

They could be alive today

→ Anna Wagstaff

Every year thousands of people die unnecessarily from cancer because their care is sub-optimal or arrives too late. Europe has known where the problems are for more than a decade and has the knowledge to improve matters. It is the political will that is lacking.

During the 1990s, a series of reports emanating from the EuroCare project revealed significant differences between survival rates for a wide variety of cancers in European countries.

Five years after being diagnosed, a stomach cancer patient in Iceland was around three times more likely to be alive than a similar patient in Slovakia, the UK, Denmark, or Poland. The differences were not just about resources, because Denmark and the UK are relatively affluent with access to the latest drugs and up to date equipment. Many factors may have skewed the results, but it was hard to avoid the conclusion that some patients were dying because their cancer care was not up to scratch.

The EuroCare statistics shocked the UK into overhauling cancer serv-

ices, with an emphasis on reducing waiting times and ensuring equal access to specialist care. Denmark also took measures to improve the quality of its cancer care.

Many lessons were learnt. But there is plenty of evidence to show that patients are continuing to die across Europe because available knowledge and techniques are not being used to best effect. Indeed, some experts believe that the situation is likely to get worse.

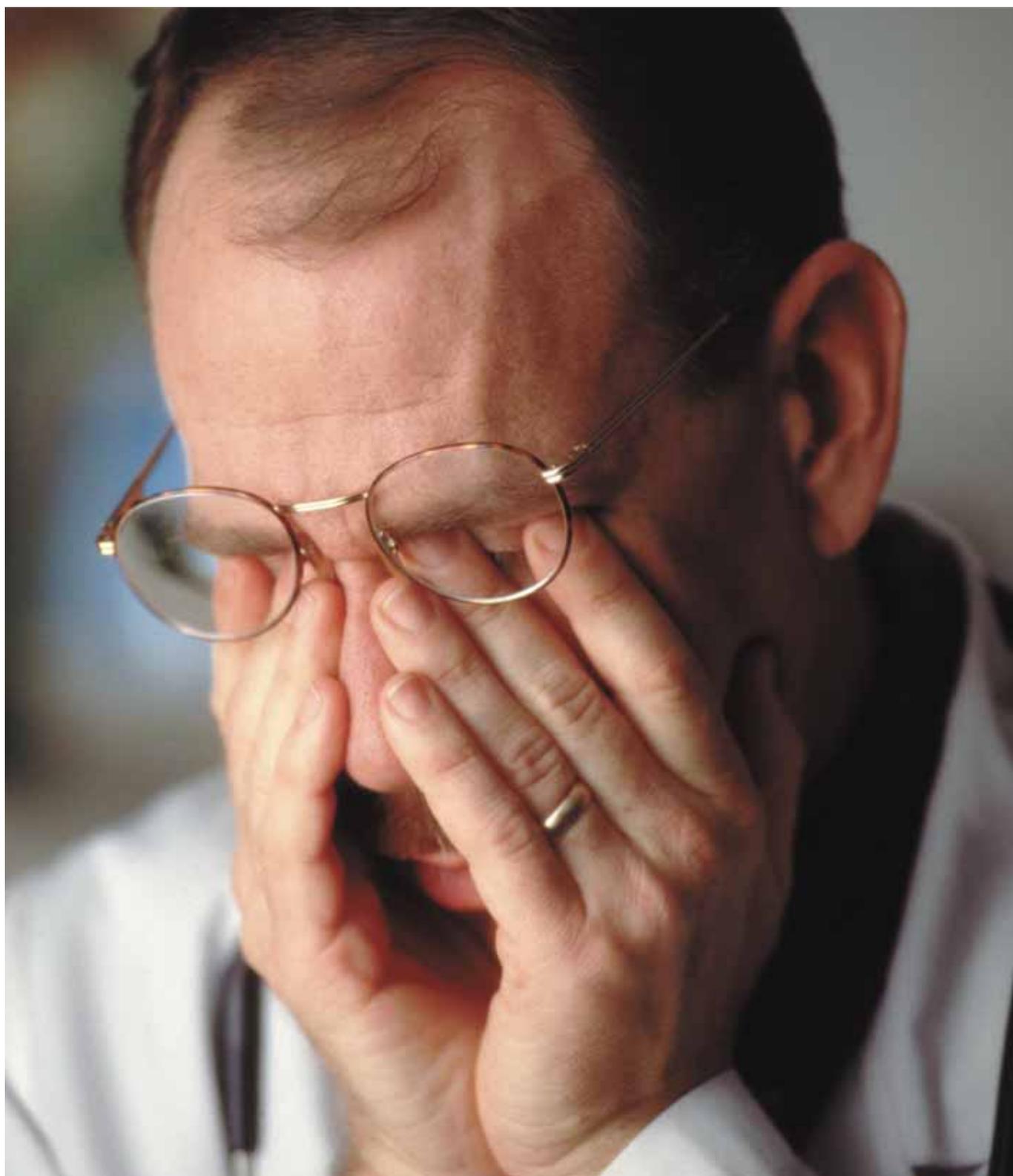
KNOW YOUR DISEASE

Oncologists need to know an increasing amount about the pathology of the disease. If the tumour has been incorrectly defined or wrongly staged, the treatment will be sub-optimal. Guiseppe Viale, professor of pathology at the University of Milan – European Institute of Oncology (EIO), believes that most oncologists

would be horrified to know how frequently this happens.

