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Secular trends in prostate cancer mortality, incidence and treatment: England and Wales, 1975-2004

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Abstract

Objective—Prostate cancer mortality fell in the UK in the early 1990s for unknown reasons. To aid interpretation of these trends, we investigated prostate cancer death rates, incidence and treatments in England and Wales between 1975-2004.

Methods—Join-point regression of secular trends in mortality and incidence (source: Office of National Statistics), radical prostatectomy and orchidectomy (source: Hospital Episode Statistics database) and androgen-suppression drugs (source: Intercontinental Medical Statistics).

Results—Prostate cancer mortality fell from 1992 (95% CI: 1990-1994). The relative mortality decline to 2004 was greater and more sustained amongst 55-74 year olds (annual percentage mortality reduction: 2.75%; 95% CI: 2.33-3.18 %) compared with those aged ≥ 75 years (0.71%; 0.26-1.15). Radical prostatectomies increased between 1991 (n=89) and 2004 (n=2788) amongst 55-74 year olds. Androgen- suppression prescribing increased between 1987 (33,000 prescriptions) and 2004 (470,000 prescriptions).

Conclusions—The fall in prostate cancer mortality was greater amongst 55-74 than ≥ 75 year olds but predates substantial use of PSA screening and radical prostatectomy operations in the UK. A rise in radical therapy amongst younger age groups with localised cancers and screen-detected low-volume locally advanced disease as a result of stage migration, as well as prolonged survival from increased medical androgen suppression therapy, may partly explain recent trends.

Keywords

prostate cancer; radical prostatectomy; anti-androgens; LHRH analogues; PSA screening; secular trends; mortality

Introduction

In Europe and North America prostate cancer is the second commonest cause of male cancer deaths¹. Prostate cancer incidence and mortality increased steadily in several countries during the 1980s², but while mortality rates continued to increase in most areas in the 1990s, sizeable declines were observed in seven countries (Canada, USA, Austria, France, Germany, Italy, UK) beginning in 1988-1991³. Some authors have attributed falling death rates to the introduction of screening based on prostate-specific antigen (PSA) testing, either through an empirical demonstration of inverse ecological associations between PSA screening intensity and prostate cancer mortality⁴ or by pointing out that screening has resulted in the earlier diagnosis⁵ and increased radical treatment⁶ of localised, well differentiated prostate cancer.

Whether screening explains these favourable mortality trends is controversial for several reasons⁷⁻⁹. Firstly, the effectiveness of PSA screening has not been demonstrated in well-conducted randomized controlled trials. Secondly, there is uncertainty over the effectiveness of treatments for screen-detected disease⁹, which may have limited impact at a population level¹⁰ because of considerable potential for overdiagnosis and overtreatment of clinically insignificant prostate cancer^{11,12}. Thirdly, the mean lead time (the time by which diagnosis is advanced by screening) for prostate cancer is over 10 years¹², whereas mean lead times of 3 years or less would be required to explain the reductions in mortality that were observed within 3-4 years of the introduction of widespread PSA screening in 1988 in the USA¹³. Finally, several comparisons of mortality patterns between regions, both within and outside the USA, where PSA screening intensity levels are markedly different, reveal no^{3,14-17} or a very weak¹⁸ relationship between prostate cancer death rates and the intensity of screening or increased levels of radical treatment. In Australia, mortality rates have continued to increase despite high uptake of screening³.

Trials of PSA testing are ongoing in the UK¹⁹, USA²⁰ and the European mainland²¹, but are not due to report their results for several years. In the absence of trial data, considerable interest remains in determining whether PSA testing has had an impact on mortality at a population level. As well as the issues of interpretation outlined above, previous ecological studies have been hampered by lack of data beyond the first few years following the introduction of PSA testing and because other factors, such as changes in treatment patterns, were often not considered. We examined age-specific trends in prostate cancer mortality between 1975 and 2004 in England and Wales in the context of age-specific trends in prostate cancer incidence, use of radical prostatectomy and hormone therapy.

Methods

DATA SOURCES

Age-specific prostate cancer incidence between 1975 and 2004 was obtained from the MB1 series published by the Office of Population Censuses and Surveys (OPCS) until 1996 and the Office of National Statistics (ONS) thereafter. These volumes cover cancer registrations for both England and Wales until 1994, and England only from 1995 onwards. The validity of these data has been established for comparisons of cancer risk over time²².

