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PROGRESS AGAINST CANCER: ARE WE WINNING THE WAR?

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Abstract

The conclusion of two biostatisticians that 'with respect to cancer as a whole we have lost ground' was based on the rise in the age-standardized mortality from cancer. Trends in mortality at all ages combined may be misleading, as the effect of recent progress may be obscured by the effect of changes in the distant past on the incidence of cancer in old age. Recent progress is best assessed by examining trends at young ages, which can be affected only by relatively recent changes in treatment, behaviour, and the environment. These trends are mostly encouraging, but a few indicate a need for preventive action or research.

Key words: Cancer epidemiology, mortality, trends, overview.

Fifty years is a short time in the history of Man, but the last 50 have seen changes that have qualitatively altered the way of life of a large proportion of the world's population. Food supply has been increased, the need for physical labour reduced, the ease of travel and communication transformed, and much disease eliminated or made amenable to cure. Not all changes, however, have been beneficial. The earth's resources have been diminished and the biosphere and surrounding atmosphere contaminated with chemicals that may cause disease and threaten to modify the climate of the whole globe. The old idea that increase in knowledge and its application by industry is synonymous with progress has been abandoned and society is beginning to accept the need to evaluate the potential impact of new discoveries and to introduce some system for the international control of their application. Medicine is no exception and the long term effects of the lengthening of life, to which it has notably contributed, could prove to be one of the most disastrous changes of all, unless it is accompanied by effective limitation of the number of births. The immediate harmful effects of new forms of therapy have, however, been small in comparison with the benefits conferred and physicians generally have continued to believe that in their own field at least progress continued to be good. It was, therefore, a severe shock to those of us concerned with the treatment and prevention of cancer to discover two years ago that the authors of an article, validated by its acceptance in the prestigious New England Journal of Medicine, had come to the conclusion that the war against cancer was being lost (1).

Bailar and Smiths's review

US data

Bailar & Smith, the authors of the article, are competent and experienced biostatisticians at, respectively, the Harvard School of Public Health and the University of Iowa Medical Centre and their opinions cannot be dismissed out of hand. To measure progress against cancer they examined trends in the incidence of cancer, the survival rate of those affected, and the mortality attributed to it, over the period 1950 to 1982.

For incidence they took the results of the so-called SEER programme, an acronym for the Surveillance, Epidemiology and End Results programme that had been developed under the auspices of the National Cancer Institute. This provides research quality data for the incidence of cancer for 10 areas of the USA covering about 10% of the total population since 1973. Relatively few non-whites are included in the population and Bailar & Smith examined only the data for whites, which showed an overall increase of 8% in the 8 years to 1981, with notable increases for cancers of the lung, colon and rectum, breast, and prostate.

For survival they again took the SEER data and examined relative survival rates after 5 years (that is, the ratio of the observed survival rates to the survival rates of all

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people of the same ages in the general population) which avoids the complexity of having to allocate an individual's death to a specific cause. These showed an increase for all cancer from 46.8% for men and women treated in 1973 to 49.2% for men and women treated in 1978. Small increases of a few per cent were observed for colo-rectal, lung, and breast cancer and substantial increases were observed for prostate cancer (from 60.7 to 69.4%), for Hodgkin's disease (from 61.5 to 72.6%), and for non-Hodgkin's lymphoma (from 40.9 to 47.1%). Several of these increases, however, were thought to be artefacts consequent on increases in the reported incidence of the disease, attributable to an increase in the amount of screening and the consequent registration as cancer of lesions that appeared malignant histologically, but were clinically benign.

The resultant difficulty in interpreting the changes in incidence and survival led Bailar & Smith (1) to prefer mortality as the most reliable indicator of progress in the control of the disease. For this purpose they chose as the best single measure of progress the total age-adjusted mortality rate, divided only by sex and by race into whites and non-whites. Their results showed that the rates rose progressively in both groups in males, while in females they rose in whites and fell slightly in non-whites before subsequently stabilizing. When the whole population was treated as a single unit the rate was found to have risen progressively. There were of course different trends for different types of cancer and Bailar & Smith noted that this 'generally dismal picture' (to use their words) obscured some notable successes, such as a reduction in mortality from all cancers combined under 30 years of age and from non-seminoma testicular cancer; but their general conclusion was that the data (again I quote) 'provide no evidence that some 35 years of intense and growing effort to improve the treatment of cancer have had 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 rates in the very old distorts the results as deaths that used to be attributed to senility or some other such non-specific term have been investigated with progressively greater intensity and attributed to specific causes (2). Secondly, 1982 was too soon to see the effects on the mortality rate of some of the major advances in treatment that have affected, for example cancer of the breast (3). The general picture would, however, have been only slightly altered if these two factors had been taken into account. Bailar & Smith (4) pointed out, in reply, that most cancer deaths occur within two to three years after diagnosis and that any effect of major improvements in survival by 1981 should have been visible in the 1983 data, which had by then become available, and that

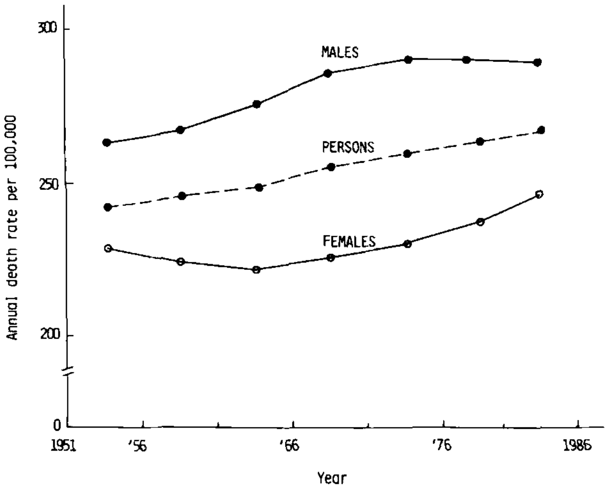

Fig. 1. Trend in mortality from all neoplasms by sex, England and Wales 1951–1955 to 1981–1985: deaths per 100000 people per year, standardized for age.

