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Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons

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Summary

The international patterns and trends in prostate cancer incidence, survival, prevalence and mortality were examined. Age-standardized incidence and death rates among men in a variety of countries worldwide were obtained from various sources, survival rates from European sources and elsewhere, and prevalence estimates from the EUROPREVAL study. Results from many published studies were summarized. The incidence of prostate cancer varies widely around the world, with by far the highest rates in the USA and Canada. There has been a gradual increase in the incidence of prostate cancer since the 1960s in many countries and in most continents; there were large increases in the late 1980s and early 1990s in the USA, but increases have also occurred in countries with comparatively low incidence, e.g. India. Survival from prostate cancer improved during the 1970s and 1980s; further increases in the 1990s may be largely a result of earlier diagnosis. There were wide differences in survival across Europe, with rates in the UK well below the average, but all European rates were far below those in the USA. There was wide variation in the prevalence of prostate cancer in Europe; in some countries with high incidence and high life-expectancy, prostate cancers formed ≈15% of all prevalent cancers in men. Mortality from prostate cancer has also increased in many countries, but to a lesser extent than incidence; this is consistent with the observed trends in survival. Mortality decreased slightly in the mid to late 1990s in several countries, including the USA, Canada, England, France and Austria. Part of the apparent increases in the incidence of prostate cancer has been associated with diagnostic artefacts (particularly detecting preclinical tumours through the increased use of transurethral resection) which may also have had an effect on death certification through the incorrect attribution of prostate cancer as the underlying cause of death. However, the greatest effect on the registration of new cases of prostate cancer has been the increased availability of prostate specific antigen testing during the early- to mid-1990s. Possibly, in addition to the effect of attribution bias, the earlier diagnosis of prostate cancers has contributed to the recent slight decreases in mortality. However, this is unlikely to account for much of the reduction, given the slow development of the disease from onset to death. Changes in disease management are probably more important. There are many strong arguments against introducing population-based screening for prostate cancer.

Introduction

The latest estimates of global cancer incidence show that prostate cancer has become the third most common cancer in men, with half a million new cases each year, almost 10% of all cancers in men [1–3]. Prostate cancer is a disease of the elderly; around the world, three-quarters of cases occur in men aged ⩾65 years. It is therefore more common in countries with higher proportions of elderly men in their population, and so accounts for ≈15% of cancers in men in developed countries, but only 4% in developing countries [3]. Prostate cancer is a large and growing public health problem, with rapidly increasing numbers of cases because incidence rates have been rising (even before the advent of screening, see below) and the age distributions of many populations have been shifting towards the elderly. For example, in England and Wales the age-standardized incidence increased by nearly 60% (more than 2.5% each year) during the 1970s and 1980s, during which time the number of men aged ⩾80 years increased by >70%, from ≈330 000 (1.4% of the total male population) to almost 980 000 (2.3%); the total number of new cases more than doubled, from 6200 to 12 500 [4].

Several reviews of the evidence on the causes and risk factors for prostate cancer have been published [5–8] but the causes are essentially unknown. There are no known primary preventive measures that men can take to minimize the risk of developing prostate cancer [9]. A few risk factors have been identified, although many (too) small studies have given conflicting or inconclusive results. Prostate cancer probably results from a combination of factors, including age,

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endogenous hormones and the environment in its widest sense, particularly dietary fat [5,10]. One recent study [11] has, in contrast to many previous studies, found a positive association between the risk of prostate cancer and the moderate consumption of spirits (but not wine or beer). Another [12] found that the risk of prostate cancer in middle-aged men increased directly in relation to the number of female sexual partners they had had, but not with the frequency of sexual intercourse. The proportions of cases attributable to genetic factors [13,14], ionizing radiation, occupational exposure to cadmium or, possibly, vasectomy, appear low [2,3,15]. Little is known about the natural history of prostate cancer, but it has long been recognized that many cancers exist in men not (or not yet) clinically diagnosed [16–19]. Recent research suggests that prostate cancer is a single disease, which may have a very long history [20]. The apparent unpredictability of the course of prostate cancer may result from a large proportion of small tumours (resulting from slow growth in the early stages of development) which do not give rise to symptoms, rather than a separate type of latent tumour [20]. Progression of the disease is also poorly understood and is not inevitable in the lifetime of a patient with histological evidence of the cancer [14].

If prostate cancer is detected at an early stage, curative treatment by radical prostatectomy [21], or radiotherapy [22] is possible. However, surveillance (with no treatment) appears to give similar outcomes for patients with low-grade tumours [23,24]. The side-effects of prostatectomy include pain, impotence in a large proportion of cases, incontinence in a small proportion, and (albeit rarely) death [8].

The apparent increases in the incidence of prostate cancer in the 1970s and 1980s have partly been attributed to the increased use of TURP [25] for treating BPH, which results in the incidental detection of preclinical cases in ≈10% of patients [26].

Even before the rapid increases in the incidence of prostate cancer seen in some countries (particularly the USA) in the early 1990s as a result of increased PSA testing, there was substantial variation in rates around the world. As noted above, some part of the apparent variability is caused by different age structures in the populations, but wide differences remain after age standardization. Differences between countries in registration of the disease have been identified where latent carcinomas are diagnosed at post mortem or after investigations for BPH [27]. The increased detection of insignificant tumours may be accelerated by the introduction of better diagnostic techniques, e.g. TRUS, TRUS-guided biopsy and PSA testing [25,28,29].

Survival with prostate cancer is moderately good: the European average 5-year relative survival rate for patients diagnosed in the late 1980s was ≈55%, but there was considerable variation among countries [28,30]. The results of that study were not affected by PSA testing which, by advancing the diagnosis, gives apparent improvements in survival even if patients do not actually live longer (lead-time bias) [28].

As would be expected from the wide range of variations in incidence and survival, the prevalence of prostate cancer (i.e. the number or proportion of patients diagnosed during a given period who are still alive at the end of it) also varies widely [31]. In developed countries, the combination of high incidence and fairly good survival means that, despite the high proportion of cases which occur in elderly men, prostate cancer cases make up a large proportion of the total number of prevalent cases of cancer. Mortality from prostate cancer also varies considerably around the world, but the differences among countries are much smaller than for incidence [27,32].

This review brings together a wide range of data on prostate cancer incidence, survival, prevalence and mortality. Part I contains the Methods section and compares international patterns and trends, while Part II concentrates on results for individual countries and includes the Discussion.

Methods

The definitions and explanations of some of the terms used in descriptive epidemiology, including incidence, crude and relative survival, prevalence, mortality and age-standardized rates, are given in the Appendix.

Directly age-standardized incidence rates per 100 000 (using the World standardized population) were obtained from the 'Cancer Incidence in Five Continents' series [33–35]. The data from the largest registry in each selected country were chosen where national values were not available. The data cover the periods 1978–82, 1983–87 and 1988–92. The map of global incidence was based on the data in 'GLOBOCAN' [36]. Age-specific incidence rates for England and Wales were based on data from regional cancer registries collated by the Office for National Statistics (ONS) [4,37,38]. Age-standardized incidence rates (using the European standard population) in local authority areas in Great Britain were produced by ONS in collaboration with the Scottish Cancer Registry [39]. Age-specific incidence rates for the USA were based on data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) cancer registries [40] which cover ≈10% of the USA population (although not a random sample, and the areas covered are geographically dispersed, so the results are not necessarily representative of the USA as a whole).

Relative survival results for countries in Europe have been produced by the EUROCARE project [30] which covered 45 cancer registries in 17 countries with data for ≈3.5 million patients; there was a high degree of standardization of data collection, checking and analysis procedures. From these results, an in-depth analysis of survival from prostate cancer in Europe was produced [28].

