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Editor
Kathy Redmond
editor@eso.net

Assistant Editor
Anna Wagstaff

Editorial Assistant
Corinne Hall

Editorial Advisors
Jacques Bernier
Fatima Cardoso
Franco Cavalli
Alberto Costa
Vincent T. DeVita

Contributing Writers
Marc Beishon, Simon Crompton, Janet Fricker, Susan Mayor, Aliasgar Moiyadi, Tiffany O'Callaghan, Sandipan Ray, Sanjeeva Srivastava, Anna Wagstaff, Howard (Jack) West

Publishing Advisors
Gillian Griffith, Fedele Gubitosi

Website Liaison
Corinne Hall

Art Editor
Jason Harris

Production
HarrisDPI
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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 Turati 29
20121 Milano, Italy
e-mail: magazine@eso.net
Tel: +39 02 8546 4522
Fax: +39 02 8546 4545
All correspondence should be sent to the Editor at editor@eso.net

Cancerworld
Shaping the future of cancer care

Contents

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We need to get serious about management

KATHY REDMOND EDITOR

Management practices within hospitals play an important role in determining the quality of care. A strong relationship has been shown between hospital-specific management practices and patient outcomes (e.g. mortality) as well as financial efficiency. Yet management practices are known to vary widely both between and within countries, and much more effort needs to be made to improve poorly performing hospitals.

A number of factors are thought to be associated with better management. There is a particularly strong relationship between better management scores and clinically qualified managers, and high-performing hospitals tend to give their managers higher levels of autonomy. Competition has been shown to improve management standards, and private hospitals tend to perform better than public hospitals (http://tiny.cc/health_management). These findings have important implications for cancer policy and for how clinicians are trained.

Given the positive relationship between high-performing hospitals and the number of managers with clinical degrees, it appears to make sense to give clinicians management responsibilities. However, few oncologists have formal management skills training and many feel ill-equipped to take on this role. In the current healthcare environment, clinicians are being increasingly called upon to take on management responsibilities including managing people and budgets.

Managing an oncology unit in a complex, resource-constrained and rapidly changing environment is not easy at the best of times, but it is even more challenging if the leader lacks sufficient management and leadership skills. Many clinicians are understandably reluctant to take on this role. This means that decisions that can have a profound impact on the quality of cancer care are often made by managers who lack insight into clinical realities and patient needs.

In the cancer world we focus so much on helping clinicians develop their knowledge and skills in disease management that we seem to overlook the need to train these clinicians to be good managers. Post-graduate training programmes need to address this deficit as a matter of urgency. Professional societies can also help by incorporating management skills training into different CME activities. The renowned Milan-based business school, SDA Bocconi School of Management, is taking a lead by offering a training programme for oncology leaders. The POLE programme, which Bocconi is running in partnership with Novartis Oncology and with endorsement from the European School of Oncology, aims to help oncologists become more effective managers (see www.eso.net).

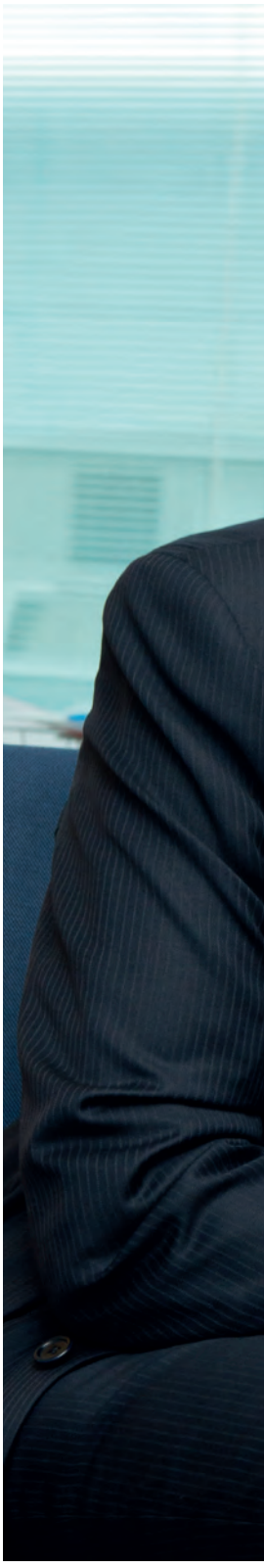
Clearly, much more is required to achieve a high-performing cancer service, but it would be good to start with the basics and make sure that the people who lead the service know what they are talking about. ■

David Cameron:

What do we really know about the quality of care we provide?

SIMON CROMPTON

We won't improve cancer care until we know more about how well we are doing and how alternative approaches compare. It sounds obvious, but it's not happening, says "the real" David Cameron.



JASON HARRIS

Something in the cancer world doesn't add up. The influential medical oncologist who voices the sentiment is a mathematician by background, so he should know.

Unlike his namesake the British Prime Minister, Professor David Cameron (known to friends as "the real David Cameron") is troubled by politics – the way it overrides the cool, research-based assessments of data that could improve patient care. Politics gets in the way of good health.

It isn't that this particular Cameron shuns the corridors of power. In fact, he's been at the heart of government-directed initiatives, and has made it a career credo to combine research with management. He is currently Professor of Oncology at the University of Edinburgh and Director of Cancer Services for NHS Lothian (in Scotland) – a role combining the academic with the service-centred. Before that, between 2006 and 2010, he was Director of the English National Cancer Research Network – a government initiative to support clinical research within the National Health Service, and to integrate it better into cancer care services.

And as a member of the government-commissioned UK Panel on Breast Cancer Screening, he tried to reconcile divergent views on screening's relative risks and benefits. Reporting in the *Lancet* in October 2012, the panel concluded that screening reduces breast cancer deaths, but at the cost of over-diagnosis – the extent of

which is uncertain given current data.

But being in the political thick of it has made him realise how badly skewed top level decision-making can be: "There are a number of political initiatives in the UK to try and improve health services where building in evaluation isn't even part of the process," he says.

"The attitude is: 'Come up with a better way of doing things, and we'll give you the money.' But if you respond that you need to have the data to show you the best way, the answer is: 'No, sorry, you have to know the answer or you don't get the money.' That's what we keep doing wrong, and there's some education needed. Health systems will never be perfect as long as people keep tweaking and changing rather than seriously asking the right questions about the best ways of delivering care."

Lack of data is deeply worrying to a man who trained and practised as a maths teacher before deciding to go into medicine at the age of 24. He's a firm advocate of the National Health Service in the UK, but it frustrates him that the collection, analysis and effective use of information is not central to everything health service managers and clinicians do – not just in the UK, but all over the world.

"People tend to see research as some sort of luxury extra which is owned by universities or drug companies," he says. "But there's clear evidence that embedding research into clinical care improves patient outcomes. Research is a core part of what we should all do, and I don't just mean drugs trials, or even randomised controlled trials. I mean a deep and thoughtful process which evaluates what we do, and uses research methodology to find ways of doing things better."

"How do you implement the right developments? For treatments, you learn from randomised controlled trials, you follow the patients up to answer questions. We should do the same for health services. How do we really know the outcomes for patients at a centre which claims to be a world leader? Show us the data, as you would in a clinical trial, indicating that your patients do better than anyone else. This is missing from the assessment of quality delivery all over the world."

Cameron is involved in some of the most

"We make all sorts of politically motivated changes which cannot be assessed with the same rigour"

important trials of breast cancer drugs. He is the UK chief investigator of the APHINITY study with pertuzumab, the EORTC LAPATAX trial, the multinational adjuvant BEATRICE trial, the UK TACT2 adjuvant breast cancer trial. He has been involved in the data safety monitoring boards for several advanced breast cancer trials.

But he acknowledges there is a problem: around 85% of the clinical trials within the National Cancer Research Network in the UK focused on questions about drug treatments. Why isn't there more research into other areas? Two reasons, he believes. One, because funding for drug studies is much more easily available from commercial companies wanting to prove a new product. Two, because drug studies are usually easier to do than other types of research.

"Could you run a randomised controlled trial to find out whether moving surgical treatment for less common cancers into fewer centres brings better outcomes? Some of the methodologies we use in clinical research for drugs trials don't naturally lend themselves to health services research. So I think one of the issues is that the methodological approaches required are more difficult, and the second is who's going to fund them. Apart from Health Technology Assessment programme in the UK, the Institut National du Cancer in France, who else in Europe will fund high-quality, methodological type research about the way we deliver healthcare services?"

What's needed is a recognition from those who commission health care services – insurance companies, politicians, managers – that research and evaluation is integral to good care, and ultimately good value for money. But currently, their understanding of this appears weak.

Those who worry that embedding research into all health services is simply too expensive are looking at the problem in the wrong way, he says. The English government, he points out, spent approaching £1 billion (€1.2 billion) on the recent National Health Service reorganisation. That is the same as the government's allocation to supporting research within the NHS. If half the reorganisation money was instead spent on asking questions about the best ways to deliver healthcare, the research budget would be boosted by 50% and half a billion pounds would have been saved.

"There is enough money," he concludes. "But politics gets in the way."

These kinds of figures put the debates about ever-increasing bills for new cancer drugs into a different perspective. The subject of cost-effectiveness in cancer services is often dominated by drugs – which take up between 10% and 20% of cancer expenditure in many European countries. "My opinion is that this is probably one of the more minor areas where we need to examine cost-effectiveness," he says. "People focus on it because it is easily measured. We make all sorts of other politically motivated changes which cannot be assessed with the same rigour. They may well be cost-effective, but we never ask the question."

For all his emphasis on logic and data, Cameron is no simple "bean-counter". Born in Edinburgh, the son of an army officer (latterly a clergyman) and a teacher, he took a maths degree at Cambridge University, and then taught mathematics in schools for a couple of years. But he knew something wasn't right: "I just didn't see my future as a mathematics school teacher." So he worked for a management consultancy firm for 18 months while he considered his options. "They were doing a lot of economic evaluations for infrastructure projects across the world – asking questions like: 'If the cost of digging a 22-mile tunnel through the Alps is *x* million, what are the economic spin-offs?' Maybe that's where my interest in health economics comes from."

In the end, however, he decided to go into medicine. He realised he needed personal

involvement with people – something which maths and health economics could not provide. Medicine involved applying knowledge systematically, but also face to face contact with a person in need.

So he went to St George's Medical School in London, spent two years as a junior doctor in London, then came to Edinburgh in 1989 to specialise in infectious diseases including HIV, and then switched to oncology. The area had much in common with HIV – the way patients are managed, balancing drug toxicity with efficacy, dealing with people who are dying. "Various options in infectious diseases had closed down for various reasons, and oncology just seemed to embrace all the areas that interested me."

After completing a fellowship and MSc in Clinical Oncology at the University of Edinburgh, he received a MD with distinction in 1997. He took up administrative responsibility for medical oncology in his department in 2001. It was in 2003 that his career really began to multi-track, when he was appointed consultant and part time senior lecturer in medical oncology at the Western General Hospital, Edinburgh, and research programme lead for cancer with NHS Lothian, and clinical lead for the South East Scotland Cancer Research Network.

Between 2006 and 2009 he went to the University of Leeds, where he was Professor of Oncology and Director of the National Cancer Research Network. Then he came back to Edinburgh for his current dual role, dividing his time between managing cancer services for the NHS Lothian region, treating patients, and researching breast cancer.

His life and career have centred on the city of Edinburgh. He was drawn back there after Leeds not because it is beautiful or because of friends and relatives, but because of the nature of the job he was offered – one that matched his conviction that research and clinical work should be inextricably linked. "There's such wonderful potential here," he says. We are sitting in his office in the Edinburgh Cancer Research UK Centre, established in 2010 and run jointly by the University of Edinburgh, Cancer Research UK and NHS Lothian. He points outside the window: "The radiotherapy machines are just there. There aren't that many cancer departments in the UK where you have basic science so close to the clinic. My job is built between two partners, the university and the health service, and their relationship is pretty good."

LEWIS HOUGHTON

"There's been a commitment by the university to invest in cancer research – more on basic science than the clinical. So my job is to build the clinical research within cancer services, and there's a commitment from NHS Lothian to do this. So the bricks that you need are here."

What really shaped his career, he says, and

"We need to ask questions about the quality of healthcare we deliver"

influenced his beliefs and priorities as an oncologist and researcher, have been teachers and colleagues. Bob Leonard, who Cameron worked with in Edinburgh, taught him about the importance of seeing the patient as well as the scientific facts; biochemist Bill Miller taught him to be methodical and beware any assumptions during research; John Smyth from Edinburgh University helped him understand the political side of oncology services. "All three believed fundamentally in clinical research," he says. When in Leeds, Peter Selby taught him the value of data in understanding services and how to improve them.

As one of the UK's leading researchers in breast cancer, Cameron was selected by the UK's National Cancer Director in 2012 to join an independent panel investigating the effectiveness of breast screening. This was in response to years of high profile, sometimes heated, debate in the UK and widespread concern that the information given to women before screening didn't help them make informed decisions.

The panel reviewed all available research and concluded that breast screening extends lives – the best evidence points to a 20% reduction in mortality in women invited to screening. But, due to lack of evidence, the panel was less categoric about the negative effects on women's wellbeing that might result from "overdiagnosis" and treatment of cancers found by screening that might ultimately never have led to their death – ductal carcinoma in situ in particular. Estimates of overdiagnosis vary from 0% to 50% (see also The Cruellest Cut, p28).

What does this mean for breast screening programmes elsewhere, particularly in countries currently considering one or in the process of setting one up? Does it constitute a recommendation that all countries should push ahead with national screening?

Cameron is cautious. The review, he says, was designed to look at an existing programme within the context of the UK population and UK breast cancer characteristics. It didn't attempt to ask the question of whether there was evidence that other countries should set up a programme, especially given variations in breast cancer characteristics from country to country. But he sees no evidence to suggest that other countries with similar breast cancer characteristics and demographics to the UK should not set up a similar screening programme.

"However, I don't think you can assume the same balance between benefits and overdiagnosis in every country," he says. "In Turkey, for example, the median age for breast cancer is 50, and here it's 62. If you want to screen under the age of 50 [in the UK screening begins at 50] you're going to need to run a randomised trial, because we don't have evidence that screening under the age of 50 is effective."

As Chairman of the EORTC Breast Cancer Group, Cameron is keen that international dialogue continues on breast screening, particularly on the kind of information that women should receive before they are screened.

"We also need to understand better whether it's possible to identify those cancers picked up by screening that we don't need to treat," he says. But putting your finger on these "less dangerous" types is not easy: working out whether a cancer is unlikely to be life-threatening for an individual involves not just crunching some population-based probabilities, but knowing the probability for a particular person's biology. "At the moment, we don't understand enough about the genetic drivers," he says.

The hour allocated for our interview is nearly up – Cameron has managed to squeeze me in between two important NHS meetings, called at short notice. I want to return to his concerns about the lack of research in and about health services. What is the way ahead?

"At a European level we should be asking

JASON HARRIS

questions about the quality of healthcare we deliver. The data exist to measure it, but we never pull it together properly." He points out that many European countries don't even have a comprehensive cancer registry, even though all the relevant data are sitting somewhere in computer files. "More and more complex data about cancer patients and the effectiveness of their treatment is going to become available as the genomic era progresses. But we risk drowning in the data unless we work out ways to use it – with all the right security and ethics – to answer bigger questions."

So how is that achieved? One barrier at the moment is the concern that patient confidentiality will be compromised if personal records are fed into larger databases. There has been outrage in some sections of the British press this year about government plans to create a central database of patient records, from which data might be sold to private companies.

"We're going to have to build ways of collaborating so that data is pulled together in systems which have the right governance," he says. "There have to be safeguards to confidentiality, but they shouldn't be barriers. Then you can start to answer questions about how different treatments affect different subgroups of patients. As you bring in more and more genomic data, you can look at which genomic differences are important. For the less common cancers, you may need to pull together data from several European countries."

"However, people will need a lot of reassuring that that they're not going to be open to political or legal challenge."

The other big challenge facing the cancer community is the cost of cancer drugs, he says. This is a common concern among oncologists in the UK, but it is intriguing in Cameron's case

"The costs of new drugs are escalating. This is a problem for all of us, and everyone needs to get round the table"

JASON HARRIS

because he has also publicly criticised the fact that newer, expensive cancer drugs are not available to patients in some parts of the UK. He explains that his problem is inconsistency: in a supposedly national health service, a drug that has been judged cost-effective by national bodies such as the National Institute for Health and Clinical Excellence should be available in every part of the country.