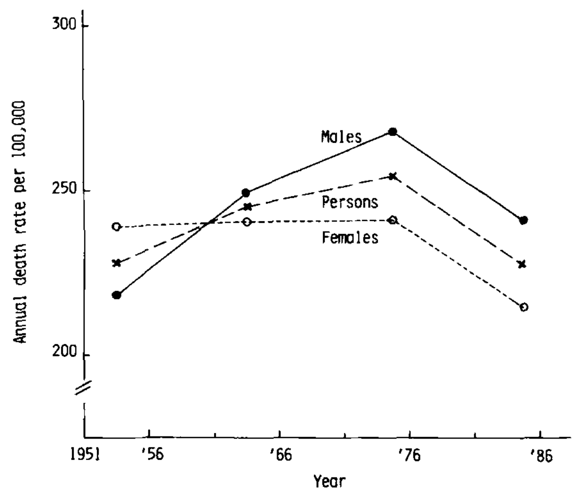

Fig. 2. Trend in mortality from all neoplasms by sex, Sweden 1951–1955 to 1981–1985: deaths per 100000 people per year, standardized for age.

no such effect could be seen. 'The ugly fact remains' they concluded, '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.'

British and Swedish data

I agree with Bailar & Smith that to assess progress the most appropriate indicator is the trend in all cancer mortality, not only since the risk of death is the risk with which the individual is most concerned, but also because trends in incidence may be distorted by the prevalence of screening and the efficiency of registration. I have, therefore, examined the position in Sweden and the United Kingdom in the same way. To make comparison with the

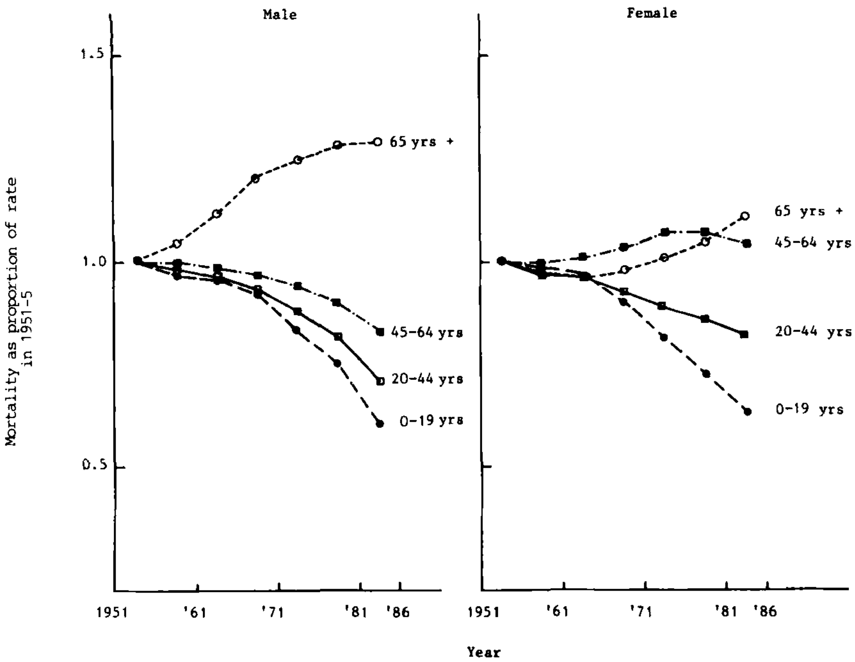

Fig. 3. Trend in mortality from all neoplasms by sex at ages under 20 years, 20 to 44 years, 45 to 64 years, and 65 years and over, England and Wales 1951–1955 to 1981–1985: death rates standardized for age within each broad age group expressed as a proportion of the mortality in 1951–1955.

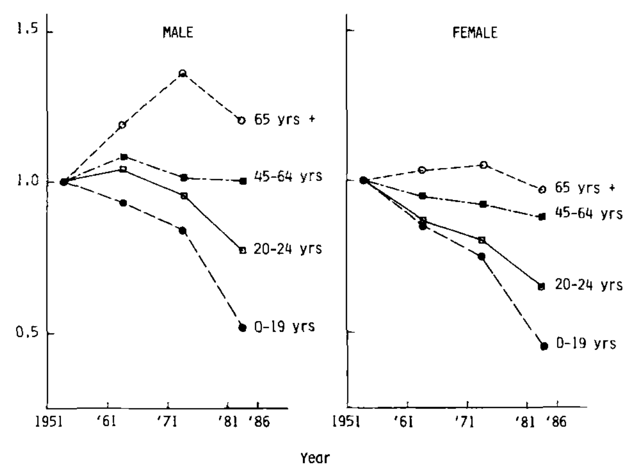

Fig. 4. Trend in mortality from all neoplasms by sex at ages under 20 years, 20 to 44 years, 45 to 64 years, and 65 years and over, Sweden 1951–1955, 1961–1965, 1971–1975, and 1981–1985: death rates standardized for age within each broad age group expressed as a proportion of the mortality in 1951–1955.

US data as close as possible age-adjusted rates have been calculated, standardized for the sex and age distribution of the population for the same year (1980), and the quinquennium 1951–1955 has been taken as the starting point. The results, however, have been brought more up to date by including mortality to 1985. Those for England and Wales are shown in Fig. 1 and, for both sexes combined, are very similar to the American ones. They differ in that the male rate has stabilized since 1971, while the female rate has increased to a greater extent and is now higher than the male rate was 30 years ago. The Swedish rates, which are shown in Fig. 2, give more encouragement. For, although the male rate is now higher than in the early 1950s, the female rate is lower and both rates have fallen in the last 10 years. As a result the rate for both sexes combined is now the same as it was 30 years ago.

