Published in final edited form as:

Cancer Causes Control. 2018 August ; 29(8): 707–719. doi:10.1007/s10552-018-1052-x.

Height, waist circumference, body mass index, and body somatotype across the life course and risk of glioma

David J. Cote^{1,2,3}, Mary K. Downer^{1,2,4}, Timothy R. Smith³, Stephanie A. Smith-Warner^{2,4}, Kathleen M. Egan⁵, and Meir J. Stampfer^{1,2,4}

¹Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

²Department of Epidemiology, Harvard T. H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, USA

³Computational Neurosciences Outcomes Center, Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

⁴Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA

⁵Division of Population Sciences, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Abstract

Purpose—Recent studies have suggested height as a risk factor for glioma, but less is known regarding body mass index (BMI) or other anthropomorphic measures. We evaluated the association between body habitus and risk of glioma.

Methods—We evaluated the association of measures of height, BMI, waist circumference, and somatotypes with risk of glioma in two prospective cohorts, the Nurses' Health Study and the Health Professionals Follow-Up Study.

Results—We documented 508 incident cases of glioma (321 glioblastoma [GBM]). In both cohorts, we found no significant association between adult BMI or waist circumference and risk of glioma, with pooled HR for BMI of 1.08 (95% CI 0.85–1.38 comparing 30 to < 25 kg/m²) and for waist circumference of 1.05 (95% CI 0.80–1.37 highest vs. lowest quintile). Higher young adult BMI (at age 18 in NHS and 21 in HPFS) was associated with modestly increased risk of glioma in the pooled cohorts (pooled HR 1.35, 95% CI 1.06–1.72 comparing 25 kg/m² vs. less; HR 1.34 for women and 1.37 for men). Analysis of body somatotypes suggested reduced risk of glioma among women with heavier body types at all ages this measure was assessed (HRs ranging from 0.52 to 0.65 comparing highest tertile to lowest tertile), but no significant association among men. Height was associated with increased risk of glioma among women (HR 1.09, 95% CI 1.04–

David J. Cote david_cote@hms.harvard.edu.

Compliance with ethical standards

Conflicts of interest The authors declare no potential conflicts of interest.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10552-018-1052-x>) contains supplementary material, which is available to authorized users.

1.14 per inch), but not significantly among men. Within the 8 years prior to diagnosis, cases had no material weight loss compared to non-cases. All results were similar when limited to GBM.

Conclusion—Adult BMI and waist circumference were not associated with glioma. Higher BMI at age 21 for men and at age 18 for women was modestly associated with risk in the pooled cohort. Based on body somatotypes, however, women with heavier body types during childhood and young adulthood may be at lower risk of glioma, although this association was not observed later in life with measurements of BMI. Greater height was associated with increased risk, and the trend was more pronounced in women.

Keywords

Body habitus; Body mass index; Glioblastoma; Glioma; Height; Waist circumference; Weight

Introduction

Recent studies have examined the relationship between multiple measures of body habitus and risk of glioma, the most common primary brain malignancy [1–8]. Whereas height has consistently been identified as a risk factor for glioma, evidence for body mass index (BMI) and waist circumference has been inconsistent, despite their association with cancers of other sites [9, 10]. No prior studies have reported on associations of BMI or other measures of adiposity using repeated measures or examined associations with such measures from early life.

Additionally, the duration and physiological effects of subclinical disease are not well understood in the context of glioma [11]. Although the disease is often rapidly fatal, particularly glioblastoma multiforme (GBM), some evidence suggests that patients with low-grade glioma may have a preclinical period of many years, during which subtle weight loss may be detectable [11]. If so, it is possible that prediagnostic weight loss may have confounded analysis of BMI as a risk factor in prior case–control studies, perhaps resulting in an underestimation of the association between higher BMI and glioma.

In this study, we analyzed data in two large, independent, prospective cohort studies, the Nurses' Health Study (NHS) and the Health Professionals Follow-Up Study (HPFS), to evaluate possible associations of various measures of body habitus, including height, BMI, waist circumference, body somatotype, and birth weight with risk of glioma and GBM. Additionally, we analyzed prospectively collected BMI data to determine whether patients ultimately diagnosed with glioma experience pre-diagnostic weight loss compared to those who remained free from glioma.

Methods

Study participants

The methods of both the NHS and the HPFS have been described in detail elsewhere [12, 13]. NHS began in 1976 with 121,701 female nurses aged 30–55 years. HPFS began in 1986, with 51,529 male health professionals aged 40–75 years. In both cohorts, participants completed a baseline questionnaire and subsequent biennial follow-up questionnaires to

provide updated information. Follow-up rates in these two cohorts have exceeded 90% [14]. After exclusion of participants without reported height and weight or with reported glioma at baseline, we followed 121,696 women from NHS and 51,400 men from HPFS. The Institutional Review Boards at the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health approved this study.

Assessment of anthropometric measures

Participants were asked to report height and weight on the baseline questionnaire for both cohorts. Subsequently, weight was ascertained on each biennial questionnaire. A validation study demonstrated a strong correlation for measured and self-reported weight (0.97 for both men and women) [15]. In 1980, NHS participants retrospectively reported their weight at age 18; in 1986, HPFS participants retrospectively reported their weight at age 21. These values were used to calculate young adult BMI, assuming that participants had achieved their adult height at ages 18 (NHS) and 21 (HPFS). This measure of BMI at age 18 was previously validated among women in the Nurses' Health Study II cohort, a study with similar demographic characteristics as the NHS cohort, where the correlation between recalled and measured past weight was 0.87 and the correlation between reported current height and measured past height was 0.94 [16]. Waist circumference was assessed three times in each cohort: 1986, 1996, and 2000 in NHS, and 1987, 1996, and 2008 for HPFS. Measures of waist circumference were also previously validated, with correlations between self-reported waist circumference and technician-measured waist circumference of 0.95 for men and 0.89 for women [15]. The 1988 questionnaire in both cohorts included a question that asked participants to identify their approximate body type (somatotype) from a range of nine images of different body types developed by Stunkard et al. at age five, 10, 20, 30, 40, and current age in 1988 (Fig. 1) [17]. This measure of body shape in early life was previously validated among 181 participants in the Boston-based Third Harvard Growth Study aged 71–76 years, by comparing retrospective reports with measured contemporaneous assessments in early life. The Pearson correlation coefficients for women were 0.60 at age five, 0.65 at age 10, 0.66 at age 20, and 0.75 at current age, and for men, 0.36 at age five, 0.66 at age 10, 0.53 at age 20, and 0.60 at current age, respectively [18]. Self-reported birth weight was assessed in 1992 for NHS and in 1994 for HPFS. Participants were asked to categorize their birth weight into one of the five categories (< 5.5, 5.5–6.9, 7.0–8.4, 8.5–9.9, 10 lbs.).