Take breast cancer. Pathologists were once simply required to define the extent and type of tumour through examining its morphology; today, they have to characterise the cancer in far greater detail. They report on how many lymph nodes are involved and evaluate the tumour for oestrogen, progesterone and HER2 expression. On the basis of these reports, fundamental decisions are made such as whether the patient requires adjuvant chemo- and/or radiotherapy, whether hormonal therapy is sufficient, or whether the patient can safely forego adjuvant therapy following surgery.

Viale says that confidence in these reports is often misplaced. “We know that 20–25% of patients who have been assessed as node-negative have disease recurrence and will



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eventually die of the disease. If we go back to those regional lymph nodes and examine more sections, we will find metastases in the large majority of these patients. The risk to these patients was not assessed correctly in the beginning.”

The story on endocrine response status is hardly more encouraging. Quality control in the UK has established that the false-negative result for oestrogen and progesterone receptors lies somewhere between 15% and 25%; the picture in Germany is a little better (11–24%). Many European countries have no quality control procedures, and the results coming out of their labs could be even more unreliable. Viale estimates the false-negative figures in Italy to be closer to 20–25%.

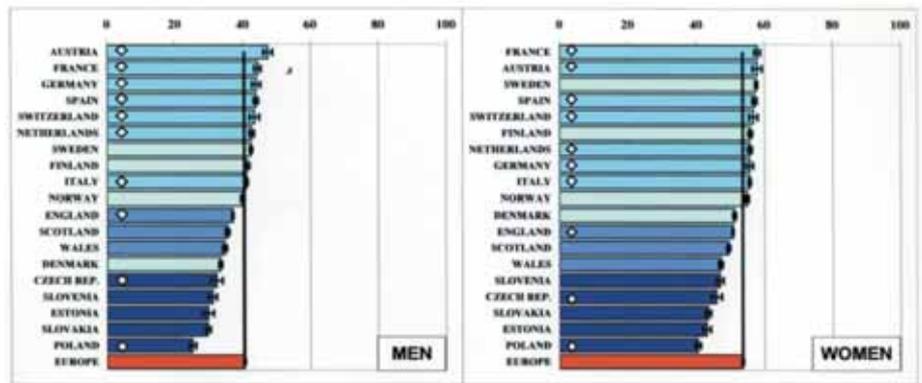
There are also problems with HER2 evaluation. False-positive rates of up to 30% are common and this is true whether the assay is done by immunohistochemistry or using the FISH (phosphorescence in situ) procedure. The problem, says Viale, lies with the pathologist rather than the test.

“You can see that a large fraction of breast cancer patients are not treated properly... it makes you a bit nervous about what is happening around you.”

