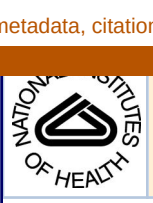

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Body mass index at early adulthood, subsequent weight change, and cancer incidence and mortality

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Abstract

Obesity later in adulthood is associated with increased risks of many cancers. However, the effect of body fatness in early adulthood, and change in weight from early to later adulthood on cancer risk later in life is less clear. We used data from 13,901 people aged 45-64 in the Atherosclerosis Risk in Communities cohort who at baseline (1987-1989) self-reported their weight at the age of 25 and had weight and height measured. Incident cancers were identified through 2006 and cancer deaths were ascertained through 2009. Multivariable Cox proportional hazard models were used to relate body mass index (BMI) at age 25 and percent weight change from age 25 to baseline to cancer incidence and mortality. After adjusting for weight change from age 25 until baseline, a 5 kg/m^2 increment in BMI at age 25 was associated with a greater risk of incidence of all cancers in women [hazard ratio (95% confidence interval): 1.10 (1.02-1.20)], but not in men. Associations with incident endometrial cancer were strong [1.83 (1.47-2.26)]. After adjusting for BMI at age 25, a 5% increment in weight from age 25 to baseline was associated with a greater risk of incident post-menopausal breast cancer [1.05 (1.02-1.07)] and endometrial cancer [1.09 (1.04-1.14)] in women and incident colorectal cancer [1.05 (1.00-1.10)] in men. Excess weight during young adulthood and weight gain from young to older adulthood may be independently associated with subsequent cancer risk. Excess weight and weight gain in early adulthood should be avoided.

Keywords

body mass index; cancer risk; early adulthood; obesity; weight gain

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Introduction

Excess body fatness in mid- and later-life has been consistently linked to increased risks of postmenopausal breast, endometrial, colorectal, kidney, pancreatic and esophageal cancers [1]. Cancer has a complex etiology and often has a long latent period; the process of tumor initiation, promotion, and progression can take decades. Therefore, exposure at an earlier time may influence risk of cancer later in life. However, the effect of body fatness in early adulthood, and change in weight from early to later adulthood on cancer risk later in life is less clear.

The prevalence of obesity in young adults aged 18-29 years tripled between 1971-1974 and 2005-2006 [2]. This escalation in the prevalence of obesity in young adults may lead to an increased cancer burden in the future. The purpose of this study was to estimate the association of BMI at age 25 and percent weight change from age 25 to later adulthood with incidence and mortality of overall cancer and cancer at sites that have strong evidence linking them to obesity measured in mid- and later-life.

Material and Methods

Study population

The Atherosclerosis Risk in Communities (ARIC) study is a cohort study of atherosclerosis and cardiovascular disease in four U.S. communities. From 1987 to 1989, 15,792 men and women aged 45-64 were recruited from Forsyth County, North Carolina; Jackson, Mississippi; the northwestern suburbs of Minneapolis, Minnesota; and Washington County, Maryland [3]. Upon entering the study, the participants received an extensive baseline examination, including medical, social and demographic data. Follow-up examinations occurred three times at approximately 3-year intervals. Annual follow-up telephone calls were made between exams to maintain contact with participants and ascertain interim clinical events. The ARIC study was approved by the Institutional Review Board (IRB) of each field center. This analysis was approved by the University of North Carolina at Chapel Hill non-Biomedical IRB on research involving human subjects.

Exposure assessment

All exposures included in this analysis were ascertained at the baseline visit. Participants were asked to recall their weight in pounds at age 25. Baseline height to the nearest centimeter (cm) and weight to the nearest pound were measured by clinic technicians with the participants wearing a scrub suit and no shoes. Body mass index (BMI) at age 25 was calculated using baseline height with the formula weight (kg)/height^2 (m^2). BMI at age 25 were categorized as underweight (<18.5 kg/m^2), normal weight (18.5 to <25.0 kg/m^2), overweight (25.0 to <30.0 kg/m^2) or obese (≥30.0 kg/m^2). The percent weight change from age 25 to baseline was calculated as [(weight at baseline-weight at age 25)/weight at age 25] × 100% and categorized [4] as weight loss (<−3%), weight maintenance (−3 to <3%), weight gain 1 (3 to <10%) and weight gain 2 (≥10%).

Covariates assessed by interviewer-administered questionnaires at baseline included education, cigarette smoking, alcohol consumption, physical activity and reproductive

history. Education was categorized as less than high school graduate, high school graduate and at least some college. From the participants' responses on smoking, we coded the cigarette smoking status at age 25 (yes/no) and at baseline (never, former or current smoker). The participants were asked about the frequency and the number of drinks they usually have per week for wine, beer and hard liquor respectively. The usual ethanol intake (g/wk) was calculated as the sum of the product of the daily frequency of each type of beverage and the typical ethanol content of each type of beverage (4-oz glass of wine: 10.8 g, 12-oz bottle or can of beer: 13.2 g, 1.5-oz shot of hard liquor: 15.1 g [5]. The participants' drinking status was classified as never or rare, former, current light (0-30 g/wk), current moderate (30-70 g/wk in women and 30-140 g/wk in men) and current heavy (>70 g/wk in women and >140 g/wk in men) [6]. Physical activity was assessed using the Baecke questionnaire [7] and the participants were categorized according to tertiles of the sport index during leisure time. The female participants were asked their age when menstrual periods started; whether they had reached menopause; and age when menopause began.