Identification of cases

Primary brain malignancy cases were self-reported on biennial questionnaires and then confirmed by medical record review. Deaths were identified through the National Death Index, next-of-kin, and postal authorities. For all deaths that may have been due to primary brain tumor, we sought medical records to confirm the diagnosis. Data on tumor subtype were extracted from medical records. Follow-up for mortality through these methods assured nearly complete ascertainment of deaths and their causes [19]. Only cases with confirmed diagnoses indicating primary malignant neuro-epithelial neoplasms of the brain (i.e., gliomas) were included in this analysis.

Statistical analyses

We began follow-up time at the date of return of the baseline questionnaire and continued to the date of glioma diagnosis, death from another cause, or the end of follow-up (30 June 2014 for NHS; 28 February 2015 for HPFS, due to questionnaire mailing cycles), whichever came first. For calculations involving variables that were identified only in later questionnaires, such as BMI at age 18 and 21, waist circumference, body somatotypes, and birth weight, follow-up was calculated from the return of the questionnaire that first asked about that variable. We used age-adjusted Cox proportional hazards models to calculate age-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) to evaluate risk of glioma by various measures of body habitus, using months as the time metamer and age and calendar year as stratification variables. Because few risk factors for glioma have been established, we did not perform multivariate-adjusted Cox models.

For all measures of BMI we used simple updating, using the most recent BMI measure available. For weights that were missing on follow-up questionnaires, we used the most recent reported weight for up to two cycles (4 years) prior to calculate BMI; otherwise, missing data were coded as missing. For periods when individuals were missing data for a particular exposure variable, they did not contribute person-time to the Cox models. BMI was analyzed both continuously and as a categorical variable according to the standard World Health Organization definition ($< 25 \text{ kg/m}^2$, $25\text{--}29.9 \text{ kg/m}^2$, $\geq 30 \text{ kg/m}^2$). To address reverse causation, because BMI among cases may have changed due to preclinical tumor effects, we applied BMI from 2, 4, 6, and 8 years prior to the current period in separate lagged analyses, resulting in exclusion of the first 2, 4, 6, and 8 years of follow-up for these calculations. We also analyzed baseline BMI both continuously and categorically, as well as lifetime maximum BMI, for which we used continuous updating through follow-up with the highest previously reported BMI used for each cycle. BMI at age 18 and 21 was additionally analyzed both continuously and categorically; because so few participants (2.1% of cases, 1.8% of non-cases) had a BMI above 30, at those ages, we dichotomized the population as < 25 or $\geq 25 \text{ kg/m}^2$ for this measure.

For analyses using waist circumference, we used simple updating, carrying forward previously reported values for waist circumference in the case of missing data. Waist circumference was analyzed both continuously and in quintiles, as was height. To evaluate the possibility of outliers skewing the results of the analyses, we also performed sensitivity analyses for all of the above analyses by excluding the top and bottom 2.5% for BMI, BMI with a 2, 4, 6, and 8 year lag, BMI at age 18 and 21, maximum lifetime BMI, baseline BMI, waist circumference, and height, separately for each exposure.

For the analysis of body somatotypes at age 5, 10, 20, 30, 40, and current in 1988, we analyzed the data in approximate tertiles for each category, separately for each cohort. Participants who did not respond to these questions were excluded from the analysis.

For the analysis of birth weight, we analyzed in the categories assessed in the HPFS questionnaire (< 5.5 , $5.5\text{--}6.9$, $7.0\text{--}8.4$, $8.5\text{--}9.9$, ≥ 10), with $5.5\text{--}6.9$ lbs. as the reference category. The NHS questionnaire had one additional category that was collapsed to match the HPFS categorization.

To evaluate potential reverse causation related to the effect of brain tumor diagnosis on pre-diagnostic weight change, we regressed the weight (in pounds) of all participants against age, age-squared, height, and time period, to adjust for secular changes in weight, and saved the residuals for cases only. The residuals for cases were then plotted against time for the 8, 6, 4, 2, and 0 years prior to diagnosis to show the weight trend of cases in the years immediately prior to diagnosis.

All analyses were performed for gliomas overall and GBM specifically, due to the possibility that risk factors may differ by tumor type and the high number of GBM cases available compared to other non-GBM gliomas. Analyses of each cohort were combined by meta-analysis using the fixed effects model. All statistical analyses were performed using the SAS 9.1 statistical package (SAS Institute, Cary, NC), and all *P* values were derived from two-sided tests.

Results

Case incidence

We documented 508 cases of glioma (NHS: 328, HPFS 180) during an average 34.2 (NHS) and 23.6 (HPFS) years of follow-up. Of these, 321 were GBM (NHS: 194, HPFS: 127). Baseline characteristics by case status and cohort are presented in Table 1.

Body mass index and waist circumference

Age-adjusted Cox proportional hazards models showed no significant risk of glioma by categorical or continuous adult BMI in either the non-lagged or lagged analyses among women or men (Table 2). Additionally, we observed no significantly different associations in risk by maximum adult BMI or BMI at baseline, modeled continuously or categorically. Waist circumference was not significantly associated with risk of glioma in either NHS or HPFS when modeled continuously or in quintiles.

When modeled continuously, higher BMI at age 21 was associated with increased risk of glioma among men (HR 1.26, 95% CI 1.01–1.57 for each 5 kg/m² increase), but not among women at age 18 (HR 1.07, 95% CI 0.87–1.31 for each 5 kg/m² increase). Young adult BMI 25 kg/m² was associated with increased risk of glioma when compared to BMI < 25 kg/m² (HR 1.34 in women at age 18, 1.37 in men at age 21, and 1.35, 95% CI 1.06–1.72 combined), but this association was not statistically significant in the cohorts individually.