But the fact remains that new cancer drugs are very expensive, and health systems are struggling to afford them. "We don't want to destroy the capitalist system of drug development which seems to work quite well. But we need to reduce the cost of developing new drugs so that drug companies no longer charge so much to cover their costs, and therefore the price to the payer can be brought down."

"I'm not sure I understand the solution, but I am seriously worried that the costs of new drugs are escalating, and it won't be just the UK that starts to struggle. There are going to have to be some complex high-level discussions – a dialogue between the companies that develop the drug, the payers, the health economists, the clinicians and the patients. This is a problem for all of us, and everyone needs to get round the table. We're very bad at doing that."

It's time for his next meeting. He whisks on his jacket, guides me out of the Cancer Research UK Centre, says goodbye, and disappears through the door of a neighbouring building consulting his papers. I imagine him at the meeting, and perhaps every meeting, telling his colleagues, whether they be clinicians or managers: "Show me the data." ■

A coordinated approach to multidisciplinary guidelines

MARC BEISHON

Oncologists put their faith in evidence-based guidelines. But when the treatment is multidisciplinary, who decides on the evidence and how? ECCO's new Guidelines Forum has come up with a plan.

Clinicians in most medical specialities do not lack guidelines for their day-to-day treatment of patients, and oncologists certainly have many to choose from at both national and international levels, issued by cancer societies and government healthcare agencies. Guidelines – if followed properly – can have a significant impact on outcomes, as they can help address the variations of clinical practice between countries and within countries, complement professional education, provide auditing and evidence for healthcare decision making, and provide patients with reliable information about standards of care. They have been widely issued for certain treatments where specialist knowledge from a branch of oncology is applied.

But there's a big problem with much of the current guideline work, according to Dirk Schrijvers, head of oncology at the Ziekenhuis Netwerk Antwerpen (ZNA) in Belgium, and that is a lack of guidelines that bring together evidence in a multidisciplinary way, and which also conform to international standards for guideline development. That's because so much in optimal treatment and care in cancer now depends on teams of professionals working together.

Schrijvers is chair of ECCO's recently established Multidisciplinary Clinical Guidelines Forum, which was set up by the pan-European cancer society to help fill this gap in the guidelines by networking among oncology societies, and also promoting quality criteria that should extend across guidelines of all types in oncology.

"There is no doubt that cancer is becoming more multidisciplinary, with not only the various physicians involved in care but also nurses, psycho-oncologists and others too. But most current guidelines are unidisciplinary, as cancer societies are mainly producing guidelines specific to their subjects," he says.

That is not a problem, he adds, for situations such as a patient with metastatic disease where the main or only treatment path is with drug therapy. "Then specific guidelines for medical oncology are fine for

clinical practice. But there are problems when there are several modalities involved in treatment, and here the uni-disciplinary guidelines often lack the multidisciplinary character."

A key example is rectal cancer. "Depending on the stage of the cancer, you can give radio and/or chemotherapy, perform surgery and may need to provide follow-up care for temporary or permanent stoma – all these aspects and more need to be covered by a guideline."

There are examples of multidisciplinary guidelines for rectal cancer, but they may not yet fit all the criteria that ECCO is proposing – and that health service funders are starting to demand, says Schrijvers. In the case of his own society, ESMO (European Society for Medical Oncology), which has a strong guideline development group, its current rectal cancer guideline is co-authored by a surgeon, a medical oncologist and a radiotherapist – but it is not a collaboration between European societies. Although there is a delegation procedure, it is an ESMO guideline, not a formal joint one that would also include ESSO and ESTRO (the surgeon and radiation oncologist societies) and possibly other organisations, such as EONS, the oncology nursing society. "Other guidelines have been produced by groups that do not have any endorsement from any cancer society," says Schrijvers. "For high-quality multidisciplinary guidelines we are looking for involvement from all the relevant societies."

SHUTTERSTOCK

"For high-quality multidisciplinary guidelines we are looking for involvement from all the relevant societies"

"We want to be a platform or 'switchboard' for organisations to come to when they intend to produce a guideline"

WHO IS DEVELOPING GUIDELINES?

This is a key aim of the Multidisciplinary Guidelines Forum, and was prompted first by the EU Eurocancercoms project which funded a survey in 2010, carried out by Schrijvers and colleagues, to find out which European organisations involved with oncology are developing guidelines. Thirty European cancer organisations were contacted, and 21 responded to the questionnaire. Of these, 13 were involved in the production of clinical practice guidelines. Almost all of these organisations developed guidelines for their members or their institutions, but more than half stated that their guidelines were also aimed at policymakers (53.9%). A majority have some multidisciplinary input, mainly from the medical specialties and nursing, and to a lesser extent from professionals in communications, social science, health economics, epidemiology, and statistics and informatics (a median of three to five disciplines were involved). Patient representatives were also involved by five organisations.

There was a wide variation in quality control in review, piloting and consensus procedures and, significantly, only a small minority required any methodological training for members of the guideline development group. The costs involved were considerable, at €25,000–50,000 for development and €5,000–10,000 for distribution for each guideline.

"Once we saw that there were so many guidelines being produced independently, we thought it could be possible to bring the societies together, specifically to improve multidisciplinary working," says Schrijvers. That led to the establishment of the ECCO forum and a working group, which first developed a consensus paper. The societies were then polled again on questions such as whether they have a system to contact other ECCO members for participation in guideline development, and on procedures and formats for guideline production (presenting guidelines as flowcharts, though rarely done, can help usability, as can producing different versions – short and long – and factsheets for patients).

ECCO QUALITY CRITERIA

ECCO says it will endorse and disseminate multidisciplinary oncology guidelines if they fulfil these quality criteria:

- Guidelines must be multidisciplinary and must involve representatives of the societies of the relevant disciplines
- Validated methodologies must be used and must be explicit and transparent
- A conflict of interest policy must be in place and transparent
- Representatives of patient organisations must be involved.

COORDINATION NOT COMPETITION

There is one fact that Schrijvers wants to make clear: ECCO is not setting up its own guideline development group, as some have thought. "We want to be a platform or 'switchboard' for organisations to come to when they intend to produce a guideline – so they can ask for help in involving other societies to make it truly multidisciplinary," he says. "There's no doubt that oncology societies do an excellent job with their own guideline development groups – we are not opening up the process to competition.

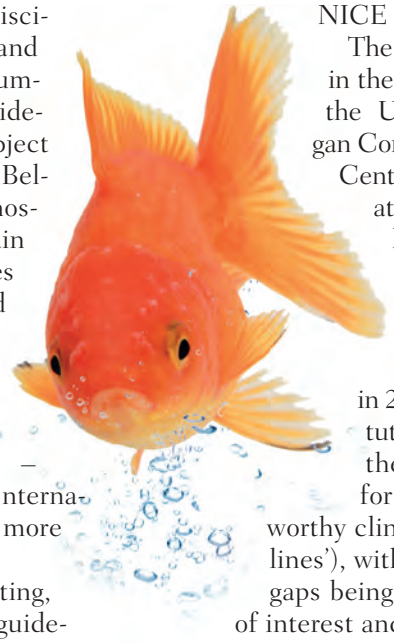
"So far, we have issued the consensus about how we want to proceed, and have also prepared a statement paper that outlines the multidisciplinary guideline process. The next step is to make it operational."

Apart from European societies, there are also national guidelines produced by agencies such as INCa in France and NICE in the UK, and many more by national oncology societies, but Schrijvers says there is a distinction to be made between these and European guidelines. "Ours is a European effort that we are putting forward based on science – an issue with national guidelines is that they are also often based on whether reimbursement is available for certain treatments and drugs, and on the resources of healthcare systems.

"There will always be these differences and we are not against that, but we need a standard that is the state of the art for patients." It is the same approach, he adds, that ESMO

has applied with its minimum clinical recommendations series, which was translated and distributed throughout Europe by 2002, with a particular aim of reaching central and eastern European countries.

Schrijvers notes, however, that with national health systems moving to evidence-based care, such as with mandatory multidisciplinary consultations, and requiring minimum numbers of procedures, guidelines are also being subject to quality criteria. In Belgium, he says, each hospital now has to maintain a book of guidelines that are mostly adapted from high-quality international guidelines (Belgium uses a methodology called ADAPTE to do this – see the Guidelines International Network for more information).



He recalls one meeting, at the Belgian national guidelines group for prostate and testicular cancer, where he suggested including an ESMO guideline as a source, but it was pointed out by the Belgian Healthcare Knowledge Centre (KCE) that it didn't at that time comply with AGREE (Appraisal of Guidelines for Research and Evaluation) – one of the most used international instruments for assessing methodological rigour and transparency – and so was excluded.

In the most recent survey of members of the ECCO forum, AGREE is now used by ESMO and others including ESSO and the European School of Oncology, but others such as ESTRO do not, although some have other quality evaluations. But a majority do at least use a development procedure based on recommendations from WHO, NICE and others.

The variability is echoed in the US – researchers at the University of Michigan Comprehensive Cancer Center recently looked at 169 guidelines for lung, breast, prostate and colorectal cancers and found that none fully met standards set in 2011 by the US Institute of Medicine (see the IoM's 'Standards for developing trustworthy clinical practice guidelines'), with the most common gaps being managing conflicts of interest and including patients or other lay people in the process. Co-author Sandra Wong does point out that for trustworthiness, some standards such as patient involvement may not be as important as, say, carrying out systematic literature reviews.

When it comes to multidisciplinary work, only four societies surveyed by ECCO have a system to contact other societies for involvement, which is one of the key reasons for the forum, says Schrijvers. "We are also finding some good systems from some organisations that could be implemented by others. The European Association of Urology (EAU), for example, has an excellent database for compiling and evaluating evidence."

The 'headline' quality criteria that ECCO says should applied to multidisciplinary guidelines are straightforward and to the point (see box), and it intends to endorse guidelines that fit the bill. The type of work that should result in endorsed European multidisciplinary guidelines includes that of consensus groups, such as EURECCA colorectal, led by current ECCO president, Cornelis van de Velde, which has recently published a multidisciplinary mission statement on better care of patients with colon and rectal cancer in Europe (see *Eur J Cancer* 2013, 49:2784-90).

That's a big and complex undertaking, but for a good example of a short, practical guideline that is in line with ECCO multidisciplinary aims, Schrijvers suggests the joint ESMO–EONS guideline on management of chemotherapy extravasation – the potentially serious problem of drugs leaking into tissue when they are administered. This is a collaboration between medical oncologists and oncology nurses – as EONS says, extravasations are a shared responsibility. It was published simultaneously in *Annals of Oncology* and the *European Journal of Oncology Nursing* in 2012… and it has flow charts. ■

Only four societies surveyed by ECCO have a system to contact other societies for involvement

Navigating uncharted waters: a guide to shared decision making

MARC BEISHON

The principle of involving patients in decisions about their own care is no longer very controversial. The question is how you put that into practice when every option carries a level of uncertainty, patients may be feeling overwhelmed and none of the options may match their hopes or expectations.

'Nothing about us without us' has been the rallying call for cancer advocacy that has helped to expose the lack of patient voices in decisions about care and treatments. Since the 1990s, enlightened doctors and healthcare organisations, aware of the hierarchical nature of the physician–patient relationship, have joined the movement to better inform people so they can be part of decisions, and the result is that in many countries the picture has radically improved. There is no doubt that attitudes about truth telling and provision of information – as witnessed by the proliferation of patient decision aids and websites – have changed for the better.

In turn, this has led to the rise of shared decision making (SDM) – which is defined, briefly, as involving a patient in a decision to the extent they would wish by providing and discussing information about options. It has become a topic that has attained specialist status, at least when judged by the number of research groups, con-

RADIUS IMAGES / ALAMY

ferences and organisations reporting and adopting shared decision making.

In 2010 the Salzburg Statement on Shared Decision Making was agreed at a global seminar (http://tiny.cc/SDM), which issued a call to clinicians, policymakers and patients to work together, and in the UK there has recently been a major push to embed this approach in care to "make no decision about me, without me, a reality".

There's also a strong movement in the US to incorporate shared decision making into clinical practice, including by legislation in a few states so far, and some other European countries such as Germany have enacted a right to informed decisions.

Another word for good communication?

There is a debate about whether shared decision making is deserving of this status, or if it is really just one part of overall communications in patient-centred care. Psycho-oncology has, after all, pioneered much effective doctor–patient communication in cancer without using this terminology, while younger people, growing up in the communications age, are anyway driving a less formal and more informed culture from both patient and doctor viewpoints. But the term does focus minds on patient involvement – which all professionals with an interest in communications agree is still widely lacking and poorly practised in healthcare.

Shared decision making has a particular relevance in cancer because of the complex and profound decisions that often have to be made at various points in the cancer journey. But that complexity also poses a particular challenge in terms of presenting information to patients in a way that they can readily apply to their own specific situation.

As Ron Epstein, professor of family medicine, psychiatry, oncology and nursing, and director of the Center for Communication and Disparities Research, at the University of Rochester, New York, points out, there are simple situations where you hardly need a medical degree to consult with a patient, such as treating a urinary tract infection. "A decision about whether to have prostate cancer screening is more complicated – while there may not be one correct answer for everyone, there are a limited number of options and there is clinical evidence to guide decisions," he says.

"But if someone has advanced colon cancer, it is hard to navigate. You can't make a list of all the possibilities. Clinical evidence is lacking and often derived from populations that are different from this patient. Treatment regimens are changing. No one can predict what's going to happen even in the next month, say if you give another line of chemotherapy. It's more like navigating a ship through uncharted waters. It takes skill, but you often have to 'muddle through' – make provisional decisions, then take stock and make the next set of decisions."

Those situations are especially difficult for oncologists to handle on a shared basis with patients, because of the lack of evidence about risk and treatments. Epstein has a particular interest in developing communications strategies in end of life care, where pursuing care that is unlikely to be effective is all too common despite attempts to foster more informed decisions.

But he makes the point that information is not enough. "There's a view that if you provide people with enough information they will make wise decisions. The psychologists tell us it doesn't always happen this way. Making choices about say surgery, radiotherapy or watchful waiting for prostate cancer is anxiety provoking. Patients can clearly be influenced by particular health beliefs and factors such as an oncologist subtly favouring one approach. And more information is not always better – sometimes patients get overwhelmed," he says.

Shared decision making, Epstein notes, has grown up alongside the development of decision aids that aim to help patients understand the implications of such choices, which of course can be irreversible and with high stakes.

A stepped approach

Providing information is one of two steps in 'doing shared decision making', as British expert Glyn Elwyn (at Cardiff University, Wales, and Dartmouth, New Hampshire) and colleagues put it in a paper on a model for clinical practice. "The first task of SDM is to ensure that individuals are not making decisions when insufficiently informed about key issues," they write, noting that many tools have been designed to help achieve this goal.

"Choices can be influenced by particular health beliefs and factors like an oncologist subtly favouring one approach"

"The first step is to make sure that the patient understands there are key choices that they can make"

A MODEL FOR SHARED DECISION MAKING

Choice talk
- Step back
- Offer choice
- Justify choice – preferences matter
- Check reaction
- Defer closure

Option talk
- Check knowledge
- List options
- Describe options – explore preferences
- Harms and benefits
- Provide patient decision support
- Summarise

Decision talk
- Focus on preferences
- Elicit preferences
- Move to a decision
- Offer review

Source: Elwyn at al. (2012) Shared decision making: a model for clinical practice. *J Gen Intern Med* 27:1361–1367

The second step is to support patients to think about the options. "When offered a role in decisions, some patients feel surprised, unsettled by the offer of options, and uncertainty about what might be best," they continue.

Adrian Edwards, a professor at the Cochrane Institute of Primary Care and Public Health (Cardiff Univeristy, Wales) with interests in risk communication and shared decision making, and a co-author of the paper, says: "The public don't assume that doctors use SDM – they assume they get on and make decisions. Clinicians assume they are doing SDM but come to realise there is often much more they could do. Patients also assume there is a right answer and a right treatment and if a doctor is going through options they are kidding them – but in early-stage breast cancer, for example, there are genuine choices. So the first step is to make sure the patient understands there are key choices that they can make."

