

Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry

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Summary

Background Cancer trends in young adults, often under 50 years, reflect recent changes in carcinogenic exposures, which could foreshadow the future overall disease burden. Previous studies reported an increase in early onset colorectal cancer, which could partly reflect the obesity epidemic. We examined age-specific contemporary incidence trends in the USA for 30 common cancers, including 12 obesity-related cancers.

Methods We obtained incidence data for invasive cancers among people aged 25–84 years diagnosed from Jan 1, 1995, to Dec 31, 2014, for 25 population-based state registries in the USA. All patients in the registry were included in the analyses. We considered the 20 most common cancer types and 12 obesity-related cancers (30 cancer types in total). We used age-period-cohort modelling to estimate average annual percentage change in incidence rates by 5-year age group (25–29 years to 80–84 years in 5-year increments) and incidence rate ratios (IRR) by birth cohort (10-year overlapping birth cohorts from 1910–19 to 1980–89 in 5-year increments). No exclusion criteria were applied after including all invasive cancer cases based on age group and diagnosis year.

Findings From 1995 to 2014 there were 14 672 409 incident cases for 30 types of cancer. Incidence significantly increased for six of 12 obesity-related cancers (multiple myeloma, colorectal, uterine corpus, gallbladder, kidney, and pancreatic cancer) in young adults (25–49 years) with steeper rises in successively younger generations. Annual increases ranged from 1·44% (95% CI –0·60 to 3·53) for multiple myeloma to 6·23% (5·32–7·14) for kidney cancer at age 25–29 years, and ranged from 0·37% (0·03–0·72) for uterine corpus cancer to 2·95% (2·74–3·16) for kidney cancer at age 45–49 years. Compared with people born around 1950, IRRs for those born around 1985 ranged from 1·59 (95% CI 1·14–2·21) for multiple myeloma to 4·91 (4·27–5·65) for kidney cancer. Conversely, incidence in young adults increased in successively younger generations for only two cancers (gastric non-cardia cancer and leukaemia), and decreased for eight of the 18 additional cancers, including smoking and HIV infection-associated cancers.

Interpretation The risk of developing an obesity-related cancer seems to be increasing in a stepwise manner in successively younger birth cohorts in the USA. Further studies are needed to elucidate exposures responsible for these emerging trends, including excess bodyweight and other risk factors.

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Introduction

Monitoring cancer occurrence in young adults, often under 50 years, is informative because it often reflects relatively recent changes in exposure to carcinogenic factors.¹ Moreover, these cancer trends often serve as a sentinel for the future disease burden in older adults, among whom most cancer cases occur.¹

Exposures to carcinogens during early life can affect an individual's cancer risk by acting during crucial developmental periods and increasing cumulative mutagenic damage.² Due to the obesity epidemic over the past 40 years, younger generations worldwide are experiencing an earlier and longer lasting exposure to excess adiposity over their lifetime than previous generations.³ Numerous cancers are associated with excess bodyweight, and evidence from experimental studies from murine models suggests that obesity and an obesogenic diet accelerate the multistage transition from

normal tissue to invasive malignancy and metastatic disease.⁴ Increases in the incidence of early onset colorectal cancer have been reported in several high-income countries over the past decade, including the USA,^{5,6} and could in part reflect the obesity epidemic.

We extended our previous study on early onset colorectal cancer⁵ by systematically examining recent temporal trends in invasive cancer incidence in the USA among young adults by age and year of birth for 30 common cancers, including 12 well established obesity-related cancers.⁷

Methods

Study design

We used the Cancer in North America database of the North American Association of Central Cancer Registries to obtain information on invasive cases of 30 cancer types diagnosed in patients aged 25–84 years from Jan 1, 1995,

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For the Cancer in North America database see <https://www.naacrr.org>

Research in context**Evidence before this study**

We searched PubMed for papers in English of population-based studies of trends in incidence by age and birth cohort for 13 obesity-related cancers in the USA published from Jan 1, 1990, to May 30, 2018, with the terms “incidence trends”, “obesity-related cancers”, and “young adults” and separately “obesity-related cancers”, “birth cohort”, and “young adults”.

Previous studies have reported rising colorectal cancer incidence rates in young adults in the USA and many high-income developed countries, but none have examined trends for a comprehensive list of cancers and compared patterns between cancers in terms of their association with obesity.

Added value of this study

This study is the first, to our knowledge, to systematically examine the contemporary incidence trends for 12 obesity-related cancers and 18 additional cancers in young adults in the USA with nationally representative population-based data. Incidence increased for half of the

obesity-related cancers (colorectum, corpus uteri, gallbladder, kidney, multiple myeloma, and pancreas) in young adults and in successively younger birth cohorts in a stepwise manner in contrast to the declining or stabilising incidence trends for smoking-related and infection-related cancers. Whether similar patterns have occurred in other populations with similar obesity trends warrants further investigation.

Implications of all the available evidence

The future burden of obesity-related cancers in the USA might be exacerbated as younger cohorts age, potentially halting or reversing the progress achieved in reducing cancer mortality over the past several decades. Further aetiological studies focusing on modifiable risk factors in early life and adult cancer risk are needed to elucidate causes responsible for these emerging trends. Meanwhile, innovative strategies are needed to mitigate morbidity and premature mortality associated with obesity-related diseases, primarily by health-care providers and policy makers.

to Dec 31, 2014. We limited our analysis to 25 US state registries that had data for all study years (appendix p 4), covering 67% of the US population. All invasive cases of 30 cancer types diagnosed in patients aged 25–84 years during the study period in these registries were included in the study.