Height

Among women, higher attained height was associated with increased risk of glioma (HR 1.09, 95% CI 1.04–1.14 for each 1 inch increase); this association was less pronounced and not significant in men (HR 1.03, 95% CI 0.98–1.09 for each 1 inch increase). When analyzed by quintiles, women in the fourth and fifth tallest quintiles of height had significantly increased risk of glioma (HR 1.58, 95% CI 1.11–2.24; HR 1.41, 95% CI 1.01–1.97, respectively, when compared to the shortest quintile). Height in men remained non-significant in the analysis by quintiles, with HRs of 1.44 and 1.16, compared to the shortest quintile.

The results for all anthropometric measures were similar when modeling glioblastoma (Table 3). The results of the sensitivity analyses after excluding the top and bottom 2.5% for each exposure did not result in any material changes to the results (data not shown).

Body somatotypes

Among women, having a higher self-reported body somatotype was associated with reduced risk of glioma when compared to a lower body somatotype at all ages that were assessed, with hazard ratios comparing highest to lowest tertile ranging from 0.52 to 0.79 (Table 4). Among men, no associations with body somatotype were statistically significant.

Birth weight

We observed significantly lower risk of glioma among those in the < 5.5 lb. category (HR 0.57, 95% CI 0.35–0.93), 7–8.4 lbs. category (HR 0.34, 95% CI 0.25–0.47), and 8.5–9.8 lb. category (HR 0.62, 95% CI 0.39–0.98) compared to the 5.5–6.9 lb. category for women (Supplementary Table 1). Men in the 8.5–9.9 lb. category had lower risk of GBM compared to the 5.5–6.9 lb. category (HR 0.24, 95% CI 0.08–0.77), but no other associations were statistically significant for either glioma or GBM.

Pre-diagnostic weight loss

Compared to participants who remained free of glioma, participants who developed glioma did not have significant weight differences during the 8 years prior to diagnosis, after controlling for height, age, age-squared, and time (Supplementary Fig. 1). For glioma cases, the absolute magnitude of the difference in weight over the 8 years preceding diagnosis was less than three pounds at all 2-year increments, with cases slightly heavier than non-cases. Results for GBM only were not materially different (Supplementary Fig. 2).

Discussion

Across two large, prospective cohort studies of more than 150,000 American adults, neither adult BMI nor waist circumference were associated with risk of glioma. Based on the analysis of body somatotypes, a heavier body type compared to a thin body type during childhood, adolescence, and young adulthood may be associated with lower risk among women, though these findings were not identified among men, where higher BMI measured at age 21 may be associated with greater risk. Taller height was associated with increased glioma risk, particularly among women.

Strengths of the current study include its prospective design, large sample size, and the detailed and accurate data collected, including medical record confirmation of primary brain malignancy diagnosis. Many studies of risk factors for glioma have used population-based registries, which lack specific data and long-term follow-up with repeated measures of body habitus. Limitations include relatively few participants with high BMI or high waist circumference relative to the general population. Additionally, the number of cases, while adequate for statistical comparison, remains relatively low due to the rarity of the disease.

BMI and waist circumference

Excess body weight during adulthood does not appear to contribute significantly to risk of glioma. Both BMI and waist circumference have previously been associated with risk of cancers of other sites, including the esophagus, stomach, colon, rectum, liver, gallbladder, uterus, ovary, kidney, meninges, and thyroid [9, 10, 20]. Proposed mechanisms for this association include higher levels of inflammation and circulating inflammatory markers among those who are obese compared to those of lower body weight, which may promote malignant transformation [9, 21, 22]. Previous reports have identified potential mechanisms for glioma pathogenesis also predicated on inflammation, including a history of measles and traumatic brain injury [23–25]. Although these associations have not been borne out in large epidemiological studies, they are suggestive of a relationship between ongoing inflammation and possible later development of malignancy, even in the central nervous system. However, higher BMI may not produce inflammation specific to the central nervous system, and thus may not provide evidence against the hypotheses relating inflammation to glioma risk [24].

There has been less research on body habitus and glioma risk as compared to cancers of other sites, but findings from both cohort and case–control studies have shown risks similar to those we report. In a study of 340 cases of glioma from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, Michaud et al. also found no associations between adult BMI and glioma [6]. A meta-analysis of 12 studies and 3057 glioma cases identified no increased risk of glioma among overweight and obese individuals when compared to those with normal weight [4]. A separate meta-analysis of 22 studies and 3683 cases did report an association between overweight/ obesity and increased risk of glioma (pooled RR = 1.17) among women but not men [1]. This meta-analysis included 14 cohort studies and eight case–control studies, but the majority of included cohort studies assessed BMI at baseline only, without ongoing follow-up through adulthood. A more recent study of 4382 gliomas among 1.8 million Norwegian men and women published after the two meta-analyses also demonstrated no association between overweight and obesity and any glioma subgroup [2].

Overall, BMI during adulthood appears to play a minimal role, if any, in contributing to the overall risk of glioma. Higher BMI during adolescence, however, may play a role in later development of glioma. In a case–control study of 1111 glioma cases, Little et al. found that being underweight at age 21 ($\text{BMI} < 18.5 \text{ kg/m}^2$) was associated with a decreased risk of glioma among women (multivariate OR 0.68) [7]. In the prospective NIH-AARP Diet and Health Study, significant positive association was identified with obesity at age 18. Comparing those BMI 30–34.9 kg/m^2 to those BMI 18.5–24.9 kg/m^2 , the authors reported increased risk of GBM among those who were obese at age 18 (RR = 3.53, 95% CI 1.72–7.24) [3]. Together, these significant associations during childhood and adolescence suggest that early-life exposures may be more strongly related to glioma risk than exposures during adulthood [7, 26]. Similarly, in the current study, risk of glioma is higher among those who were obese during young adulthood (defined as age 18 for women and 21 for men), particularly among men.

On the other hand, Kitahara et al. reported results from a prospective study of Danish boys and girls aged 7–13, and found no association between BMI at these ages and risk of adult

glioma [27]. This study did not include follow-up data on weight and height for later adolescence or adulthood and the results differ from those reported here, where higher BMI at age 21 among men was found to be associated with later glioma risk. This could possibly be explained by the variation in ages at which BMI was assessed (7–13 years old vs. 18 and 21 years old in our own study), particularly given the significant differences in growth trajectories for boys and girls around the time of puberty.