An alternative assessment

I believe, however, that Bailar & Smith's assessment of the US situation was profoundly wrong, as would be a similar assessment of the situation anywhere else. For, by taking all ages together, Bailar & Smith allowed the effects of recent progress to be overshadowed by the effects of changes in behaviour and the prevalence of carcinogenic agents in the distant past, which can manifest themselves only in the old. If, instead of looking at the trend at all ages, we look at the trends in 4 broad age groups (standardizing for age within each of the 4 groups) the picture looks entirely different.

The 4 trends for ages under 20 years, 20 to 44 years, 45 to 64 years, and 65 years and over in each sex are shown for England and Wales in Fig. 3. In each age group the rates in successive quinquennia have been expressed as proportions of the rate in 1951–1955. In males, the mortality has fallen at all ages under 65 years. At older ages, in contrast, 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 mid-1970s and then began to decline, while over 65 years of age the increase, in contrast to the increase in men, began only in the late 1960s and has recently accelerated.

Comparable trends for Sweden are shown in Fig. 4. For males, the picture is qualitatively the same, except that the rate at 65 years and over has fallen appreciably in the last 10 years. In fermales, the reductions have been greater and the increases less and, in particular, there has been no recent increase in the old.

That these changes should be so different at different ages and in the two sexes is the result of a complex interaction of changes in the efficacy of treatment, human behaviour, and the prevalence of carcinogenic factors at different times over the last 80 years, and, to some minor extent, and principally at the oldest ages, to changes in the standards of medical diagnosis. To assess the effect of recent changes in the efficacy of treatment and our attempts at prevention, we should concentrate on the changes in the two youngest age groups shown in Figs 3 and 4 as these can be determined only by changes in the relatively recent past, unless they are occasionally determined by the previous experience of the individuals' parents. They are, therefore, the most sensitive indicators of our efforts at control and the best predictors of what the future holds, except perhaps for the incidence of cancers that are largely dependent on hormonal secretions late in life, as may be the case for breast cancer in postmenopausal women and for prostate cancer, which is more characteristically a disease of old age than cancer of any other type.

Children and adolescents

Consider first the decrease in mortality in children and adolescents. This owes very little to changes in incidence, which has probably not altered over time to a material extent in any developed country. Some small changes may have occurred as a result of the introduction of diagnostic radiography and the subsequent reduction in its use during pregnancy, when the risk to the fetus began to be appreciated; but the large increaese in childhood leukaemia that was recorded in the first half of the century seems likely to have been more apparent than real and due to a reduction in the fatality of common infections, thereby allowing the disease to develop to a stage at which it was easily recognized (5, 6). Nor are there many large differences between the incidence of childhood cancers in different communities that would suggest the existence of avoidable factors, apart from the great excess of Burkitt's lymphoma in areas of intense malarial infection and the 5 to 10-fold difference in the incidence fo Hodgkin's disease between some Central and South American and Middle Eastern populations and others in the Far East and (to a less extent) in Scandinavia (7).

The reductions in mortality that have occurred in this age group, which are shown for 4 countries in Table 1,

Table 1

Change in mortality from cancer under 20 years of age: 1950 to 1985

Country	Period	Per cent reduction	
		Male	Female
England and Wales	1951–1955 to 1981–1985	40	42
Federal Republic of Germany	1952–1955 to 1981–1985	37	40
Sweden	1951–1955 to 1981–1985	49	55
USA (whites)	1950–1953 to 1980–1983	46	46

must, I think, be attributed almost entirely to more efficacious treatment. The results of treatment are, however, less satisfactory than the increased survival rate might suggest, as the end results include in some cases 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. In this group all the types of cancer that are common in old age begin to appear and changes in human behaviour and the environment compete with changes in therapeutic efficiency as causes of the change in mortality. In these circumstances we cannot rely on examining all types in combination, but must examine each type separately, as the cause of the disease and the efficacy of treatment vary greatly from one type to another. For this purpose I have limited my analysis to the data for England and Wales, as interpretation of the trends for specific cancers is hazardous without personal knowledge of local circumstances.

Examination of the trend in 49 sex-specific types of cancer that accounted for more than 1 death per million persons per year at ages 20 to 44 years at either the beginning or the end of the period, shows that the mortality decreased over the 30 years of observation by more than 10% in 28, increased by more than 10% in 13, and left only 8 relatively unchanged. Nine types for which decreases of more than 10% were recorded in both sexes are shown in Table 2. Large contributions to the overall reduction in mortality are seen to have been made by cancers of the stomach, colon, rectum, and central nervous system, and by Hodgkin's disease.

Cancer of the stomach. The mortality from cancer of the stomach shows the same dramatic decline in mortality that has been recorded nearly everywhere in the developed world. No new and effective form of treatment has been introduced and the reduction must be due almost entirely to a reduction in the incidence of the disease—something that is confirmed by the 29% drop in the cancer registration rate since the early 1970s, when figures for

Table 2

Cancers showing substantial decreases in mortality in both sexes. Ages 20–44 years

Type of cancer	Mortality in 1981–1985 as per cent of mortality in 1951–1955		Annual mortality per million in 1981–1985	
	Men	Women	Men	Women
Pharynx	86	41	2.4	1.4
Stomach	31	28	12.0	7.0
Colon	67	50	14.4	12.4
Rectum	67	47	9.0	6.0
Gall bladder*	50	67	0.8	0.8
Larynx	88	13	1.4	0.2
Bladder	52	60	2.2	1.2
Brain and other+	74	71	28.0	20.4
CNS Hodgkin's disease	51	53	12.4	6.6

* Mortality as per cent of rate in 1961–1965.
+ Including benign tumours and tumours of undetermined type.

