Eur J Cancer, Vol. 26, No. 4, pp. 500–508, 1990.
Printed in Great Britain

0277–5379/90$3.00 + 0.00
Pergamon Press plc

Feature Articles

Are We Winning the Fight Against Cancer? An Epidemiological Assessment

EACR—Mühlbock Memorial Lecture

Sir Richard Doll

INTRODUCTION

In the last 60 years the proportion of deaths attributed to cancer has increased progressively. In some countries the proportion has doubled from one in eight to one in four and in middle-aged women it is now almost six in ten. The principal reason for this increase is, of course, the successful treatment or virtual elimination of many other diseases; but it is not surprising if personal experience of the relative importance of cancer as a cause of death and a steady stream of reports in newspapers, on radio, and on television of a risk of cancer associated with (for example) life in the vicinity of nuclear installations, pesticide residues in food, nitrates in drinking water, and a wide variety of occupations—including laboratory research into the causes of cancer—has led many people to believe that our success in discovering new avoidable causes and in improving treatment is outweighed by the spread of new hazards.

Bailar and Smith's review of trends in the U.S.A.

This pessimistic view is not limited to non-scientists but has also been voiced by some cancer research workers, including experienced biostatisticians. It was expressed most forthrightly by Bailar and Smith [1] when, 3 years ago, they reported the trends in the incidence and mortality attributable to cancer in the U.S.A. The incidence, they found, showed an overall increase of 8% in whites over the years 1973–1981, with notable increases in cancers of the lung, colon, rectum, breast, and prostate; but they preferred to base their conclusions on the trend in mortality as several of the recorded increases in the incidence of cancer could have been artefacts due to the spread of screening and the consequent registration as cancers of lesions that appeared malignant histologically but were clinically benign.

They chose, therefore, as the most reliable indicator of progress in the control of the disease, the total age adjusted mortality rate, divided only by sex and race into whites and non-whites. Their results showed that the rates rose progressively over the period 1950 to 1982 in males, while in females, they rose in whites and fell slightly in non-whites before subsequently stabilizing. There were, of course, different trends for different types of cancer, including a reduction in mortality from all cancers combined under 30 years of age, but their general conclusion was that the data (I quote) 'provide no evidence that some 35 years of intense and growing effort to improve the treatment of cancer have much overall effect on the most fundamental measure of clinical outcome—death. Indeed, with respect to cancer as a whole, we have lost ground, as shown by the rise in age-adjusted mortality rates in the entire population.'

This conclusion was challenged, as might be expected, and two criticisms, at least, carried some weight. First, the inclusion of mortality in the very old distorts the results as deaths that used to be attributed to senility or some other non-specific term have been investigated with progressively greater intensity and attributed to specific causes. Secondly, 1982 was too soon to see the effect on mortality of some of the major advances of treatment that have affected, for example, the fatality of cancer of the breast [2]. The general picture is, however, affected only slightly if these two factors are taken into account and Bailar and Smith [3] concluded that (I quote again) 'The ugly fact remains that overall cancer mortality is rising . . . This cannot be explained away as a statistical artefact obscured by the clear evidence of progress here and there, or submerged by rosy rhetoric about research results still in the pipeline.'

TRENDS IN MORTALITY IN EUROPE

If, following Bailar and Smith, we were to accept the trend in the age-adjusted mortality rate as our prime indicator of progress in the fight against cancer, we would find that European data would, for the most part, lead to a similar conclusion, as Becker *et al.* [4] found for the Federal Republic of Germany. This is illustrated in Figs 1 and 2, which show the trends in age-adjusted mortality from all neoplasms in men and in women from the early 1950s to the early 1980s in six countries, drawn from the North, East, South, and West of Europe, which have been provided by Dr Muir and Dr Estéve of the International Agency for Research on Cancer (personal communication) together with the data for England and Wales, which have been extended to include mortality for 1986–1987.

The picture in men is truly dismal enough. In all seven countries the mortality was higher in 1980–1984 than in the

Correspondence to: R. Doll, Imperial Cancer Research Fund, Cancer Studies Unit, Radcliffe Infirmary, Oxford, U.K.
Presented at the Xth Meeting of the European Association for Cancer Research on 10 September 1989 in Galway, Ireland.

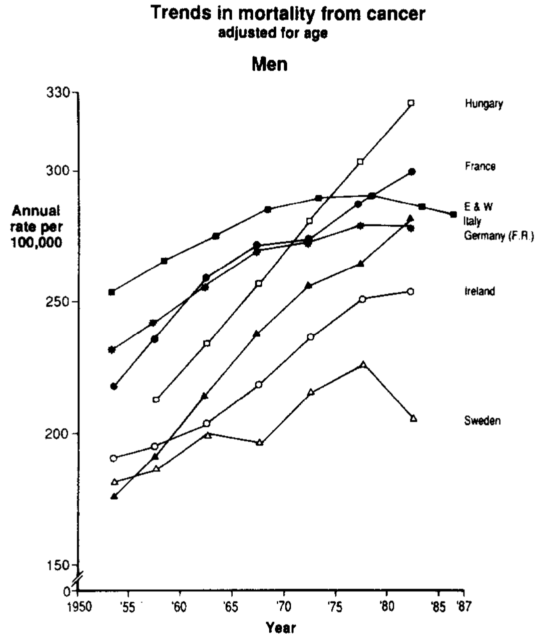

Fig. 1. Trends in mortality from cancer, standardized for age, in men in seven European countries from 1952–1954 to 1980–1984 (Hungary from 1955–1959, Italy to 1980–1983, England and Wales 1951–1955 to 1986–1987): annual death rate per 100,000.

early 1950s. In Hungary, Italy, and France the increase has been large and shows no sign of abating. In the Federal Republic of Germany and Ireland there is a suggestion that the increase has stopped or is slowing down, while in Sweden* and England and Wales there is evidence of a reduction since the late 1970s.