The simple model described in their paper, Edwards adds, shows how doctors can introduce shared decision making to their practice. "First is to introduce this idea of choice. Then you explore the options. Lastly, you focus on preferences that can move to a decision." However, within these stages there is a lot to appreciate about truly giving patients the time and information to come to a preference, from checking reactions to choices and that information is understood, especially on the harms and benefits of the options, to deferring a decision where the patient isn't ready. "And even if patients say they don't want to be involved in decisions, they may want to later. You need to be aware of when people become more informed and confident."

Decision aid tools for patients, he adds, are not essential, but there is growing evidence that they have a positive effect. A Cochrane review by Stacey Bennett and colleagues found that "decision aids increase people's involvement, and improve knowledge and realistic perception of outcomes," and can lead to people making more conservative choices, for instance, by not opting for surgery. "They also help options to be discussed in a standardised way, which can reduce the problem of healthcare professionals in different specialities saying different things," says Edwards.

The healthcare quality group at Cardiff University, which Edwards is part of, has developed a set of option grids for use by patients with their doctors to compare treatment and screening choices, including one for early-stage breast cancer, which can also be found at BresDex (breast cancer decision explorer), a website that sets out the choices between lumpectomy with radiotherapy, and mastectomy. The option grids are now part of an international collaboration, including with the Dartmouth Center for Health Care Delivery Science in the US, says Edwards. But such decision aids now abound – the UK NHS, for example, now has at least 25 online aids as part of its shared decision making programme, including tools for localised prostate cancer and bladder cancer.

Oncologists are also beginning to use their own prediction tools in discussion with patients, but it can be difficult to present the information in a way patients can readily make sense

of. The Adjuvant Online! tool to help decision making in breast cancer has been shown to result in lower uptake of drugs (see *Cancer World* September-October 2013), but a study has shown that patients would understand it better if pictograms were used rather than bar charts.

The Maastro clinic in the Netherlands has developed an information tool for patients with lung cancer (treatment-choice.info) that is separate from the prediction model they developed for oncologists, but as radiation oncologist Philippe Lambin, who is leading this work notes, so far they have not been able to integrate the two. "That's complicated," he says, "We tried to do it but our first attempt was a total failure, not least because patients vary enormously – some can barely read."

Surgeons too are doing their bit to develop tools that can help patients make informed decisions, for example imaging software that shows how a woman's breast will look after breast-conserving surgery. The tool models simulations of cosmetic outcomes according to what is possible for a woman's breast, given what needs to be removed (see overleaf). Maria João Cardoso, head breast surgeon at the Champalimaud Foundation in Lisbon, who is involved in this project, says this puts women in a better position to make an informed choice, and their preferences can then be fed into multi-disciplinary team meetings so the right decisions are made about margins and other factors. If none of the conserving options are good, the woman may opt for mastectomy, she says.

Weighing up the options. The Maastro clinic is piloting this decision aid tool to help patients with lung cancer choose whether to go for radiotherapy alone or in combination with chemotherapy

In the US, several medical and cancer centres have set up dedicated decision units to support patients. Dartmouth was among the first, while the decision services department at the breast care centre at the University of California, San Francisco, has become particularly well known because of the work of Jeff Belkora, who has been prolific in discussing the 'secrets' of putting shared decision making into practice. Decision aids play a part, but Belkora's team majors on helping patients prepare for consultations – or the typical 'visit cycle' with various cancer specialists as he puts it – by viewing videos, making notes, drawing up questions and recording the visits as audio files. Key to this is deploying a team of pre-medical trainees who help patients prepare in this way, and oncologists report that they are able to start discussions at a higher level of explanation.

It is a clever use of scarce resources – people in the shape of pre-meds – and Belkora reckons that other centres could do the same, if not with medical trainees, then with other trainee professionals on rotation in nursing, mental health and social work. "They can help patients prepare for two hours so a 30 minute visit with an oncologist goes as productively as possible," he says. In the UK, the NHS SDM programme is training nurses with at least ten years' experience to offer telephone support to patients who use online decision tools.

Epstein's team at the University of Rochester runs educational programmes for oncologists in communications. He talks about the need for doctors to understand their own role as only part of the process by which patients construct their preferences, alongside other influences such as family and the media, all of which might affect a patient's expression of their own values, especially in the very unsettling context of cancer. "It is important to be 'in tune' with their patients and foster a 'shared mind' where new ideas and perspectives emerge among two people." Often, oncologists have had little training in communication and can feel overwhelmed, especially when talking to

"Decision aids increase people's involvement, and improve knowledge and realistic perception of outcomes"

"Some feel they are doing a good job, but often they are not asking patients what their goals are"

patients about bad news and treatment choices, says Epstein. "Some do feel they are doing a good job, but when we have sent in 'sleuth' patients as part of a study we are doing, it is often the case that they are not asking patients what their goals are, and they assume patients understand the information they have been given."

Patients, he says, often leave a visit with misunderstandings about prognosis. They may understand terms such as 'response rate' as 'cure'. Several studies show that up to 40% of patients with stage 4 solid cancers believe cure is somewhat likely, whereas the overwhelming majority of their oncologists said not. "This can have major implications for treatments and what people choose to do with their lives," he says.

Oncologists, he adds, really do need to learn ways to check that patients have understood and are on the same wavelength. These skills cannot be learnt from reading books. "We carry out communication training in oncologists' offices – it's remarkable what you can accomplish in a couple of one-hour sessions and they love it because they don't have to travel and perform in front of their peers. Calculating chemotherapy doses is much easier for them – this is the hard stuff."

Epstein supports the use of decision aids. "We need all the tools we can get for patients and their families," he says, and adds that doctors must respect decisions made by adults that could be seen as unreasonable, as long as they are not operating out of fear or mistaken beliefs. For example, in the US, many patients believe that surgery actually spreads cancer, and can be influenced by persuasive advertisements for alternative medicines."

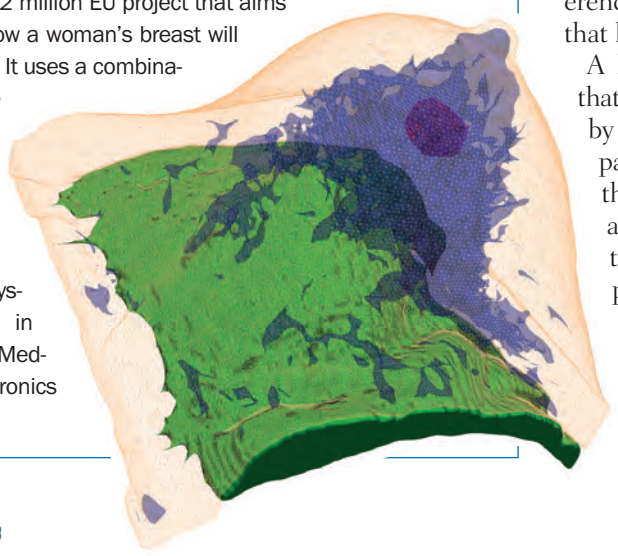
A case study he gives highlights how important it is to empower people to make their own decisions. It concerns a geriatrician in hospital with terminal colorectal cancer and with various conditions such as a massive ulcer and a biliary tract infection. "He was struggling with the decision about whether to leave the hospital and die at home or try one more procedure. I spoke with him and his family and the hospital team about the options, and he said he knew it was his choice. But he said that he was too overwhelmed to think clearly.

"I asked him if he would like a recommendation – it was his decision to accept my offer or not – and he said yes. He seemed to be relieved to be unburdened from the obligation to make a choice for which he was overwhelmed. He was comfortable making a decision, following the recommendation, to go home and spend time with his family, despite the preference of some of his family members that he 'fight'."

A key point, concludes Epstein, is that decision making should be guided by compassion, quality of life and patient autonomy. Balancing the three involves 'muddling through' and a patient-centred approach to communication where patient preferences are sought, informed and enacted in difficult, complex situations in which clinical evidence alone is insufficient to guide decisions. ■

A cosmetic model for breast surgery choice

PICTURE (Patient Information Combined for the Assessment of Specific Surgical Outcomes in Breast Cancer) is a €2.2 million EU project that aims to develop a tool that can predict how a woman's breast will look after breast-conserving surgery. It uses a combination of 3D photography and routine radiological images (from mammography, ultrasound and MRI) together with information about the tumour (size, location, shape) to model the anatomy of the breast. Partners include the Institute for Systems and Computer Engineering in Porto, UCL in London, the University Medical Centre in Leiden, and the electronics firm, Philips.



UCL, CENTRE FOR MEDICAL IMAGE COMPUTING

Going public on DCIS

Ending the overtreatment of women with DCIS will require enough women to have the courage and insight to demand something better. Tiffany O'Callaghan won a Best Cancer Reporter Award for opening up the debate with her article in the New Scientist, which is republished here.

The lump in her right breast was smaller than a pea. When she first noticed it, last August, 28-year-old photographer Ellen Doherty was busy working on an exhibition. She put off visiting the doctor for a month.

When Doherty finally went, the doctor said it was probably nothing to worry about. But they did a scan to be sure – and that led to several more tests. Finally they said she had a 2.8-millimetre tumour known as ductal carcinoma in situ, or DCIS.

Like many women given this diagnosis, Doherty had never heard of it before. She quickly devoured any information she could find, but came away confused.

The term "in situ" means that the cancerous cells are contained within the breast's milk ducts and have not invaded the surrounding tissue. This kind of lesion is not harmful unless it progresses past that stage and becomes invasive, but it is treated just as aggressively as invasive cancer. Yet this approach is increasingly being questioned, as evidence emerges that for some women DCIS would not turn out to be dangerous.

Tiffany O'Callaghan

In fact, DCIS could be regarded as a creation of modern medicine, as most cases are found through breast screening – 30 years ago it was rarely diagnosed. The fear is that screening may be leading us to cut out lumps that, left alone, would have never caused a problem. "Are we helping people by diagnosing it, or are we making things worse?" asks Beth Virnig, who monitors cancer surveillance and detection data at the University of Minnesota in Minneapolis. Breast cancer used to be discovered only if it formed a noticeable lump or caused other symptoms such as nipple discharge. Since the advent of breast screening programmes using X-rays known as mammograms in the 1980s, it is more commonly found that way. And that means growing numbers of DCIS cases are being detected. In the US, the incidence has grown more than eight-fold since the 1980s. DCIS now makes up about a quarter of breast cancer cases found through screening.

When a mammogram turns up an abnormality the next step is a biopsy to remove a small sample of the tissue in question. If the diagnosis is DCIS, the options are the same as

for invasive cancer: excision of a lump containing the growth, if possible, or removal of the breast. To Doherty this seemed bizarre: "How can they cut one of your boobs off for something that's not going to kill you?"

Doherty had a lumpectomy in November, but while she was recovering, a doctor called to say the affected tissue was more widespread than they thought and they hadn't cut out enough. In January she had a mastectomy.

This zero-tolerance approach to DCIS is based on the assumption that, given the chance, it will progress to invasive cancer. Yet no one knows how often that assumption is correct.

Disappearing tumours

It may sound surprising but people can have small cancers that do them no harm; autopsies can reveal "incidental cancers" that were not the cause of death. Some tumours are so slow-growing that they never cause a problem, while others, including some cases of breast cancer, go away on their own, presumably eliminated by the immune system.

Scour the medical literature for a figure for how often DCIS progresses to invasive cancer if left untreated and you will find estimates as low as 14 per cent and as high as 75 per cent, a range so broad as to be almost meaningless. There has never been a large study of women given this diagnosis who don't have surgery, so the progression rate can only be inferred by indirect means.

Take, for instance, a study of laboratory tissue samples from women who had a breast lump biopsied many decades ago, and went untreated because tests at the time indicated it was benign. Re-examining those biopsies turned up some in which a mistake had been made and the woman actually had DCIS. Of 71 such cases where they could track down the women, about half had gone on to develop invasive breast cancer.

That figure is probably an overestimate, though, because the women in that study had DCIS that had grown big enough to be felt as a lump. "Mammographically detected DCIS has a much lower risk of invasive cancer than DCIS detected [as a lump]," says Karla Kerlikowske, an epidemiologist at the University of California, San Francisco (UCSF).

There is another kind of evidence that suggests our current approach might be wrong. If this condition usually progresses to invasive cancer, then catching and cutting out more cases of DCIS should lead to a drop in cases of invasive cancer. That is what has happened with colon cancer: the removal of small precancerous growths, or polyps, in the colon detected through screening by colonoscopy has coincided with falling rates of colon cancer.

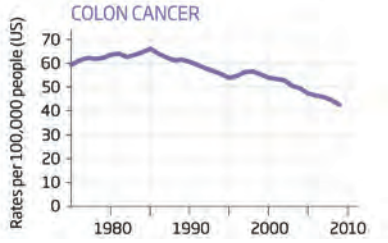
This isn't happening with breast cancer, which suggests one of two things: either the rate of invasive breast cancer is rising, or most cases of DCIS would not go on to become invasive cancer. While DCIS incidence rates have steadily climbed over the past 30 years, the figures for invasive breast cancer dipped only slightly in the mid 2000s. Because of the timing this is largely attributed to fewer women using hormone replacement therapy, which can stimulate tumour growth. "Not until the decrease in hormone therapy did we

"How can they cut one of your boobs off for something that's not going to kill you?"

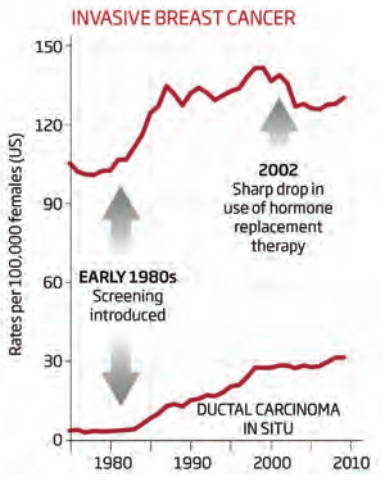
"If DCIS was a true precursor, one would expect a decline in invasive cancer much sooner."

CANCER MYSTERY

If detecting breast cancer early prevents it from spreading, why has there been no decline in invasive breast cancer rates since screening programmes started in the 1980s?



The incidence of colon cancer has fallen since the introduction of screening and removal of the polyps thought to lead to cancer.



Breast cancer screening led to a rise in cases of ductal carcinoma in situ, seen as an early form of cancer and removed surgically. But rates of invasive breast cancer have not fallen as a result.

US NATIONAL CANCER INSTITUTE

see a decline in invasive cancer," says Kerlikowske. "If DCIS was a true precursor, one would expect a decline in invasive cancer much sooner."

If we are indeed going wrong with our treatment of DCIS, what are the alternatives? About three-quarters of breast cancers are fuelled by the female reproductive hormone oestrogen, and drugs that block this hormone are already used alongside surgery. Could they be used instead of surgery?

In a recent study, 14 women whose DCIS was oestrogen-sensitive chose to forego surgery and receive drug treatment alone. Eight nevertheless ended up having surgery, and five of these women were found to have had progression to invasive cancer. The other six carried on without surgery, and two stopped the drugs. After up to seven years of follow-up, none of the non-surgery six had any signs of invasive breast cancer. "What we really want to do is identify the women who are stable without any intervention – or are stable with hormone therapy alone," says Shelley Hwang, a breast cancer specialist at Duke University Hospital in Durham, North Carolina, who led that study (*Breast*, vol 20, p 529).

Could we go a step further? It is becoming more common for men diagnosed with prostate cancer to be offered the option of "watchful waiting" instead of surgery, getting regular blood tests and biopsies to monitor signs of progression. Some breast surgeons are starting to wonder if this might also be an option for women with low-grade DCIS, where the cells still look similar to normal duct cells. Laura Esserman, a breast cancer specialist at UCSF, believes change will be driven by patients. She points out that until the 1970s, the standard response to breast cancer was a painful and debilitating "radical mastectomy", removing the entire breast, underlying chest muscle and nearby lymph nodes. Now that is rarely done. "The reason we don't do radical mastectomies anymore is because of the courage that patients had to want to come up with something else," she says. It is something their doctors can learn from, she adds.

Breast cancer surgeon Adele Francis at University Hospital Birmingham in the UK may have what it takes. She is planning a five-year trial in 1000 women with low-grade DCIS. The trial will compare surgery with monitoring through annual mammograms. Like Esserman, Francis believes it will take determined patients to chart the way. "To take part in any sort of clinical trial once you've had a diagnosis like this, it takes courage," she says.