the whole of England and Wales were first obtained. The cause of the reduction remains a mystery. Two factors seem likely to have contributed: changes in the methods of food preservation (in particular the use of refrigeration and perhaps the addition of antioxidants in place of preservation by salt) and increased consumption of fruit and vegetables. The latter is inversely associated with the risk of the disease in almost all case-control studies; but the size of the increase is inadequate to account for the decreased incidence of the disease and changes in the former 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 in food and nitrites, derived principally by bacterial reduction of nitrates in the mouth or in the achlorhydric stomach, is attractive and is supported by the fact that nitrosation is inhibited in the presence of vitamin C. It is not generally supported, however, by epidemiological studies, most of which have failed to relate the incidence of the disease to the amount of nitrate in water or food, in the air in the manufacture of nitrate fertilisers, or in saliva or urine. Nitrosation *in vivo* may, perhaps, be responsible; but, if it is, the intake of nitrates is not generally the rate-limiting factor (8).

Cancers of colon and rectum. That the incidence of gastric cancer has been declining has been known for many years, but the decline in colo-rectal cancer has not. A better standard of surgery may have contributed to a higher survival rate, but much of the reduction must have been due to reduced incidence. Registration of cancer has not been sufficiently complete in Britain for long enough to put much trust in the size of the recorded trends, but the fact that the registration rates in this age group declined by 7% in men and 18% in women from 1971–1974 to 1981–1984 provides support for the belief that the decline in mortality is due in part to a decline in incidence. The decline is, moreover, greater under 45 years of age than at older ages and this supports the idea that recent changes in dietary habits, particularly the increased consumption of vegetables and of fibre in wholemeal bread, help to prevent the disease.

Hodgkin's disease. The reduction in mortality from Hodgkin's disease accords with clinical experience and must be due in large part, if not wholly, to the great improvements in treatment that followed the introduction of more intensive radiotherapy, careful staging, and the use of chemotherapy.

Cancers of central nervous system. The reduction in the mortality from cancers of the brain and other parts of the central nervous system is, at first sight, less easy to explain, as there has been no great improvement in therapy and the incidence of the disease is sometimes reported to have increased. Reports of an increase have, however, failed to take account of the need to group together malignant and benign tumours and tumours of unspecified type, as has been done in Table 2. Failure to do this results in the appearance of a spurious increase in mortality from malignant tumours, as diagnosis has been progressively more precise and the nondescript diagnosis of a cerebral tumour as the cause of death (classified by WHO rules as non-malignant) has given way to histological diagnoses like astrocytoma. As a result, the number of deaths attributed to malignant neoplasms of the brain has increased while the total number attributable to all neoplasms of the brain has not. The reduced mortality from this heterogeneous group is, I suspect, due to a reduced fatality from benign tumours, which have been diagnosed and treated more effectively. Some, however, may be an artefact due to the more precise diagnosis of secondary tumours arising primarily from other sites.

Cancers of the bladder, pharynx, and larynx. There remain cancers of the bladder, pharynx, larynx, and gall-bladder. The reduction in mortality from the first three in men can be attributed, in part, to the same factors that have been responsible for the reduction in lung cancer, to which I shall refer later, but there is no such simple explanation for the reduction in women. The elimination of 2-naphthylamine, the reduction in the use of benzidine, and improvements in treatment will all have helped to reduce the mortality from bladder cancer in both sexes and improved treatment may well have contributed to the reduced mortality from cancer of the larynx; but the extent of the fall in mortality from cancers of the pharynx and larynx in women remains unexplained. Nutritional deficiencies have been thought to contribute to the production of pharyngeal cancer, notably in North Sweden, and some of the fall may be due to their correction.

Cancer of the gall-bladder. Cancer of the gall-bladder can be studied in national mortality statistics only from 1959, when it began to be classed separately from cancer of the liver. Why the mortality from it should have de-

Table 3

Cancers showing substantial decreases in mortality in one sex with small decreases or no relevant data for other sex. Ages 20–44 years

Type of cancer	Mortality in 1981–1985 as per cent of mortality in 1951–1955		Annual mortality per million in 1981–1985	
	Men	Women	Men	Women
Lung	45	94	36.6	19.8
Myeloma	90	83	1.8	1.0
Leukaemia	94	80	25.4	16.4
Small intestine	67	+	0.8	+
Thyroid	+	33	+	0.4
Testis	69	–	9.8	–
Corpus uteri	–	40	–	1.6
Ovary	–	73	–	22.8
Vagina, vulva, etc.	–	48	–	1.0

+ Annual mortality less than 1 per million throughout.

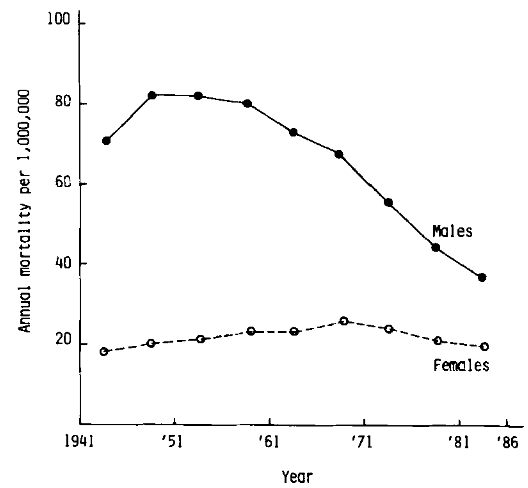

Fig. 5. Trend in mortality from lung cancer at ages 20 to 44 years by sex, England and Wales 1941–1945 to 1981–1985: deaths per 1000000 people per year, standardized for age.

creased is unclear. The numbers of deaths are small, but the fall is too great to be attributed to random variation. It can hardly be due to prophylactic cholecystectomy at these young ages.

