival is fundamental. An early venture into the 'targeted world' for pancreatic adenocarcinoma, thus far, has been disappointing and, in relative terms, cytotoxic-based combinations are enjoying an indirect re-endorsement. Hence, treatment options in 2008 include single-agent gemcitabine, gemcitabine-based cytotoxic combinations, gemcitabine and erlotinib and, where possible, an emphasis on clinical trial participation.

Details of the references cited in this article can be accessed at www.cancerworld.org/magazine

NEWSROUND

Selected reports edited by Janet Fricker

Shorter radiotherapy courses may not increase risk of breast cancer relapse

➜ Lancet Oncology

Giving a lower total dose of radiotherapy, delivered in fewer, slightly higher-dose treatments over a shorter period of time is as effective in reducing local relapses in women with early breast cancer as standard radiotherapy of a higher total dose delivered over a longer time, and has no more side-effects, according to a large UK study. However, specialists have cautioned that longer-term follow-up is needed to ensure that this radiotherapy regimen achieves a sustained reduction in the risk of breast cancer relapse.

Radiotherapy after surgery for breast cancer has been shown to reduce local recurrence. This is important, as previous research has shown that avoiding four local recurrences saves one woman from dying of breast cancer. The treatment is traditionally given in 25 daily doses (called fractions) of 2.0 Gy, achieving a total dose of 50 Gy over five weeks. However, hospitals in the UK and Canada have been delivering a lower total dose in fewer, larger fractions – termed hypofractionation – for some time, and retrospective studies have shown that it appears to be as effective as standard radiotherapy in reducing the risk of relapse, without increasing adverse events.

UK researchers have now carried out two prospective studies randomly allocating women to different radiotherapy regimens and following them up for five to six years to assess the rate of recurrence of breast cancer and the adverse effects associated with the different approaches.

In the first study, the UK Standardisation of Breast Radiotherapy (START) Trial A, researchers randomly allocated 2,236 women who had undergone surgery for early breast cancer to receive the standard radiotherapy schedule (50 Gy in 25 fractions of 2.0 Gy over five weeks), or a lower total dose of 41.6 Gy (13 fractions of 3.2 Gy over five weeks) or 39 Gy (13 fractions of 3.0 Gy over five weeks). After an average follow-up of just over five years, the results showed that the rate of locoregional tumour relapse in women given 41.6 Gy (3.5%) was similar to that in women given 50 Gy (3.6%). However, it was slightly higher in women given the lowest total radiotherapy dose of 39 Gy (5.2%).

In the second study, START Trial B, a further 2,215 women with early breast cancer were randomly allocated, following surgery, to the standard radiotherapy schedule or a hypofractionated schedule (40 Gy in 15 fractions of 2.67 Gy over three weeks).

Results showed similar rates of local-regional tumour relapse after five years: 3.3% of women given standard radiotherapy and 2.2% of those given the hypofractionated regimen. A significant reduction was also seen in the rate of distant metastasis and overall risk of death at five years among women treated with the hypofractionated schedule, as well as lower rates of late side-effects.

"The results suggest that a high total dose given in 25 small treatments is no better than simpler schedules, using fewer exposures to a total dose," said John Yarnold, chief investigator for the two studies. "Shorter therapies giving fewer, larger treatments are obviously convenient for patients. These results support the current use of shorter schedules in the UK and in other countries," he added.

Other breast cancer specialists, however, have questioned the findings, arguing that increasing the radiation dose per fraction would be expected to increase normal tissue damage and reduce the therapeutic benefit. They point out that the results from the START trials seemed to be contrary to those seen in studies in head and neck cancer, which show that reducing the radiation dose per fraction at the same time as increasing the number of fractions (hyperfractionation) and the total dose leads to better tumour control and survival without increased toxicity. Much longer follow-up is needed, they argue, to see if the apparently similar reduction in rate of relapse with hypofractionated radiotherapy to standard radiotherapy is maintained over time.

■ The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation

for treatment of early breast cancer: a randomised trial. The START Trialists' Group. *Lancet Oncol* 4 April 2008, 9:331–341

■ The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. The START Trialists' Group. *Lancet* 29 March 2008, 371:1098–1107

Delays in adjuvant chemotherapy worsen ovarian cancer outcomes

➜ British Journal of Cancer

Ovarian cancer patients who start chemotherapy more than six weeks after debulking surgery and those receiving an abbreviated course of treatment are more likely to die than those starting therapy within six weeks and completing the full course of treatment, according to an analysis of two US cancer registries.

Previous studies in ovarian cancer examining the time from surgery to initiation of adjuvant chemotherapy have produced varying results. A theoretical basis for the benefits of early administration of cytotoxic agents was suggested by a mouse mammary tumour model, where removal of primary lesions resulted in increased tumour proliferation.

Dawn Hershman and colleagues, from the Herbert Irving Comprehensive Cancer Center, used the US National Cancer Institute's SEER cancer registry and the linked Center for Medicare and Medicaid Services (CMS) data base to identify 6,047 women aged 65 years or older with stages III–IV epithelial ovarian cancer. A total of 3,585 women underwent surgery and 2,558 (71%) received at least one cycle of chemotherapy. Of these, 1,712 (67%) started chemotherapy within six weeks of debulking surgery, while 846 (33%) began treatment at least six weeks after debulking surgery.

Results show the median survival for women initiating treatment within six weeks of surgery was 34 months compared to 28 months for those beginning therapy after six weeks. Women who initiated treatment after six weeks had poorer overall survival (P<0.0001) and ovarian cancer-specific survival (P=0.009) than women who did not delay treatment.

