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Original article

International variation in childhood cancer mortality rates from 2001-2015: comparison of trends in the International Cancer Benchmarking Partnership countries

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Key words

Childhood cancer, mortality trends, epidemiology.

Abbreviations

AAPC: Average annual percentage change.

ASR: Age standardized mortality rate.

AYA: Adolescents and young adult.

CI: Confidence interval

CNS: Central nervous system.

ICBP: International Cancer Benchmarking Partnership.

ICD-10: International Classification of Diseases 10th revision.

WHO: World Health Organization.

Article category

Research Article: Cancer Epidemiology.

Novelty and Impact

We compared mortality among children, adolescents and young adults (AYA), and older adults across six countries between 2001-2015. We show a consistent temporal reduction in mortality rates in all populations. Changes in cancer mortality rates were larger among children than AYAs or older adults. This may reflect the more centralised childhood cancer service provision, more consistent uptake of treatment protocols and trial recruitment rates in these high-income countries among children than in other age groups.

Abstract

Despite improved survival rates, cancer remains one of the most common causes of childhood death. The International Cancer Benchmarking Partnership (ICBP) showed variation in cancer survival for adults. We aimed to assess and compare trends over time in cancer mortality between children, adolescents and young adults (AYAs) and adults in the six countries involved in the ICBP: UK, Denmark, Australia, Canada, Norway and Sweden.

Trends in mortality between 2001 and 2015 in the six original ICBP countries were examined. Age standardized mortality rates (ASR per million) were calculated for all cancers, leukaemia, malignant and benign CNS tumours, and non-CNS solid tumours. ASRs were reported for children (age 0-14 years), AYAs aged 15-39 years, and adults aged 40 years and above. Average annual percentage change (AAPC) in mortality rates per country were estimated using Joinpoint regression.

For all cancers combined, significant temporal reductions were observed in all countries and all age groups. However, the overall AAPC was greater for children (-2.9; 95% CI -4.0 to -1.7) compared to AYAs (-1.8; -2.1 to -1.5) and adults aged>40 years (-1.5; -1.6 to -1.4). This pattern was mirrored for leukaemia, CNS tumours and non-CNS solid tumours, with the difference being most pronounced for leukaemia: AAPC for children -4.6 (-6.1 to -3.1) vs AYAs -3.2 (-4.2 to -2.1) and over 40s -1.1 (-1.3 to -0.8). AAPCs varied between countries in children for all cancers except leukaemia, and in adults over 40 for all cancers combined, but not in subgroups.

Improvements in cancer mortality rates in ICBP countries have been most marked among children aged 0-14s in comparison to 15-39 and over 40 year olds. This may reflect better care, including centralised service provision, treatment protocols and higher trial recruitment rates in children compared to older patients.

Introduction

Survival from childhood cancer has improved substantially over the last 50 years in high income countries, with estimated 5-year survival exceeding 80% in many European countries[1]. International studies of childhood cancer mortality have shown a decrease in rates since the 1960s but with considerable variation between countries[2-6]. A recent paper on childhood mortality comparing data from 33 European countries between 1990 to 2017 showed large reductions for all cancers combined, leukaemia and CNS tumours, with an overall decline of 2.8% per year[6]. However, cancer remains one of the most common causes of death for children[7].

The International Cancer Benchmarking Partnership (ICBP) was established to quantify international differences in cancer survival in all ages and to identify factors that might influence observed variations to inform policy[8]. All countries included in the ICBP are high income nations with universal health coverage and well established cancer registration systems in place. The countries included in the first phase of the ICBP were Australia, Canada, Denmark, Norway, Sweden and the UK[8], with the second phase including Australia, Canada, Denmark, Ireland, New Zealand, Norway and the UK[9]. Studies from this partnership have focused on cancers common in adults, specifically excluding those aged under 15 years. Results from phase 1 of the ICBP showed variation in cancer survival with poorer outcomes in the UK and Denmark for four cancers common in adults (colorectal, lung, breast and ovarian) compared to Australia, Canada, Norway and Sweden[10]. Results from phase 2 included seven cancer sites (including non-CNS solid tumours) and showed improvements in survival and mortality over time. Despite improvements in mortality for stomach, colorectal, pancreatic, lung (males only) and ovarian cancers, disparities between countries persisted with survival generally higher in Australia, Canada and Norway[11].

Cancer mortality rates and trends are a measure of the success of public health policy for cancer. They are a function of both cancer incidence and survival[12]. In this study we evaluate childhood

mortality rates and trends in the six original ICBP countries from 2001-2015 where cancer was the

underlying cause of death in those aged 0-14 years and for the first time make comparisons with

equivalent data for adolescents and young adults (AYA) aged 15-39 years and adults aged 40 years

and above over the same time period.

Materials and Methods

Data sources

Data were extracted from the World Health Organization (WHO) mortality database which includes

age, sex and cause of death reported from national vital registration systems, and corresponding

population data[13]. Data were included from Australia, Canada, Denmark, Norway, Sweden and the

UK from 2001-2015. Mortality data were not available for Australia in 2005, therefore for this year

mortality data for children were obtained from the Australian Childhood Cancer Registry[14] whilst for

adults the mean of deaths in 2004 and 2006 were used to estimate the number of deaths in 2005.

