ORIGINAL ARTICLE: GLOBAL EPIDEMIOLOGIC METHODS

Use of Statistics to Assess the Global Burden of Breast Cancer

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■ **Abstract:** A variety of statistics are used to quantify the burden (occurrence and outcome) of cancer generally and of breast cancer specifically. When undertaking any cancer control program, understanding these statistics, their source, and their quality is important for assessing the current situation, allocating resources to different control strategies, and evaluating progress. Two core statistics are the cancer incidence rate and the cancer mortality rate, which provide estimates of the average risk of acquiring and of dying from the disease, respectively. About 16% of the world's population is covered by registration systems that produce cancer incidence statistics, while mortality data are available for about 29%. Breast cancer incidence and mortality vary considerably by world region. In general, the incidence is high (greater than 80 per 100,000) in developed regions of the world and low (less than 30 per 100,000), though increasing, in developing regions; the range of mortality rates is much less (approximately 6–23 per 100,000) because of the more favorable survival of breast cancer in (high-incidence) developed regions. The incidence of breast cancer is increasing almost everywhere. This unfavorable trend is due in part to increases in risk factors (decreased childbearing and breast-feeding, increased exogenous hormone exposure, and detrimental dietary and lifestyle changes, including obesity and less physical activity). On the other hand, mortality is now decreasing in many high-risk countries due to a combination of intensified early detection efforts and the introduction of mammographic screening, resulting in the diagnosis of more small, early stage tumors, and advances in treatment. ■

Key Words: breast cancer, burden of illness, health care evaluation mechanisms, health planning, outcomes assessment, program evaluation, registries, resource allocation, statistics

Several statistics are used to quantify the burden (occurrence and outcome) of cancer generally and of breast cancer specifically. Understanding these statistics, their source, and their quality is important for the planning and evaluation of cancer control programs. In this article we review the core statistics commonly used for planning and assessing the effectiveness of a cancer control program, the strengths and limitations of selected statistics, and the key sources of global cancer statistics. In addition, we discuss regional differences and temporal trends in breast cancer incidence and mortality, as well as possible explanations for the observed patterns.

CORE STATISTICS FOR ESTIMATING CANCER BURDEN

Although the general idea of the burden of a disease such as cancer to a community seems fairly straightforward, there are multiple dimensions in which it may be expressed.

Incidence

Cancer incidence is the number of new cancer cases occurring in a specific population during a period of time. It can be expressed as an absolute number of cases per year (the volume of new patients presenting for treatment) or as a rate per 100,000 persons per year. The latter provides an approximation of the average risk of developing a cancer. Because the risk of cancer is strongly related to age, comparison of the risk of cancer among populations (e.g., countries, ethnic groups, or populations at different time periods within a country) may use age-standardized incidence rates to allow for the effect of differences in their age structure (1). When evaluating the impact of primary prevention strategies, a reduction in incidence (occurrence of new cases) is the appropriate statistic to use.

Mortality

Cancer mortality is the number of deaths occurring due to cancer, and the cancer mortality rate is the number of deaths due to cancer per 100,000 persons per year in a defined population. The number of deaths provides one measure (and a rather unambiguous one) of the outcome

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or impact of cancer. It is the product of the incidence and the fatality of a given cancer. Fatality, the inverse of survival, is the proportion of cancer patients that die. The cancer mortality rate therefore measures the average risk to the population of dying from a specific cancer, while fatality (1 – survival) represents the probability that an individual with cancer will die from it. Mortality rates are frequently used as a convenient proxy measure of the risk of acquiring the disease (the incidence rate) when comparing different populations or groups because they may be more generally available (as described below). However, such use introduces an assumption of equal survival/fatality in the populations being compared. This may be reasonable for cancers with poor survival rates (liver, lung, esophagus), but for breast cancer, for example, there are quite large variations in survival between countries and over time. It is safer therefore to use mortality as a measure of outcome rather than occurrence.

Prevalence

Prevalence refers to the proportion (or percentage) of the population that has the disease in question at a given point in time. For cancer, this sometimes refers to individuals who have developed a cancer at some time in their life (1). However, this definition includes as cancer cases those who are cured of the disease, and it is not particularly useful for health care planning purposes. Partial prevalence, which limits the number of patients to those in whom cancer was diagnosed during a fixed time in the past, is therefore a more practical measure of cancer burden (2). The prevalence of cases diagnosed within 1, 3, and 5 years is likely to be of relevance to the different stages of cancer therapy, namely, initial treatment (1 year), clinical follow-up (3 years), and cure (5 years). Patients who are still alive 5 years after diagnosis are usually considered cured, since for most cancers, the death rates of such patients are similar to those of the general population. Breast cancer is a notable exception, however, as the risk of death remains higher than that of the general population for many more years.

Life-Years Lost

Several other more complex statistics have been used to measure the impact of cancer, particularly in health economics. Person-years of life lost (PYLL) quantifies the years of normal life span that are lost due to deaths from cancer, and the years of life lost (YLL) may be weighted according to age, so that, for example, a year saved at age 20 is valued more highly than one at age 60. A further refinement is to calculate disability-adjusted life-years (DALYs) or quality-adjusted life-years (QALYs) lost. These involve a further weighting (between 0 and 1) of the years of life lived between diagnosis and death, reflecting the quality of these life-years (where 0 = dead and 1 = perfect health). Such estimates require a lot of data on incidence and duration of disease, as well as a lot of guesswork about quality of life in different circumstances and cultures.

Survival

The survival time of a patient with cancer is defined as the time that elapses between diagnosis and death. The most basic measure of patient survival is the observed survival. The 5-year observed survival is the probability for an individual of survival at 5 years from the date of diagnosis. Not all deaths among cancer patients will, however, be due to the primary cancer in question. Deaths from other causes reduce the observed survival and preclude comparison between groups for which probabilities of death in the general population vary. This problem is avoided by the use of relative survival—the observed survival in a patient group divided by the expected survival of a comparable group in the general population with respect to age, sex, and calendar period of investigation.