Cancer of the lung. Nine types of cancer that show decreases of more than 10% in only one sex, with smaller decreases or no relevant data in the other, are shown in Table 3. For only 3 of these types are the decreases of any material importance: that is, for cancers of the lung, testis, and ovary. For cancer of the lung the decrease in men has been so great that it accounts for a 13% decrease in the mortality from all types of cancer combined. The fatality of the disease has been affected only very little by improved treatment and the decrease has been principally brought about by reduction in the amount smoked and a change in the quality of the smoke. That the amount smoked is by far the most important is established by the observations on men and women who have smoked different amounts, but have lived otherwise under similar conditions (9), while the importance of the quality of tobacco smoke is established both by case-control studies (10) and by comparison of the trends in young people in countries in which tar levels long continued to be high (for example Czechoslovakia, Federal Republic of Germany, France, and Hungary) and those in countries in which the levels have been greatly reduced (for example Australia, England, Hong Kong, and USA). Trends in the mortality from lung cancer in men and women at 20 to 44 years of age in England and Wales are shown in Fig. 5, in the amount smoked in Fig. 6, and in the amount of tar delivered per cigarette in Fig. 7. Whether the early drop in tar delivery is sufficient to account for the start of the reduction in mortality is unclear and the decline may also have been contributed to by the reduction in atmospheric pollution from the combustion of coal that began as a result of

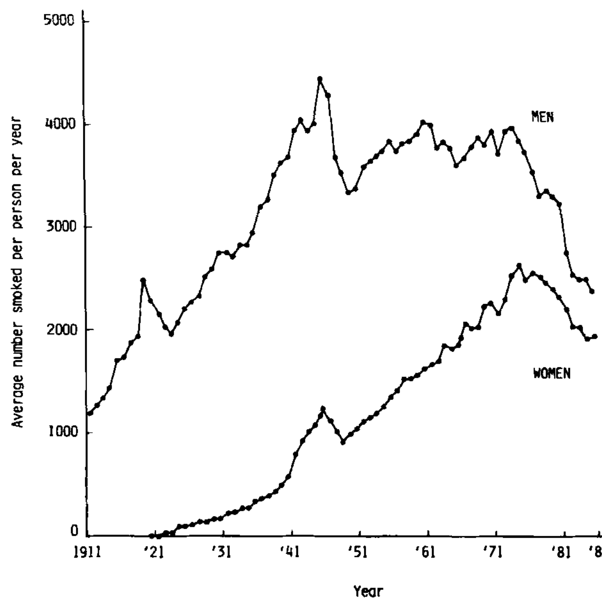

Fig. 6. Trend in cigarette consumption by sex, United Kingdom 1911 to 1985: average number of cigarettes smoked per year per person aged 15 years and over (ref. 20).

government intervention after the disastrous for of 1952. This would be consistent with the idea, based on epidemiological studies, that atmospheric pollution may have been responsible, in conjunction with cigarette smoking, for some 5–10% of all lung cancers in men (11).

Cancers of the testis and ovary. The other two cancers that showed important decreases in Table 3 were cancers of the testis and ovary. Their trends in mortality since 1911 are shown in Fig. 8. In both cases there was a small artificial break in the trend around 1950. For both types the mortality was recorded as increasing between the two

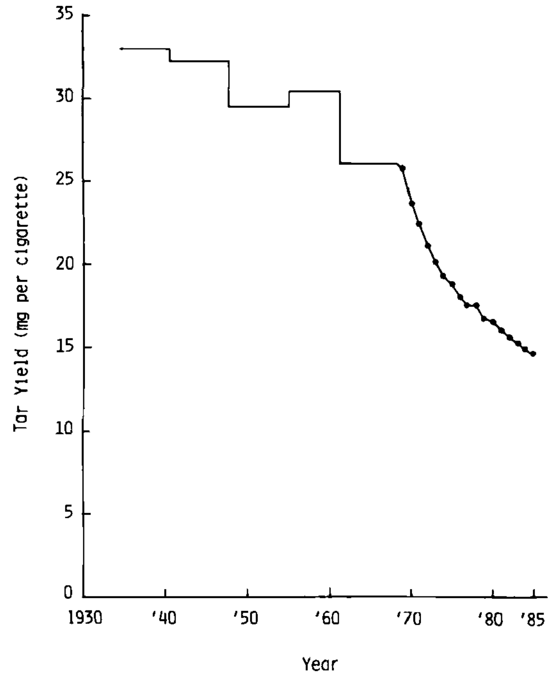

Fig. 7. Trend in delivery of tar per cigarette, United Kingdom 1934 to 1985: mg per cigarette, weighted for sales for period of manufacture. (ref. 20).

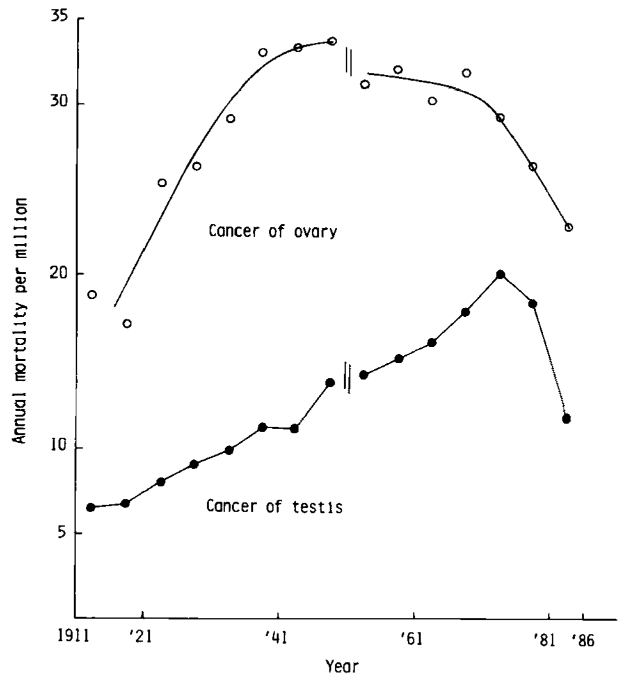

Fig. 8. Trends in mortality from cancer of the ovary in women and cancer of the testis in men at ages 20 to 44 years, England and Wales, 1911–1915 to 1981–1985: deaths per million people per year, standardized for age.