Body somatotypes

Our results for body somatotypes suggest that a heavier body type during childhood, adolescence, and young adulthood may be protective for glioma among women, but not among men. These findings are relatively consistent across all ages of somatotype, for both sexes. Few other studies have assessed body somatotypes, and to our knowledge, none have evaluated glioma risk. Based on our null results for waist circumference and adult BMI in the cohorts, however, it is possible that the early-life association may wane in later life. Because these cohorts have generally tracked participants through the fifth and later decades of life, we hypothesize that the null association demonstrated between adult BMI and waist circumference and glioma risk may not hold at younger ages. Future studies should focus on measures of body habitus during childhood and early adulthood in relation to glioma risk, as the results presented here are suggestive of associations that may change over the life course. The results presented here are plausible given that the overall risk of glioma for women is considerably lower than that for men, so the finding of inverse associations of larger body types among women but not among men may be consistent with population trends that have not yet been explained by other risk factors [8].

Nevertheless, it is important to note that the somatotypes at age 20 and the young adult BMI measured at age 18 in NHS and at age 21 in HPFS do not align—whereas the young adult BMI measures suggest increased risk with higher BMI, the somatotype measures suggest reduced risk among heavier women. The categorization of young adult BMI as above or below 25 kg/m² was chosen based on the distribution of responses, in that few individuals reported high BMI at these ages. Therefore, many of the individuals in the > 25 kg/m² category may fit into the second tertile, rather than the third tertile, of somatotypes, so these results cannot be compared exactly. Additionally, in a sub-cohort analysis of only those individuals who responded to the somatotype questionnaire in 1988, the hazard ratios for young adult BMI among men were attenuated, while those for women were materially unchanged.

Birth weight

Most studies of birth weight and risk of central nervous system malignancies have focused on associations with childhood brain tumors rather than adult glioma. These studies have generally demonstrated increased risk of childhood brain tumors with increasing birth weight [28, 29]. The study by Kitahara et al. also found evidence of increased risk of adult glioma with higher birth weight (HR 1.13, 95% CI 1.04–1.24, per 0.5 kg) [27]. In the present study, we observed a higher risk in the 5.5–6.9 lb. category, with reduced risk of adult glioma at both higher and lower weights, particularly among women. Our study had only modest statistical power to observe differences in risk by birth weight, however, and the

late ascertainment of this exposure resulted in inclusion of only 136 cases from NHS and 68 cases from HPFS. To help clarify the observed associations between birth weight and risk of glioma, this question should be further explored using large birth cohorts with adequate duration of follow-up.

Height

We found that increased height was associated with higher risk of glioma among women, but not significantly so among men. Prior studies on this association have consistently shown increased risk of glioma with increased height. The study of 1.8 million Norwegian men and women by Wiedmann et al. observed increased risk of glioma with increased adult height (HR 1.18 per 10 cm increase) [2]. The NIH-AARP cohort also found significant associations between taller height (1.9 vs. <1.6 m) and increased risk of glioma [3]. Benson et al. similarly observed a relative risk of glioma of 1.19 per 10 cm increase in height (95% CI 1.10–1.30). The EPIC study of 340 gliomas reported no association with height [6]. Most studies have not stratified by sex; however, differences in association by sex have been previously reported. Kitahara et al. identified increased risk among Danish boys ages 7–13 (HR 1.17, 95% CI 1.05–1.30 for each 5.1 cm at age 7; HR 1.21, 95% CI 1.09–1.35 for each 7.6 cm at age 13), but no increased risk among Danish girls at either age [27]. These results are interesting in light of the aforementioned differences in growth trajectories between boys and girls at these ages.

Height is a risk factor for cancers of other sites, including prostate [30] and breast [10]. Hypotheses for this relationship include the higher total body mass of individuals of higher height, resulting in a larger number of cells that could possibly undergo malignant transformation. Prior studies have suggested that brain weight increases with higher adult height, with one study reporting approximately a 3 g increase in brain weight for each 1 cm of body length [31]. Alternatively, others have hypothesized that factors promoting higher growth during adolescence, such as circulating growth factors, may increase risk of malignant transformation [10, 30]. This hypothesis would not explain the long latent period between adolescent growth and diagnosis of primary brain malignancies observed in this study, however.

Pre-clinical weight change

Some investigators have suggested that glioma may exert effects years before diagnosis [11]. Schwartzbaum et al. reported excess epilepsy among participants who later developed glioma as long as 8 years prior to diagnosis when compared to healthy controls who remained free of cancer [11]. However, we found no evidence for pre-diagnostic weight loss, either with lagged analyses of BMI, or with the analysis of weight residuals in the years preceding diagnosis. This suggests that reverse causation by pre-diagnostic weight loss does not represent a significant issue in studies of BMI and glioma risk, and that prior cross-sectional assessments of the association between higher BMI and glioma risk are not downwardly biased by subclinical weight loss.

In this study, results were not materially different for any analyses when restricting to GBM, but the number of non-GBM cases ($n = 187$) was limited. This finding is consistent with

previous reports that have not demonstrated differences comparing GBM to lower grade glioma on measures such as height and BMI [2]. Nevertheless, some studies have identified possible differences by more granular glioma subtypes, including by isocitrate dehydrogenase (IDH) mutation status [2]. Future studies should identify these subtypes to evaluate if there are differences between subgroups of this highly heterogeneous diagnosis.

Conclusion

Adult BMI and waist circumference were not associated with glioma risk. Greater height was associated with higher risk in women but less so in men; inconsistent findings were observed for BMI during childhood and adolescence. Based on body somatotypes, women with heavier body types during childhood and young adulthood may be at lower risk, although this association was not observed later in life with measurements of BMI. We found no evidence of significant weight loss in the years preceding diagnosis of glioma or GBM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We would like to thank the participants and staff of the Nurses' Health Study and the Health Professionals Follow-Up Study for their valuable contributions as well as the following state cancer registries for their help: AL, AZ, AR, CA, CO, CT, DE, FL, GA, ID, IL, IN, IA, KY, LA, ME, MD, MA, MI, NE, NH, NJ, NY, NC, ND, OH, OK, OR, PA, RI, SC, TN, TX, VA, WA, and WY. The authors assume full responsibility for analyses and interpretation of these data.

Funding National Institutes of Health (NIH) Training Grant T32 CA 009001 (DJC, MKD). The authors acknowledge support from the following Grants: UM1 CA186107, P01 CA87969, and UM1 CA167552.