INTERNATIONAL CANCER STATISTICS

Sources

The sources of information on international cancer incidence, mortality, and survival have been summarized by Parkin and Bray (3). Incidence data derive from population-based cancer registries. Registries cover about 16% of the world population, although the distribution is very uneven by region (Table 1). Cancer incidence data from

Table 1. Percentage of the Population Covered by Incidence and Mortality Registration Systems in Various World Regions

Region	Incidence (% covered)		Mortality (% covered)
	Based on registries in CI5 vol. VIII	Based on all registries	
Africa	1	8	0.1
North America	32	99	99
Latin America and Caribbean	3	10.5	50
Japan	12.7	19.6	100
Asia (other)	4.7	7	8.6
Europe	26.2	36.5	98.3
Oceania	82	86	84
World total	**8.1**	**16.3**	**28.7**

CI5 vol. VIII, *Cancer Incidence in Five Continents*, vol. VIII (4).

registries meeting stringent quality criteria (of completeness and validity) are included in the series *Cancer Incidence in Five Continents* (4). Cancer registries also produce survival statistics, and population-based figures have been published from many developed countries; for example, the Surveillance, Epidemiology, and End Results (SEER) program comprising 14 cancer registries covering 26% of the U.S. population (5) and the EUROCARE-3 project covering 12 countries of Europe (6). Survival data from populations in China, the Philippines, Thailand, India, and Cuba have been published by Sankaranarayanan et al. (7).

Statistics on cancer mortality are derived from the information on death certificates, which are collected by civil registration systems that record vital events (births, marriages, deaths). National-level mortality statistics are collated and made available online by the World Health Organization (WHO) (http://www3.who.int/whosis); this source also provides tables of estimated coverage and completeness of the data from the different countries. Mortality data are available for about 29% of the world's population (Table 1).

Estimation

Cancer incidence and mortality data are available for only a small number of the world's countries, and estimation procedures are required to obtain a comprehensive global picture of the cancer profile and its evolution over time. In its GLOBOCAN estimates, the International Agency for Research on Cancer prepares national estimates of incidence, mortality, and prevalence of cancer that uses all available sources of information from the different countries. The level of accuracy depends on the extent and quality of locally available data. The most recent country-level estimates have been provided for 24 different cancers and 5 broad age-groups in GLOBOCAN 2002. These estimates are available on CD-ROM (8) and, in a format allowing rather less flexibility for analysis and presentation, on the Internet (http://www.dep.iarc.fr/globocan/globocan.html).

REGIONAL VARIATIONS IN BREAST CANCER INCIDENCE AND MORTALITY

Breast cancer is by far the most common cancer of women, comprising 23% of all female cancers, and there were an estimated 1.15 million new cases in 2002 (9). It ranks second overall when both sexes are considered. More than half of all cases occur in industrialized countries—about 361,000 in Europe (27.3% of cancers in women) and 230,000 in North America (31.3%). Incidence rates are high in most of the developed areas of the world (except for Japan, where breast cancer is third after colorectal cancer and stomach cancer), with the highest age-standardized incidence in North America (99.4 per 100,000) (Fig. 1). Within the United States, certain populations, such as white women in California and Hawaiian women, have age-adjusted rates of 100 per 100,000 or higher (4). In part, the high incidence in the more affluent world areas is likely due to the presence of screening programs that detect early invasive cancers, some of which would otherwise have been diagnosed later or not at all (10). The incidence is more modest in eastern Europe, South America, southern Africa, and western Asia, but breast cancer is still the most common cancer of women in these regions. In contrast, low rates (less than 30 per

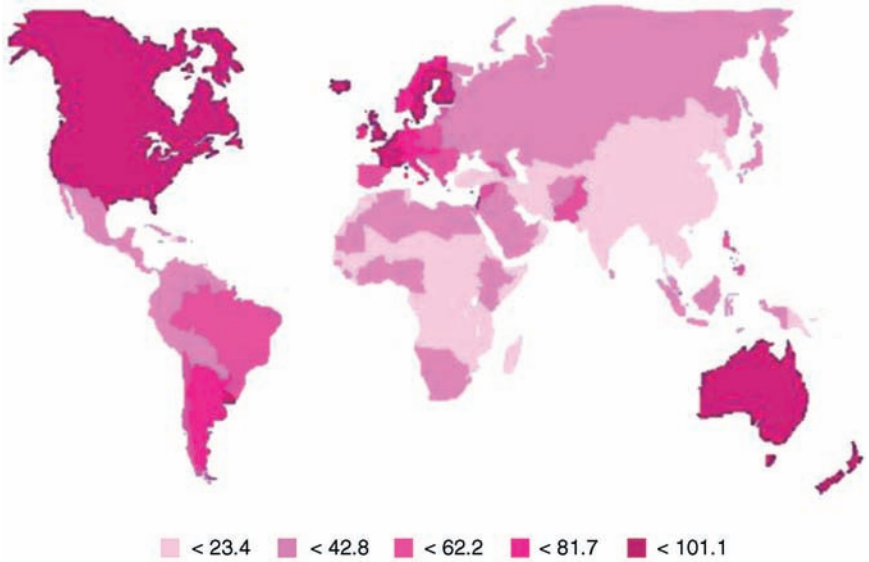


Figure 1. Breast cancer incidence rates worldwide according to GLOBOCAN 2002 (18). Rates are age-standardized (world standard) rates (per 100,000).

100,000) are found in most African and Asian populations, although they are increasing; in some Asian populations, they are already the same as in southern Europe, and in others (e.g., the Philippines), they are even higher. The incidence in the Jewish population of Israel is especially high (87.1 per 100,000). The lowest incidence internationally is in central Africa, where the age-standardized rate is 16.5 per 100,000.

The prognosis of breast cancer is generally rather good, so that this cancer ranks as the fifth cause of death from cancer overall, although it is still the leading cause of cancer mortality in women (the 411,000 annual deaths worldwide represent 14% of female cancer deaths). The very favorable survival of breast cancer cases in western countries—for example, 89% at 5 years in cases registered by the U.S. SEER program in 1995–2000 (5)—is also in part a consequence of the presence of screening programs.

Because of the very favorable survival of breast cancer in the more affluent developed countries and the poor survival in some of the least affluent developing countries, differences in mortality rates worldwide are much less marked than differences in incidence rates (Fig. 2). The estimated mortality rates in Africa and the Pacific (Micronesia and Polynesia), for example, are not greatly inferior to those in Europe.

The combination of its high incidence and relatively good prognosis make breast cancer the most prevalent cancer in the world today; there are an estimated 4.4 million women alive in whom breast cancer was diagnosed within the last 5 years (compared with just 1.4 million survivors—male and female—from lung cancer). It has been estimated that 1.5% of the U.S. female population are survivors of breast cancer (11).