Prevalence at any particular 'reference date' depends on both the incidence of and survival from cancer over a very long period before that date. Until recently, information on the prevalence of cancer cases has been sparse, but the first results from 'EUROPREVAL', a European collaborative study involving 38 registries in 17 countries with data on almost 3 million cancers and standardized data collection, checking and analysis, have recently been published [31]. The method calculated age-specific prevalence based on the available data, and estimated the additional proportions of prevalent cases that would have been diagnosed *before* the observation periods of the various cancer registries.

Mortality data from the OECD Health Database [41] were examined for the period 1985 to the latest year available for over 20 countries. Rates were age-standardized using the 1980 OECD population. Age-specific rates for England and Wales were based on data from the deaths database at ONS [42–44]. All trends in mortality in England and Wales were adjusted to take into account a change during the period 1984–92 in the interpretation of WHO Rule 3, which governs how information in the two parts of the death certificate is used to determine the underlying cause of death. The change meant that deaths from causes such as pneumonia declined steeply in 1984, whereas deaths from causes often mentioned in part II of the death certificate increased [45]. There was an artefactual increase in mortality from prostate cancer in 1984, which was most marked in the elderly. The adjustments [42] mean that rates presented here for 1984–92 will be lower than given elsewhere [46]. Mortality data for geographical areas below state level in the USA were taken from the database on the National Cancer Institute's website.

Detailed information on trends in prostate cancer has been published for many countries, including England and Wales [4,42,47–49], Scotland [50], Denmark [51,52], France [53], Germany [54], Luxembourg [55], The Netherlands [49,56,57], Spain [58], Switzerland [59], the USA [60–71], Canada [72–74], Mexico [75], Australia [76–78], New Zealand [79] and Japan [80]. Several recent overviews have also been published [81–84] updating the two large volumes on trends in cancer incidence and mortality published in the early 1990s [27,85].

Results

Incidence

The recorded incidence of prostate cancer varies enormously around the world. The rates in the USA (before the peak in 1992) were more than twice those in Sweden and Australia, over three times the rates in the UK and elsewhere in Europe, and 10 times the levels in the Far East in countries such as Singapore, Japan, India and China (Fig. 1a). The complete global picture of prostate cancer incidence [36] is illustrated in Fig. 2.

Directly age-standardized incidence rates (using the World standard population) for 17 countries around the world for three periods (1978–82, 1983–87 and 1988–92) are given in Table 1, together with the percentage changes in rates between the periods. There were substantial increases in rates during the 1980s in all countries except Denmark, Ecuador and Japan.

Very few cases of prostate cancer occur in men aged <50 years, but rates then increase very steeply with age. For example, in England and Wales the incidence in 1997 exceeded that of lung cancer for men aged $\geqslant 75$, and the rate in the very elderly (those $\geqslant 85$ years) was ≈1000 per 100 000 population, i.e. 1% [4,37]. The distribution of cases across the age groups differs substantially from that for breast cancer, the most common cancer in women, for which 8–11% of cases occur in all age groups from 45 to 49 years upwards; $<15\%$ of cases of prostate cancer occur in those aged <65 compared with 55% of cases of breast cancer (Fig. 3).

The age-standardized trends in incidence and mortality for England and Wales and for the USA are shown in Fig. 4. They clearly show the differences between the countries in the incidence rates during the 1970s and 1980s, the timing and extent of the increase caused by PSA testing, and the subsequent reductions. (The age-specific rates of incidence and mortality are described and illustrated in Part II).

Survival

On average, the 5-year relative survival in England and Wales in the late 1980s, before PSA testing became widespread, was just over 40%, some 6 percentage points lower than in Scotland. However, survival in England, Wales and Scotland was well below rates in most countries in western Europe [28,30] where the average level was 56% (Fig. 5). There was considerable variation in survival across Europe, with the lowest rates in former 'Eastern bloc' countries, e.g. Estonia (40%) and in the UK, and the highest in

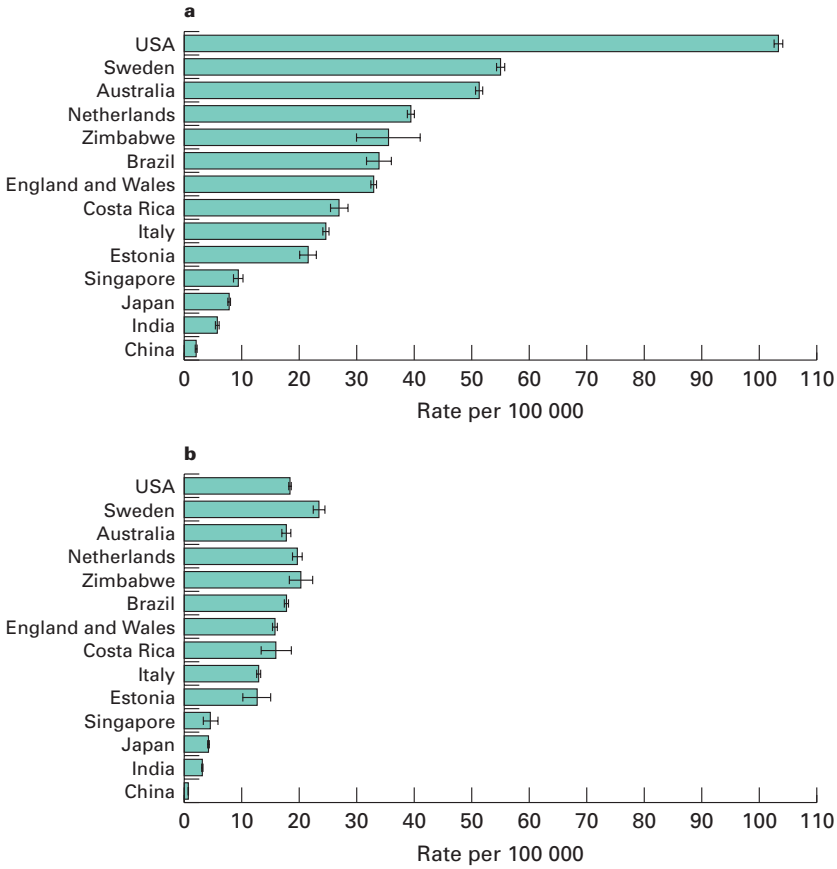

Fig. 1. The international **a**, incidence of and **b**, mortality from prostate cancer. Both rates are directly age-standardized using the World standard population.