Case ascertainment

The case ascertainment method was described previously [8, 9]. Briefly, incident cancer was ascertained from 1987 to 2006 through linkages to cancer registries and supplemented by hospital records. Cancer deaths through the end of 2009 were ascertained from death certificates. Nine deaths from pancreatic cancer and another 9 deaths from esophageal cancer before 2006 were found to be the first report of these cancers, and these deaths were considered incident cancer cases as well.

Exclusions

From the original ARIC cohort (n=15,792), we excluded participants who were not black or white (n=48) and those from Minneapolis, MN and Washington County, MD who were black (n=55) as a standard in this cohort [10]. We also excluded those whose weight at age 25 was missing (n=187); those whose weight at baseline was missing (n=26); those who reported a prior cancer diagnosis at baseline (except non-melanoma skin cancer); and those with missing information on cancer (n=1052), education, cigarette smoking, alcohol consumption or physical activity at baseline (n=131), or cigarette smoking at age 25 (n=63). In addition, we excluded those diagnosed with cancer (except non-melanoma skin cancer) during the first 3 years of follow-up (n=331) to minimize reverse causation. The analysis sample size was 13,901 (7,569 women and 6,332 men).

Statistical analysis

The analysis was conducted separately for men and women. The associations of BMI at age 25 and percent weight change from age 25 to baseline with cancer incidence and mortality were examined for cancer overall (any cancer except non-melanoma skin cancer), the group of obesity-related cancers (in women: colorectal, endometrial, kidney, pancreatic and esophageal cancer combined; in men: colorectal, kidney, pancreatic and esophageal cancer combined), and the following obesity-related cancer sites: post-menopausal breast cancer, colorectal cancer and endometrial cancer [1]. Cancer-specific analyses were not done for kidney cancer, pancreatic cancer and esophageal cancer due to the small number of cases (<55 in both men and women). When examining post-menopausal breast cancer, we used

the first visit at which the participant self- reported reaching menopause as the “baseline” visit; because this baseline differed from that of the other cancers, we did not include post-menopausal breast cancer in the group of obesity-related cancers in women. Time to cancer incidence was calculated as the time from baseline to December 31, 2006, the date of the first primary cancer diagnosis, death or loss to follow-up, whichever occurred first. Time to cancer mortality was calculated as the time from baseline to December 31, 2009, death or loss to follow-up, whichever occurred first.

Adjusted hazard ratios (HR) were calculated using Cox proportional hazards regression. If the overweight or obese categories had <10 cases, then the two BMI categories were combined to increase stability of the effect estimates. To test for linearity of the associations, we examined the association between continuous BMI and hazard rates by fitting models with linear, quadratic forms, or quadratic splines and then comparing the nested models using likelihood ratio tests at significant level of 0.05. If a linear association was supported, adjusted HRs were also calculated for a 5 kg/m^2 increment of BMI. Three adjusted models were fit: model 1 included race-center, age and height at baseline, education, cigarette smoking status at age 25, and age at menarche (for breast cancer, endometrial cancer, and obesity-related cancers in women); model 2 included the above covariates and the following variables at baseline: cigarette smoking, alcohol consumption and physical activity, menopause status (for endometrial cancer and obesity-related cancers in women) and age at menopause (for post-menopausal breast cancer; model 3 further included percent weight change category from 25 to baseline. Similarly for percent weight change categories, two models were fit to calculate HRs adjusted for above covariates with and without BMI at age 25. If a linear association was supported, adjusted HRs were also calculated for a 5% increment of weight change. The proportional hazards assumption was tested with correlation of scaled Schoenfeld residuals with time. The proportional hazards assumption was not met for age, thus interaction terms of age with time were added to the models. Interaction between BMI at age 25 and weight change was tested at an α-level of 0.10, and none was detected.

In order to further separate the effects of BMI at age 25 and weight change, we conducted two subgroup analyses: one among those who maintained weight, a second among those who had normal weight at age 25. For the first analysis, models were fitted adjusting for all covariates except weight change to examine the effect of BMI at age 25. Similarly, for the second analysis, models were fitted to examine the effect of weight change.

Results

The descriptive characteristics of the cohort are presented in Table 1. Seventy-seven percent of women and 62% of men were normal weight at age 25, while only 36% of women and 27% of men were in the normal weight range at baseline when participants were between 45 and 64 years of age. On average women gained 33 lbs (27%) and men gained 22 lbs (15%) between age 25 and baseline.

As shown in Table 2, the association of BMI at age 25 with cancer incidence was mainly seen in women. After adjustment for lifestyle factors and weight change from age 25 to

baseline, being overweight or obese at age 25 was associated with an increased risk of 5 obesity-related cancer combined in women. Examined separately, the association with incident endometrial cancer was especially strong. Being underweight at age 25 was associated with lower risk of post-menopausal breast cancer.

