If nothing is done...

Prize-winning article tells the story behind falling cancer mortality rates

The more we know about cancer, the harder it becomes to present a coherent and accurate picture of the nature of the threat and what can – and what cannot – be achieved through changing lifestyles, screening and investing in the search for a cure. **Ulrich Bahnsen** won a Best Cancer Reporter Award for his comprehensive article in the leading German weekly *Die Zeit*, which is republished below.

Cancer is a complicated disease. There are 230 different types of cancer. It occupies tens of thousands of doctors and scientists. It is big business. And if nothing is done it will kill more than 200 million people – one in four of all Europeans and Americans alive today.

Elizabeth Ward records the horrors. Year by year she and her colleagues in the American Cancer Society (ACS) collate the figures which speak of so much hope, anxiety, living, suffering and dying: new cases, cure rates, survival times, mortality.

It is hardly an uplifting activity, but Elizabeth Ward is upbeat. She has encouraging news. Fewer and fewer people are dying of cancer – even though more are developing the disease. American epidemiologists are convinced that they are witnessing the start of a continuing decline. "It is a robust trend," says Ward, "and we expect numbers to fall further in the next few years."

In Europe, too, there is a growing mood of confidence. Nevertheless, cancer is still a long way from being conquered. The decline starts from a high level: 553,888 people in the US died from cancer in 2004, but that is nevertheless 3,000 fewer than in the previous year. In 2003 the researchers had already recorded a lower number of deaths than in 2002. In Germany, deaths from cancer peaked in 1993. Since then the mortality figures have fallen by around 4,000 cases per year.

The evidence on the causes of the long-awaited turnaround now seems clear. On this point the epidemiologists are unequivocal. The breakthrough on the cancer front, says Ward, is primarily the result of prevention and early diagnosis. The celebrated advances in cancer medicine have apparently made only a minor contribution to the success story.

Ulrich Bahnsen

The health researchers' verdict is that it will be possible to reduce cancer deaths significantly, provided that politicians, and in particular the general public, adhere to the policy of prevention, or at least early diagnosis followed by prompt and state-of-the art treatment: this is the new success strategy. According to Otmar Wiestler, director of the DKFZ (German Cancer Research Centre), preventive oncology – long

Comprehensive coverage. This well-researched piece was the first in a series of three – the subsequent article looked at current efforts to improve the care of German cancer patients, followed by a piece exploring the late effects of treatment

regarded as indispensable in the US – has so far been completely neglected in Germany.

70,000 DEATHS COULD HAVE BEEN AVOIDED

Every year Germany has more than 70,000 cancer deaths that could have been easily avoided. Even though there are particular risk factors for many types of cancer, the majority – and in particular the most frequent types – are influenced by the three fatal factors of smoking, obesity and lack of exercise. Hence, at Germany's first National Oncological Prevention Conference, held in mid-June in Essen, the assembled experts did not want to confine themselves to appeals to politicians. Their call was addressed to the person on the street: cancer prevention is the responsibility of everyone, through giving up tobacco and through an active lifestyle. Even non-smokers can dramatically reduce their risk of cancer.

It is not only the Germans' pot bellies that are held to be dangerous. The researchers are also concerned by the wasting muscles of the nation's citizens. The two together – love handles, plus chicken wings where arms ought to be – are regarded as having particular cancer-causing potential. The proliferating fat tissue floods the body with cancer-stimulating hormones and pumps inflammation-causing signal substances into the blood. By contrast, muscles that are hardened by sport drive away these troublemakers: substances that inhibit the cascade of inflammation are released into the bloodstream by the muscle fibres. Thus people who are unfit and overweight slide even further into a state of systemic inflammation – a condition, in the words of DKFZ director Wiestler, in which cancer can flourish.

Smoking exacerbates the hormonal imbalance of overweight couch potatoes even further. The genotoxic effect of the poisons in tobacco smoke encourages the emergence of cancer, and the smoke contains substances which further stimulate the dangerous inflammation process. Exactly how inflammations promote the formation of tumours is not fully understood. It is likely that they encourage the malign degeneration of stem cells in the organs.