A second analysis, which looked at duration of treatment, showed that women treated for three to seven months had 16% lower mortality than women treated less than three months.

"Prospective studies of factors that influence the quality of care in women with OC [ovarian cancer] are needed," write the authors, "but until such studies are completed, efforts should be made to facilitate prompt initiation and full completion of adjuvant chemotherapy."

■ Variability in chemotherapy delivery for elderly women with advanced stage ovarian cancer and its impact on survival. JD Wright, T Doan, R McBride et al. *Br J Cancer* 1 April 2008, 98:1197–1203

Lymphadenectomy advised for nodal metastasis from an unknown primary melanoma

➜ Journal of Clinical Oncology

Overall survival is significantly better for patients with melanomas of unknown primary origin than for patients where the primary melanoma is of known origin, according to a recent US study.

For 10%–20 % of patients presenting with palpable evidence of regional metastatic melanoma, no primary lesion can be identified. Proposed causes of unknown primary melanoma (MUP) include failure to recognise the primary lesion during clinical examination, prior removal of the primary lesion during traumatic injury or by excision without pathologic diagnosis, and the unrecognised primary lesion undergoing spontaneous regression.

Some studies have reported poorer outcomes for MUP compared to known primary melanoma (MKP), while others have reported equivalent or better outcomes. The need for clarification prompted Chris Lee and colleagues, from the John Wayne Cancer Institute in Santa Monica, to review clinical records for 13,000 melanoma patients registered on a prospective melanoma database between 1 April 1971 and 31 December 2005.

The study identified a subgroup of 1,571 patients in the database managed with regional lymphadenectomy for palpable nodal metastases within three months of presentation. Of these, 262 had MUP and 1,309 had MKP. For each patient, age (whether they were under or over 60), sex, site of tumour involvement, number of tumour nodes, decade of diagnosis, status of primary (MUP or MKP) and clinical outcome were recorded.

Results show that five-year overall survival was significantly better for the 262 patients with MUP than for the 1,309 patients with MKP (55% ±6% vs 44% ±3%, P=0.0021). Computerised matching of MUP and MKP by four significant covariables (age, sex, nodal tumour burden and decade of diagnosis) yielded 221 matched pairs. Median and five-year overall survival rates were 165 months and 58% ±7% for MUP, compared with 34 months and 40% ±7 % for MKP (P=0.0006).

The most likely explanation for MUP, say the authors, is that an unrecognised primary lesion has undergone spontaneous regression mediated by an endogenous immune response. "Our data strongly suggest that the initial treatment of MUP with nodal metastasis should be regional lymphadenectomy," they write, stressing the importance of an accurate staging work-up that includes complete imaging to rule out distant disease.

"Unless the results of this work-up are positive for metastasis beyond the regional basin, patients should undergo therapeutic (and potentially curative) regional lymphadenectomy as the standard of care."

■ Improved survival after lymphadenectomy for nodal metastasis from an unknown primary melanoma. C Lee, M Faries, L Wanek et al. *J Clin Oncol* 1 February 2008, 26:535–541

One in four do not adhere to aromatase inhibitor prescription

→ Journal of Clinical Oncology

Around one-quarter of early-stage breast cancer patients taking the aromatase inhibitor (AI) anastrozole do not adhere to treatment, according to the largest study of adherence to adjuvant endocrine therapy ever undertaken outside a clinical trial. The US study suggests that a substantial proportion of women with early-stage breast cancer receive suboptimal treatment.

In 2001 the ATAC study showed a statistically significant improvement in disease-free survival for postmenopausal women taking initial anastrozole compared with initial tamoxifen as adjuvant therapy for hormone-receptor-positive early-breast cancer. Previous studies have suggested adherence to tamoxifen among women with early stage breast cancer in the range of 25%–96%. This is important because, across all disease types, adherence has been cited as the single most important modifiable factor compromising treatment outcomes.

In the present study, Ann Partridge and colleagues from the Dana-Farber Cancer Institute in Boston looked at whether similar patterns of non-adherence occur in women prescribed AIs for early-stage breast cancer. The study focused on anastrozole, since it was the only AI approved for early-stage breast cancer during the study period.

Investigators used longitudinal claims data from three large commercial US health programmes: Plan A, Plan B and the Market Scan, which included information on 1,111 women, 1,587 and 4,434 women respectively. For the purposes of the study, receiving medication on less than 80% of days was defined as 'non-adherence'.

Results show the number of days a patient took anastrozole, known as the medication possession ratio (MPR), declined from year 1 to year 3 of the study. For patients in Plan A, in year 1 the mean MPR was 86%, declining to 79% in year 3. For those in plan B, mean MPR decreased from 78% to 62%, while for those in the Market Scan it fell from 84% to 72%. Across all three data sets the proportion of women considered non-adherent ranged from 22% to 31% in year 1, rising to 32% to 50% in year 3.

The results of the study have important implications, say the investigators. "Patients who are non-adherent to adjuvant endocrine therapy may be compromising their care. Oncologist and patient awareness of the problem of non-adherence, and communication regarding the importance of adherence to therapy, may improve health outcomes," they write, adding that future research should focus on identifying patients at risk for non-adherence and on developing interventions to improve adherence.

■ Adherence to initial adjuvant anastrozole therapy among women with early-stage breast cancer. AH Partridge, A LaFountain, E Mayer et al. *J Clin Oncol* 1 February 2008, 26:556–562

Better survival for HPV-positive squamous cell head and neck cancer

→ JNCI

Patients with human papillomavirus- (HPV)-positive head and neck squamous cell carcinoma (HNSCC) show better survival than patients with HPV-negative tumours, according to a US study. The authors are calling for cancer staging systems to reflect these differences.