12 cancer types were chosen on the basis of their association with obesity according to the International Agency for Research on Cancer:⁷ colorectal, oesophageal (adenocarcinoma), gallbladder, gastric cardia, kidney, liver and intrahepatic bile duct, multiple myeloma, pancreatic, and thyroid cancer, and, in women, uterine corpus (including endometrial cancer and uterine sarcoma), breast, and ovarian cancer. Meningioma is related to obesity, but was excluded because of its rarity in young adults based on the number of cases from the registries. We also included a further 18 cancers ranking in the most common 20 cancers in men and women aged 25–49 years based on incidence data from the North American Association of Central Cancer Registries between 2010 and 2014 (appendix p 5): anal, brain and other central nervous system, cervical, oesophageal (squamous cell), gastric non-cardia, Kaposi sarcoma, laryngeal, leukaemia, lung and bronchial, lymphoma (Hodgkin and non-Hodgkin), skin melanoma, oropharyngeal (HPV-related and smoking-related), prostate, testicular, urinary bladder, and vulval. Cases were classified according to the International Classification of Diseases for Oncology and further grouped, when appropriate, into anatomical, histological, and causal subtypes for some cancers (cardia and non-cardia for stomach; adenocarcinoma and squamous cell carcinoma for oesophagus; smoking-related and HPV-related for oropharynx; appendix pp 6–7). The 2001 WHO classification scheme reclassified chronic lymphocytic leukaemia from leukaemia to non-Hodgkin

lymphoma; therefore, we included chronic lymphocytic leukaemia as a subtype of non-Hodgkin lymphoma (appendix pp 6–8).⁸ SEER*Stat (version 8.3.4) was used to tabulate case data and person-years-at risk.

Statistical analysis

To obtain stable parameter estimates across cancer types, 5-year intervals were used to categorise age (ie, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84) and calendar period of diagnosis (ie, 1995–99, 2000–04, 2005–09, 2010–14). Nominal birth cohorts were constructed by subtracting the the mid-year of age (the age halfway between the youngest and oldest age in each age category) from the mid-year of diagnosis (the year halfway between the first and last year in each diagnosis calendar period), resulting in 15 partly overlapping 10-year birth cohorts, referenced by mid-year of birth (from 1910–19 [the 1915 cohort] to 1980–89 [1985 cohort]). An age-period-cohort model was fitted to each cancer type, yielding estimated temporal trends in incidence by 5-year age group and expressed as annual percent change per calendar year.⁹ The significance of the trend in annual percent changes across age groups was tested using a Wald test. Because of the substantially lower incidence among younger adults than older people for most cancers, small increases in absolute case numbers among young adults might cause large annual percent increases in incidence rates. Therefore, we also visualised trends in age-specific incidence rates by 5-year age group and birth cohort. We estimated age-adjusted and period-adjusted incidence rate ratios (IRRs) by birth cohort and accompanying 95% CIs to compare incidence rates for a given birth cohort to corresponding age groups among people in the 1950 birth cohort (1945–54). We chose 1950 as the

See Online for appendix

referent birth cohort because it is midway between examined cohorts; however, the referent cohort is arbitrary and does not influence the interpretation of results. These estimates are predicted on the assumption that the age-period-cohort model provides an adequate description of the data. We assessed the goodness-of-fit of the age-period-cohort models by comparing the observed age-specific incidence rates across birth cohort with the 95% CIs of the corresponding fitted rates. All statistical tests were two-sided and considered significant at $p < 0.05$.

Sensitivity analyses were done for female breast cancer by race (appendix pp 8, 15, 21) and for leukaemia and non-Hodgkin lymphoma by major histological subtypes (acute lymphoid leukaemia, acute myeloid leukaemia, and chronic myeloid leukaemia for leukaemia, and diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukaemia for non-Hodgkin lymphoma; appendix pp 8, 16–17, 22–23).

All statistical analyses were done with MATLAB R2017b (version 9.4).

Role of the funding source

The funders of the study reviewed the final version of the manuscript but had no role in study design, data collection, data analysis, data interpretation, or writing of the report. HS had full access to all the data in the study, and AJ had final responsibility for the decision to submit for publication.

Results

From 1995 to 2014, there were 14 672 409 incident cases for 30 types of cancers during 2 481 416 140 person-years of observation. Figure 1 shows average annual percent change in age-specific incidence for obesity-related cancers. From 1995 to 2014, the incidences of multiple myeloma and cancers of the colorectum, corpus uteri, gallbladder, kidney, pancreas, and thyroid increased in younger adults (25–49 years), with the magnitude of the increases steeper with younger age (all $p_{\text{wald}} < 0.05$) except for thyroid cancer (appendix pp 9–10). For example, the average annual percent change in pancreatic cancer incidence increased with decreasing age, from 0.77% (95% CI 0.57–0.98) for ages 45–49 years to 2.47% (1.77–3.18) for ages 30–34 years, and 4.34% (3.19–5.50) for ages 25–29 years. Similarly, the annual percent change by age was largest in individuals aged 25–29 years for cancers of the kidney (6.23%; 95% CI 5.32–7.14), gallbladder (3.71%; 1.46–6.00), corpus uteri (3.34%; 1.80–4.90), and colorectum (2.41%; 0.57–4.29), and in individuals aged 30–34 years for multiple myeloma (2.21%; 1.20–3.23; figure 1; appendix pp 9–10). Incidences were stable for breast cancer.

Age-specific incidence in older adults (≥ 50 years) increased for the same obesity-related cancers (gallbladder, kidney, multiple myeloma, pancreas, and thyroid) that increased in younger adults, except for colorectal cancer,

which declined, and uterine corpus cancer, which increased in ages 50–69 years, but decreased in older women aged 75–84 years (figure 1). However, the magnitudes of the increases in older adults were smaller than in younger adults, except for thyroid cancer. Incidence increased for liver cancer and oesophageal adenocarcinoma in older age groups, was generally stable for gastric cardia cancer, and declined for ovarian cancer across almost all age groups.

Figure 2 shows the age-adjusted and period-adjusted IRR by birth cohort for obesity-related cancers using incidence in the 1950 birth cohort as the reference (appendix pp 9–10). Incidence increased in successively younger birth cohorts for most of the 12 obesity-related cancers. For example, compared with individuals born around 1950, the IRR for uterine corpus cancer increased to 1.25 (95% CI 1.16–1.34) for individuals born around 1970 and 2.05 (1.60–2.62) for individuals born around 1985; for pancreatic cancer, these IRRs rose from 1.18 (1.13–1.24) for the 1970 birth cohort and 2.25 (1.89–2.69) for the 1985 group, and for kidney cancer rose from 1.98 (1.90–2.07) to 4.91 (4.27–5.65). By contrast, IRRs remained relatively stable for gastric cardia cancer and declined continuously in every subsequent birth cohort since 1915 for ovarian cancer. The risk of developing breast cancer generally remained unchanged in younger generations.