Age-specific prostate cancer mortality in England and Wales between 1975 and 2004 was obtained from the ONS Series DH2, Mortality statistics: Cause. The process of collecting and coding death registrations changed over the study period. These changes included: updates of International Classification of Diseases (ICD) codes from ICD-8 to ICD-9 in 1979 and from ICD-9 to ICD-10 in 2001^{23,24}, introduction of automated cause of death coding in 1993²⁵ and changes to the interpretation of WHO Rule 3 for selecting underlying

cause of death in 1984, 1993^{26,27} and 2001²⁶. Rule 3 allows a condition reported in either Part I or Part II of the death certificate to take precedence over a condition selected using other coding rules if the latter is obviously a direct consequence of that condition. Between 1984 and 1992, a revised interpretation of WHO Rule 3 was introduced by the OPCS. Consequently, deaths from causes such as pneumonia declined steeply in 1984, whereas deaths from causes often mentioned in part II of the certificate increased²⁷. This change resulted in an increase in the death rate from prostate cancer in 1984, which was most marked in the elderly. The change in 1993 was a move back to the internationally accepted interpretation of Rule 3 operating in England and Wales before 1984. Under ICD-10 adopted in January 2001, the interpretation of Rule 3 is similar to that adopted by the OPCS for deaths in 1984-1992. A bridge coding exercise demonstrated that for cancers coded by ICD-9 Rule 3 between 1993-2000, the application of ICD-10 Rule 3 would have selected prostate cancer more often as the underlying cause of death^{23,24}, the ratio of the number of deaths coded to prostate cancer using ICD-10 compared with applying ICD-9 rules being 1.008, 1.031 and 1.358 at ages <75 years, 75-84 and ≥ 85, respectively²³. The influence of these procedural changes on the mortality data is investigated by applying the multipliers 1.008 (for deaths <75 years) and 1.031 (for deaths ≥ 75 years) to the data between 1993-2000 to give an expected number of deaths that would have been coded to prostate cancer in ICD-10.

The Hospital Episode Statistics (HES) database for England holds information on the care provided to those admitted to NHS hospitals and for NHS hospital patients treated elsewhere. This includes details of surgical procedures carried out, coded using OPCS-4 codes. HES records were extracted from the database held by the Department of Social Medicine, Bristol using the OPCS procedure codes M 61.1 (radical prostatectomy) and N051, N052, N061, N063 (orchidectomy) when the underlying diagnosis was prostate cancer (ICD 9 185 and ICD10 C61). This information was available from 1991 to 2004.

Data on overall prescribing in England and Wales (1975 to 2004) of hormonal therapy for prostate cancer (that is, oestrogens, luteinizing hormone-releasing hormone (LHRH) analogues and antiandrogens) were obtained from IMS Health (Intercontinental Medical Statistics) Medical Data Index²⁸. Age-specific prescribing data were not available. Since 1967, IMS Health has collected quarterly data on drug prescribing in the UK. A prescription is defined as every drug item on a prescription form given as a result of a consultation. Since 1994, anonymised prescribing data have been collected electronically every day from a stratified sample of 500 general practitioners, giving a total of 26,000 doctor weeks per year. Sample data are projected to the whole of the UK, weighted by a regional factor, and the figures adjusted to reflect the total number of prescriptions dispensed in the UK as indicated by data published by the UK Prescription Pricing Authority.

Statistical methods

Age-specific rates for prostate cancer incidence and mortality and radical prostatectomy were estimated for the age groups < 55, 55-74 and ≥ 75 years using the year by year information on mid-year resident population of England and/or Wales, as appropriate, from 1975 to 2004 as provided by the Population Estimates Unit of the ONS. The mid-year population of men resident in England only was used for calculating age-specific incidence rates from 1995-2004 and age specific rates for orchidectomy and radical prostatectomy from 1991-2004. The population of men aged 55 and over in England in 2004 was 6.26 million compared to 0.40 million in Wales, so if trends differ in the two countries this would only have a minor impact on our results. Unless otherwise noted, all rates are expressed per 100,000 population per year.