EXPLAINING REGIONAL VARIATIONS IN BREAST CANCER INCIDENCE

Genetic factors, including the major susceptibility genes (*BRCA-1*, *BRCA-2*), may account for up to 10% of breast cancer cases in developed countries (12), but their prevalence in the population is too low to explain much of the international or interethnic variation in risk. Most must therefore be a consequence of different environmental exposures. This is clear from studies of migrants, which show quite clearly that incidence changes following migration; for example, an increase in the risk of breast

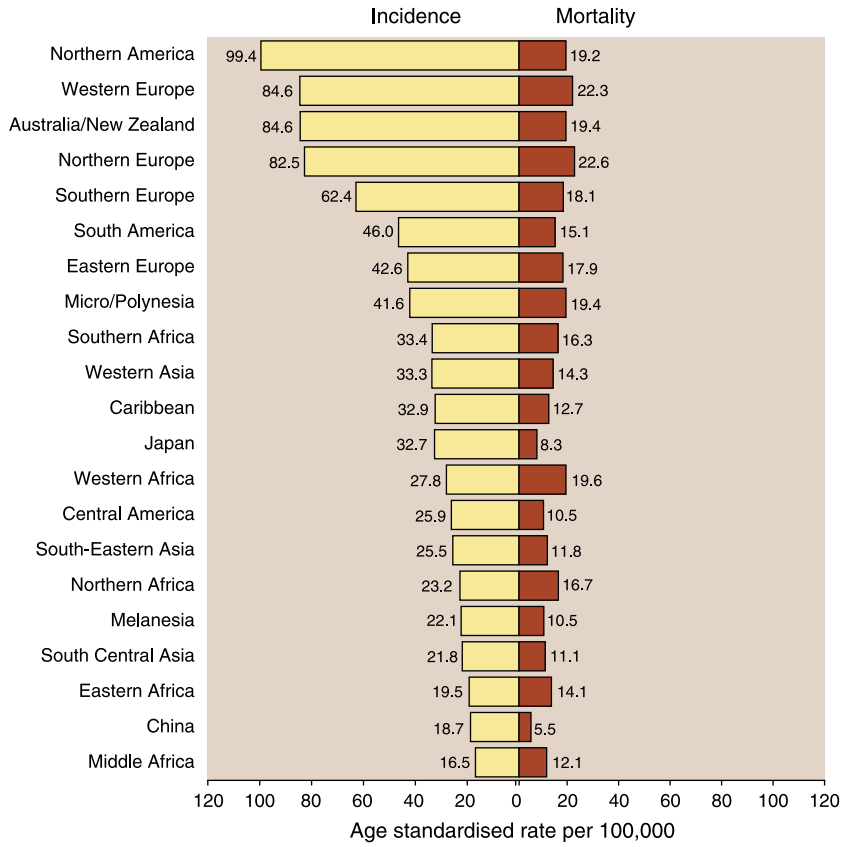


Figure 2. Breast cancer incidence and mortality rates per 100,000 by region or country. Reprinted with permission from Parkin et al. (21). Copyright 2002, Lippincott, Williams and Wilkins.

cancer in populations from European countries at relatively low risk (Italy, Poland) occurs after migration to Australia, particularly if they migrate as children (13,14). Furthermore, studies comparing the risks in migrants and their offspring (particularly among Asians migrating to the United States) demonstrate that there are major increases in risk between first, second, and third generations (15).

The major influences on breast cancer risk appear to be certain reproductive factors (low parity, late age at first pregnancy), larger body size/obesity, and less certainly, diet (16). There have, however, been few attempts to quantify the magnitude of risk differentials between populations that might be explained by such factors. Internationally there is some association between national incidence (or mortality) rates of breast cancer and population averages for various variables related to fertility (17) or body weight (18). However, such models can explain only a minor component of the variation in incidence. In the United States, Brinton et al. (19) calculated that the difference in incidence between whites and blacks, at least among women age 40–54 years (20%), was entirely explicable in terms of the different prevalences of certain reproductive and lifestyle variables.

REGIONAL TRENDS IN BREAST CANCER INCIDENCE AND MORTALITY

The changing profile of breast cancer incidence and mortality among populations in each world region, and within populations over time, has been recently reviewed by Bray et al. (20).

Europe

In countries where national screening programs started in the mid- to late 1980s (the Nordic countries, England, Wales, and The Netherlands), incidence rates were increasing at an annual rate of 1–3% before organized screening activity began (Fig. 3) (21). In several countries, such as England and Wales (22) and Sweden (23), a screening-related increase—a short-duration "bump" in the incidence curve—can be seen in the age groups being screened as a result of the detection of prevalent cancers during the first screening round. Quite substantial increases in incidence (greater than 2% per year) up to the mid-1990s were also seen in several countries where there was no national program, or where screening was very limited (e.g., Spain and Slovakia) (Fig. 3). Annual increases of 2–4% per year have been reported for the incidence of breast cancer in the former Soviet Union between 1971 and 1987 (24).

The most recent data indicate some signs of a slowdown or leveling off of the increase in incidence in several countries since the mid-1990s, particularly in The Netherlands, Sweden, and England and Wales (21). This may be a result of a cohort-specific peak in incidence (25), although the observations are also consistent with what would be expected after the initial breast screening round: a decline after the postscreening increase to a level slightly higher than that before screening (26).