Problems are more evident in breast cancer, because we know more about subtypes and the implications for treatment than for many other cancers. But differentiation and tailored treatment is the future for most cancers, giving the role of the pathology labs even greater importance.

Viale believes that pathologists who are not working as part of a multidisciplinary team are not aware of how their conclusions determine treatment.

This is something Viale himself



Source: M P Coleman, G Gatta, A Verdecchia et al. EUROCORE-3 summary: cancer survival in Europe at the end of the 20th century. *Annals of Oncology* (2003) vol 14 (Suppl 5): v128–v149. Reprinted with permission of Oxford University Press

learnt only after he left his job in a general hospital. “I thought I knew breast cancer, but when I started working at the EIO, I changed my approach completely. I started to realise, for instance, that saying ‘10% progesterone positive’ is completely different to saying ‘80% positive’ in terms of treatment – it’s not just a question of saying ‘negative’ or ‘positive’. Once you realise that, you are ready to spend the necessary time to make an accurate evaluation.”

One way to help pathologists become more aware of the significance of their role would be to make funding available for pathologists from centres participating in clinical trials to attend coordinating meetings. They should also receive feedback on the quality of their evaluations in real time, rather than several years later after the trial has closed.

In some countries poor access to the latest diagnostic and imaging techniques is an obstacle to accurately defining the disease.

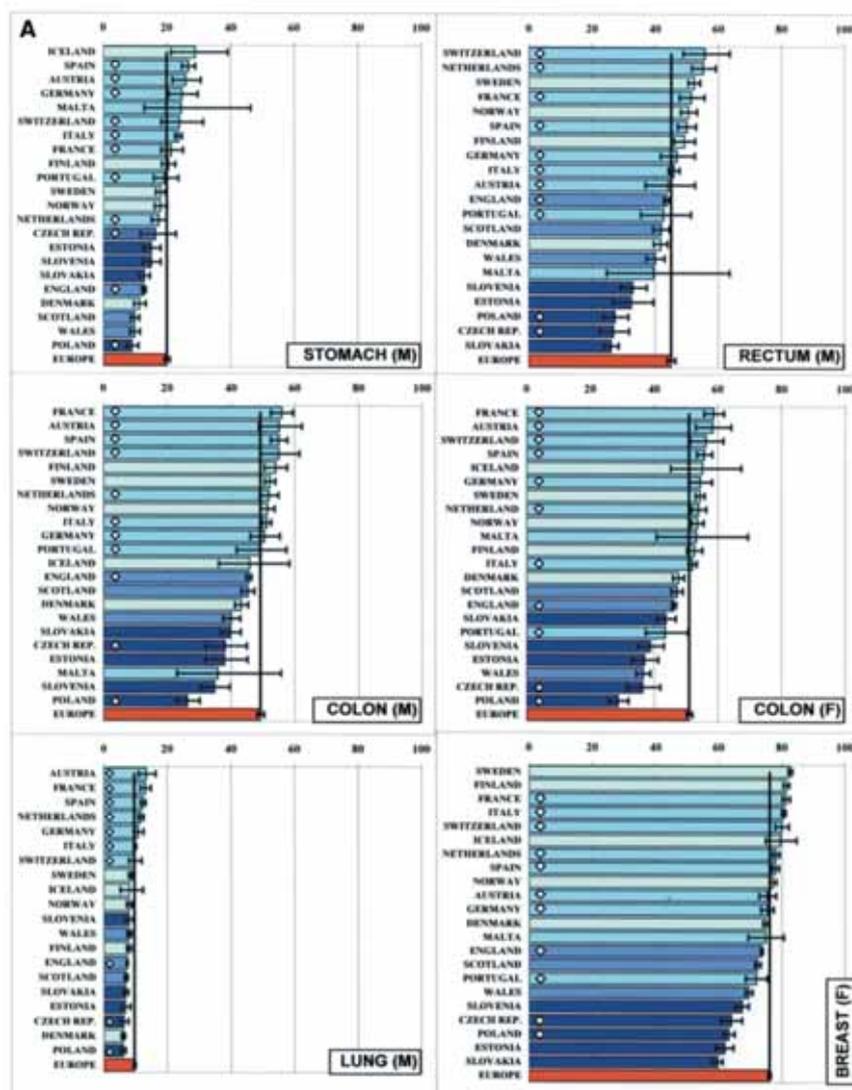
Adrian Udrea, who works in the chemotherapy department at the Oncological Institute of Cluj, Romania, says that the standard of

medical oncology training is very similar to that in Western Europe and that money is available for cancer drugs. However, clinicians cannot always treat patients effectively because they are unable to characterise the disease.

