25 year trends in cancer incidence and mortality among adults aged 35-69 years in the UK, 1993-2018: retrospective secondary analysis

Jon Shelton,[1] Ewa Zotow,[2] Lesley Smith,[3] Shane A Johnson,[1] Catherine S Thomson,[4] Amar Ahmad,[1] Lars Murdock,[1] Diana Nagarwalla,[1] David Forman[5]

[1]Cancer Research UK, London, UK
[2]University College London, London, UK
[3]Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, UK
[4]Public Health Scotland, Edinburgh, UK
[5]Faculty of Medicine and Health, University of Leeds, Leeds, UK

Correspondence to: J Shelton
jon.shelton@cancer.org.uk
(ORCID 0000-0001-6290-8717)

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ABSTRACT

OBJECTIVE

To examine and interpret trends in UK cancer incidence and mortality for all cancers combined and for the most common cancer sites in adults aged 35-69 years.

DESIGN

Retrospective secondary data analysis.

DATA SOURCES

Cancer registration data, cancer mortality and national population data from the Office for National Statistics, Public Health Wales, Public Health Scotland, Northern Ireland Cancer Registry, NHS England, and the General Register Office for Northern Ireland.

SETTING

23 cancer sites were included in the analysis in the UK.

PARTICIPANTS

Men and women aged 35-69 years diagnosed with or who died from cancer between 1993 to 2018.

MAIN OUTCOME MEASURES

Change in cancer incidence and mortality age standardised rates over time.

RESULTS

The number of cancer cases in this age range rose by 57% for men (from 55 014 cases registered in 1993 to 86 297 in 2018) and by 48% for women (60 187 to 88 970) with age standardised rates showing average annual increases of 0.8% in both sexes. The increase in incidence was predominantly driven by increases in prostate (male) and breast (female) cancers. Without these two sites, all cancer trends in age standardised incidence rates were relatively stable. Trends for a small number of less common cancers showed concerning increases in incidence rates, for example, in melanoma skin, liver, oral, and kidney cancers. The number of cancer deaths decreased over the 25 year period, by 20% in men (from 32 878 to 26 322) and 17% in women (28 516 to 23 719); age standardised mortality rates reduced for all cancers combined by 37% in men (−2.0% per year) and 33% in women (−1.6% per year). The largest decreases in mortality were noted for stomach, mesothelioma, and bladder cancers in men and stomach and cervical cancers and non-Hodgkin lymphoma in women. Most incidence and mortality changes were statistically significant even when the size of change was relatively small.

CONCLUSIONS

Cancer mortality had a substantial reduction during the past 25 years in both men and women aged 35-69 years. This decline is likely a reflection of the successes in cancer prevention (eg, smoking prevention policies and cessation programmes), earlier detection (eg, screening programmes) and improved diagnostic tests, and more effective treatment. By contrast, increased prevalence of non-smoking risk factors are the likely cause of the observed increased incidence for a small number of specific cancers. This analysis also provides a benchmark for the following decade, which will include the impact of covid-19 on cancer incidence and outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

No recent studies have investigated cancer incidence and mortality rates over such a long time frame within the 35-69 year age group in the UK

Short term trends for specific cancer sites are related to known risk factors, screening programmes, and improved treatment

Trends in the 35-69 years age group can be indicative of future patterns of cancer in older people

WHAT THIS STUDY ADDS

Decreased rates of many cancers, including lung and laryngeal, is positive, and likely to be driven by the decrease in smoking prevalence across the UK

An increase in rates of other cancer sites, including uterine and kidney, was noted, which may be a result of the increasing prevalence of overweight/obesity and other risk factors

Organised population screening programmes have led to an increase in cancer incidence but also look to have contributed to a reduction in cancer mortality across the UK

Introduction

The availability of comprehensive cancer registration data across the UK since 1993 makes comparison of cancer incidence and mortality trends over 25 years possible. We examined UK trends in cancer incidence and mortality for men and women, aged 35-69 years, for all cancers combined and for the most common sites (or site groups) of cancer between 1993 and 2018.

This study focuses on the 35-69 years age group because cancer trend data are more reliable and easier to interpret in this age range.[1] Diagnostic accuracy is better in this age range than in older patients who have a greater proportion of clinical and uncertain diagnoses, as evidenced by the relatively low proportion of microscopically verified tumours,[2] especially in the earlier part of the period analysed. By the age of 35 years, the pattern of cancer broadly represents the usual adult profiles because specific cancers that are observed in childhood, adolescence, and young people would not impact on the overall pattern. Trends in the 35-69 years age group are also reflective of causal factors in the more recent and

medium term past rather than in the longer term and, therefore, will be more indicative of future patterns of cancer in the older populations.

This time period has also seen the introduction of three population screening programmes across the UK, which have affected trends by diagnosing some cancers at an earlier stage, preventing cancers, but also had the potential for diagnosing some cancers that would not have otherwise caused harm to the individual, particularly breast cancer.[3 4] Cervical smear tests have been used since the 1960s and the national screening programme was introduced in 1988, with over 85% coverage of the target population (women and people with a cervix aged 25-64 years) in the UK by 1994.[5] The breast screening programme was introduced in 1988 and covered all UK countries by the mid-1990s, with women aged 50-70 years being invited.[6] The bowel screening programme was introduced from 2006 and took a number of years to reach full roll-out. Currently, people aged 60-74 across England, Wales, and Northern Ireland, and 50-74 for Scotland are eligible. Prostate specific antigen testing is not part of the national screening programme. Anyone older than 50 years with a prostate can request a prostate specific antigen test from their family doctor (general practitioner).

The past 25 years have seen differing trends in cancer risk factors, with the two most important risk factors displaying trends in opposing directions. In one direction, smoking prevalence is reducing due to introductions of tax rises on tobacco products, further advertising bans, and smokefree policies, including education and encouraging quitting, and, in the other direction, the proportion of the population classified as overweight or obese is increasing, of which diet and exercise contribute to, as well as being independent risk factors for cancer.[7]

Methods

Cancer registration data are currently collected by four national registries in the UK. These organisations collect detailed information on newly diagnosed primary tumours, referred to as registrations. Prior to 2013, cancer registrations in England were collected by eight regional registries and compiled by the Office for National Statistics,[8] with these regional registries producing complete population coverage for England since 1971.[9] Cancer Research UK aggregate these data from the UK registries, with incidence, mortality, and corresponding national population data provided by the Office for National Statistics, Public Health Wales,[10] Public Health Scotland,[11] the Northern Ireland Cancer Registry,[12] NHS England,[13] and the General Register Office for Northern Ireland.[14] Coding of cancer registrations is consistent between countries of the UK, using internationally accepted codes from the International Classification of Diseases 10th revision (ICD-10) and collaboration through the UK and Ireland Association of Cancer Registries.[15]

Cancer sites (for single sites) or site groups (with multiple sites, such as oral) included in these analyses were selected as the most common causes of cancer incidence or death. These cancer sites are: all cancers combined (excluding non-melanoma skin cancer for incidence) (C00-C97, excluding C44); bladder (C67); bowel (C18-C20); brain and central nervous system (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, D44.3-D44.5); breast (women only) (C50); cervix (C53); Hodgkin lymphoma (C81); kidney (C64-C66, C68); larynx (C32); leukaemia (C91-C95); liver (C22); lung (C33-C34); melanoma skin(C43); mesothelioma (C45); myeloma (C90); non-Hodgkin lymphoma (C82-C86); oesophagus (C15); lip, oral cavity, and pharynx (oral) (C00-C06, C09-C10, C12-C14); ovary (C56-C57.4); pancreas (C25); prostate (C61); stomach (C16); testis (C62); and uterus (C54-C55). In addition, sex specific all cancer groups are also presented without breast and prostate cancers to inspect the overall trends in the absence of the most common cancer site for each sex. Sex is reported as recorded by the cancer registries at the time of registration. Mesothelioma was a new specific code introduced in ICD-10 and no reliable mortality data are available for this site before 2001, hence, we have not included this type of cancer prior to then. Non-malignant brain and central nervous system codes (ICD-10 D codes) are included despite their benign nature because they can cause mortality due to their location in the cranial cavity. The codes included for the brain and central nervous system have been chosen following clinical engagement and discussion with cancer registries across the UK. Non-melanoma skin cancer is excluded for incidence data because of the lack of completeness in the recording of these cancers and therefore unreliability of the data; this process is standard practice among UK cancer registries.[16] A proportion of non-melanoma skin cancer cases can be diagnosed and treated within primary care and have not consistently been captured within cancer registration data.[17]

To overcome yearly variation for sites with low numbers of cases, we calculated three-year rolling average age standardised rates per 100 000 population.[18] These rates were based on the European standard population 2013 for men and women separately for each cancer site or site group for both incidence and mortality, restricted to the 35-69 years age group.[19]

The estimated annual percentage change is commonly computed using a generalised linear regression model with Gaussian or Poisson link function.[18 20] In this analysis, a generalised linear model was performed with quasi-Poisson link function as overdispersion is very common when modelling rates and count data.[21] The outcome was the age standardised cancer (incidence or mortality) rate per 100 000 and the independent variable was the period variable, which was defined as the three year period for each data point, starting from 1993-95 and ending with 2016-18. Estimated annual percentage change was estimated as (exp (β^−1)' 100, where β^ is the estimated slope of the period variable,