In women the position is different. The mortality has increased in four countries, but in no case has the increase been greater than 15% and only in England and Wales is it clearly continuing. In three countries (the Federal Republic of Germany, France, and Sweden*) the rate is now lower than it was 35 years ago. If the data for both sexes are combined, the situation is clearly worse than it was, though only marginally so in Sweden.*

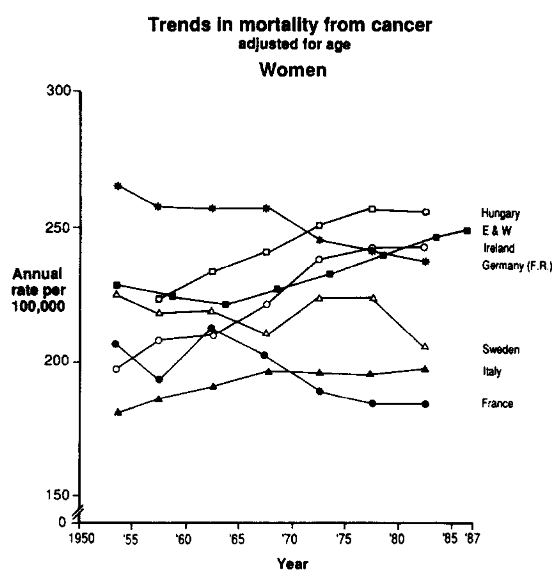

Fig. 2. Trends in mortality from cancer, standardized for age, in women in seven European countries from 1952–1954 to 1980–1984 (Hungary from 1955–1959, Italy to 1980–1983, England and Wales 1951–1955 to 1986–1987): annual death rate per 100,000.

I agree with Bailar and Smith that to assess progress the most appropriate indicator is the trend in mortality from all types of cancer combined, not only because the risk of death is the risk with which the individual is principally concerned, but also because trends in incidence may be distorted by the efficiency of registration and the prevalence of screening. That is not to disparage the value of incidence data, which are becoming progressively more important as survival improves for the detection of new hazards and assessment of the efficacy of measures for prevention. For our present purpose, however, incidence data must be relegated to second place. But although I agree with Bailar and Smith about the choice of indicator, I believe their assessment of the progress of the fight against cancer to be profoundly wrong; for by taking all ages together they allow the effects of recent progress to be outweighed by the effects of changes in behaviour and the prevalence of carcinogenic agents in the distant past, which are irrelevant to our assessment of current trends. If, instead of looking at the trend at all ages, we look at the trends separately for each sex in four broad age groups (standardizing for age within each of the four groups) the picture is entirely different.

This is illustrated by the rates for England and Wales at ages under 20 years, at 20–44 years, at 45–64 years, and at 65 years and above which are shown in Fig. 3. In each age group the rates in successive quinquennia have been expressed as proportions of the rates in 1951–1955. In males, the mortality has fallen at all ages under 65 years. At other ages it has risen progressively throughout, although the rate of increase is now falling off. In females the pattern is the same only in children and adolescents. In young adults the decrease has been less marked and there has actually been an increase at all ages over 45 years. At 45–64 years of age mortality rose until the 1970s and then began to decline, while over 65 years of age, the increase, in contrast to that in men, began only in the late 1960s and has recently accelerated.

That these trends should be so different at different ages and in the two sexes is the result of a complex interaction of the mix of different types of cancer at different ages and the prevalence of different carcinogenic factors, the patterns of human behaviour, the efficacy of treatment, and, to a minor extent, the standards of medical diagnosis that have characterized different periods over the last 80 years. To assess the effect of recent changes in the efficacy of treatment and of our efforts at prevention, we should concentrate on the changes in the two youngest age groups as these can have been determined only by changes in the recent past, unless perhaps they are occasionally determined by the previous experience of the individual's parents.

Children and adolescents

Consider first the change in mortality in children and adolescents. This owes little or nothing to changes in incidence. Whether there was a substantial increase in the incidence of childhood leukaemia in the first half of the century corresponding with the recorded increase in mortality is still open to doubt. It is possible that the reduction in the prevalence of infection in infancy postponed the time when the immunological system was first intensively stimulated and, so, according to Greaves' [5]

*See Addendum.

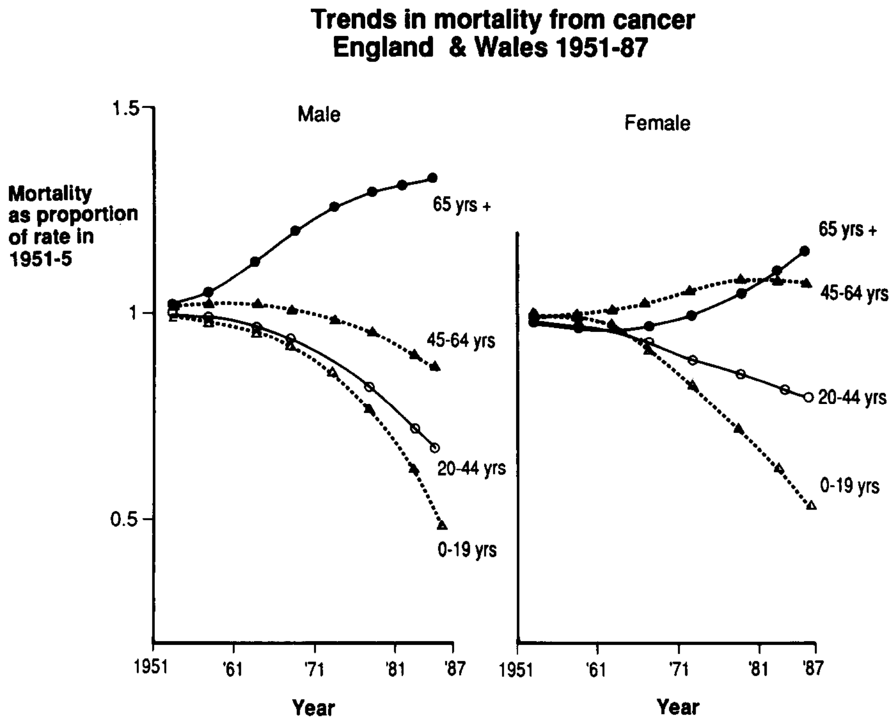

Fig. 3. Trends in mortality from cancer in England and Wales from 1951–1955 to 1986–1987, by sex in four age groups (under 20 years, 20–44 years, 45–64 years, and 65 years and over): standardized for age within each age group. Mortality expressed as percentage of rate in 1951–1955.