All mortality statistics were based on the underlying cause of death. Underlying cause of death was

coded according to the International Classification of Diseases 10th revision (ICD-10). The number of

deaths by 5-year age group, year and country were extracted for all cancers combined (ICD-10 C00-

C97, D32-D33, D42-D43, D46), leukaemia (ICD-10 C91-C95, D46), malignant and benign central

nervous system (CNS) tumours (ICD-10 C70-C72, D32-33, D42-43), and malignant non-CNS solid

tumours (ICD-10 C00-C69, C73-C80, C97). Leukaemia and CNS tumours were included as separate

groups as these are the two major diagnostic groups that contribute most to childhood cancer

mortality. Further comparisons were made based on acute leukaemias (which account for most

childhood leukaemias) (ICD-10 C91.0, C91.8, C92.0, C 92.4, C92.5, C92.6, C92.8, C93.0, C94.0, C94.2,

and C95.0) and unspecified leukaemias (ICD-10 C91.9, C92.3, C92.9, C93.9, C95.7 and C95.9).

Statistical analysis

Age standardized mortality rates (ASR) were calculated using the world standard population[15] for each country for three age groups: children aged 0-14 years, AYAs aged 15-39 years and adults aged 40+ years. Given the rarity of childhood cancer and the small number of deaths observed annually in some countries, ASRs were calculated for 5-year time periods (2001-2005, 2006-2010 and 2011-2015). ASRs were reported per million person-years for children and per 100,000 person-years for AYA and older adults.

To assess temporal trends in mortality rates the Joinpoint Regression Program (version 4.6.0) was used[16]. Joinpoint regression analysis was based on the natural logarithm of the annual age standardized rates for each country and used to calculate the average annual percentage change (AAPC) and 95% confidence intervals. The Joinpoint program runs a series of models to identify changes in trend and joinpoints (the years of change) using permutation tests[17]. The simplest model assumes no joinpoints or constant linear change over time. Models were compared including up to 2 joinpoints (the maximum number recommended[16]) and the simplest model selected based on the permutation test[17]. If at least one joinpoint was detected the annual percentage change was calculated for each linear segment and AAPC for the total period calculated as the weighted average of these, equal to the length of each interval in years. Where joinpoints were detected, the annual percentage change for each segment was estimated. We report the overall AAPC in the main tables and information on the significant joinpoints detected are included in Supplementary Table 1 . Joinpoint analysis was conducted separately for children, AYA and older adults. Tests of heterogeneity in AAPCs by country were assessed for each age group and tumour group by fitting a statistical interaction term into the models. A regression model was run using the log ASRs for each country, weighted by the standard error, including year and an interaction with country whilst assuming a linear trend for year.

Results

The population of the six countries ranged from 5.2 million in Norway to 65.1 million in the UK, and childhood populations ranged from 0.9 million in Norway to 11.5 million in the UK in 2015. Coverage of death registration was high in all countries (100% in five countries, 98.5% in Denmark) and the percentage of deaths registered with ill-defined (non-specific) cause ranged from 5% to 13% for all ages (Table 1). Data were not available broken down by age to determine whether there were any differences between children, AYAs and older adults.

All cancers combined

In 2001-2005 childhood mortality (ASR) ranged from 24.8 per million (95%CI 22.9, 26.7) in Canada to 32.5 per million (27.5, 37.5) in Denmark (Table 2). In 2011-2015 ASRs ranged from 18.5 per million (14.6, 22.4) in Denmark to 24.1 per million (20.7, 27.5) in Sweden. Significant temporal reductions in mortality were observed in most countries with the AAPC ranging from -0.9 (-2.0, 0.2) in Canada to -6.6 (-10.0, -3.4) in Denmark (Table3, Figure 1). Nonetheless, many confidence intervals for each country overlapped with each other including Denmark.

For ages 15-39 and 40+, mortality rates consistently decreased over time with the AAPC ranging from -1.1 in Sweden to -2.6 in Denmark for AYAs, and from -1.1 in Sweden to -1.8 in Denmark for adults over 40 (Table 3, Figure 1). Differences in the size of the AAPCs between country were much lower for 15-39 and especially 40+ year olds than for children (Figure 1).

A small number of tumour and age groups were identified for certain countries showing evidence of significantly different time period trends (n=8). Details of these, showing time period specific AAPCs and the number of joinpoints, are provided in Supplementary Table 1.

Leukaemia

In 2001-2005, childhood leukaemia mortality ranged from 6.6 per million (5.6, 7.6) in Canada to 10.1 per million (7.8, 12.4) in Sweden. In 2011-2015 the rates ranged from 4.6 per million (2.6, 6.7) in Denmark to 7.4 per million (4.9, 10.0) in Norway (Table 4). Childhood mortality rates decreased significantly over time for all countries except Norway; AAPCs ranged from -2.5 (-7.2, 2.5) in Norway to -6.0 (-10.9, -0.9) in Denmark (Tables 3, Figure 1).

Leukaemia mortality for AYAs and older adults also decreased over time in all countries with the AAPC ranging from -1.5 in Sweden to -4.4 in Australia for AYAs, and from -0.9 in Canada to -1.3 in Denmark and the UK for those aged 40+ years (Tables 3, Figure 1).