There are no immunohistochemistry testing facilities outside the main cancer centres in Bucharest and Cluj, and these centres do not offer services to smaller hospitals. Access to imaging techniques such as bone scan, CT and MRI is also extremely limited. The ultrasound equipment is 20 years old, and unreliable.

“There must be some way to organise the system to work better with the money we have,” says Udrea. “We are spending money for expensive drugs, but we don’t know what we need to know in order to use them effectively.”

The problem is not confined to central and eastern European countries. In Italy, for instance, though costly trastuzumab prescriptions are reimbursed by the national health system, the HER2 test that indicates whether the tumour might respond to the drug is not.



Comparative index of 5-year relative survival (%) by country for adults diagnosed in the period 1990-1994, followed up to 1999. These were the graphs that shamed the UK into improving cancer services

15 rectal or 15 oesophageal or 15 pancreatic or 15 gastric cancers a year, you shouldn't do any at all, because you are automatically associated with worse outcomes."

This principle has been recognised in Europe for 20 years, and many countries encourage regional or national specialisation – but bad practice still continues. Eggermont says that there is a need for a new referral culture, where different units work collaboratively rather than competing for patients, and agree a rational way to divide specialist services.

Even in the Netherlands, with its excellent referral culture and commitment to regional specialisation, it is proving hard to stop a few errant small hospitals carrying out low volumes of oesophageal or pancreatic operations. The situation is probably far worse in other countries, particularly those with weaker public health sectors and poorly coordinated cancer treatment delivery, and in poorer and more rural areas.

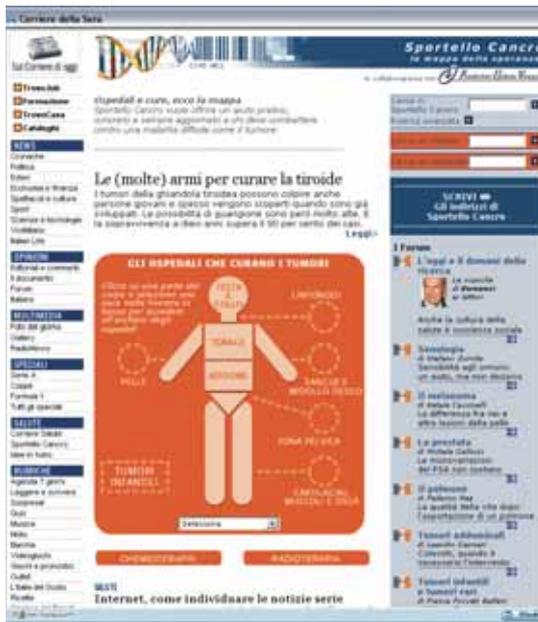
The public have little access to information about volume. However, www.corriere.it/sportello-cancro, a website supported by the leading Italian daily the *Corriere della Sera* and the Umberto Veronesi Foundation, provides a fascinating insight into how surgical procedures are divided

KNOW YOUR PROCEDURE SURGERY

Since the 1980s, studies have shown that referring a patient to a specialist centre for difficult procedures to excise pancreatic, gastric and rectal cancers significantly lowers their risk of dying from postoperative complications. The latest figures from the Netherlands show patients operated for pancreatic cancer in small hospitals are ten times more likely to die than those treated in the larger centres.

Expert surgery is also associated with far lower local recurrence rates – between five and ten times lower in the case of rectal surgery.