Previous analyses of HNSCC tumours have suggested HPV-positive oropharyngeal tumours are clinically and molecularly distinct from HPV-negative tumours, and are associated with different prognostic outcomes. In a prospective multicentre study, Carole Fakhry and colleagues from the John Hopkins Medical Institutions in Baltimore evaluated the association of tumour HPV status with response to treatment and survival among 96 patients with stage III or IV HNSCC of the oropharynx or larynx. The subjects – who were participants in an Eastern Cooperative Oncology Group (ECOG) phase II trial – had been administered two cycles of induction chemotherapy with intravenous paclitaxel and carboplatin, followed by concomitant weekly intravenous paclitaxel and standard fractionation radiation therapy. For each subject, formalin-fixed and paraffin-embedded biopsy specimens were evaluated for the presence of HPV16 DNA by *in situ* hybridisation.

Results show that, compared with patients with HPV-negative tumours, patients with HPV-positive tumours have a significantly better rate of response following induction chemotherapy (82% vs 55%; 95%CI 9.3% –44.7%, P=0.01), and following chemoradiation treatment (84% vs 57%; 95%CI 9.7%–44.3%, P=0.007). Furthermore, patients with HPV-positive tumours showed an overall two-year survival of 95% compared with 62% for HPV-negative tumours (95% CI 18.6%–47.4%, P=0.005).

The association of tumour HPV status with survival and response to treatment, say the authors, is sufficiently strong to warrant consideration in the design and analysis of future head and neck cancer clinical trials. "Our data suggest that the risks and benefits of intensive combined modality therapies should be considered separately for HPV-positive and -negative patients," they write, adding that failure to take such differences into consideration could lead to confounding results.

■ Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. C Fakhry, WH Westra et al. *J Natl Cancer Inst* 20 February 2008, 100:261–269

No difference between sequential and concomitant chemotherapy and hormonal therapy in breast cancer

→ Annals of Oncology

No difference in overall survival is evident between pre- and post-menopausal breast cancer patients given sequential or concomitant

hormonal therapy with adjuvant chemotherapy, according to an Italian study. A slight advantage, however, was noted for concomitant treatment in pre-menopausal patients.

Adjuvant chemotherapy and hormonal therapy are currently administered sequentially, with hormonal therapy following chemotherapy. The study by Lucia Del Mastro and colleagues, from the Istituto Nazionale per la Ricerca sul Cancro in Genova, set out to clarify optimum timing for treatments. A potential advantage of concomitant administration, say the authors, is the possibility of avoiding detrimental effects of delaying tamoxifen. Preclinical studies, however, have suggested negative interactions between tamoxifen and chemotherapy when given concomitantly. So far, randomised clinical trials have reported conflicting results: two trials found no difference between sequential and concomitant treatment, while sequential therapy was found to be better in a third trial. The current study is the first to include pre-menopausal women.

The study retrospectively analysed outcomes for 1,096 patients entered into two phase III trials receiving adjuvant chemotherapy and tamoxifen either concomitantly or sequentially.

In the MIG-1 study, patients had been randomly assigned to receive either six courses of FEC21 (5-fluorouracil, epirubicin and cyclophosphamide every 21 days) or six courses of dose-dense FEC14 (same as FEC21 but given every 14 days, with granulocyte colony-stimulating factor support).

In the MIG-5 study, patients had been randomly assigned to receive either the FEC21 treatment or four courses of epirubicin and paclitaxel every 21 days. In both trials, tamoxifen was given either after completion of chemotherapy or concomitantly at the physician's discretion.

Of the total population of eligible patients from the two trials, 507 had received concomitant tamoxifen and 589 sequential tamoxifen.

Results show no significant difference in overall survival between the two groups (P=0.384). The cumulative overall survival at five years was 94% (95%CI 92%–96%) in both the concomitant and the sequential groups. By 10 years, however, the survival rate had fallen to 83% in the concomitant group (95%CI 78%–88%) and 80% (95%CI 74%–86%) in the sequential group.

The cumulative 10-year event-free survival was 63% (95%CI 56%–70%) in the concomitant group and 54% (95%CI 42%–66%) in the sequential group (P=0.570).

In terms of overall survival, a significant decreasing trend in the hazard ratio for death or reoccurrence was observed with increasing age, indicating that concomitant therapy, as compared with sequential therapy, might be more effective in younger patients. "A potential explanation of this finding is that the early commencement of tamoxifen could counterbalance the bad prognosis reported in young pre-menopausal patients with ER-positive tumors who are treated with chemotherapy alone," write the authors. The potential advantage of concomitant tamoxifen in young patients needs to be further addressed in prospective trials, they add.

■ Timing of adjuvant chemotherapy and tamoxifen in women with breast cancer: findings from two consecutive trials of Gruppo Oncologico Nord-Ovest–Mammella Intergruppo (GONO-MIG) Group. L Del Mastro, B Dozin, E Aitini et al. *Ann Oncol* February 2008, 19:299–307

Quality of life changes in prostate cancer

➜ New England Journal of Medicine

Each of the three common primary therapies for prostate cancer – radical prostatectomy, brachytherapy and external beam radiotherapy – produce unique quality of life changes in patients relating to urinary symptoms, sexual and bowel function, vitality and hormonal function, according to a recent American study.