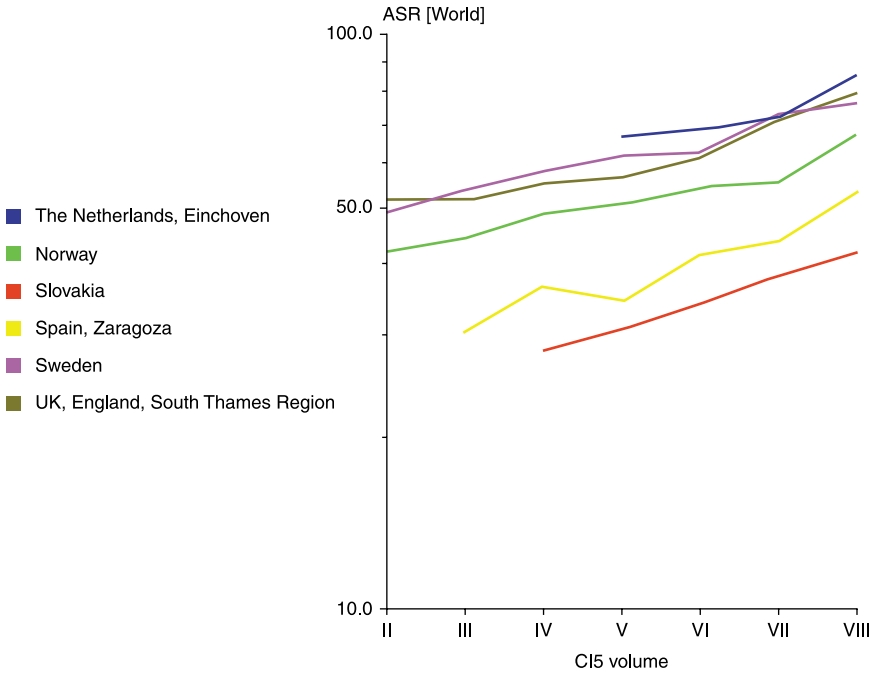


Figure 3. Breast cancer incidence rate in selected European and Scandinavian countries. ASR, age-standardized rate (world standard) (per 100,000). CI5, *Cancer Incidence in Five Continents*.

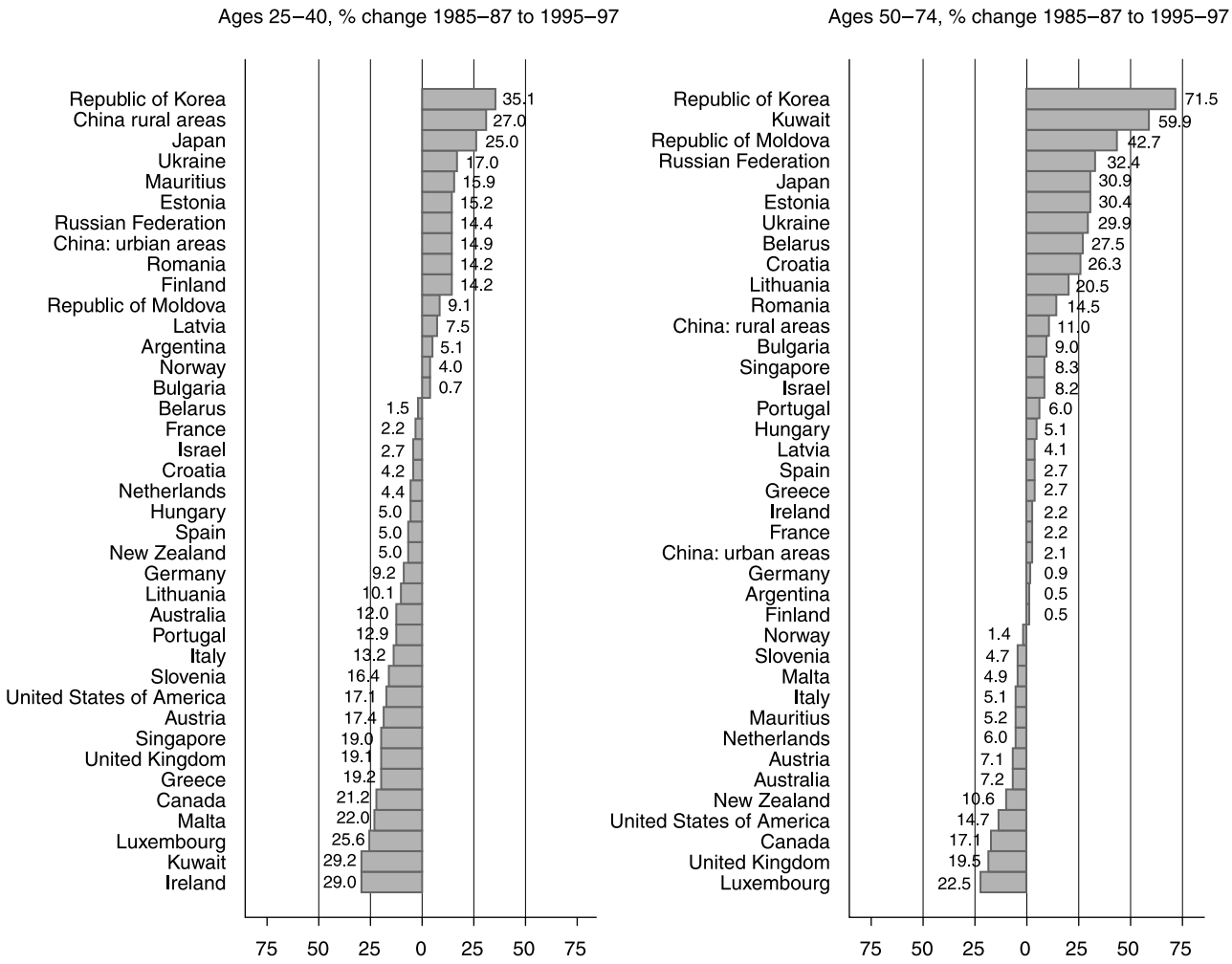
Mortality in most countries has increased from the 1950s until at least the 1980s, particularly in countries of eastern and southern Europe. A leveling off and subsequent decline in breast cancer mortality from the early 1990s is now evident in several other European countries (21), although the declines are often confined to women younger than 50 years of age (Fig. 4).

Some recent decreases in mortality are also evident in several countries that do not have national screening programs, although these tend to be confined mainly to younger age groups. Mortality is still increasing in several eastern European or former Soviet countries, where rates were relatively low in the past (Russian Federation, Estonia, Romania, and Hungary).

North America

The pattern observed in the United States and Canada is broadly similar to that in Europe, with increases in incidence among both white and black women (Fig. 5) (27). Most of this increase occurred in the period between 1980 and 1987 (5) and is related to increases in mammographically detected incident cases as a result of the intensification of breast screening at this time (28). The overall rate of increase has slowed to 0.6% per year since the late 1980s (29).

The leveling off in mortality and subsequent decline noted in several northern European countries in the 1980s was also observed in both the United States (30) and



Peroentage change in breast cancer mortality between 1995–97 and 1995–97 in women aged 50–74 and 25–49 years in selecled countries worldwide, sorted by descending order of magnitude of the change (earlier period is 1989–90 for China, later period is 1994–96 for Argentina). Source: http//www-depdb.iarc.fr/who/menu.htm.

Figure 4. Percentage change in breast cancer mortality in selected countries. (For China, the earlier period is 1988–1990; for Argentina, the later period is 1994–1996.) Countries are sorted in descending order of the magnitude of the change. Source of data: http://www.dep.iarc.fr/. Reprinted with permission from Bray et al. (32). Copyright 2004, BioMed Central Ltd.