It's a hard decision to make while the current approach of surgery for all still has many defenders. "While [DCIS] may be 'overtreated', early detection and treatment saves lives," says Kimberly Van Zee, a breast cancer specialist at the Memorial Sloan-Kettering Cancer Center in New York City.

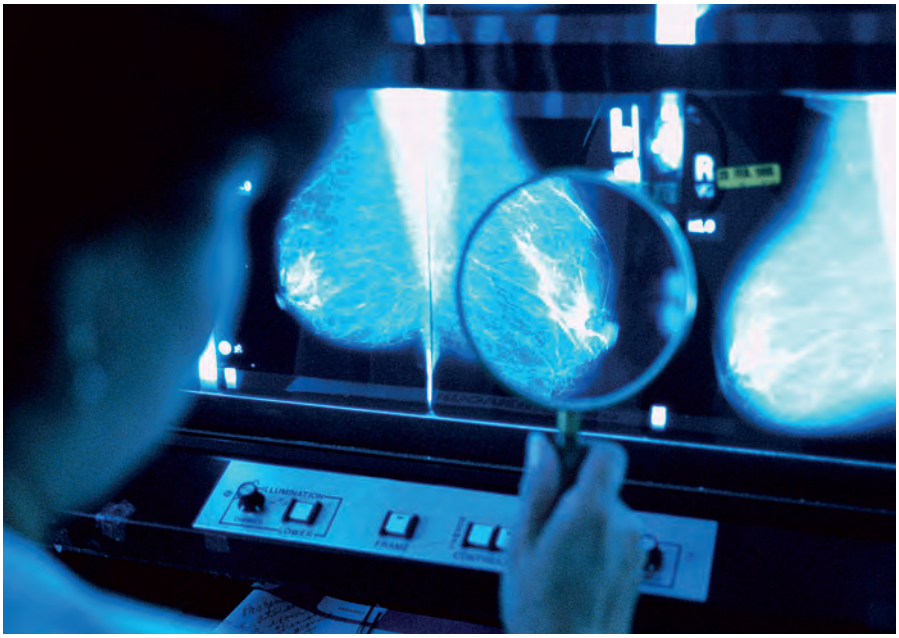
Yet Francis says about 80 per cent of the 54 colleagues she contacted about the trial were keen to take part. "The only way that this uncertainty can be addressed is by treating patients within trials," she says.

As well as changing the way we treat DCIS, there may be other ways to improve matters. One recommendation of a 2009 conference on DCIS held by the US National Institutes of Health was to do away with the term carcinoma, which most people are aware is synonymous with cancer. "The fear attached to the word cancer leads people to overreact and makes it hard to develop more prudent and cautious approaches," says H. Gilbert Welch, a professor of medicine at Dartmouth College in New Hampshire.

Not all agree. According to the grading system applied to all tumours, DCIS is currently classed as stage 0, and Van Zee believes this already makes it clear it is different to invasive breast cancer. The emotional impact of this issue is clear in online forums. One woman with DCIS who had a lumpectomy, mastectomy and radiotherapy summed it up: "Don't tell me I didn't have cancer."

Sense of urgency

With or without a name change, it would help if healthcare systems were better geared up to distinguish between DCIS and invasive cancer. UK guidelines, for instance, require all cancer patients to be treated within one month of diagnosis, and that sense of urgency can put undue pressure on women still grappling with a confusing diagnosis. "With DCIS, women don't need to jump to make a decision," says Joann Elmore, an epidemiologist at the University of Washington in Seattle. "You don't need to have a mastectomy tomorrow."



ER PRODUCTIONS/CORBIS

Mammograms revolutionised breast cancer diagnosis

One day we may be able to make better informed decisions by using cancer biomarkers – testing the molecular make-up of biopsied DCIS tissue to see which are most likely to progress to invasive cancer. Kerlikowske has found that people whose tissue was positive for three proteins, COX-2, p16 and ki67, had nearly a 20 per cent risk of developing invasive cancer after surgery to remove the lesion, while those who were triple negative had just over a 4 per cent risk.

While efforts continue to better distinguish the deceptive from the deadly, women with DCIS are still left with uncertainty. On the day Doherty was scheduled for surgery it was an act of considerable will to show up at the hospital. Had it been an option, she would gladly have taken part in a trial investigating alternatives. Without that chance, she was grateful to a nurse for her candour. "She didn't make any attempt to bluff," Doherty says. The nurse told her: "It's shit – we don't know what it is."

Doherty was left stunned by her experience. "The uncertainty is an eye-opener," she says. "However advanced we are as a society, there is so much we still don't know about the human body." ■

Tiffany O'Callaghan is an opinion editor at the *New Scientist*

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"To take part in any sort of clinical trial once you've had a diagnosis like this, it takes courage"

Managing the sexual consequences of cancer and its treatment

The impact cancer and cancer treatment can have on a person's sex life can cause physical, emotional and relationship difficulties. This overview describes the many problems that can be triggered, and a step-wise approach to addressing them, with a special focus on step one: asking patients about their sexual concerns.

Sexual difficulties can affect everyone at some point in their lives and we need to be aware of the rates of sexual dysfunction reported in healthy populations when considering how cancer might cause sexual difficulties in addition to those occurring generally. A cross-sectional survey of healthy US adults aged 18–59 found that 31% of men and 43% of women reported some degree of sexual difficulty. Ten per cent of men had difficulty achieving or maintaining an erection, 15% had low sexual desire, 8% of men couldn't reach orgasm and 30% of men experienced rapid ejaculation. In women, 32% reported a lack of interest in sex, around 14% had arousal difficulties and 7% of women reported sexual pain (*J Sex Med* 2008, 5:289–300). Estimates from a range of studies suggest about 25% of women have difficulty achieving orgasm. Age is a major risk factor for increased rates of sexual difficulties in both men and women.

European School of Oncology e-grandround

The European School of Oncology presents weekly e-grandrounds which offer participants the chance to discuss a range of cutting-edge issues with leading European experts. One of these is selected for publication in each issue of *Cancer World*. In this issue Isabel White, a clinical research fellow in psychosexual practice at the Royal Marsden NHS Foundation Trust in London, provides insights into how to manage the sexual consequences of cancer and its treatment. Gail Dunberger, of the Jubileumsklinik, in Göteborg, Sweden, poses questions arising during the live presentation.
Edited by Susan Mayor.

The recorded version of this and other e-grandrounds is available at www.e-eso.net

Impact of cancer treatment on phases of the human sexual response cycle

Cancer treatment can affect all phases of the human sexual response cycle.

Desire phase

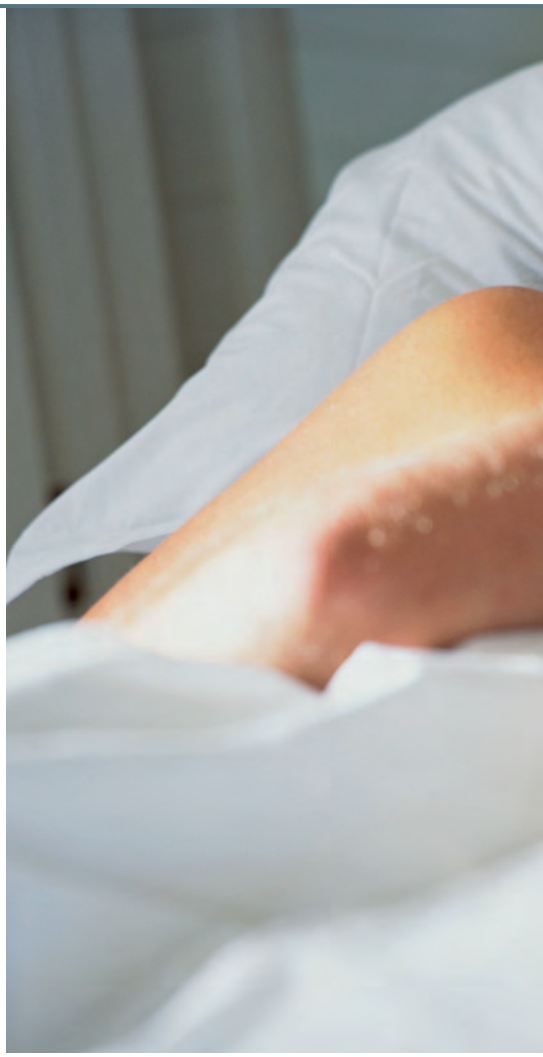
The ability to feel desire and to feel that others might desire you sexually can be affected by body image changes, altered masculinity and femininity caused by treatment, and anxiety or depression associated with being diagnosed with cancer. Sexual interest is also affected by fatigue as a consequence of radiotherapy and chemotherapy, changes in hormones as a direct result of cancer therapy – particularly after breast, gynaecological or prostate cancer, and treatment side-effects including loss of hair, feeling nauseated, problems with diarrhoea and mucositis (painful inflammation or ulceration in the mouth or digestive tract).

Arousal phase

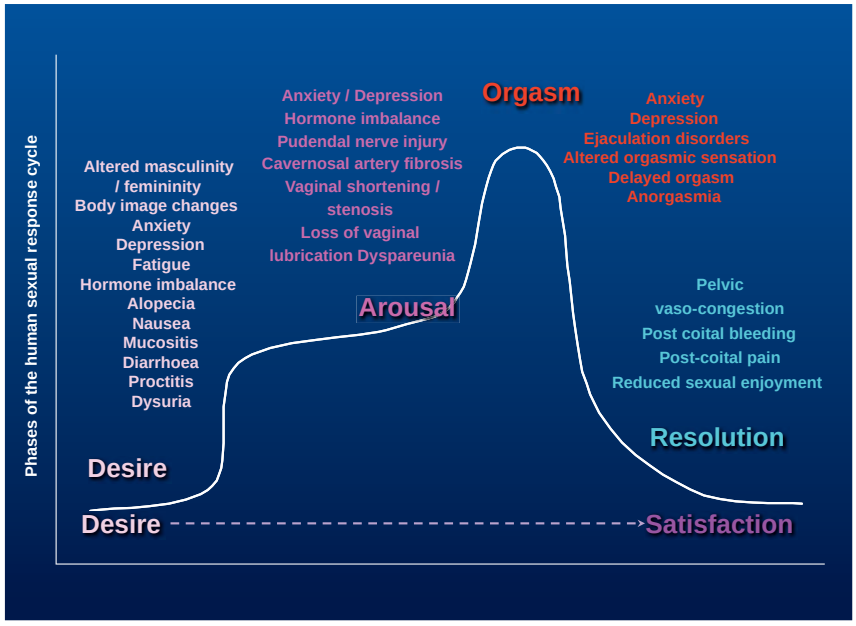
During the arousal phase, a man's ability to get and keep an erection can be indirectly affected by changes in testosterone and directly affected by nerve injury to the pudendal nerve or through scarring and fibrosis of the cavernosal arteries caused by radiotherapy or by surgery. In women, changes to the vagina in terms of shortening or narrowing caused by surgery or pelvic radiotherapy and loss of vaginal lubrication can lead to sexual pain and reduce the ability to relax and enjoy arousal.

Orgasm

Anxiety and depression and drug treatments for them can have a negative impact on the ability to reach the threshold necessary to have an orgasm. Even when an orgasm is achieved, it may be less intense and less enjoyable. Nerve damage can also cause problems with ejaculation. Men may fail to ejaculate at all or may have retrograde ejaculation, where the ejaculate passes back into the bladder, rather than being expelled forwards out of the end of the penis. There can also be delays in being able to achieve an orgasm, or loss of orgasm altogether.

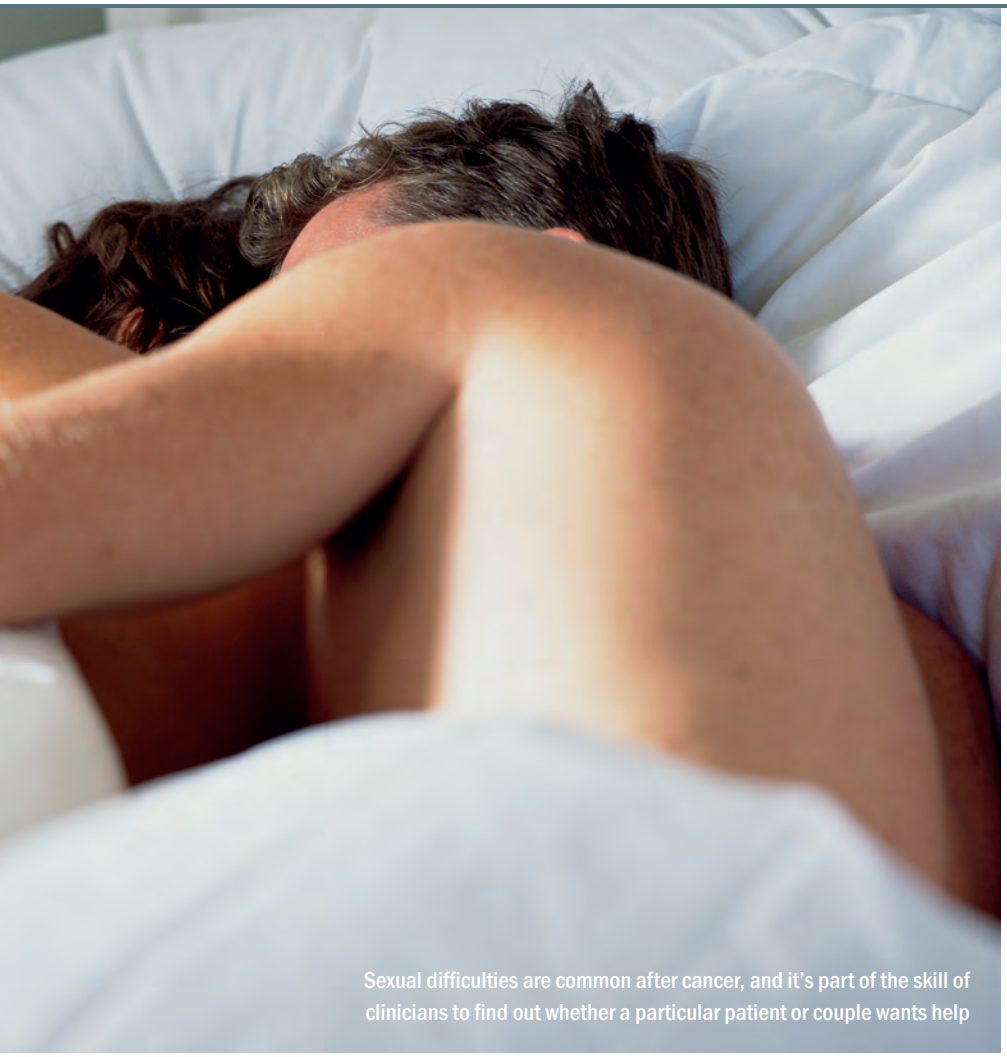


IMPACT OF CANCER TREATMENT



Question: *How can you help women with reduced sensation after pelvic cancer to reach orgasm?*

Answer: *The first point is to ensure we ask the question about whether any aspect of a woman's sexual well-being has been adversely affected by her cancer treatment. If she reports a change in orgasm, there are a variety of techniques and approaches that might be suggested, usually by someone trained as a sex therapist or a*



Sexual difficulties are common after cancer, and it's part of the skill of clinicians to find out whether a particular patient or couple wants help

IMAGE SOURCE / ALAMY

psychologist or a nurse with training in cognitive behavioural approaches for sex therapy. We would usually use a technique called sensate focus, which helps women, through a series of exercises carried out at home with her partner, to identify different erogenous zones and what types of stimulation and touch are enjoyable. She might also consider using a lubricant that can help stimulate sensation or a vibrator, which may help orgasm where stimulation by oral sex or fingers might not be sufficient.

Prevalence of sexual difficulties after cancer

The prevalence of sexual difficulties is generally higher after cancer than in the general population. A survey by Macmillan Cancer Support, "Worried Sick: the Emotional Impact of Cancer", found that 43% of UK patients said that their sex life had suffered as a direct consequence of their cancer treatment. The rate of sexual difficulties is higher – 50% to 80% – in patients who've had pelvic radiotherapy for cervical cancer (*BMJ* 1994, 308:869–870; *Int J Radiat Oncol Biol Phys* 1995, 31:399–404). After breast cancer, particularly after treatment-induced menopause, the prevalence of sexual difficulties can be as high as 70% (*J Sex Med* 2010, 8:294–302). The rate is similarly high (70%) after prostate cancer, irrespective of whether treated surgically or by radiotherapy and hormone therapy (*Int J Radiat Oncol Biol Phys* 2006, 66:439–444; *Sexologies* 2007, 16:273e278). After rectal cancer treatment 86% of men report sexual difficulties (*J Sex Med* 2010, 7:349–373), but there are limited data for women with rectal cancer.