Lex Eggermont, head of surgical oncology at the Erasmus University Medical Centre in Rotterdam, says observing simple principles will minimise unnecessary deaths from poor surgery. "First you must be well trained. Second, there is a direct volume effect – the more you do, the better you are. If you don't do more than



The Italian website www.corriere.it/sportello-cancro. For the best chance of survival, click the relevant part of the body to find out which hospitals in your region have the greatest experience in dealing with your type of cancer – and which hospitals to avoid

between major centres and peripheral hospitals across Italy. It shows that around 230 hospitals are carrying out surgical procedures for cancers of the digestive tract even though their annual case load is less than the recommended 15. When the figures are broken down to surgery on the oesophagus or rectum, the number of hospitals carrying out between 1 and 15 procedures is very much higher.

RADIOTHERAPY

Of all cancer treatments, radiotherapy is the easiest to systematise. It is concentrated in larger centres, with fewer problems associated with low volumes of treatment. Decades of quality control prevents most easily identifiable mistakes, but controversy remains over long-term effects. Radiation for testicular cancer has been associated

with new cancers up to 20 years later and there is some evidence to show that high-dose radiotherapy to treat Hodgkin’s lymphoma or breast cancer can damage the heart.

Intensity modulated radiotherapy allows for more aggressive and effective treatment, concentrating firepower on the tumour and sparing normal tissue to a greater extent. However, if mistakes are made, the damage can be all the greater. Jacques Bernier of the Oncology Institute of Southern Switzerland in Bellinzona, says, “We have to have much stricter controls before irradiating, because if the plan calculation and the delivery don’t correspond, you can give two, three or four times the dose you calculated.”

Gross errors are rare however. One UK study of almost 2000 patients treated with 95,000 individual doses showed an error rate of 0.18%, all of minor clinical significance.

Of greater concern, is the under-investment in latest equipment and software, leading to increased waiting time or treatment using outdated methods. Radiotherapy now forms a part of the treatment of more than 50% of all cancer patients, but according to the European Society for Therapeutic Radiology and Oncology (ESTRO), the services in many countries cannot cope with this level of demand, and access to treatment is now a major problem.

KNOW YOUR PATIENT

Medical oncology has emerged as the defining mode of treatment for most

cancers and the arena in which major advances are expected. Unfortunately, it is also least amenable to quality control.

In the 1980s and ’90s, huge variations in the way patients were being treated led to much greater emphasis on evidence-based medicine. The idea was to educate all oncologists to act according to the best available evidence rather than relying on empirical knowledge or on the established policy in their departments.

Recently published studies show that following guidelines has an impact on survival. However, the key to success lies in how guidelines and evidence is applied to each patient.

Aron Goldhirsch of the Department of Medicine at the European Institute of Oncology, worries that too many medical oncologists use guidelines uncritically and prescriptively.

“Every patient is absolutely unique, but part of a population. Statistics and epidemiology have brought medicine away from individual patients, so that what is said is actually ‘on average’. It’s like ‘one-size-fits-all’. If we don’t recognise patterns of diversity from one individual to another, and we take an average answer as a good answer for everyone, we are likely sometimes to be wrong.”

Statistics in cancer medicine is typically used to group people into wider populations in order to analyse outcome and factors that influence response to treatment. Goldhirsch’s concern is that no-one is teaching the methodology of applying those statistics to the individual patient.

Goldhirsch is involved in the MINDACT breast cancer trial (Micro-array for Node negative Disease may Avoid ChemoTherapy), which seeks to find out how responses to therapies vary according to the

specific genetic and pathologic characteristics of subgroups of node negative breast cancer.

He says that, while breast cancer is ahead of the field in defining subtypes and identifying oncogenes, the same process is now happening elsewhere, and all cancers will require ever more precise treatments. The trouble is that as much of the evidence that oncologists currently use represents only an average response, some tumour subgroups will respond better than the average, and others may not respond at all.

A wise oncologist, says Goldhirsch, does not apply evidence unquestioningly, especially when detailed information is not available. 'Average' data are just not precise enough. "Doubt is very important. When you don't have anything else, evidence-based is by far the best, but you must use it critically or you end up stagnating knowledge."

Encouraging oncology departments to participate in well-structured clinical trials that apply tailored treatments, would be one of the most effective ways to improve their methodological approach, he says.