Table 1 | Number of newly diagnosed cancer cases (% of total) in the UK for all cancers, excluding non-melanoma skin cancer, (ICD-10 C00-C97 excluding C44) by sex and age group in 1993 and 2018

	Men, no. (%)		Women, no. (%)	
Age group, years	1993	2018	1993	2018
0-34	3799 (3.0)	4416 (2.2)	4303 (3.4)	5950 (3.2)
35-69	55 014 (43.5)	86 297 (43.2)	60 187 (47.2)	88 970 (48.2)
≥70	67 775 (53.5)	109 135 (54.6)	62 916 (49.4)	89 764 (48.6)
Total	126 588	199 848	127 406	184 684

ICD-10=International Classification of Diseases (10th revision).

with corresponding 95% confidence interval, which is derived from the fitted quasi-Poisson regression model.[22] The determination of trends was based on the following criteria: firstly, an increasing trend was identified when the estimated annual percentage change value and its 95% confidence interval were greater than zero. This value suggests a statistically significant increase in the age standardised rate over time. Secondly, a decreasing trend was indicated when both the estimated annual percentage change value and its 95% confidence interval were less than zero, signifying a statistically significant decline in the age standardised rate over the period considered. Finally, in cases where these conditions were not met, the age standardised rate was concluded to have remained relatively stable. This designation means that no significant change in the age standardised rate over the period examined was noted. These criteria ensure a thorough and precise interpretation of the estimated annual percentage change values and their corresponding trends. These analyses were carried out for each sex and site or site group separately. Statistical analysis was performed using R version 4.0.2.[23]

Patient and public involvement

This work uses aggregated and non-identifiable routine data that have been provided by patients and collected by the health services of the UK as part of their care and support. Given the aggregated nature of the data, attempts to identify or involve any of the patients whose data are included is not possible nor permitted. Although patients and the public were not involved in the design and conduct of this research, the aim of this research is to provide an assessment of trends in cancer incidence and mortality and the impacts of treatment and policy changes to improve outcomes for cancer patients across the UK. Dissemination to the public will include a press release and a summary published online, written using layman's terms, and a webinar to discuss the results.

Results

Table 1 and table 2 show the percentage of all newly diagnosed cancer cases and deaths by age group in 1993 and 2018. For male registrations, around 43% of all registrations were in the 35-69 years age group in 1993 and 2018, while for female registrations, between 47% and 48% of all registrations were in this age group in 1993 and 2018, respectively. For mortality, around 40% of male cancer deaths occurred in the 35-69 years age group in 1993 and this value was lower at 30% in 2018. For female cancer deaths, a slightly smaller reduction was noted, from 38% in the 35-69 years age group in 1993 to 31% in 2018.

Figure 1 shows the number of newly diagnosed cancer cases and deaths in the 35-69 years age group between 1993 and 2018 by sex. Across the UK, of cancer registrations in 2018, 83% were from England, and 5.1% from Wales, 9.2% from Scotland, and 2.7% from Northern Ireland; for deaths in 2018, 81.4%, 5.3%, 10.4%, and 2.9% were from England, Wales, Scotland, and Northern Ireland, respectively. These proportions remained relatively stable over the study period. For men, the number of cancer registrations increased by 57% from 55 014 cases registered in 1993 to 86 297 cases registered in 2018, while for women, cases increased by 48% from 60 187 in 1993 to 88 970 in 2018. The rate of increase in the number of cases of cancer was more marked between 2003 and 2013 for both sexes than in other time periods in the study.

The number of cancer deaths in men and women aged 35-69 years decreased: by 20% in men from 32 878 in 1993 to 26 322 deaths in 2018 and by 17% in women from 28 516 in 1993 to 23 719 deaths in 2018. The main decrease in the number of deaths per year occurred before the year 2000 (fig 1) with a decrease of 14% in males and 11% in females between 1993 and 2000. Since 2000, the number of deaths each year in both men and women has remained fairly constant (fig 1).

Table 2 | Number of deaths (% of total) in the UK for all cancers, (ICD-10 C00-C97) by sex and age group in 1993 and 2018

	Men, no. (%)		Women, no. (%)	
Age group, years	1993	2018	1993	2018
0-34	976 (1.2)	615 (0.7)	928 (1.2)	666 (0.9)
35-69	32 878 (39.5)	26 322 (29.6)	28 516 (37.5)	23 719 (30.5)
≥70	49 339 (59.3)	62 026 (69.7)	46 673 (61.3)	53 397 (68.6)
Total	83 193	88 963	76 117	77 782

ICD-10=International Classification of Diseases (10th revision).

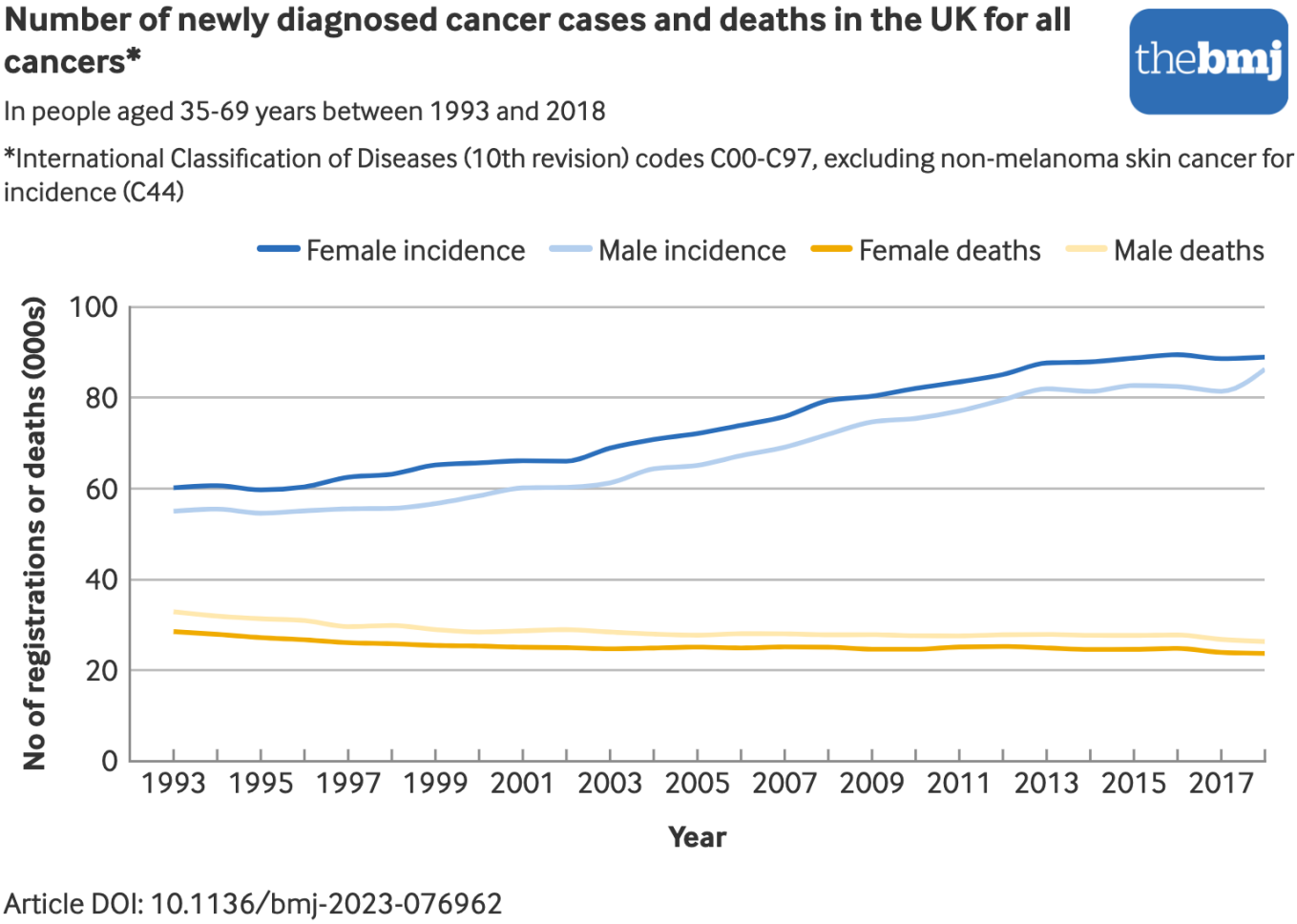

Fig 1 | Number of newly diagnosed cancer cases and deaths in the UK for all cancers, excluding non-melanoma skin cancer for incidence (International Classification of Diseases (10th revision) codes C00-C97 (excluding C44 for incidence)), men and women, 35-69 years, 1993 to 2018. An interactive version of this graphic is available at https://bit.ly/4acPDjP

Table 3, table 4, figure 2 and figure 3, and figure 4 and figure 5 show the trends over time in both incidence and mortality rates by sex and cancer site or site group. The tables only include specific age standardised incidence and mortality rates for the first (1993-95) and last (2016-18) period to give an indication of the change over the 25 year period. The trends in incidence and mortality age standardised rates for all years are shown in the figures. Figure 6 and figure 7 show the age adjusted average annual percentage change in the rates. Between 1993-95 and 2016-18, the age standardised incidence rate for all cancers (excluding non-melanoma skin cancer) increased slightly in men and women with age adjusted annual increases of 0.8% for both sexes. The trends in prostate and breast cancer, as the two largest cancer sites in men and women, respectively, substantially contribute to the overall all sites trends for cancer incidence. Figure 3 shows the trends for each sex without the largest cancer site. In contrast to the male age standardised incidence rate for all cancers, which showed a general increase, the incidence trend for men for all cancers excluding non-melanoma skin and prostate cancer, showed a decrease before 2000, but very little change in the following period. For women, an increase in age standardised incidence rates for all cancers excluding non-melanoma skin and breast cancer is still observed but the rate of increase is lower, at 0.7% per annum on average, over the 25 year period. Over the same period reductions in age standardised mortality for all cancers, including non-melanoma skin cancer, were −2.0% per year in men and −1.6% in women. Exclusion of prostate cancer from the mortality trends for men had a negligible effect on the average annual percentage change. For women, the exclusion of breast cancer from mortality trends led to a smaller decrease in mortality of −1.3% per annum.