Analysis of prostate cancer incidence and mortality trends was conducted by join point regression, in which trend data are described by a number of contiguous linear segments and 'join points' (points at which trends change). Join point regression was used to estimate annual change in incidence and mortality rates and the number and location of join points²⁹. Models were based on linear regression with incidence and mortality rates as the dependent variables and year as the independent variable. To identify the best-fitting combination of line segments and join points, a series of permutation tests was performed, first testing the null hypothesis (H_0 = no join points) versus the alternative hypothesis (H_a = 3 join points). Hypothesis testing proceeded sequentially, increasing the number of join points under H_0 by 1 if the null hypothesis was rejected and decreasing the number of join points under the alternative hypothesis if H_0 was accepted. The maximum number of join points tested was 3 in each analysis. For each model, the locations (i.e. years and 95% confidence intervals) of the best-fitting join points were identified using a grid search algorithm³⁰. A Bonferroni correction was applied by conducting each test at the $\alpha/3$ level, ensuring that the probability of a type I error (i.e., concluding that there are 1 or more join points when there are in fact none) was at most 0.05. Analyses were conducted using Joinpoint software (version 3 April 2005) made available by the National Cancer Institute (srab.cancer.gov/joinpoint).

Results

Figure 1 summarizes secular trends in age-specific prostate cancer incidence. Overall the annual number of new cases of prostate cancer increased from 7,168 in 1975 (England and Wales) to 29,406 in 2004 (England). Incidence rates amongst < 55 year olds were low but did increase 6-fold between 1975 (3.07 per 100,000) and 2004 (18.30 per 100,000).

Amongst 55-74 year olds, prostate cancer incidence increased four-fold between 1975 and 2004. The rise in prostate cancer incidence began in 1985 (95% CI for year of change: 1982 to 1989) (p for slope change < 0.0001). The estimated mean increase in incidence between 1985 and 1998 was 10.35 additional new cases per 100,000 per year (95% CI: 8.76 to 11.94; p < 0.0001 for test of null hypothesis that annual change = 0). From 1998 (95% CI: 1995 to 2000) until 2004, there was an acceleration in prostate cancer incidence amongst this age group (p for slope change = 0.0001), the incidence increasing to a mean of 21.83 additional new cases per 100,000 per year (95% CI: 17.28 to 26.38; p < 0.0001). Table 1 summarises the annual change and join points for trends in age-specific incidence (as well as mortality rates).

Amongst 75 year olds, prostate cancer incidence rose slowly between 1975 and 1986, a mean annual increase of 5.46 per 100,000 (95% CI: 1.42 to 9.50). The rise in incidence increased steadily after 1986 (95% CI: 1983 to 1988) (p for slope change < 0.0001), peaking in 1994 (95% CI: 1992 to 1995). From 1994, new registrations of prostate cancer amongst 75 year olds plateaued (p for slope change < 0.0001) with little evidence of any annual change in incidence up to 2004 (p = 0.3).

Figure 2 summarizes age-specific prostate cancer mortality rates. The numbers of deaths due to prostate cancer in England and Wales doubled from 4,421 in 1975 to 9,169 in 2004. Death rates amongst < 55 year olds were low in 1975 (0.31 per 100,000) and 2004 (0.45 per 100,000). Death rates amongst 55-74 year olds started to increase in 1979 (95% CI: 1977 to 1983) from 46.33 per 100,000 to a peak of 67.33 per 100,000 in 1992 (95% CI: 1990 to 1993). The estimated mean increase in mortality between 1979 and 1992 was 1.72 additional deaths per 100,000 per year (95% CI: 1.50 to 1.94; p < 0.0001). There was strong evidence that mortality amongst 55-74 year olds started to decline steadily after 1992 (p for slope change < 0.0001): the estimated mean decrease in deaths between 1992 and 2004 was 1.61 per 100,000 per year (95% CI: 1.39 to 1.83; p < 0.0001), from 67.33 to 49.64 deaths per

100,000. In relative terms, the annual percentage reduction in mortality was 2.75% (95% CI: 2.33 to 3.18 %) in this age group between 1992 and 2004 (an overall 26% fall in mortality rates). The observed and fitted values for the 55-74 year old mortality trend are shown in more detail in Figure 3, with a shorter y-axis scale from 0-80 per 100,000.