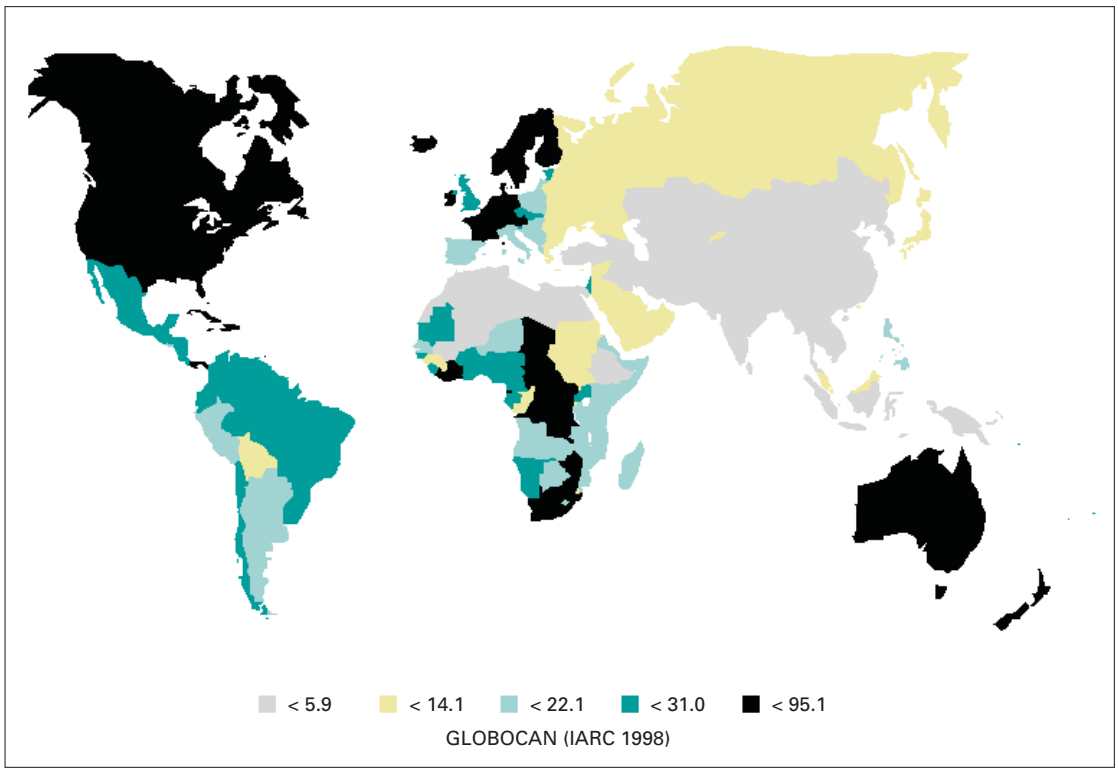

Fig. 2. The incidence of prostate cancer world-wide, age-standardized using the World standard population.

Table 1 The incidence of prostate cancer in selected countries from 1978–82 to 1988–92

	*Incidence**				
Country	*1978–82*	*1983–87*	*% change†*	*1988–92*	*% change†*
Australia	33.8	39.0	15	53.5	37
Canada	43.7	51.4	18	63.0	23
Denmark	27.7	29.9	8	31.0	4
Ecuador	na	23.0	na	22.4	−3
England & Wales	20.9	23.1	11	28.0	21
France	27.4	31.1	14	48.1	55
Iceland	36.2	52.4	45	61.0	16
India	8.2	6.9	−16	8.0	16
Israel	18.8	17.5	−7	23.9	37
Japan	5.1	6.6	29	6.8	3
Netherlands	28.3	29.6	5	39.6	34
Norway	42	43.8	4	48.4	11
Poland	11.5	13.3	16	15.5	17
Slovakia	15.8	19.9	26	22.0	11
Spain	17	18.6	9	21.0	13
Sweden	45.9	50.2	9	55.3	10
USA					
White	45.6	61.8	35	100.8	63
Black	78.4	82.0	5	137.0	67

*Rate per 100 000 population, directly age-standardized using the World standard population; †compared with the earlier period. Sources [33–35].

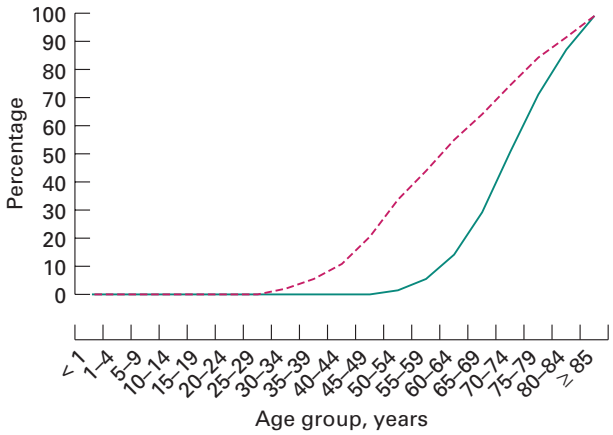

Fig. 3. The cumulative percentages of cases of breast (red dashed line) and prostate cancer (green solid line) by age group, England and Wales, 1997.

Switzerland and the Nordic countries (except Denmark). However, European differences in survival become insignificant when compared with the apparent rate of 86% in the USA. Regardless of any difference in the efficacy of treatment, there can be little doubt that prostate cancers registered in the USA are biologically quite different [4], although survival rates in black men

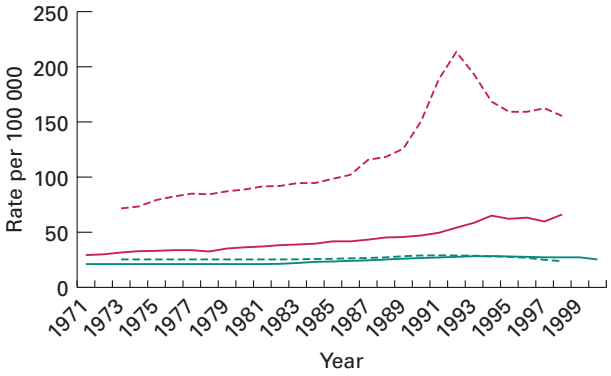

Fig. 4. The age-standardized (using the European standard population) incidence of (red) and mortality from (green) prostate cancer, England and Wales (solid lines) and USA (dashed lines), 1971–2000.

in the USA are lower and have not improved as rapidly as those in white men.

Prevalence

Estimates of the crude (i.e. not age-standardized) prevalence of prostate cancer in 17 European countries for cases diagnosed in various periods up to the reference date of 31 December 1992 are shown in Fig. 6 (the rank order of the countries based on age-standardized results was closely similar) [31]. The prevalence in Sweden was markedly higher than elsewhere, at almost 600 per 100 000 population compared with the second highest rate of just over 400 per 100 000 in Switzerland. Even excluding the highest and lowest rates (the latter only 40 per 100 000 in Poland), there was a five-fold range across the countries.

Mortality

In contrast to the very wide variation in the incidence of and survival from prostate cancer around the world, there was relatively little variation in mortality (Fig. 1b). In particular, mortality in the USA was not very different from levels in other developed countries, suggesting that a large proportion of prostate cancers in the USA have a very good prognosis. However, mortality in Singapore, Japan, India and China was lower than in the other countries and consistent with the pattern in incidence (Fig. 1a).

Worldwide trends in prostate cancer mortality have recently been systematically analysed by Boyle *et al.* [82]. They calculated truncated (age 50+) age-standardized mortality using the World standard population for all European countries for which a long time series was available, and for the USA, Canada,