hypothesis, provided time for mutated pre-B lymphocytes to proliferate in the marrow, and cause a real increase in the incidence of the disease. Alternatively, the large increase in recorded mortality could have been an artefact due to the reduction in the fatality of common infections occurring in an early stage of the disease, thus allowing it to develop to a stage at which it was easily recognized [6, 7]. In any case there is nothing to suggest that childhood leukaemia or any other type of childhood cancer has changed much in incidence over the last 40 years, while there is ample clinical evidence that survival has improved enormously. The changes in mortality that have occurred under 20 years of age are shown for the seven European countries and the U.S.A. in Table 1. Only in Hungary has the rate increased. In several others it has declined by more than 40% and it may by now be substantially lower, as the British data for the 1980s show an acceleration in the rate of improvement.

Table 1. *Change in mortality from cancer under* 20 *years of age*: 1951–1987

Country	Period	Recent mortality as a percentage of rate in 1950s	
		Male	Female
England and Wales	1951–1955 to 1986–1987	48	53
France	1955–1959 to 1980–1984	76	78
Germany (F.R.)	1955–1959 to 1980–1984	58	54
Hungary	1955–1959 to 1980–1984	108	110
Ireland	1955–1959 to 1980–1984	67	88
Italy	1955–1959 to 1980–1983	72	73
Sweden	1955–1959 to 1980–1984	59	51
U.S.A.	1950–1953 to 1980–1983	54	54

Treatment is, however, less satisfactory than the reduced mortality would suggest, as it has sometimes led to stunted growth, mental retardation, infertility, and an increased risk of other cancers later in life.

Young adults

In young adults the position is very different, as the trends vary with sex and substantially also with geographical location. In women the mortality has decreased in each of the seven selected European countries. This is shown in Fig. 4, which shows the rates for each country expressed as percentages of the rate for that country in 1952–1954. The greatest fall has occurred in Germany, where the rate has been reduced by more than 30%. In five countries, the decline appears to be continuing; but in France it has almost ceased and in Hungary it has reversed, so that the rate is now almost back to its original level.

In men, the trends in Fig. 5 show a remarkable diversity, mortality in the early 1980s ranging from 72 to 164% of that recorded 30 years earlier. In three countries the rates are now lower than they used to be and in four they are higher. Six, however, show a decrease in the last decade and an increase has continued only in Hungary. This diversity accords with the fact that many of the types of cancer that occur at these ages are known to vary in incidence from place to place and from period to period and changes in human behaviour and the environment begin to compete with changes in the efficacy of treatment as an explanation for the change in mortality. We can, therefore, disentangle the various effects of changing hazards, measures for prevention, and improving treatment only by examining separately the incidence and mortality attributable to each type of the disease. This requires an intimate knowledge of local conditions so that, for this purpose, I must limit my analysis to the data for England and Wales, where the mortality in 1986–1987 was only 74% of that 35 years earlier.

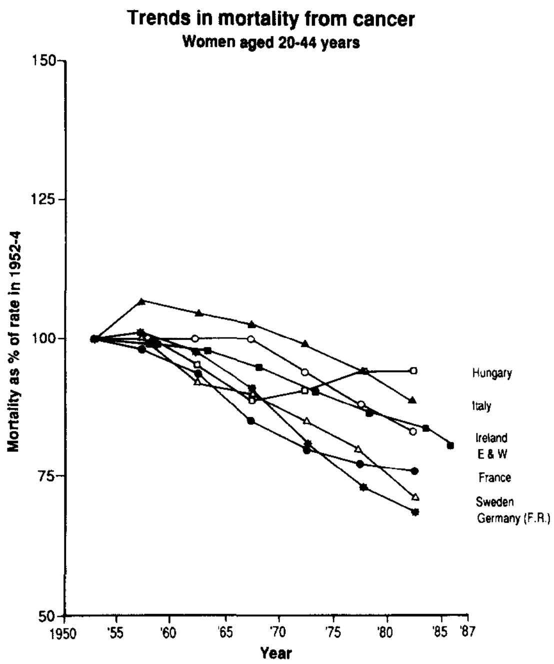

Fig. 4. Trends in mortality from cancer in seven European countries from 1952–1954 to 1980–1984 (Hungary from 1955–1959, Italy to 1980–1983, England and Wales 1951–1955 to 1986–1987): women at ages 20–44 years, standardized for age. Mortality expressed as percentage of rate in initial period.

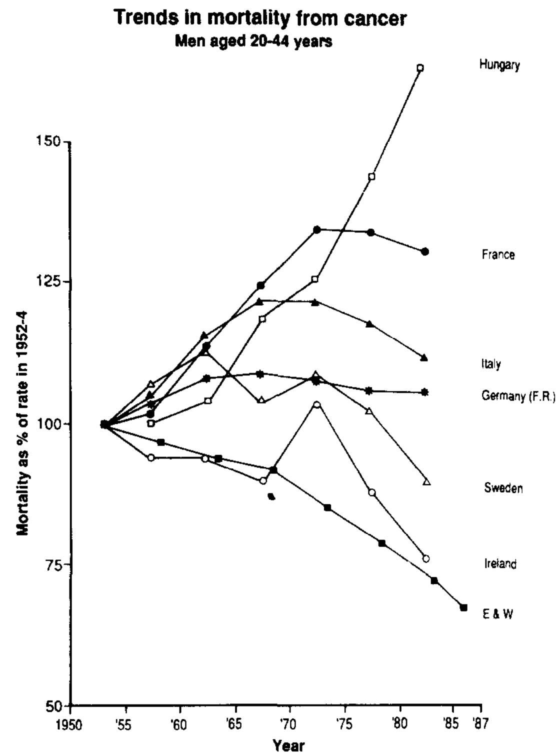

Fig. 5. Trends in mortality from cancer in seven European countries from 1952–1954 to 1980–1984 (Hungary from 1955–1959, Italy to 1980–1983, England and Wales 1951–1955 to 1986–1987): men aged 20–44 years, standardized for age. Mortality expressed as percentage of rate in initial period.