Quality-of-life outcomes are important for prostate cancer patients. Early studies reviewing outcomes following prostatectomy or conventional radiotherapy raised concerns about urinary incontinence, bowel function and sexual activity. Less is known, however, about quality of life after brachytherapy and androgen-suppression therapy.

Martin Sanda and colleagues from Harvard University, in Boston, sought to identify determinants of health-related quality of life after primary treatment for prostate cancer and to determine how quality of life relates to overall satisfaction with the outcome of treatment for patients and their partners. Patients who underwent elected prostatectomy, brachytherapy or external-beam radiotherapy between March 2003 and March 2006 were enrolled in the study. In phone surveys, 1,201 patient and 626 partners responded to questionnaires, including the Expanded Prostate Cancer Index Composite (EPIC-26) and Service Satisfaction Scale for CancerCare (SCA). Responses were obtained before treatment and at 2, 6, 12, and 24 months after starting treatment.

Results show adjuvant hormone therapy exacerbated the adverse effects of radiotherapy or brachytherapy, whereas nerve-sparing surgical procedures mitigated the adverse effects of prostatectomy. Factors associated with worse patient-reported outcomes were obesity, a large prostate size, a high pretreatment prostate-specific antigen (PSA) score, and older age. At one year, 5% of partners reported being bothered by the patient's incontinence after prostatectomy or brachytherapy, while 7% of partners in the brachytherapy group and 3% each in the radiotherapy and prostatectomy groups reported being bothered by the patient's symptoms of urinary obstruction, such as urinary frequency.

Black patients reported lower satisfaction with the degree of overall treatment outcomes than other patients. "We could not determine whether these differences in outcome reflected disparities in the quality of care, in the expectations of patients, or in cancer biology," write the authors, adding that further study will be required to answer these questions.

■ Quality of life and satisfaction with outcome among prostate-cancer survivors. MG Sanda, RL Dunn, J Michalski et al. *N Engl J Med* 20 March 2008, 358:1250–1261

Europe must tackle health illiteracy to avoid a health 'underclass'

Peter McIntyre

A quarter of Europe's citizens may miss out on better health, unless policy makers address functional illiteracy and improvements in the way information is presented.

"The most shocking thing is that 20%–30% of Europeans in each and every society are functionally illiterate. They cannot function adequately in our modern society, and that means they cannot function adequately in a modern healthcare system. That is an enormous challenge that our societies have to pick up."

Ilona Kickbusch has been trying to put the concept of health literacy onto the European agenda for more than three years – and it seems that she and her co-thinkers are succeeding, even if many people still find the term baffling and many European languages do not even have a word for it.

Kickbusch, former director of Health Promotion, Education and Communication at the World Health Organization and former Yale Professor of Global Health, sees health literacy as a core component of inequality – a matter of life and death.

She defines health literacy as "the capacity to make sound health decisions in the context of everyday life – at home, in the community, at the workplace, in the healthcare system, the market place and the political arena".

Those that that lack this ability are at a double disadvantage. "We know that people who are less educated and are poorer already have a lower health status and life expectancy. Now when they enter the health system with low health literacy, they are again disadvantaged compared to other patients. The healthcare systems are not geared up towards responding to patients with low health literacy. Professionals are not even trained to recognise it."

Health literacy is firmly on the agenda of the new EU Health Commissioner Androulla Vassiliou, who had barely started in the job when she spoke alongside Kickbusch at the European Patients' Forum (EPF) spring conference on health literacy in Brussels in April. She warns that there is a danger of two classes of citizens in Europe if some people lack the capacity to describe symptoms, ask questions, evaluate health information, analyse risks and navigate complex healthcare systems.

"Inadequate health literacy can result in little or no knowledge of medical care and medical conditions, decreased understanding of medical information, reduced use of preventive services, poorer self-reported health, poorer compliance rate, poorer health status, increased hospitalisation, higher inequality and increased healthcare costs.

"My belief is that within every member state we should have a set of patients' rights and within the patients' rights should be reliable information to patients especially from health professionals, especially to understand whatever they are reading about

ALAMY

themselves and their particular illness or medicine."

Vassiliou points to a number of EU initiatives to improve information, including the EU Public Health Portal (http://ec.europa.eu/health-eu/) which provides health information in 22 languages. (It is worth noting that this is a nicely laid out site, but hardly aimed at people with low health literacy. On the first cancer page, the reader must understand "primary and secondary prevention", "a cancer surveillance system" and "the incidence of malignant neoplasm of the breast".)

More to the point, perhaps, the EU Public Health Executive Agency is putting money towards a Europe-wide survey of health literacy that will create a network of organisations researching health literacy across the continent. The survey builds on work done by a team led by Jen Wang from the Institute of Social and Preventive Medicine at the University of Zurich.

His Swiss Health Literacy Survey, based on 30 measurable competencies, showed that 35% of Swiss people find choosing medication a highly complex process, and 34% say the same about treatment options. More than one in five regards choosing a doctor as a highly complex decision.

But there is an appetite for involvement – 85% of patients want to participate in treatment decisions, while only 49% believe that they do so.

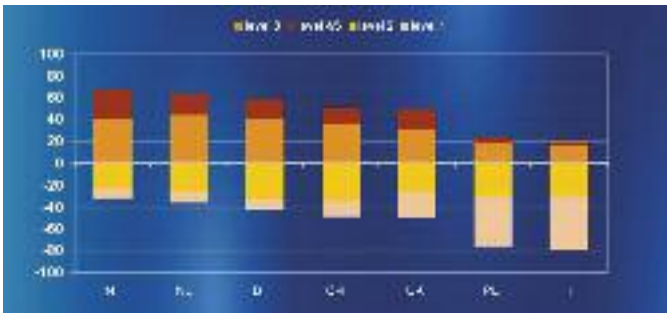
Perhaps the most revealing finding concerns sources of information that people find easy to understand. While 94% of Swiss patients find information from their doctor 'easy' or 'somewhat easy', only 76–77% say this about the media, the Internet and patient information leaflets. Hardest to understand are food labels, regarded as 'easy' or 'somewhat easy' by only half the population.