Amongst 75 year olds, death rates started to increase in 1981 (95% CI: 1979 to 1984), from 296.23 per 100,000 to a peak of 456.97 per 100,000 in 1992 (95% CI: 1990 to 1994) (Figure 2). The estimated mean increase in mortality between 1981 and 1992 was 14.84 additional deaths per 100,000 per year (95% CI: 12.41 to 17.27; $p < 0.0001$). There was strong evidence that mortality amongst 75 year olds started to decline after 1992 (p for slope change < 0.0001): the estimated mean slope between 1992 and 2004 indicating 3.81 fewer deaths per 100,000 per year (95% CI: 1.97 to 5.65; $p < 0.0001$). In relative terms, the annual percentage reduction in mortality was 0.71% (95% CI: 0.26 to 1.15%) in this age group between 1992 and 2004 (an overall 7% fall in mortality). There was little effect of adjusting for the return between 1993 and 2000 to the internationally accepted interpretation of Rule 3 operating in England and Wales before 1984 (which particularly affected 75 year olds): using adjusted estimates suggested that the decline in mortality started after 1993 (95% CI: 1991 to 1994) and may have been slightly greater than estimated using the original data (-5.42 deaths per 100,000 per year; 95% CI: -3.60 to -7.24). There was borderline statistical evidence that the data fit a 3 join point model ($p = 0.05$). In this model, death rates increased in 1981 (95% CI: 1979 to 1983) and declined in 1993 (95% CI: 1991 to 1995), in line with the 2 join point model, but there was a suggestion visually and in the 3 join point model that mortality rates may have plateaued in 1999 (95% CI: 1996 to 2002).

Figure 4 shows the annual age-specific radical prostatectomy and orchidectomy rates per 100,000 men in England, 1991-2004. The number of radical prostatectomies performed in patients with prostate cancer increased nineteen-fold from 164 in 1991 to 3070 in 2004. The rise in radical prostatectomy was mainly amongst 55-74 year old men (a 31-fold increase from 89 in 1991 to 2788 in 2004). In this age group, there appeared to be an acceleration in the annual increase in operation rates after 1997 (95% CI: 1995 to 1999) (p for slope change < 0.0001). Amongst 55-74 year olds, orchidectomy rates for prostate cancer fell each year from 28.07 per 100,000 in 1991 to 2.45 per 100,000 in 2004; the corresponding fall amongst 75 year olds was from 106.58 to 15.17.

Figure 5 shows the rates per 100,000 men of prescriptions for LHRH analogues, anti-androgens and oestrogens for the treatment of prostate cancer in the UK between 1975-2004. The number of prescriptions for LHRH analogues steadily increased from 1987 (95% CI: 1985 to 1989) to 2004, from 4000 (14.5 per 100,000) to 319,000 (1089.8 per 100,000) per annum over this time (an estimated annual increase of 17,810 prescriptions; 95% CI: 16,338 to 19,282). Prescriptions for anti-androgens also increased from 0 in 1982 to 151,000 (515.9 per 100,000) in 2004 (an estimated annual increase of 7,508 prescriptions; 95% CI: 6,950 to 8,066). Prescriptions of oestrogens for the treatment of prostate cancer fell from 139,000 (508.0 per 100,000) in 1975 to a nadir of 14,000 (49.5 per 100,000) in 1996, thereafter rising steadily to 34,000 (116.2 per 100,000) in 2004.

Discussion

We found strong evidence that prostate cancer death rates in England and Wales began to increase steadily in the late 1970s / early 1980s, plateaued around 1992 and then started to decline. This decline was steady amongst 55-74 year old men until the end of data collection in 2004, falling by 26%. In the older men, aged 75 years or greater, prostate cancer mortality declined by 7% between 1992 and 2004, although there was some evidence that death rates

plateaued in 1999. Changes to the interpretation of WHO coding Rule 3 in 1993-2000 did not explain the mortality declines, as has been suggested by others.

In order to distinguish possible explanations for these mortality trends we have placed them in the context of concomitant changes in disease incidence and advances in treatments for prostate cancer. In interpreting the findings, it is important to recognize the main limitations of the study, which are the lack of data on secular changes in radiotherapy management of prostate cancer and systematically obtained data on PSA testing rates. There are no long-term national sources of these data, although we are aware that steps are being taken to rectify this. We also lacked data on age-specific prescribing of medical anti-androgen therapy, although we did have indication-specific data.