Cancers showing a reduction in mortality

Fourteen types of cancer have shown a fall of 10% or more in both sexes or in the one sex to which they are limited. These are shown in Table 2. Some are uncommon causes of death and contribute little to the total mortality from the disease (cancers of the small intestine, gall bladder, larynx, and thyroid). Seven, however, were each responsible for more than 5% of the total cancer mortality in one or other sex in this age group in the early 1950s and these are shown separately on the left of the table.

By far the most important are the reductions in mortality from cancers of the stomach and lung. The first, alone, would have brought about a reduction in the mortality from all cancers of 8.5% in men and 7.6% in women. Treatment has made little impact on the fatality of the disease and the reduction must be due to a reduction in incidence, which is confirmed by cancer registration data for those parts of the country in which cancer registration has been reasonably complete for the last 20 years. The reasons for the reduction remain a mystery. Two factors may have contributed, namely, changes in the methods of food preservation, in particular the use of refrigeration and perhaps the addition of antioxidants and the decline in the use of salt, and secondly, an increased consumption of fruit and vegetables. The latter has been inversely related to the rise of the disease in almost all case-control studies in which it has been investigated, but the size of the increase is inadequate to account for the

Table 2. Cancers showing substantial decreases in mortality in both sexes or in the one relevant sex: ages 20–44 years

Important causes of mortality, 1951–1954	Mortality in 1986–1987 as percentage of mortality in 1951–1954		Other cancers	Mortality in 1986–1987 as percentage of mortality in 1951–1954	
	Men	Women		Men	Women
Stomach	26	25	Small intestine	67	75
Colon	63	53	Rectum	49	36
Lung	37	88	Gall bladder*	63	83
Ovary	—	71	Larynx	50	25
Brain and CNS	67	60	Testis	61	—
Hodgkin's disease	46	64	Bladder	48	45
Leukaemia	90	81	Thyroid	33	33

*Mortality as a percentage of the rate in 1961–1965.

decreased incidence of the disease and changes in food preservation seem likely to have been more important. There is, however, no direct evidence that they are. The idea that the disease is caused by carcinogenic nitrosamines formed *in vivo* from amines and nitrites, derived principally from bacterial reduction of nitrates in the mouth or the achlorhydric stomach, is attractive and is supported by the fact that nitrosation is inhibited by vitamin C. It is not supported, however, by the generality of epidemiological studies, most of which have failed to relate the incidence of the disease to the amount of nitrate in drinking water or food, in the air during the manufacture of nitrate fertilizers or in the saliva or urine of individuals. Nitrosation *in vivo* may, perhaps be responsible; but, if it is, the intake of nitrates is not generally the rate-limiting factor.

The other principal contributor to the reduction in mortality has been cancer of the lung, which has caused a much bigger reduction in the total mortality from cancer in men (15.1%) than in women (1.1%). That the mortality should have been so substantially reduced is, perhaps, surprising when cigarette smoking, which is by far the most important cause of the disease [8], remained at a fairly constant level in men from the 1930s until it began to fall in the late 1960s and increased in women until it began to fall in 1978. The explanation would seem to be the change in the quality of the tobacco, which has delivered progressively less tar per cigarette smoked since before the Second World War, a change that was accelerated intentionally by the tobacco industry in the mid-1960s. Whether the early drop in tar delivery is sufficient to account for the start of the reduction in mortality is unclear and a small part of the decrease may also have been due to the reduction in atmospheric pollution from the combustion of coal that began as a result of government intervention after the disastrous fog of 1952. This would be consistent with the idea that atmospheric pollution may have interacted with cigarette smoking to produce perhaps 5–10% of all lung cancers in men [8].

Reductions in mortality from cancer of the colon and rectum have each made worthwhile contributions, the combined effect of which has been to reduce the total mortality from cancer by 4.4% in men and 5.1% in women. An improved standard of surgery throughout the country may have caused a higher average rate of survival, but much of the reduction must have been due to a reduction in incidence. Registration of cancer has not been sufficiently complete in Britain to put much trust in the size of the recorded trends, but the fact that the registration rates in this age group declined by 22% in men and 30% in women from the early 1970s to the early 1980s provides support for the belief that much of the decline in mortality must have been due to a decline in incidence. This could have been brought about, in part, by an increase in the consumption of green vegetables, but only to a very small extent by the increased consumption of wholemeal bread which has been material only in the last decade.