Table 4

Cancers showing discrepant changes in each sex or at different ages. Ages 20–44 years

Type of cancer	Mortality in 1981–1985 as per cent of mortality in 1951–1955		Annual mortality per million in 1981–1985	
	Men	Women	Men	Women
Oesophagus	155	65	6.2	2.2
Cervix				
20–34 years	–	163	–	22.3
35–44 years	–	87	–	65.5

world wars and decreasing in the last 10 years. The underlying changes in incidence were, however, quite different.

Cancer of the testis is easy to diagnose, the increase in mortality has been paralleled in many other developed countries, and it must reflect a true increase in incidence. The explanation for the increase is unknown and it is, therefore, particularly fortunate that the platinum therapy introduced in about 1970 should have been so brilliantly successful.

Cancer of the ovary, in contrast, has been difficult to diagnose and some of the early increase could be due to improved medical services. Much of it, however, was due to an increased incidence associated with reduced fertility (12, 13). The recent reduction in mortality is likely to reflect, in part, the response to platinum and other forms of chemotherapy and in part a reduction in incidence due to the prolonged use of steroid contraceptives, which can halve the risk of the disease.

Cancer of the oesophagus. Two types of cancer show discrepant changes in each sex or at different ages, even within the narrow range of 20–44 years. This is illustrated in Table 4. Why the trends for cancer of the oesophagus should have been so different in men and women and so different from those recorded for cancer of the lung is unclear, as smoking is a major cause of both diseases. Lung cancer mortality showed a reduction of only 6% in women against a reduction of 35% for cancer of the oesophagus and a *reduction* of 55% in men against an *increase* of 55% for cancer of the oesophagus. One contributory factor is the effect of alcohol, which acts synergistically with tobacco to increase the risk of oesophageal but not lung cancer and is relatively more important than smoking in that the rate of increase in risk with the amount drunk is greater than with the amount smoked. As the consumption of alcohol has increased, this goes some way towards explaining the increase in the incidence of oesophageal cancer in men. Another factor affecting particularly women, may be an improvement in nutrition, which has been referred to as contributing to a similar marked fall in female mortality from cancers of the pharynx and larynx.

Cancer of the cervix uteri. The other discrepant finding is the different direction of the trends in mortality from cervix cancer at different ages. Taken altogether the mortality at 20–44 years of age has remained practically unchanged, but this conceals a 63% increase under 35 years of age and a 13% decrease at 35–44 years. The decrease over 35 years of age is paralleled throughout the developed world and has been variously attributed to improved sexual hygiene and the routine use of vaginal smears to detect premalignant disease in healthy women. At younger ages the trend was the same until it began to reverse in the cohort born in and around 1936. This is illustrated in Fig. 9 in which the age specific rates in the cohorts born in and around 1921 and 1936 are linked by dotted lines. The former cohort reached sexual maturity just before the beginning of the Second World War, the latter just before the sexual revolution of the 1960s. The increase in cohorts born since 1936 corresponds to an increase in venereal disease and presumably results from increased spread of infection with putatively malignant types of the human papilloma virus, exacerbated perhaps by cigarette smoking and the use of steroid contraceptives, both of which appear to increase the risk of the disease independently of sexual behaviour.

Cancers of the pancreas, kidney, and tongue and mouth. Eight types of cancer have shown increases of more than 10%. Three, listed in Table 5, are caused in part by smoking and have shown increases in only one sex. Other things being equal, any increase in their mortality rates might have been expected to be greater in women than in men. This was so for cancers of the pancreas and kidney, but not for cancer of the buccal cavity including the tongue. The last is closely associated with the consumption of alcohol and probably also with some aspects of nutrition in common with other cancers of the upper digestive tract. The trends in mortality from cancers in different parts of the upper digestive tract are, however, very different from one another (Tables 2, 4, and 5) despite the absence of any great difference in the trends in fatality and we evidently have only a very incomplete picture of their causation. The only consistent feature is that, in each case, the trend has been more favourable (or less unfavourable) in women.

Mesothelioma. A fourth type of cancer to have increased substantially in only one sex is mesothelioma, which was widely recognized as a specific type of cancer affecting both the pleura and the peritoneum only in the early 1960s and has been classified as a separate cause of death in national statistics only since 1968. Sporadic cases occurred in the 19th century, due possibly to background radiation, but the disease has become at all common only in the last 30 years as a result of the increased use of asbestos. The increase in mortality in young men is now levelling off and should soon be reversed as a result of the measures that have been taken to reduce exposure to the material.

Melanoma of the skin. Four other cancers have shown increases in both sexes. There are listed in Table 6. The most important is melanoma of the skin, which, despite improvements in therapy, has shown a progressive increase in mortality in both sexes in all developed countries since the Second World War. The increase is due to increased exposure to ultraviolet light, but the risk depends not so much on the total dose as on the dose to the untanned skin and the frequency of sunburn.

