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Associations between BMI in youth and site-specific cancer in men—A cohort study with register linkage

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Abstract

Objective: This study examined BMI in young men and incident site-specific cancer to estimate population attributable fractions due to BMI based on projected obesity prevalence.

Methods: A population-based cohort study with measured height and weight at age 18. Cox regression models assessed linear associations for BMI and included age, year, and site of conscription as well as parental level of education as covariates.

Results: Primary analyses were performed in 1,489,115 men, of whom 78,217 subsequently developed cancer during a mean follow-up of 31 years. BMI was linearly associated with risk of developing all 18 site-specific cancers assessed (malignant melanoma; leukemia; myeloma; Hodgkin lymphoma; non-Hodgkin lymphoma; and cancer in the lungs, head and neck, central nervous system, thyroid, esophagus, stomach, pancreas, liver and gallbladder, colon, rectum, kidney, and bladder), in some instances evident at BMI levels usually defined as normal (20–25 kg/m^2). Higher BMI was associated with lower risk of prostate cancer. The highest hazard ratios and population attributable fractions were seen for some gastrointestinal cancers.

Conclusions: This study reports linear associations between BMI at age 18 and subsequent site-specific cancers, calling for rapid action to stem the obesity epidemic and to prepare the health care system for steep increases in cancer cases.

INTRODUCTION

Obesity in adulthood is an established risk factor for cancer in the esophagus, gastric cardia, colon and rectum, liver, gallbladder, pancreas, kidney, and thyroid as well as for multiple myeloma in men according to the International Agency on Research on Cancer (IARC) [1]. Reports on the association between overweight or obesity in youth and future cancer risk are scarcer. A recent study on body mass index (BMI) in youth confirmed several of the associations reported for adults and added associations between BMI in youth and cancers in the oral cavity, thyroid, and male breast as well as with Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, and melanoma [2].

High BMI early in life has been proposed to have a stronger association with development of cancer in adulthood than obesity developed later in life [2]. This would imply that the current obesity epidemic that has already resulted in many millions of children, adolescents, and young adults with overweight or obesity [3] will lead to a drastic increase in several types of cancer for decades to come even if the course of the epidemic could be changed. Physical activity (PA) has protective effects for several site-specific cancers through improving cardiorespiratory fitness (CRF) [4–6]. Because of the inverse association between PA and BMI [4], some of the associations between BMI and site-specific cancers may be confounded by CRF.

The first aim was to examine the associations between BMI and future incidence of site-specific cancer in a large cohort of young men, adjusting for CRF. The second aim was to estimate cancer site-specific population attributable fractions (PAFs) of overweight and obesity in youth, based on current and past prevalences of youth overweight and obesity in Sweden and the United States.

Study Importance

What is already known?

- In men, obesity is an established risk factor for cancer in the esophagus, gastric cardia, colon and rectum, liver, gallbladder, pancreas, kidney, and thyroid and for multiple myeloma.
- In contrast, the evidence is weaker in adolescents and young adults, although generally consistent with associations in older adults, according to the International Agency for Research on Cancer.

What does this study add?

- We provide effect sizes for associations between BMI in youth and site-specific cancers from a population-based sample of 1.5 million men and can report linear associations between BMI and leukemia; myeloma; Hodgkin lymphoma; non-Hodgkin lymphoma; and cancer in the lungs, central nervous system, and urinary bladder.
- The uniform age at BMI assessment and the extended follow-up period allowed us to provide projections of attributable fractions accounting for the global obesity epidemic.

How might these results change the direction of research or the focus of clinical practice?

- If current obesity trends continue, our findings provide additional support for rapid action to stem the course of the obesity epidemic and, with a large prevalence of youth overweight and obesity already in existence, to prepare the health care system for a steeply increasing number of cancer cases.

METHODS

Design

This is a Swedish nationwide, register-based, observational cohort study with prospective data. Ethical permission for conducting the study was obtained on November 16, 2021, from the Swedish Ethical Review Authority, EPN Dnr 462-14 with addendums Dnr 2021-05638-02 and 2023-04937-02. Because data were retrieved from registers, no consent was obtained from individuals included in the study. All men who underwent the conscription examination between 1968 and 2005 at ages from 16 to 25 years were included. Exclusion criteria were a cancer diagnosis before or within 5 years after the military conscription and death or emigration within 5 years after conscription.

Data sources

Conscripts were identified in the Swedish military service conscription register. Until 2010, conscription was compulsory by law for all male citizens, except for imprisoned individuals or those with severe chronic conditions or functional disabilities [7]. Data from conscription were linked on the person level with sociodemographic data from Statistics Sweden, the Swedish national patient register [8], and the Swedish cause of death register [9].

Exposure

Height was measured using a stadiometer and weight with weight scales by a licensed nurse, and BMI was calculated as kilograms/meters squared [7]. It was categorized into underweight (<18.5 kg/m^2), overweight (25–29.9), and obesity (≥30). Although the World Health Organization defines 18.5 to 25 as normal, this concept is derived from middle-aged people. From previous studies in this and other cohorts on

BMI and cardiovascular disease and mortality, it has been shown that the risk increase starts below BMI 25 for BMI assessed in youth [10, 11]. Hence, we categorized normal weight into three categories (18.5–19.9, 20.0–22.4, and 22.5–24.9) and used the lowest normal weight category as reference in the analyses.

Outcome

Information on a cancer diagnosis was collected from the Swedish national patient register and the cause of death register. Eighteen types of site-specific cancers were defined according to International Classification of Diseases 8/9/10 codes (Table S1). The first time a relevant cancer diagnosis was registered during an inpatient or outpatient visit was used as diagnosis date. With some exceptions, diagnoses of different subtypes were treated independently. For tumors in the lungs, central nervous system (CNS), and liver, only diagnoses without any other preceding cancer diagnosis were registered to reduce to risk for misclassification of metastatic cancer.

Covariates

Information on CRF at conscription was assessed as maximal aerobic workload on a cycle ergometer test in Watt max [7]. Two test procedures were used for muscle strength, previously described in detail [7]. Parental level of education was collected from Statistics Sweden and categorized according to highest level attained by either parent: up to 9 years of compulsory school, high school to ≤2 years at university, or ≥3 years at university. Cognitive testing was measured in different ways over the years, although a low score was never a criterion for avoiding conscription. The test consisted of four domains, initially including verbal, spatial, inductive logic, and technical ability [7]. In 1968 to 1970 and 2002 to 2005, questions on smoking were included in the conscription procedures. These were categorized into the following: no active smoking, 1 to 10 cigarettes or equivalent per day, and >10 cigarettes or equivalent per day.

Statistical methods

A statistical analysis plan was specified before any statistical analyses were performed (supplementary material). No sample size calculation was performed. Cox proportional hazards models were used with follow-up starting at conscription and continuing until a registered cancer diagnosis, date of death, first emigration after conscription, or end of follow-up (December 31, 2019). The main analyses assessed linear associations between BMI and site-specific cancer, with additional analyses of categorized BMI for interpretation of the effect sizes. The proportional hazards assumption was checked graphically for categorical predictors. Results were given in terms of hazard ratios (HR) with 95% confidence intervals. The main analysis included the following covariates, as deemed relevant according to a directed acyclic graph: year, site, age, and parental education level at conscription. We also assessed results in unadjusted models (Table S2). Missing values lead to listwise deletion. All significance tests were two-sided with a 5% significance level and performed in STATA/SE software (17.0).

There were two prespecified sensitivity analyses. In the first, we assessed confounding by CRF. In the second, we assessed how smoking could confound the results. Associations were assessed between BMI (dichotomized into underweight/normal weight vs. overweight/obesity) and site-specific cancer in the subpopulation for which smoking information was available ($n = 24{,}505$) with and without smoking at baseline as covariate. We also tested models including interaction terms between CRF and BMI categories with likelihood ratio testing of the interaction terms. Ad hoc sensitivity analyses were performed to see how adding cognitive ability as covariates changed the estimates.