Incidence rates varied over time across the different cancer sites and site groups. The largest average annual percentage increases over time for cancer incidence rates for men aged 35-69 years were for cancers of the liver (4.7%), prostate (4.2%), and melanoma skin cancer (4.2%). Increases of 1% or more per annum were also seen for oral cancer (3.4%), kidney

Table 3 | Age standardised* incidence and mortality rates in 1993-95 and 2016-18 and percentage change by cancer type, men aged 35-69 years, UK

	Incidence			Mortality		
Cancer type	1993-95	2016-18	Annual % change (95% CI)†‡	1993-1995	2016-2018	Annual % change (95% CI)†‡
All cancers: C00-C97 excluding C44§	512.3	588.2	0.79 (0.69 to 0.88)	300.0	190.3	−1.96 (−2.02 to −1.90)
All cancers excluding prostate: C00-C97 excluding C44 and C61	454.4	423.5	−0.13 (−0.27 to 0.00)	284.0	179.6	−1.97 (−2.03 to −1.91)
Bladder: C67	37.9	14.6	−4.1 (−4.41 to −3.78)	9.3	4.4	−3.24 (−3.44 to −3.04)
Bowel: C18-C20	71.0	70.7	0.01 (−0.19 to 0.21)	33.7	20.0	−2.47 (−2.60 to −2.33)
Brain and central nervous system: C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, D44.3-D44.5	19.0	22.0	0.75 (0.63 to 0.87)	12.0	10.8	−0.69 (−0.77 to −0.61)
Hodgkin lymphoma: C81	3.2	4.0	1.46 (1.25 to 1.66)	1.0	0.4	−2.56 (−2.88 to −2.25)
Kidney: C64-C66, C68	18.0	30.1	2.65 (2.37 to 2.93)	8.8	7.3	−0.77 (−0.85 to −0.69)
Larynx: C32	10.6	7.4	−1.49 (−1.65 to −1.32)	3.3	1.9	−2.5 (−2.71 to −2.28)
Leukaemia: C91-C95	14.2	16.5	1.04 (0.89 to 1.20)	7.2	4.8	−1.62 (−1.86 to −1.38)
Liver: C22	4.8	12.5	4.68 (4.41 to 4.95)	4.9	8.9	2.97 (2.70 to 3.24)
Lung: C33-C34	109.3	64.2	−2.09 (−2.29 to −1.90)	94.2	44.1	−3.07 (−3.21 to −2.92)
Melanoma skin: C43	12.6	29.0	4.15 (3.76 to 4.54)	3.9	3.7	0.33 (0.03 to 0.63)
Mesothelioma§: C45	6.3	3.6	−1.93 (−2.68 to −1.17)	6.2	3.0	−4.17 (−4.76 to −3.58)
Myeloma: C90	7.1	9.9	1.61 (1.52 to 1.70)	4.6	3.1	−1.72 (−1.90 to −1.55)
Non-Hodgkin lymphoma: C82-C86	21.0	25.1	1.03 (0.89 to 1.18)	9.7	5.5	−2.90 (−3.13 to −2.66)
Oesophagus: C15	18.0	20.4	0.77 (0.60 to 0.94)	17.3	15.6	−0.35 (−0.49 to −0.20)
Oral: C00-C06, C09-C10, C12-C14	14.4	28.6	3.37 (3.23 to 3.52)	5.8	7.4	1.12 (0.89 to 1.35)
Pancreas: C25	13.5	15.0	0.56 (0.47 to 0.66)	12.7	12.6	−0.05 (−0.12 to 0.01)
Prostate: C61	57.9	164.8	4.21 (3.51 to 4.92)	16.0	10.7	−1.76 (−1.88 to −1.64)
Stomach: C16	26.0	10.6	−4.18 (−4.33 to −4.02)	17.5	6.0	−5.13 (−5.45 to −4.82)
Testis: C62	6.2	8.6	1.27 (1.05 to 1.50)	0.4	0.2	−2.77 (−3.21 to −2.34)

CI=confidence interval.
*European standard population.[19]
†Age adjusted annual percent change in incidence/mortality rate.
‡All P values are P<0.05 except All cancers excluding C44 and C61 (incidence), bowel (incidence), and pancreas (mortality).
§Mesothelioma mortality data only available from 2001.

cancer (2.7%), myeloma (1.6%), Hodgkin lymphoma (1.5%), testicular cancer (1.3%), non-Hodgkin lymphoma (1.0%), and leukaemia (1.0%). The largest annual decreases over the two decades were seen for stomach (−4.2%), bladder (−4.1%), and lung cancers (−2.1%), with decreases of more than 1% per annum also observed for mesothelioma (−1.9% from 2001 onwards) and laryngeal cancer (−1.5%).

Table 4 | Age standardised* incidence and mortality rates in 1993-95 and 2016-18 and percentage change by cancer type, women aged 35-69 years, UK

	Incidence			Mortality		
Cancer type	1993-95	2016-18	Annual % change (95% CI)†‡	1993-95	2016-18	Annual % change (95% CI)†‡
All cancers (C00-C97 excluding C44)	520.6	601.7	0.78 (0.71 to 0.86)	242.2	163.1	−1.64 (−1.69 to −1.59)
All cancers excluding breast (C00-C97 excluding C44 and C50)	326.0	363.8	0.68 (0.56 to 0.81)	182.6	132.0	−1.32 (−1.37 to −1.28)
Bladder: C67	11.0	4.9	−3.59 (−4.01 to −3.18)	3.0	2.1	−1.64 (−1.88 to −1.40)
Bowel: C18-C20	47.4	47.4	0.16 (−0.03 to 0.34)	21.6	13.1	−2.24 (−2.51 to −1.96)
Brain and central nervous system: C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, D44.3-D44.5	16.0	23.0	1.80 (1.61 to 1.99)	8.2	6.8	−0.88 (−0.96 to −0.80)
Breast: C50	194.7	238.0	0.93 (0.77 to 1.08)	59.6	31.1	−2.78 (−2.84 to −2.71)
Cervix: C53	17.8	12.9	−1.31 (−1.75 to −0.87)	7.0	3.2	−3.58 (−3.93 to −3.23)
Hodgkin lymphoma: C81	1.7	2.2	1.59 (1.26 to 1.93)	0.5	0.2	−2.84 (−3.28 to −2.39)
Kidney: C64-C66,C68	8.2	14.7	2.87 (2.63 to 3.10)	4.0	3.1	−1.01 (−1.19 to −0.83)
Larynx: C32	2.1	1.7	−0.91 (−1.12 to −0.70)	0.7	0.5	−2.03 (−2.47 to −1.59)
Leukaemia: C91-C95	8.5	9.2	0.90 (0.72 to 1.09)	4.7	2.9	−2.13 (−2.31 to −1.94)
Liver: C22	2.1	4.8	3.87 (3.69 to 4.06)	2.4	4.3	2.74 (2.44 to 3.04)
Lung: C33-C34	52.7	57.7	0.80 (0.60 to 0.99)	44.4	35.2	−0.55 (−0.75 to −0.34)
Melanoma skin: C43	16.1	31.6	3.48 (3.19 to 3.76)	3.1	2.4	−0.69 (−0.98 to −0.40)
Mesothelioma§: C45	0.8	0.7	0.01 (−1.01 to 1.04)	1.0	0.6	−2.01 (−2.90 to −1.11)
Myeloma: C90	5.4	6.5	1.05 (0.91 to 1.20)	3.3	2.0	−2.29 (−2.42 to −2.16)
Non-Hodgkin lymphoma: C82-C86	14.9	18.0	1.04 (0.78 to 1.30)	6.4	3.2	−3.24 (−3.51 to −2.97)
Oesophagus: C15	7.0	6.3	−0.15 (−0.26 to −0.03)	5.9	4.4	−1.19 (−1.35 to −1.03)
Oral: C00-C06, C09-C10, C12-C14	5.4	11.1	3.29 (3.13 to 3.44)	1.9	2.4	1.24 (0.99 to 1.48)
Ovary: C56-C57.4	31.1	27.0	−0.87 (−1.02 to −0.72)	19.5	10.9	−2.81 (−2.99 to −2.63)
Pancreas: C25	9.7	11.0	0.93 (0.80 to 1.07)	9.2	8.9	0.18 (0.03 to 0.34)
Stomach: C16	9.3	4.9	−3.12 (−3.31 to −2.94)	6.6	2.7	−4.23 (−4.52 to −3.94)
Uterus: C54-C55	25.0	36.8	1.85 (1.61 to 2.10)	4.2	5.2	1.06 (0.97 to 1.15)

CI=confidence interval.
*2013 European standard population.[19]
†Age adjusted annual percent change in incidence/mortality rate.
‡All P values are P<0.05 except bowel (incidence) and mesothelioma (incidence).
§Mesothelioma mortality data only available from 2001.

