The absolute benefits of anti-cancer drugs and of tobacco control

Sir Richard Peto

Cancer treatment and cancer prevention are both important. Even 50 years ago, before there were effective anti-cancer drugs, many people with some of the common types of cancer were completely cured by successful surgery. Nowadays, helped by screening and early detection, cancer surgery and radiotherapy still save more lives than cancer drugs do. The first anti-cancer drugs were, unfortunately, effective only against uncommon forms of the disease, such as the cancers of childhood or of early adult life. So, although for the few young people who actually had cancer the benefit from those old chemotherapy regimens could be large (because their risk of death was halved), for the population as a whole the absolute gain was relatively small. Modern drug treatments for the cancers of childhood and early adult life have reduced the population risk of dying from cancer before age 35 from 0.4% in the 1950s to 0.2% today, but this is an absolute gain of only 0.2%.

Only 25 years ago there was still, in many countries, a widespread nihilistic belief among many doctors about the drugs then available for the common types of cancer that although medical treatment could shrink such a tumour temporarily it couldn't ever cure the patient. Indeed, in the early 1980s many of the doctors who collaborated in randomised trials of drugs for common diseases like breast cancer or intestine cancer expected merely to help demonstrate that in the long run treatment with nasty anti-cancer drugs did not cure anybody, thereby at least protecting future patients from inappropriate over-treatment by over-zealous colleagues.

The trouble was, however, that back in the 1980s all of the randomised trials of the treatment of common cancers were too small to be statistically reliable on their own. So, in the mid-1980s we in Oxford got all of the breast cancer trialists in the world to collaborate and share their data with us. To our surprise and theirs, when the results from many different trials that had addressed much the same therapeutic question in breast cancer were added together, we did see some small but definite effects on five-year survival — hormonal therapy did something small but real, and so did chemotherapy.

Nobody really knew whether these small survival differences would be transient or permanent, so the trialists agreed that they would all share their data again every 5 years, in 1990, 1995, 2000, 2005 and so on; they've continued to do so, and they'll do it again next year, in 2010. The good news was that the small gains in 5-year survival did not disappear. Indeed, long follow-up showed that the differences in 10-year and in 15-year survival from hormonal therapy, from chemotherapy and from radiotherapy were slightly bigger than the differences in 5-year survival had been, and although the 10-year benefits still weren't very big, hormone therapy and chemotherapy can both be given, adding the two benefits together. Moreover, continuation of the worldwide collaboration between many trials over many years showed that some of the newer types of chemotherapy and hormonal therapy were slightly better than the older ones, and eventually, by a series of small but definite steps forward over the past 25 years, we've got to the point where about half the women who would have died of their breast cancer will not now do so, because of earlier diagnosis and better treatment. Hence, even though more women develop breast cancer nowadays, the national breast cancer mortality rates in many countries are definitely falling, and I hope they'll keep on doing so. It's still not a very big absolute gain, but it is real. In the UK female population, for example, the probability of death before age 70 from breast cancer has gone down over the past 20 years from about 2.5% to 1.5%, which is an absolute gain of 1%. Not good enough, but not bad.

Control of the main cause of cancer offers considerably greater absolute benefits, however, and in Europe and North America much the biggest cause of cancer is tobacco. Smoking is more important than all other known causes of cancer added together, and it causes even more deaths from other diseases than from cancer.

When we compared men in Britain who had smoked cigarettes throughout adult life with men who had never smoked, we found a 10-year difference in life expectancy. (Men who had

stopped at age 30 did almost as well as the never-smokers.) That 10-year difference is about twice as big as other studies had suggested, because ours was the first clean study of men who had smoked substantial numbers of cigarettes throughout adult life. Partly as a result of our study, two-thirds of the smokers my age in Britain have now stopped, lung cancer rates are falling, and, as smoking kills even more people by other diseases than by lung cancer, the overall death rates from smoking are falling substantially, particularly in men. The proportion of UK males killed by smoking at ages 35-69 has already decreased from 20% in 1970 to 5% today, which is an absolute population gain of 15%, and it's still falling. British men have had the best decrease in tobacco deaths in the world (partly because they used to have the worst death rates from tobacco in the world), but there are also substantial decreases in tobacco deaths in several other developed countries, though not in all.

The really bad news today comes from big developing countries like China and India. We have worked with Chinese scientists in the 1980s and with Indian scientists in the present decade on large nationwide studies of tobacco deaths. Both in China and in India there are already about one million tobacco deaths a year, the annual number is rising, and tobacco consumption isn't falling.

Worldwide, there were about 100 million deaths from tobacco during the 20th century and there will be about 1000 million this century, if current smoking patterns continue (with widespread uptake of smoking and, at least in developing countries, little cessation until people are already ill). Practicable changes in public policy could avoid tens of millions of premature deaths over the next few decades, and could avoid hundreds of millions over the whole century. For example, the French government recently tripled the price of cigarettes, French cigarette consumption fell by half, and the government got richer. It's a much easier way to save lots of lives than improving cancer treatment is, but fortunately we can do both.