PAFs were calculated for overweight and obesity for each site-specific cancer with linearly increased risk for cancer with increasing BMI. We used this equation for multicategorical exposures [12]:

$$\mathrm{PAF} = \frac{\sum_{i=1}^{n} p_i \mathrm{RR}_i - 1}{\sum_{i=1}^{n} p_i \mathrm{RR}_i}$$

We wanted to illustrate the expected change in PAF with increasing proportions of youth overweight and obesity in Sweden as well to illustrate it for a country with considerably higher prevalence of youth overweight and obesity. Hence, the proportions of 19-year-old men with overweight and obesity in Sweden and the United States in 1989 and 2016 were used [3] (Table S3). With a mean time of 34 years between the BMI assessment at age 18 and the cancer diagnosis in our study (Table S3), the distributions in 1989 correlate to cancers occurring in 2023, whereas the distribution in 2016 corresponds to cancers occurring in 2050.

We used restricted cubic splines with four knots in combination with Cox proportional hazard regression. To this end, we applied the STATA subroutines rcsgen and partpred [13]. BMI = 20 was chosen as reference value, which corresponds to the upper limit of the reference interval in Table 3. To reduce the influence of outliers, BMI values were restricted to the interval 15 to 35.

RESULTS

After exclusions, 1,665,224 individuals were included in the study population (Figure 1) and 1,489,115 could be included in the primary analyses. Mean age at conscription was 18 years and mean BMI was 21.9, with 2.3% with BMI ≥ 30. Obesity increased gradually over time, from 1.1% in 1968 to 1979 to 3.6% in 1990 to 2005, and the change in prevalence corresponded to a decreasing prevalence of BMI < 20,

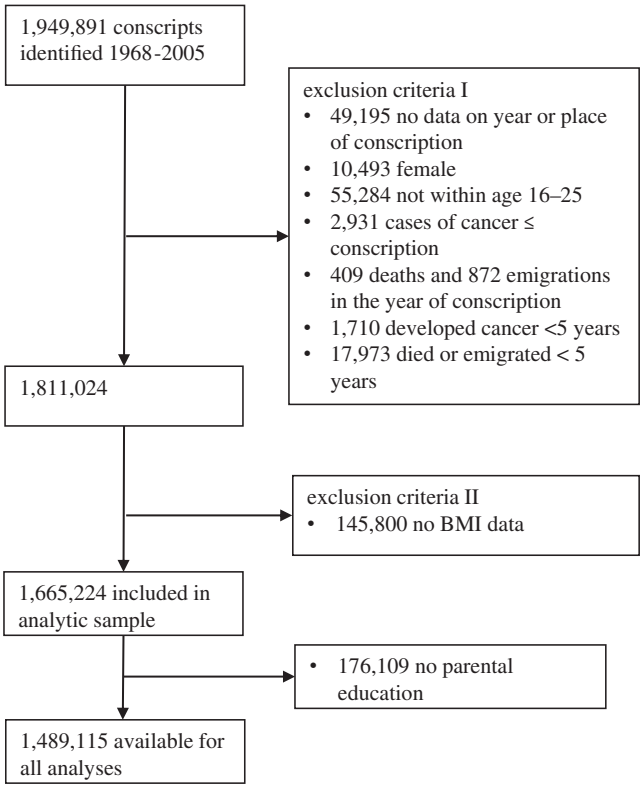

FIGURE 1 Flowchart of individuals included in the study.

an increasing prevalence of BMI ≥ 25, and a relatively consistent prevalence of BMI from 20 to 24.9 (Table S3). Mean follow-up time was 31 years with mean age at cancer diagnosis varying between 39 years for Hodgkin lymphoma and 59 years for prostate cancer (Table S4). Men across BMI categories were similar in terms of age, height, and prevalence of diabetes, kidney disease, and alcohol abuse at conscription (Table 1). Men with obesity were more likely to have lower cognitive ability and hypertension and their parents were slightly less likely to have higher education. Men with underweight and with obesity had lower CRF than their peers with normal weight.

In 1968 to 1970 ($n = 24{,}505$), 58% reported any current smoking (Table 1). The proportion of smokers was similar in men with normal weight and overweight whereas men with underweight and obesity were more likely to smoke, with the highest proportion of men smoking >10 cigarettes per day seen in those with obesity (38%). In 2002 to 2005, only 10% of conscripts reported any current smoking, with only 2% reporting smoking >10 cigarettes per day (Table 1). Table S4 shows the absolute number of events.

Malignant melanoma

There was a linear association between BMI and increasing risk of being diagnosed with malignant melanoma (Tables 2 and 3). This did not seem to be confounded by smoking (Table S5).

Bronchi and lungs

In the primary analysis, there was no linear association between BMI and the risk of lung cancer (Table 2). This was explained by a u-shaped association, with higher risk in underweight men as well as in those with obesity, Table 2. Adjusting for CRF removed the risk increase for underweight men with less pronounced changes for men with overweight and obesity (Table 3), and the linear analysis was now borderline significant. Although smoking was strongly associated with lung cancer, the estimates for overweight/obesity remained similar with and without adjusting for smoking (Table S5).

Head and neck

There was a linear association between BMI and the risk of developing head and neck cancer (Table 2), with risk increases starting above BMI 20 (Table 3). Adjusting for smoking (Table S5) did not change the results.

CNS

There was a weak linear association between BMI and CNS tumors (Table 2), with low risk increases with increasing BMI (Table 3). A borderline linear association was seen in analyses adjusted for CRF (Table 3). The effect sizes were the same before and after adjusting for both CRF and cognitive ability, and the loss of associations seemed to be due to a smaller sample size in those analyses and not due to confounding by these variables. Sensitivity analyses adjusted for smoking were not possible to perform due to too few events.

Thyroid gland

There was a linear association between BMI and the risk of developing thyroid cancer (Table 2). Adjusting for smoking did not change the results (Table S5).

Gastrointestinal cancer

There were strong linear associations between BMI and cancer in the esophagus, stomach, pancreas, liver and gallbladder, colon, and rectum in the fully adjusted models including CRF (Table 3). For most of the cancer sites, there were relatively large risk increases starting above BMI 20. No tendency for confounding by smoking was seen for any of the associations (Table S5).

Urological cancer

There was a linear protective association between BMI and the risk of being diagnosed with prostate cancer (Table 2). Conversely, there