Restricting analysis to acute leukaemias only, substantial reductions in childhood mortality were observed with AAPCs ranging from -1.3 (-1.8, -0.7) in Canada to -6.5 (-7.8, -5.2) in Sweden, while for adults aged 40+ significant reductions in rates were only observed in Australia and Sweden, with stable mortality trends observed in other countries (Supplementary Tables 2-3). For AYAs, there was a modest reduction in mortality rates, although ASRs were very low and all below 1.0. For completeness, results for unspecified leukaemia are also shown (supplementary Table 4) although numbers of childhood deaths were too small to draw any robust conclusions.

Malignant and benign CNS tumours

Temporal trends in childhood malignant and benign CNS tumour mortality varied by country with slightly greater variation observed than for all cancers, mainly due to the sharp reduction in mortality in Denmark of 8.3% per year (2.8, 13.5) (Table 5, Figure 1). In 2001-2005, childhood CNS tumour mortality ranged from 9.4 per million (8.2, 10.6) in Canada to 10.9 per million (9.4, 12.4) in Australia (Table 5). In 2011-2015, childhood CNS tumour mortality similarly ranged from 6.5 per million (4.3, 8.8) in Denmark to 10.2 per million (7.3, 13.1) in Norway. Besides Denmark, mortality decreased in Australia (AAPC-2.3 (-3.9, -0.6)) and the UK (-1.6 (-2.8, -0.4)), whilst they remained stable in Canada, Sweden and Norway (Table 3, Table 5, Figure 1).

Changes in CNS tumour mortality among adults aged 40+ were similar by country (Table 3, Figure 1) and was most pronounced in Denmark, AAPC=-1.2 (-1.7, -0.6). Slightly greater reductions in mortality rates over time were seen for AYAs compared to older adults, with AAPCs ranging from -0.5 (-3.2, 2.2) in Norway to -1.9 (-4.7, 1.0) in Denmark.

Non-CNS solid tumours

Childhood non-CNS solid tumour mortality rates were highest in the UK and Denmark between 2001 and 2005 with ASRs ranging from 5.8 per million (3.5, 8.1) in Norway to 10.2 per million (7.4, 13.0) in Denmark. In 2011-2015 the mortality in Norway decreased to 3.9 per million (2.1, 5.7), while Australia, Canada and the UK had the highest rates (Table 6). AAPCs ranged from -6.2 (-10.1, -2.2) in Denmark to -1.0 (-3.3, 1.4) in Canada (Table 3, Figure 1). There were few deaths in most countries, illustrated by the wide confidence intervals (Table 6). Such small numbers precluded more detailed comparisons between countries.

In adults aged 40+, non-CNS solid tumours comprised the majority (88%) of cancer deaths. The highest mortality rates for this group were observed in Denmark and lowest in Sweden (Table 6). Mortality rates decreased in all countries but AAPCs showed much less variation than for children, ranging from -1.8 (-2.0, -1.6) in Denmark to -1.1 (-1.3, -0.8) in Sweden; all countries retained their ranks between 2001-2005 and 2011-2015 (Table 3, Table 6, Figure 1).

For AYAs, highest mortality rates were seen in the UK and lowest in Sweden (Table 6). Mortality rates fell in all countries with the greatest reduction seen in Norway with an AAPC of -2.4 (-3.6, -1.2) and smallest reduction observed in Sweden with an AAPC of -0.5 (-1.6, 0.6) (Table 3, Figure 1). The variation in AAPCs by country was again much smaller than for children.

Discussion

In this population-based study we compared the changes in cancer mortality between children and adults aged both 15-39 and 40 years and above in countries participating in the ICBP. Generally, cancer mortality rates decreased between 2001 and 2015 for most countries and the rate of decline

was greater for children (2.9%; 1.7 to 4.0%) compared to AYAs (1.8%; 1.5-2.1%) and adults aged 40+ (1.5%; 1.4-1.6%). Variations in trends were observed by cancer type.

There was greater variation in AAPC by country for childhood mortality compared to AYAs and adults over 40, for all cancers combined, CNS and non-CNS solid tumours. The AAPC for AYAs with leukaemia, however, did show some variation (range: -1.5 to –4.4) in contrast to all other tumour groups but this was not statistically significant.

Regarding childhood cancer mortality rates, Denmark and the UK were not different from other countries as in adults, and the few differences present in 2001-2005 disappeared almost completely by 2011-2015. In contrast, the large numbers of deaths included in the analyses for adults aged 40+ permitted unambiguous ranking of country-specific mortality for all cancers and non-CNS malignant tumours and demonstrated a similar improvement in all countries.

Mortality is influenced by both incidence and survival. Within Europe, childhood cancer incidence increased on average by 0.5% per year up to 2010[18] in parallel with increasing survival rates[1]. International data from CONCORD-3 showed that survival estimates for children and adults were stable or increased steadily for leukaemia, CNS tumours and non-CNS solid tumours between 2000-2014[19]. The observed decreases in mortality reported here are likely to be due to such increased survival from improved treatment and supportive care, given the general pattern of stable or increasing incidence rates over time. Adult cancer mortality (ages 40+) will also be influenced by life expectancy within each country, which may also differ. Nonetheless, our findings for childhood mortality appear to mirror those from a study examining trends from 1990-2017 across selected European countries which found an average annual reduction in all cancer mortality of 2.8% (vs 2.9%), 4.0% (vs 4.6%) for leukaemia and 1.6% (vs 1.7%) for CNS tumours[6].