SCREENING AND RADICAL THERAPY

Annual PSA testing rates in NHS general practice in England and Wales, amongst men who were initially free from prostate cancer, increased from 1.4% overall in 1994³¹ to 4.2% (55-69 year olds) and 5.3% (≥ 70 years) in 1999³² and to 8.8% (55-74 year olds) and 14.0% (≥ 75 years) in 2002³³. Our data suggest that the secular increase in prostate cancer incidence accelerated from 1998 amongst 55-74 year olds, possibly reflecting an upsurge in PSA testing. The mortality reduction, which commenced around 1992 in both 55-74 and 75 year olds, predates even the modest use of PSA testing in the UK in the late 1990s³³, and the wider use of radical prostatectomy in clinically localised disease observed since 1991³⁴. Prostate cancer death rates in the first decade following the diagnosis of localised disease are relatively low in both screen detected prostate cancer (because of the more than 10-year lead-time¹²) and clinically identified disease³⁵⁻³⁷. The above considerations suggest that factors other than increased detection and radical treatment of early-stage disease contributed to the start of the mortality decline starting in 1992. The commencement of this decline in approximately the same year in both 55-74 and ≥ 75 year olds, suggests a period effect operating at that time (for example, some aspect of prostate cancer management, if real, or cause of death assignment, if artefactual) rather than a cohort effect (which tends to implicate an environmental cause).

The cause(s) of the start of the prostate cancer mortality decline in the early 1990s in many countries has been very difficult to determine because of inconsistent international mortality patterns reported soon after the introduction of PSA testing^{3,14-16,18,38}. With longer term monitoring of trends, however, our age-specific data may provide some clues. Of particular interest is the finding that between 1992-2004 relative reductions in death rates were greater and sustained in those aged 55-74 years compared with those aged ≥ 75 years. Although probably not a factor in the commencement of the mortality decline, it is possible that the rapidly increasing use of radical prostatectomy that was observed in the younger age group (Figure 4) may be having some mortality benefit on the long-term trends at a population level. Between 1992 and 2004, prostate cancer deaths in those aged 55-74 years fell by a total of 529, from 3071 to 2542 (approximately 44 fewer deaths per annum) while radical prostatectomy rose from 89 in 1991 to 2788 in 2004 (approximately 208 extra operations per annum). These extra operations may be having an observable impact on mortality trends to 2004 on the 50% of men with lead times < 10 years¹². The observed trends would be consistent with an improved prognosis amongst younger men with clinically significant aggressive prostate cancer, and relatively short lead times¹³, who are being diagnosed by PSA testing and undergoing radical treatment before the disease has metastasized – the very population that may be deriving real benefit from screening and early intervention. Such a scenario would be expected to impact on mortality more in the younger than older age group, amongst whom radical prostatectomy rates were low and stable, but an age-related divergence in mortality rates should only be observed around 5-10 years after the introduction of PSA testing and increased use of radical therapy³⁵, which is what we

observed. This hypothesis of an improved prognosis through earlier detection of prostate cancer is consistent with declines in the mortality rate of disease diagnosed at an advanced stage in the PSA era in the USA³⁸. However, it is likely that such benefits are restricted to a relatively small proportion of screen-detected men, the majority of whom have indolent disease and may be receiving unnecessary treatment³⁹.

HORMONES

Androgen suppression using oestrogens and surgical castration by bilateral orchidectomy was used for palliation in advanced prostate cancer, declining markedly in favour of LHRH analogues during the time-period of this study, perhaps because of concerns about adverse effects in the case of oestrogens, and acceptability of orchidectomy. Starting in the mid-1980s, there were rapid rises in prescribing of alternative forms of hormonal therapy, i.e. LHRH analogues and anti-androgens, in the UK. In the USA rapid increases in use of these androgen deprivation therapies commenced in the late 1980s⁴⁰⁻⁴². We are unable to determine whether earlier or more aggressive use of androgen deprivation therapies (such as occurred in the USA⁴⁰⁻⁴²) explain their rise in the UK, but such changes in management would be in line with increased interest in their use in early disease⁴³⁻⁴⁵. Even though hormonal therapy is not curative, trial data suggest that increased uptake earlier in the course of the disease^{46,47} or as maximum androgen blockade in advanced disease^{43,48-50}, could have contributed to the recent mortality declines by delaying death from prostate cancer long enough for the man to die from other causes^{40,51}. Such a possibility is supported by an ecologic relationship between the intensity of early hormone ablation therapy and declines in mortality¹⁸. This hypothesis would be consistent with mortality declines starting before any plausible effects of increased use of radical treatment for localised disease could be observed. The combined effect of stage migration through screening and the detection of asymptomatic early extracapsular cancers treated aggressively with radiotherapy and androgen suppression may explain the early mortality effect reported in a study from Austria, where approximately 5 years after the introduction of mass screening, lower mortality from prostate cancer was observed in the Tyrol region⁴. Radiotherapy alone with dose escalation may also have played a role in delaying death from prostate cancer⁵², but we do not have any data on this issue.