Age standardised incidence and mortality rates in the UK for all cancers*

In people aged 35-69 years between 1993-95 and 2016-18. Each year shown represents the first year of a three year period, eg, 1993-95

*International Classification of Diseases (10th revision) codes C00-C97, excluding non-melanoma skin cancer for incidence (C44)

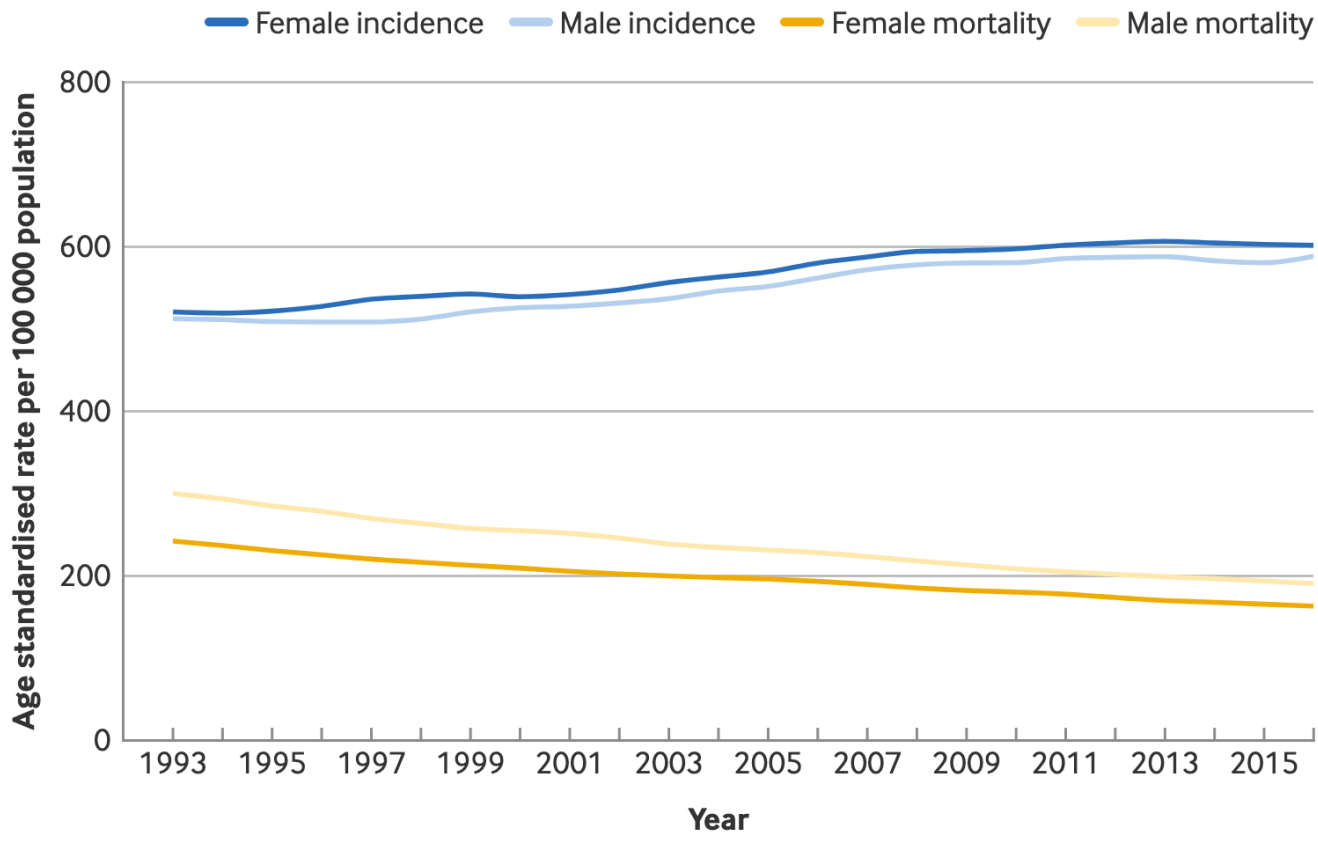

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Fig 2 | European 2013 population age standardised incidence and mortality rates in the UK for all cancers,[19] excluding non-melanoma skin cancer for incidence (International Classification of Diseases (10th revision) codes C00-C97 excluding C44 for incidence), men and women, 35-69 years, 1993-95 to 2016-18. An interactive version of this graphic is available at https://bit.ly/4a484aE

For women, the largest average annual percentage increases in incidence rates were noted for liver (3.9%), melanoma skin (3.5%), and oral (3.3%) cancers with increases in incidence of more than 1% per annum also observed for kidney (2.9%), uterus (1.9%), brain and central nervous system cancers (1.8%), Hodgkin lymphoma (1.6%), myeloma (1.1%), and non-Hodgkin lymphoma (1.0%). The largest annual decreases were reported for bladder (−3.6%) and stomach (−3.1%) cancers while the only other site showing a decrease of more than 1% per annum was cervical cancer (−1.3%). Although breast cancer represents the largest individual cancer site for women and therefore plays a large part in all cancer trends, the average annual increase was only 0.9%. All the incidence changes mentioned, for both men and women, and most incidence changes shown in table 3 and table 4 and in figure 6 and figure 7 were statistically significant ($P<0.05$) even when the size of change was relatively small.

Mortality rates mainly decreased over time in both sexes. For men, the cancer sites that showed average annual percentage reductions in mortality rates of more than 1% per annum were stomach (−5.1%), mesothelioma (−4.2% from 2001), bladder (−3.2%), lung (−3.1%), non-Hodgkin lymphoma (−2.9%), testis (−2.8%), Hodgkin lymphoma (−2.6%), bowel (−2.5%), larynx (−2.5%), prostate (−1.8%), myeloma (−1.7%),

Age standardised incidence and mortality rates in the UK for all cancers, excluding breast and prostate cancers

In people aged 35-69 years between 1993-95 and 2016-18. Each year shown represents the first year of a three year period, eg, 1993-95

*International Classification of Diseases (10th revision) codes C00-C97, excluding C44 (for incidence) and C50 and C61