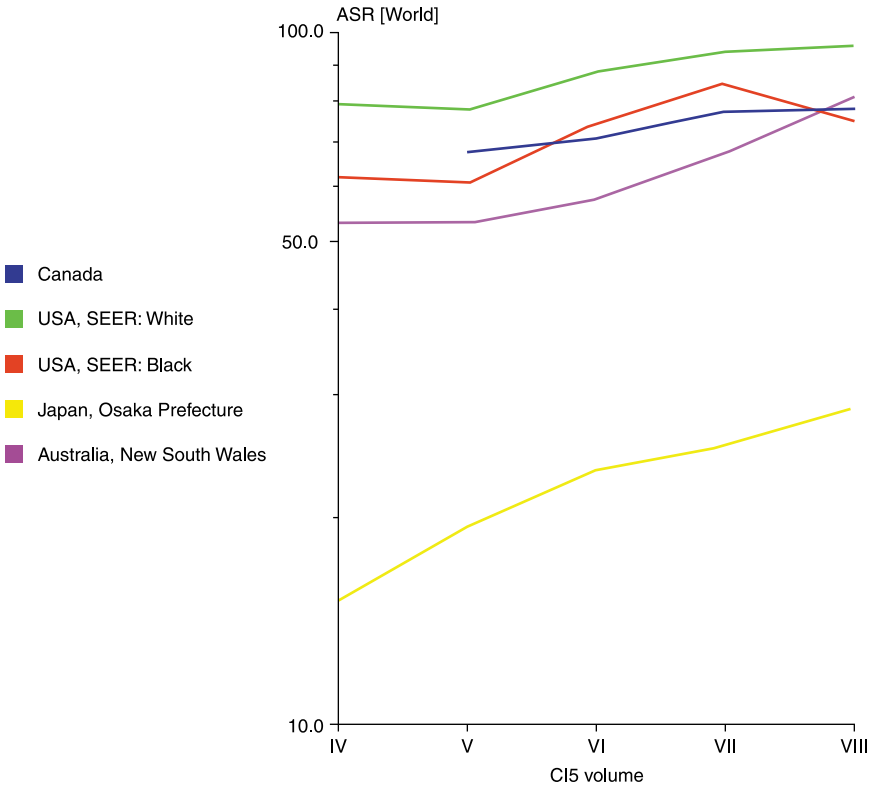


Figure 5. Breast cancer incidence rates in Canada, the United States, Japan, and Australia. SEER, Surveillance, Epidemiology, and End Results; ASR, age-standardized rate (world standard) (per 100,000); CI5, *Cancer Incidence in Five Continents*.

Canada (31), and the extent of the decrease in both younger and older women is shown in Figure 4. Since the mid-1980s, the trends in U.S. whites and blacks have diverged, with white women experiencing a leveling off and subsequent decline in mortality from the early 1990s, but black women experiencing a slight increase in mortality throughout the same period (27).

Australia and New Zealand

The incidence of breast cancer in New South Wales (representing about one-third of Australian women) increased steadily from the early to mid-1980s (Fig. 5), and by 1995 was nearly 50% higher than in 1983. The greatest increase was in the target age group for mammography screening (50–69 years), which became available in 1984 on a limited basis and in 1992 was nationwide and accessible to all women at least 40 years of age (32). In New Zealand, there were steady increases in incidence rates among both Maori and non-Maori women from 1978 to 1992 (33).

Breast cancer mortality in Australia rose steadily from the early 1970s to the late 1980s (34). Between 1985 and 1989 and 1990–1994, breast cancer mortality fell by 3.2% among women 50–69 years of age and by 4.2% among women 25–49 years of age, with little change (–0.2%) among older women (34). The proportion of women screened in all age groups increased substantially between 1988 and 1994, and by 1994 nearly 65% of women in the target age group had had at least one mammogram (34).

Japan

Although breast cancer remains relatively rare in Japan, the incidence (Fig. 5) and mortality (Fig. 4) have been increasing quite rapidly, which is consistent with increasing risk in successive generations of women (35). The overall incidence has been increasing since the mid-1970s (35,36), although the increase has been much larger than that for mortality, demonstrating improving prognosis over time (35).

Developing Countries

There are few data from developing countries, but where they are available, increases in breast cancer incidence and mortality are seen, an observation often more apparent within recent birth cohorts (37), and a probable consequence of the adoption of western lifestyles (38).

Latin America. Most Latin American countries have intermediate rates of breast cancer occurrence. Incidence

and mortality rates have been observed to be increasing in most countries (38); incidence has at least doubled, for instance, in Cali, Colombia (Fig. 6), and in Puerto Rico between the early 1970s and the mid-1990s. In Uruguay, Argentina, and Chile, women are at high or intermediate risk, and mortality rates in younger women have been reported to be more or less constant over time (37).

Asia. The age-adjusted incidence is low in most Asian countries, although world-standardized rates are greater than 50 per 100,000 in Manila, Philippines, and in Karachi, Pakistan. Rates in Singapore, particularly among the Chinese population, are also relatively high for the region. Rising incidence has been observed in India (39) and also in Singapore (40) (Fig. 6). In China, breast cancer mortality increased during the period 1987–1999 in both rural and urban areas, with a more marked rise among rural women, although the rates have remained lower than those among urban women (41). Substantial increases are reported also in Taiwan between the 1960s and 1990s (42), and in Hong Kong (43).

Africa. In Africa as a whole, breast cancer is less common than cervical cancer (8); however, it is the most common malignancy in North Africa and in urban populations in sub-Saharan Africa (44). Few datasets are available for the study of time trends in Africa, but some increases in incidence are apparent, for example, in Ibadan, Nigeria (44), and in Kampala, Uganda (45), between the 1960s and the late 1990s. Steady increases in breast cancer mortality rates of the same order of magnitude have also been noted from the early 1960s in Mauritius (44).

EXPLAINING REGIONAL TRENDS IN BREAST CANCER INCIDENCE AND MORTALITY

In general, the largest increases in breast cancer risk have been seen in populations of women historically at lowest risk, often within developing countries, whereas relatively recent departures from the long-term upward trend have been observed in several, mainly western countries. In contrast, as described above, there have been declines in mortality rates from breast cancer in several developed countries in Europe, North America, and Australia and New Zealand, dating from around 1990 (Fig. 7). A variety of factors are contributing to these trends.