Figure 3 shows trends in age-specific incidence by 5-year age group and birth cohort for 12 obesity-related cancers, with trends for the remaining 18 additional cancers given in the appendix (pp 18–20). Age-specific incidence in individuals aged younger than 50 years generally continued to increase in successively younger birth cohorts for cancers of the corpus uteri, colorectum, gallbladder, kidney, pancreas, and multiple myeloma, supporting the findings in figure 2 from the age-period-cohort model. By contrast, incidence increased across all ages and all birth cohorts for thyroid cancer and among middle-aged and older adults and birth cohorts born before around 1960 for liver cancer, whereas incidence was relatively stable for the remaining cancers.

Incidence in young adults increased significantly for two of the additional cancers (gastric non-cardia cancer and leukaemia), decreased for most younger age groups for eight cancers (bladder, brain, cervix, oesophageal squamous cell carcinoma, Kaposi sarcoma, larynx, lung, and non-Hodgkin lymphoma), and was otherwise stable or variable across age groups (figure 4; appendix pp 11–14). Among older age groups, incidence generally decreased for 10 of the 18 cancers (bladder, brain, cervix, oesophageal squamous cell carcinoma, gastric non-cardia, Kaposi sarcoma, larynx, lung, and smoking-related oropharynx, and prostate), increased for four cancers (ie, anus, melanoma, oropharyngeal HPV-related cancers, and vulva), and was otherwise variable across age groups (figure 4).

Figure 5 shows the age-adjusted and period-adjusted IRRs by birth cohort for 18 additional cancers (appendix pp 11–14). Compared with the incidence in

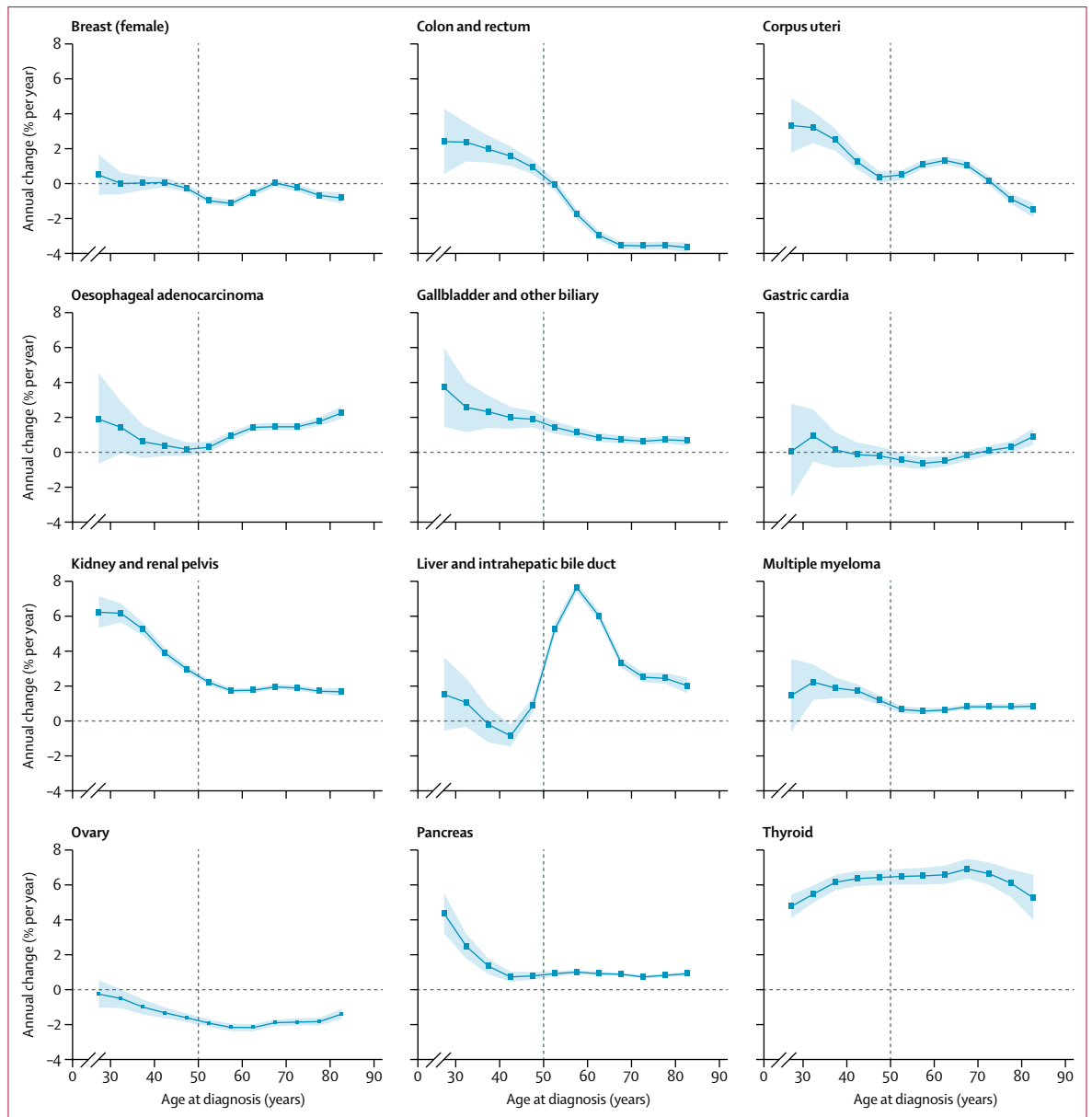


Figure 1: Age-specific annual percent change in incidence for 12 obesity-related cancers, 1995–2014

Dots and shaded areas represent the net annual percentage changes (% per year) and 95% CIs in incidence from the age-period-cohort models for 12 age groups (5-year increments from age 25 years).

people born around 1950, age-specific incidence was slightly elevated across subsequent generations for testicular cancer but increased consistently and more rapidly in successively younger generations for gastric non-cardia cancer and leukaemia. The IRRs for gastric non-cardia cancer increased to 1.36 (95% CI 1.27–1.45) in individuals born around 1970 and 1.68 (1.38–2.06) in individuals born around 1985. IRRs also increased in successive generations born since around 1950 for melanoma and cancers of the anus, HPV-related oropharynx, prostate, and vulva, but declined or stabilised in individuals born after the mid-1960s. By contrast, IRRs

decreased in successive generations for many cancers, including bladder, brain, cervix, oesophageal squamous cell carcinoma, Kaposi sarcoma, larynx, lung, and non-Hodgkin lymphoma. Age-specific incidence by birth cohort for each of the additional 18 cancers corresponded with estimated annual percent changes by age group and IRRs by birth cohort (appendix pp 18–20).