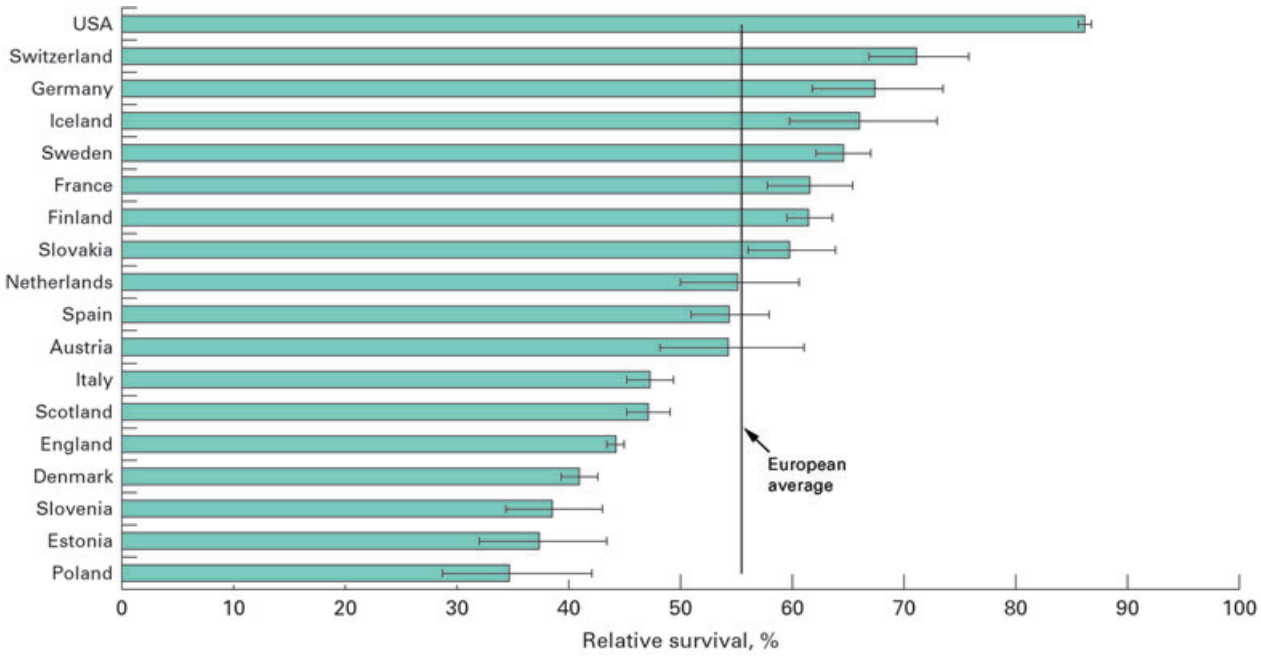

Fig. 5. International 5-year relative survival from prostate cancer, 1985–89.

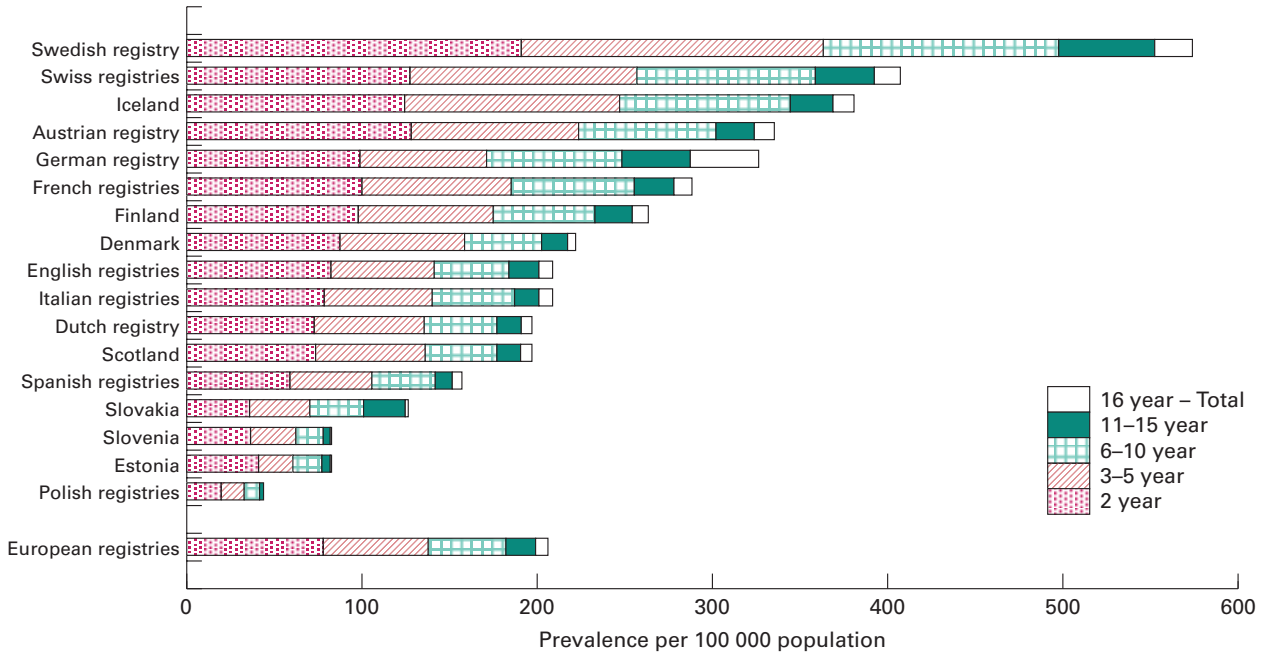

Fig. 6. Prevalence of prostate cancer in European countries by time since diagnosis, 1992.

Australia, New Zealand and Japan. Despite there being very wide differences in mortality among the countries, there were large increases in rates in virtually all of them, although the timing and rates of increase varied among them. Declines in mortality in the late 1990s were recorded in the USA, Canada, England, France and Austria.

Recent trends in prostate cancer mortality for many of the same countries are illustrated in Fig. 7, in which the countries have been grouped. (Note that these three charts have different scales on their vertical axes). Figure 7a includes those countries (several in the Far East or in southern Europe) where mortality was <25 per 100 000 in 1985; in most of these there have

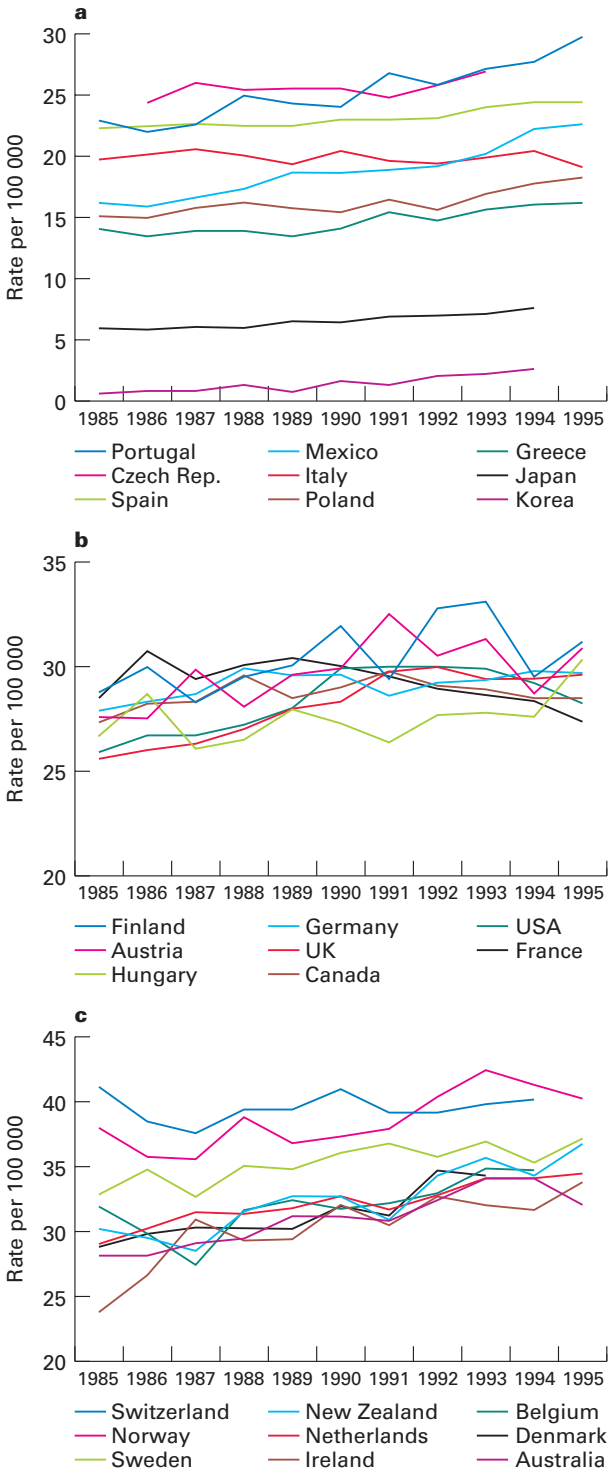

Fig. 7. International trends in mortality from prostate cancer.