Changes in Risk Factors

Changing patterns of childbearing and breast-feeding, of exogenous hormonal exposure, and of lifestyle factors

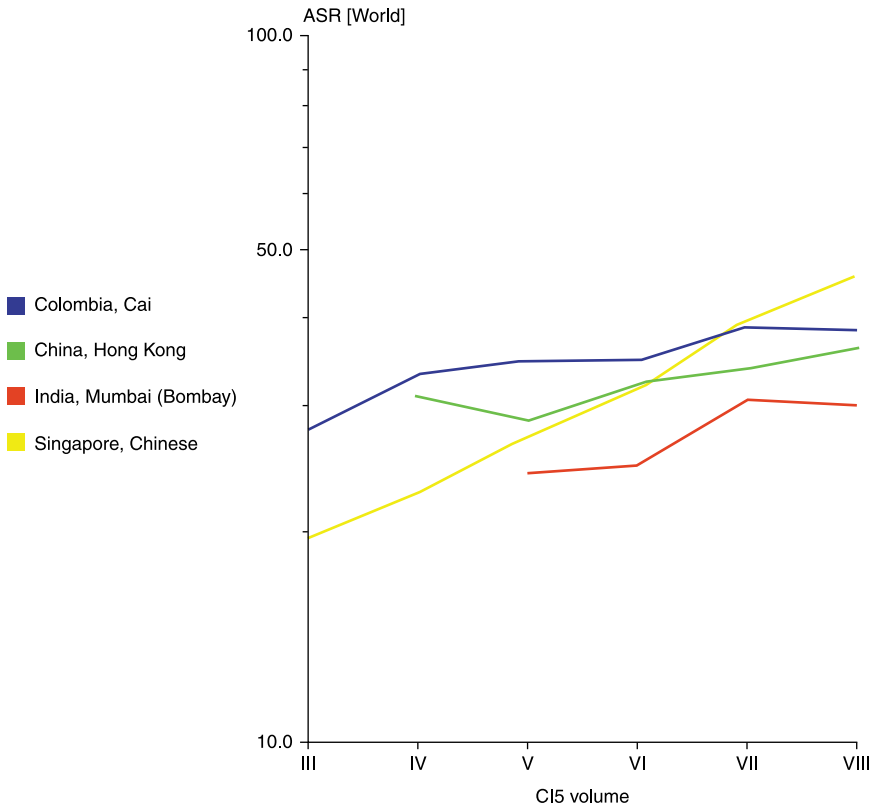


Figure 6. Breast cancer incidence rates in selected developing countries in Latin America and Asia. ASR, age-standardized rate (world standard) (per 100,000); CI5, *Cancer Incidence in Five Continents.*

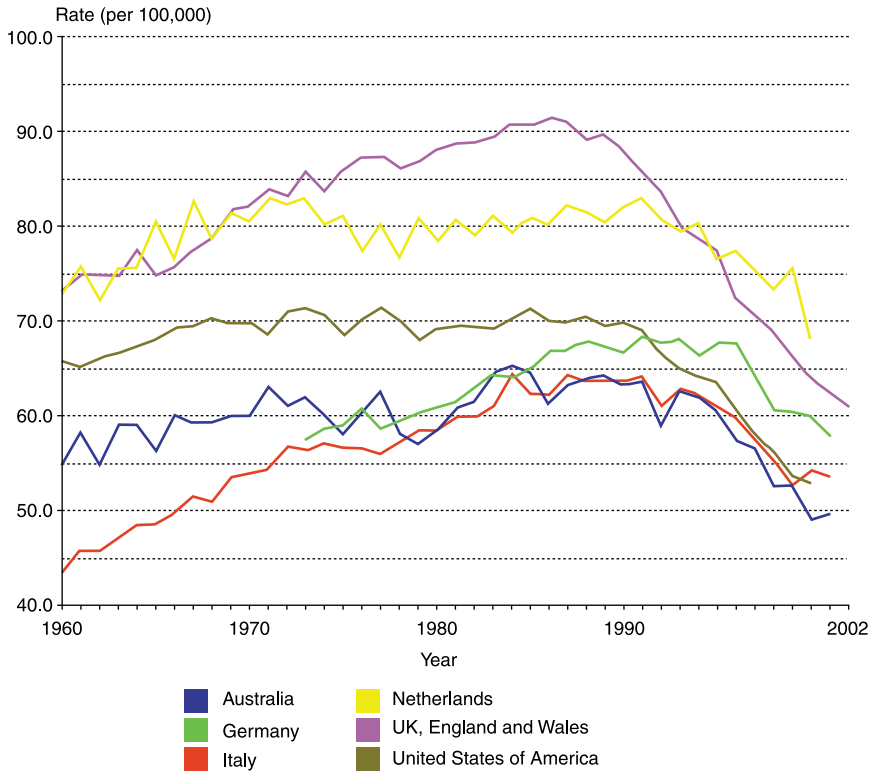


Figure 7. Breast cancer mortality rate in six countries, 1960–2002. Rates are age-standardized rates (world standard) per 100,000 at ages 45–74 years. UK, United Kingdom.

including obesity, alcohol consumption, and reduced physical activity have certainly contributed to trends in incidence and mortality. Earlier menarche and later menopause associated with better nutrition and greater body weight, resulting in an increasing lifetime length of exposure to endogenous estrogen, are consistent with upward trends in the incidence of breast cancer, particularly in developed countries.

Early Detection and Mammographic Screening

Mammographic screening for women age 50–69 years is effective in reducing breast cancer mortality, and reductions in mortality have been observed where screening has been introduced (46,47). Evidence that at least part of this decline can be attributed to screening comes from the expected increase in incidence of early stage and in situ breast cancers, followed by a decline in the incidence of advanced cancers and in subsequent mortality in the United Kingdom, northern Europe, and Australia (48–51). It has been estimated that about one-third of the overall 21% reduction in breast cancer mortality in the United Kingdom by 1998 (10 years after screening began) was due directly to screening (52), although the time lag before any benefits from screening can be expected (53), together with the reduction in mortality resulting from notable advances in treatment (discussed below), makes quantification of the contribution of each of these factors problematic. Part of the beneficial effect of screening is probably due to a shift toward earlier diagnosis of breast cancer as a consequence of better awareness of the disease following the extensive publicity surrounding the breast cancer and its prevention.