In sensitivity analyses of breast cancer by race, and haematological cancers by major histological subtypes, we found that breast cancer risk in successive younger birth cohorts stabilised among white and black women but increased among Asian Pacific Islander women (appendix

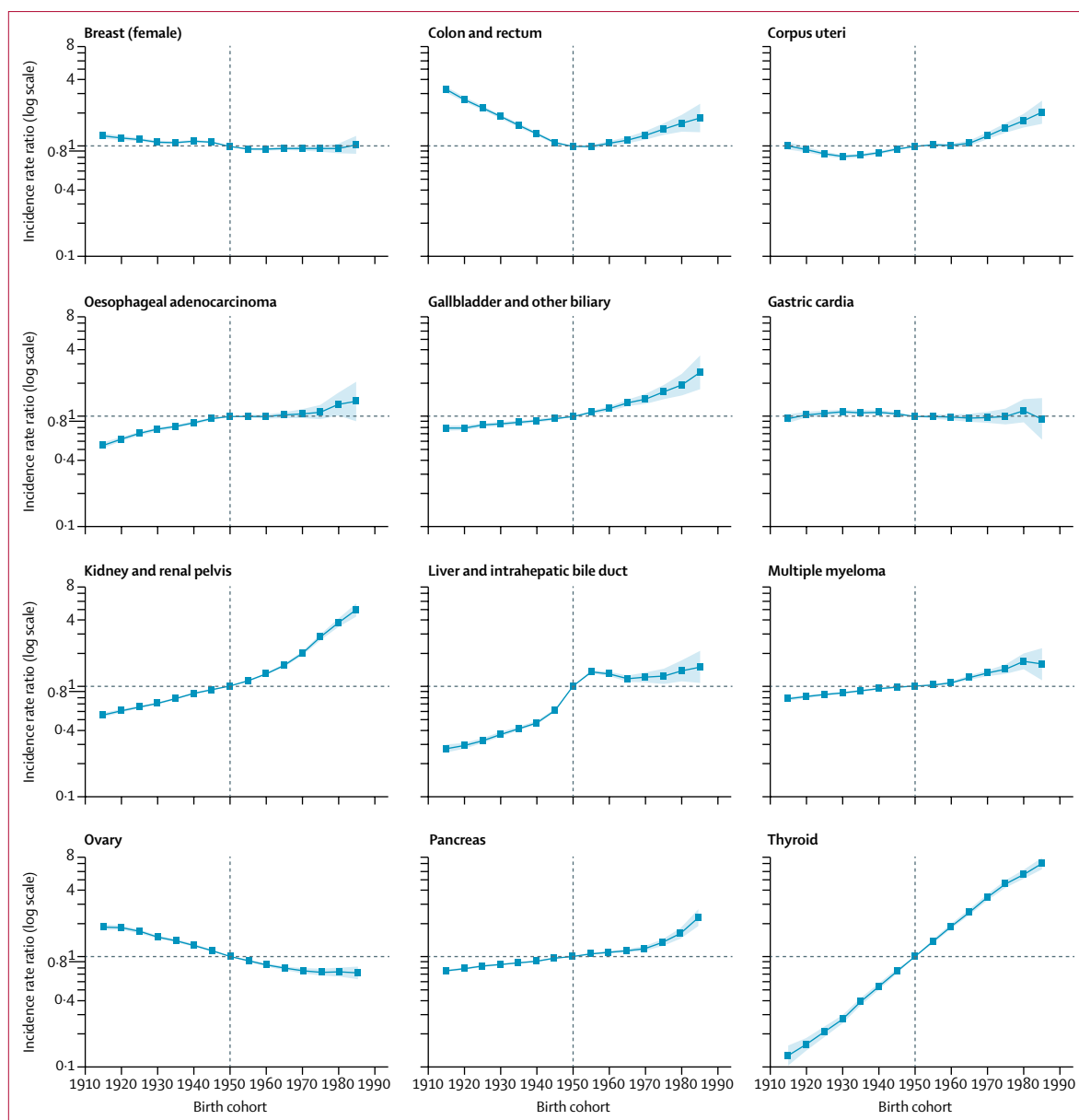


Figure 2: Incidence rate ratio by birth cohort from 1915 (1910–19) to 1985 (1980–89) for 12 obesity-related cancers, 1995–2014

Dots and shaded areas represent incidence rate ratios and 95% CIs for a given birth cohort relative to the 1950 birth cohort (1945–54; reference) for 15 partly overlapping 10-year birth cohorts.

pp 15, 21). For leukaemia, risk increased in successive younger birth cohorts for all three major subtypes (acute lymphoid leukaemia, acute myeloid leukaemia, and chronic myeloid leukaemia; appendix pp 16, 22). For non-Hodgkin lymphoma, in contrast, risk decreased for diffuse large B-cell lymphoma and follicular lymphoma but increased for chronic lymphocytic leukaemia in successively younger birth cohorts (appendix pp 17, 23).