been steady increases in mortality. Figure 7b includes the USA, Canada, the UK and several countries in 'central' Europe, e.g. Austria, Germany and Hungary, where the mortality was 25–30 per 100 000 in 1985; most of these showed only slight increases over the period, clustering at ≈30 per 100 000 in 1995. Figure 7c includes several, but not all, of the Nordic countries, and Australia and New Zealand, where mortality was generally >25 per 100 000 in 1985 and/or there were noticeable increases over the period.

References

1 Parkin DM, Laara E, Muir CS. Estimates of the worldwide frequency of sixteen cancers in 1980. *Int J Cancer* 1988; **41**: 184–97

2 Parkin DM, Pisani P, Ferlay J. Estimates of the world-wide incidence of 25 major cancers in 1990. *Int J Cancer* 1999; **80**: 827–41

3 Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000: the global picture. *Eur J Cancer* 2001; **37** (Suppl. 8): 4–66

4 Quinn MJ, Babb PJ, Brock A, Kirby L, Jones J. *Cancer trends in England and Wales, 1950–99.* Studies on Medical and Population Subjects No. 66. London: The Stationery Office, 2001

5 Pienta KJ, Esper PS. Risk factors for prostate cancer. *Ann Intern Med* 1993; **118**: 789–803

6 Pack RS. Epidemiology of prostate cancer; with emphasis on familial clusters. *Cancer Bull* 1993; **45**: 384–9

7 Meikle AW, Smith JA. Epidemiology of prostate cancer. *Urol Clin North Am* 1990; **17**: 709–19

8 Selley S, Donovan J, Faulkner A, Coast J, Gillat D. Diagnosis, management and screening of early localised prostate cancer. *Health Technol Assess* 1997; **1** (2)

9 Department of Health. *National Cancer Plan.* London: Department of Health, 2000

10 Muir CS, Nectoux J, Statszewski J. The epidemiology of prostatic cancer. *Acta Oncol* 1991; **30**: 133–40

11 Sesso HD, Paffenbarger RS Jr, Lee J-M. Alcohol consumption and risk of prostate cancer: the Harvard Alumni Health Study. *Int J Epidemiol* 2001; **30**: 749–55

12 Rosenblatt KA, Wicklund KG, Stanford JL. Sexual factors and the risk of prostate cancer. *Am J Epidemiol* 2001; **153**: 1152–8

13 Pienta KJ. The epidemiology of prostate cancer: clues for chemo-prevention. *In Vivo* 1994; **8**: 419–22

14 Whitmore WF. Localised prostatic cancer. Management and detection issues. *Lancet* 1994; **343**: 1263–7

15 Schottenfeld D. Prostate cancer. In Schottenfeld D, Fraumeni JF eds, *Cancer Epidemiology and Prevention*, 2nd edn. Oxford: Oxford University Press, 1996

16 Franks LM. Latent carcinoma of the prostate. *J Pathol Bacteriol* 1954; **68**: 603–16

17 Breslow N, Chan CW, Dhom G. Latent carcinoma of prostate at autopsy in seven areas. *Int J Cancer* 1977; **20**: 680–8

18 Guileyardo JM, Johnson WD, Welsh RA, Akazaki K, Correa P. Prevalence of latent prostate carcinoma in two US populations. *J Natl Cancer Inst* 1980; **65**: 311–6

19 Schröder FH. Detection of prostate cancer. *Br Med J* 1995; **310**: 140–1

20 McNeal JE, Kindrachur RA, Freha FS *et al.* Patterns of progression in prostate cancer. *Lancet* 1998; **i**: 60–3
21 Zincke H, Bergstralh EJ, Blute ML *et al.* Radical prostatectomy for clinically localised prostate cancer. Long term results of 1,143 patients from a single institution. *J Clin Oncol* 1994; **12**: 2254–63
22 Bagshaw MA, Cox RS, Hancock SL. Control of prostate cancer with radiotherapy: long term results. *J Urol* 1994; **152**: 1781–5
23 Chodak GW, Thisted RA, Gerber GS *et al.* Recent results of conservative management of clinically localised prostate cancer. *N Engl J Med* 1994; **330**: 242–8
24 Lu-Yao GL, Yao S-L. Population based study of long term survival in patients with clinically localised prostate cancer. *Lancet* 1997; **349**: 906–10
25 Potosky AL, Kessler L, Gridley G, Brown CC, Horm JW. Rise in prostatic cancer incidence associated with increased use of transurethral resection. *J Natl Cancer Inst* 1990; **82**: 1624–8
26 Rohr LR. Incidental adenocarcinoma in transurethral resections of the prostate. Partial versus complete microscopic examination. *Am J Surg Pathol* 1987; **11**: 53–8
27 Coleman MP, Estève J, Damiecki P, Arslan A, Renard H. *Trends in Cancer Incidence and Mortality.* IARC. Scientific Publications no. 121. Lyons: International Agency for Research on Cancer, 1993
28 Post PN, Damhuis RAM, van der Meyden APM and the EUROCARE Working Group. Variation in survival of patients with prostate cancer in Europe since 1978. *Eur J Cancer* 1998; **34**: 2226–31
29 Potosky AL, Miller BA, Albertsen PC, Kramer BS. The role of increasing detection in the rising incidence of prostate cancer. *J Am Med Assoc* 1995; **273**: 548–52
30 Berrino F, Capocaccia R, Estève J *et al. Survival of cancer patients in Europe – the EUROCARE Study II.* IARC. Scientific Publications no. 151. Lyons: International Agency for Research on Cancer, 1999
31 Micheli A, Mugno E, Krogh V *et al.* Cancer prevalence in European registries Areas. *Acta Oncol* 2002; in press
32 Whittemore AS. Prostate cancer. In Fraumeni JF Jr, Muir CS eds, *Trends in Cancer Incidence and Mortality.* Cancer Surveys, Vol. 19/20. Imperial Cancer Research Fund/Cold Spring Harbor Laboratory Press, 1994
33 Muir CS, Waterhouse J, Mack T, Powell J, Whelan S eds, *Cancer Incidence in Five Continents.* Vol. V. IARC Scientific Publications no. 88. Lyons: International Agency for Research on Cancer, 1987
34 Parkin DM, Muir CS, Whelan SL, Gao Y-T, Ferlay J, Powell J eds. *Cancer Incidence in Five Continents*. Vol. VI. IARC Scientific Publications no. 120. Lyons: International Agency for Research on Cancer, 1992
35 Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J eds, *Cancer Incidence in Five Continents.* Vol. VII. IARC Scientific Publications no. 143. Lyons: International Agency for Research on Cancer, 1997
36 Ferlay J, Parkin DM, Pisani P. GLOBOCAN 1: Cancer Incidence and Mortality Worldwide. [CD-ROM]. Lyons: IARC Press, 1998
37 Office for National Statistics. Booth H, Babb PJ, Quinn MJ eds. *Cancer Statistics – Registrations, 1995–97, England.* Series MB1 no. 28. London: The Stationery Office, 2001
38 Office for National Statistics. Booth H, Cooper N, Quinn MJ eds. *Cancer Statistics – Registrations, 1998, England.* Series MB1. no. 29. London: The Stationery Office, 2002
39 Harris V, Sandridge AL, Black RJ, Brewster DH, Gould A. *Cancer Registration Statistics Scotland 1986–95.* Edinburgh: ISD Scotland, 1998
40 Ries LAG, Eisner MP, Kosary CL *et al.* SEER Cancer Statistics Review 1973–1998. Bethesda MD, USA: National Cancer Institute, 2001
41 OECD Health Data 2000 Version 17/05/2000. OECD, 2000
42 Majeed A, Babb PJ, Jones J, Quinn MJ. Trends in prostate cancer incidence, mortality and survival in England and Wales 1971–98. *BJU Int* 2000; **85**: 1–5
43 Office for National Statistics. *Mortality statistics: cause, England and Wales 1999.* Series DH2 No. 26. London: The Stationery Office, 2000
44 Office for National Statistics. *Deaths in 2000; excess winter mortality in 1999–2000 and 2000–1*. London: Office for National Statistics, October 2001
45 Rooney C, Devis T. Mortality trends by cause of death in England and Wales 1980–94: the impact of introducing automated cause coding and related changes in 1993. *Population Trends* 1996; **86**: 29–35
46 Office of Population Census and Surveys. *Mortality statistics: cause, England and Wales 1984.* Series DH2 No. 11. London: HMSO, 1985
47 Murphy M, Johnston C, Whelan P, Rider L, Lloyd SN. Changing trends in prostatic cancer. *BJU Int* 1999; **83**: 786–91
48 Oliver SE, Gunnell D, Donovan JL. Comparison of trends in prostate cancer mortality in England and Wales and the USA. *Lancet* 2000; **355**: 1788–9
49 Post PN, Stockton D, Davies TW, Coebergh J-WW. Striking increase in incidence of prostate cancer men aged <60 years without improvement in prognosis. *Br J Cancer* 1999; **79**: 13–7
50 Brewster DH, Fraser LA, Harris V, Black RJ. Rising incidence of prostate cancer in Scotland: increased risk or increased detection? *BJU Int* 2000; **85**: 463–73
51 Brasso K, Friis S, Kruger Kjær S, Jørgensen-Iversen P. Prostate cancer in Denmark: a 50-year population-based study. *Urology* 1998; **51**: 590–4
52 Møller H. Trends in incidence of testicular cancer and prostate cancer In Denmark. *Human Reprod* 2001; **16**: 1007–11
53 Menegoz F, Colonna M, Exbrayat C *et al.* A recent increase in the incidence of prostatic carcinoma in a French population: role of ultrasonography and prostatic specific antigen. *Eur J Cancer* 1995; **31**: 55–8
54 Schuz J, Schon D, Batzler W *et al.* Cancer registration in Germany: current status, perspectives and trends in incidence 1973–93. *J Epidemiol Biostat* 2000; **5**: 99–107
55 Lamy S, Hein T, Wilmart JF *et al.* Prostatic cancer in the Grand Duchy of Luxembourg. Role of PSA. *Bull Soc Sci Med Grand Duche Luxemb* 1998; **135**: 11–23