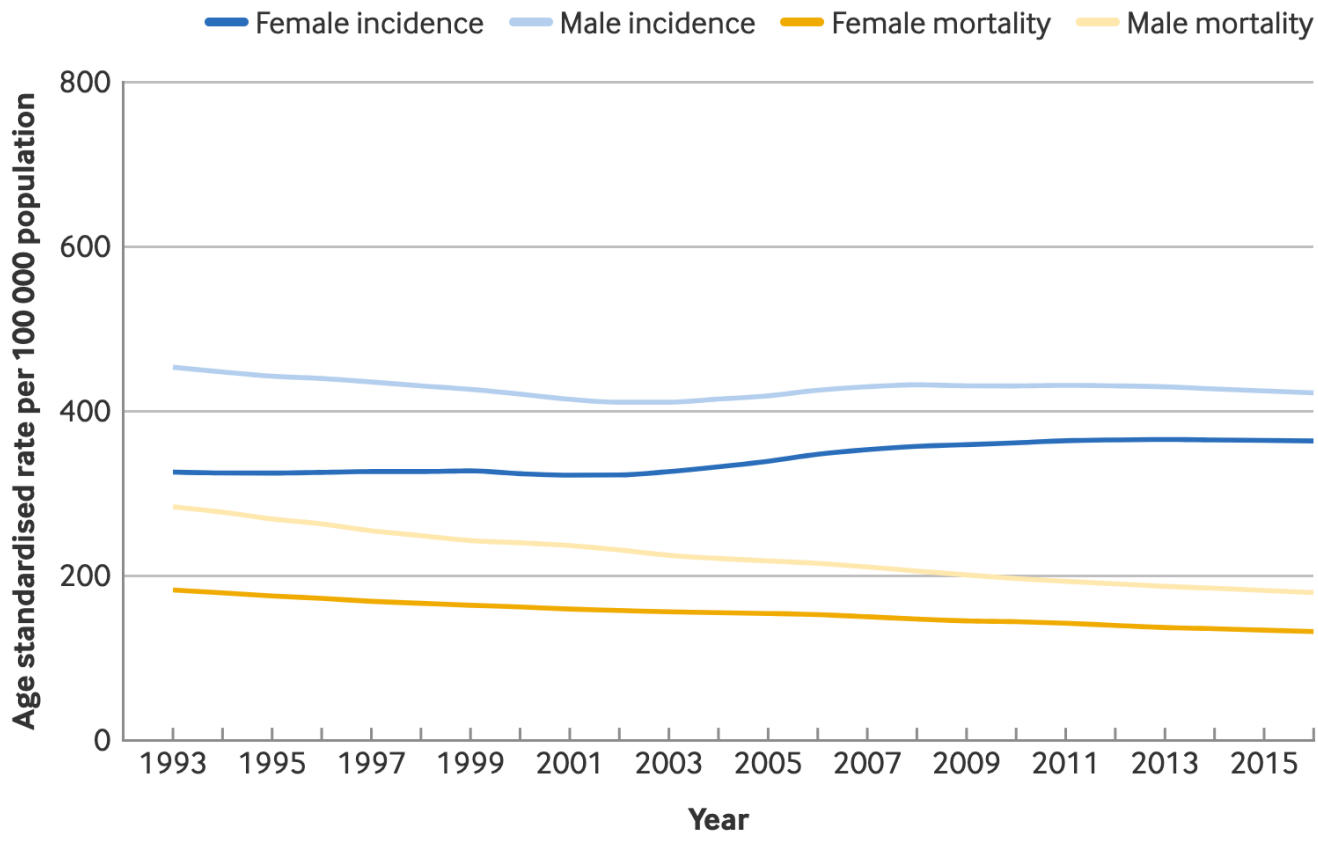

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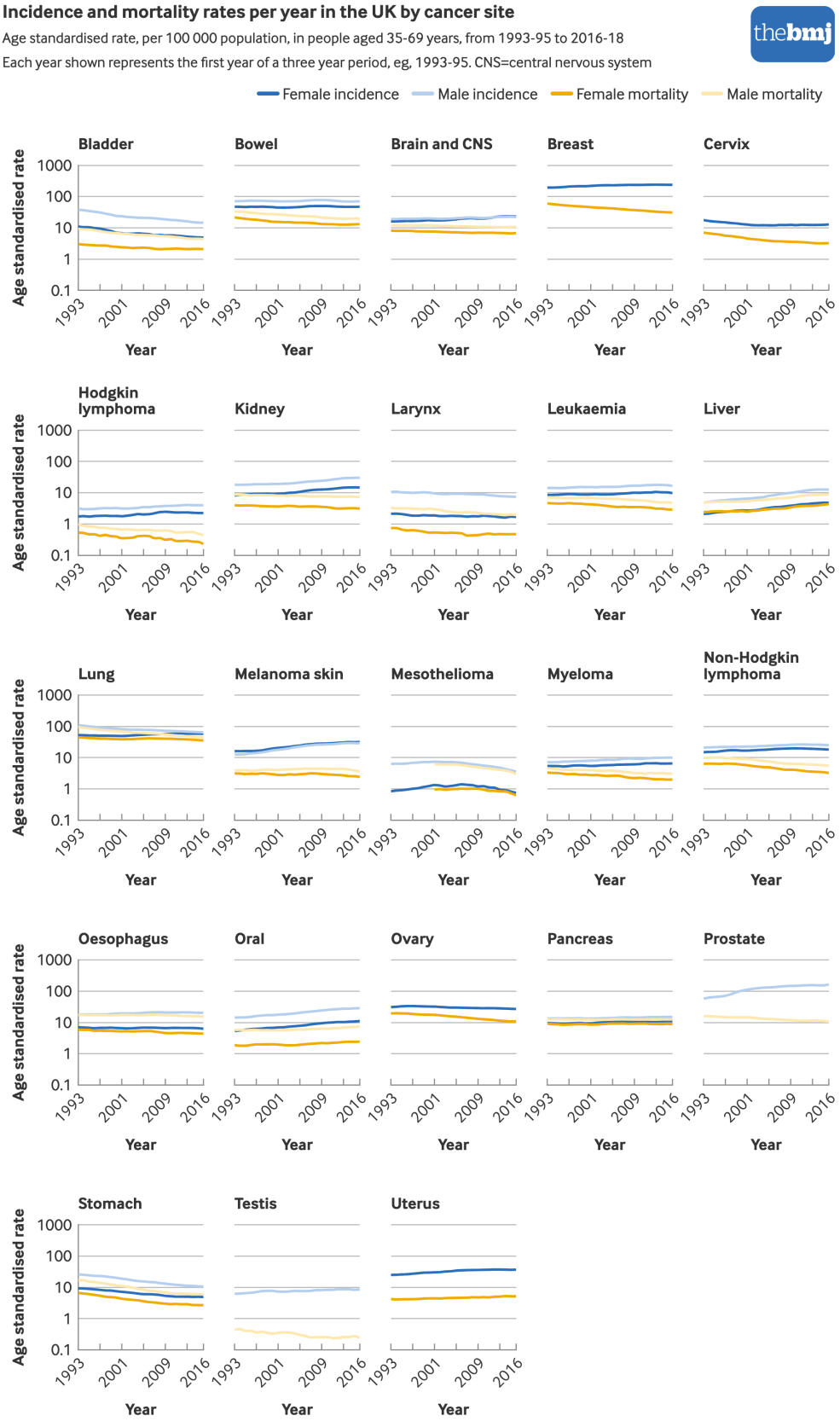
Fig 3 | European 2013 population age standardised incidence and mortality rates in the UK for all cancers in men and women aged 35-69 years during 1993-95 to 2016-18,[19] excluding non-melanoma skin cancer for incidence, and breast cancer in women and prostate cancer in men were excluded for incidence and mortality (International Classification of Diseases (10th revision) codes C00-C97 excluding C44 for incidence, C50, C61). An interactive version of this graphic is available at https://bit.ly/3vakQoX

and leukaemia (−1.6%). Only liver (3.0%) and oral (1.1%) cancers showed an average annual increase in mortality of 1% or more with melanoma skin cancer (0.3%) the only other site showing an increase. For women, the cancer sites with average annual decreases in mortality per year of 1% or more were stomach (−4.2%), cervix (−3.6%), non-Hodgkin lymphoma (−3.2%), breast (−2.8%), Hodgkin lymphoma (−2.8%), ovary (−2.8%), myeloma (−2.3%), bowel (−2.2%), leukaemia (−2.1%), larynx (−2.0%), mesothelioma (−2.0% since 2001), bladder (−1.6%), oesophagus (−1.2%), and kidney (1.0%). As with men, liver (2.7%) and oral (1.2%) cancers showed average annual increases of more than 1%, in addition to uterine cancer (1.1%). For both men and women, the mortality changes mentioned previously and most mortality changes shown in table 3 and table 4 and in figure 6 and figure 7 were statistically significant (P<0.05), even when the size of change was relatively small.

Discussion

Principal findings

The most striking finding in this analysis of UK cancer trends among the 35-69 years age group is the substantial decline in cancer mortality rates observed in both sexes (37% decline in men and 33% decline



Article DOI: 10.1136/bmj-2023-076962

Fig 4 | European 2013 age standardised incidence and mortality rates by year,[19] in the UK, for men and women aged 35-69 years from 1993-95 to 2016-18, by cancer site. An interactive version of this graphic is available at https://bit.ly/49a6ovn