ARTEFACT

If it is accepted that the rise in disease incidence was largely an artifact of greater surveillance, because of increased use of transurethral resection of the prostate (TURP)⁵³ and PSA testing¹⁴ (see below), then the rise in mortality between 1979-1992 may also have been an artifact. It is unlikely that increased diagnosis adversely impacted on prostate cancer specific survival during this time by increasing iatrogenic deaths, as radical prostatectomy was limited before 1992 and the operative mortality is low⁵⁴, although concerns have been recently raised about fatal myocardial infarction associated with androgen suppression therapy⁵⁵. Perhaps a more plausible explanation is increased attribution of deaths, that would have previously been labeled as death from other causes, as being from prostate cancer, merely as a result of the cancer being detected^{38,56,57}. ICD-9 / 10 coding rules may select prostate cancer as the underlying cause of death despite clinical uncertainty, if a diagnosed prostate cancer is entered at some point on the death certificate⁵⁸. It is possible that the changes to the interpretation of WHO coding Rule 3 in 1984, which increased deaths from causes often mentioned in part II of the certificate²⁷, explains the sharp rise in prostate cancer mortality between 1983 to 1984, but not the continued rise in mortality trends until 1992. Incidence rates have not declined, but the recent mortality declines could have been artefactual, if the bias in cause of death attribution was reduced once physicians recognised the relatively good prognosis of localised prostate cancer and therefore may have been less likely to record prostate cancer on the death certificate³⁸. One report suggests

biased under-attribution of prostate cancer as the underlying cause of death amongst men who underwent radical treatment⁵⁹; this may partly explain the mortality decline amongst 55-74 year olds. In the 55-74 year age group, however, mortality has declined to below levels that were observed prior to the rise in incidence rates in 1985, indicating that reduced misattribution bias probably does not explain all the declining mortality. The continued rising incidence rate in this age group is more likely to be masking larger mortality declines.

PROSTATE CANCER INCIDENCE

We found that prostate cancer incidence increased steadily from the mid-1980s. A cohort analysis indicates that there may have been a real increase in risk in the Netherlands⁶⁰. In Japan, large increases in childhood height⁶¹, a marker for early childhood nutrition and levels of the dietary regulated, anti-apoptotic peptide insulin-like growth factor (IGF)-I⁶², have been followed by steady increases in the rate of prostate cancer⁶³. Since the majority of prostate cancers that can be potentially detected have an indolent natural history, however, a large proportion of the increasing incidence is likely to reflect improvements in the detection of cancers that formerly were undiagnosed^{53,64,65}. This hypothesis is supported by strong positive ecological correlations between utilization rates of techniques that increase diagnosis and incidence of prostate cancer^{53,64-66}, by the similarity in mortality patterns between areas with markedly divergent incidence rates^{3,15,16,64}, and by the suggestion that period effects explain declining mortality in many countries^{3,16}. During the 1980s, increased use of TURPs for benign prostatic hyperplasia (BPH) probably explains the increased incidence observed during the 5 years before the introduction of PSA testing in the UK in 1990^{53,64,67}.