56 Post PN, Kil PJM, Crommelin MA, Schapers RFM, Coebergh J-WW. Trends in incidence and mortality rates for prostate cancer before and after prostate-specific antigen introduction. A registry-based study in Southeastern Netherlands 1971–95. *Eur J Cancer* 1998; **34**: 705–9
57 Post PN, Straatman H, Kiemeney LA, Coebergh JW. Increased risk of fatal prostate cancer may explain the rise in mortality in Netherlands. *Int J Epidemiol* 1999; **28**: 403–8
58 Lopez-Abente G, Pollan M, Vergara A *et al.* Time trends in cancer incidence in Navarra and Zaragoza, Spain. *Gac Sanit* 2000; **14**: 100–9
59 Levi F, La Vecchia C, Randimbison L, Erler G, Te VC, Francheschi S. Incidence, mortality and survival from prostate cancer in Vaud Neuchatel, Switzerland, 1974–94. *Ann Oncol* 1998; **9**: 31–5
60 Brawley OW. Prostate carcinoma incidence and mortality. The effects of screening and early detection. *Cancer* 1997; **80**: 1857–63
61 Dennis LK, Resnick ML. Analysis of recent trends in prostate cancer incidence and mortality. *Prostate* 2000; **42**: 247–52
62 Etzioni R, Legler JM, Feuer EJ, Merrill RM, Cronin KA, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer – Part III. Quantifying the link between population prostate-specific antigen testing and recent declines in prostate cancer mortality. *J Natl Cancer Inst* 1999; **91**: 1033–9
63 Farkas A, Schneider D, Perrotti M, Cummings KB, Ward WS. National trends in the epidemiology of prostate cancer, 1973 to 94: evidence for the effectiveness of prostate-Specific antigen screening. *Urology* 1998; **52**: 444–8
64 Feuer EJ, Merrill RM, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer – Part II. Quantifying the link between population prostate-specific antigen testing and recent declines in prostate cancer mortality. *J Natl Cancer Inst* 1999; **91**: 1025–32
65 Hankey BF, Feuer EJ, Clegg LX *et al.* Cancer surveillance series: interpreting trends in prostate cancer – Part I. Quantifying the link between population prostate-specific antigen testing and recent declines in prostate cancer mortality. *J Natl Cancer Inst* 1999; **91**: 1017–24
66 Legler JM, Feuer EJ, Potosky AL, Merrill RM, Kramer BS. The role of prostate-specific antigen (PSA) testing patterns in the recent prostate cancer incidence decline in the United States. *Cancer Causes Control* 1998; **9**: 519–27
67 Merrill RM, Stephenson RA. Trends in mortality rates in patients with prostate cancer during the era of prostate specific antigen screening. *J Urol* 2000; **163**: 503–10
68 Mettlin C. Impact of screening on prostate cancer rates and trends. *Microscopy Res Technique* 2000; **51**: 415–8
69 Newcomer LM, Stanford JL, Blumenstein BA, Brawer MK. Temporal trends in rates of prostate cancer: declining incidence of advanced stage disease, 1974 to 1994. *J Urol* 1997; **158**: 1427–30
70 Perrotti M, Rabbani F, Farkas A, Ward WS, Cummings KB. Trends in poorly differentiated prostate cancer 1973–94: observations from the Surveillance, Epidemiology and End Results Database. *J Urol* 1998; **160**: 811–5
71 Tarone RE, Chu KC, Brawley OW. Implications of stage specific survival rates in assessing recent declines in prostate cancer mortality rates. *Epidemiology* 2000; **11**: 167–70
72 Levy IG, Gibbons L, Collins JP, Perkins DG, Mao Y. Prostate cancer trends in Canada: rising incidence or increased detection? *Can Med Assoc J* 1993; **149**: 617–24
73 Meyer F, Moore L, Bairati I, Fradet Y. Quebec prostate cancer mortality dropped in 1996. *Cancer Prev Control* 1998; **2**: 163–6
74 Meyer F, Moore L, Bairati I, Fradet Y. Downward trend in prostate cancer mortality in Quebec and Canada. *J Urol* 1999; **161**: 1189–91
75 Tovar-Gutzman V, Hernandez Giron C, Lopez-Rios O, Lazcano-Ponce EC. Prostate cancer mortality trends in Mexico. *Prostate* 1999; **39**: 23–7
76 Giles GG, Thursfield V eds. *Prostate Cancer. Canstat 30*. Carlton: Anti-Cancer Council of Victoria, Australia, 2000
77 Threlfall TJ, English DR, Rouse IL. Prostate cancer in Western Australia: trends in incidence and mortality from 1985 to 1996. *Med J Aust* 1998; **169**: 21–4
78 Smith DP, Armstrong BK. Prostate specific antigen testing in Australia and association with prostate cancer incidence in New South Wales. *Med J Aust* 1998; **169**: 17–20
79 Cohen RJ, Robinson E, McRae CU. Prostate cancer mortality in New Zealand: the past and projections for the future. *Aust N Z J Surg* 1997; **67**: 781–4
80 Nakata S, Takahashi H, Ohtake N, Takei T, Yamanaka H. Trends and characteristics in prostate cancer mortality in Japan. *Int J Urol* 2000; **7**: 254–7
81 Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. *Int J Cancer* 2000; **85**: 60–7
82 Boyle P, Baglietto L, Severi G, Gandini S, Robertson C. *Trends in Prostate Cancer World-Wide. Results of a Systematic Analysis.* Proceedings of the Conference of the American Urology Association, Anaheim, 2001
83 Levi F, Lucchini F, Negri E, La Vecchia C. The decline in cancer mortality in the European Union in 1988–96. *Eur J Cancer* 2000; **36**: 1965–8
84 Vercelli M, Quaglia A, Marani E, Parodi S. Prostate cancer incidence and mortality trends among elderly and adult Europeans. *Crit Rev Oncol Haematol* 2000; **35**: 133–44
85 Doll R, Fraumeni JF Jr, Muir CS eds. *Cancer Surveys*, Vol. 19/20: Trends in Cancer Incidence and Mortality. Imperial Cancer Research Fund/Cold Spring Harbor Laboratory Press, 1994
86 Sant M, Gatta G. The EUROCARE database. In Berrino F, Sant M, Verdecchia A, Capocaccia R, Hakulinen T, Estève J eds, *Survival of Cancer Patients in Europe – the EUROCARE Study*. IARC Scientific Publications no. 132. Lyons: International Agency for Research on Cancer, 1995:15–31
87 World Health Organisation. *International Classification of Diseases – Eighth Revision*. Geneva: WHO, 1967
88 World Health Organisation. *International Classification of Diseases – Ninth Revision*. Geneva: WHO, 1977