The survey put health literacy onto the agendas of the Swiss Federal Office of Public Health and other key bodies. In fact Switzerland is one of only three countries in Europe (together with the UK and Ireland) to have any policies on health literacy. "Outside the English-speaking world, health literacy is not a very common topic in Europe yet," said Wang. "The term for health literacy may not even exist in your country."

Levels of basic literacy vary widely between countries. In the figure overleaf, only those above the zero line (levels 3 or 4/5) meet the minimum OECD skills to function in 21st century society. Those below the line are struggling, while those in the bottom band are functionally illiterate. In Poland and Italy, this amounts to almost half the population, and in the UK, almost a quarter. In Norway, the Netherlands and

"The healthcare systems are not geared up towards responding to patients with low health literacy"

DOCUMENT LITERACY IN SELECTED COUNTRIES (16–65 YEARS)



This figure shows adult skills in deriving information from documents. Those above the zero line are considered to have adequate literacy skills to function in society. The yellow band consists of people who can derive information from written communication only if it is very clear and simple (level 2). Level 1 is considered functional illiteracy.
Source: *International Adult Literacy Survey, 1993–1997, Adult Literacy and Life Skill Survey, 2003*

Germany, only 9%–10% are in this bottom band.

In research in Ireland, one in five people were not fully confident that they understand all the information they receive from healthcare professionals. A full 60% did not fully understand the word 'prognosis' – a term often used in patient consultations.

Wang believes his research has the potential to increase accountability and help bridge the gap between patient information and health education. Whether the broader European research can achieve this is less certain. Although academic units in 16 European countries have signed up, Wang has been given the money to carry out the research in only six. He is looking for partners who can provide a further €1 million to make the research truly pan European.

Patient stories

Much of the discussion about health literacy is about how health professionals and authorities can communicate better with patients. But patient groups say that patients' own stories can be the most helpful in explaining choices and issues to new patients.

Akiki Vrienniou from the Greek Multiple Sclerosis Society recalls how, despite being a university graduate, she struggled to take in the impact of her diagnosis. "When the doctor told me I had MS, I was totally confused because I did not know what this was and how it would affect my life. There are a lot of questions and doctors do not have the time to answer all these questions. They focus on the therapy."

She compares the mental process of using information to make decisions with the physical process of digestion. "The digestive system keeps the nutritious things for the body to function and the rest is just garbage and it goes out from the body. I think health information is more or less the same. At the end you need to reject unreliable information."

Hildrun Sundseth, from the European Cancer Patient Coalition, believes that patient advocates play a critical role in helping newly diagnosed patients deal with the information jungle.

She was diagnosed with melanoma 15 years ago and was very bruised by the experience. "I rung up my consultant and she gave me my diagnosis over the phone two days before Christmas. I thought that was my last Christmas. I was sitting there crying.

"After Christmas I went to see my GP and he said, 'I have someone on my patient list who has had the same condition as you for 20 years and she is still alive.' That lifted me up."

She says, "I feel sorry for doctors – they are human as well. But if you are giving information to patients, then you have to put the patient at the centre."

Who gives information?

There is a debate over who can best give information. Naturally enough, at the EPF conference, patient groups were the clear favourites for this role.

Kickbusch says that health literacy implies a choice about where to get information, and there is a need for a significant extra effort to reach the 20% with low literacy. Patient groups will be central to the process. "There is a certain type of health literacy that only patients have. Without the experience of women with breast cancer, I guess they would still be cutting our breasts off."

But while Vassiliou, the Health Commissioner, paid tribute to the work of patient groups, she also

"We are trying to create a dynamic doctor–patient relationship, based on dialogue and problem solving"

sounded a note of caution. "It is mainly the medical profession that can give this information, because they are the most qualified," she told the EPF. "What is dangerous very often is that one patient gets information from another patient, but his or her circumstances might be very different. It is not very reliable to take for granted information from other patients. You have to corroborate the information you get from health providers and physicians."

Strangely, perhaps, Michael Wilks, President of the Standing Committee of European Doctors (CPME), does not agree that doctors always know best. "We want information that is understandable and relevant to that patient at the right time and I don't think any doctor in the world is going to have that range of skills.

"We are trying to create a much more dynamic doctor–patient relationship, in which we get the concept of dialogue and problem solving, together with a joint plan; an agreement about how the doctor and patient go forward together in the interest of improving self-care and self-knowledge and improving trust – a very precious commodity for both of us."

One way in which he feels this could be done is to ensure that the patient has the right to access their own electronic records. "Large parts of the medical profession have scepticism because they don't want to lose control of that data. I think they need to be reminded that it is not their data. The record may be in their computer, but the information actually belongs to the patient."

There were also strong calls at the EPF conference to recognise the key roles of nurses and pharmacists in the process of improving information to patients.

There is an ongoing debate about the role of the pharmaceutical industry in giving information. Currently, patient information leaflets inside medicine packets are the most difficult of all information to read (because of the tiny type) and to understand (because of the language).