For childhood cancers, cancer service provision is similar in the countries included in these analyses with equivalent trial recruitment rates, treatment protocols and centralization of services[1, 20]. This is in contrast to AYA and older adult services where there is greater variation in cancer service delivery between and within countries [21-23]. It is reassuring there was little variation in childhood mortality between countries in 2011-2015. In contrast, AYA mortality rates were consistently higher in the UK, whereas for older adults, mortality rates were higher in Denmark in line with findings based upon survival from the ICBP[10, 11]. Older adult cancer mortality rates may decrease over time as a consequence of successful screening programs (due to improved survival or earlier cancer detection) or reduced exposure to harmful risk factors affecting incidence (e.g. smoking, alcohol and obesity). Differences in referral pathways to specialist or diagnostic services could impact on mortality. Further exploration of variation in routes and time to diagnosis for each tumour group across countries may generate intelligence to improve access and reduce mortality. This could be particularly helpful for CNS tumour subgroups since variation in levels of disability could emerge as a consequence of delays in diagnosis.

The greatest reduction in childhood mortality rates was observed for leukaemia with rates falling by between 2.5% and 6.0% per year. Restricting analysis to acute leukaemias enables a more comparable outcome for children and adults, as less chronic leukaemia is diagnosed in children than in adults. Significant annual declines in childhood acute leukaemia mortality rates ranged from 1.3% to 6.3%, whilst more stable trends occurred in AYAs and older adults with significant reductions in three countries ranging between 0.3% and 4.2%. The greater decline in childhood mortality is likely to have arisen from treatment protocol advancements in the early time period. However, such comparisons between childhood and adult cancer mortality are non-trivial as most childhood leukaemia is acute lymphoid leukaemia (ALL) and most older adult leukaemia is acute myeloid leukaemia (AML) with AYA a mixture of the two, each with different treatment strategies. Similarly, adult CNS tumours and non-CNS solid tumours are notably different to their childhood tumour

counterparts. For example, for CNS tumours there are virtually no pilocytic astrocytoma or medulloblastomas diagnosed in adults compared to around 20% in children. For non-CNS solid tumours, the majority of these in adults occur as carcinomas in contrast to mainly embryonal tumours in children.

Variations in registration of non-malignant (and malignant) CNS tumours by population-based cancer registries are important when assessing geographical variation in CNS incidence and survival. Our study includes deaths from both malignant and benign CNS tumours, therefore variation between countries in registration processes for CNS tumours are unlikely to have affected our results. Furthermore, non-malignant tumours form a substantial proportion of total CNS tumours for ages 0-14 and 15-39 years and their survival rates, while high, are less than 100% and will therefore make a contribution to mortality. Even if levels of case ascertainment varied for non-malignant CNS tumours between countries, this is unlikely to have influenced the results because of the way in which mortality data are reported, i.e. malignant tumours have different codes to non-malignant tumours, and both of these tumour groups were included in this evaluation. This cancer type showed the greatest variation for both children and older adults, possibly reflecting different treatment modalities for the different types of CNS tumours, although AYA mortality showed relatively little heterogeneity.

The focus on deaths under the age of 15 years was chosen as it is commonly used in epidemiological studies of childhood cancer and was excluded in previous ICBP studies. Limitations of including such children are that mortality rates do not capture all deaths due to childhood cancer in countries with high survival, for example many deaths diagnosed aged 10-14 years would occur within the AYA and 40+ age groups. The larger reduction of mortality in those aged under 15 years compared with AYAs and older adults may be accounted for by deferral of death to an older age range.

Cause of death was reliant on coding quality on death certificates. This may have varied between countries and over time. In Table 1, we were only able to report the % of deaths with a registered cause and ill-defined cause in certain years or periods for each country. These data were unavailable for childhood or AYA mortality. Nonetheless, these figures are unlikely to have varied markedly throughout the study period across such high income countries, ensuring consistent data quality. Although rare, cancer is the leading disease-related cause of death in childhood in ICBP countries and likely to be recorded more accurately because of significant quantities of treatment-related medical records preceding death for most cases. This variation is also mitigated through national quality assurance policies such as the child death review mandatory process in the UK and Canada[24, 25]. Incomplete mortality data for adults from Australia for 2005 is unlikely to influence the results since this value was imputed from 2004 and 2006, results were aggregated across 5-year periods minimising year-on-year variation, and annual variation in mortality numbers ranged from -5% to +1%.

We also acknowledge the high number of comparisons in mortality rates and trends made between countries, disease groups and age groups as a potential limitation. However, we have been careful not to undertake inappropriate, multiple statistical testing to mitigate against type I errors.

Conclusion

Childhood cancer mortality rates have declined steadily since 2001, reflecting continuing success in outcomes for childhood cancer. Rates of decline were generally greater in children than AYAs and older adults. Compared to marked variation in cancer mortality rates in older adults, there was relatively little variation between national cancer mortality rates in children, reflecting similar centralised childhood cancer service provision, treatment protocols and trial recruitment rates in these high-income countries. Investigation of structural differences in cancer care pathways for

different ages may identify areas of improvement to further enhance outcomes and reduce

inequalities.

Conflict of interest

The authors have declared no conflicts of interest.

Data Availability Statement

This study uses data from the WHO mortality database which is freely available to download from

https://www.who.int/data/data-collection-tools/who-mortality-database. Further information is

available from the corresponding author upon request.