TABLE 1 Baseline demographics at conscription by BMI level

Characteristic	BMI < 18.5 (n = 129,584)	BMI 18.5–19.9 (n = 297,820)	BMI 20.0–22.4 (n = 665,649)	BMI 22.5–24.9 (n = 364,312)	BMI 25.0–29.9 (n = 169,551)	BMI ≥ 30.0 (n = 38,308)	Overall (n = 1,665,224)
Year for conscription, mean (SD)	1984 (10)	1984 (10)	1986 (10)	1987 (10)	1989 (10)	1991 (10)	1986 (10)
Age at conscription, mean (SD)	18.3 (0.6)	18.3 (0.6)	18.3 (0.6)	18.3 (0.7)	18.3 (0.8)	18.3 (0.8)	18.3 (0.7)
Years of follow-up, mean (SD)	33.2 (10.9)	32.5 (10.6)	31.3 (10.5)	29.9 (10.4)	28.6 (10.2)	26.4 (9.6)	31.0 (10.6)
Height, mean (SD) (cm)	180 (7)	179 (7)	179 (7)	179 (7)	179 (7)	179 (7)	179 (7)
BMI, mean (SD)	17.6 (0.7)	19.3 (0.4)	21.2 (0.7)	23.5 (0.7)	26.7 (1.3)	33.0 (3.0)	21.9 (3.1)
Cardiorespiratory fitness, *n* (%)							
Low	49,134 (53)	80,926 (36)	118,852 (23)	60,292 (22)	44,332 (39)	12,338 (66)	365,874 (30)
Moderate	36,717 (40)	102,673 (46)	221,043 (44)	112,058 (42)	43,086 (38)	4075 (22)	519,652 (42)
High	6416 (7)	41,113 (18)	167,978 (33)	97,286 (36)	25,835 (23)	2324 (12)	340,952 (28)
Missing	37,317 (29)	73,108 (25)	157,776 (24%)	94,676 (26%)	56,298 (33)	19,571 (51)	438,746 (26)
Systolic blood pressure, mean (SD)	126 (11)	127 (11)	128 (11)	130 (11)	132 (11)	134 (11)	129 (11)
Missing, *n* (%)	7459 (6)	12,414 (4)	28,512 (4)	18,356 (5)	11,485 (7)	5859 (15)	84,085 (5)
Diastolic blood pressure, mean (SD)	67 (10)	67 (10)	67 10)	68 (10)	69 (10)	71 (11)	68 (10)
Missing, *n* (%)	7554 (6)	12,641 (4)	29,063 (4)	18,628 (5)	11,598 (7)	5881 (15)	85,365 (5)
Diabetes mellitus, *n* (%)	71 (0.05)	160 (0.05)	471 (0.07)	305 (0.08)	122 (0.07)	24 (0.06)	1153 (0.07)
Hypertension, *n* (%)	98 (0.08)	232 (0.08)	783 (0.12)	622 (0.17)	571 (0.34)	312 (0.81)	2618 (0.16)
Cardiovascular disease, *n* (%)	3968 (3.06)	7957 (2.67)	16,220 (2.44)	7973 (2.19)	3380 (1.99)	837 (2.18)	40,335 (2.42)
Kidney disease, *n* (%)	143 (0.11)	324 (0.11)	633 (0.10)	347 (0.10)	165 (0.10)	46 (0.12)	1658 (0.10)
Alcohol abuse, *n* (%)	229 (0.18)	617 (0.21)	1194 (0.18)	696 (0.19)	331 (0.20)	67 (0.17)	3134 (0.19)
Substance abuse, *n* (%)	657 (0.51)	1186 (0.40)	1886 (0.28)	681 (0.19)	256 (0.15)	48 (0.13)	4714 (0.28)
Cognitive ability, mean (SD)	5.2 (2.0)	5.3 (1.9)	5.3 (1.9)	5.2 (1.9)	4.9 (1.9)	4.6 (1.9)	5.2 (1.9)
Missing, *n* (%)	52,306 (40)	104,105 (35)	218,563 (33)	123,273 (34)	68,263 (40)	21,672 (57)	588,182 (35)
Parental education, *n* (%)							
Compulsory school	31,792 (29)	69,204 (26)	147,354 (25)	79,492 (24)	39,327 (25)	9087 (26)	376,256 (25)
High school to ≤2 years university	61,207 (55)	145,353 (56)	336,409 (57)	193,491 (58)	93,962 (61)	22,575 (64)	852,997 (57)
>2 years university	18,229 (16)	46,910 (18)	111,489 (19)	57,865 (17)	21,619 (14)	3750 (11)	259,862 (17)
Missing	18,356 (14)	36,353 (12)	70,397 (11)	33,464 (9)	14,643 (9)	2896 (8)	176,109 (11)
Smoking 1968–1970, *n* (%)	3548	6089	9679	3638	1369	182	24,505
No active smoking	1295 (37)	2249 (37)	3986 (41)	1583 (44)	563 (41)	60 (33)	9736 (40)
Smoking 1–10 cigarettes	1258 (35)	2084 (34)	3065 (32)	1005 (28)	373 (27)	49 (27)	7834 (32)
Smoking >10 cigarettes	920 (26)	1626 (27)	2427 (25)	969 (27)	392 (29)	70 (38)	6404 (26)
Not answered	75 (2)	130 (2)	201 (2)	81 (2)	41 (3)	3 (2)	531 (2)

(Continues)

TABLE 1 (Continued)

Characteristic	BMI < 18.5 (n = 129,584)	BMI 18.5–19.9 (n = 297,820)	BMI 20.0–22.4 (n = 665,649)	BMI 22.5–24.9 (n = 364,312)	BMI 25.0–29.9 (n = 169,551)	BMI ≥ 30.0 (n = 38,308)	Overall (n = 1,665,224)
Smoking 2002–2005, *n* (%)	5872	14,055	38,042	28,310	17,522	5393	109,194
No active smoking	5076 (86)	12,439 (89)	34,276 (90)	25,890 (91)	15,552 (89)	4541 (84)	97,774 (90)
Smoking 1–10 cigarettes	589 (10)	1244 (9)	2970 (8)	1926 (7)	1530 (9)	590 (11)	8849 (8)
Smoking >10 cigarettes	207 (4)	372 (3)	796 (2)	494 (2)	440 (3)	262 (5)	2571 (2)

were linear associations between increasing BMI and a higher risk of developing cancer in the kidney. For bladder cancer, there was a relatively weak linear association in the full cohort (Table 2), not reaching statistical significance in the cohort restricted to having information on CRF (Table 3). No confounding was seen for smoking (Table S5).

Hematological malignancies

There were linear associations between BMI and all hematological malignancies (Table 2), with increasing risk for leukemia, myeloma, Hodgkin lymphoma, and non-Hodgkin lymphoma. Significant risk increases were seen from BMI 22.5. No confounding by smoking was seen for Hodgkin or non-Hodgkin lymphomas, whereas it could not be analyzed for leukemia or myeloma due to few events in the cohort with information on smoking (Table S5).

Sensitivity analysis for smoking

Adjusting for smoking had no or very little effect on the estimates (Table 3). Smoking was associated with a lower risk of malignant melanoma and prostate cancer and a higher risk of cancer in the lungs, head and neck, esophagus, stomach, pancreas, liver and gallbladder, and urinary bladder and a higher risk of non-Hodgkin lymphoma and any cancer.

Adjusting for CRF

In the linear analyses, adjusting for CRF had minor effects on the associations, with strengthened associations between BMI and the risk of developing cancer in the lungs and bladder (Table 3). This was explained by the effect sizes for underweight going toward protective associations. The most pronounced confounding by CRF for underweight men was seen for lung cancer after adjusting for CRF (Table 3). Adjusting for CRF also increased the HRs for overweight and obesity for many cancer sites, especially gastrointestinal cancers. This is probably explained by the reference population having a relatively low CRF (Table 1) and low CRF being an independent risk factor for many of the site-specific cancers [5]. Hence, the unadjusted analyses shown in Table 1 underestimate the effect size of body fat due to confounding by low CRF for the reference category. Therefore, the results adjusted for CRF are more appropriate, and we calculated PAF based on these HRs.

Table S6 shows analyses stratified by CRF status at conscription. These show that although higher BMI was associated with higher risk for cancers both in men with low and moderate/high CRF, the higher risk with BMI > 25 was more pronounced in men with low fitness for cancer in the head and neck, esophagus, stomach, liver, colon, kidney, and urinary bladder as well as for Hodgkin lymphoma. For urinary bladder cancer, the association with higher BMI was only true in men with low CRF and not for men with moderate/high CRF.