CONCLUSION

Prostate cancer mortality has been falling steadily in England and Wales since 1992, following a period of rising artefactual incidence and mortality in the 1980s. The availability of PSA screening is unlikely to explain the initial decline in mortality, as the fall coincides with the period during which PSA testing and aggressive treatment in England was limited and is inconsistent with the long lead-time involved in prostate cancer progression. Radical prostatectomy, which was largely limited to 55-74 year olds, may have been a factor in the continued steady mortality decline in 55-74 year olds compared with those aged ≥ 75 years. Increasing use of medical androgen deprivation therapy may be responsible for at least part of the mortality decline, by improving survival long enough for competing causes of death to feature. Even if early detection and radical treatment of localised prostate cancer does explain some of the continued mortality decline in middle-aged men in England, the dilemma remains that current screening tests cannot differentiate between cancers that have low biological likelihood of progression from those with aggressive potential⁶⁸, in whom early radical treatment may be justified³⁹. There is thus potential for a population-based screening programme to result in substantial overdiagnosis (estimated at between 18%-84%) and overtreatment of clinically insignificant prostate cancer^{11 69}, and the prospect of substantial morbidity as a result of treatment⁷⁰. The relative effectiveness of the major forms of treatment for localised disease (radical prostatectomy, radical radiotherapy and active monitoring [regular PSA testing with radical intervention for tumours that progress]) remain the subject of a large ongoing trial⁷¹. The debate about the effectiveness of screening and subsequent treatment will continue until the results of ongoing trials are known⁹.

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Figure 1. Annual age-specific prostate cancer incidence rates per 100,000 men in England and Wales, 1975-2004

Source: MB1 series, Office of National Statistics (formerly Office of Population Censuses and Surveys)

Figure 2. Annual age-specific prostate cancer mortality rates per 100,000 men in England and Wales, 1975-2004

Shaded area = Revised interpretation of WHO Rule 3 was introduced by the OPCS. Source: DH2, Mortality statistics: Cause. Office of National Statistics (formerly Office of Population Censuses and Surveys)

Figure 3. Observed and fitted prostate cancer mortality rates amongst 55-74 year olds per 100,000 men in England and Wales, 1975-2004

Source: DH2, Mortality statistics: Cause. Office of National Statistics (formerly Office of Population Censuses and Surveys)

Figure 4. Annual age-specific radical prostatectomy and orchidectomy rates per 100,000 men in England, 1991-2004

Source: Hospital Episodes Statistics Database, England. Rates for < 55 years not shown because of very low numbers.

Figure 5. Rates per 100,000 men of prescribing for hormone treatment for prostate cancer UK, 1975-2004

Source: IMS Health (Intercontinental Medical Statistics) Medical Data Index

Table 1
Summary of annual change and join points for trends in age-specific incidence and mortality rates, England and Wales, 1975-2004

	Annual change (95% CI) for period 1 (1975 to join point 1)		Join point 1 (95% CI) [‡]	Annual change (95% CI) for period 2 (join point 1 to join point 2)		Join point 2 (95% CI) [‡]	Annual change (95% CI) for period 3 (join point 2 to 2004)	
	Absolute* (per 100,000)	Relative [†] (%)		Absolute* (per 100,000)	Relative [†] (%)		Absolute* (per 100,000)	Relative [†] (%)
Incidence								
55-74 years	0.38 (-1.72; 2.48)	0.52 (-0.93; 1.99)	1985 (1982, 1989)	10.35 (8.76; 11.94)	7.06 (6.59; 7.52)	1998 (1995, 2000)	21.83 (17.28; 26.38)	-
75 years +	5.46 (1.42 to 9.50)	1.10 (0.32; 1.89)	1986 (1983, 1988)	37.93 (29.93; 45.93)	6.19 (5.05; 7.35)	1994 (1992, 1995)	2.74 (-1.92; 7.40)	0.27 (-0.51; 1.04)
Mortality								
55-74 years	0.15 (-1.05; 1.35)	0.66 (-1.67; 3.05)	1979 (1977, 1983)	1.72 (1.50; 1.94)	3.08 (2.63; 3.54)	1992 (1990, 1993)	-1.61 (-1.83; -1.39)	-2.75 (-3.18; -2.33)
75 years +	0.02 (-5.25; 5.28)	0.10 (-1.34; 1.57)	1981 (1979, 1984)	14.84 (12.41; 17.27)	4.43 (3.61; 5.25)	1992 (1990, 1994)	-3.81 (-5.65; -1.97)	-0.71 (-1.15; -0.26)

* Annual rate change, based on the linear model option in Joinpoint.

[†] Annual percentage rate change, based on the log-linear model option in Joinpoint.

[‡] Based on the linear model option, but join points based on the log-linear model option were little different.