The celebrated advances in cancer medicine have made only a minor contribution to the success story

Nothing can be done about fitness and weight loss unless people agree to take action. Smokers, however, are having change forced upon them. Since 2004 the EU has been taking the battle against nicotine addiction seriously. Even in Germany, smoking bans are due to be imposed. The justification for clamping down on the civil liberties of smokers is the risk inherent in passive smoking, which claims up to 80,000 victims a year in the EU.

It would, however, be naïve to suppose that this move is primarily for the protection of non-smokers. The real aim of the ban on smoking in public places is to protect future generations by thoroughly repressive means. "Smoking bans establish non-smoking as the social norm," says Elizabeth Ward bluntly. In her view social proscription is necessary if the great goal of the health strategists is to be achieved: "All tobacco-dependent cancers are entirely preventable." Lung cancer is not the only form of cancer involved: cancers of the bladder, colon, breast, mouth, oesophagus, larynx and even the pancreas are also stimulated by the toxins in tobacco. One smoker in ten goes down with lung cancer; 90% of cases of the disease occur in addicted smokers.

But one of the worst killers could soon be history. The story also demonstrates the effectiveness of even unintentional cancer prevention. It seems that stomach cancer, which in the middle of the last century was still one of the commonest fatal cancers, has been held at bay by the refrigerator. Since we have taken to keeping food fresh by chilling it instead of by pickling, salting or smoking it, cases of stomach cancer and deaths from it have fallen rapidly. Now that the once rampant stomach ulcer has been conquered too, stomach cancer is likely to become a rarity. Stomach ulcers represent a chronic inflammation of the stomach lining as a result of infection with the stomach bacterium *Helicobacter pylori*; like the toxic substances in conventionally preserved food, it stimulates the emergence of cancer. Deaths from stomach cancer in industrialised countries have fallen by 80% since 1950.

This "unplanned triumph", in the words of the US doctor Christopher Howson, is now likely to be followed by a strategic victory. Doctors are hoping that cervical cancer will soon be eradicated by means of a vaccination. Worldwide some 250,000 women per year die of this cancer. The disease is always the long-term consequence of an infection with a papilloma virus. In Germany, the death rate has already fallen sharply as a result of smear tests (Pap smears), which enable the cancer to be identified at an early stage. It is hoped that two new vaccines against the papilloma viruses 16 and 18 will finally put the brake on the disease.

However, they have no effect on an already existing infection. Following a resolution of Germany's Standing Vaccination Commission (Stiko), the emphasis will therefore be on immunising girls and young women between the ages of 12 and 17.

Infections lie behind one in five cancers

Experts estimate that one cancer case in five is ultimately caused by a normally avoidable infection. Thus it seems that deaths from liver cancer are also largely preventable. Alongside alcohol abuse, which paves the way first for cirrhosis of the liver and then for cancer, infection with one of the various forms of the hepatitis virus poses the greatest risk. Although the liver infection leads on to cancer in only a small proportion of chronic cases (and then only after many years), the viruses are nevertheless the principal cause of this cancer.

According to the gastroenterologist Markus Cornberg of the medical university in Hanover, testing has revealed that half the liver cancer patients in his clinic are carriers of the virus. At least one million people in Germany are permanently infected with either the hepatitis B (HVB) or hepatitis C (HVC) virus. Since 1992 blood products, previously the principal source of infection, have been tested to guarantee their safety. Yet many people continue to become infected with hepatitis C – drug addicts through exchanging needles, and others through

The real aim of the ban on smoking in public places is to protect future generations

A message for you. With its talk of 'the German potbelly' and discussion of the national disquiet over 'repressive' anti-smoking laws, the Die Zeit article addresses key cancer issues in a way readers can readily relate to

simple foolishness that can put them at risk. "Getting yourself tattooed on the beach during your holiday in Egypt is not at all a good idea," says Cornberg, "One person in five there carries the virus."