TABLE 2 HRs for BMI at conscription and incidence of cancer ($n = 1{,}489{,}115$)

Cancer site	*n* cases	BMI < 18.5, HR (95% CI)	BMI 20.0–22.4, HR (95% CI)	BMI 22.5–24.9, HR (95% CI)	BMI 25.0–29.9, HR (95% CI)	BMI ≥30.0, HR (95% CI)	Linear analysis[a]	
							HR (95% CI)	*p*
Malignant melanoma	8102	0.87 (0.79–0.96)	1.08 (1.02–1.15)	1.21 (1.13–1.30)	1.20 (1.10–1.31)	0.96 (0.79–1.16)	1.02 (1.02–1.03)	<0.001
Bronchi and lung	2000	1.19 (1.02–1.38)	0.79 (0.70–0.89)	0.86 (0.75–0.98)	0.92 (0.76–1.10)	1.67 (1.23–2.28)	0.99 (0.98–1.01)	0.51
Head & neck	3283	1.05 (0.91–1.21)	1.07 (0.97–1.18)	1.14 (1.02–1.27)	1.18 (1.02–1.35)	1.34 (1.02–1.76)	1.02 (1.01–1.03)	0.001
Central nervous system	2537	0.96 (0.81–1.14)	1.06 (0.95–1.19)	1.10 (0.98–1.25)	1.14 (0.98–1.33)	1.11 (0.83–1.50)	1.02 (1.00–1.03)	0.02
Thyroid gland	851	0.73 (0.53–1.00)	0.97 (0.80–1.17)	1.06 (0.86–1.31)	1.03 (0.79–1.35)	1.47 (0.95–2.27)	1.03 (1.01–1.05)	0.01
Gastrointestinal cancers								
Esophagus	835	1.17 (0.87–1.56)	1.27 (1.04–1.56)	1.49 (1.19–1.87)	2.36 (1.82–3.05)	3.61 (2.36–5.52)	1.09 (1.06–1.11)	<0.001
Stomach	1072	1.10 (0.85–1.42)	1.21 (1.01–1.45)	1.34 (1.10–1.64)	2.17 (1.74–2.72)	3.13 (2.16–4.54)	1.08 (1.06–1.10)	<0.001
Pancreas	1538	1.19 (0.98–1.46)	1.12 (0.97–1.30)	1.35 (1.15–1.58)	1.70 (1.40–2.06)	1.85 (1.26–2.71)	1.05 (1.03–1.07)	<0.001
Liver, bile ducts, and gallbladder	1401	1.14 (0.93–1.41)	1.08 (0.93–1.26)	1.14 (0.96–1.35)	1.53 (1.25–1.88)	1.93 (1.34–2.79)	1.04 (1.02–1.06)	<0.001
Colon	3917	1.05 (0.93–1.19)	1.01 (0.92–1.10)	1.06 (0.96–1.17)	1.31 (1.15–1.48)	1.62 (1.29–2.03)	1.03 (1.02–1.04)	<0.001
Rectum	2811	1.05 (0.91–1.22)	1.04 (0.94–1.16)	1.04 (0.93–1.17)	1.15 (0.99–1.34)	1.65 (1.26–2.16)	1.02 (1.01–1.03)	0.003
Urological cancers								
Prostate	16,313	0.94 (0.89–1.00)	1.03 (0.99–1.08)	0.99 (0.94–1.04)	0.91 (0.85–0.97)	0.59 (0.49–0.72)	0.99 (0.98–1.00)	<0.001
Kidney	2138	1.07 (0.89–1.28)	1.17 (1.03–1.32)	1.38 (1.20–1.59)	1.92 (1.63–2.25)	2.60 (1.98–3.43)	1.08 (1.06–1.09)	<0.001
Bladder	2715	1.03 (0.89–1.20)	1.01 (0.92–1.13)	1.10 (0.98–1.24)	1.15 (0.98–1.34)	1.48 (1.09–1.99)	1.02 (1.00–1.03)	0.02
Hematological cancers								
Leukemia	2498	0.96 (0.81–1.14)	1.11 (0.99–1.24)	1.22 (1.07–1.38)	1.38 (1.18–1.61)	1.53 (1.15–2.04)	1.04 (1.03–1.05)	<0.001
Myeloma	1081	0.84 (0.65–1.10)	1.14 (0.96–1.35)	1.41 (1.17–1.70)	1.22 (0.95–1.57)	1.48 (0.91–2.41)	1.04 (1.02–1.06)	<0.001
Hodgkin lymphoma	1155	1.06 (0.82–1.37)	1.02 (0.86–1.21)	1.24 (1.03–1.49)	1.53 (1.23–1.90)	1.50 (1.04–2.19)	1.04 (1.02–1.06)	<0.001
Non-Hodgkin lymphoma	3178	0.98 (0.84–1.14)	1.12 (1.02–1.24)	1.19 (1.06–1.33)	1.26 (1.09–1.45)	1.81 (1.43–2.28)	1.04 (1.02–1.05)	<0.001

Note: Adjusted for year, site, age, BMI, and parental education at conscription. Reference is BMI 18.5–19.9.

Abbreviation: HR, hazard ratio.

[a]Linear trends tested continuous BMI.

TABLE 3 HRs for BMI at conscription and incidence of cancer, unadjusted and adjusted for cardiorespiratory fitness in population with information on CRF (n = 1,078,000)