References

1. Sergentanis TN, Tsvigoulis G, Perlepe C et al. (2015) Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a metaanalysis. *PloS ONE* 10:e0136974 [PubMed: 26332834]
2. Wiedmann MK, Brunborg C, Di Ieva A et al. (2016) The impact of body mass index and height on the risk for glioblastoma and other glioma subgroups: a large prospective cohort study. *Neuro-Oncology* 19:976–985
3. Moore SC, Rajaraman P, Dubrow R et al. (2009) Height, body mass index, and physical activity in relation to glioma risk. *Cancer Res* 69:8349–8355 [PubMed: 19808953]
4. Niedermaier T, Behrens G, Schmid D, Schlecht I, Fischer B, Leitzmann MF (2015) Body mass index, physical activity, and risk of adult meningioma and glioma: a meta-analysis. *Neurology* 85:1342–1350 [PubMed: 26377253]
5. Wiedmann M, Brunborg C, Lindemann K et al. (2013) Body mass index and the risk of meningioma, glioma and schwannoma in a large prospective cohort study (The HUNT Study). *Br J Cancer* 109:289–294 [PubMed: 23778522]
6. Michaud DS, Bove G, Gallo V et al. (2011) Anthropometric measures, physical activity, and risk of glioma and meningioma in a large prospective cohort study. *Cancer Prev Res* 4:1385–1392
7. Little RB, Madden MH, Thompson RC et al. (2013) Anthropometric factors in relation to risk of glioma. *Cancer Causes Control* 24:1025–1031 [PubMed: 23456313]

8. Ostrom QT, Gittleman H, Xu J et al. (2016) CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2009–2013. *Neuro-Oncology*. 18: v1–v75 [PubMed: 28475809]
9. Arslan AA, Helzlsouer KJ, Kooperberg C et al. (2010) Anthropometric measures, body mass index, and pancreatic cancer: a pooled analysis from the pancreatic cancer cohort consortium (PanScan). *Arch Intern Med* 170:791–802 [PubMed: 20458087]
10. Warner ET, Hu R, Collins LC et al. (2016) Height and body size in childhood, adolescence, and young adulthood and breast cancer risk according to molecular subtype in the nurses' health studies. *Cancer Prev Res* 9:732–738
11. Schwartzbaum J, Jonsson F, Ahlbom A et al. (2005) Prior hospitalization for epilepsy, diabetes, and stroke and subsequent glioma and meningioma risk. *Cancer Epidemiol Biomark Prev* 14:643–650
12. Wolpin BM, Chan AT, Hartge P et al. (2009) ABO blood group and the risk of pancreatic cancer. *J Natl Cancer Inst* 101:424–431 [PubMed: 19276450]
13. Khalili H, Wolpin BM, Huang ES et al. (2011) ABO blood group and risk of colorectal cancer. *Cancer Epidemiol Biomark Prev* 20:1017–1020
14. Smith-Warner SA, Spiegelman D, Ritz J et al. (2006) Methods for pooling results of epidemiologic studies: the pooling project of prospective studies of diet and cancer. *Am J Epidemiol* 163:1053–1064 [PubMed: 16624970]
15. Rimm EB, Stampfer MJ, Colditz GA, Chute CG, Litin LB, Willett WC (1990) Validity of self-reported waist and hip circumferences in men and women. *Epidemiology* 1:466–473 [PubMed: 2090285]
16. Troy LM, Hunter DJ, Manson JE, Colditz GA, Stampfer MJ, Willett WC (1995) The validity of recalled weight among younger women. *Int J Obes Relat Metab Disord* 19:570–572 [PubMed: 7489028]
17. Stunkard AJ, Sorensen T, Schulsinger F (1983) Use of the Danish adoption register for the study of obesity and thinness. *Res Publ Assoc Res Nerv Mental Dis* 60: 115–120
18. Must A, Willett WC, Dietz WH (1993) Remote recall of childhood height, weight, and body build by elderly subjects. *Am J Epidemiol* 138:56–64 [PubMed: 8333427]
19. Stampfer MJ, Willett WC, Speizer FE et al. (1984) Test of the national death index. *Am J Epidemiol* 119:837–839 [PubMed: 6720679]
20. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K (2016) Body fatness and cancer—viewpoint of the IARC working group. *N Engl J Med* 375:794–798 [PubMed: 27557308]
21. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 348:1625–1638 [PubMed: 12711737]
22. Oh SW, Yoon YS, Shin SA (2005) Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea national health insurance corporation study. *J Clin Oncol* 23:4742–4754 [PubMed: 16034050]
23. Tyagi V, Theobald J, Barger J et al. (2016) Traumatic brain injury and subsequent glioblastoma development: review of the literature and case reports. *Surg Neurol Int* 7:78 [PubMed: 27625888]
24. Gu J, Liu Y, Kyritsis AP, Bondy ML (2009) Molecular epidemiology of primary brain tumors. *Neurotherapeutics* 6:427–435 [PubMed: 19560733]
25. Lehrer S, Green S, Rendo A, Rosenzweig KE (2015) Measles may be a risk factor for malignant brain tumors. *Brain Tumor Res Treat* 3:65–67
26. Brenner AV, Linet MS, Shapiro WR et al. (2004) Season of birth and risk of brain tumors in adults. *Neurology* 63:276–281 [PubMed: 15277620]
27. Kitahara CM, Gamborg M, Rajaraman P, Sorensen TI, Baker JL (2014) A prospective study of height and body mass index in childhood, birth weight, and risk of adult glioma over 40 years of follow-up. *Am J Epidemiol* 180:821–829 [PubMed: 25205831]
28. Harder T, Plagemann A, Harder A (2008) Birth weight and subsequent risk of childhood primary brain tumors: a meta-analysis. *Am J Epidemiol* 168: 366–373 [PubMed: 18579539]

29. Georgakis MK, Kalogirou EI, Liaskas A et al. (2017) Anthropometrics at birth and risk of a primary central nervous system tumour: a systematic review and meta-analysis. *Eur J Cancer* 75:117–131 [PubMed: 28219020]
30. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Willett WC (1997) Height, body weight, and risk of prostate cancer. *Cancer Epidemiol Biomark Prev* 6:557–563
31. Skullerud K (1985) Variations in the size of the human brain. Influence of age, sex, body length, body mass index, alcoholism, Alzheimer changes, and cerebral atherosclerosis. *Acta Neurol Scand* 102:1–94