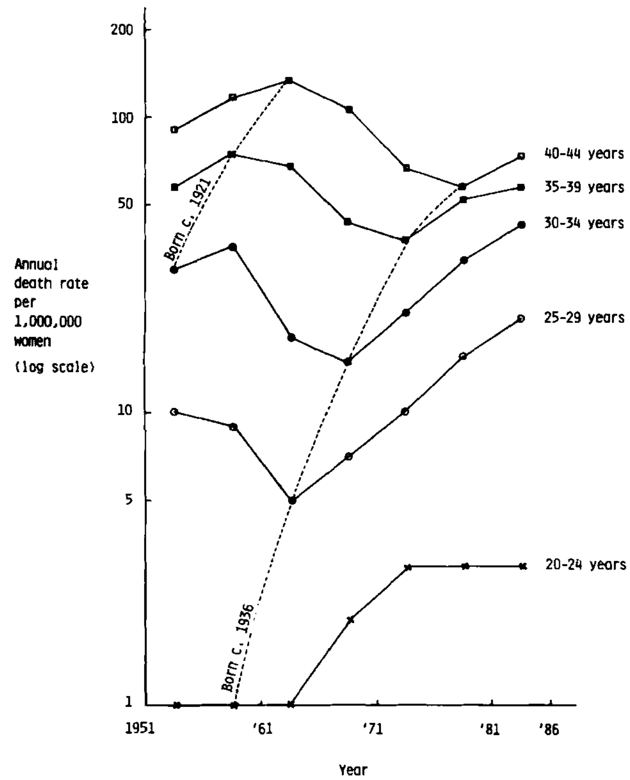

Fig. 9. Trends in mortality from cancer of the cervix uteri by age from 25–29 years to 40–44 years, England and Wales 1951–1955 to 1981–1985 showing age specific mortality rates for cohorts born around 1921 and around 1931: deaths per million women per year.

Table 5

Cancers showing substantial increases in one sex with no change or no relevant data in the other. Ages 20–44 years

Type of cancer	Mortality in 1981–1985 as per cent of mortality in 1951–1955		Annual mortality per million in 1981–1985	
	Men	Women	Men	Women
Tongue and mouth	157	100	2.2	1.2
Pancreas	100	115	8.6	4.6
Kidney	100	120	5.6	3.6
Mesothelioma*	235	+	3.1	+

* Mortality in 1982–1983 as per cent of rate of 1968–1969.
+ Annual mortality less than 1 per million throughout.

Cancer of the liver. The reasons for the increase in the other 3 types are less clear. Infection with the hepatitis B

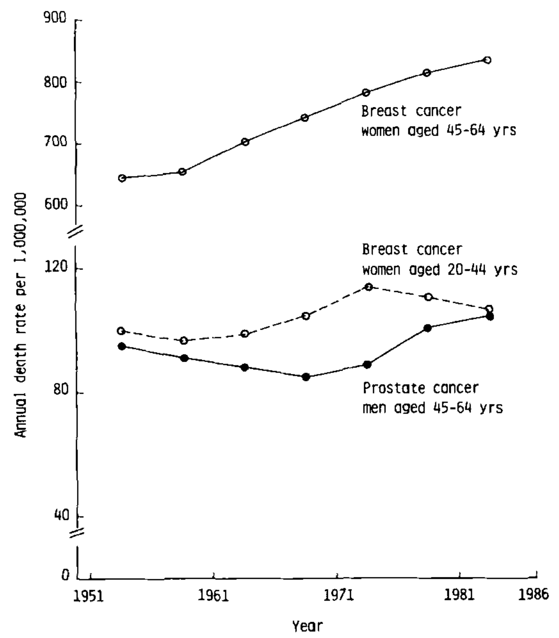

Fig. 10. Trends in mortality from cancer of the breast in women at ages 20–44 years and 45–64 years and from cancer of the prostate in men at ages 45–64 years, England and Wales 1951–1955 to 1981–1985: deaths per million people per year standardized for age.

Table 6

Cancers showing substantial increases in mortality in both sexes. Ages 20–44

Type of cancer	Mortality in 1981–1985 as per cent of mortality in 1951–1955		Annual mortality per million in 1981–1985	
	Men	Women	Men	Women
Liver*	114	138	3.2	2.2
Melanoma	245	170	10.8	10.2
Non-Hodgkin's lymphoma	134	136	15.4	9.0
Connective tissue	164	163	4.6	3.8

* Mortality as per cent of rate in 1961–1965.

virus, steroid contraceptives, and vinyl chloride are all proven causes of liver cancer in humans and an increase in the prevalence of the virus, the use of the steroid contraceptives, and occupational exposure to vinyl chloride must all have contributed to the increased mortality from the disease. Many other chemicals that have been introduced into social use have been shown to 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, the smallness of its size.

Non-Hodgkin's lymphoma and soft tissue sarcoma. The introduction of new chemicals has, however, been linked to the development of both non-Hodgkin's lymphomas and soft tissue sarcomas. Specific associations have

Table 7

Cancers examined at older ages

Type of cancer	Age (years)	Mortality in 1981–1985 as per cent of mortality in 1951–1955	Annual mortality per million in 1981–1985
Prostate	20–44	+	+
(men)	45–64	111	94.5
Breast	20–44	108	107.2
(women)	55–64	130	837.0

+ Annual mortality less than 1 per million throughout.

been reported between both types of tumour and exposure to organic solvents, chlorophenols, and phenoxyacids in case-control studies in Sweden (14, 15) and between non-Hodgkin's lymphomas and the use of farm herbicides in a case-control study in Kansas (16). Laboratory evidence to support the idea that these agents cause either disease is, however, weak and the associations have not generally been confirmed in case-control studies elsewhere or in cohorts of occupationally exposed workers (17–19).

A large increase in non-Hodgkin's lymphoma due to infection with the EB virus has occurred in transplant patients receiving intensive immunosuppression and in patients with AIDS. The total number of such cases is, however, too few and too recent to account for the increase in young adults that occurred on a national scale in Britain, Sweden, and the USA before the mid-1970s and the recorded increase in mortality is still not satisfactorily explained.