Cancer site	*n* cases	BMI < 18.5, HR (95% CI)	BMI 20.0–22.4, HR (95% CI)	BMI 22.5–24.9, HR (95% CI)	BMI 25.0–29.9, HR (95% CI)	BMI ≥ 30.0, HR (95% CI)	Linear analysis[a]	
							HR (95% CI)	*p*
Malignant melanoma	6681	0.90 (0.81–1.00)	1.11 (1.04–1.19)	1.24 (1.15–1.34)	1.26 (1.15–1.39)	0.96 (0.75–1.22)	1.03 (1.02–1.04)	<0.001
Adjusted for CRF		0.96 (0.86–1.08)	1.05 (0.98–1.13)	1.15 (1.06–1.24)	1.21 (1.10–1.34)	0.99 (0.7–1.26)	1.02 (1.01–1.03)	<0.001
Bronchi and lung	1635	1.17 (0.99–1.39)	0.77 (0.68–0.87)	0.82 (0.71–0.96)	0.91 (0.75–1.12)	1.63 (1.13–2.37)	0.99 (0.97–1.01)	0.36
Adjusted for CRF		1.04 (0.88–1.23)	0.86 (0.75–0.98)	0.97 (0.83–1.14)	1.04 (0.85–1.28)	1.71 (1.18–2.48)	1.02 (1.00–1.04)	0.05
Head & neck	2738	1.13 (0.97–1.31)	1.12 (1.01–1.24)	1.21 (1.08–1.37)	1.27 (1.09–1.48)	1.30 (0.92–1.84)	1.02 (1.01–1.04)	0.001
Adjusted for CRF		1.07 (0.92–1.25)	1.17 (1.05–1.30)	1.30 (1.15–1.47)	1.33 (1.13–1.55)	1.30 (0.92–1.83)	1.03 (1.02–1.04)	<0.001
Central nervous system	2014	0.93 (0.76–1.12)	1.05 (0.93–1.19)	1.11 (0.97–1.27)	1.09 (0.91–1.31)	1.03 (0.69–1.54)	1.02 (1.00–1.03)	0.05
Adjusted for CRF		0.92 (0.76–1.12)	1.05 (0.93–1.19)	1.11 (0.97–1.28)	1.10 (0.91–1.31)	1.03 (0.69–1.54)	1.02 (1.00–1.03)	0.05
Thyroid gland	685	0.76 (0.53–1.09)	1.07 (0.87–1.33)	1.18 (0.93–1.49)	1.17 (0.86–1.59)	1.87 (1.11–3.17)	1.05 (1.02–1.07)	<0.001
Adjusted for CRF		0.75 (0.52–1.09)	1.08 (0.87–1.34)	1.19 (0.93–1.51)	1.18 (0.87–1.60)	1.86 (1.10–3.15)	1.05 (1.02–1.07)	<0.001
Gastrointestinal cancers								
Esophagus	689	1.14 (0.83–1.58)	1.25 (1.00–1.56)	1.57 (1.23–2.01)	2.40 (1.81–3.19)	4.06 (2.51–6.56)	1.09 (1.07–1.12)	<0.001
Adjusted for CRF		1.01 (0.73–1.40)	1.40 (1.11–1.75)	1.86 (1.45–2.40)	2.76 (2.07–3.68)	4.29 (2.66–6.94)	1.11 (1.08–1.13)	<0.001
Stomach	902	1.19 (0.90–1.58)	1.26 (1.03–1.53)	1.41 (1.13–1.75)	2.35 (1.84–3.00)	3.06 (1.95–4.81)	1.08 (1.06–1.10)	<0.001
Adjusted for CRF		1.11 (0.84–1.47)	1.34 (1.10–1.64)	1.55 (1.24–1.94)	2.52 (1.97–3.23)	3.10 (1.97–4.87)	1.09 (1.07–1.11)	<0.001
Pancreas	1280	1.20 (0.96–1.49)	1.12 (0.96–1.31)	1.31 (1.10–1.56)	1.79 (1.45–2.22)	1.47 (0.88–2.44)	1.05 (1.03–1.07)	<0.001
Adjusted for CRF		1.13 (0.91–1.41)	1.18 (1.01–1.39)	1.41 (1.18–1.69)	1.90 (1.53–2.36)	1.49 (0.90–2.48)	1.06 (1.04–1.08)	<0.001
Liver, bile ducts and gallbladder	1111	1.07 (0.84–1.36)	1.08 (0.91–1.27)	1.15 (0.95–1.39)	1.60 (1.27–2.01)	2.04 (1.31–3.16)	1.05 (1.03–1.07)	<0.001
Adjusted for CRF		0.96 (0.75–1.22)	1.20 (1.01–1.42)	1.34 (1.10–1.63)	1.80 (1.43–2.26)	2.08 (1.34–3.24)	1.06 (1.04–1.08)	<0.001
Colon	3222	1.03 (0.89–1.18)	1.02 (0.93–1.12)	1.06 (0.95–1.19)	1.28 (1.12–1.47)	1.75 (1.34–2.28)	1.03 (1.02–1.04)	<0.001
Adjusted for CRF		0.98 (0.85–1.13)	1.06 (0.96–1.17)	1.12 (1.00–1.26)	1.33 (1.16–1.53)	1.74 (1.34–2.28)	1.04 (1.02–1.05)	<0.001
Rectum	2337	1.07 (0.91–1.26)	1.04 (0.93–1.16)	1.05 (0.92–1.20)	1.19 (1.01–1.41)	1.69 (1.22–2.33)	1.02 (1.01–1.04)	0.005
Adjusted for CRF		1.05 (0.90–1.24)	1.06 (0.95–1.19)	1.08 (0.94–1.23)	1.21 (1.02–1.44)	1.69 (1.22–2.34)	1.03 (1.01–1.04)	0.001
Urological cancers								
Prostate	14,232	0.92 (0.87–0.99)	1.02 (0.98–1.06)	0.98 (0.93–1.03)	0.91 (0.84–0.98)	0.58 (0.46–0.73)	0.99 (0.98–1.00)	0.004
Adjusted for CRF		0.94 (0.88–1.00)	1.00 (0.96–1.05)	0.96 (0.91–1.01)	0.89 (0.82–0.96)	0.58 (0.46–0.72)	0.98 (0.98–0.99)	<0.001
Kidney	1753	1.07 (0.87–1.32)	1.24 (1.08–1.42)	1.42 (1.22–1.66)	1.98 (1.65–2.37)	2.73 (1.97–3.80)	1.08 (1.06–1.10)	<0.001
Adjusted for CRF		1.01 (0.82–1.24)	1.30 (1.13–1.50)	1.54 (1.31–1.80)	2.09 (1.74–2.51)	2.74 (1.97–3.81)	1.09 (1.07–1.10)	<0.001
Bladder	2259	0.96 (0.82–1.14)	0.99 (0.89–1.11)	1.11 (0.97–1.26)	1.06 (0.89–1.26)	1.17 (0.78–1.73)	1.01 (0.99–1.03)	0.20
Adjusted for CRF		0.94 (0.79–1.11)	1.02 (0.91–1.14)	1.15 (1.01–1.31)	1.09 (0.91–1.30)	1.17 (0.79–1.75)	1.02 (1.00–1.03)	0.07
Hematological cancers								
Leukemia	1991	0.97 (0.80–1.18)	1.13 (0.99–1.28)	1.22 (1.06–1.40)	1.50 (1.26–1.79)	1.71 (1.20–2.42)	1.05 (1.03–1.06)	<0.001
Adjusted for CRF		0.99 (0.81–1.20)	1.11 (0.98–1.26)	1.19 (1.03–1.38)	1.48 (1.25–1.77)	1.71 (1.21–2.43)	1.05 (1.03–1.06)	<0.001

TABLE 3 (Continued)

Cancer site	*n* cases	BMI < 18.5, HR (95% CI)	BMI 20.0–22.4, HR (95% CI)	BMI 22.5–24.9, HR (95% CI)	BMI 25.0–29.9, HR (95% CI)	BMI ≥ 30.0, HR (95% CI)	Linear analysis[a]	
							HR (95% CI)	*p*
Myeloma	915	0.84 (0.62–1.13)	1.19 (0.99–1.43)	1.38 (1.13–1.70)	1.30 (0.99–1.71)	1.69 (0.98–2.93)	1.04 (1.02–1.07)	<0.001
Adjusted for CRF		0.86 (0.64–1.16)	1.16 (0.96–1.39)	1.33 (1.08–1.64)	1.26 (0.95–1.66)	1.69 (0.97–2.91)	1.04 (1.01–1.06)	0.003
Hodgkin lymphoma	843	1.21 (0.90–1.63)	1.11 (0.91–1.36)	1.24 (1.00–1.55)	1.67 (1.29–2.16)	1.36 (0.78–2.36)	1.04 (1.01–1.06)	0.001
Adjusted for CRF		1.20 (0.89–1.62)	1.12 (0.91–1.37)	1.25 (1.00–1.57)	1.67 (1.29–2.16)	1.35 (0.77–2.35)	1.04 (1.01–1.06)	0.001
Non-Hodgkin lymphoma	2559	0.95 (0.80–1.12)	1.13 (1.01–1.26)	1.18 (1.04–1.34)	1.26 (1.08–1.48)	1.86 (1.40–2.49)	1.04 (1.02–1.05)	<0.001
Adjusted for CRF		0.96 (0.81–1.15)	1.11 (0.99–1.24)	1.15 (1.02–1.31)	1.25 (1.06–1.46)	1.88 (1.41–2.51)	1.04 (1.02–1.05)	<0.001

Note: Adjusted for year, site, age, CRF, and parental education at conscription. Reference is BMI 18.5–19.9.
Abbreviation: CRF, cardiorespiratory fitness; HR, hazard ratio.
[a]Linear trends tested using continuous BMI.

Conversely, the association between BMI and cancer in the CNS, thyroid, and pancreas and with leukemia was more pronounced in men with high/moderate CRF compared with men with low CRF.

Further sensitivity analyses

Adjusting for cognitive ability (Table S7) or muscle strength (Table S8) at conscription had little effect on the results. Individuals in the full target population, the study sample, the analyses not adjusting for CRF, and the analyses adjusted for CRF were comparable at baseline except for chronic disease at age 18, with diabetes especially being more common in the full target population (Table S9). Analyses stratified by year of conscription showed consistent directions of the associations and overlapping confidence intervals between men who underwent conscription from 1968 to 1979 and from 1980 to 2005 (Table S10).

Cancer site-specific PAF for overweight and obesity

The PAF for overweight and obesity based on current and historic prevalences of youth overweight and obesity in Sweden and the United States were calculated for each site-specific cancer, reflecting the fractions in the two countries in 2023 and 2050, assuming no change in other risk factors (Figure 2) [3]. These showed the highest PAF for gastrointestinal cancer sites, with the estimates based on current prevalences of youth overweight and obesity and the United States exceeding 50% for cancers in the esophagus and stomach.

Restricted cubic splines

Figure 3 shows the associations with the risk of each site-specific cancer along the BMI continuum. Except for cancer in the bronchi and lungs, the risk did not decrease above BMI 20, and for most site-specific cancers the risk started increasing already at BMI 20.