Discussion

We found that, in the USA, the risk of developing cancer has increased in younger adults for six of 12 obesity-related

cancers, with a steeper increase in progressively younger ages ($p_{\text{wald}} < 0.05$) and successively younger generations born since around 1950. Although incidences for these cancers, except for colorectal cancer, also rose in older adults, the magnitudes of annual percent increases were smaller than in young adults. By contrast, incidence increased in successive younger generations for only two of the 18 additional cancers, and decreased for about half of the remaining cancer types, especially for those related to smoking or HIV infection (eg, lung cancer and Kaposi sarcoma). These trends might have been influenced by the rapid rise in overweight or obesity prevalence in the

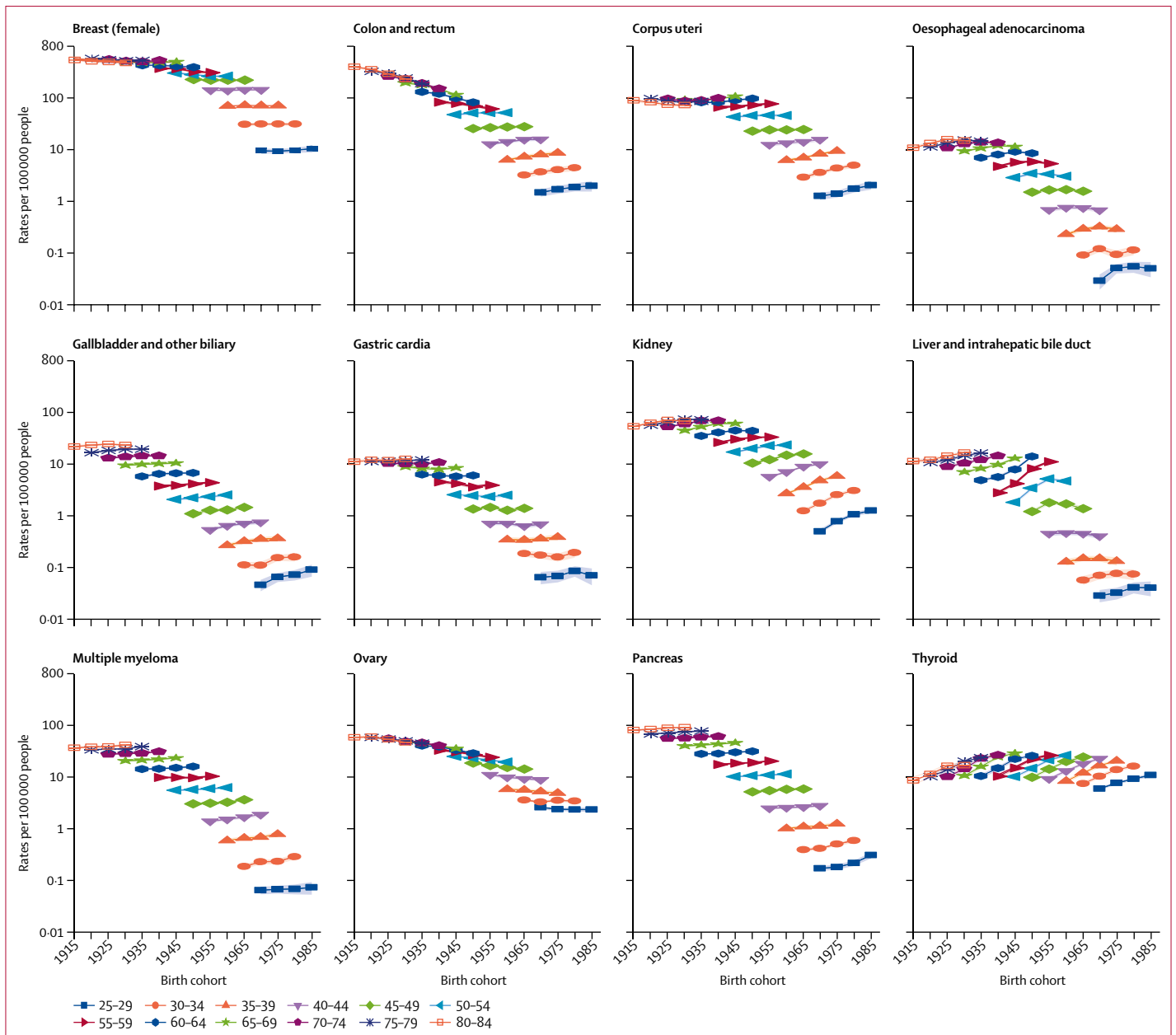


Figure 3: Age-specific incidence by birth cohort from 1915 (1910–19) to 1985 (1980–89) for 12 obesity-related cancers, 1995–2014

Dots denote observed incidence for 5-year age groups by 15 partly overlapping 10-year birth cohorts and shaded areas indicate 95% CIs of the corresponding fitted rates from the age-period-cohort models.

USA. Between 1980 and 2014, overweight or obesity prevalence in the USA increased by more than 100% (from 14.7% to 33.4%) among children and adolescents and by 60% among adults aged 20–74 years (from 48.5% to 78.2%).¹⁰

In adults aged 30 years and older in the USA, excess bodyweight could account for up to 60% of all endometrial cancers, 36% of gallbladder cancers, 33% of kidney cancers, 17% of pancreatic cancers, and 11% of multiple myelomas in 2014.¹¹ Because most epidemiological studies have primarily focused on older populations, the

effect of excess bodyweight in early life or of weight change from young adulthood on cancer risk in different stages of the life course is not well characterised.² Nevertheless, growing evidence supports an association between childhood or adolescent obesity and increased risk of colorectal, endometrial, and pancreatic cancers and multiple myeloma.¹² Adult weight gain has also been associated with several cancers, including those of the colorectum, endometrium, ovary, pancreas, and thyroid.¹² A recent study of data from 20 pooled prospective cohorts suggests that excess bodyweight during early adulthood