Ethics statement

No research ethical approval was required for this study.

Disclaimer:

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article and they do not necessarily represent the decisions, policy or views of the International

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Symbol	Country
●	AUS
◆	CAN
▲	DEN
■	NOR
+	SWE
×	UK
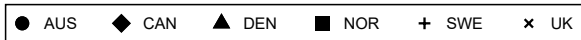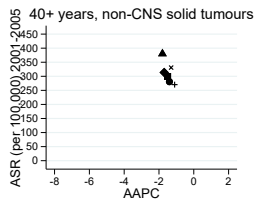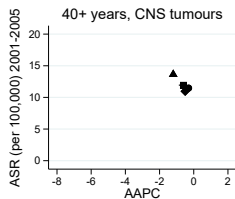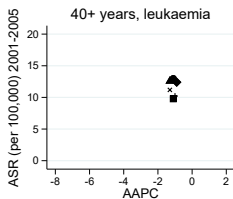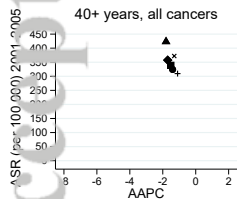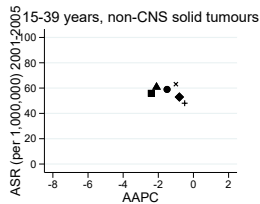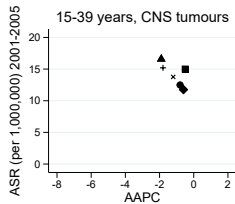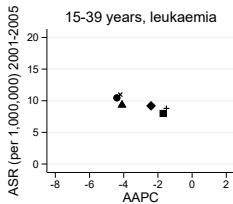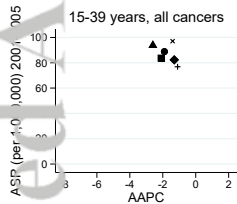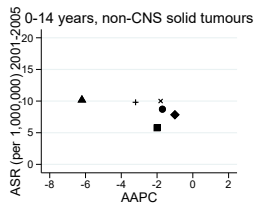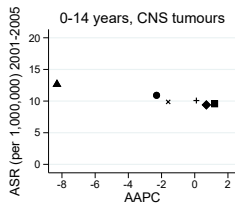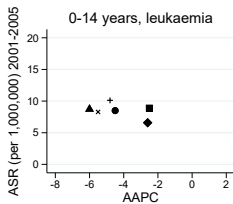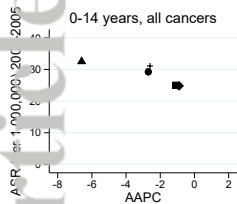
Country	Total population all ages (millions)	Population 0-14 years (millions)	% of population aged 0-14 years in total	% deaths with registered cause (all ages*)	% deaths with ill-defined cause (all ages†)
Australia	23.8	4.5	18.9%	100	5
Canada	35.9	5.7	15.9%	100	5
Denmark	5.7	1.0	17.5%	98.5	13
Norway	5.2	0.9	17.3%	100	11
Sweden	9.7	1.7	17.5%	100	10
UK	65.1	11.5	17.7%	100	5

Table 1: Populations in 2015 and quality indicators of mortality statistics in the included countries

Source: WHO mortality database and WHO Global Health Observatory[13].

*Years 2010-2012 for Denmark, Norway and Sweden, 2010 for UK, and 2009-2011 for Australia and Canada.

†Year 2016 for Sweden, 2015 for Australia, Denmark Norway and UK, and 2013 for Canada.

Country	Mean deaths per year	Age 0-14 years 2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)	Mean deaths per year	Age 15-39 years 2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)	Mean deaths per year	Age 40+ years 2001-2005 ASR per 100,000 (95%CI)	2006-2010 ASR per 100,000 (95%CI)	2011-2015 ASR per 100,000 (95%CI)
Australia	101	29.2 (26.8, 31.6)	23.2 (21.1, 25.3)	21.7 (19.7, 23.7)	675	88.8 (85.8, 91.8)	78.0 (75.3, 80.7)	73.3 (70.8, 75.9)	40,378	324.3 (322.7, 325.9)	303.5 (302.1, 305.0)	281.6 (280.3, 282.9)
Canada	136	24.8 (22.9, 26.7)	24.8 (22.9, 26.7)	22.6 (20.8, 24.3)	985	82.3 (80.0, 84.6)	75.6 (73.5, 77.8)	71.8 (69.7, 73.9)	70,175	357.6 (356.3, 358.9)	327.9 (326.7, 329.0)	301.2 (300.2, 302.3)
Denmark	23	32.5 (27.5, 37.5)	20.4 (16.4, 24.5)	18.5 (14.6, 22.4)	167	93.7 (87.7, 99.8)	82.2 (76.4, 88.0)	70.6 (65.3, 75.9)	15,209	423.4 (420.1, 426.6)	391.8 (388.8, 394.8)	354.8 (352.1, 357.5)
Norway	21	25.0 (20.4, 29.7)	21.2 (17.0, 25.5)	22.8 (18.5, 27.2)	140	83.7 (77.6, 89.8)	75.9 (70.2, 81.7)	66.9 (61.6, 72.2)	10,606	339.5 (336.2, 342.8)	316.9 (313.9, 319.9)	291.0 (288.3, 293.7)
Sweden	42	31.1 (27.1, 35.1)	25.9 (22.3, 29.5)	24.1 (20.7, 27.5)	243	76.8 (72.5, 81.2)	71.4 (67.3, 75.5)	70.4 (66.4, 74.5)	21,934	309.8 (307.7, 311.9)	290.0 (288.1, 292.0)	271.9 (270.1, 273.7)
UK	287	29.6 (28.1, 31.1)	25.8 (24.5, 27.2)	23.0 (21.7, 24.2)	2094	97.1 (95.3, 98.9)	89.0 (87.3, 90.8)	82.7 (81.0, 84.3)	157,545	372.1 (371.2, 373.0)	347.9 (347.0, 348.7)	327.3 (326.5, 328.1)
All countries combined	611	28.5 (27.5, 29.4)	24.7 (23.8, 25.6)	22.6 (21.7, 23.4)	4304	90.2 (89.1, 91.4)	82.0 (80.9, 83.1)	76.5 (75.4, 77.6)	315, 847	358.6 (357.9, 359.2)	333.4 (332.8, 334.0)	310.3 (309.8, 310.8)