These figures show that sexual difficulties are common after cancer. But not all patients necessarily want to pursue treatment for these problems, and it's part of the skill of clinicians to find out whether sexual recovery is something that's important to a particular patient or couple.

We automatically think of patients with cancers that pose high risk of sexual difficulties, but we also need to consider lower profile patient groups. These include patients treated for haematological cancers, particularly those treated with stem cells or bone marrow transplantation, who often need advice on how to prevent infection, how to reduce the risk of bleeding associated with sexual activity during treatment and where there might be difficulties with vaginal or penile graft versus host disease. Other patient groups that are also neglected include those treated for head and neck cancer, cerebral tumours, people who have had amputations or limb-preserving surgery that affects their mobility and ability to adopt certain sexual positions and teenagers and young adults, where research is lacking.

Question: *We know a lot about how surgery and radiotherapy affects sexual functioning in men and women but what about chemotherapy?*

Answer: *The effects are mainly to do with whether or not it's safe to have sexual activity during periods where patients might be immunosuppressed or where their thrombocyte count is significantly reduced. Generally, the sort of advice that we might give would be to suggest that barrier contraceptives can reduce*

the risk of sexually transmitted infections while someone is immunosuppressed, as well as protecting against unplanned pregnancy. Patients also worry about whether they may bleed more heavily, associated with chemotherapy-induced thrombocytopenia, and advice may include using a good lubricant to reduce friction and being gentle during penetrative sex.

The other area that is sometimes asked about is anal sex – and it's not just gay male couples that engage in anal sex, heterosexual couples may include it in their sexual repertoire. Patients who are immunosuppressed or thrombocytopenic are advised not to practice rectal penetration because the risk of infection is higher with anal sex. Rectal or anal intercourse can be dangerous in patients who are thrombocytopenic because there is a greater risk of mucosal damage and bleeding.

Other chemotherapy-associated problems relate to complications such as fatigue. Patients ability to enjoy sexual contact might be reduced during the immediate post-treatment period when fatigue is most severe.

Cancer and sex: myth or reality?

There are lots of myths that seem to surround cancer and sexual activity. These myths are often not volunteered and may need to be skilfully brought into the conversation to normalise their existence in order to correct misconceptions. A common myth is the fear of contamination from radioactivity. Patients who have had pelvic radiotherapy may worry that they can pass radiation on to their partners. But there is no possibility of patients treated with external beam radiotherapy passing on radioactivity. The only situation where you would recommend avoiding sexual contact would be in a patient treated with sealed or unsealed sources such as iodine-131, who may still be considered radioactive.

PHOTO COURTESY OF THE ROYAL MARSDEN NHS FOUNDATION TRUST

Isabel White in her consulting room at the Royal Marsden Hospital. Responsibility for asking about sexual issues lies with health professionals and not patients, but studies have shown that, even in high-risk patients, the question of sexual recovery is not addressed in around half the consultations

Some patients worry about cytotoxic contamination of their partner. There is a theoretical fear about being contaminated by the breakdown products of chemotherapy agents, but there is no research to indicate that this has ever happened, and I've never come across male or female patients whose partners developed irritation or difficulty associated with sexual contact. Patients who are very nervous about this might be advised to use a barrier contraceptive, but there is no theoretical or research evidence to back up this advice.

Some patients worry about whether their cancer can be passed on to their partner and can be reassured that this is not possible. Patients on treatment to suppress hormone levels, such as in prostate or breast cancer, can worry that having sex might lead to a surge in oestrogen or testosterone levels, but there is no evidence to suggest that this happens so we advise that sexual activity is perfectly safe.

A more common fear is that sex might cause pain or damage.

Patients can be reassured that it's quite safe to have gentle sex during or after treatment for cancer. Some patients worry that sexual contact in the past has caused their cancer. For human papillomavirus associated cancers, it is helpful to explain that most sexually active adults are exposed to HPV, but not all of them contract a cancer that is associated with that exposure. For HIV-related cancers, advice should include safe sex messages with the use of appropriate barrier contraceptive methods to reduce the likelihood of HIV transmission.

Some patients worry about being re-infected after successful treatment for a virally associated cancer if they believe their partner is the source of the virus. This often requires a conversation between the patient, their treatment team (maybe with advice from a virologist) and a sexual counsellor, to work through the period of fear or anxiety.

Asking patients about sexual concerns

Clinicians are reluctant to ask cancer patients about sex during reviews in outpatient or follow-up clinics. A study I carried out in pelvic radiotherapy clinics for women showed that sexual issues were discussed in only 25% of consultations – even though this is a high-risk group for sexual difficulty – while bowel toxicity was discussed in 81% and bladder toxicity in 70% of consultations (see figure *above*).

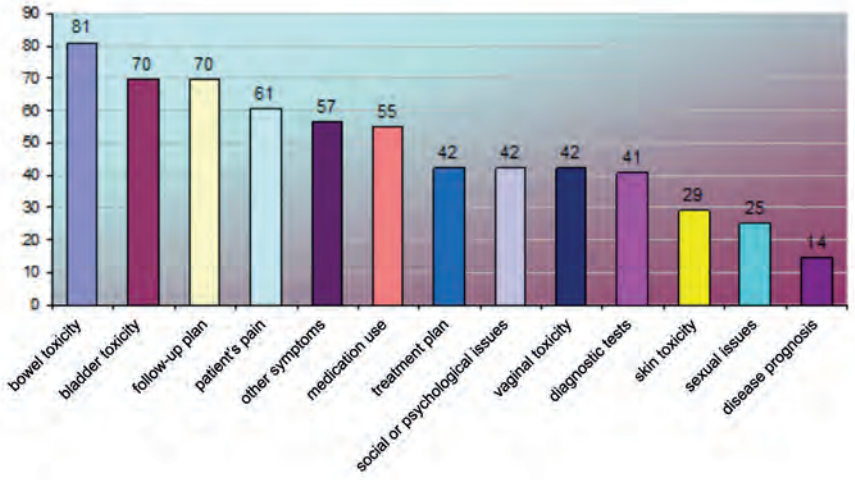
In men undergoing treatment for prostate cancer, the prevalence of inquiry about sexual difficulties was 52% in radiotherapy clinics and 54% in urology clinics (*Br J Urol Int* 2011, 109:98–103). Questions about sexual recovery were generally raised by healthcare professionals. They asked about sexual concerns in 48% of radiotherapy consultations and 30% of urology consultations observed (figures for patients were 4% and 22%, respectively). However, even though this is a high-risk group of patients, the question of sexual recovery wasn't addressed in around half of consultations, although this is better than the 25% figure in female patients.

It is important to recognise that the majority of people whose sexual lives are affected by cancer treatment can benefit from timely accurate information given by their treatment team regarding the common sexual consequences they may encounter and where to seek support/information if they have concerns. Some may benefit from brief sexual counselling or more detailed information, given by advanced practitioners or nurse specialists in oncology or sexual health. Those likely to require psychosexual therapy or specialist counselling are usually a small number of individuals with more persistent or complex sexual difficulties and high levels of individual or couple distress.

Question: *Could you give an example of a question that you could ask a patient when you start to talk about sex?*
Answer: *You need to help the patient to feel as though it is alright to ask a question, so I say things like: "Many patients who have had your kind of treatment (or cancer) have fears or worries about what it might feel like to get back into sexual activity again afterwards. Is that something that is worrying you?"*

For research purposes, it's helpful to use established instruments such as the International Index of Erectile Function and the Female Sexual Function Index to assess sexual functioning to provide consistency when you're

TOPICS DISCUSSED IN CONSULTATIONS



Sexual issues were discussed with only one in four women in this observational study of 69 consultations in pelvic radiotherapy clinics

Source: I D White, H Allan and S Faithfull (2011) *BJC* 105:903–910. Reprinted by permission from Macmillan Publishers Ltd on behalf of Cancer Research UK

MANAGING SEXUAL DIFFICULTIES: A STEPPED APPROACH

Step One	Step Two	Step Three	Step Four	Step Five
		Vaginal Dilation		
		Intimate Lubricants	Vacum pumps (male)	Vaginal reconstruction
Allow time for tissue recovery post treatment	Vardenafil (10-20mg)	Vaginal Moisturisers	Constriction rings	Penile Implants Rigid Semi-rigid Inflatable
Identify the problem	Sildenafil (50-100mg)	Topical Oestrogen	Vaginal / clitoral vibrators	
Involve partner	Tadalafil (5mg daily or 10-20mg)	MUSE (alprostadil) pellets	Vaginal prosthesis	
Sexual growth programme	Hormone replacement therapy Testosterone replacement	Alprostadil IC injections	Penile prosthesis (strap-on)	
Communicate	**Drug therapy**	**Mildly invasive**	**Mechanical**	**Surgical**
Psychological support throughout assessment and management of sexual difficulties				
Identify the problem and assess likelihood of nerve / vascular integrity. Check co-morbidities and current medications				

reviewing patients at regular intervals during follow-up. Many of the EORTC quality of life instruments, including those for breast, cervical, prostate, endometrial and rectal cancer, have a small number of questions on sexual function. The EORTC is currently developing male and female modules specifically addressing sexual recovery or adjustment after cancer.

Managing sexual difficulties

The figure above shows a stepwise approach to sexual difficulties caused by cancer or cancer treatments.

Step 1: The initial step is to identify the problems through assessment, involving the partner where that is appropriate, and helping the patient communicate their difficulties and anxieties about sexual recovery.

Step 2: If we identify sexual difficulties, step two is to consider drug treatment, including drugs for erectile dysfunction or hormone replacement therapy for someone with a treatment-induced menopause or testosterone deficiency that's adversely affecting their sexual function, as long as it's oncologically safe to do so.

Step 3: We might also consider step three, including advising patients on the use of vaginal dilators if they've had either pelvic radiotherapy or pelvic surgery, particularly where they may have had vaginal reconstruction. (International Guidelines can be found on the National Cancer Survivorship website www.ncsi.org.uk). We also commonly suggest the use of intimate lubricants, vaginal moisturisers or topical oestrogens, to help with treatment-induced vaginal changes. For men, we may use alprostadil for erectile dysfunction not responding to oral therapy.

Step 4: Step four provides mechanical options, including vacuum pumps, constriction rings, and vaginal or clitoral vibrators for orgasmic difficulties. We might consider a vaginal prosthesis for a woman without a vagina who wants to have penetrative sex, or a penile prosthesis (strap-on) for a male patient who cannot maintain an erection by other means.

Step 5: Lastly, step five is surgical interventions, with vaginal reconstruction techniques or penile implants for patients where other approaches have not been successful.

Psychological support, either through psychotherapy, sexual counselling

or psychosexual therapy, should be available throughout assessment and management. Psychosexual therapy can be useful for a variety of sexual difficulties, including persistent loss of sexual desire, orgasmic difficulties, or for patients who are fearful of having lost femininity/masculinity. Strategies helping patients to adjust to non-coital alternatives can be used where biomedical treatments for erectile dysfunction have not worked. A couples therapy approach would be preferred where both people in a couple are distressed.

A Cochrane review on interventions for sexual dysfunction following cancer treatment (Interventions for sexual dysfunction following treatments for cancer, Issue 4. Art. No.: CD005540. doi: 10.1002/14651858.CD005540.pub2) found the strongest evidence for oral phosphodiesterase 5 inhibitors for erectile dysfunction after radical prostatectomy or radiotherapy. Only one of the studies reviewed explored the effectiveness of a vaginal cream containing oestrogen after radiotherapy for cervical cancer, and found some evidence for efficacy. More research is needed in this field.

Question: *Women with pelvic cancers such as gynaecological cancers and rectal cancer are afraid of topical oestrogen. Is that your experience as well?*
Answer: *Yes. For women with cervical cancer or rectal or anal cancer, I usually explain that as their cancers are not hormone responsive we don't think that there are any safety concerns with topical oestrogen. The only women who should not use vaginal oestrogen are those who've been treated for endometrial cancer, or women treated for breast cancer where their consultants consider it not advisable.*

Take home messages

- Multimodality cancer therapy increases the likelihood of sexual consequences.
- Be aware of high-risk patient groups: breast cancer and pelvic malignancies.
- It is important to increase rates of routine screening and assessment of treatment-induced sexual difficulties in patients with cancer.
- It is the responsibility of health professionals, not patients, to initiate discussion.
- We need to improve knowledge and provision of specialist services and referral pathways for sexual rehabilitation in oncology.

Psychosexual therapy

Sex therapists work across three domains of sexual function:

Physical function, such as hormonal, vascular, and neurological changes, other physical illnesses and drug therapy that might be causing problems with sexual recovery,

Psychological response, including anxiety, depression and other concurrent mental health difficulties that might make psychological well-being a challenge.

Couple interaction. Not all couple relationships are supportive and there might be fear, blame, anger or a history of abuse requiring further psychosexual therapy and support.

We look at three sets of factors when assessing patients with sexual difficulties that they can't overcome without help. These include predisposing factors for being unable to adjust to sexual changes, such as previous abuse; precipitating factors, such as the cancer diagnosis and treatment, or relationship breakdown; and factors that maintain difficulties, such as poor couple communication or fear and anxiety in one or both members of the couple.

A retrospective cohort study of 259 women attending a survivorship programme after a variety of cancers (37% gynaecological, 92% postmenopausal) found the commonest sexual problems were dyspareunia (painful intercourse), atrophic vaginitis (changes to the skin and lubrication of the vagina walls that can result in the vagina becoming shorter, less elastic and drier), and decreased sexual desire. Orgasmic difficulties occurred in a minority of patients (*J Sex Med* 2006, 3: 646–649).

Treatment recommendations included hormone therapy (89%), psychosexual counselling (46%), vaginal oestrogens (34%), and vaginal dilators (25%). There was 63% compliance at six months and 70% of the women reported a subjective improvement in their symptoms. A literature review suggested moderate support for the effectiveness and the feasibility of psychological interventions for sexual dysfunction after cancer and cancer treatments (*J Cancer Survivorship* 2010, 4:346–360) I think that this shows that, with increased awareness, there are more patients that we can help with approaches that go beyond drug-focused interventions for sexual difficulties after cancer and cancer treatment. ■

Head and neck cancers are coming out of the closet

ANNA WAGSTAFF

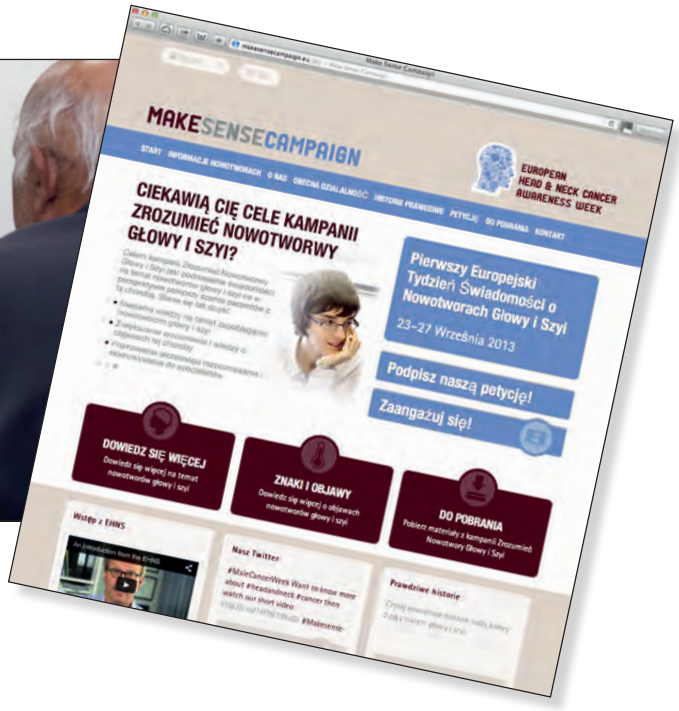
If detected early, 80–90% of head and neck cancers can be cured. Yet lack of awareness means that two out of three cases are picked up late. The Make Sense campaign takes a message of hope to the streets and subway stations and to the media and politicians.