Cancer caused by hepatitis B can be even more easily avoided. A vaccine against the virus, which can also be transmitted sexually, has long been available. What can be achieved by a campaign of vaccination against liver cancer was demonstrated 20 years ago by the island state of Taiwan. The government launched a mass HVB vaccination campaign for children in an attempt to control the rampant virus. The incidence of the cancer subsequently fell by half among those who had been vaccinated.

The health strategists would like to be able to report similar successes in other key areas of oncology. They don't want to carry on waiting for the hoped-for breakthrough in the treatment of advanced cancers. According to Michael Bamberg, president of the German Cancer Society, treatments in the late stages of cancer will in future need to be very carefully weighed up. In his view we should instead be spending the majority of the available funds on prevention and screening. "In the case of metastasised tumours we have already missed the bus; we must take pre-emptive action."

This change in thinking is the result of depressing experiences. The bitter realisation is that cancer cannot be conquered by the classical methods of oncology alone. In the 1970s, after spectacular successes brought about by the introduction of chemotherapy, it looked at first as though the war was already as good as won. The experts prophesied that victory over cancer was only a question of time and money. The aim was to halve the number of deaths from the disease by the year 2000. And there were indeed indisputable triumphs: in virtually hopeless cases such as testicular cancer cure rates rose to 90%; for leukaemia they rose to 75%. Likewise, Hodgkin's lymphoma, a type of cancer of the lymph glands, is now regarded as 80%–90% curable.

But since those days, cancer therapy has to a large extent stagnated. In the last four decades industrialised countries and pharmaceutical companies have pumped hundreds of billions of euros into basic research and the development of more effective treatments and new drugs. The American

National Cancer Institute alone has an annual budget of $4.5 billion. And it would be wrong to claim that the money has been pointlessly squandered. Highly effective drugs, ultra-precise radiation techniques and the increased refinements of surgery have increased cure rates for many types of cancer and extended the life expectancy of many patients. They have also improved sufferers' quality of life and reduced the side-effects of treatment which, with justification, were formerly feared. But progress is excruciatingly slow.

At this year's prestigious gathering of experts, the meeting of the American Society of Clinical Oncology in Chicago, it was again made clear that any hope for a 'magic cancer bullet' will remain an illusion. The 32,000 attendees were presented not with therapeutic miracles but with a wide range of small improvements – a couple of new drugs, better chemotherapies, the application to another type of cancer of a drug that has proved itself in a different area. "More of the same", sighed a US reporter resignedly during one of the daily press conferences.

The current situation can be summed up by saying that more and more patients are living longer and better lives with their cancer, but in the end almost as many are dying as 20 years ago. For cancers of the lung and kidney, which tend not to be diagnosed until a late stage, the outcomes of treatment are depressing; for pancreatic cancer they are disastrous.

In the middle of the 1990s, a quarter of a century after US President Nixon had declared the country's 'war on cancer', it was already evident that far-reaching success as a result of new treatments was not going to be as readily achievable as had been hoped. As the experts resigned themselves to the situation, heretics began to raise their voices. In 1997 the epidemiologists John Bailar and Heather Gornik of the University of Chicago caused a stir with a hard-hitting progress report. "The effect of new treatments for cancer on mortality has been largely disappointing," was the researchers' verdict in the *New England Journal of Medicine*; any hope of a substantial reduction in death figures before the year 2000 was "clearly misplaced". The professional world reacted with outrage, but it was impossible to refute the gloomy calculations coming from Chicago.

Early detection has a lot more to offer

As it turns out, Bailar and Gornik were wrong and yet at the same time they were right. When they spoke out, the fall in mortality rates had in fact already begun; it was to continue until the present day – a consequence of the declining number of smokers and the first early detection campaigns. "Cancer is a disease that is easier to prevent than to treat," wrote the oncologist Michael Sporn in *The Lancet*. "Our obsession with curing advanced cancers rather than preventing the disease in the first place or stopping it at an early stage has shifted victory into the far future." A fundamental reorientation was what Bailar and Gornik had also called for. They realised that, alongside intensive research, prevention and screening were key issues that must be accorded the status of a 'national priority'.