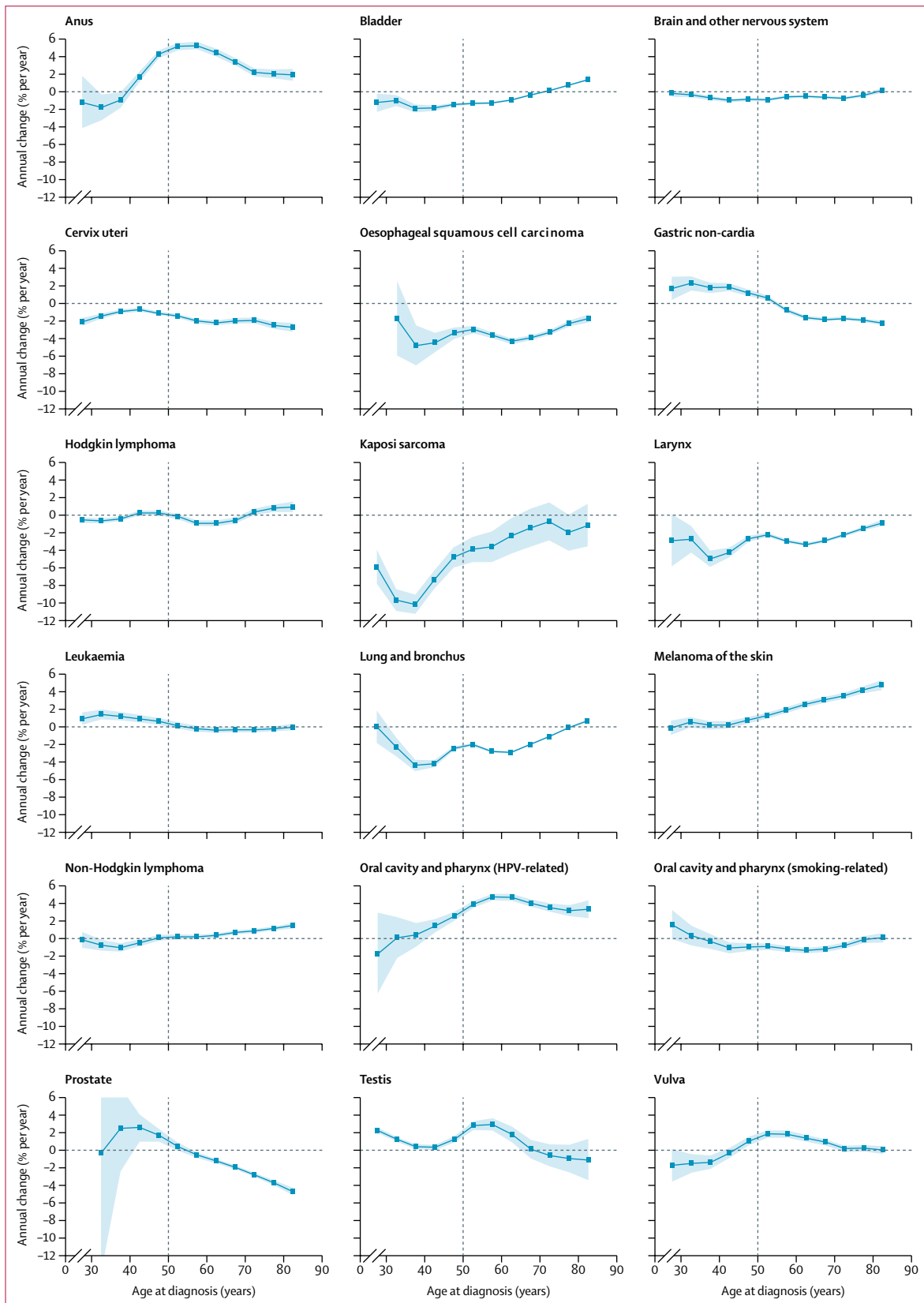


Figure 4: Age-specific annual percent change in incidence for 18 additional cancers, 1995–2014
 Dots and shaded areas represent the net annual percentage changes (% per year) and 95% CIs in incidence rates from the age-period-cohort models for 12 age groups (5-year increments from age 25 years). For oesophageal squamous cell carcinoma and prostate cancer, age group 25–29 years was excluded because of rarity of cases. HPV=human papillomavirus.