89 World Health Organisation. *International Statistical Classification of Diseases and Related Health Problems – Tenth Revision*. Geneva: WHO, 1992
90 Coleman MP, Aylin P eds. *Death Certification and Mortality Statistics: an International Perspective*. Studies on Medical and Population Statistics No. 64. London: The Stationery Office, 2000
91 Tabar L, Fagerberg CJ, Gad A *et al.* Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the breast cancer screening working group of the Swedish National Board of Health and Welfare. *Lancet* 1985; **i**: 829–32
92 Day NE. Screening for breast cancer. *Br Med Bull* 1991; **47**: 400–15
93 Coleman MP, Babb PJ, Stockton D, Forman D, Møller H. Trends in breast cancer incidence, survival and mortality in England and Wales. *Lancet* 2000; **356**: 590–1
94 Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet RG eds. *Cancer Registration: Principles and Methods*. IARC. Scientific Publications no. 95. Lyons: International Agency for Research on Cancer, 1991
95 Estève J, Benhamou E, Raymond L. Descriptive Epidemiology. Statistical methods. In *Cancer Research.* Vol. IV. IARC. Scientific Publications no. 128. Lyons: International Agency for Research on Cancer, 1994
96 dos Santos Silva I. *Cancer Epidemiology: Principles and Methods*. Lyons: International Agency for Research on Cancer, 1999
97 Carstairs V, Morris R. Deprivation and mortality: an alternative to social class? *Community Med* 1989; **11**: 210–9
98 Estève J, Benhamou E, Croasdale M, Raymond L. Relative survival and the estimate of net survival: elements for further discussion. *Statistics Med* 1990; **9**: 529–38
99 Coleman MP, Babb PJ, Damiecki P *et al. Cancer survival trends in England and Wales 1971–95: deprivation and NHS Region.* Studies on Medical and Population Subjects No. 61. London: The Stationery Office, 1999

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Appendix – Epidemiological terms

Ascertainment

Ascertainment is the proportion of the true incidence in a population which is recorded by a cancer registry. Cancer registries around the world (and even within countries such as the UK) differ considerably in their overall levels of ascertainment, but the best are known to have very high levels [4]. High proportions of registrations made solely from a 'death certificate only' (DCOs) or a low mortality to incidence ratio compared with a neighbouring registry, may indicate under-ascertainment. Ascertainment within a registry will vary by cancer site, usually being higher for cancers with poor survival, e.g. lung cancer, because most patients die from the cancer and this is recorded on the death certificate (and in many countries notified to the registry). Ascertainment will also generally have improved over time as procedures and computer systems have been enhanced, e.g. comparison of the trends in incidence and mortality for lung and stomach cancers in England and Wales clearly indicate some under-ascertainment for these (and so probably other) cancers in the early 1970s [4].

DCO registrations

In the UK and elsewhere, cancer registries are notified if an individual's death certificate mentions cancer. If the case is already registered, the record is updated with the information about the death. If it is not, the registry searches for further information. If after a set period, usually 6 months or a year, the search is unsuccessful, a registration is then made solely from the information on the death certificate. The true incidence date is unknown and has to be taken as the date of death. Tables giving the proportions of DCO registration by registry are given in [33–35]. A high DCO rate is an indicator of potentially poor-quality registration, because: (i) the registry's procedures are not detecting cases when they are still alive, and so there must be some degree of under-ascertainment because some patients, particularly those with cancers with good survival, e.g. breast cancer, may die from other causes (e.g. heart attack or road traffic accident); (ii) the true incidence date may have been some considerable time before death, and so the case may be recorded in the wrong incidence year; and (iii) the cases that are missed are more likely to be the longer survivors, who have more chance of dying from causes other than their cancer, and so the registry's survival rates may appear lower than they really are [86].

Deaths

The reported number of deaths from a particular disease in a population in a given period are those for which the disease was the underlying cause of death, determined from the information on the death certificate according to rules specified by the WHO [87–89]. The practice of death certification, and the WHO rules and their interpretation, have varied over time and among places [90] (see also [35–45] in Appendix H of 'Cancer Trends in England and Wales' [4]). [See mortality, below.]

Incidence

The incidence of a particular disease in a population is the number of new cases which develop in that population during a specific period. [see also ascertainment; rate].

Lead-time bias

A screening programme for cancer (other than for cervical cancer, where pre-cancerous lesions are detected) should detect cases earlier than they would have been diagnosed clinically as a result of reported symptoms. However, a screening programme will only be effective in reducing mortality if the earlier diagnosis and treatment actually extend the life of the patient beyond the point that they would have died had they not been screened. This can only be determined by large randomized controlled trials such as those on breast cancer screening [91,92]. Thus the apparent improvement in survival rates after introducing screening is made up of (i) the gain in 'lead-time' from earlier diagnosis, and (ii) the additional period (if any) of life gained.

Length bias

The efficacy of a screening programme also depends on the speed with which cancers develop from being detectable by screening to causing symptoms leading to clinical diagnosis. People with faster growing tumours are more likely to be diagnosed clinically between scheduled screens. So screening tends to detect proportionally more of the slower growing tumours which are less likely eventually to kill the patient. Thus patients with screen-detected cancers may appear to have better survival than those with clinically detected ones simply because the latter include a higher proportion of fast-growing tumours.