Bob Pinedo, director of the VUmc Cancer Centre at Vrije Universiteit hospital in Amsterdam, emphasises the diversity of patients, as well as the diversity of tumour types and believes that young oncologists need more training in internal medicine to allow them to tailor treatment to their patient.

Medical oncologists give toxic drugs to people who may not only be weakened by cancer, but have co-

morbidities such as heart conditions or diabetes. They may be taking other medicines and their organs may not be functioning normally. Pinedo feels young oncologists are not being taught to take this into account when they prescribe medication, and some patients are being put at risk as a result. "You need to know what is going on with the patient. You need to do a lot of research making use of their tissues and blood to understand the biology, to understand their pharmacodynamics. It's not just a question of measuring drugs, you need to know the effects of your drugs on the organs."

Knowing your patient also means knowing who is at extra risk of cancer. Pinedo is frustrated at lack of effective monitoring for people known to be at very high risk.

He wants to see women who have a family history of BRCA positive breast cancer routinely screened by MRI, to detect disease earlier than by mammography.

People with familial colon cancer also need more effective screening he says. Studies coming out of the US and the Netherlands have shown that only half of the patients in whom adenomatous polyps had been identified by colonoscopy show positive for colon cancer using the faecal occult blood (FOB) test. So why, asks Pinedo, are we still relying on this method of detection for people known to be at high risk? "I foresee a big problem here. We will get angry people who have been screened with the FOB test and they get cancer, and they will say why did this happen?"

MULTIDISCIPLINARY TREATMENT

Top quality pathology, medical oncology, surgery and radiotherapy are all essential to save every patient who can be saved. But each mode of treatment becomes significantly more effective in the presence of the vital ingredient: multidisciplinary collaboration.

The majority of treatments involve two or three types of therapy, often interlinked. Almost 90% of all radiotherapy now takes place within a multidisciplinary framework.

Effective multidisciplinary working makes it possible to select the most effective treatments with the least damage to the patient. Supportive care is also essential. Nutrition, for instance, can make the difference between surviving or dying for very ill patients. Monitoring and dealing promptly with life-threatening side-effects such as thrombocytopenia and neutropaenia is essential; the involvement of expert cancer nurses in the multidisciplinary teams can make a difference here.

Such a multidisciplinary approach is impractical outside of larger hospitals or networks of collaborating centres. Where cancer patients make up only a small proportion of a surgeon's or pathologist's work, they will not be able to organise their timetables around multidisciplinary meetings, which would in any event happen too infrequently for them to build a relationship or to understand the roles and problems of other specialists.

It is the combination of specialist surgery and multidisciplinary working that has been credited with significant differences in survival rates

If we don't recognise patterns of diversity from one individual to another, we will make mistakes

Involving pathologists, cancer nurses and dieticians in the team can make a difference to survival

between larger centres and peripheral hospitals in a number of studies, notably in Scotland in the early 1990s. Finding a way to deliver specialist multidisciplinary treatment to all patients, no matter where they live, is one of the logistical challenges for good cancer care.

TEACHING CANCER

Decades after the multidisciplinary approach was recognised as effective, it is still rarely taught as a concept in medical schools.

Franco Cavalli of the Oncology Institute of Southern Switzerland, Bellinzona, says the fragmented way in which cancer is taught lies at the heart of many problems. "There is no overall teaching in oncology. You will have the internist, who will talk a little bit about cancer, the surgeon, who will talk a little bit about cancer, the pathologist and so on. Most universities do not have well-structured teaching on cancer, and because of that most physicians, when they finish their training, do not know enough about cancer."

WAITING TO DIE

The best cancer services are undermined if patients do not receive a diagnosis and treatment when they need it. Evidence shows that in some tumours, making patients wait weeks, sometimes months, for radiotherapy reduces their chance of a cure, allowing the tumour to grow beyond a 'curative size' or to metastasise. ESTRO, the professional body for European radiologists and radiotherapists, says

very few EU countries have sufficient linear accelerators and trained staff to provide an adequate service, and that a high proportion of patients are treated outside clinically acceptable time limits.