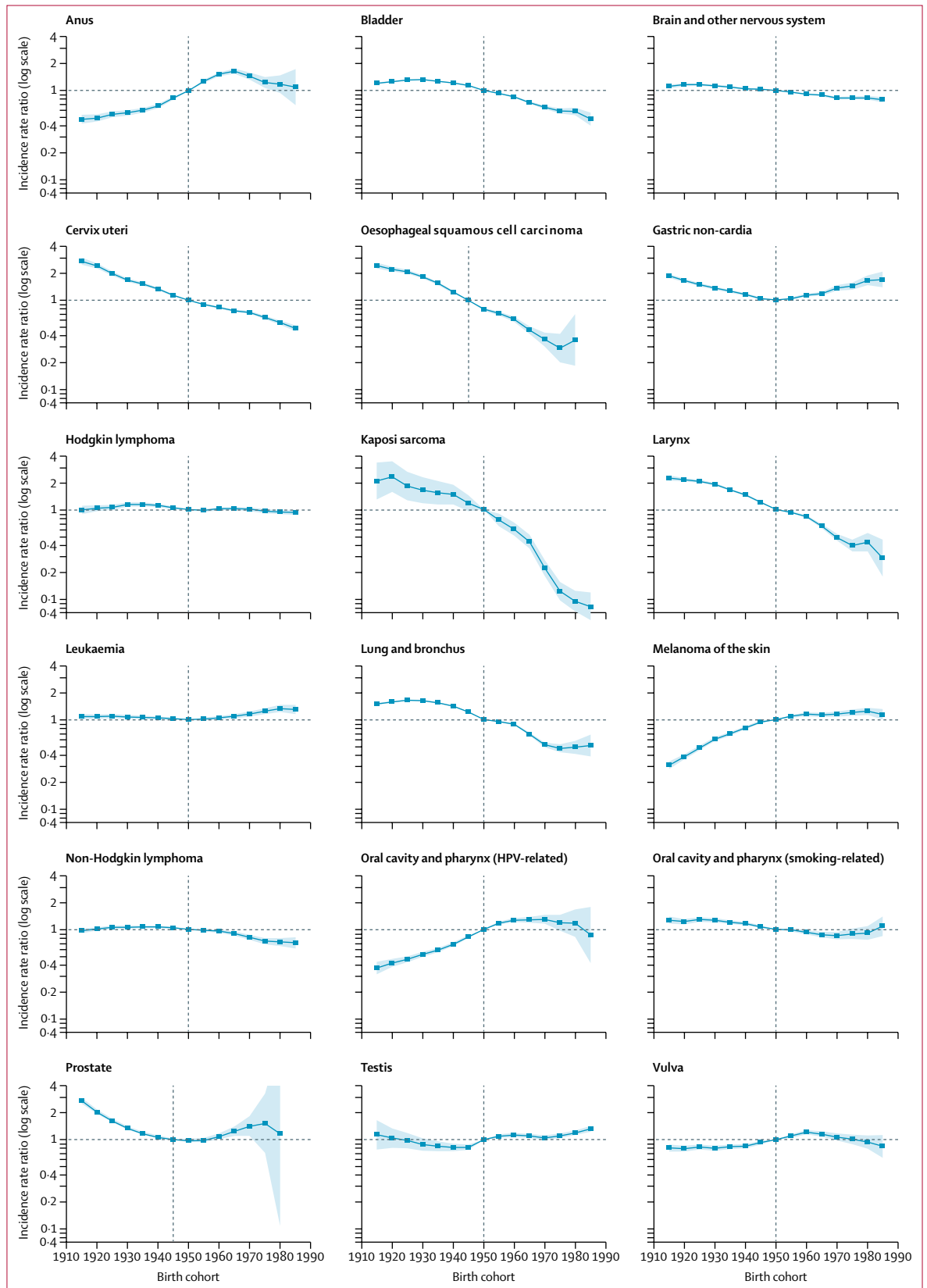


Figure 5: Incidence rate ratio by birth cohort from 1915 to 1985 for 18 additional cancers, USA, 1995–2014
 Dots and shaded areas represent incidence rate ratios and 95% CIs for a given birth cohort relative to the 1950 birth cohort (referent) for 15 partly overlapping 10-year birth cohorts. For oesophageal squamous cell carcinoma and prostate cancer, 1945 birth cohort served as the referent. HPV=human papillomavirus.

(ages 18–21 years) could be a more important influence on pancreatic cancer risk than weight gain later in life.¹³

Evidence from multiple murine models suggests that obesity and obesogenic diets can shift the development of cancer to younger age groups by promoting the rate of cancer progression, thereby reducing the length of latency.^{4,14} In mouse models, increased number and size of adipocytes have been shown to enhance mutation rates by generating reactive oxygen species and accelerating tumour growth by releasing proinflammatory cytokines and growth-promoting hormones and growth factors.¹⁴ Despite accumulating evidence from experimental studies, evidence from observational studies remains limited. In a recent population-based study, Chang and colleagues¹⁵ reported a faster rate of transformation from monoclonal gammopathy of undetermined significance to multiple myeloma among patients who are obese (median age 67 years) compared with individuals of normal weight (median age 75 years),¹⁵ supporting the hypothesis that obesity can contribute to a shortened latency period from benign to malignant disease. However, studies focusing on young adults are scarce, given the rarity of monoclonal gammopathy of undetermined significance, particularly among young adults.

In concert with excess bodyweight, obesity-related health conditions and lifestyle factors can contribute to the increasing burden of obesity-related cancers in young adults, which include diabetes, gallstones, inflammatory bowel disease, and poor diet. There is strong evidence for an association between type 2 diabetes and excess risk for cholangiocarcinoma and cancers of the colorectum, endometrium, liver, and pancreas.¹⁶ The incidence of diabetes has been increasing rapidly in children and young adults¹⁷ since the 1980s. Similarly, the prevalence of paediatric gallstones, the primary risk factor for gallbladder cancer in adults, has increased in the USA.¹⁸ An approximately linear relationship exists between bodyweight and gallstone development, suggesting that even moderate weight gain could be an important determinant of risk.¹⁹ The prevalence of inflammatory bowel disease, a risk factor for colorectal cancer, also increased in paediatric and adult populations in the USA from 2004–05 to 2008–09, although these data are based on commercially insured people in a limited geographical area.²⁰ Low intake of fruits or vegetables and high intake of red meat and processed meat are associated with increased risk of colorectal cancer.²¹ The quality of diet has worsened in recent decades among young adults in the USA,²² with more than half of adults aged 20–49 years in 2010–12 reporting poor dietary habits, characterised as low consumption of fruits and vegetables, whole grains, and fish and shellfish, and high consumption of sodium and sugar-sweetened beverages.²³

Given the similar set of risk factors for gastric cardia cancer and oesophageal adenocarcinoma, it is not clear why trends diverge with stable rates of gastric cardia cancer versus significant (older adults, 50–84 years) and

non-significant (young adults, 25–49 years) increases in oesophageal adenocarcinoma. A similar diverging trend was reported in the Netherlands, where the stable rates of gastric cardia cancer were explained by the presence of a subtype of gastric cardia cancer associated with *Helicobacter pylori* infection,²⁴ the prevalence of *H pylori* infection decreased. The steep increase in liver cancer incidence in middle-aged adults is largely attributed to the high prevalence of chronic hepatitis C virus infection in Americans born between 1946 and 1964 (so-called baby boomers) through sharing of contaminated needles among intravenous drug users in the 1960s–80s.²⁵ Although the rapid increase in thyroid cancer incidence has been attributed to overdiagnosis of small and indolent tumours, several studies have also shown an increase in advanced-stage papillary thyroid cancer,²⁶ suggesting the role of other factors including obesity. Rising obesity prevalence has probably attenuated declines in ovarian cancer attributed to the strong, long-lasting protective effect of oral contraceptives, which have been used widely since the 1960s.²⁷

Stable breast cancer incidence has been previously shown to reflect diverging trends of rising rates of oestrogen receptor-positive tumours and falling rates of oestrogen receptor-negative tumours.²⁸ The increase in incidence of oestrogen receptor-positive breast cancer in younger women in the USA is not consistent with the rising obesity trend as obesity is expected to decrease oestrogen-related breast cancers in premenopausal women. This finding suggests additional factors are in play, such as changes in reproductive factors and influence of detection practice as mammography detects oestrogen-positive tumours with greater propensity than oestrogen-negative tumours. Stratified analysis by race has shown increasing risk in successively younger birth cohorts in Asian people in contrast to stabilised trends in other races (appendix p 15, 21), which might in part reflect the distinct association of obesity with premenopausal breast cancer reported among Asian women.²⁹