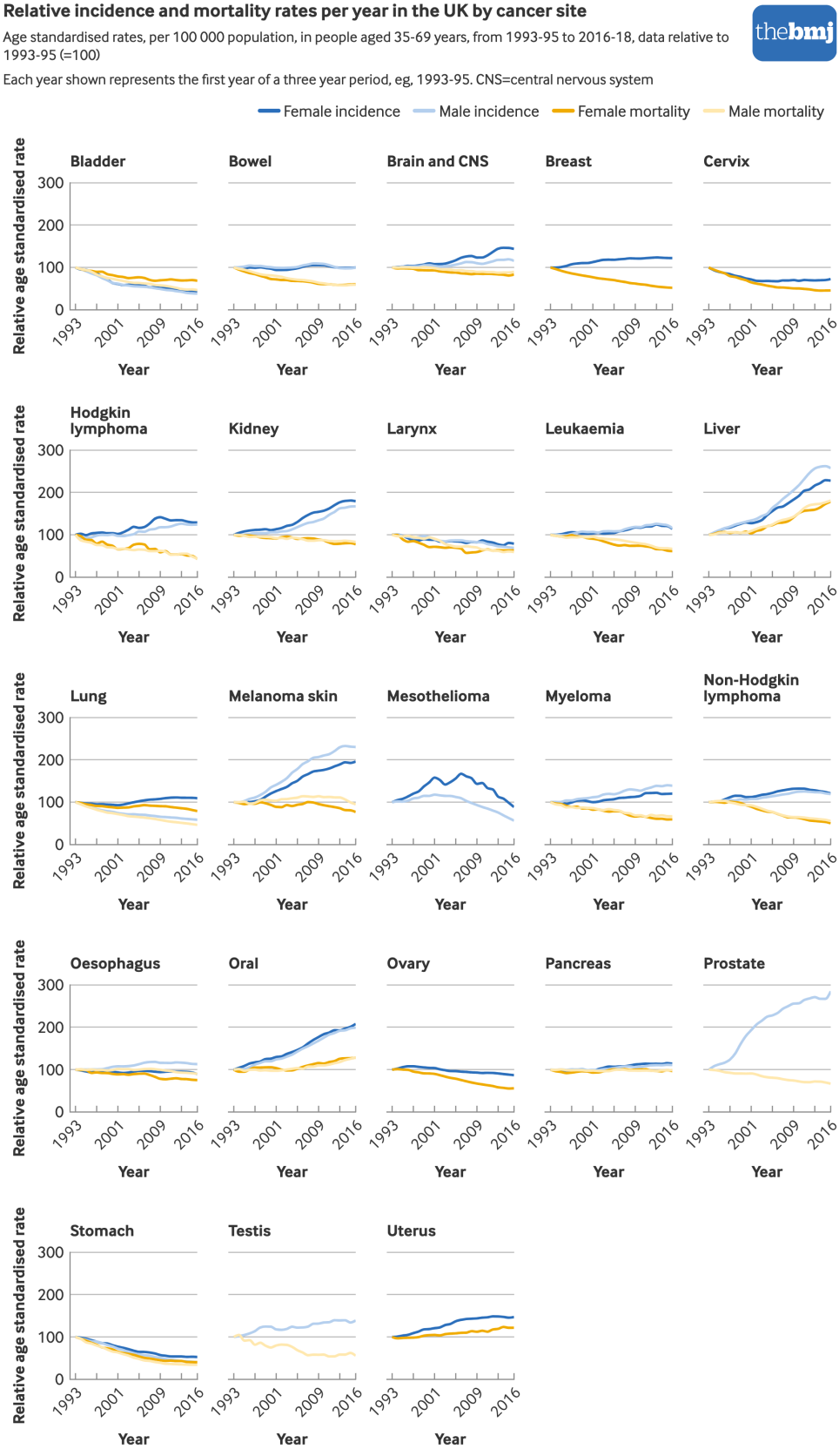


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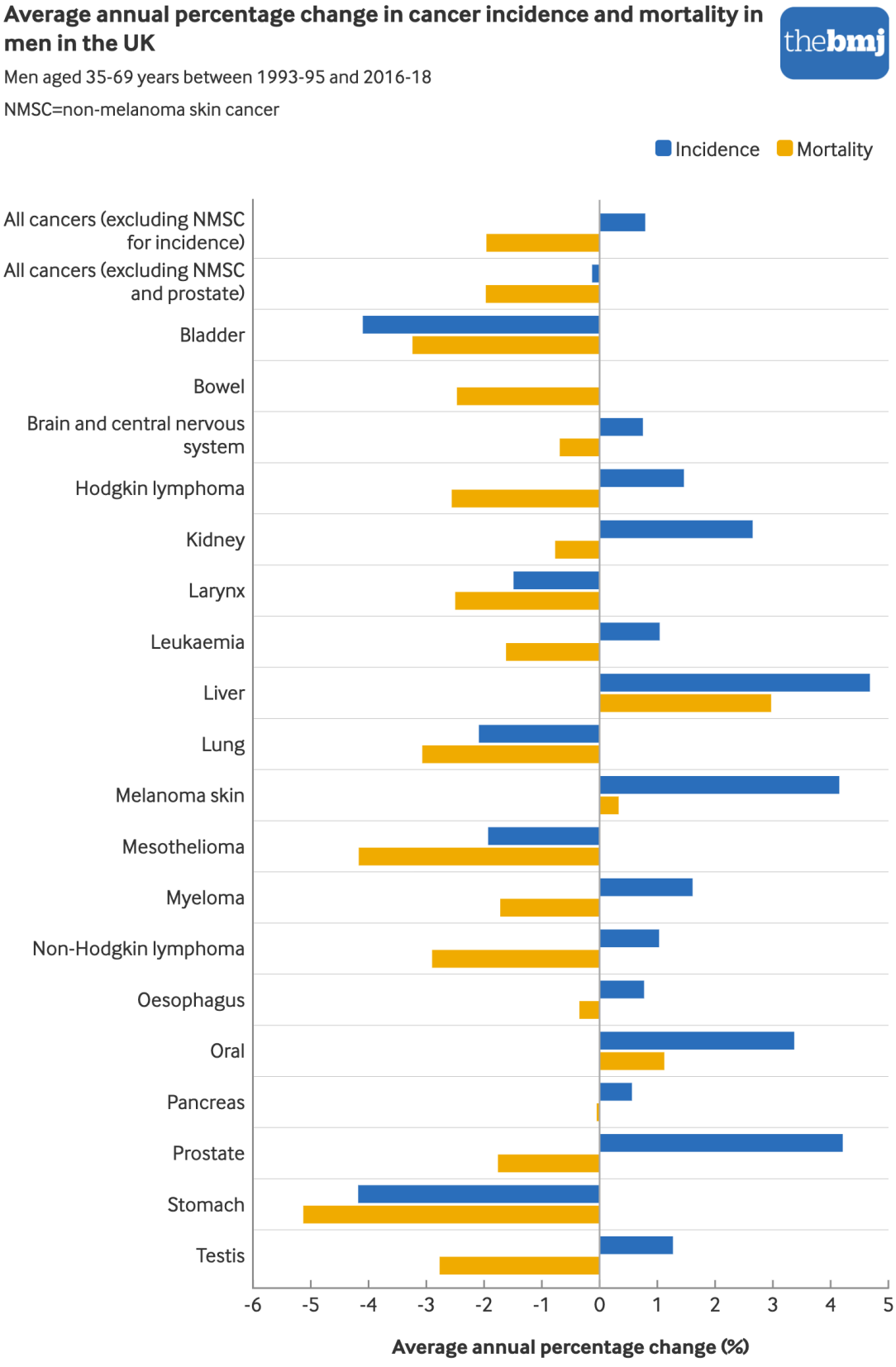
Fig 5 | Relative European 2013 age standardised incidence and mortality rates by year,[19] in the UK, for men and women aged 35-69 years from 1993-95 to 2016-18 (the reference year is 1993-95=100), by cancer site. CNS=central nervous system. An interactive version of this graphic is available at https://bit.ly/3PiKGOk



Article DOI: 10.1136/bmj-2023-076962

Fig 6 | Average annual percentage change in incidence and mortality rates, in the UK, for men aged 35-69 years from 1993-95 to 2016-18 by cancer site. An interactive version of this graphic is available at https://bit.ly/3wMR6yU