Improved Treatment and Management

Reductions in mortality before the introduction of screening, and in those countries without screening, suggest that improvements in disease treatment and management might be responsible for observed declines in mortality (53,54). In the United Kingdom (55) and Finland (49), the rapid decline in mortality rates was probably due in part to an increased use of tamoxifen among postmenopausal women with node-positive disease. The Early Breast Cancer Trialists' Collaborative Group (56) reported in a meta-analysis of 55 randomized adjuvant trials that tamoxifen reduced the incidence of contralateral breast cancers by 47% at 5 years. It is likely that the increasing use of this antiestrogen has contributed to decreases in mortality from breast cancer in women with estrogen receptor-positive tumors in developed countries during the 1990s (57). However, it has been suggested that the absolute benefit is more modest (58), because most trials reported on women with estrogen receptor-positive tumors who had early disease, whereas about one-third of women have tumors that are negative for this

receptor, and many women with breast cancer do not present with early disease.

Additional factors that have likely contributed to the decline in mortality, as noted in the United Kingdom, have been the establishment of treatment protocols, improvement in chemotherapeutic options, and development of better therapeutic guidelines (52). Specific structural changes that have embraced the specialization of breast cancer care (such as centralized treatment, adjustments in clinician workload, and use of multidisciplinary teams) have been shown to improve outcome (59).

CONCLUSION

Existing data confirm the magnitude of the problem of breast cancer—the number one cancer of women worldwide. Although the introduction of screening programs has perturbed the preexisting trends in incidence (by bringing forward the date of diagnosis), they do not disguise the steady increase in risk of breast cancer almost everywhere. Combating this will be difficult: primary prevention strategies require changes in lifestyles that run counter to the aspirations of the majority of women worldwide. Fortunately many countries with a high risk of breast cancer have achieved something of a triumph as far as improved outcome (better survival and decreased mortality) is concerned. The data on stage of disease at diagnosis, survival, and mortality suggest that this is the consequence of earlier diagnosis of clinically detectable cancers, detection of nonpalpable lesions by mammography, and improved treatment with hormonal therapy and chemotherapy. How much more improvement is possible with this combination in these countries is unclear, but it clearly offers room to reduce the mortality and morbidity in countries in which the epidemic of breast cancer is still emerging. The intelligence derived from statistical information systems is an important component of breast cancer control programs everywhere.

REFERENCES

1. Parkin DM, Bray FI. Descriptive studies. In: Ahrens W, Pigeot I, eds. *Handbook of Epidemiology*. Berlin: Springer, 2004.
2. Pisani P, Bray F, Parkin DM. Estimates of the worldwide prevalence of cancer for 25 cancers in the adult population. *Int J Cancer* 2002;97:72–81.
3. Parkin DM, Bray FI. International patterns of cancer incidence and mortality. In: Schottenfeld D, Fraumeni JF Jr, eds. *Cancer Epidemiology and Prevention*, 3rd ed. New York: Oxford University Press, in press.
4. Parkin DM, Whelan SL, Ferlay J, Storm H. *Cancer Incidence in Five Continents*, vols. I–VIII. IARC CancerBase no. 6. Lyon, France: IARC Press, 2005. Available at http://www-dep.iarc.fr; accessed September 27, 2005.
5. Ries LAG, Eisner MP, Kosary CL, *et al.*, eds. *SEER Cancer Statistics Review*. Bethesda, MD: National Cancer Institute, 2004:1975–2001. Available at http://seer.cancer.gov/csr/1975_2001; accessed April 11, 2005.
6. Sant M, Aareleid T, Berrino F, *et al.* EUROCARE-3: survival of cancer patients diagnosed 1990–94—results and commentary. *Ann Oncol* 2003;14(suppl. 5):v61–118.
7. Sankaranarayanan R, Black RJ, Parkin DM, eds. *Cancer Survival in Developing Countries*. Scientific publication no. 145. Lyon, France: IARC Press, 1998.
8. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002. Cancer incidence, mortality and prevalence worldwide. IARC CancerBase no. 5, version 2.0 [data on CD-ROM]. Lyon, France: IARC Press, 2004.
9. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005;55:74–108.
10. IARC Working Group on the Evaluation of Cancer-Prevention Strategies. *Handbooks of Cancer Prevention*, vol. 7, *Breast Cancer Screening*. Lyon, France: IARC Press, 2002.
11. Hewitt M, Breen N, Devesa S. Cancer prevalence and survivorship issues: analyses of the 1992 National Health Interview Survey. *J Natl Cancer Inst* 1999;91:1480–86.
12. McPherson K, Steel CM, Dixon JM. Breast cancer—epidemiology, risk factors and genetics. *BMJ* 2000;321:624–28.
13. Geddes M, Parkin DM, Khlat M, Balzi D, Buiatti E, eds. *Cancer in Italian Migrant Populations*. Scientific publication no. 123. Lyon, France: IARC Press, 1993.
14. Tyczynski J, Tarkowski W, Parkin DM, Zatonski W. Cancer mortality among Polish migrants to Australia. *Eur J Cancer* 1994;30A:478–84.
15. Ziegler RG, Hoover RN, Pike MC, *et al.* Migration patterns and breast cancer risk in Asian-American women. *J Natl Cancer Inst* 1993;85:1819–27.
16. Kelsey JL, Bernstein L. Epidemiology and prevention of breast cancer. *Annu Rev Public Health* 1996;17:47–67.
17. Parkin DM. Cancers of the breast, endometrium and ovary: geographic correlations. *Eur J Cancer Clin Oncol* 1989;25:1917–25.
18. Bergström A, Pisani P, Wolk A, Adami HO. Overweight as an avoidable cause of cancer in Europe. *Int J Cancer* 2001;91:421–30.
19. Brinton LA, Benichou J, Gammon MD, Brogan DR, Coates R, Schoenberg JB. Ethnicity and variation in breast cancer incidence. *Int J Cancer* 1997;73:349–55.
20. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. *Breast Cancer Res* 2004;6:229–39.
21. Botha JL, Bray F, Sankila R, Parkin DM. Breast cancer incidence and mortality trends in 16 European countries. *Eur J Cancer* 2003; 39:1718–29.
22. Quinn M, Allen E. Changes in incidence of and mortality from breast cancer in England and Wales since introduction of screening. United Kingdom Association of Cancer Registries. *BMJ* 1995;311:1391–95.
23. Persson I, Bergstrom R, Barlow L, Adami HO. Recent trends in breast cancer incidence in Sweden. *Br J Cancer* 1998;77:167–69.
24. Zaridze DG, Basieva TH. Incidence of cancer of the lung, stomach, breast, and cervix in the USSR: patterns and trends. *Cancer Causes Control* 1990;1:39–40.
25. Nab HW, Mulder PG, Crommelin MA, van der Heijden LH, Coebergh JW. Is the peak in breast cancer incidence in sight? A study conducted in the southeastern Netherlands. *Eur J Cancer* 1994;30A:50–52.
26. Walter SD, Day NE. Estimation of the duration of a preclinical disease state using screening data. *Am J Epidemiol* 1983;118:865–86.
27. Lacey JV Jr, Devesa SS, Brinton LA. Recent trends in breast cancer incidence and mortality. *Environ Mol Mutagen* 2002;39:82–88.