Advocacy and awareness campaigns have transformed public attitudes to cancer in recent decades. By challenging the silence and taboo associated with the disease, they have promoted life-saving messages about risk factors and symptoms and put access to prevention, screening and high-quality care onto the political agenda.

The breast cancer lobby, with its ubiquitous pink ribbon, was first and the most successful. Other advocacy networks followed, such as for prostate cancer, leukaemia, and brain tumours. Conspicuously absent from the list has been head and neck cancers, although they seem ideal candidates for advocacy. The sixth most common cancer in Europe, they have recognisable symptoms, and if detected early can be cured in 80–90% of cases. Yet lack of awareness among the public and primary healthcare professionals means that two out of three cases are currently picked up at a late stage.

Patients treated for head and neck cancer have a pressing need for help to rebuild their lives after treatment, when disfigurement to the face and loss of ability to speak or swallow normally can leave them feeling isolated and unable to pick up the strands of their lives.

Jean-Louis Lefebvre, president of the European Head and Neck Society, has been preoccupied with the question of why head and neck cancers have remained in the shadows for so long. Last summer he spoke to *Cancer World* about his efforts to promote greater awareness, especially among those most at risk (Breaking Boundaries, July–August 2012). The fruits of



A message of hope. A week-long high-profile campaign, conducted across 13 countries, spread the word about risk factors and symptoms, with hospitals opening their doors to offer free check-ups

his labours were realised this September with the launch of Make Sense (www.makesensecampaign.eu), a Europe-wide campaign, led by the European Head and Neck Society and supported by Merck Serono, Transgene and Boehringer Ingelheim, that aims to raise the profile of head and neck cancers.

Make Sense has three target audiences:

- The public – to raise awareness about head and neck cancers, risk factors, symptoms, and the importance of getting symptoms checked early,
- Health professionals – to improve early detection, treatment, care and rehabilitation,
- Policy makers – to advocate for governments to ensure equal access to high-quality services.

The foot-soldiers of the campaign are members of national affiliates of the European Head and Neck Society, who helped to launch the "First European Awareness of Head and Neck Cancer Week", with five days of action coordinated across 13 countries.

Into the streets

For Ana Castro, a medical oncologist and member of the executive board of the Portuguese Head and Neck Cancer Society, the week offered an opportunity to get the message about early detection across to some of those most at risk, and to persuade them to attend a free check-up.

"Most of our patients are people who drink and smoke a lot, and many are extremely poor," she said. "Our dentists are good at referring patients with suspicious symptoms, but these people never go, partly because they can't afford to, so they tend to be referred by their GPs when they have a lump in their neck."

The best way to reach this target audience, she says, is through the media, or by "going into the streets". In Porto and Lisbon, doctors, patients and volunteers handed out leaflets to people passing through subway stations, inviting them to attend a free screening day if they felt they had reason to be concerned.

The campaign was supported by articles on head and neck cancers in national and regional newspapers and radio and television interviews with leading doctors.

Two days later, 28 institutes across the country opened their doors to people who wanted to be screened, overwhelming some centres. Though precise figures are not yet in, Castro says that around 10% of those who attended were referred for further tests. Media interviews with some of the men and women who turned up to be screened reinforced the message about awareness of risk and symptoms and the importance of seeking medical advice.

Castro's one regret is that most of the people who came to be screened were not smokers or drinkers, meaning they probably didn't reach their target audience. "Next year we will think about actions for special groups, like taxi drivers or people who go out at night."

Later the same week, Castro and her Make Sense team organised for doctors to visit two high schools in Porto and Lisbon, where they showed a cartoon. Rastreio do cancro da cabeça e pescoço, available on You Tube, tells the story of a typical young man who is into smoking,

"GPs often spend months treating patients for hoarseness or other symptoms, while the neoplasm is rapidly growing"

drinking and many girlfriends, exposing him to the three big risk factors (HPV infection from oral sex is estimated to account for almost one in three throat cancers). The young man changes his lifestyle after the death of his father from head and neck cancer.

The cartoon has had well over 2000 viewings. "The message is about moderation," says Castro, and she believes it was very helpful in getting students to think about their own risk behaviour. An offer to screen students, she says, also led to a number of HPV-related lesions being picked up. She is now planning to organise similar sessions in other schools throughout the coming year.

Castro insists the results of this hard work were worth "every minute of it", especially conducted as a pan-European event.

Standardising quality of care

The policy agenda was addressed with the launch of a White Paper at the European Parliament (makesense-campaign.eu/white-paper). This was a chance to show policy makers the devastating impact of head and neck cancers, and the need for high-quality care and rehabilitation. The White Paper highlighted the need to involve not only medical and radiation oncologists, head and neck surgeons, and radiologists, but also oncology nurses, speech therapists, social workers, psychologists, plastic and/or reconstructive surgeons and dentists specialised in these types of cancer.

It called on the European Commission to promote policies which ensure that all patients across Europe have access to care from specialised multidisciplinary teams – currently delivered as standard practice in only a handful of countries.

It also proposed that patient advocacy groups should be involved in providing assistance and support to patients, from diagnosis through to rehabilitation, as well as being involved in awareness campaigns, and providing updates on new treatments, research programmes and clinical trials.

Reaching out to health professionals

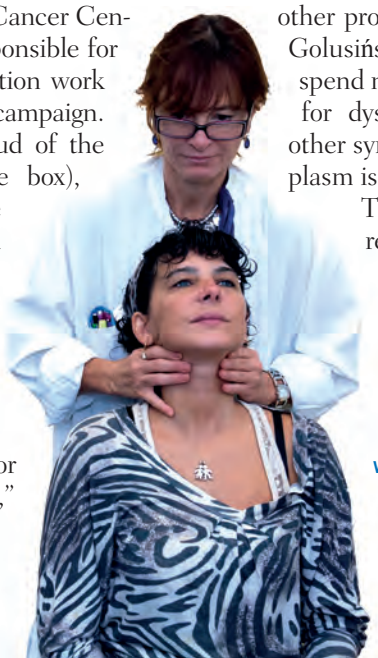
The final day of the awareness week reached out to healthcare professionals, with a meeting at the ECCO cancer conference, where delegates were invited to hear about Make Sense. In participating countries information about detection and best practice for care and rehabilitation was distributed to GPs, community dentists, pharmacists, maxillofacial specialists, ear/nose/throat doctors as well as all those directly involved in care and rehabilitation.

Wojciech Golusiński, head of the department of Head and Neck Surgery at the Greater Poland Cancer Centre in Poznań, was responsible for the professional education work of the Make Sense campaign. He is particularly proud of the "1 for 3" slogan (see box), which describes the symptoms that should prompt patients to get checked out, and alert professionals to refer patients for further examinations. "We selected the six main symptoms for head and neck cancers," says Golusiński. "If you have any one of these symptoms for more than three weeks you should seek medical advice. It is very easy to understand, not just for the public but for healthcare professionals."

In Poland, 150,000 leaflets were distributed in the 16 administrative regions, where each local Make Sense campaign was led jointly by a surgeon and a medical oncologist or radiotherapist.

Some of the best responses came from the nurses and medical students, who were eager to participate in the campaign. Dentists and GPs – key to early detection – were far less responsive. In Poland, says Golusiński, dentists accept no responsibility for the wider health of a patient, and most see their job purely as a way to earn a living. "They don't examine the oral cavity, and they see themselves responsible for the teeth only." GPs on the other hand don't always have the necessary expertise, they don't receive specialist training, and they deal with a lot of other problems. The result, says Golusiński, is that "they often spend months treating patients for dysphagia, hoarseness or other symptoms, while the neoplasm is rapidly growing."

This problem cannot be resolved by a one-week campaign, he says. The next step must be to present Make Sense at



Walk-in clinic, Lisbon. This woman was among the many who took advantage of the offer of a free check-up

all the national and international conferences of the GPs, dentists and other health professionals. Ultimately, he hopes to see the key information incorporated into curricula at medical, dentistry, pharmacy and nursing schools. He believes it will take at least two years of hard work to make real progress.

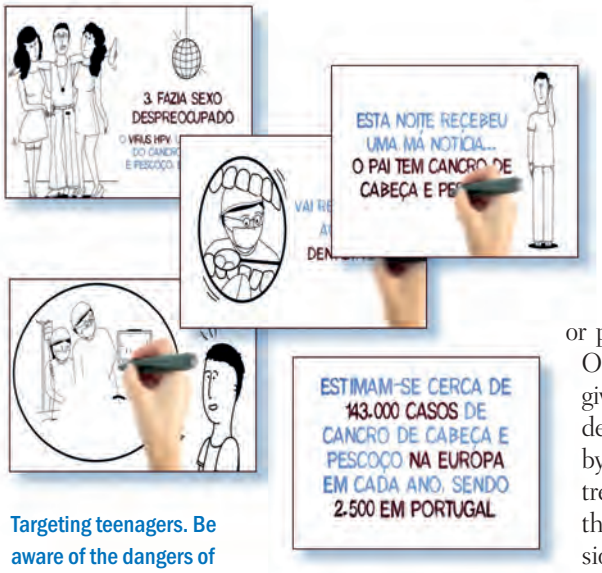
A partnership with patients

Lisa Licitra, chief of the Head and Neck Cancer Medical Oncology Unit, at the Istituto Nazionale dei Tumori, Milan, agrees that Make Sense must be a long-term campaign. She has taken responsibility for developing a sustainable partnership with European patient advocacy groups, and believes that patients are very powerful. "It is really very impressive when you speak with a patient who has been rehabilitated, who has no voice, but just a stoma."

In Italy active groups have taken on the task of helping people with voice rehabilitation, "which takes hours, and hours and hours, and is not always successful." They are also lobbying on things like prostheses and medical benefits. However, across Europe, she has found patient advocacy groups to be "very dispersed and poorly coordinated."

Building a strong advocacy partnership will take time and negotiation, as some groups are wary of being expected to provide support and advocacy, without being given a say when it comes to key decisions that affect patients.

This is certainly the view of Henrike Korn, who founded the German Head and Neck Cancer Foundation (khts.org) after her husband died from tongue cancer. She has more reason than most to welcome the efforts of the Make Sense in educating health professionals on early detection. Her husband might be alive today if one of the five doctors he visited – including a GP, dentist, maxillofacial specialist, dermatologist and ear/nose/throat specialist – had recognised the gravity of any of the symptoms that she now knows to be typical of tongue cancer.



Targeting teenagers. Be aware of the dangers of smoking, drinking and many sexual partners is the message of this cartoon

She also welcomes efforts to promote access to care by specialist multidisciplinary groups. Germany, she says, has been very slow to move towards this way of working, and as a consequence patients often find themselves on their own after leaving hospital. Henrike spends much of her spare time "substituting" for the role of outpatient nurse or case manager, helping patients who have no voice and don't leave their homes.

Enablement and empowerment is what she feels patients value. "Give them the tools to be able to live alone, let the nurses go out and tell them how to deal with all these things they have at home, the tubes and everything, so they are enabled to get along with their illness without a nurse or physician as far as possible."

Only when patient groups are given a say, for instance, in deciding the quality indicators by which head and neck centres are evaluated, will she see the relationship with professionals as a true partnership.

In Milan, Licitra agrees that patients must be given a say. "What the Make Sense campaign was trying to do was to put together a partnership between them and us, and ask them the direction we should take in this disease. I would also advocate that they should participate in research planning, because we know that there may be very different opinions in terms of outcome from research."

These are early days for the campaign, and participants are thrilled it got off to such a good start. Golusiński describes the media response as "amazing". "In Poland, like the rest of Europe, campaigns on head and neck cancers did not exist until now." Licitra also sees it as a big step forward, "I've been in head and neck cancers for 25 years and I've not seen anything like this. It's good to be part of a pan-European project." ■

1 FOR 3 – THE SYMPTOMS TO LOOK FOR

The Make Sense campaign came up with the 1 for 3 slogan as a simple guide to suspicious symptoms.

If you have ONE of these symptoms for THREE weeks, seek medical advice:

- Sore tongue, non-healing mouth ulcers and/or red or white patches in the mouth
- Pain in the throat
- Persistent hoarseness
- Painful and/or difficulty in swallowing
- Lump on the neck
- Blocked nose on one side and/or bloody discharge from the nose

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Biorepositories for cancer research in developing countries

SANDIPAN RAY, ALIASGAR MOIYADI AND SANJEEVA SRIVASTAVA

Well-documented biorepositories are essential for cancer research. Currently, major biobanks are located in the developed world, which represents the minority global population; however, countries with low-resource settings contribute more than 50% of the global cancer burden. Therefore, there is an urgent need to establish next-generation biorepositories in developing countries.

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Biospecimens are a precious and irreplaceable resource for cancer research, which requires a large number of specimens in the form of well-annotated biobanks or biorepositories.[1] Biobanking is the organised collection and storage of biospecimens and clinicopathological information, and is undoubtedly highly useful for the study of complex human diseases such as cancer. In addition to primary tumour specimens, biopsy of metastatic cancer is now becoming a standard procedure before second-line and salvage therapy. The specimens from these metastatic tumours are increasingly regarded as an invaluable resource for cancer research to accelerate the knowledge of intrinsic and acquired resistance to treatment.[2]

The establishment of next-generation biobanks (storing primary and metastatic samples with the relevant clinical annotation) in developing countries is crucial to build comprehensive and globally inclusive biorepositories and provide an unbiased platform for cancer research, especially for genomic-based translational studies. The existence of heterogeneous patterns of cancer, owing to diverse ethnic populations in countries such as India, provides a highly attractive source for research materials. Moreover, cancers of the cervix, stomach, liver, lip and oral cavity are predominantly found in the population of developing countries, but are rare in resource-rich countries.[3] Consequently, repositories of biological specimens collected from limited geographical regions might not accurately reflect the complexity and heterogeneity of cancers in a global context. This limitation severely constrains the extrapolation of data emerging for tumours, particularly those of specific geoethnic background or similar cancers in different parts of the world, and might account for the seemingly variable patterns of treatment response among patient populations. To obtain an inclusive spectrum of cancer pathobiology, and accelerate cancer research and manage-

ment, there is an indispensable need to encourage biobanking activities across the globe. This need is particularly acute in developing and resource-limited regions, where cancer-related mortality rates are much higher and survival rates are poorer compared to the developed regions of the world. According to the WHO GLOBOCAN estimation, 56% of total cancer incidence and 64% of cancer-related deaths occur in the economically developing world.[4] The total number of new cancer cases is expected to greatly increase in developing countries during the coming decade.[3]

Given the research potential of biobanks, significant financial support has been raised for such resources in many countries, including the Iceland DeCode Biobank (US$0.8 million annually), the UK Biobank (US$109 million), Biobank Japan (US$218 million for 5 years), Genomic Research in African Diaspora* (US$18 million), and the Gambian National DNA Bank (US$0.6 million for the first 5 years).[5,6] However, there is a lack of comprehensive initiatives to harmonise biobanking processes and regulations across the world. Unfortunately, at present, there are only a limited number of notable biobank initiatives in developing countries, including: the Cancer Centre Tissue Bank, Fudan University, China; the Tata Memorial Hospital Tissue Bank, India; the Malaysian Tissue Bank; the Iran National Tumour Bank; and the Bangkok Biomaterial Centre, Thailand,[5] primarily owing to the lack of awareness, paucity of designated research budgets and infrastructure, and social, ethical and political barriers.[6] For example, clinical trial irregularities have led to stricter ethical committee reviews and governmental intervention, which make clinical research more difficult. Downstream analysis of biospecimens yields a plethora of information about a patient, so protection of patient confidentiality and obtaining prior informed consent are essential to avoid legal and social concerns. Over the past two decades, a few promising biobanks, containing very large population collections (≥10,000 samples), have been established in developing countries across Asia and Africa to support multidisciplinary cancer research.[5] However, the procedure to obtain samples contained in these biobanks is not well organised, and often resources are not open for sharing with other institutes owing to ethical and logistical concerns.[7]

Completion of the Human Genome Project has provided an impetus for new approaches to cancer research. The post-genomic era has seen advancement in next-generation sequencing, high-throughput transcriptomics, proteomics and metabolomics technologies for molecular diagnostics and targeted therapeutics of cancer, leading to personalised medicine.[8] The integrative 'omics' profiling of individual patients with cancer has opened new opportunities for comprehensive biomarker discovery and oriented clinical trials in cancer research.[9] Developing countries, such as India and China, have a significant role in cancer-related research in a global context. However, a lack of comprehensive biorepositories in most developing countries affects this progress of 'omics'-based cancer research. There are difficulties in obtaining bigger clinical cohorts for designing conclusive studies, and pre-analytical variations arising from sample collection, storage and handling procedures impair the validity of results, especially for trials involving biomarkers. Additionally, a lack of guidelines and stringent, time-consuming ethical approval procedures to obtain clinical specimens often slow the pace of research activities.