The middle aged

Lastly there are two types of cancer for which the trends in mortality under 45 years of age may be misleading as predictors of future trends at older ages, namely cancers of the breast and prostate. The former may be affected differently to an important extent by different agents when it occurs before and after the menopause, while the latter is unique in that it is one of the most common cancers after 65 years of age, but is so rare under 45 years of age that the trend in the young age group may be materially affected by random variation.

Breast cancer. The changes in the mortality from breast and prostate cancers at 45 to 64 years of age over the last 30 years, and the change in breast cancer in younger women are shown in Table 7. The increase in breast cancer premenopausally is small; but, even so, it is important as the disease is relatively so common that it accounts for a third of all cancer deaths in women at 20 to 44 years of age. Fig. 10 shows that the increases have not been uniform over time and that the mortality from breast cancer in the younger age group was even higher in the mid-1970s. The increases, which must reflect real increases in incidence, cannot be due to the use of steroid contraceptives, which were not introduced into Britain until 1961 and have little effect on the incidence of the disease within 10 years; but they could be due in part to changes in fertility and to a richer diet in childhood, with a consequent earlier age at menarche and greater physical development.

The decline in the younger age group since the mid-1970s could be partly due to the use of cytotoxic chemotherapy, which has been found in controlled trials to have produced a statistically significant benefit only in young patients, as is shown in Table 8. At older ages, in contrast, benefit has been obtained from the use of tamoxifen. This presages well for the future; but it has not yet been used long enough on a large enough scale for any material effect to be seen in national statistics. Nor has there been time for benefit to be seen from mammographic screening, which is only now becoming widely available. We must not, however, attribute all the reduction at young ages to better treatment, as the incidence of the disease at these ages declined by 8% over the same period.

Cancer of the prostate. Changes in the mortality from cancer of the prostate have been relatively small, but the increase in the last 15 years has been over 20% and there is no indication that it is yet levelling off. Despite many investigations, the aetiology of the disease remains obscure. Case-control studies have associated a high fat diet with prostate cancer more consistently than with any other type, but there has been no corresponding increase in the fat content of the national diet that could account for the observed increase in mortality. Nor is there any new treatment on the horizon which would encourage us to think that the trend will shortly be reversed.

Table 8

Effect of chemotherapy on mortality from early breast cancer. Overview of 28 trials (ref. 21)

Chemotherapy	Per cent reduction in annual odds of death ± SD
Cytotoxic (13 442 women)*	
age under 50 yrs	22±6
age 50 yrs and over	4±5
Tamoxifen (16 513 women)*	
age under 50 yrs	−1±8
age 50 yrs and over	20±3

* Including 1 059 women in trials of both regimes.

Discussion

In this review of progress against cancer I have based my assessment on changes in the mortality from cancer that have occurred since 1951 in children and adolescents and in adults under 45 years of age or, in two exceptional cases, in adults somewhat older. I have concentrated on the experience at young ages for two reasons. First, childhood cancers need to be examined separately because they respond differently to treatment and have different causes from the cancers that occur later in life. Secondly, the cancers that occur in adults occur at all adult ages but those that occur under 45 years of age can, of necessity, have been produced only by agents that have been prevalent in the recent past (in so far as they are due to environmental factors or to personal behaviour) whereas the risk of developing cancer at a later age will have been affected by the prevalence of agents that existed many years before. A slow spread of epidemics from the young to the 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 often given more intensively in the young) but, irrespective of this, the evidence of the waxing and waning of cancer epidemics makes it clear that if we want to predict what is likely to happen in the near future, we need to examine primarily the recent changes in the relatively young.

So far as childhood cancers are concerned, the evidence is plain. The mortality has been approximately halved in developed countries as a result of progressive improvements in the efficacy of treatment and there is nothing to suggest that the improvement is coming to an end.

For the cancers that occur in adult life, 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 ovary, corpus uteri, and pharynx, and from leukaemia in women, that are attributable in part to improved treatment, in part to active prevention, and in part (in the case of cancer of the stomach and to a large extent in the case of cancer of the overy) to serendipitous social change. In the absence of any other change these would alone have reduced the total mortality from cancer since the early 1950s by 33% in men and by 18% in women, and smaller decreases in one or other sex from 11 other sex specific types of cancer would have increased the reductions to 34 and 20% respectively.

Counterbalancing part of this improvement there have been substantial increases in mortality from melanoma and non-Hodgkin's lymphoma in both sexes, from cancer of the oesophagus and mesothelioma in men, and from cancer of the breast in women and smaller increases from five other types of cancer, most of which are still relatively uncommon. Altogether these could have added 5% to the total cancer mortality in men and 4% to the total in women. In addition, however, 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.

Conclusion

The fact that the mortality from some types of cancer has increased shows that we have been losing some battles. In several cases, the reason for the increase is known and we have grounds for thinking that the foe can be stopped if this has not happened already. In others, the reason is unknown and the increase has continued. These urgently require investigation. For the majority of cancers, however, the incidence or the fatality has been materially reduced in that age group whose experience is likely to be the best predictor of the future and the totality of the evidence shows that we are clearly winning the war.

If this is true for Britain, where the regular use of cervical smears to detect premalignant lesions of the cervix and of mass mammography to detect early cancers of the breast have yet to be applied effectively on a large scale, it is certainly true in Sweden where the value of prophylactic screening has been clearly demonstrated.

In this review I have limited myself to the actual trends in mortality and current knowledge of the way in which these trends can be modified, because I have wanted to refute Bailar & Smith's (1) gloomy conclusion on their chosen ground, rather than take refuge in 'rosy rhetoric about research results still in the pipeline'. I cannot conclude, however, without affirming my belief that even if the 'rosy rhetoric' to which Bailar & Smith referred may sometimes paint an overoptimistic picture of the immediate future, the steady progress that is being made into our understanding of the nature of malignant cells and the mechanism by which malignant clones are formed will lead to increasingly rapid advances in therapy and prevention in the future.

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