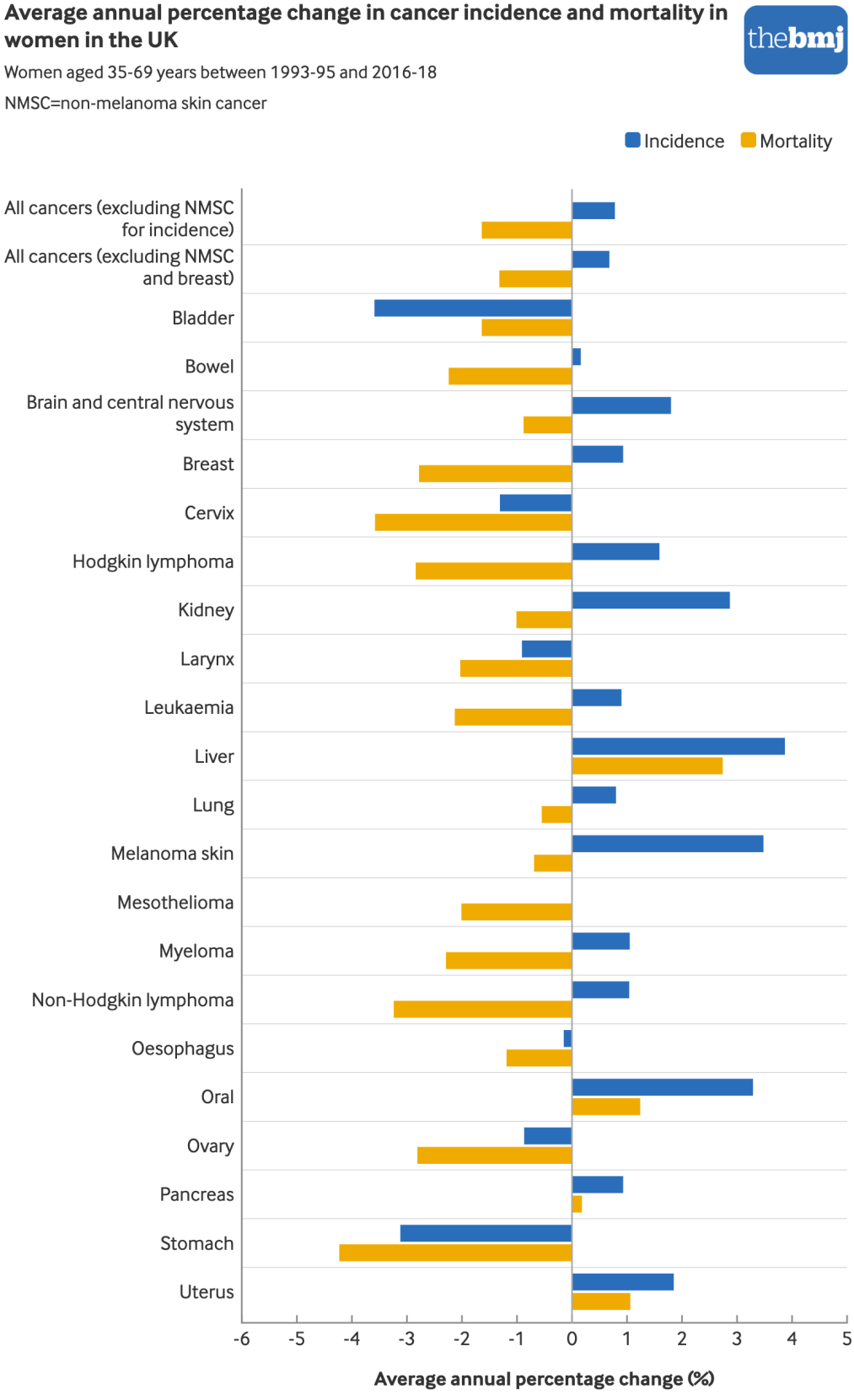


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Fig 7 | Average annual percentage change in incidence and mortality rates, in the UK, for women aged 35-69 years, from 1993-95 to 2016-18, by cancer site. An interactive version of this graphic is available at https://bit.ly/3v0QdT7

in women) across the period examined. A decrease in mortality was reported across nearly all the specific types of cancer examined (23 in total), with only liver, oral, and uterine cancers showing an increase together with melanoma skin cancer in men and pancreatic cancer in women, both showing small increases. By contrast, the incidence trends in this age group showed varying patterns with some sites increasing, some decreasing and some remaining relatively constant. Over all sites, a modest increase was noted in cancer incidence rates of around 0.8% per annum in both sexes, amounting to an increase of 15% in men and 16% in women over the 25 year time frame.

The increase in prostate cancer incidence over this period, especially in the 35-69 years age group considered here, is very likely to be a direct result of the uptake of prostate specific antigen testing, which results in the detection of early stage disease and, to an unknown extent, indolent disease that may otherwise never have been regarded as clinically significant.[24 25] The results do, however, affect people diagnosed and represent a large increase in workload for clinical staff. The fact that the overall mortality trends for men show no difference whether prostate cancer is included or excluded in the analysis indicates that the incidence increase for this cancer has largely been of non-fatal disease. That the specific mortality rates for prostate cancer showed an appreciable rate of decline during this time (−1.8% per annum) also indicates improved clinical treatment of the disease or an increase in the proportion of men diagnosed with a favourable prognosis, or both.[24 26] However, the increase in prostate cancer incidence still results in thousands of men each year dealing with the concerns of a cancer diagnosis and the impact this may have on their lives.

Breast cancer comprehensively dominated incidence and mortality trends in female cancer. Even though the average annual incidence increase of breast cancer over this period (0.9%) was modest in comparison to the prostate cancer increase in men (4.2%), breast cancer incidence rates remained substantially higher than those for any other cancer site in either sex. Inspection of figure 4 shows that breast cancer incidence rates (age standardised) increased at a faster rate until around 2003-05 (from 194.7 in 1993-95 to 229.9 in 2003-05), a slower rate from then until 2013-15 (240.8) but have levelled off in the most recent years analysed (238.0 in 2016-18). These changes in the incidence trend likely reflect a reduced effect of the initial incidence increases brought about by mammography screening in the UK introduced from the late 1980s or a possible effect of a decline in usage of hormone replacement treatment.[27 28] However, the effect of hormone replacement treatment on breast cancer risk is small in comparison to other risk factors,[7] and trends in this treatment has varied over time, such as changes in preferred formulations, doses, and treatment durations,[29-31] which may impact breast cancer risk levels.[32 33] As has been reported elsewhere,[34-36] mortality for breast cancer has declined substantially despite the incidence increase, which is indicative of improvements in early detection (including through screening[37]) and improved treatment.

The other two major sites of cancer in men apart from prostate cancer, namely lung and bowel cancers, showed substantial reductions in mortality. These results are likely from primary prevention (historical reduction in smoking rates)[38-41] for lung cancer and earlier detection (including screening) and improved treatment for bowel cancer.[42-44] While lung cancer incidence substantially decreased, the incidence rates of bowel cancer remained unchanged. However, closer inspection of the bowel cancer incidence trends over the full period shows an increase from the point the bowel screening programme was first introduced from 2006 in the UK. This rate, however, has now decreased back to the observed level prior to the introduction of the screening programme. As others have shown, the introduction of bowel screening leads to an initial short-term increase in cancer incidence due to detection of as-yet undiagnosed cancer cases, followed by a decrease because of removal of adenomas.[42 45 46] Therefore, bowel cancer incidence trends can reasonably be assumed to decrease further over the coming years, unless other preventable risk factors for bowel cancer affect the trend.

Similarly, lung and bowel were the other two major cancer sites for women (alongside breast cancer), and both showed reductions in mortality. The decline in lung cancer mortality was, however, not as extensive as that for men (−0.5% compared with −3.1% per annum) likely reflecting the different demographic pattern in smoking rates that led to peak smoking prevalence in women occurring around 30 years later than men, albeit at around half the peak prevalence observed in men.[40 47] Smoking prevalence in women has always been lower than in men.[39 48] The lung cancer incidence trends showed a significant increase in women of 0.8% per annum as opposed to the −2.1% per annum decrease in men. That the incidence rate in 2016-18 was still higher in men than in women again is almost certainly a reflection of historical differences in smoking patterns.[39 49 50] Bowel cancer incidence in women followed a similar pattern to men and is equally reflective of the introduction of the bowel screening programme. Bowel cancer mortality in women has declined at a similar rate to men (−2.2% compared with −2.5% per annum), indicative of the same improvements in early detection and improved treatment.

These reductions in mortality across the most common cancers in both sexes are likely a representation of considerable success in cancer prevention, diagnosis, and treatment. Further improvements are likely to be realised from the continued reduction in smoking prevalence, of which smoking prevention policies continue to contribute,[51] alongside the recent move to faecal immunochemical testing in the bowel screening programme adopted throughout the UK during 2019.[52] The recommended rollout of targeted lung screening is expected to further help with the earlier diagnosis of

lung cancer where surgery is a viable treatment option and outcomes are vastly improved.[53 54]

Although four major sites influenced the overall pattern of cancer incidence and mortality, increases in rates among some of the less common sites do raise concerns. Four cancers showed substantial increases in incidence (more than 2% per annum) in both sexes: liver, melanoma skin, oral, and kidney cancers. All have strong associations with established risk factors: alcohol consumption, smoking, and HPV for oral cancer;[7 55 56] overweight and obesity, smoking, alcohol, and hepatitis B and C for liver cancer;[7 57 58] ultraviolet light for melanoma;[59 60] and obesity and smoking for kidney cancer.[61-63] Increases in liver cancer incidence and mortality for both men and women are very concerning, with nearly one in two attributable to modifiable risk factors.[7] With high prevalence of overweight and obesity and diabetes in the general population, other studies expect the rates to remain high.[64] For oral and kidney cancer, despite the association with smoking, incidence rates have not followed the decrease seen for lung cancer incidence in men. This is likely to be due to the smaller proportion of cases attributable to smoking in these two sites. Whilst smoking accounts for around 17% of oral cancers, over one in three are attributed to alcohol consumption.[7] For kidney cancer, smoking is attributable to 13% of cases whereas obesity causes around 25%, however, increasing trends in kidney mortality are shown for this age group and period.[7] Therefore, the increasing incidence trends could potentially have been worse, especially in men, if the reduction in smoking prevalence had not occurred. The increased incidence of melanoma skin cancer is likely to be caused by the increased sunlight and ultraviolet exposure caused by the availability of cheaper air travel to countries with a warmer climate and insufficient regulation of tanning beds until 2010.[65 66]

In women, uterine cancer incidence increased by 1.9% per annum; although, this increase was predominantly seen over the period 1993-2007 and since then incidence trends have increased at a slower rate. One of the main risk factors for uterine cancer is the use of oestrogen-based hormone replacement therapy,[67 68] and since around 2000, use has substantially declined.[27] Around a third of uterine cancers in the UK are also attributed to overweight and obesity, but the increase in incidence is also likely to be caused by a decrease in the number of women undergoing hysterectomies for menorrhagia, in favour of endometrial ablation.[69]

Other cancers that showed increases in incidence were cancers of the pancreas, brain, and central nervous system, together with Hodgkin and non-Hodgkin lymphoma, myeloma, and leukaemia in both sexes, and oesophageal and testicular cancers in men. With the exception of pancreatic cancer, which only decreased in women, all these cancers also showed a reduction in mortality in both sexes, indicating improving treatment or earlier detection, or both. Generally, the causes of these cancers are not well understood although obesity is associated with the adenocarcinoma histological subtype of oesophageal cancer,[70] especially in men,[7] while a combination of smoking and alcohol is implicated in the squamous cell carcinoma subtype.[71] The considerable male excess in oesophageal adenocarcinoma in comparison with squamous cell carcinoma rates,[72] possibly underlined by the higher incidence of gastroesophageal reflux disease in men [73] and the protective effect of oestrogen,[74 75] may explain the differing trends now observed between men and women.