Biological specimens collected from limited geographical regions might not reflect the heterogeneity of cancers

Biobanking-related activities are significantly lower in the developing world. For example, India is a geographically diverse country that has a population of over one billion people, but has only one cancer tissue biorepository – the Tata Memorial Hospital Tissue Bank in Mumbai. Cancer research efforts are plentiful in developing countries, and there is strong support from the governmental funding agencies, but most studies are investigator-driven and limited to very few biological samples. We want to emphasise the importance of an effective downstream research process, which is heavily dependent on the availability of good quality disease and control clinical samples in large numbers. The need to establish next-generation biorepositories in developing countries should, therefore, attract the attention of global policy makers, governmental and non-governmental funding agencies. Additionally, quality checks, and complete annotation of each sample with clinicopathological and sociodemographic details, are both important to ensure the authenticity of results from downstream analysis. Initiatives that include the establishment of the International Society for Biological and Environmental Repositories to address the technical, legal, ethical, uniformity and quality assurance issues associated with biobanks are appreciable. Further-

more, there is a lack of dialogue and cooperation among the small regional biorepositories existing in the majority of the developing countries.

Aside from the establishment of new biorepositories, there is also a need to integrate existing biobanks thereby building larger clinical resources that can be easily accessed by the researchers from different parts of the world.[1] A recent comprehensive survey by the Global Business Intelligence Research team revealed that, even at the global level, only 30% of biobanks have connections with other biobanks or research institutions. The remaining 70% were stand-alone, which clearly indicates the paucity of cross-talk among the existing biorepositories; the international sharing of biobank resources is still a long way off.[10] To that end, there is a successful endeavour in India to establish a national cancer grid, connecting the existing and proposed cancer centres and establishing a high-quality uniform standard to diagnose and treat patients with cancers across the country. Similar initiatives will be appreciable for nationalisation of individual stand-alone biorepositories that exist in different parts of a country. We suggest that development of regional cancer biobanks should be linked with such national cancer biobanks. However, standardised operating procedures, including maint enance of uniformity in sample collection, storage and documentation, is essential for the success of biorepositories for cancer research. ■

* This was renamed in 2006 as Translational genomic Research in the African Diaspora (TgRIAD), which is part of The National Human Genome Center at Howard University

Author affiliations
Sandipan Ray and Sanjeeva Srivastava, Wadhwani Research Centre for Biosciences and Bioengineering, Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Powai, Mumbai, India; Aliasgar Moiyadi, Department of Neurosurgery, Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Kharghar, Navi Mumbai, India

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Details of the references cited in this article can be found at www.cancerworld.com

newsround

Selected reports edited by Janet Fricker

Cancer survivors less likely to be treated for infertility

■ Lancet Oncology

Although women who survive childhood cancer face increased risks of infertility, nearly two-thirds who had tried unsuccessfully for at least one year to become pregnant eventually conceived, the latest findings from the Childhood Cancer Survivors Study (CCSS) show. However, when compared to siblings, cancer survivors were almost half as likely to be medically treated for infertility.

While substantial improvements in treatment have greatly increased five-year survival for childhood cancers (which now exceed 80% in the USA), the infertility effects of treatment represent a major concern for patients. In the latest CCSS analysis, Sara Barton and colleagues from the Dana Farber Cancer Institute quantified the risk of infertility in survivors of childhood cancers on the basis of clinical definitions of infertility.

CCSS is a collaborative study, conducted at 26 clinical centres in Canada and the US, in which a cohort of five-year cancer survivors, diagnosed before the age of 21 with eligible malignancies (leukaemia, CNS cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, Wilms' tumour, neuroblastoma, soft-tissue sarcoma, and bone tumours), have been assembled.

Survivors were asked to identify all their living siblings, of whom a random sample of closest-aged siblings were asked to participate. Both cancer patients and siblings answered a baseline questionnaire gathering information about demographics, medical care, medical disorders, and reproductive history.

For the current analysis, 3531 female cancer survivors aged 18–39 years, who had enrolled in CCSS between November 1992 and April 2004 and who reported having ever been sexually active, were compared to 1366 female sibling controls. Women with known ovarian failure were excluded from the analysis.

Results show that, in comparison to siblings, survivors had an increased risk of clinical infertility (defined as >1 year of attempts without success; RR=1.48, 95%CI 1.23–1.78, $P<0.001$). Relative risk was most pronounced at early reproductive ages (RR=2.92 for participants <24 years; 1.61 for those aged 25–29 years; and 1.37 for those aged 30–40 years). Altogether 292 survivors with self-reported clinical fertility (64%) achieved a pregnancy. Despite being equally likely to seek treatment for infertility, survivors were less likely than their siblings to be prescribed drugs for infertility (RR=0.57, 95%CI 0.46–0.70, $P<0.0001$).

"We do not have data about why providers did not prescribe infertility drugs, but are concerned about a provider bias against treating cancer survivors for infertility. Perhaps providers assessed the chance of success as poor and therefore decided not to attempt therapy, or perhaps survivors were less motivated to take drugs after previous extensive treatment. Alternatively, reproductive medicine providers might have been uncomfortable with perceived medical comorbidities," write the authors.

In an accompanying editorial, Richard Anderson, from the MRC Centre for Reproductive Health in Edinburgh, writes, "Barton and colleagues' data highlight the risk of infertility in childhood cancer survivors beyond the risk of ovarian failure and the need for this risk to be addressed by oncologists at the time of diagnosis and during follow-up as a key part of long-term care."

■ S Barton, J Najita, E Ginsburg et al. Infertility, infertility treatment, and achievement of pregnancy in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. *Lancet Oncol* August 2013, 14:873–881

■ R Anderson. Infertility in women after childhood cancer. *ibid* pp797–798

Colorectal cancer patients do better with adjuvant chemotherapy following metastatic surgery

■ Clinical Colorectal Cancer

Adjuvant chemotherapy following the surgical removal of metastases in patients with colorectal cancer produced significant benefits in disease-free survival (DFS), reports an Italian study.

Approximately 50% of patients with stage III and 20% of patients with stage II colorectal cancer develop metastatic spread, of which the liver is the main target followed by the lung. Surgical resection, where feasible, offers the only hope of long-term survival for patients with liver or lung metastases, resulting in five-year survival rates ranging from 25% to 50%. Two

recent randomised trials, when analysed together, suggested a potential benefit on DFS for patients treated with systemic chemotherapy after radical surgery on metastatic sites, but taken separately, neither study proved conclusive.

In the current study, Giovanni Brandi and colleagues, from the University of Bologna, Italy, evaluated the relative impact of adjuvant systemic chemotherapy and other established prognostic factors on DFS after first resection of liver and lung colorectal cancer metastases.

Between 1997 and 2004 the team retrospectively reviewed data from 181 consecutive unselected patients who underwent R0 resection of colorectal liver (*n*=156) or lung (*n*=25) metastases. Altogether 30 patients were excluded due to factors such as being aged over 75 years and having comorbidities, making them unsuitable for adjuvant chemotherapy following surgery.

This left 151 patients for review (131 with liver metastases, 20 with lung metastases). Due to the lack of conclusive evidence of the benefit of adjuvant chemotherapy, each eligible patient was informed of the possible advantages and disadvantages of each option, and left to choose whether to receive chemotherapy or not. Altogether 78 chose adjuvant treatment and 73 observation. The chemotherapy regimens used in the study varied according to the progress of disease, first-line chemotherapy and the availability of the drugs in clinical practice. Regimens used included 5-FU alone, FOLFIRI (folinic acid, 5-FU, irinotecan hydrochloride [CPT-11]) or FOLFOX (folinic acid, 5-FU, OHP), capecitabine, CAPOX (capecitabine OHP) or CAPIRI (CPT-11, capecitabine).

Results showed that the median DFS of patients who underwent systemic adjuvant chemotherapy was 16 months, versus 9.7 months for patients with observation alone (HR=1.56, *P*=0.014) The overall survival (OS) was 42 months for the adjuvant chemotherapy group versus 39 months for untreated patients (*P*=0.8).

"Our study emphasizes the importance of adjuvant chemotherapy in a postmetastasectomy setting, which showed a significant benefit on DFS, but formal recommendations have yet to be established," write the authors.

A control with surgery alone, they add, is now needed to demonstrate a benefit for adjuvant chemotherapy. This, they caution, may prove an obstacle for accrual. "The clearly established benefit of adjuvant chemotherapy in resected stage III colon cancer had led some authors to consider surgery alone unethical after resection of stage IV disease and that adjuvant chemotherapy should be given even without unquestionable proof of its benefit," they write.

■ G Brandi, E Derenzini, A Falcone et al. Adjuvant systemic chemotherapy after putative curative resection of colorectal liver and lung metastases. *Clin Colorectal Cancer* September 2013, 12:188–194

CT lung screening delivers least benefit for patients at low risk

■ New England Journal of Medicine

Screening with low-dose CT prevented the greatest number of deaths from lung cancer among participants at highest risk and caused the lowest number of false-positives in this group. The study, funded by the US National Cancer Institute, provides 'empirical' support for risk-based targeting of smokers for screening.

Recent results from the National Lung Screening Trial (NLST) showed that screening with low-dose computed tomography (CT) resulted in a 20% reduction in lung-cancer mortality among participants aged between 55 and 74 years with a minimum of 30 pack years of smoking, and no more than 15 years since quitting. Although it is widely agreed that screening should be limited to high-risk persons for whom potential benefits of low-dose CT outweigh potential harms, uncertainty exists as to how high-risk target populations should be defined.

In the current analysis, Stephanie Kovalchik, from the National Institutes of Health in Bethesda, Maryland, and colleagues, used data from the previously completed NLST trial to compare findings from 26,604 NLST participants who underwent low-dose CT and 26,554 who underwent chest radiography, according to the quintile of five-year risk for lung cancer mortality.

The team identified factors known to be associated with death from lung cancer and created an *a priori* prediction model based on such variables. To analyse the efficacy of lung cancer screening they divided the NLST population into five equal quintiles of lung cancer risk (with quintile 1 having the lowest risk) and inserted the NLST outcomes data to analyse efficacy of lung cancer screening. The authors do not share their formula for calculating the *a priori* risk in the paper.

Results show that the number of lung-cancer deaths per 10,000 person-years prevented in the CT-screening group (in comparison to the radiography group) increased according to risk quintile – 0.2 in quintile 1, 3.5 in quintile 2, 5.1 in quintile 3, 11.0 in quintile 4, and 12.0 in quintile 5 (*P*=0.01 for trend).

Furthermore, across risk quintiles, there were significant decreasing trends in the number of participants with false-positive results per screening-prevented lung-cancer death (1648 in quintile 1, 181 in quintile 2, 147 in quintile 3, 64 in quintile 4, and 65 in quintile 5). The 60% of participants at highest risk for lung-cancer death (quintiles 3 through 5) accounted for 88% of the screening-prevented lung-cancer deaths and for 64% of participants with false-positive results. The 20% of participants at lowest risk (quintile 1) accounted for only 1% of prevented lung-cancer deaths.

"Our estimates of the expected benefits and potential harms of such screening across risk groups provide the empirical framework for evaluating the cost-effectiveness of low-dose CT screening, investigating optimal risk cutoffs for screening, and communicating the potential benefits and harms of such screening tailored to each patient's individual risk," write the authors.

■ S Kovalchik, M Tammemagi, C Berg et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. *NEJM* July 18 2013, 369:245–254

Neuropathy persists long term after colorectal cancer treatment

■ Journal of Clinical Oncology

Neuropathy symptoms remain widely reported by patients from 2 to 11 years after diagnosis with colorectal cancer, a Dutch registry study has found. Neuropathy should be screened for and alleviated, the investigators conclude, with more research focused on preventing this condition.

Neuropathy, a common adverse effect of the platinum agent oxaliplatin, has a negative impact on patients' health-related quality of life (HRQOL). Due to the increasing prevalence of colorectal cancer, and increased use of oxalipatin, neuropathy represents a growing issue for cancer survivors. Symptoms for acute neuropathy, often triggered by cold, include distal paraesthesias, dysaesthesias, and mild muscle contractions of hands, feet and perioral regions. A significant proportion of patients experience chronic neuropathy, which is mainly sensory, after oxaliplatin is discontinued.

In the current study, Floortje Mols and colleagues, from the Centre of Research on Psychology in Somatic Diseases, Tilburg University, set out to gain insights into the prevalence and severity of chemotherapy-induced neuropathy and its influence on HRQOL.

All patients diagnosed with colorectal cancer between 2000 and 2009 enrolled in the Dutch population-based Eindhoven Cancer Registry and still alive were eligible. Altogether 83% of patients (n=1643) responded to the request to fill out the EORTC Quality of Life Questionnaire and the EORTC QLQ Chemotherapy-induced Peripheral Neuropathy (CIPN) 20 instrument. Of the respondents, 500 (31%) had been treated with chemotherapy.

The five neuropathy-subscale-related symptoms that bothered patients with colorectal cancer most during the week prior to the survey were erectile problems (42% of men), trouble hearing (11%), trouble opening jars or bottles (11%), tingling toes/feet (10%), and trouble walking stairs or standing up (9%). Additionally, 29% of patients who received oxaliplatin reported tingling versus 8% of those not treated with chemotherapy (P=0.001). Numbness was reported by 17% who were receiving chemotherapy versus 5% who were not (P=0.05), and aching or burning pain by 13% receiving chemotherapy versus 6% not (P=0.03). Those with neuropathy symptoms in the upper 10% reported statistically significant and clinically worse HRQOL scores on all EORTC QLQ-C30 subscales.

"This study is one of the first to show that those with many neuropathy symptoms report a lower HRQOL compared with those with less neuropathy symptoms. Because our results are based on a large population-based study with a high response rate, extrapolating these results to the larger population of CRC survivors seems justified," write the authors.

Future studies, they add, should be prospective in nature, assess neuropathy both objectively and subjectively, and take the dose of oxaliplatin in every cycle and the duration of therapy (cumulative dose) into account. Studies should also focus on possible ways to prevent or alleviate these symptoms, preferably without dose reduction or early cessation of the treatment.

■ F Mols, T Beijers, V Lemmens et al. Chemotherapy-induced neuropathy and its association with quality of life among 2- to 11-year colorectal cancer survivors: results from the population-based PROFILES Registry. *JCO* July 20 2013, 31:2699–2707

Study defines use of neoadjuvant chemotherapy in advanced ovarian cancer

■ European Journal of Cancer

Ovarian cancer patients with stage IIIC disease and less extensive metastatic tumours show higher survival with primary surgery; while patients with stage IV disease and large metastatic tumours have higher survival with neoadjuvant chemotherapy, reports a Dutch study. The analysis of earlier EORTC data found that, in patients who did not meet these criteria, both treatment options showed comparable survival.

The standard treatment for patients with advanced ovarian cancer has been primary debulking surgery followed by chemotherapy. However, in 2010 the EORTC 55971 trial compared outcomes for three cycles of neoadjuvant chemotherapy followed by interval debulking surgery and three cycles of postsurgical chemotherapy (n=334) with primary debulking surgery followed by six cycles of postsurgical chemotherapy (n=336). Results showed that overall survival and progression-free survival were similar for both groups and that there were no significant advantages for either approach in terms of adverse effects, quality of life or postoperative morbidity or mortality. Questions remain whether these conclusions apply to all subgroups of patients presenting with stage IIIC or IV ovarian cancer, and if the selection of the best approach to treatment could be made before the start of therapy.

In the current study Hannah van Meurs, from the Academic Medical Centre in

Amsterdam, and colleagues, set out to investigate whether patient characteristics recorded at baseline in the EORTC trial could help identify subgroups who would benefit more from primary surgery or neoadjuvant chemotherapy. Altogether 10 different baseline clinical and pathological characteristics were identified, and to test the presence of interaction between the biomarkers and treatments the authors undertook Subpopulation Treatment Effect Pattern Plots (STEPP).