Mortality

Mortality, or death rates, which may be crude, age-specific, indirectly or directly age-standardized, are calculated in exactly the same way as incidence rates. [See also rate.]

Mortality to incidence ratio

The number of deaths from a cancer in a particular period (usually a calendar year) divided by the number of new cases in the same period. Where trends in both incidence and mortality are stable, the ratio approximates to (1 – the long-term survival rate). However, it is not clear what group or population the ratio applies to, because for cancers with good survival, those dying in a given year may have been diagnosed many years previously. Tables giving mortality to incidence ratios have been published (e.g. Appendix D of [4] and Table 9 in [37]) but they are principally an indicator of the quality of registration; there are variations in the ratios among regions of the UK, and over time, which would be difficult to explain unless there were similar variations in ascertainment.

Advantages and disadvantages of incidence and mortality data

The advantages of incidence data compared with mortality are that it has a higher quality of diagnostic coding; both the cancer site and the histology are known; there is a very low proportion of cases with site 'unspecified' (compared with $\approx$10% for mortality); and the incidence date is known (except for small proportion registered solely from a death certificate) whereas deaths in any one year result from cases diagnosed over a long previous period. The disadvantages of incidence data are that they may not be timely or sufficiently complete (see ascertainment), whereas mortality data are timely and virtually complete; in many countries, cancer registries have only recently been established and/or may not cover the whole country, whereas mortality is available for nearly all countries and over a very long period, although the data may be affected by ICD or other coding changes [45,46,87–89]. Cancer mortality trends are therefore an imperfect and 'fuzzy' indicator of trends in the efficacy of treatment; they reflect earlier trends in both incidence and survival, and cannot be interpreted sensibly without them. None of these indicators is perfect, and none is adequate alone [93].

Prevalence

The prevalence of a particular disease in a population at a given point in time (or index date) is the number or proportion of people who have been diagnosed with that disease in a specified period before the index date and who are still alive. Total prevalence is the number or proportion who have ever been so diagnosed. If a population has been covered by a cancer registry for a very long time, total prevalence can be calculated directly from the register. However, in most countries there will be patients alive who were diagnosed before the registry started, and to obtain the total prevalence, estimates of their numbers must be added to the observed prevalence [31].

Rate

The incidence of and mortality from cancer varies greatly with age. All other factors being equal, the numbers of cases or deaths from cancer in a population will therefore depend on (a) the size of the population, and (b) its age structure. To make unbiased comparisons of incidence and mortality in different areas or over time, several types of rates can be calculated which allow for differences in the various populations. Rates are usually expressed per 100 000 population: (i) the crude rate, which takes into account the size, but not the age structure of the population, is simply the total number of cases or deaths divided by the total population at risk:

$$N/P \times 100\,000$$

where there are k age groups, usually 0–4, 5–9, ..., 80–84, $\geqslant$85; n_k and p_k are the numbers of cases and the population, respectively, in age group k; and

$$N = \Sigma_k n_k \quad \text{and} \quad P = \Sigma_k p_k.$$

(ii) The age-specific (incidence) rate in age group k is

$$i_k = n_k/p_k \times 100\,000.$$

(iii) To allow for both different size and age distributions in the populations, two methods are used:

(a) indirect age standardization is often used for comparing rates in different areas within a country. One set of age- (and sex-) specific rates, often those for a country as a whole, is taken as the standard. These rates are then applied to the populations in the areas being compared, giving the number of cases (or deaths) which would have been expected had these populations experienced the cancer rates of the country as a whole. This 'expected' incidence is then compared with the actual number observed, and the ratio usually multiplied by 100 to give an index called the standardized incidence or registration ratio (SIR). For example, the SIR for stomach cancer in the Trent region of England is calculated as:

$$[(\text{number of registrations of cancer of the stomach in Trent})]/(\Sigma_k I_k \times p_k) \times 100$$

where I_k = incidence rate in age group k in England and p_k = population in age group k in Trent.

(b) with direct age-standardization, age- (and sex-) specific rates in each group to be compared are multiplied by the corresponding number of people in a standard population and then summed to give an overall rate per 100 000 population. The two most commonly used standard populations are the World and European (see Appendix F in [4]). The directly age-standardized incidence rate using the European standard population is given by:

$$I_{(ASR/E)} = (\Sigma_k i_k \times P_k)/\Sigma_k P_k$$

where i_k = incidence rate per 100 000 population in age group k; and P_k = European standard population in age group k.

An advantage of indirect standardization is that it is not necessary to know the number of cases in each age group in all the populations being compared, only the total. Disadvantages are that, strictly, it is not valid to compare ratios for several areas with each other; any area's ratio should only be compared against the standard of 100. It is possible, given large differences in the age structures of the regional and national populations, for most or even all of the age-specific rates in a region to be higher than in the standard (national) population, and yet the SRR to be <100. Further details, including the calculation of the precision and confidence intervals around the various rates, can be found in [94–96].

Socio-economic deprivation

The Carstairs index [97] (and other similar indices) are used to measure deprivation. The value of the Carstairs index for each census enumeration district (ED) is calculated using four variables from the 1991 census in Great Britain, i.e. the percentage of unemployed (economically active) males; the percentage of people in overcrowded households (density of >1 person per room); the percentage of residents in households with no car; and the percentage of residents in households with an economically active head of household in social classes IV or V. The values of each variable for each ED are 'normalised' (by subtracting the average value for Great Britain and dividing by the standard deviation of the distribution) and then summed. EDs with low values are termed 'affluent' and those with high values 'deprived'. EDs were categorized into fifths or 20ths based on the distribution of values for Great Britain. Values of the index were assigned to each individual case of or death from prostate cancer using a directory which links postcode to ED, and thus everyone living in a particular ED is assigned the same level of socio-economic deprivation.

Survival

Three types of survival rates are commonly calculated. Crude survival is simply the proportion of a group of patients diagnosed during a specified period who are still alive after the particular length of time being considered. For example, of the 46 000 patients with prostate cancer diagnosed in England during 1993–95, almost 27 600 had died within 5 years of their diagnosis, and thus $\approx$18 400 had survived at least 5 years. The crude 5-year survival rate for this group of patients was therefore 18 400/46 000, or 0.40, or 40%. This rate can be interpreted as the probability of survival from prostate cancer and all other causes of death combined.

In addition, cancer registries around the world adjust the crude survival rate by taking into account the 'background' mortality in the general population (of the same age and sex as the group of patients). This is called relative survival, i.e. relative to an equivalent group in the general population. Thus, for example, $\approx$15 200 of the original group of 46 000 patients with prostate cancer mentioned above would have been expected to die within 5 years. Therefore 30 800, or $\approx$67%, would have been expected to have survived. The relative survival rate is the crude survival rate divided by the general or population survival rate, i.e. 40/67 = 60%. The actual calculations are more complicated than this [98]; further details of the statistical methods used to produce the ONS cancer survival statistics can be found in Chapter 3 of [99].

Another method, sometimes used by academic researchers, distinguishes for each individual patient between those who died from their cancer and those who died from other causes. This is called net or cause-specific survival, and requires information about the cause of death to be linked to the cancer case record. Survival can then be calculated (e.g.) for only those men diagnosed with prostate cancer who also died from prostate cancer. The two main problems with this approach are the linking of the cause of death information, and the reliability and comparability of the cause of death information over time and between places [90]. Cause-specific survival rates are generally close to those obtained by the relative survival method.