Table 2: All cancer mortality: annual numbers of deaths (2001-2015) and age standardized rates using world standard population [15] by age group and time period in the included countries.

Source: WHO mortality database[13]

ASR: age standardized rate; CI: confidence interval.

	Average annual percentage change (AAPC) (95%CI)											
	Age 0-14 years				Age 15-39 years				Age 40+ years			
Country	All cancers	Leukaemia	CNS tumours	Non-CNS solid tumours	All cancers	Leukaemia	CNS tumours	Non-CNS solid tumours	All cancers	Leukaemia	CNS tumours	Non-CNS solid tumours
Australia	-2.7 (-4.2, -1.2)	-4.5 (-7.4, -1.4)	-2.3 (-3.9, -0.6)	-1.7 (-4.0, 0.6)	-1.9 (-2.4, -1.4)	-4.4 (-5.7, -3.2)	-0.8 (-2.3, 0.7)	-1.5 (-2.0, -0.9)	-1.4 (-1.5, -1.3)	-1.1 (-1.4, -0.8)	-0.3 (-0.6, 0.1)	-1.4 (-1.5, -1.3)
Canada	-0.9 (-2.0, 0.2)	-2.6 (-4.2, -1.0)	0.7 (-1.6, 3.0)	-1.0 (-3.3, 1.4)	-1.3 (-1.7, -0.8)	-2.4 (-3.2, -1.6)	-0.6 (-1.3, 0.1)	-0.8 (-1.3, -0.3)	-1.7 (-1.8, -1.6)	-0.9 (-1.3, -0.5)	-0.5 (-1.1, 0.1)	-1.7 (-1.8, -1.6)
Denmark	-6.6 (-10.0, -3.1)	-6.0 (-10.9, -0.9)	-8.3 (-13.5, -2.8)	-6.2 (-10.1, -2.2)	-2.6 (-3.6, -1.5)	-4.1 (-9.3, 1.5)	-1.9 (-4.7, 1.0)	-2.1 (-3.6, -0.5	-1.8 (-2.0, -1.6)	-1.3 (-1.9, -0.7)	-1.2 (-1.7, -0.6)	-1.8 (-2.0, -1.6)
Norway	-1.1 (-4.1, 2.1)	-2.5 (-7.2, 2.5)	1.2 (-3.5, 6.1)	-2.0 (-9.6, 6.1)	-2.1 (-3.2, -1.1)	-1.7 (-4.0, 0.6)	-0.5 (-3.2, 2.2)	-2.4 (-3.6, -1.2)	-1.5 (-1.7, -1.4)	-1.1 (-1.9, -0.2)	-0.6 (-1.3, 0)	-1.5 (-1.7, -1.4)
Sweden	-2.6 (-4.6, -0.7)	-4.8 (-8.4, -1.1)	0.1 (-2.8, 3.0)	-3.2 (-6.4, 0.2)	-1.1 (-1.9, -0.3)	-1.5 (-4.4, 1.4)	-1.8 (-4.1, 0.6)	-0.5 (-1.6, 0.6)	-1.1 (-1.3, -0.9)	-1.0 (-1.5, -0.4)	-0.7 (-1.3, -0.1)	-1.1 (-1.3, -0.8)
UK	-2.7 (-3.4, -1.9)	-5.5 (-7.1, -4.0)	-1.6 (-2.8, -0.4)	-1.8 (-2.0, -0.5)	-1.4 (-2.1, -0.8)	-4.2 (-4.8, -3.6)	-1.2 (-2.0, -0.4)	-1.0 (-1.4, -0.6)	-1.3 (-1.4, -1.2)	-1.3 (-2.2, -0.3)	-0.6 (-1.1, -0.2)	-1.3 (-1.4, -1.3)
P interaction	0.009	0.55	0.017	0.073	0.0587	0.42	0.83	0.78	<0.001	0.90	0.23	0.23
All countries combined	-2.9 (-4.0, -1.7)	-4.6 (-6.1, -3.1)	-1.7 (-2.7, -0.8)	-2.7 (-4.0, -1.4)	-1.8 (-2.1, -1.5)	-3.2 (-4.2, -2.1)	-1.2 (-2.3, -0.1)	-1.4 (-1.8, -1.0)	-1.5 (-1.6, -1.4)	-1.1 (-1.3, -0.8)	-0.7 (-0.9, -0.4)	-1.5 (-1.6, -1.4)

Table 3: Average annual percentage change (AAPC) in the mortality rates over the period 2001-2015 by age group and diagnostic group in the included countries.