The US set up early detection programmes long before Germany. Their success is now apparent. A DKFZ study published in the spring showed that the better prognosis for American breast cancer patients compared with those in Germany is a consequence of the more thorough mammography screening that is carried out in the US. In the US 80% of women aged over 40 are screened in this way. As a result, breast cancer is detected earlier there. Germany did not start to develop a quality-assured mammography programme until 2004.

Early detection does indeed appear to have great potential. According to the German Cancer Society's president, Michael Bamberg, one-third of the common malignant cancers are not detected until metastases are already rife in the patient's body, and more often than not it is they that are the

The bitter realisation is that cancer cannot be conquered by the classical methods of oncology alone

In practice, however, early detection verges on being both a blessing and a curse

killers. "Even with the most modern targeted therapies it is very difficult to achieve a cure in that situation," says DKFZ director Wiestler. In other words: more screening saves lives.

In practice, however, early detection verges on being both a blessing and a curse. Early detection tests are available for only a few types of cancer. Furthermore, most procedures are imprecise. All too often tests give the all-clear when in reality a tumour is already growing; too frequently they report a cancer which is not in fact there or which does not require treatment. As a result patients are lulled into a false sense of security and may skip the next examination because "nothing showed up last time." Many prostate cancer patients, on the other hand, suffer from the consequences of unnecessary surgery – because the check-up does not reveal whether what was found was a rare type of aggressive prostate cancer or one of the forms that will never prove fatal.

Although there is an absence of clear evidence, colonoscopy is regarded as an effective method of early detection. The examination can be used not only to identify early signs of cancer; suspicious colon polyps, the precursors of colon cancer, can be immediately removed, thus preventing the cancer developing. Despite this, the procedure is not as popular as it deserves to be. Scarcely 10% of Germans undergo screening. "A lot can be done for colon cancer," says DKFZ epidemiologist Nikolaus Becker, "and quite a lot with quality-assured mammography."

Genome research may predict individual risk in the future

In the eyes of the experts, a crucial means of further reducing deaths from cancer will be the development of more precise early detection techniques. Here the results of basic research are giving grounds for hope. In tumour biology the age of the genome has dawned. While scientists previously had to search painstakingly for individual genetic defects within tumours, researchers of the Cancer Genome Atlas Consortium are now decoding the complete genetic make-up of tumours. The aim is to systematically identify all the genetic changes that take place in cancer cells. The $100m pilot project for the Cancer Genome Atlas is already under way. As a first step researchers are decoding and analysing the genetic make-up of the cancer cells of 500 patients with ovarian cancer, lung cancer and the almost invariably fatal brain tumour glioblastoma multiforme. It is already clear that defects in hundreds of genes control the emergence, growth and metastasising of cancer sites. Gene profiling opens up new opportunities for drug treatments, but its primary purpose is to facilitate effective diagnostic procedures.

The American drugs authority has already licensed the first genetic cancer profiler. The test systems, which go under the names of MammaPrint and Oncotype DX, measure the activity of a number of genes in breast cancer samples. The results can be used to predict whether a patient requires chemotherapy after surgery in order to prevent the tumour returning.

This is but the first move in a new era of cancer medicine. Similar procedures for other types of cancer are already at an advanced stage of development. For example, scientists at the University of Cologne are working on a test that would actually predict lung cancer. Doctors could then intervene before the patient becomes ill. However, it will be some years before the wonder tool is ready for clinical use. It takes almost as long to validate such diagnostic tools as it does cancer drugs.

Until then, we must continue to make full use of all available means of cancer prevention. Everyone can do something. Elizabeth Ward suggests as a starting point "Smoking? Don't even think about it."

This is an abridged version of an article first published in Die Zeit on 12 July 2007 under the title Die Wende im Kampf gegen Krebs. It is republished here with permission