DISCUSSION

This large population-based study of Swedish young men presents linear associations between BMI and site-specific cancer. In this young population, we were able to confirm the associations between higher BMI in adulthood and higher risk for site-specific cancers indicated by the IARC as related to obesity (cancer in the esophagus, stomach, liver, colon, rectum, pancreas, kidney, and thyroid) [1] and show that these associations are independent of CRF. In addition, we can report linear associations between BMI in youth and the risk of developing leukemia; myeloma; Hodgkin lymphoma; non-Hodgkin lymphoma; and cancer in the lungs, CNS, and urinary bladder as previously reported in single reports but without consensus for BMI in neither youth nor adulthood in the IARC statement [2]. Based on these results, we have calculated current cancer site-specific PAF and estimated PAF for the

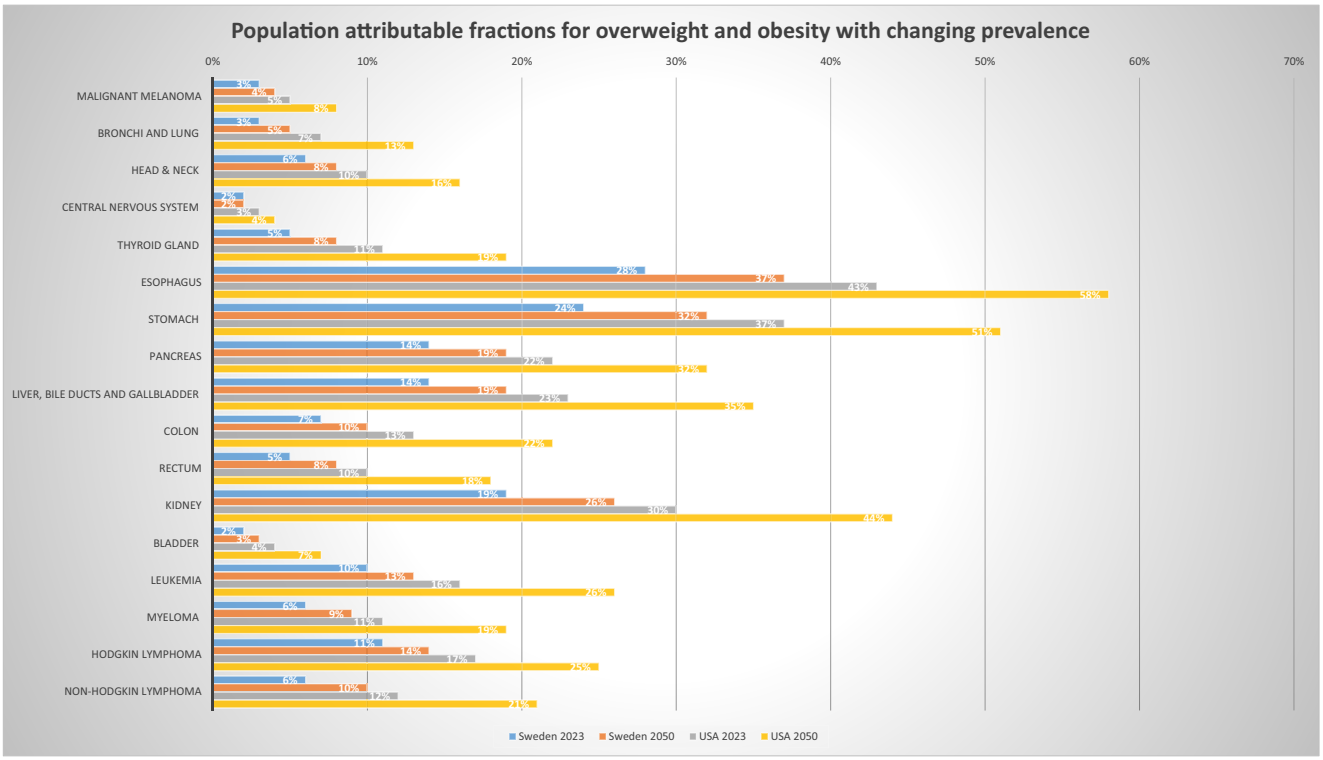

FIGURE 2 PAF for overweight and obesity for each of the site-specific cancers. Estimated for cancers diagnosed in Sweden and the United States in 2023 (based on proportions of youth overweight and obesity in 1989 with a mean lag time of 34 years to cancer) and in 2050 (based on levels of overweight and obesity in 2016). *PAF includes only obesity for lung cancer. PAF, population attributable fraction. [Color figure can be viewed at wileyonlinelibrary.com]

year 2050, based on current proportions of youth overweight and obesity in Sweden and the United States, respectively.

This study has several strengths, including the population-based approach, the use of prospectively registered data with high validity, the large sample size, and the long follow-up. These strengths increase both internal validity and generalizability and contribute to novel information for some site-specific cancers. Another strength is the possibility to adjust for CRF. We can show that the associations between BMI and site-specific cancers are independent of the protective associations between CRF and cancer previously reported [6] that could be explained by differences in PA and its effects on mechanisms involved in tumor development [4, 14]. We could not confirm previously reported J-shaped associations between BMI and cancer, possibly explained by the possibility of adjusting for CRF, and removing the risk for reverse causality with the long time between BMI assessment and cancer development in our study. We could also show that higher BMI was associated with these cancer sites in men with both low and moderate/high CRF. The use of BMI 18.5 to 20.0 as a reference is an additional strength, because previous studies have shown that the risk of both cardiovascular disease and mortality increases already below the conventional threshold of BMI 25 for younger people, but not older people [10, 11]. Our results show that this was the case for site-specific cancer as well and add to previous information that the broad category of 18.5 to 25.0 indicating normal weight may not be applicable in young people. The BMI assessment during a narrow age span in youth made it possible to assess both youth-specific associations and to estimate future PAF, taking the increasing proportion of youth overweight and obesity into account. The results illustrate the effect of moving the population from BMI ≥ 25 to BMI 18.5–19.9 that is, reversing the shift over time illustrated in Table S3. The PAF in our study do not consider the risk increase seen from BMI 20 or 22.5. Although interesting, these PAF only consider the change in BMI and are not an attempt to include changes in other risk factors in the population [15]. The major limitation in this study is the lack of full data on other known lifestyle risk factors, especially smoking, which increases the risk of confounding. We have used the information on smoking habits from a subpopulation of more than 24,000 individuals for which this information was available to see how adjusting for smoking changed the estimates. This detected smoking as a risk factor for cancers in the lungs, head and neck, esophagus, stomach, pancreas, liver, and urinary bladder but did not suggest any confounding by smoking for the associations between BMI and site-specific cancer. However, the borderline significant results for smoking and the risk increase associated only with obesity should lead to caution in interpreting the results for lung cancer. Smoking declined dramatically in Sweden during the study period. Hence, any confounding from smoking should be less prominent than that observed in the 1968 to 1970 cohort where smoking was frequent.

The relatively low proportion of men with obesity in this population limits the statistical power for categorical analyses of obesity,