Health literacy initiatives

Health literacy initiatives in Europe are increasing rapidly, even if they do not always use this language. The growth of information services such as IQWiG in Germany, La haute autorité de santé (HAS) in France and NHS Direct in the UK reflects a growing desire to validate and disseminate clear accurate information.

In Ireland, the winners have just been announced in the first annual Crystal Clear Health Literacy Awards, established by the National Adult Literary Agency. A €1,000 award went to Ursula Courtney, Director of Services at the ARC Cancer Support Centre, in Dublin, who established the 'talk-together learn-together' psycho-educative group for women with gynaecological cancers. Many described this as

PLAIN TALKING FOR CLINICIANS

The following list of user-friendly alternatives to common medical terms was published by the American Medical Association Foundation and American Medical Association in a helpful manual for clinicians, *Health literacy and patient safety: Help patients understand* (2007), which is available on the Internet.

Analgesic	Pain killer
Anti-inflammatory	Lessens swelling and irritation
Benign	Not cancer
Carcinoma	Cancer
Cardiac problem	Heart problem
Contraception	Birth control
Enlarge	Get bigger
Heart failure	Heart isn't pumping well
Hypertension	High blood pressure
Infertility	Can't get pregnant
Lateral	Outside
Menopause	Stopping periods, change of life
Menses	Period
Monitor	Keep track of, keep an eye on
Oral	By mouth
Referral	Send you to another doctor
Terminal	Going to die
Toxic	Poisonous

"I put all the papers in a closed envelope. I have not read any of them. I could not understand it"

their first real opportunity to talk about their fears and thoughts about their cancer.

Albert Jovell, who is a professor of Public Health and Preventative Medicine in Barcelona, is also a cancer patient and President of the Spanish Patients' Forum. He has been instrumental in starting a 'patients university' in Barcelona, billed as 'a knowledge alliance of patients and citizens'. Jovell talks about the crisis in the whole family, when a patient is diagnosed. "They feel paralysed. They have three diseases, not only the physical disease but the emotional and social aspects. You have all these things we do not teach in a school of medicine. You can find a lesson on pain, but you cannot find a lesson on fear, ignorance or uncertainty."

There is no lack of information, but a lack of guidance through it. One patient told them, "I put all the papers in a closed envelope. I have not read any of them. I could not understand it."

Key recommendations

The European Patients' Forum made a number of recommendations following its conference, including the following:

- More resources to extend the EU Health Literacy Research Project across Europe
- A guide on how to make information user friendly
- Explore an EU 'quality mark' for health information
- EU funding for NGOs to translate information into more languages
- A right for patients to access and 'own' their electronic health records
- An EU programme to involve patient experts in training healthcare providers on good communication
- Greater recognition of a patient rights agenda in promoting health literacy among marginalised groups
- A clearing house for patient organisations, so they can adapt existing high-quality information
- Health literacy as part of a broader patients' and citizens' information strategy across Europe

On the other hand, doctors have told them they do not have time to talk to the patients properly, let alone the family. "It is very difficult for us to communicate with patients because the way we are trained to think is very complex. We follow organograms; we don't follow the normal language people use."

The patient university has both a physical and virtual presence. "We try to help patients and families navigate through the disease, like GPS navigation in cars. We started what we call the 'friendly hospital'. Every time the cancer patient comes to the hospital, there is someone who is going to take care of all the emotional and social aspects along the process. We say, don't walk alone with the disease."

In the UK, a dozen pilots are taking place of an 'information prescription' to support patients. The Long Term Conditions Alliance, a grouping of 110 patient organisations, won support for this from all political parties before the last election. However, David Pink, chief executive of the Alliance, sees dangers as well as benefits in the term 'health literacy'. "To some people it will tell us that the problem is in the patient. Blaming the people served for the failings of the service is a real temptation."

He is also concerned about the possibility of mixed motives. "Some healthcare professionals want information prescriptions simply as a way of trying to get patients to do as they are told, and patients are unlikely to do as they are told as soon as they have access to the full information. The Government's support may well be based on the hope and expectation that, with these prescriptions, patients will go home and manage their own diseases and won't demand so much from the health services and that costs will be contained."

Whatever the motivation, however, there is a consensus emerging, and Pink is clear who should be leading it. "Patient organisations should be leading the discussions about health literacy in Europe. Patient groups understand the patient perspective, they are trusted by patients and they understand that healthcare is something that must always be seen within the context of real lives of real people."

We're back!

How an alliance of patients and politicians put cancer back on the EU agenda

Anna Wagstaff

When Europe Against Cancer ended, the need for a Europe-wide strategy to tackle Europe's growing cancer problem fell off the political agenda. Now, thanks to an impressive two-year campaign by patients and their parliamentary allies, key EU bodies are starting to give this issue the attention it deserves.

An afternoon of political speeches in the Committee of the Regions in Brussels is not everyone's cup of tea. Even Alojz Peterle, founding chair of MEPs Against Cancer and vintage political campaigner, admitted that conferences like this 'can be boring'. The April 7–8 summit of the European Cancer Patient Coalition (ECPC), however, really wasn't.

The top table brought together a combination of people who have the ability to make things happen for European cancer patients. Not only were they all singing to the same tune, but the tune sounded pleasingly similar to that composed by MEPs Against Cancer when they put forward an action plan for tackling cancer in Europe at their first meeting, in 2006.

There was Georgs Andrejevs, one of the founding members of MEPs Against Cancer. He was sponsoring a comprehensive resolution due to go before the Parliament on combating cancer in the enlarged European Union.