Source: WHO mortality database[13]

AAPC: average annual percentage change; CI: confidence interval

	Age 0-14 years				Age 15-39 years				Age 40+ years			
Country	Mean deaths per year	2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)	Mean deaths per year	2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)	Mean deaths per year	2001-2005 ASR per 100,000 (95%CI)	2006-2010 ASR per 100,000 (95%CI)	2011-2015 ASR per 100,000 (95%CI)
Australia	25	8.5 (7.2, 9.8)	4.9 (4.0, 5.9)	5.0 (4.0, 5.9)	67	10.5 (9.4, 11.5)	9.0 (8.1, 10.0)	6.8 (6.0, 7.6)	1832	13.0 (12.7, 13.3)	12.3 (12.0, 12.5)	11.6 (11.4, 11.9)
Canada	32	6.6 (5.6, 7.6)	5.9 (5.0, 6.8)	4.9 (4.1, 5.7)	95	9.2 (8.4, 10.0)	8.0 (7.2, 8.7)	7.1 (6.4, 7.8)	2783	12.4 (12.2, 12.6)	11.6 (11.4, 11.8)	11.4 (11.2, 11.6)
Denmark	6	8.7 (6.1, 11.3)	6.0 (3.8, 8.2)	4.6 (2.6, 6.7)	14	9.3 (7.3, 11.4)	8.3 (6.4, 10.3)	5.9 (4.0, 7.5)	523	12.6 (12.0, 13.1)	12.0 (11.5, 12.5)	11.1 (10.7, 11.6)
Norway	7	8.9 (6.2, 11.6)	5.4 (3.2, 7.5)	7.4 (4.9, 10.0)	12	8.0 (5.9, 10.1)	7.4 (5.5, 9.4)	6.3 (4.6, 8.1)	349	9.8 (9.2, 10.3)	9.5 (9.0, 10.0)	9.0 (8.5, 9.5)
Sweden	13	10.1 (7.8, 12.4)	8.9 (6.8, 11.0)	6.6 (4.8, 8.4)	23	8.8 (7.2, 10.3)	6.7 (5.3, 8.0)	7.6 (6.2, 9.0)	826	10.2 (9.9, 10.6)	9.7 (9.3, 10.0)	9.4 (9.1, 9.7)
UK	71	8.3 (7.5, 9.1)	6.0 (5.3, 6.7)	5.0 (4.4, 5.6)	187	11.0 (10.3, 11.6)	8.7 (8.1, 9.3)	7.1 (6.5, 7.6)	5329	11.2 (11.0, 11.3)	10.5 (10.4, 10.7)	10.2 (10.0, 10.3)
All countries combined	155	8.1 (7.6, 8.6)	5.9 (5.5, 6.4)	5.1 (4.7, 5.5)	398	10.1 (9.7, 10.6)	8.4 (8.0, 8.8)	7.0 (6.7, 7.3)	11,641	11.6 (11.5, 11.7)	11.0 (10.9, 11.1)	10.6 (10.5, 10.7)

Table 4: Leukaemia mortality: annual numbers of deaths (2001-2015) and age standardized rates using world standard population [15] by age group and time period in the included countries

Source: Data obtained from the WHO mortality database[13]

ASR: age standardized rate; CI: confidence interval.

Country	Mean deaths per year	Age 0-14 years			Mean deaths per year	Age 15-39 years			Mean deaths per year	Age 40+ years		
		2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)		2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)		2001-2005 ASR per 100,000 (95%CI)	2006-2010 ASR per 100,000 (95%CI)	2011-2015 ASR per 100,000 (95%CI)
Australia	39	10.9 (9.4, 12.4)	9.1 (7.8, 10.4)	8.4 (7.2, 9.7)	95	12.5 (11.4, 13.6)	10.8 (9.8, 11.8)	11.1 (10.1, 12.2)	1291	11.5 (11.2, 11.8)	11.2 (10.9, 11.5)	11.2 (10.9, 11.4)
Canada	52	9.4 (8.2, 10.6)	9.0 (7.9, 10.2)	9.4 (8.2, 10.5)	143	11.8 (10.9, 12.6)	11.3 (10.4, 12.1)	11.1 (10.3, 11.9)	2004	11.0 (10.7, 11.2)	10.5 (10.3, 10.7)	10.3 (10.1, 10.5)
Denmark	9	12.7 (9.5, 15.8)	6.8 (4.5, 9.1)	6.5 (4.3, 8.8)	28	16.6 (13.9, 19.2)	13.3 (11.0, 15.6)	13.5 (1.11, 15.9)	441	13.6 (13.0, 14.3)	13.3 (12.7, 13.8)	12.2 (11.7, 12.8)
Norway	9	9.6 (6.7, 12.4)	9.3 (6.4, 12.1)	10.2 (7.3, 13.1)	25	15.0 (12.4, 17.7)	12.2 (9.9, 14.6)	13.9 (11.4, 16.3)	323	11.9 (11.2, 12.6)	11.6 (11.0, 12.2)	11.2 (10.6, 11.8)
Sweden	15	10.1 (7.8, 12.4)	9.2 (7.0, 11.4)	9.6 (7.5, 11.8)	45	15.2 (13.2, 17.2)	13.4 (11.6, 15.2)	13.0 (11.2, 14.8)	725	11.9 (11.5, 12.4)	12.0 (11.6, 12.5)	11.2 (10.8, 11.6)
UK	103	9.9 (9.0, 10.7)	9.9 (9.0, 10.7)	8.5 (7.7, 9.2)	295	13.8 (13.1, 14.5)	13.1 (12.4, 13.8)	12.2 (11.6, 12.9)	4395	12.0 (11.8, 12.2)	11.6 (11.4, 11.8)	11.5 (11.3, 11.7)
All countries combined	226	10.1 (9.5, 10.6)	9.3 (8.8, 9.9)	8.7 (8.2, 9.3)	630	13.3 (12.9, 13.8)	12.3 (11.8, 12.7)	11.9 (11.5, 12.3)	9179	11.8 (11.6, 11.9)	11.4 (11.3, 11.5)	11.2 (11.1, 11.3)