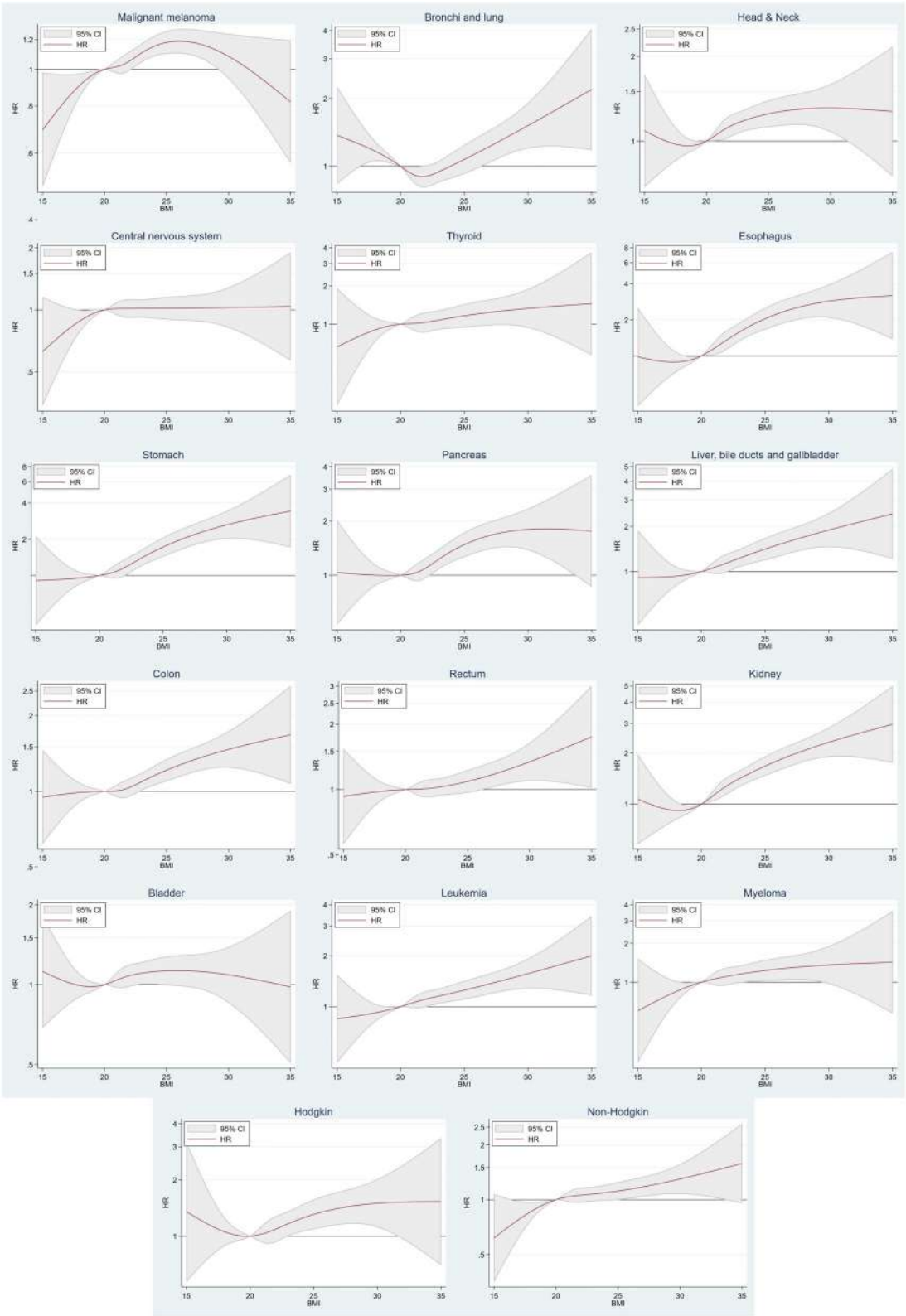

FIGURE 3 Restricted cubic splines illustrating the HR (y-axis) along the BMI continuum (x-axis) for each site-specific cancer. Adjusted for age, year, and site of conscription, parental level of education, and cardiorespiratory fitness. HR, hazard ratio. [Color figure can be viewed at wileyonlinelibrary.com]

which probably explains some nonsignificant associations for obesity despite linear associations. Our study is also limited by a lack of information on other lifestyle risk factors, such as alcohol and diet. Another limitation is the lack of data on changes of BMI during the long follow-up. Although BMI generally increases during midlife, BMI in adolescence has been shown to have a strong predictive value for

predicting BMI in midlife [16, 17]. This single timepoint assessment can also be considered a strength. Although some previous studies have assessed BMI at ages differing by decades [18], we have an assessment at a specific age. This strengthens the generalizability of these results to the age group we have studied and facilitates accurate estimates of future PAF due to the obesity epidemic. Because our study only included men, our results are only applicable to men. However, the IARC concluded that the risk increase from body fatness seems to be similar in men and women [1].

There is a similar Israeli study on BMI in youth and future risk of site-specific cancer [2]. Our study contributes with the possibility of validating those results in a population-based sample with different ethnicity and to assess confounding by fitness [19]. Unfortunately, the Israeli study had no information on smoking patterns for the BMI categories. Because the BMI categories differed, the effect sizes are hard to compare. Our results were similar for cancer in the stomach, colon, rectum, pancreas, prostate, kidney, brain, and thyroid as well as for Hodgkin and non-Hodgkin lymphomas, multiple myeloma, leukemia, and malignant melanoma. However, the Israeli study reported an inverse association between BMI and lung cancer and tendencies toward reverse associations for cancer in the esophagus and liver and gallbladder, whereas we reported linear risk increases with increasing BMI. Interestingly, these three cancer sites were the sites where our analyses showed the strongest confounding by adjusting for CRF, while our sensitivity analyses did not suggest any significant confounding by smoking. This shows the importance of adding a measure more related to PA to strengthen the interpretation of causal effects from BMI from those from PA. Our finding that the increased cancer risk for underweight was confounded by CRF might also explain previously reported nonlinear association between BMI and cancer from other studies [20]. Our results support the finding of an association between BMI in youth and melanoma in the Israeli study [2], where the IARC concluded that there was inadequate evidence in the general adult population [1].

Prostate cancer showed an inverse association with BMI in our study. Wang et al. reported a lower prostate cancer angiogenesis, a proxy for tumor growth, for individuals with weight gain early in life but a higher angiogenesis with weight gain later in life [21]. Similarly, Kelly et al. reported a nonsignificant lower risk for fatal prostate cancer with increasing BMI at age 18 but a higher risk with higher BMI in men in their 60s [22]. In parallel studies in the same study population, we have assessed the risk of 5-year mortality after prostate cancer as well as the risk of fatal prostate cancer and found a higher 5-year mortality in men with obesity and prostate cancer but no difference in the risk of fatal prostate cancer [23, 24]. This has also been reported in a similar British study in which they wrote that a possible explanation was that diagnoses could be delayed or missed in people with overweight or obesity. Hence, it is probable that the protective association between body fatness and prostate cancer diagnosis in our current study is confounded by differences in prostate cancer testing (e.g., with the prostate-specific antigen test). There was no organized cancer screening program in place in Sweden for prostate cancer or any other cancer site included in the current study during the study period.

Neither the IARC statement nor the Israeli study have reported associations between body weight and cancer in the CNS or urinary bladder. A systematic review described associations between BMI and any brain tumor, including malignant tumors and meningiomas, and reported separate results for gliomas and meningiomas [25]. No significant association for obesity was found, but a small increase for overweight for malignant brain tumors. Our results further indicate a small risk increase for malignant brain tumors with higher BMI. For the urinary bladder, results from a Danish study showed higher risk of developing bladder cancer with higher childhood BMI and with weight gain during childhood [26], while a systematic review identified no results for bladder cancer [27]. Hence, our results with HR 1.48 for men with obesity add new knowledge on a possible association between BMI and bladder cancer.

Our results do not raise any controversies with the consensus statement on associations between BMI in adults and cancer from the IARC, [1] although our study does add new information and strengthens the evidence base for BMI measured in youth. The IARC reported that relative risks from meta-analyses were 1.2 to 1.5 for overweight and 1.5 to 1.8 for obesity with respect to cancers of the colon, stomach, liver, gallbladder, pancreas, and kidney [1]. In our analyses adjusted for fitness, overweight and obesity in youth were associated with risk increases in that range for colon and pancreas, whereas they were associated with higher risk increases for the liver and gallbladder, stomach, and kidney. For multiple myeloma, the IARC reported relative risks of 1.2 for both overweight and obesity [1]. For cancer in the esophagus, the IARC reported a relative risk of 4.8 for a BMI of 40 or more [1]. We could not assess the risk increase in that BMI range with the BMI distribution in our population, but BMI ≥ 30 in youth was associated with HR 4.3. The generally higher risk increases in our study might partially be explained by our reference category for BMI being lower than in previous studies. The similar Israeli study did not report any association between adolescent BMI and esophagus cancer [2]. For thyroid cancer, the IARC reported a relative risk of 1.1 for the highest weight category [1], whereas we report HR 1.9 for obesity, the Israeli study HR 1.3 [2], and an Australian study reported HR 1.66 for overweight and 2.07 for obesity in men [28].