28. Wun LM, Feuer EJ, Miller BA. Are increases in mammographic screening still a valid explanation for trends in breast cancer incidence in the United States? *Cancer Causes Control* 1995;6:135–44.

29. Weir HK, Thun MJ, Hankey BF, *et al.* Annual report to the nation on the status of cancer, 1975–2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst* 2003;95:1276–99.

30. Smigel K. Breast cancer death rates decline for white women [news]. *J Natl Cancer Inst* 1995;87:173.

31. National Cancer Institute of Canada. *Canadian Cancer Statistics 1998*. Toronto, Ontario, Canada: National Cancer Institute of Canada, 1998.

32. Giles GG, Amos A. Evaluation of the organised mammographic screening programme in Australia. *Ann Oncol* 2003;14:1209–11.

33. Armstrong W, Borman B. Breast cancer in New Zealand: trends, patterns, and data quality. *N Z Med J* 1996;109:221–24.

34. Smith CL, Kricker A, Armstrong BK. Breast cancer mortality trends in Australia: 1921–94. *Med J Aust* 1998;168:11–14.

35. Wakai K, Suzuki S, Ohno Y, Kawamura T, Tamakoshi A, Aoki R. Epidemiology of breast cancer in Japan. *Int J Epidemiol* 1995;24:285–91.

36. Nagata C, Kawakami N, Shimizu H. Trends in the incidence rate and risk factors for breast cancer in Japan. *Breast Cancer Res Treat* 1997;44:75–82.

37. Parkin DM. Cancer in developing countries. *Cancer Surveys* 1994;19/20:519–61.

38. Coleman MP, Esteve J, Damiecki P, Arslan A, Renard H. *Trends in Cancer Incidence and Mortality*. Lyon, France: IARC Press, 1993.

39. Yeole BB, Kurkure AP. An epidemiological assessment of increasing incidence and trends in breast cancer in Mumbai and other sites in India, during the last two decades. *Asian Pac J Cancer Prev* 2003;4:51–56.

40. Seow A, Duffy SW, McGee MA, Lee J, Lee HP. Breast cancer in Singapore: trends in incidence 1968–1992. *Int J Epidemiol* 1996;25:40–45.

41. Yang L, Parkin DM, Li L, Chen Y. Time trends in cancer mortality in China: 1987–1999. *Int J Cancer* 2003;106:771–83.

42. Chie WC, Chen CF, Lee WC, Chen CJ, Lin RS. Age-period cohort analysis of breast cancer mortality. *Anticancer Res* 1995;15:511–15.

43. Leung GM, Thach TQ, Lam TH, *et al.* Trends in breast cancer incidence in Hong Kong between 1973 and 1999: an age-period-cohort analysis. *Br J Cancer* 2002;87:982–88.

44. Parkin DM, Ferlay J, Hamdi-Cherif M, *et al.*, eds. *Cancer in Africa: Epidemiology and Prevention*. Scientific publication no. 153. Lyon, France: IARC Press, 2003.

45. Wabinga HR, Parkin DM, Wabwire-Mangen F, Nambooze S. Trends in cancer incidence in Kyadondo County, Uganda, 1960–1997. *Br J Cancer* 2000;82:1585–92.

46. Shapiro S, Coleman EA, Broeders M, *et al.* Breast cancer screening programmes in 22 countries: current policies, administration and guidelines. International Breast Cancer Screening Network (IBSN) and the European Network of Pilot Projects for Breast Cancer Screening. *Int J Epidemiol* 1998;27:735–42.

47. International Agency for Research on Cancer. *Breast Cancer Screening*. Lyon, France: IARC Press, 2002.

48. McCann J, Stockton D, Day N. Breast cancer in East Anglia: the impact of the breast screening programme on stage at diagnosis. *J Med Screen* 1998;5:42–48.

49. Hakama M, Pukkala E, Heikkila M, Kallio M. Effectiveness of the public health policy for breast cancer screening in Finland: population based cohort study. *BMJ* 1997;314:864–67.

50. Tabar L, Fagerberg G, Duffy SW, Day NE, Gad A, Grontoft O. Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin North Am* 1992;30:187–210.

51. Kricker A, Farac K, Smith D, Sweeny A, McCredie M, Armstrong BK. Breast cancer in New South Wales in 1972–1995: tumor size and the impact of mammographic screening. *Int J Cancer* 1999;81:877–80.

52. Blanks RG, Moss SM, McGahan CE, Quinn MJ, Babb PJ. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990–1998: comparison of observed with predicted mortality. *BMJ* 2000;321:665–69.

53. Jatoi I, Miller AB. Why is breast-cancer mortality declining? *Lancet Oncol* 2003;4:251–54.

54. Chlebowski RT, Collyar DE, Somerfield MR, Pfister DG. American Society of Clinical Oncology technology assessment on breast cancer risk reduction strategies: tamoxifen and raloxifene. *J Clin Oncol* 1999;17:1939–55.

55. Peto R, Boreham J, Clarke M, Davies C, Beral V. UK and USA breast cancer deaths down 25% in year 2000 at ages 20–69 years [correspondence]. *Lancet* 2000;355:1822.

56. Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer: an overview of the randomised trials. *Lancet* 1998;351:1451–67.

57. Chu KC, Tarone RE, Kessler LG, *et al.* Recent trends in US breast cancer incidence, survival, and mortality rates. *J Natl Cancer Inst* 1996;88:1571–79.

58. Peto R. Five years of tamoxifen—or more? *J Natl Cancer Inst* 1996;88:1791–93.

59. Selby P, Gillis C, Haward R. Benefits from specialised cancer care. *Lancet* 1996;348:313–18.