Table 5: CNS tumour mortality: annual numbers of deaths (2001-2015) and age standardized rates using world standard population [15] by age group and time period in the included countries

Source: Data obtained from the WHO mortality database[13]

ASR: age standardized rate; CI: confidence interval.

Country	Mean deaths per year	Age 0-14 years			Mean deaths per year	Age 15-39 years			Mean deaths per year	Age 40+ years		
		2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)		2001-2005 ASR per 1,000,000 (95%CI)	2006-2010 ASR per 1,000,000 (95%CI)	2011-2015 ASR per 1,000,000 (95%CI)		2001-2005 ASR per 100,000 (95%CI)	2006-2010 ASR per 100,000 (95%CI)	2011-2015 ASR per 100,000 (95%CI)
Australia	33	8.7 (7.4, 10.0)	8.3 (7.0, 9.6)	7.3 (6.1, 8.4)	473	59.0 (56.6, 61.4)	53.6 (51.4, 55.8)	51.6 (49.5, 53.7)	34,948	280.8 (279.3, 282.3)	264.1 (262.8, 265.5)	243.9 (242.7, 245.1)
Canada	46	7.8 (6.8, 8.9)	9.2 (8.0, 10.3)	7.4 (6.4, 8.4)	664	53.0 (51.2, 54.7)	49.9 (48.2, 51.6)	48.5 (46.8, 50.2)	61,417	313.7 (312.5, 315.0)	287.9 (286.8, 289.0)	263.3 (262.3, 264.3)
Denmark	7	10.2 (7.4, 13.0)	6.1 (3.9, 8.2)	6.3 (4.0, 8.6)	114	60.8 (56.0, 65.5)	55.2 (50.5, 59.9)	47.8 (43.4, 52.1)	13,657	380.3 (377.2, 383.4)	352.4 (349.6, 355.3)	318.5 (316.0, 321.1)
Norway	5	5.8 (3.5, 8.1)	6.0 (3.7, 8.3)	3.9 (2.1, 5.7)	97	55.9 (51.0, 60.8)	52.8 (48.1, 57.6)	44.3 (40.1, 48.6)	9363	299.4 (296.3, 302.5)	279.6 (276.7, 282.4)	256.2 (253.7, 258.7)
Sweden	12	9.8 (7.5, 12.1)	6.9 (5.0, 8.8)	7.0 (5.2, 8.9)	163	48.1 (44.7, 51.4)	47.7 (44.4, 51.1)	46.7 (43.4, 49.9)	19,174	270.5 (268.5, 272.5)	253.5 (251.7, 255.3)	237.4 (235.8, 239.1)
UK	100	10.0 (9.2, 10.9)	9.1 (8.3, 9.9)	8.4 (7.6, 9.2)	1446	63.1 (61.7, 64.5)	59.9 (58.5, 61.4)	57.6 (56.2, 59.0)	140,279	331.1 (330.2, 332.0)	309.6 (308.8, 310.4)	290.4 (289.7, 291.2)
All countries combined	204	9.1 (8.6, 9.7)	8.6 (8.0, 9.1)	7.6 (7.2, 8.1)	2958	58.6 (57.7, 59.6)	55.2 (54.3, 56.1)	52.7 (51.9, 53.6)	278,837	316.7 (316.1, 317.3)	294.7 (294.2, 295.3)	273.3 (272.8, 273.8)

Table 6: Non-CNS solid tumour mortality: annual numbers of deaths (2001-2015) and age standardized rates using world standard population [15] by age group and time period in the included countries

Source: Data obtained from the WHO mortality database[13]

ASR: age standardized rate; CI: confidence interval.

Cancer mortality rates and trends are a function of both cancer incidence and survival and reflect the success of public health policy. Here, the authors compared mortality among children, adolescents and young adults, and older adults across six high-income, universal health-coverage nations between 2001 and 2015. They found a consistent temporal reduction in mortality rates in all populations. Changes in cancer mortality rates were larger among children than among adolescent and young adults or older adults. This may reflect the more centralised cancer care provision, more consistent uptake of treatment protocols, and higher trial recruitment rates in children compared to other age groups in these high-income countries.