Previous studies have assessed the burden of BMI on cancer. With studies varying in terms of underlying assumptions on size of risk increases, time lag, and with different distributions of overweight and obesity, it is hard to directly compare PAF between studies. Because our study included assessment at a specific age [18], and we know that the effects sizes were true for a mean 34-year follow-up between the assessment and the cancer diagnosis, we can use this information to make more precise predictions. Andersson et al. calculated the proportion of avoidable cancers due to overweight and obesity in the Nordic countries [29]. They had to assume relative risks for both overweight and obesity for several cancer types. Of the cancer sites that overlapped, their estimated PAFs for overweight/obesity for year 2016 to 2045 were similar to our estimates for Sweden 2023 for cancers in the colon (9% vs. 7%), rectum (5% vs. 5%), kidney (16% vs. 19%), liver and gallbladder (14%–17% vs. 14%), thyroid (4% vs. 5%),

and esophagus (24% vs. 28%), although it differed somewhat for pancreas (6% vs. 14%) and myeloma (11% vs. 6%). It is possible that the risk increase associated with higher BMI varies with length of follow-up, and the duration of this period is not well-established in previous studies linking obesity to cancer incidence, making assumptions regarding the exposure time lag [18, 30]. Bhaskaran et al. estimated the PAF for overweight and obesity for cancer cases in the United Kingdom [18]. Their estimates were in the same range as ours for the cancer sites that were included in both studies: colon (11% vs. 7%), liver and gallbladder (16%–20% vs. 14%), kidney (17% vs. 19%), thyroid (2% vs. 5%), and leukemia (6% vs. 10%). Arnold et al. estimated the global burden of cancer attributable to BMI > 25 in 2012 and presented results by world region [30] They reported considerably higher PAFs than ours for cancer in the esophagus (44% vs. 28%), colon (18% vs. 7%), and rectum (10% vs. 5%). However, their estimates were similar to ours for cancer in the pancreas (12% vs. 14%) and kidney (22% vs. 19%). The agreement between our results and those from both Nordic and international studies support the validity of our results.

Our results indicate some future research directions. First, to confirm the results for cancer sites that have not been previously reported. Second, to clarify the effect of body fatness on cancer in different periods of life. Third, to establish whether a higher risk of developing cancer also translates into a higher mortality after being diagnosed with cancer.

In conclusion, we report that higher BMI in young men is associated with a higher risk of developing malignant melanoma, leukemia, myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and cancer in the lungs, head and neck, CNS, thyroid, esophagus, stomach, pancreas, liver and gallbladder, colon, rectum, kidney, and urinary bladder. We used these results for BMI at age 18 to estimate the change in PAF for site-specific cancers due to the obesity epidemic. These results could be used in public health policymaking, further strengthening the incentive for public health effort in reversing the obesity epidemic in children and adolescents.O

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The data in this study is not available for data sharing.

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REFERENCES

1. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer — viewpoint of the IARC working group. *N Engl J Med*. 2016; 375:794-798.
2. Furer A, Afek A, Sommer A, et al. Adolescent obesity and midlife cancer risk: a population-based cohort study of 2.3 million adolescents in Israel. *Lancet Diabetes Endocrinol*. 2020;8:216-225.
3. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet*. 2017; 390:2627-2642.
4. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med*. 2020;54:1451-1462.
5. Pozuelo-Carrascosa DP, Alvarez-Bueno C, Cavero-Redondo I, Morais S, Lee IM, Martinez-Vizcaino V. Cardiorespiratory fitness and site-specific risk of cancer in men: a systematic review and meta-analysis. *Eur J Cancer*. 2019;113:58-68.
6. Onerup A, Mehlig K, Af Geijerstam A, et al. Associations between cardiorespiratory fitness in youth and the incidence of site-specific cancer in men: a cohort study with register linkage. *Br J Sports Med*. 2023;57:1248-1256.
7. Ludvigsson JF, Berglind D, Sundquist K, Sundstrom J, Tynelius P, Neovius M. The Swedish military conscription register: opportunities for its use in medical research. *Eur J Epidemiol*. 2022;37:767-777.
8. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011;11:450.
9. Brooke HL, Talback M, Hornblad J, et al. The Swedish cause of death register. *Eur J Epidemiol*. 2017;32:765-773.
10. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju SN, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. 2016;388:776-786.
11. Rosengren A, Aberg M, Robertson J, et al. Body weight in adolescence and long-term risk of early heart failure in adulthood among men in Sweden. *Eur Heart J*. 2017;38:1926-1933.
12. Zapata-Diomedi B, Barendregt JJ, Veerman JL. Population attributable fraction: names, types and issues with incorrect interpretation of relative risks. *Br J Sports Med*. 2018;52:212-213.
13. Dickman P. Cox_hr_pred.do. Available from: http://www.pauldickman.com/survival/.
14. Locasale JW. Diet and exercise in cancer metabolism. *Cancer Discov*. 2022;12:2249-2257.
15. Soerjomataram I, Bray F. Planning for tomorrow: global cancer incidence and the role of prevention 2020–2070. *Nat Rev Clin Oncol*. 2021;18:663-672.
16. Kvaavik E, Tell GS, Klepp KI. Predictors and tracking of body mass index from adolescence into adulthood: follow-up of 18 to 20 years in the Oslo Youth Study. *Arch Pediatr Adolesc Med*. 2003;157:1212-1218.

17. Rundle AG, Factor-Litvak P, Suglia SF, et al. Tracking of obesity in childhood into adulthood: effects on body mass index and fat mass index at age 50. *Child Obes*. 2020;16:226-233.
18. Bhaskaran K, Douglas I, Forbes H, Dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet*. 2014;384:755-765.
19. Reinehr T. Obesity in adolescents and cancer risk: causal relationship or epiphenomenon? *Lancet Diabetes Endocrinol*. 2020;8:179-180.
20. Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. *Lancet Diabetes Endocrinol*. 2018;6:944-953.
21. Wang QL, Song M, Clinton SK, Mucci LA, Lagergren J, Giovannucci EL. Longitudinal trajectories of lifetime body shape and prostate cancer angiogenesis. *Eur J Epidemiol*. 2022;37:261-270.
22. Kelly SP, Lennon H, Sperrin M, et al. Body mass index trajectories across adulthood and smoking in relation to prostate cancer risks: the NIH-AARP Diet and Health Study. *Int J Epidemiol*. 2019;48:464-473.
23. Onerup A, Mehlig K, Af Geijerstam A, et al. Cardiorespiratory fitness and BMI measured in youth and 5-year mortality after site-specific cancer diagnoses in men - A population-based cohort study with register linkage. *Cancer Med*. 2023;00:1-15.
24. Onerup A, Mehlig K, Af Geijerstam A, et al. Cardiorespiratory fitness and BMI in youth and site-specific cancer mortality in men: a population-based cohort study with register linkage. *J Clin Oncol*. 2023;41(16_suppl):10534-10534.
25. Zhang D, Chen J, Wang J, et al. Body mass index and risk of brain tumors: a systematic review and dose-response meta-analysis. *Eur J Clin Nutr*. 2016;70:757-765.
26. Sørensen KK, Jensen BW, Thomas PE, et al. Early life body size and its associations with adult bladder cancer. *Ann Hum Biol*. 2020;47:166-172.
27. Choi EK, Park HB, Lee KH, et al. Body mass index and 20 specific cancers: re-analyses of dose-response meta-analyses of observational studies. *Ann Oncol*. 2018;29:749-757.
28. Laaksonen MA, MacInnis RJ, Canfell K, et al. Thyroid cancers potentially preventable by reducing overweight and obesity in Australia: a pooled cohort study. *Int J Cancer*. 2022;150:1281-1290.
29. Andersson TM, Weiderpass E, Engholm G, et al. Avoidable cancer cases in the Nordic countries - the impact of overweight and obesity. *Eur J Cancer*. 2017;79:106-118.
30. Arnold M, Pandeya N, Byrnes G, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. *Lancet Oncol*. 2015;16:36-46.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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