Fig. 1. Body somatotypes. This figure shows the body somatotypes from which participants were asked to identify at ages 5, 10, 20, 30, 40, and current in the 1988 questionnaire for both cohorts [17]

Table 1

Age-adjusted demographics of study participants by cohort at baseline, 1976 for NHS and 1986 for HPFS

	NHS (n = 121,696)		HPFS (n = 51,400)		Overall cohort (n = 51,220)
	Incident cases (n = 328)	Overall cohort (n = 12,1368)	Incident cases (n = 180)		
Age, years (mean ± SD)	45.5 ± 6.9	42.9 ± 7.2	56.3 ± 9.0		54.8 ± 10.0
Height, inches (mean ± SD)	65.0 ± 2.0	64.5 ± 2.4	70.3 ± 3.0		70.1 ± 2.8
BMI, kg/m ² (mean ± SD)	23.9 ± 3.1	23.8 ± 4.2	25.7 ± 4.2		25.5 ± 3.4
Smoking status (%)					
Never smoker	41	43	49		44
Former smoker	27	23	42		42
Current smoker	32	33	5		10
Unknown	0	0	4		4

All values apart from age are age adjusted to the distribution of the cohort

BMI Body mass index, HPFS Health Professionals Follow-Up Study, NHS nurses' health study, SD standard deviation

Table 2
Age-adjusted risk of glioma in HPFS and NHS by body habitus, using Cox proportional hazard modeling

	NHS (n =328)				HPFS (n =180)				Total (n =508) ^a			
	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	P heterogeneity		
BMI ^b												
<25	168	Ref		85	Ref		253	Ref				
25–29.9	90	0.85	0.66–1.10	74	0.80	0.58–1.10	164	0.83	0.68–1.01	0.78		
30	70	1.14	0.86–1.51	21	0.92	0.57–1.49	91	1.08	0.85–1.38	0.45		
Continuous (per 5 kg/m ²)	328	1.06	0.95–1.17	180	1.11	0.92–1.34	508	1.07	0.98–1.17	0.65		
2-year lagged BMI ^c												
<25	158	Ref		77	Ref		235	Ref				
25–29.9	91	0.94	0.72–1.21	76	0.96	0.70–1.32	167	0.95	0.77–1.16	0.88		
30	70	1.26	0.94–1.67	18	0.93	0.55–1.55	88	1.17	0.91–1.50	0.31		
Continuous (per 5 kg/m ²)	319	1.06	0.95–1.18	171	1.13	0.93–1.37	490	1.07	0.98–1.18	0.57		
4-year lagged BMI ^c												
<25	159	Ref		69	Ref		228	Ref				
25–29.9	94	0.99	0.76–1.28	66	0.96	0.69–1.34	161	0.98	0.80–1.20	0.89		
30	57	1.07	0.78–1.45	22	1.34	0.83–2.18	78	1.14	0.88–1.48	0.43		
Continuous (per 5 kg/m ²)	309	1.02	0.91–1.14	156	1.14	0.93–1.41	465	1.05	0.95–1.15	0.34		
6-year lagged BMI ^c												
<25	147	Ref		66	Ref		213	Ref				
25–29.9	94	1.06	0.82–1.38	52	0.74	0.52–1.05	147	0.93	0.76–1.15	0.10		
30	50	1.03	0.74–1.42	18	1.09	0.65–1.84	67	1.04	0.79–1.38	0.85		
Continuous (per 5 kg/m ²)	290	1.01	0.90–1.13	134	1.07	0.84–1.36	424	1.02	0.92–1.13	0.71		
8-year lagged BMI ^c												
<25	150	Ref		63	Ref		213	Ref				
25–29.9	86	1.01	0.77–1.31	45	0.73	0.50–1.06	132	0.90	0.73–1.12	0.17		
30	44	0.96	0.68–1.35	16	1.16	0.67–2.01	59	1.01	0.76–1.35	0.57		
Continuous (per 5 kg/m ²)	277	1.02	0.90–1.15	122	1.11	0.86–1.42	399	1.03	0.93–1.15	0.54		

	NHS (<i>n</i> = 328)			HPFS (<i>n</i> = 180)			Total (<i>n</i> = 508) ^a			<i>P</i> heterogeneity
	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	
Baseline BMI ^d										
<25	215	Ref		90	Ref		305	Ref		
25–29.9	79	1.21	0.93–1.56	71	0.82	0.60–1.11	150	1.03	0.84–1.25	0.06
30	32	1.28	0.88–1.86	17	1.12	0.67–1.89	49	1.23	0.91–1.66	0.70
Continuous (per 5 kg/m ²)	326	1.02	0.99–1.04	178	1.02	0.97–1.06	504	1.02	1.00–1.04	0.93
Maximum lifetime BMI										
<25	132	Ref		73	Ref		205	Ref		
25–29.9	107	0.95	0.74–1.24	81	0.71	0.52–0.98	189	0.85	0.69–1.04	0.16
30	89	1.12	0.85–1.48	26	0.76	0.48–1.20	114	1.01	0.80–1.28	0.16
Continuous (per 5 kg/m ²)	328	1.06	0.96–1.17	180	1.06	0.87–1.28	508	1.06	0.97–1.15	0.99
Young adult BMI ^e										
<25	223	Ref		126	Ref		349	Ref		
25	36	1.34	0.94–1.89	47	1.37	0.98–1.91	83	1.35	1.06–1.72	0.93
Continuous (per 5 kg/m ²)	259	1.07	0.87–1.31	173	1.26	1.01–1.57	432	1.15	0.99–1.33	0.29
Waist circumference quintiles ^{f,g}										
1	25	Ref		27	Ref		52	Ref		
2	27	0.78	0.51–1.18	24	0.75	0.47–1.20	51	0.77	0.56–1.04	0.91
3	34	0.93	0.64–1.36	24	0.90	0.56–1.43	58	0.92	0.68–1.23	0.90
4	34	0.91	0.62–1.33	26	0.73	0.47–1.15	60	0.83	0.62–1.11	0.47
5	39	1.02	0.72–1.47	34	1.08	0.72–1.63	73	1.05	0.80–1.37	0.84
Continuous (per 1 inch)	159	1.02	0.99–1.05	135	1.02	0.97–1.06	294	1.02	0.99–1.04	0.93
Height quintiles ^h										
1	64	Ref		25	Ref		89	Ref		
2	28	0.82	0.53–1.28	34	0.95	0.56–1.59	62	0.87	0.62–1.22	0.69
3	101	1.18	0.86–1.62	33	1.25	0.74–2.11	134	1.20	0.92–1.57	0.85
4	60	1.58	1.11–2.24	59	1.44	0.90–2.31	119	1.53	1.15–2.02	0.77
5	75	1.41	1.01–1.97	29	1.16	0.67–1.99	104	1.34	1.01–1.78	0.54
Continuous (per 1 inch)	328	1.09	1.04–1.14	180	1.03	0.98–1.09	508	1.07	1.03–1.11	0.15