Where waiting lists are long, radiotherapy departments systematically treat patients when they know it is too late, and doctors have to choose which patient will receive the best care today, and which will have to wait – or be assigned to palliative treatment simply because their chance of a cure is below the threshold that makes them a priority within an overstretched system.

Pinedo believes there is also a critical shortage of oncology specialists across Europe that will become more acute as more patients survive longer. "We know that the prognosis for colorectal cancer improves if you do secondary surgery. But if you have a waiting list of months for a primary colon cancer, you are not going to take a patient with a little metastasis and put them on the list." Pinedo still goes to multidisciplinary meetings and argues for that surgery to be done, but he is aware of the pressure. "You know the surgeon is already very upset because of his waiting list. I know I'm asking them something I shouldn't ask, because there are certain things you just cannot ask these days, even though you know it is the best for the patient."

He worries that the medical profession seems to accept delays as a fact of life. "If 30 years ago you would say, 'operate within four weeks', now

you accept an operation within eight weeks. I just cannot work that way. I find it horrible, because we don't tell our patients the risks."

WHAT NEXT?

All over Europe, patients who could have been saved are dying because they did not get high-quality treatment when they needed it. We know a lot about the training and systems of care delivery needed to avoid unnecessary deaths. We need now to know how to get there from here.

PATIENT POWER

Many argue that patients hold the key, through exercising informed choice over where they are treated.

Eggermont says the most effective thing to do is "bombard" patients with advice to ask their hospital the crucial questions: "How often are these procedures performed here? What is your track record? What are your mortality figures?" And if the answer is not reassuring, they should go elsewhere.

Patient groups have been advocating this approach for years, but they have precious little information to go on; the Sportello Cancro website is an exception. Eggermont would like to see similar statistics on volume and track record available in all countries. "That would force the system to reform."

In the Netherlands, the Breast Cancer Patients Association is setting its own agenda. It has drawn up quality guidelines, covering issues such as waiting lists, expertise and choices between different interventions, and

has set a deadline of January 1 2007 for treatment centres to comply or face a boycott by patients.

A Europe-wide accreditation system for specialist breast cancer units, developed and operated by the European Society of Mastology, is in the pipeline. This will set standards for specialist centres in breast cancer care, and will offer an important marker for patients deciding where to go for treatment.

But directing patients to the best treatment centres creates its own waiting list problems. Patients may have to choose between waiting eight weeks for top-quality treatment, or immediate treatment at a hospital with less expertise. In the end, says Pinedo, pressure on centres of excellence can compromise the quality of care they can offer.

The European Court of Justice believes that patients should be able to use their power. In three landmark cases between 1998 and 2003, it ruled that patients have the right to be reimbursed for treatment in another Member State if they cannot get the treatment they need from their own health system within a reasonable time.

This is not a solution, since it does not create any new resources in the offending state, but it establishes the legal principle that timely treatment is a right that health services cannot ignore.

PLAN AHEAD

In the end, the answer lies in networks of adequately resourced centres that can provide all sectors of the pop-

ulation with access to specialist facilities. This is the system that has kept Sweden, Finland and the Netherlands at the top of the cancer survival league. It is now being emulated by countries like the UK, Ireland and France, which can build on a strong base of 20 regional cancer centres.

Building new state of the art cancer centres is not always the issue. The Netherlands, for instance, is developing a structure designed to achieve top-quality treatment in smaller hospitals that agree to specialise and coordinate their work. It does, however, require a system in which there is no big financial loss in referring a patient elsewhere. It is also easier in more concentrated populations, although Sweden pioneered this system, and distances there can be great.

The French national cancer plan, introduced in 2003, represents a welcome attempt to address all aspects of cancer care: training and continual medical education, equal access, a mandatory multidisciplinary approach and patient information. Importantly, it also supports the work of the French cancer registries, which should provide information that can be used to further improve the system.

Despite these encouraging signs, Cavalli cautions that France has always believed in a strong state, and is probably an exception. He argues that the current European economic and political climate is driving the organisation of public services towards greater liberalisation, which may be counterproductive since cancer care needs well-planned systems driven by collaboration not competi-

tion. If, for instance, hospitals are obliged to contract out specialist pathology services, there is no way that pathologists will be able to work within a multidisciplinary team.