Prevention must have played a part in the reduction in mortality from cancers of the bladder and ovary, principally, in the case of cancer of the bladder, by the elimination of 2-naphthylamine and benzidine from industrial use. The mortality attributed to cancer of the ovary increased substantially in the first half of the century, as is illustrated in Fig. 6, due principally to the reduction in fertility, but partly also perhaps as a result of better diagnosis. The decrease in mortality, which began in the early 1970s, must partly reflect the response to platinum and other forms of chemotherapy, but it must also reflect the introduction of oral contraceptives which have the same effect

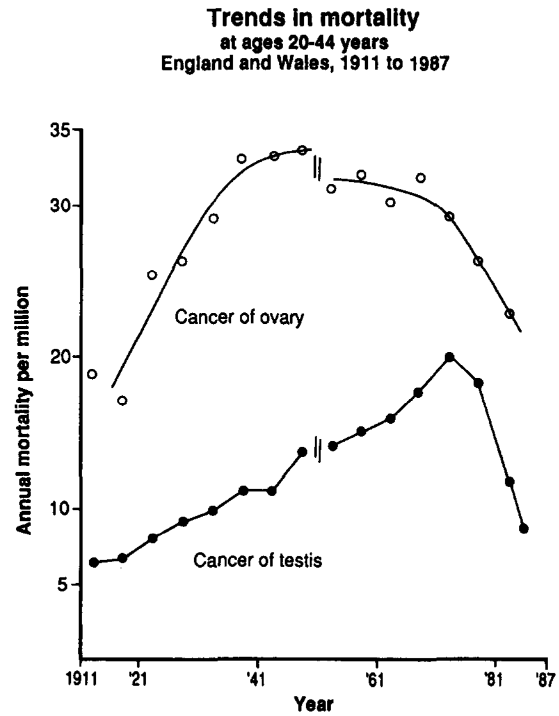

Fig. 6 Trends in mortality from cancer of the ovary in women and from cancer of the testis in men, in England and Wales from 1911–1915 to 1986–1987, at ages 20–44 years, standardized for age: annual death rate per million. The break in 1950 reflects a change in the rules for classifying causes of death.

on the risk of developing the disease as multiparity, and will reduce the risk by 50% if used for more than five years.

For three of the remaining cancers, the reduction may be wholly due to improved treatment—more intensive radiotherapy, careful staging, and the use of chemotherapy in the case of Hodgkin's disease, chemotherapy and marrow transplantation in the case of leukaemia, and chemotherapy in the case of cancer of the testis. That the reduction in the last should have been barely 40% may appear surprising in view of the dramatic effect of the platinum drugs that were introduced at the beginning of the 1970s. In fact, the reduction has been greater, as the disease has become progressively more common since about the time of the First World War and the mortality has been reduced by 57% from its peak rate in 1971–1975, as is shown in Fig. 6. Why the disease should have become more common, is a mystery; but it is certainly fortunate that the platinum drugs were discovered when they were, or it would by now be a major cause of death in young men.

Time precludes consideration of the trends in the relatively uncommon causes of death, but we must note the surprising reduction in the mortality attributed to tumours of the brain and central nervous system of 30–40%: surprising that is to me, because there has been no great improvement in therapy and the disease has sometimes been thought to have become more common. Reports of an increase have, however, failed to take account of the need to group together malignant, benign, and unspecified types of tumours. Failure to do this results in the appearance of a spurious increase in the mortality attributed to malignant tumours, as diagnosis has become progressively more precise and the nondescript diagnosis of a cerebral tumour as the cause of death (classified by WHO rules as of unspecified malignancy) has given way to histological diagnoses, like astrocy-

Table 3. Cancers showing little change in mortality: ages 20–44 years

Type of cancer	Mortality in 1986–1987 as percentage of mortality in 1951–1954	
	Men	Women
Breast*	—	103
Myelomatosis	100	89

*Causing 25% of the total mortality from cancer in women in 1951–1954.

toma. As a result the number of deaths attributed to malignant neoplasms of the brain has increased, while the number attributed to all neoplasms of the brain has not. The reduced mortality from this heterogenous group is, I suspect, primarily due to the better provision for the treatment of benign tumours plus, perhaps, the elimination of some incorrectly diagnosed secondary tumours arising from other sites.

Cancers showing little or no change

Two types of cancer listed in Table 3 have practically the same mortality as they did 35 years ago. Myelomatosis probably hasn't changed much in incidence and the treatment, though possibly prolonging life, has had little effect on the ultimate outcome. The unchanged mortality from cancer of the breast is, however, misleading, as the mortality increased by 16% from the late 1950s to the early 1970s and has decreased since. The increase cannot have been due to oral contraceptives, as it began too soon and the reason for it is unknown. The more recent decrease can be attributed only in part to improved treatment as there was also a decrease in the registration rates of 9% between 1971–1974 and 1981–1984.

Cancers showing discrepant changes in men and women

Five types of cancer have shown discrepant changes in the two sexes. These are listed in Table 4. Four are listed by the International Agency for Research on Cancer [8] as types of cancer caused by smoking and there is much evidence that smoking may also cause the fifth (cancer of the kidney).

The small increase in mortality from cancers of the pancreas and kidney in women, with very little change in the mortality rates in men, fits with the different trends in smoking habits in the two sexes. The changes are different from those seen for cancer of the lung, but that is not surprising as the smoke from low tar cigarettes, which have long been the predominant type in Britain, spares the bronchi but is inhaled more deeply so as to produce the same blood level of nicotine as the old high tar cigarettes. It follows that, even if the smoke from low tar cigarettes contains a smaller amount of carcinogens it may cause the same amount to be present in the blood or urine.

Alcohol is a major factor in the production of the three other cancers, all of which occur in the upper digestive tract, and the increase in the consumption of alcohol will account for some of the increase in mortality of two of them in men. Why, however, should there have been such a marked decrease in the mortality in women? The enormous variation in the mortality from oesophageal cancer throughout the world is a clear indication of the importance of some factors other than alcohol and tobacco in the aetiology of the disease and there is reason to think that

Table 4. Cancers showing discrepant changes in the two sexes: ages 20–44 years

Type of cancer	Mortality in 1986–87 as percentage of mortality in 1951–1954	
	Men	Women
Tongue and mouth	200	83
Pharynx	107	41
Oesophagus	190	53
Pancreas	93	130
Kidney	100	133

nutritional deficiencies may also play a part, as they were thought to do in Sweden in relation to cancer of the pharynx in women. In this case, it may be that the reduction in women reflects a specific improvement in their standards of nutrition. Some unrecognized factor may also be required to account for the increase in mortality from cancer of the tongue and mouth in men, which has occurred widely throughout Europe, and most notably in France, where alcohol consumption has actually been reduced and where the mortality in this age-group has been increased six-fold.