In contrast to trends for obesity-related cancers, incidence of the additional cancers analysed in young adults decreased or were variable, except for gastric non-cardia cancer and leukaemia, which increased. Our findings are consistent with a previously reported increase in gastric non-cardia cancer among young adults and is thought to reflect, in part, increased prevalence of auto-immune or atrophic gastritis related to exposures to antibiotics and acid-suppressing drugs.³⁰ The stepwise increase in young adults for leukaemia was similar to that observed for some obesity-related cancers. Trends stratified by subtype were broadly similar in three major subtypes of leukaemia (appendix p 16, 22). Environmental factors known to be associated with increased risk of leukaemia include ionising radiation and some chemical carcinogens (eg, benzene or chemotherapy). Over the past decades, environmental and occupational benzene exposures have probably decreased because of reductions

in smoking and laws limiting benzene concentrations in gasoline and manufacturing.³¹ By contrast, exposure to chemotherapy drugs and ionising radiation via imaging and cancer treatment has increased.³² Although obesity is not an established risk factor for leukaemia, evidence from cohort studies showed that obesity is associated with increased risk of all major subtypes of leukaemia to varying degrees.³³ However, it remains unknown to what extent each of the known and suspected risk factors have contributed to the increasing trends in leukaemia among young adults. In addition to leukaemia, there is limited evidence for an association between obesity and one of the major histological subtypes of non-Hodgkin lymphoma, diffuse large B-cell lymphoma.⁷ However, diffuse large B-cell lymphoma decreased among young adults and increased among older adults (appendix p 17, 23).

The decline in risk of oesophageal squamous cell carcinoma and, lung, larynx, and bladder cancers in successive generations born since about 1950 is largely due to decreases in smoking initiation and increased smoking cessation, while the decline in risk of Kaposi sarcoma reflects the wide dissemination of antiretroviral therapy since 1996. For non-cervical HPV-related cancers (eg, oropharynx, anus, or vulva), risk increased among the 1960s and 1970s birth cohorts and stabilised or declined in younger cohorts. Favourable patterns in the most recent birth cohort could be due to increased awareness of sexually transmitted diseases and safer sexual practices.³⁴ By contrast with other HPV-related cancers, cervical cancer risk continued to decrease across generations, reflecting decades of high screening prevalence and successful treatment of pre-cancerous lesions.

Our finding of increasing incidence in younger generations for some obesity-related cancers has significant practical public health implications, especially for health-care providers and policy makers. Despite national guidelines recommending screening of children and adults for obesity with appropriate provision of (or referral to) “intensive, multicomponent behavioral interventions,” fewer than half of primary care physicians regularly assess body-mass index in their patients, and only a third of obese patients report receiving an obesity diagnosis or weight loss counselling.³⁵ Similarly, community-level regulatory interventions such as urban planning for promoting physical activity, taxes on sugar-sweetened beverages, and restriction of advertising for calorie-dense food and soft drinks have yet to be implemented broadly, despite growing empirical evidence for their effectiveness.³⁶

The strengths of our study are the use of high-quality population-based incidence information covering 67% of the US population and use of a systematic approach of age-period-cohort modelling for a comprehensive list of cancers in young adults. This approach allowed us to identify emerging incidence trends in young generations for multiple obesity-related cancers.

However, several limitations of our study should be noted. First, interpretation of our findings is somewhat limited by the assumptions of age-period-cohort modelling, particularly in that interactions between age and period can be described as birth cohort effects. Nevertheless, observed age-specific rates by birth cohort fell within the 95% CIs of the fitted rates, suggesting the model fits the observed rates well (figure 3; appendix pp 18–20). Second, we could not directly assess and quantify the effect of obesity (and other risk factors) or mode of detection (eg, diagnostic imaging, screening, or clinical manifestation) on the emerging incidence trends in young generations because information on these variables is absent in the Cancer in North America database. Although screening is not generally recommended for young adults, early detection and increased use of highly sensitive diagnostic imaging tests in routine medical practice could have influenced increases in rates for some cancers (eg, kidney cancer). Nevertheless, the increase in kidney cancer was greater in younger adults (2.95–6.23% per year in individuals aged 25–49 years) than older adults (1.67–2.19% per year in individuals aged 50–84 years), despite a lower likelihood of imaging use in younger adults. For those cancers with emerging trends among young adults, examination of temporal variations in stage at diagnosis might help disentangle the effect of early detection. Third, because of the descriptive and ecological nature of our study, our findings can help establish hypotheses about the relationship between the obesity epidemic and early onset cancer, but do not provide information for a causal relationship. Fourth, our results presenting aggregated incidence might conceal variations in cancer rates in subpopulations by sex and race or ethnicity, which are of interest for future studies. Finally, the IRR by birth cohort for cancers of the corpus uteri, cervix, and ovary were estimated without correction for hysterectomy prevalence, which would probably affect rates particularly among older women (>50 years),³⁷ and correspondingly among birth cohorts born before 1960. Therefore, the IRRs for younger birth cohorts relative to birth cohort born around 1950 could have been overestimated. However, the continuous stepwise increase (corpus uteri) or decrease (ovary and cervix) in IRRs in successively younger birth cohorts born since 1970, among whom hysterectomy rates are generally similar,³⁷ do not reflect differences in hysterectomy rates.

Given the large increase in the prevalence of overweight and obesity among young people and increasing risks of obesity-related cancers in contemporary birth cohorts, the future burden of these cancers might be exacerbated as younger cohorts age, potentially halting or reversing the progress achieved in reducing cancer mortality over the past several decades. Future aetiological studies focusing on modifiable risk factors in early life and adult cancer risk are needed to elucidate exposures responsible for these emerging trends, including excess bodyweight and other risk factors.

Contributors

HS and AJ designed the study, HS and PSR analysed the data. All authors contributed to interpretation of the data and wrote the manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The database “NAACCR Incidence Data—Cancer in Northern America Analytic File, 1995–2014, Public Use” is a non-confidential and publicly accessible data set obtained with a signed Data Use Agreement and distributed through SEER*Stat 8.3.4.

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