BMI/Body Mass Index, HPFS Health Professionals Follow-up Study, NHS Nurses' Health Study

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

^gObtained via meta-analysis by cohort using the fixed effects model

^hBMI in kg/m², current with continuous update

^cTo control for pre-diagnosis disease confounding, lagged analyses applied BMI from 2, 4, 6, and 8 years prior to the current period, resulting in exclusion of the first 2, 4, 6, or 8 years of follow-up

^dBMI measured in 1986 for HPFS or 1976 for NHS, without continuous update

^eFor NHS, age 18; for HPFS, age 21

^fFor HPFS, waist circumference was collected in 1987, 1996, and 2008, for NHS, waist circumference was collected in 1986, 1996, and 2000

^gFor HPFS, overall median waist circumference = 37.8 inches, IQR 35.5–40.0; for NHS, median = 32.3 inches, IQR 29.0–36.3

^hFor HPFS, overall median height = 70.0 inches, IQR 68.0–72.0; for NHS, median = 64.0 inches, IQR 63.0–66.0

Table 3

Age-adjusted risk of glioblastoma multiforme in HPFS and NHS by body habitus, using Cox proportional hazard modeling

	NHS (n = 194)				HPFS (n = 127)				Total (n = 321) ^a			
	Cases	Hazard ratio	95% CI		Cases	Hazard ratio	95% CI		Cases	Hazard ratio	95% CI	P-heterogeneity
BMI ^b												
<25	91	Ref			61	Ref			152	Ref		
25–29.9	55	0.94	0.67–1.32		52	0.78	0.54–1.13		107	0.87	0.67–1.11	0.46
30	48	1.42	1.00–2.03		14	0.85	0.47–1.53		62	1.24	0.91–1.68	0.14
Continuous (per 5 kg/m ²)	194	1.12	0.99–1.28		127	1.16	0.93–1.44		321	1.13	1.01–1.27	0.83
2-year lagged BMI ^c												
<25	93	Ref			56	Ref			149	Ref		
25–29.9	52	0.90	0.64–1.26		52	0.89	0.61–1.29		104	0.89	0.69–1.15	0.98
30	46	1.39	0.97–1.98		13	0.91	0.49–1.67		59	1.24	0.91–1.69	0.24
Continuous (per 5 kg/m ²)	191	1.12	0.98–1.28		121	1.17	0.94–1.46		312	1.13	1.01–1.27	0.73
4-year lagged BMI ^c												
<25	95	Ref			51	Ref			146	Ref		
25–29.9	52	0.91	0.65–1.28		49	0.99	0.67–1.45		101	0.94	0.73–1.22	0.76
30	40	1.25	0.85–1.81		14	1.18	0.65–2.15		54	1.23	0.89–1.69	0.89
Continuous (per 5 kg/m ²)	186	1.07	0.93–1.23		114	1.16	0.92–1.47		300	1.10	0.97–1.24	0.57
6-year lagged BMI ^c												
<25	92	Ref			50	Ref			142	Ref		
25–29.9	54	1.01	0.72–1.42		40	0.81	0.54–1.22		94	0.92	0.71–1.20	0.41
30	34	1.14	0.77–1.70		12	1.03	0.55–1.94		56	1.11	0.79–1.56	0.79
Continuous (per 5 kg/m ²)	179	1.06	0.92–1.22		101	1.09	0.83–1.43		280	1.07	0.94–1.21	0.85
8-year lagged BMI ^c												
<25	91	Ref			49	Ref			140	Ref		
25–29.9	54	1.06	0.75–1.49		32	0.71	0.45–1.11		87	0.91	0.70–1.20	0.16
30	28	1.02	0.66–1.56		11	1.08	0.56–2.09		38	1.03	0.72–1.48	0.89
Continuous (per 5 kg/m ²)	171	1.06	0.92–1.24		91	1.12	0.84–1.48		262	1.08	0.94–1.23	0.78

	NHS (<i>n</i> = 194)			HPFS (<i>n</i> = 127)			Total (<i>n</i> = 321) ^d			P-heterogeneity
	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	
Baseline BMI ^d										
<25	126	Ref		63	Ref			Ref		
25–29.9	48	1.26	0.90–1.76	50	0.81	0.56–1.17	98	1.03	0.80–1.32	0.08
30	20	1.37	0.85–2.19	12	1.12	0.61–2.08	32	1.27	0.87–1.85	0.62
Continuous (per 5 kg/m ²)	194	1.03	1.00–1.06	125	1.02	0.97–1.07	319	1.03	1.00–1.06	0.76
Maximum lifetime BMI										
<25	74	Ref		52	Ref		126	Ref		
25–29.9	62	0.95	0.67–1.33	59	0.71	0.49–1.04	121	0.83	0.65–1.07	0.28
30	58	1.24	0.87–1.76	16	0.65	0.36–1.14	74	1.03	0.77–1.40	0.06
Continuous (per 5 kg/m ²)	194	1.10	0.97–1.24	127	1.10	0.88–1.37	321	1.10	0.99–1.22	0.99
Young adult BMI ^e										
<25	134	Ref		87	Ref		221	Ref		
25	21	1.30	0.83–2.05	34	1.43	0.96–2.12	55	1.37	1.02–1.85	0.77
Continuous (per 5 kg/m ²)	155	1.10	0.83–1.39	121	1.22	0.93–1.61	276	1.14	0.95–1.38	0.51
Waist circumference quintiles ^{f,g}										
1	12	Ref		17	Ref		29	Ref		
2	19	0.92	0.56–1.53	17	0.77	0.44–1.34	36	0.85	0.59–1.23	0.63
3	19	0.87	0.53–1.45	21	1.13	0.68–1.88	40	0.99	0.69–1.42	0.48
4	25	1.13	0.72–1.78	17	0.68	0.39–1.18	42	0.92	0.65–1.31	0.16
5	24	1.06	0.67–1.68	22	0.99	0.60–1.64	46	1.03	0.73–1.45	0.85
Continuous (per inch)	99	1.02	0.98–1.06	94	1.01	0.96–1.07	193	1.01	0.98–1.05	0.81
Height quintiles ^h										
1	32	Ref		17	Ref		49	Ref		
2	15	0.88	0.48–1.62	22	0.90	0.48–1.70	37	0.89	0.57–1.39	0.96
3	68	1.59	1.04–2.42	25	1.42	0.77–2.64	93	1.53	1.08–2.17	0.77
4	37	1.95	1.21–3.13	45	1.64	0.93–2.88	82	1.81	1.26–2.61	0.64
5	42	1.58	1.00–2.51	18	1.09	0.56–2.13	60	1.41	0.96–2.05	0.37
Continuous (per inch)	194	1.11	1.05–1.17	127	1.03	0.96–1.10	321	1.07	1.03–1.12	0.08