Health budgets are generally static or shrinking, because of pressure to limit public spending. He says there is a danger of developing the two-tier health system that exists in the US – a highly sophisticated system for those who can afford it, and a fundamentally inadequate one for those who cannot.

Cavalli points out that life expectancy in Russia has decreased by around seven years since the collapse of state-led systems, some of which can be attributed to the collapse of the health system. He says there is no reason to believe that minimising the public sector and encouraging private provision in eastern Europe will provide an effective cancer service for more than a tiny part of the population.

MONITOR THE SYSTEM

Funding for the EuroCare project has dried up, and as a result many national or regional registries have lost their sense of dynamism and purpose. Many registers have also been hit by privacy legislation, though some people argue this is more of a problem of political will or legal interpretation.

Jan Willem Coebergh, of the Eindhoven Cancer Registry in the Netherlands, says he is worried by this apparent retreat from the approach that taught us much of what we now know about unnecessary can-

Very few EU countries are able to provide
an adequate radiotherapy service

cer deaths. His concern is that, without effective registries, we will no longer be able to tell which systems or procedures are working and which are not. Ian Kunkler, who analysed registries for the Scottish cancer plan, agrees. "A cancer service without cancer registration is like a clinical trial without a statistician."

Norway is swimming against the tide. The government is investing heavily in upgrading its registry system to include detailed pathological and clinical data. Surgical procedures, radiotherapy and medical treatment will be recorded as well as instances of recurrences and metastases. This huge project requires close cooperation between registries and clinicians, but the government is convinced that the information it yields about variations in survival will be worth it.

But there is also plenty that could be learnt from less ambitious projects that analyse smaller populations. The European Network of Cancer Registries has recently regrouped and is looking to promote these sorts of studies throughout Europe.

WINNING THE ARGUMENT

People will continue to die from cancer under any system. However, dying because your health system let you down, you live in the wrong country or even in the wrong part of the country, is not inevitable and should be considered unacceptable.

When the compelling voice of patients and their families joins with the medical profession and is backed by firm evidence, it is possible to capture the media and political agenda. That is what is needed to force governments to address the inequities revealed by the EuroCare data, and ensure that every cancer patient is given the best chance of life.

10 ways to prevent unnecessary deaths

1

Training. Teach oncology in a holistic way instead of splitting it between disciplines and organ specialties. Teach the importance of early detection, multidisciplinary treatment and comorbidity issues.

2

Pathology. Raise awareness among pathologists of the key role they play. Involve pathologists in planning and executing clinical trials. Introduce greater quality control, and feedback results quickly.

3

Surgery. Ensure that surgeons carrying out complex procedures do at least 15 such cases a year. Make relevant information available on the Internet and encourage patients to choose carefully where they go for treatment.

4

Radiotherapy. Ensure rigorous quality control of high-dose modern procedures. Conduct long-term studies to monitor possible late side-effects such as heart problems in breast cancer and Hodgkin's patients, or new tumours that may emerge decades after treatment.

5

Medical oncology. Promote the use of evidence-based guidelines and encourage oncology departments to participate in trials. Improve training in interpreting statistical evidence to tailor treatment to individual patients.

6

Multidisciplinary working.

Ensure that all cancer treatment takes place within a multidisciplinary setting, either within one hospital or by co-ordinating specialists from different hospitals.

7

Networks. Organise well-structured networks of specialist centres. Encourage a culture of referral where hospitals collaborate rather than compete for patients.

8

Registries. Monitor effectiveness by collating and analysing data on diagnosis, treatment and survival.

9

Waiting time. Delays can cost lives. Define acceptable time frames for imaging, pathology and specialist treatment of different cancers, and provide sufficient resources and effective systems to keep delays within those limits. Educate patients to demand treatment within that time frame.

10

Cancer plans. Organise national and regional cancer plans, covering training, resource allocation, location of specialist services, professional guidelines, quality control, and evaluation.