Marija Seljak was there representing the Slovenian Minister of Health, Zofija Kukovič, who was about to make cancer the priority item at an informal meeting of all EU health ministers, under her chairmanship, in Brdo. Slovenia holds the Presidency of the EU for the first half of 2008.

Androulla Vassiliou was present, making her first public appearance as the newly appointed European Health Commissioner. She is set to start drawing up an EC Cancer Action Plan for 2009.

Also speaking was Luc Van den Brande, president of the EU Committee of the Regions, a 'consultative' body designed to bring in the expertise and opinions of local and regional authorities before new legislation starts its journey through Parliament and the Council.

Although the COR does not have the power to veto legislation, it is important because its members tend to be close to the delivery of services to cancer patients. The COR was about to finalise its submission on the EU's draft health strategy *Together for Health: A Strategic Approach for the EU 2008–2013*.

This was a perfect line-up to open a summit entitled Making Cancer a Priority, and testimony to three years of intensive activity and nifty political footwork led by the European Cancer Patient Coalition and their political strike force, MEPs Against Cancer.

It signals a welcome return to focusing on cancer that had been all but abandoned at European level after the ending of the Europe Against Cancer programme in 2002.

Patient power. Former ECPC president Stella Kyriakides asking the new Health Commissioner whether her Cancer Action Plan will be designed to act as a permanent lobby to pressurise governments to deliver. Seated to her left is Hildrun Sundseth, ECPC's head of EU policy, and to her right Jan Geissler, ECPC vice-president, and Sandy Craine, Secretary

PHILIPPE VELDEMAN

Building political will

Europe Against Cancer (1989–2002) was an initiative of the European Commission that provided funding for key areas of cancer control, including prevention, screening and cancer registries. However, growing resistance to EC 'interference' with national healthcare policies, pressure from other disease groups, and the lack of a coherent European voice for cancer led to the programme being abandoned in favour of a health strategy that moved the focus away from tackling specific diseases.

Just as countries such as France, the UK and Denmark were beginning to accept that cancer requires a strategic, patient-centred, evidence-based, quality-controlled approach, the European Commission's health directorate, DG Sanco, redirected its efforts towards generic action to reduce smoking, improve diet and promote exercise. But despite its termination, efforts that began under the Europe Against Cancer programme continued to bear some fruit. In 2003, work conducted by the European Cancer Screening Networks generated an EC recommendation on screening for breast, cervical and colorectal cancers. In the same year, the European Parliament passed a resolution on the screening and management of breast cancer. These measures have great potential,

Only 7 countries have set up screening programmes for cervical cancer and only 11 for breast cancer

ECPC and MEPs Against Cancer became an effective double act, building support among political leaders

but their impact has been limited by lack of political will at European and Member State level. Only seven countries have so far set up cervical cancer screening programmes and only 11 provide nationwide screening for breast cancer. The EC has yet to publish a progress report, due in 2006.

A VOICE FOR PATIENTS

The formation of the European Cancer Patient Coalition in 2004 proved a turning point. Bringing together more than 250 patient groups representing millions of survivors of many different cancers, across 30 countries, it has given Europe's cancer patients a single voice to fight for their right to good care and social inclusion, to argue for a role in policy making, and to hold national and European politicians to account.

ECPC searched out sympathetic politicians to champion the cause, and by the end of 2005, MEPs Against Cancer was launched under the co-chairmanship of Adamos Adamou, Liz Lynne and Alojz Peterle.

Peterle is himself a cancer survivor. A former Prime Minister of Slovenia, he feels strongly the need to close the wide gap in cancer mortality between 'old Europe' and the newer central and eastern European Member States.

Above all, perhaps, as one of the architects of the rejected European constitution, Peterle is conscious of the dangerous distance between the structures of the European Union and the citizens of Europe – the so-called 'democratic deficit'.

He sees delivering effective action on cancer as a good way to reconnect the EU with its citizens – and he has put an extraordinary effort into achieving this.

At its first full meeting early in 2006, MEPs Against Cancer adopted a seven-point action plan that set out what it wanted from European and national political leaders (see www.mepsagainstcancer.org). Top of its list of priorities was to

- Encourage member states to draw up and implement national cancer plans
- End the socio-economic and geographic gap in cancer mortality
- Convince the Commission to create an EU cancer task force involving members of the Commission, the Parliament and the Council as a forum to exchange information and to galvanise political will to translate policy into action

ECPC and MEPs Against Cancer became an effective double act, mobilising patient advocates behind these policies and building support among political leaders and policy makers. They used the Eurocare-3 data to show the difference that good prevention policies, effective screening and high-quality care can make to mortality. They invited key players from the UK, France and Portugal to share experiences of setting up national cancer plans, and talked to patient advocates about putting pressure on political leaders to act to stem the increase in cancer cases in their own countries and to improve the experience and life chances of those diagnosed with cancer.

In November 2006, Slovenia hosted a summit on tackling cancer in the countries of central and eastern Europe, which attracted politicians and policy makers from across the region. An informal closed discussion at the start of the conference provided a rare opportunity for political leaders to hold a high-level discussion of strategies for cancer control in Europe.

Joaquim Gouveia, National Co-ordinator for Oncological Diseases in Portugal, took back to his government a suggestion from the Summit that the issues of cancer registries, screening and cancer plans should be singled out for a special discussion when Portugal assumed the EU Presidency in the second half of 2007.

A set of simple and clear recommendations on all three issues was agreed and are available in English (see figure opposite).

To promote active surveillance of the progress in cancer control across Europe, they included in this document a set of maps and charts showing how Member States are performing in terms of registering cancer diagnoses, screening their citizens and operating a cancer plan, which they intend to update in line with developments. They also included in their recommendations a provision that cancer should be included as a standard item on the agenda of every meeting of EU health ministers.