Cancers showing substantial increases in mortality

Lastly there are six types of cancer that show an increase in mortality of 10% or more in both sexes or in the one relevant sex. These are listed in Table 5. Two increases are particularly disturbing. Cancer of the cervix, which now accounts for over 12% of all fatal cancers in women in this age group, and melanoma which accounts for 3% in both sexes combined.

The increase in cervix cancer, which is opposite to what has occurred in many other European counties, is most marked in the youngest women, the rate in women under 35 years of age now being more than twice what it was 30 years ago (236%). Earlier this century the rate had declined; but the trend has

Table 5. Cancers showing substantial increases in mortality in both sexes or in the one relevant sex: ages 20–44 years

Type of cancer	Mortality in 1986–1987 as percentage of mortality in 1951–1954	
	Men	Women
Liver*	138	163
Melanoma	250	177
Cervix†	—	117
Connective tissues	164	158
Non-Hodgkin's lymphoma	126	127
Mesothelioma‡	210	131

*Mortality as a percentage of the rate in 1961–1965.

†Causing 10% of the total mortality from cancer at these ages in women in 1951–1954 and 12% in 1986–1987.

‡Mortality in 1980–1983 as a percentage of the rate in 1968–1971.

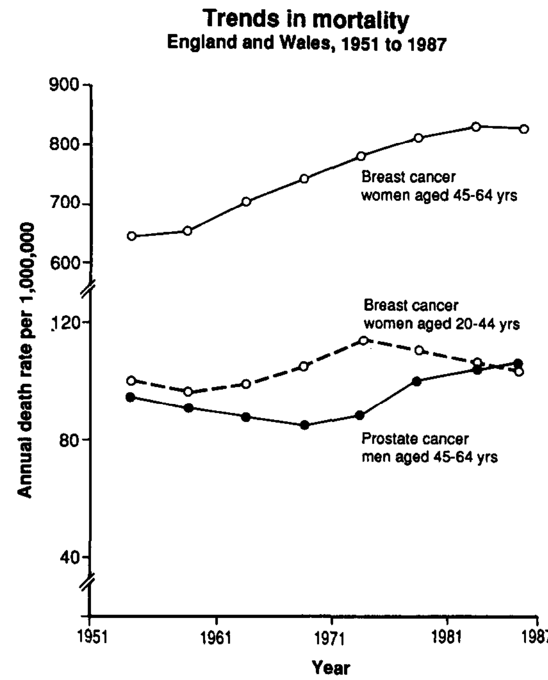

Fig. 7. Trends in mortality from cancer of the breast in women aged 20–44 years and 45–64 years and from cancer of the prostate in men aged 45–64 years in England and Wales from 1951–1955 to 1986–1987, standardized for age within each age group: annual death rate per million.

reversed and it has increased steadily in the cohorts born since 1936, that is in those which reached sexual maturity just after the sexual revolution of the 1960s. The increase in these cohorts corresponds to the increase in venereal disease and presumably results from increased spread of infection with oncogenic types of the human papilloma virus, exacerbated perhaps by cigarette smoking and the use of oral contraceptives, both of which appear to increase the risk of the disease independently of sexual behaviour.

The increase in melanoma, which had occurred in white-skinned populations throughout the world, is almost certainly explained by the increased exposure to ultraviolet light. The risk depends, however, not so much on the total dose received as on the dose to the untanned skin and the frequency of sunburn.

The four other types of cancer that show increased mortality rates are less common and their increase is less threatening. Three factors can account for the increase in cancer of the liver: the spread of infection with hepatitis B virus, the use of oral contraceptives, and the industrial use of vinyl chloride, all of which are known to cause the disease. Many other chemicals that have been introduced into social use cause liver cancer in animals, but have not been linked to the disease in humans, and the most remarkable feature of the increase is, perhaps, its small size—the disease still causing less than 1% (0.85%) of all cancer deaths in this age group.

The introduction of new chemicals has, however, been linked to the development of both non-Hodgkin's lymphoma and soft-tissue sarcomas. Specific associations have been reported between both types of tumour and exposure to organic solvents, chlorophenols, and phenoxy acids in case-control studies in Sweden [10, 11] and between non-Hodgkin's lymphoma and the use of pesticides in Kansas [12], but the evidence is weak and contradictory [13–15]. A large increase in non-Hodgkin's lymphoma due to infection with E.B. virus has occurred in transplant patients receiving intense immunosuppression and in patients with AIDS, but the total number of cases produced in these two groups is too few and too recent to account for the increase which occurred before the mid-1970s. The increases, in brief, are not satisfactorily explained.

Lastly there are mesotheliomas of the pleura and peritoneum. These have been poorly recorded in the past and the trends in mortality statistics are of little value. Sporadic cases occurred in the 19th century, due probably to background radiation, but the disease became at all common only in the last 30 years as a result of the increased use of asbestos. The figures in the table are those compiled by the British Health and Safety Executive from the national register that was established in 1967 [16]. By this time the epidemic was well under way and the increase recorded in young people between 1968 and 1983 is relatively small. In the last 6 years there was, in fact, none, which gives some encouragement to think that the measures taken to prevent the disease have been effective. Large increases must, however, be expected to continue at older ages until the epidemic has finally burnt out in perhaps 50 years time.

The middle-aged

The two age groups that I have examined cannot, of course, provide any worthwhile information about the one common cancer that is almost limited to older ages (namely, cancer of the prostate) nor could they provide information about trends in breast cancer after the menopause, if this is aetiologically different, in any important way, from the premenopausal disease. The trends in mortality from these two diseases are, therefore, shown for older ages (45–64 years of age) in Fig. 7.