Several cancer sites showed decreases in both incidence and mortality rates over the time period, notably stomach, larynx, and bladder cancer in both sexes, as well as cervical and ovarian cancers in women and mesothelioma in men. The changes in stomach cancer rates were of a similar magnitude and represented the largest percentage mortality decline in both sexes. This decline can probably be attributed to a combination of a reduction in the prevalence of *Helicobacter pylori* infection and an increase over time in fruit and vegetable consumption reducing the dependency on preserved foods.[76 77] Challenges in coding of stomach and oesophageal cancer before 2000 may also have had a role in shaping these trends. Laryngeal cancer is associated with tobacco use and alcohol consumption as well as occupational exposures,[56 78 79] and the decline in rates is most likely to be related to the decrease in smoking prevalence as well as decreases in occupational exposure.[80] The refinement of understanding pathology for bladder cancer during this period, in which previously diagnosed malignant disease is now categorised as benign,[81] is likely to have resulted in an artificial decline in incidence rates.[82 83] This artefact should not, however, have affected the decline in mortality rates given the benign nature of these tumours that do not cause death.[81] This decline in mortality, although not as marked as that for incidence, remained appreciable. The changes in cervical cancer rates, which showed the largest percentage mortality decline amongst gynaecological cancers, are almost certainly attributed to the success of the cytological screening programme during the whole of the time period considered.[84 85] With the introduction of the HPV vaccination programme for girls in 2008[86] and the subsequent expansion to boys in 2019,[87] rates of cervical cancer are expected to fall substantially over the following decades as the first cohort of vaccinated women reaches the peak age for cervical cancer incidence (aged 30-34 years). A reduction has already been shown for women aged 20-24.[88] The absolute incidence rates of mesothelioma in women were small in magnitude in 1993-95 (0.8 per 100 000 per annum) and remained similar over time (0.7 per 100 000 per annum in 2016-18). The incidence rates of mesothelioma in men were considerably greater, especially in 1993-95 (around 6.3 per 100 000 per annum), due largely to occupational asbestos exposure,[89] but a significant decrease was noted over time (to 3.6 per 100 000 per annum in 2016-18) resulting from both the decline in

asbestos exposure and the decline in heavy industries, such as coal mining. Mortality decreased substantially in both sexes over the period for which data are available (2001-03 to 2016-18).

The conclusions that can be drawn from this analysis are, overall, positive and reassuring. Within the 35-69 year age group, cancer mortality rates have shown a substantial overall decline during the last quarter of a century in both men and women. The most probable causes are a combination of changes in the underlying risk of disease for some cancers (notably lung and stomach), in increased levels of early detection (notably breast[37] and cervix[90]) and improved treatment (notably breast and bowel) for others. The specific circumstances leading to the increased incidence of breast cancer, of which risk factors are complex, need to be better understood and controlled. Similar results have been shown for incidence within Great Britain and mortality in the UK for some cancer sites.[91] Speculated overdiagnosis, where tumours are detected that would not have caused the patient any harm during their lifetimes, has been thought to increase rates for breast and prostate cancers in particular, of which prostate is especially affected by the widespread use of prostate specific antigen testing.[4 92] However, given the decreases in mortality across the wide set of cancer sites analysed here, improvements in early diagnosis, treatment, or both are having a positive effect for most cancer patients, although cancer mortality in this age group still needs reducing.

After accounting for the major two sites in men and women, the increase in overall incidence rates disappeared in men while it remained significant in women. This difference between sexes is due to a decrease in cancers with substantially higher initial incidence rates in men, such as lung, stomach, and bladder, resulting in a higher overall impact on male incidence, combined with an increase in incidence in uterine cancer, one of the most common cancers in women.

Strengths and limitations

This study benefits from high quality cancer registry data collected by all four cancer registries in each country across the UK, which allows for the inspection of a wide range of cancer sites over 25 years. ICD-10 coding changes have been minimal, only affecting trends in cancer incidence for bladder and ovarian cancers and cancer mortality for mesothelioma, whereas challenges in coding stomach and oesophageal cancer may have affected trends for these sites. Changes in registration practice may well have had a small effect on certain cancer sites. By focusing only on the 35-69 age range, we present a clear and reliable comparative picture of cancer incidence across 25 years within the UK, which provides a reliable indicator regarding future cancer incidence trends. Understanding cancer in older people and changes in the trends of different cancers is also of interest, but subject to a different study given the increasing life expectancy over this period, impact of comorbidities, and differing interaction with health services in this age group.

Limitations include the absence of staging data to substantiate any improvements in earlier diagnosis. Due to the number of sites analysed, we also have not broken down sites by histological type, which could be beneficial in certain sites to understand the trends within cancer sites—eg, small cell and non-small cell lung cancer or oestrogen receptor-positive and oestrogen receptor-negative breast cancer. In focusing on the age group selected, we are excluding older ages where rates of cancer are higher. Although this exclusion reduces the number of cases included, providing a smaller cohort for each year, the age group selected provides a more reliable comparator for future trends given the accuracy of incidence recording and also focuses on the cancers that lead to a larger number of years of life lost. The age range included in this study has been well defined; however, other studies are indicating potentially different trends worldwide in young adults with potential increases in risk factors such as dietary risk factors playing a role.[93 94] The data captured across the UK registries provides a basis for further understanding to see whether different trends are observed across younger age groups and whether the causes of this can be determined. Additionally, although we have included a broad range of cancer sites, cancers that have not been included in this study could well be showing different trends, such as a more recent increase in thyroid cancer in the UK.[95]

This study also provides a baseline covering a 25 year period uninterrupted by covid-19. Trends in cancer incidence and mortality beyond these years will be affected and therefore understanding the causes of trends will be more complicated. Having a 25 year baseline provides the observed trend for which expected cases can be assessed against observed. This benchmark will present a comparison for the following decade as the presentation, diagnosis, and treatment of cancer have been hugely affected by rules and regulations affecting public and health service staff. Mortality trends will also be impacted with decision making regarding coding of deaths with covid-19 likely to be the underlying cause of death for people with cancer if that has directly led to the patient dying, rather than their cancer.

This study focuses on the overall sex specific trends for cancer incidence and mortality in the specified age group to observe and understand trends over the 25 year period across the entire UK. Further breakdowns have not been possible. Paucity of numbers for less common cancers precluded separate analyses for the individual UK nations while data limitations precluded analyses by other demographic characteristics, for example, ethnic group and deprivation. The main obstacle to analysing data by ethnic group is the completeness of recordings in hospitals. In England, completeness improved substantially in 2012, but prior to this, the proportion of cases with unknown ethnic group renders results over time to be incomparable. In other UK countries, completeness of ethnic group recording

is still not good enough to conduct country-wide cancer incidence or mortality analyses by ethnicity. For deprivation, the measures currently available are derived within each UK nation, and a specific validated UK-wide deprivation measure does not yet exist. Given the obvious importance of looking at variation in UK trends within ethnic groups and deprivation categories, such analyses represent a priority for further research and highlights the importance of data collection across all UK nations.

Conclusions

Overall, these results substantiate the view that in this age group there is no generalised increase in cancer incidence, while there is a substantial decrease in cancer mortality in the UK over the 25 year study period. Specific concerns about individual cancer sites identified were raised, of which the most important numerically, apart from the increases in breast and prostate cancer incidence, was the need to accelerate the decrease in female lung cancer. After which, concerns about oral cancer, liver cancer, kidney cancer, uterine cancer, and melanoma skin cancer present the most pressing issues. There are also several cancer sites that showed decreases in both incidence and mortality, notably, stomach, larynx, bladder, and cervical.

This work uses data that has been provided by patients and collected by the health services as part of their care and support. The data is collated, maintained, and quality assured by NHS England, Public Health Wales, Public Health Scotland, and the Northern Ireland Cancer Registry.

Contributors: All authors participated in study conception and design, and/or the analysis and interpretation of results. Conception and design: DF, LS, and CT. Analysis and interpretation: all authors. Writing manuscript: all authors. Supervision and guarantor: JS and DF. All authors critically reviewed drafts of the manuscript, read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Ethics approval for this work was not required as the study used publicly available data.

Data sharing: Data sharing may be possible for additional analyses. All code used for analyses in this paper are also available from the Cancer Research UK website and GitHub. Information on how to access the data used in this analysis are available from the Cancer Research UK website.

The manuscript's guarantor (DF) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

Dissemination to participants and related and public communities: study results will be disseminated to the public and health professionals by a press release written using layman's terms; findings will also be shared through mass media communications and social media postings. A webinar produced alongside a patient advocacy group is also planned to accompany the publication of this study, a recording of which will be made available on the Cancer Research UK website. Since the study analyses cancer registry data collected during routine care, and provided in aggregated form, we are unable to specifically disseminate results to study participants beyond the usual channels of publication.

Provenance and peer review: Not commissioned; externally peer reviewed.

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