This was taken up with enthusiasm by Portugal's successor to the EU Presidency – Slovenia. In fact, the Slovenian government adopted cancer as the main health focus of their term of

Saints and sinners. This map, which can be viewed at www.acs.min-saude.pt/2007/12/18/health-strategies-in-europe-workshop-sobre-cancro (go to Conclusões), shows how Member States are performing on cancer control plans. Similar data can be found at the same site for other key parameters such as population screening and cancer registries

Cancer control plans in Europe

office, which started in January 2008, and senior European policy makers were invited to a conference in Brdo in February, to take an in-depth look at strategies for reducing the burden of cancer in Europe.

The Slovenian presidency also commissioned a book, *Responding to the challenge of cancer in Europe*, which brings together current knowledge about the burden of cancer across the continent, and effective strategies for collecting data, carrying out population screening, organising high-quality care, and developing comprehensive strategies for control.

A key chapter, contributed by Hildrun Sundseth and Lynn Faulds Wood of ECPC, says that Europe has shown a lack of commitment to getting to grips with the growing cancer problem. "Astonishingly," they write, "within the EU there seems to be little political will to share and apply evenly the knowledge we do have on how to prevent, diagnose and treat cancer, and how to care for patients…"

They reiterate the call for an EU cancer task force "to provide fresh impetus and a European framework for tackling inequalities and sharing best practice". They also express hopes that the Slovenian government would use its presidency to "build the political will required to force through the level of change and investment in health needed to close the gaps in cancer control, both within European countries and between the countries of east and west Europe."

Closing the gap

It's still too early to make a full assessment of the Slovenian Presidency's efforts, but the opening session of the ECPC summit in Brussels testified to significant success in pushing cancer high up on the agenda of every part of the EU's complex decision-making machinery.

The ECPC summit in Brussels testified to significant success in pushing cancer high up on the agenda

"Cancer patients have shown that working in partnership with political leaders can bring about change"

Luc Van den Brande of the Committee of the Regions – "good fighters, who feel the inequalities most," according to Peterle – said the COR Opinion on the EU's draft Health Strategy 2008–2013 prioritises action to reduce inequalities in health, since citizens "are exposed to variable levels of health services, hospitals and provision of qualified doctors". He promised, "The Committee of the Regions fully supports all efforts in helping to close the gap in cancer care in different regions of the EU."

The COR is pressing for stronger mechanisms to encourage those with day-to-day responsibility for organising and delivering healthcare at a regional level to cooperate with one another and exchange information, experiences and best practice.

They are also pressing for health considerations to be taken into account in developing EU policy on pharmaceuticals. Their Opinion notes that the health strategy currently fails to address this issue, "despite the far reaching impact on patients and the public if the provisions in place in this area are considered solely as a facet of industrial policy and not in connection with health."

Two days after the Patient Summit the European Parliament adopted the 41-point cancer resolution (http://tiny.cc/epcancerres). Crucially, point 2 calls on the Commission to "set up an interinstitutional EU Task Force composed of Members from the Commission, the Council and the European Parliament, which shall meet on a regular basis". Canny politician that he is, Georgs Andrejevs MEP grabbed the opportunity of having the new health commissioner by his side in front of an audience of cancer patient advocates, to stress his "sincere hope that this Task Force will be established soon".

Maria Seljak, Director General of Public Health in Slovenia, told the summit that recommendations from February's Brdo conference would be discussed at the next meeting of the Social Policy, Health and Consumer Affairs Council (EPSCO), in June, which the Slovenian Minister of Health would chair.

The emphasis will be on getting action throughout all Member States on the key priorities and strategies agreed at the ministerial informal meeting. Slovenia would push the Council to recommend a comprehensive cancer control strategy across the European Union.

To patient advocates, it certainly sounded as if their concerns are now being taken seriously. And by a happy twist of fate, this seems to have coincided with the appointment of a real ally in the European Commission, in the person of Androulla Vassiliou. The Health Commissioner has a track record on supporting cancer patients. She is one of the three founding patrons of ECPC, and has long served as chairperson of the board of trustees of the Cyprus Oncology Centre. Faced with searching questions from the floor, she does seem geared up to confronting some of the obstacles in the way of getting action on cancer.

For instance, she does not accept that the EU can make policy about pharmaceuticals without reference to the impact on patients. She told the summit that she had discussed this with Günter Verheugen, EC Commissioner for Enterprise and Industry, saying that an effort should be made to make the same types of medicines available in all EU countries, because these disparities cannot be maintained. "We are working towards it because we understand the inequity of this problem."

She also recognises that the success of the Cancer Action Plan for Europe 2009 that she is charged with drawing up will depend on getting the plan implemented in every Member State, since healthcare is an issue of national autonomy in the EU. "Certainly we will put pressure on Member States, though we can't force them. But if we publicise the good practices of certain states, we put other states in a difficult situation because they have to explain to their citizens why they don't take the same measures."

This, she says, is where patient advocates come in as partners for change, adding that any Cancer Task Force should include not only the Commission, Council and Parliament, but also the involvement of patients themselves.

As head of EU Policy for the ECPC, Hildrun Sundseth has been co-orchestrator, together with Peterle, of the two-year campaign to get cancer back on the EU agenda. She warmly welcomed the new willingness to tackle cancer more forcefully. "Cancer patients have demonstrated that working in partnership with political leaders and key players can bring about change. We're looking forward to taking that fight forward."