Breast cancer at these ages increased *pari passu* with the premenopausal disease until the early 1970s, but it continued on its own for the next 10 years and the mortality has only just levelled off. Why the mortality increased is unknown, but it could, perhaps, have been due to an improved diet in childhood and a consequent earlier age at menarche and greater physical development. Whether the incidence has now ceased to rise or has been counteracted by the wider use of Tamoxifen, which certainly reduces the fatality of the disease, remains for the future to show.

Changes in the mortality from prostate cancer have been small over 35 years, but the mortality fell at first and over the last 20 years there has been an increase of more than 40%. Even now there is no indication that it is slowing down. Despite much research the causes of the disease are still unknown. Case-control studies have associated it with the consumption of fat, more consistently than they have for any other type of cancer, but there has been no increase in the fat content of the British diet that could account for the change in mortality. Nor is there any new treatment on the horizon that would encourage us to think that the trend will be reversed shortly. I am not sure how widespread this increase is. A smaller increase at these ages has occurred in France [17], but the rate in Italy has remained static [6].

DISCUSSION

In this review of the progress against cancer, I have considered only the trends in mortality and, occasionally, the trends in incidence and have limited my examination to data from seven countries. There are, in consequence, many notable achievements in Europe that I have had to omit, like the model law against the use of tobacco enacted in Norway. Like Møller *et* *al.* [18] in their examination of trends in Denmark, I have emphasized the importance of examining separately the trends at different ages. But I have gone further and have based my assessment almost entirely on the changes in mortality under 45 years of age.

I have done this for two reasons. First, childhood cancers need to be examined separately, because they have different causes from cancers that occur later in life and they respond differently to treatment. Secondly, cancers that occur in adults nearly all occur to some extent at all ages and those that occur under 45 years of age can, of necessity, have been produced only in the recent past (in so far as they are due to environmental factors or to personal behaviour) whereas those that occur at a later age are at least partly determined by the prevalence of agents that existed many years before. A slow spread of an epidemic from young to old has been seen with occupational cancers due to new hazards and with lung cancer due to cigarette smoking and the reverse has been seen with the control of occupational hazards and the diminution of the epidemics of cancers of the lung and stomach. Treatment may be equally effective at all ages (though it is sometimes given more intensively in the young) but, irrespective of this, evidence of the waxing and waning of cancer epidemics make it clear that if we want to know what is likely to happen in the future, we need to examine, primarily, the recent changes in the relatively young.

So far as childhood cancers are concerned the evidence is plain. We have not been able to alter their incidence and there is little to encourage the belief that we are likely to be able to do so. We have, however, been able to halve their fatality and can almost certainly reduce it further—but we need to discover how to do it, without causing so many unpleasant side-effects.

For cancers that occur in young adult life the evidence would seem at first sight to vary from one country to another, since the trends in mortality are so extraordinarily different—at least in men. So far as Britain is concerned the evidence is mixed. Large decreases have occurred in the mortality from cancers of the stomach, colon, rectum, and central nervous system, and from Hodgkin's disease in both sexes, from cancers of the lung, bladder, and testis in men, and from cancers of the pharynx and ovary in women. These are attributable in part to improved treatment, in part to active prevention, and in part to serendipitous social change. In the absence of any other changes, the reduction in mortality from these diseases would have reduced the total mortality from cancer since the early 1950s by 33% in men and by 18% in women, and smaller decreases from 11 other sex-specific types of cancer would have contributed a further 11% and 4% respectively.

These reductions have, however, been counterbalanced in part by substantial increases in mortality from melanoma and smaller increases from non-Hodgkin's lymphoma and connective tissue sarcoma in both sexes, from mesotheliomas and from cancers of the mouth and oesophagus in men, from cervical cancer in women, and small increases from five other types of cancer, most of which are still relatively uncommon. Altogether these would have added 5% to the total cancer mortality in men and 4% in women. In addition we have to take note of increases in the mortality from cancers of the breast and prostate at older ages, that may not be adequately predicted by changes at younger ages. Both are relatively small but are absolutely important because the diseases were common before the increases began.

The fact that the mortality from some types of cancer has increased shows that we have been losing some battles. In several cases, however, the reasons are known and we have grounds for thinking that the foe can be stopped. In others the increase is continuing, the reason for it is unknown, and, even if we have some prospect for halting the increase by improved treatment, the cause for the increase needs urgent investigation.

In sum, there is, to my mind, good evidence that we have been winning the fight in Britain and in Ireland, where the trends are for the most part similar, and that is despite not having had any well-attended national screening programme to pick up premalignant lesions of the cervix and early cancers of the breast. With the sort of screening that is carried out in Sweden, we should have done better still.

In the other countries whose mortality I have examined the evidence varies. The benefits of new treatments, which have greatly improved the outlook for patients with Hodgkin's disease, cancer of the testis, and most recently, cancer of the breast, are universal; but knowledge of the methods for avoidance of cancer are not everywhere equally applied.

This is abundantly clear in relation to smoking, which has become more prevalent in many countries in the last 20 years, in some of which the old high tar cigarettes also continue to be sold. The results are seen in Table 6. This shows the mortality from lung cancer in men for a period in the early 1950s and again for a period in the 1980s, with an indication of the current trends shown by the percentage change in the last 10 years in the third column. In Hungary the rate has trebled and is now

Table 6. Changes in age-standardized mortality from cancer of the lung in seven European countries: men, aged 20–44 years

Period	Country	Annual rate per million 1950s	Annual rate per million 1980s	Percentage change in last 10 years
1951–1955 to 1986–1987	England and Wales	81.8	30.6	−44*
1955–1959 to 1980–1984	France	26.2	52.2	+22
1955–1959 to 1980–1984	Germany (F.R.)	30.4	41.0	+14
1955–1959 to 1980–1984	Hungary	30.8	92.5	+89
1955–1959 to 1980–1984	Ireland	41.0	33.0	−41
1955–1959 to 1980–1983	Italy	31.0	54.9	−4
1955–1959 to 1980–1984	Sweden	14.1	19.7	+1

*Change in 13 1/2 years (1986–1987 as a percentage of 1971–1975).