BMI/Body Mass Index, HPFS Health Professionals Follow-Up Study, NHS Nurses' Health Study

^aObtained via meta-analysis by cohort using the fixed effects model

^bBMI in kg/m², current with continuous update

^cTo control for pre-diagnosis disease confounding, lagged analyses applied BMI from 2, 4, 6, and 8 years prior to the current period, resulting in exclusion of the first 2, 4, 6 or 8 years of follow up

^dBMI measured in 1986 for HPFS or 1976 for NHS, without continuous update

^eFor NHS, age 18; for HPFS, age 21

^fFor HPFS, waist circumference was collected in 1987, 1996, and 2008, for NHS, waist circumference was collected in 1986, 1996, and 2000

^gFor HPFS, overall median waist circumference = 37.8 inches, IQR 35.5–40.0; for NHS, median = 32.3 inches, IQR 29.0–36.3

^hFor HPFS, overall median height = 70.0 inches, IQR 68.0–72.0; for NHS, median = 64.0 inches, IQR 63.0–66.0

Table 4

Age-adjusted risk of glioma and glioblastoma by nine categories of body somatotype at ages 5, 10, 20, 30, 40, and age in 1988, using Cox proportional hazard modeling

Tertile ^a	NHS (n = 201)			HPFS (n = 138)		
	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI
Glioma						
Age 5 body diagrams						
Low (1)	83	Ref		48	Ref	
Middle (2)	53	0.84	0.62–1.13	34	1.18	0.79–1.75
High (3–9)	63	0.65	0.49–0.87	52	1.08	0.76–1.51
Age 10 body diagrams						
Low (1)	65	Ref		29	Ref	
Middle (2) (2–3)	56	0.71	0.53–0.95	70	1.13	0.81–1.57
High (3–9) (4–9)	79	0.65	0.50–0.84	37	1.12	0.75–1.66
Age 20 body diagrams						
Low (1–2)	76	Ref		47	Ref	
Middle (3)	69	0.74	0.57–0.98	40	0.88	0.61–1.28
High (4–9)	56	0.79	0.59–1.06	49	0.92	0.65–1.31
Age 30 body diagrams						
Low (1–2) (1–3)	50	Ref		64	Ref	
Middle (3) (4)	84	0.65	0.50–0.84	37	0.76	0.52–1.11
High (4–9) (5–9)	65	0.54	0.41–0.72	35	0.90	0.61–1.33
Age 40 body diagrams						
Middle (1–3)	92	Ref		37	Ref	
Middle (4)	65	0.65	0.49–0.86	45	0.89	0.62–1.29
High (5–9)	44	0.55	0.40–0.76	55	0.82	0.58–1.16
Age in 1988 body diagrams						
Low (1–3) (1–4)	57	Ref		63	Ref	
Middle (4) (5)	66	0.61	0.46–0.81	46	0.79	0.56–1.12
High (5–9) (6–9)	78	0.52	0.40–0.67	29	0.82	0.54–1.24

Tertile ^a	NHS (n = 123)			HPFS (n = 100)		
	Cases	Hazard Ratio	95% CI	Cases	Hazard Ratio	95% CI
Glioblastoma						
Age 5 body diagrams						
Low (1)	50	Ref		34	Ref	
Middle (2)	37	1.01	0.70–1.47	27	1.41	0.90–2.22
High (3–9)	34	0.61	0.42–0.89	37	1.16	0.77–1.74
Age 10 body diagrams						
Low (1)	37	Ref		17	Ref	
Middle (2) (2–3)	40	0.89	0.62–1.28	56	1.47	0.99–2.18
High (3–9) (4–9)	45	0.66	0.46–0.93	26	1.29	0.80–2.10
Age 20 body diagrams						
Low (1–2)	45	Ref		30	Ref	
Middle (3)	41	0.78	0.54–1.11	31	1.08	0.70–1.67
High (4–9)	37	0.91	0.63–1.32	38	1.14	0.75–1.72
Age 30 body diagrams						
Low (1–2) (1–3)	32	Ref		45	Ref	
Middle (3) (4)	49	0.66	0.47–0.92	27	0.83	0.53–1.29
High (4–9) (5–9)	42	0.61	0.42–0.87	27	1.05	0.67–1.64
Age 40 body diagrams						
Low (1–3)	56	Ref		25	Ref	
Middle (4)	38	0.65	0.45–0.93	34	1.04	0.67–1.60
High (5–9)	29	0.63	0.42–0.94	41	0.95	0.63–1.44
Age in 1988 body diagrams						
Low (1–3) (1–4)	29	Ref		44	Ref	
Middle (4) (5)	43	0.73	0.51–1.04	33	0.81	0.54–1.23
High (5–9) (6–9)	51	0.62	0.44–0.87	21	0.84	0.51–1.36

HPFS Health Professionals Follow-Up Study, NHS Nurses' Health Study

^aSomatotypes categorized by tertiles for each cohort. Numbers in parentheses indicate which somatotypes fall into each tertile for NHS and HPFS