The results showed that patients with stage IIIC disease with metastatic tumours less than 45mm benefited more from primary surgery, while patients with stage IV disease with metastatic tumours greater than 45mm benefited more from neoadjuvant therapy. However in stage IIIC patients with larger metastatic tumours and stage IV patients with less extensive metastatic tumours both treatments were equally effective.

Furthermore, the biomarkers, age, WHO performance status, tumour grade, tumour histology, serum CA125 at study entry, pelvic mass, and omental cake showed no statistically significant difference in five-year survival between primary surgery and adjuvant chemotherapy.

"In conclusion... we found that patients with stage IIIC and less extensive metastatic tumours had a better survival after primary surgery while patients with stage IV disease and large metastatic tumours had a better survival after neoadjuvant chemotherapy," write the authors.

This strategy, they add, has the potential to result in an improved five-year survival of more than 6% in certain patient populations. "We suggest that systematic investigations of heterogeneity of treatment effects in randomised trials leading to treatment selection rules, could pave the way towards more individualised patient care."

■ H van Meurs, P Tajik, M Hof et al. Which patients benefit most from primary surgery or neoadjuvant chemotherapy in stage IIIC or IV ovarian cancer? An exploratory analysis of the European Organisation for Research and Treatment of Cancer 55971 randomised trial. *EJC* published online 15 July 2013, doi.org/10.1016/j.ejca.2013.06.013

Two years of trastuzumab shows no more effect than one

■ The Lancet

Two years of adjuvant trastuzumab is no more effective than one year in patients with HER2-positive early breast cancer, reports the latest analysis of the HERA trial. The study also demonstrated prolonged and sustained benefit from one year of trastuzumab compared to observation alone after a median follow-up of eight years.

Trastuzumab is an established treatment for patients with metastatic breast cancer with over-expression or amplification of the *HER2* oncogene. The open-label HERceptin Adjuvant (HERA) trial (*Lancet* 2007, 369:29–36) showed one year of adjuvant trastuzumab after standard neoadjuvant or adjuvant chemotherapy conferred significant overall survival benefits versus observation at a median follow-up of two years in patients with HER2-positive, early-stage, invasive disease. The original HERA trial also included a third randomised group given trastuzumab for two years, which has now been reported by Aron Goldhirsch and colleagues, from the European Institute of Oncology in Milan, for the first time.

In the open-label phase III trial, between December 2001 and June 2005, a total of 5102 patients were randomly allocated to three groups: observation (*n*=1698), trastuzumab for one year (*n*=1703), and trastuzumab for two years (*n*=1701).

Results at a median follow-up of eight years show that disease-free survival occurred in 367 (out of 1552) patients in the one-year treatment group versus 367 (out of 1553) patients in the two-year group (HR=0.99, 95%CI 0.85–1.14; *P*=0.86). Grade 3–4 adverse events, however, occurred in 16.3% in the one-year group versus 20.4% in the two-year group, and decreases in left ventricular ejection fractions were reported in 4.1% of patients in the one-year group versus 7.2% in the two-year group.

Furthermore the hazard ratios for a comparison of one year of trastuzumab treatment versus observation were 0.76 (95%CI 0.67–0.86, *P*<0.0001) for disease-free survival and 0.76 (0.65–0.88; *P*=0.0005) for overall survival, despite crossover of 884 (52%) patients from the observation group to trastuzumab therapy.

"Our results show no such additional benefit and a small but real increase in adverse events, leading to an unfavourable benefit–risk ratio for 2 years of adjuvant trastuzumab," write the authors. Taken together with the high cost of trastuzumab, this finding, they add, supports a standard duration of 12 months adjuvant trastuzumab.

In an accompanying commentary Heikki Joensuu, from Helsinki University Central Hospital, wrote, "The results of the HERA trial are in line with the biology and clinical behaviour of HER2-positive breast cancer. HER2-positive cancers are frequently aggressive tumours that usually recur early, within a few years after detection." This, he added, was in contrast to oestrogen receptor-positive HER2-negative cancers, which have a protracted clinical course, with recurrence that is sometimes detected only after the first decade of follow-up.

■ A Goldhirsch, R Gelber, M Piccart-Gebhart et al. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label randomised controlled trial. *Lancet*, http://dx.doi.org/10.1016/S0140-6736(13)61094-6

■ H Joensuu. Duration of adjuvant trastuzumab: shorter beats longer. *ibid*. published online 18 July 2013, doi.org/10.1016/S0140-6736(13)61448-8

Practising in partnership with Dr Google

The growing effect of social media in oncology practice and research

HOWARD (JACK) WEST

Online communities can help patients learn about and weigh up the options open to them. Where enough patients are involved, they are also helping to shape those options, opening up new opportunities for accelerating research and improving care.

Oncology is in the midst of transformation on several fronts. Anatomically defined diagnoses are being reclassified into molecularly defined subsets. A growing proportion of community-based oncologists are becoming employees of hospitals that are now increasingly becoming aligned into large networks covering broad geographic territories. The growing momentum of telemedicine is beginning to confer the possibility to deliver specialty and even subspecialty care to patients who would otherwise not have such ready access to it.

Along with these significant changes, access to information has been fundamentally altered by the Internet. For the first time, a significant proportion of patients and caregivers without formal medical training are turning to internet-based educational and support resources as they search online for relevant and reliable content. Through these efforts, many patients are becoming engaged in learning about their treatment options, including clinical trial opportunities, from outside sources. As is the case with any profound change, there are potential beneficial and detrimental effects of the disruptive influence of online information and support on the relationship between patients and physicians, as well as on the conduct of clinical research in a new era of molecular oncology.

The Oncologist

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More information, more complexity

The volume of new content becoming available has been escalating rapidly – more than doubling over the past 20 years – to the point where it is infeasible for any single physician to remain updated on the emerging treatment options and clinical research opportunities across anything other than the most subspecialised patient population. This is particularly true in the field of oncology, for which there are currently over 200 medical journals focused on cancer[1].

This situation is coincident with a fundamental change in cancer care, which is transitioning from anatomically defined large and relatively heterogeneous groups (e.g. breast cancer, lung cancer and colon cancer) to molecularly defined narrow subgroups based on the presence of discrete driver mutations with identifiable targets. Therefore, there is a proliferation of targeted therapies that are largely characterised by their greater efficacy in these subgroups, although they often entail an additional challenge of requiring an ever-increasing battery of treatment-directing molecular tests. The pace of new discoveries in this field has been rapid and is limited by the lag time of typically at least one year – and sometimes three or more years – from initial discovery of relevant information and its publication[2], followed by additional time for its widespread dissemination within the oncologist community.

Taken together, we can see that there is a growing volume of new clinically relevant medical information, perhaps especially in oncology, which is experiencing a transformation to increasingly molecularly defined, limited subgroups. These dramatic changes have created new challenges in the ability of the practising oncologist to remain current on a rapidly proliferating array of treatment and research options.

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

These patients are increasingly sharing links to new research options and facilitating faster enrolment in clinical trials

More patients are seeking cancer information online

Concurrent with these changes in the field of oncology, more patients and caregivers are seeking very specific and current information from online sources. As we might expect, the proportion of American adults with internet access has been increasing, from 50% in 2000 to 85% in 2012[3]. Moreover, although many elderly adults are less likely to connect online, many of these patients have children who seek information online and therefore they have 'second-degree' access. Among patients with a chronic disease, people living with cancer are most likely to be directly engaged in their care[4], using the internet for both seeking information and for connection to other patients and caregivers for support through social media.

The quality of information available online varies; however, this is recognised by the lay public, who still consistently rank healthcare professionals as the most trusted source of medical information[6]. These findings corroborate those from the Health Information National Trends Survey by the National Cancer Institute, which concluded that trust in information from healthcare professionals had increased from 2002 to 2008, while trust in health information from the internet had waned[7]. Online content is commonly sought but also recognised as complementing rather than obviating good communication between patient and physician[7].

The online experience for patients typically entails more than collecting information. One of the critical elements of time spent online is the social connection afforded from fellow patients, caregivers, family, and friends – not only emotional support but also practical advice for managing daily challenges[9]. Accordingly, clinicians may see steadily rising numbers of patients participating in online communities, especially for rare diseases[10]. Beyond providing support and background information, these sources are increasingly becoming indirectly integrated into clinical practice from patients incorporating what they learn into their own decisions. Specifically, online communities are shaping management plans about where and from whom to receive treatment, when to pursue a second opinion, and whether to seek clinical trial options that may be unavailable and even unknown to their local medical team as treatment options become more specialised on the basis of narrower subgroups.

Online patient groups are changing medical practice and facilitating clinical research

With patients seeking information online, more are requesting specific treatment and tests that they may learn about from sources other than their own physician. Although physicians may have mixed feelings about patients seeking information about treatment options from outside sources that may not be relevant to the patient's particular care, the fact remains that online groups have emerged as the "third party in the examination room" as a factor influencing patient perceptions of various management options[10]. Is this adding value or undermining patient care?

In a recent survey of over 2200 American adults by the Pew Internet Foundation, 42% of the overall population and 60% of 'e-patients' – the growing population of patients who are "equipped, enabled, empowered, and engaged in their health and health decisions"[7] – reported that they or someone they knew had been significantly helped by medical information they found online, compared with only 3% who reported that they or someone they knew had been harmed by online content[6]. Although not exhaustively studied, the limited available information does not support the contention that poor-quality information undermines the delivery of effective care.

Self-aggregating online patient groups have become instrumental in the transition into small, molecularly defined populations that are geographically distributed, essentially turning monolithic, large populations of anatomically defined cancers into subgroups that are akin to a new rare disease. These patients are increasingly sharing internet links to new research options and are facilitating faster enrolment in clinical trials seeking these rare populations, even leading patients to travel to the few locations in which very promising investigational agents are offered[11].

This beneficial effect of online communities emerged as early as a decade ago when the Life Raft Group, and several other international patient-based groups focused on advocacy and research efforts for gastrointestinal stromal tumours (GISTs), began sharing news of the growing favourable experiences with imatinib in clinical trials for patients with GISTs. This work led Dr George Demetri, one of the

pivotal leaders in these nascent clinical research efforts in GISTs, to summarise, "The new research model pioneered by the Life Raft Group is making it possible for patients and family members to contribute to clinical research for their diseases in unprecedented ways"[5].

More recently, patients with lung cancer with the newly identified and very uncommon anaplastic lymphoma kinase (ALK) or ROS-1 rearrangements, for which the ALK inhibitor crizotinib has been demonstrated to be effective, have connected online to share information in discussion forums about a wide range of emerging investigational agents for this population, including LDK378, AP26113, CH5424802 and ganetespib[12]. This range of research options would exceed the knowledge base of not only a general oncologist but also nearly all specialists in thoracic oncology. On these discussion forums, patients from multiple different trial centres often share their experiences on early clinical trials in a way that enables patients to know more about the trends of outcomes in this early research than even the investigators, who are typically aware of only the results in the patients at their own treating facility.

A glimpse of the future and patient-initiated research

In addition to the potential for online communities to facilitate efforts of ongoing investigator-led trials in limited locations, there is a potential for patients to play a more active role in accelerating clinical research by facilitating research on their own clinical conditions, including pooling their data in aggregated databases that can be queried and potentially lead to new insights. Although generally limited by a heterogeneous quality of data entry and a far more open eligibility than the research enterprise led by established clinical researchers, these databases provide the potential to draw from a wide range of subjects and identify associations that may corroborate early clinical observations and/or generate new hypotheses that can be addressed in prospective trials.

Some online communities (PatientsLikeMe.com, CureTogether.com), are developing research efforts that offer the potential to aggregate findings of efficacy and tolerability of treatments for which there is little or no financial support for prospective clinical trials. With a growing emphasis on the validity of patient-reported outcomes (PROs) as relevant endpoints in clinical trials, these communities also provide a ready source of large numbers of subjects across a broad geography who are motivated to contribute to clinical research. Such communities can help overcome limitations of cost and reach large numbers of geographically dispersed patients for PROs in many research efforts. Nascent efforts in this direction have included the collection of self-assessed efficacy and toxicity, including peer-reviewed publication of these data[13,14].

CureTogether.com has recently partnered with 23andMe.com, a company that offers genome-wide screening analyses directly to consumers for a wide range of predictive markers for development of medical conditions in the future. Together, they are initiating a series of population-based studies of people diagnosed with specific medical conditions or identified predictive genetic factors. These companies are currently seeking to accrue up to 1000 patients with any form of sarcoma or myeloproliferative neoplasm to look for genetic markers in the patients; they potentially will expand to include evaluation of genetic markers in first- and second-degree relatives of patients.

Patients, physicians, and the online community

The Internet has disrupted many industries, with the delivery of healthcare now in the midst of an ongoing, rapid transformation. Among the leading factors in this process is the dramatic increase in the sheer volume of new medical content becoming available and the need to be integrated to formulate optimal treatment recommendations; this extent of new information precludes the possibility of any single healthcare professional knowing everything that could be helpful to a patient. Second, cancer care is evolving into a new era of molecularly defined subgroups that has created new complexity that requires greater individualisation of treatment recommendations, while often limiting appealing research opportunities to a few distant trial centres. Medical information is no longer available only to healthcare professionals, but rather it is often readily searchable by the lay public. Moreover, many patients are creating new content and sharing it in real time through online patient communities.

These patient communities are poised to help navigate these transitions. Self-aggregating narrow patient subgroups are facilitating communication about promising clinical trials for these populations. Many patients and caregivers are seeking to help their own cause by providing insights into their own experiences that can be aggregated into population-based data that may lead to a better understanding of their disease and potential novel treatment options. The clinical oncology community stands to benefit by capitalising on the potential of patients and caregivers to accelerate the research process and bridge the limitations of geography through the connectivity fostered by internet-based communities. ■

Author affiliation

Howard West is affiliated to the Swedish Cancer Institute, Global Resource for Advancing Cancer Education, Seattle, Washington, USA

Details of the references cited in this article can be found at www.cancerworld.org

My World

Adel Araf is a clinical oncologist who trained in Ain Shams University, Cairo, and is now working as a specialist medical oncologist in Dubai Hospital, in the UAE. He leads a group of young oncologists from the region who are working to drive up standards of cancer care throughout the Middle East and North Africa.

Why I chose to work in cancer

I chose clinical oncology, which combines medical and radiation oncology, because I was impressed at how biology and physics come together to give magnificent results. Cancer is a very interesting and challenging branch of medicine.

What I love most about my job

Finding ways to relieve the pain and suffering of my patients. Sometimes even the smallest things can help, like giving them a quick appointment.

The hardest thing about my job

The hardest thing is telling a patient there are no more treatment options. It is particularly hard when you see patients who cannot receive the optimum treatment because it is too expensive and not covered by their insurance.

What I've learnt about myself

I like to be different, and I'm always looking to find new ways to solve problems.

I'll never forget...

A young patient with breast cancer metastasised to the lung, who I treated at the beginning of my residency in clinical oncology in Ain Shams university hospital. She was very dyspneic, and I thought she was going to die. But I was highly impressed by how she improved after chemotherapy and she did very well for a long time. I learnt never to lose hope. We always have to do our best, because we still don't really know how the disease will behave. A very bad situation can turn out quite well.

A high point in my career

Setting up my research group, MedicalSurveys-17, and the MENA breast cancer guidelines project that we started with the ESO/EASO. This project seeks to gather information about the clinical practice of oncologists in the MENA region (Middle East and North Africa) and highlight obstacles to applying international guidelines. The findings will be used to adapt the guidelines to regional circumstances. It encapsulates my interest in trying to improve the service we give to cancer patients by minimising the impact of economic and logistic issues on our treatment decisions.

I wish I were better at...

I wish I were able to do more things at the same time and to achieve more in a shorter time.

What I value most in a colleague

I value colleagues who are smart and work hard. I like people who always think outside the box and try to find new solutions.

The most significant advance in my specialism in recent years

I think the most significant advance in cancer treatment recently is personalisation of treatments and finding specific receptors and targets that can predict how each patient will respond to a given treatment and give a clue about their prognosis.

My advice to someone entering clinical oncology today would be...

Work hard and think about different ways of doing things. Success comes from innovating, not just being more clever.

What I wish I'd learnt at medical school

I wish I had learnt more about clinical research and been offered more of a chance to get involved in planning and carrying out clinical trials. ■