Table 7. Changes in age-standardized mortality from colorectal cancer in seven European countries: men, aged 20–44 years

Period	Country	Annual rate per million		Percentage change in last 10 years
		1950s	1980s	
1951–1955 to 1986–1987	England and Wales	35.0	20.2	−29*
1955–1959 to 1980–1984	France	17.7	15.0	−22
1955–1959 to 1980–1984	Germany (F.R.)	14.1	20.7	−22
1955–1959 to 1980–1984	Hungary	19.8	33.5	+26
1955–1959 to 1980–1984	Ireland	24.6	31.3	−26
1955–1959 to 1980–1983	Italy	16.3	19.4	−22
1955–1959 to 1980–1984	Sweden	24.0	15.4	−33

*Change in 13 1/2 years (1986–1987 as a percentage of 1971–1975).

higher than it ever was at the height of the epidemic in Britain. It has doubled in France and increased by 77% in Italy. In Italy, however, there is now evidence that the epidemic has begun to wane, while in Sweden it was stopped before it ever became a serious threat. With the campaign for public education and the control of smoking that the European Office of the World Health Organization has initiated and is so strongly supported by the European Community, we can reasonably expect that the trends of the past will be reversed—that is, unless it proves that the public in each country will react only after they have seen the effects of the full-fledged epidemic. In this respect there is nothing more important than the example set by the medical profession.

A more cheering example is provided by cancers of the colon and rectum, the mortality of which has decreased by more than 40% in England and Wales, but has increased in Germany, Hungary, Ireland, and Italy (Table 7). In three of these countries, however, the trend has already reversed and mortality is decreasing almost everywhere at approximately the same rate.

If the rates for young men and women are combined, the total mortality from cancer at these ages in the first half of the 1980s, compared with that 30 years before, is found to have decreased by 22% in England and Wales and Sweden, by 20% in Ireland, by 16% in the Federal Republic of Germany and by 1% in France and Italy and to have increased by 2% in Hungary. The trend, moreover, has been decreasing over the last 10 years in both sexes in five of the seven countries and increasing in both sexes only in one.

CONCLUSION

I conclude that we are, for the most part, winning the fight against cancer. This does not appear from examination of the trends in mortality at all ages, but it does when we examine the cohorts on whom the future depends. Continued progress, however, requires not only continual research into the biological mechanisms by which malignant clones are produced and allowed to grow but also the better application of the knowledge we already have, constant vigilance to detect the appearance of new hazards, and focussed research to discover how new hazards can be avoided.

ADDENDUM

A part of the decrease in mortality recorded in Sweden since 1980 is an artefact due to a change in the way causes of death were classified.

1. Bailar JG, Smith EM. Progress against cancer. *New Engl J Med* 1986, **314**, 1226–1232.
2. Early Breast Cancer Triallists Collaborative Group. The effects of adjuvant tamoxifen and of cytotoxic therapy on mortality in early breast cancer; an overview of 61 randomized trials among 28896 women. *New Engl J Med* 1988, **319**, 1681–1692.
3. Bailar JG, Smith EM. Progress against cancer. *New Engl J Med* 1986, **315**, 968.
4. Becker N, Smith EM, Wahrendorf J. Time trends in cancer mortality in the Federal Republic of Germany: progress against cancer? *Int J Cancer* 1989, **43**, 245–249.
5. Greaves M. Speculations on the causes of childhood acute lymphoblastic leukaemia. *Leukaemia* 1988, **2**, 120–125.
6. Kneale GW. Excess sensitiviy of pre-leukaemias to pneumonia. *Br J Prev Soc Med* 1971, **25**, 152–159.
7. Stewart A, Kneale GW. Role of local infections recognition of haemotopoietic neoplasms. *Nature* 1969, **223**, 741–742.
8. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Tobacco Smoking*. Lyon, International Agency for Research on Cancer 1986, Vol. 38.
9. Cederlof R, Doll R, Fowler B, Fribert J, Nelson N, Vouk V. Air pollution and cancer: risk assessment methodology and epidemiological evidence. *Environ Hlth Perspect* 1978, **22**, 1–12.
10. Eriksson M, Hardell L, Berg NO, Moller T, Axelson D. Soft tissue sarcomas and exposure to chemical substances: a case-referrent study. *Br J Industr Med* 1981, **38**, 27–33.
11. Hardell L, Sandstrom A. Case-control study: soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. *Br J Cancer* 1979, **39**, 711–717.
12. Hoar SK, Blair A, Holmes FF, Robel RJ, Hoover R, Fraumeni JF. Agricultural herbicide use and risk of lymphoma and soft tissue sarcoma. *J Am Med Ass* 1988, **256**, 1141–1147.
13. Royal Commission on the Use and Effects of Chemical Agents on Australian Personnel in Vietnam. *Final Report July 1985*, Vol. 4 (*Cancer*). Canberra, Australian Government Printing Service, 1988.
14. Wiklund K, Holm L-E. Soft tissue sarcoma risk in Swedish agricultural and factory workers. *J Natl Cancer Inst* 1986, **76**, 229–234.
15. Wicklund K, Dich J, Holm L-E. Risk of malignant lymphoma in Swedish pesticide appliers. *Br J Cancer* 1987, **56**, 505–508.
16. Jones RD, Smith DM, Thomas PG. Mesothelioma in Great Britain in 1968–1983. *Scand J Work Environ Hlth* 1988, **14**, 145–152.
17. Hill C, Benhamou E, Doyon F, Flamant R. *Evolution de la mortalité par cancer en France entre 1950 et 1985*. Paris, Editions INSERM, 1988.
18. Møller H, Melemgaad A, Jensen OM. Measuring progress against cancer. *J Cancer Res Clin Oncol* 1988, **114**, 613–617.
19. De Vita VT, Korn D. Progress against cancer. *New Engl J Med* 1986, 315, 964.