Being obese at age 25 was associated with higher risk of death from obesity-related cancers in men (Table 3). Although based on a small sample size, higher BMI at age 25 was associated with greater risk of endometrial cancer mortality in women (Table 3).

In the subgroup analysis of subjects who maintained weight (441 women and 727 men), there were only sufficient case numbers for the analyses of any cancer and obesity-related cancer combined. The results, although not statistically significant, confirmed the above findings of the effect of BMI at age 25 independent of weight change: the obese women at age 25 appeared to have a higher risk of obesity-related cancer [HR (95%CI) = 1.69 (0.19-14.92)] and the obese men at age 25 appeared to have a higher risk of death from obesity-related cancers [1.72 (0.34-8.63)] compared to those of normal weight at age 25.

For weight change, the adjusted HRs with or without BMI at age 25 were very similar (Table 4 and 5). No significant findings were observed for weight change categories. However, when using the linear form of weight change, in women higher weight change was found to be associated with higher risk of incident post-menopausal breast cancer, endometrial cancer and obesity-related cancer combined, as well as higher risk of death from post-menopausal breast cancer and colorectal cancer. In men, higher weight change was associated with higher risk of incident obesity-related cancer combined and colorectal cancer.

In the subgroup analysis of subjects who were of normal weight at age 25 (5821 women and 3929 men), the results were also consistent with the findings in the primary analyses: in women, 5% weight gain was associated with a significantly higher risk of incident post-menopausal breast cancer [1.05 (1.02-1.07)], endometrial cancer [1.08 (1.02-1.15)] and obesity-related cancer [1.04 (1.01-1.07)], as well as a higher risk of death from colorectal cancer [1.09 (1.01-1.17)]. In men, 5% weight gain was associated with a slightly increased risk of incident obesity-related cancer [1.03 (0.98-1.08)] and colorectal cancer [1.03 (0.97-1.10)], although the HRs were not statistically significant.

In the primary analysis we excluded the first three years of follow-up to minimize reverse causation. Nevertheless, the results were similar when including cases diagnosed during the first three years of follow-up (data not shown). The results were similar to overall when restricting to participants who never smoked (data not shown). The results for total cancer incidence and mortality in men were unchanged after excluding prostate cancers (data not shown).

Discussion

Our analyses showed that after controlling for subsequent weight change, higher BMI at age 25 was associated with a higher risk of any cancer and 5 types of obesity-related cancers combined in women. Examined separately, the association between BMI at age 25 and

endometrial cancer in women was especially strong. After controlling for BMI at age 25, weight gain was associated with a higher risk of 5 types of obesity-related cancers in both women and men, as well as a higher risk of post-menopausal breast cancer. Studied separately, endometrial cancer in women and colorectal cancer in men were positively associated with weight gain. Weight gain was also associated with death from any cancer, post-menopausal breast cancer and colorectal cancer in women.

Existing literature has provided convincing evidence that obesity as measured in middle and later age is associated with higher risk of the six site-specific cancers we examined [1]. Body weight at middle and later adulthood is a combination of body weight at early adulthood and the subsequent weight change. This study attempted to tease apart the effects from BMI at early adulthood and adulthood weight change on cancer risk. We identified evidence for an association of obesity-related cancer risk with both BMI at age 25 and subsequent weight gain in women, but in men the association was only seen for weight change. The findings could be translated into a public health message that avoiding adulthood weight gain is important for everybody, while keeping a healthy weight at early adulthood is particularly important for women.

The risk of excess body weight in early life has been most extensively studied for breast cancer. The majority of studies showed an inverse association between increased adiposity in early life and pre-menopausal breast cancer [11-19] or total breast cancer [20-23]. The results are less consistent for post-menopausal breast cancer, with reduced risk [13, 16, 24, 25], no association [14, 26, 27] or increased risk [28] observed with higher BMI at early adulthood (aged 18 to 20s). All these previous studies on post-menopausal breast cancer used BMI (or other body size measures for earlier studies) as a linear variable or categorized it by distribution or other arbitrary rules; none of them used WHO- defined weight status categories. When we examined the association between weight status at age 25 and incidence of breast cancer among post-menopausal women, we found that the linear form of BMI at age 25 was not adequate in our models, suggesting that the assumption of a linear relationship between BMI at age 25 and post-menopausal breast cancer risk may not be valid in certain populations. This may partly explain the inconsistencies in previous studies. We further found that those who were underweight at age 25 had a greatly decreased risk (almost half) of post-menopausal breast cancer compared to women of normal weight at age 25 after adjustment for weight change. This may be due to low estrogen levels in young women with insufficient body fat [29]. We do not want to overemphasize this observed “benefit” of being underweight at early adulthood since severe underweight or having an estrogen deficiency may lead to various health problems among young women [30].

Current literature on adult weight gain and cancer incidence is mostly on breast cancer, and post-menopausal breast cancer is the only cancer type with adequate evidence supporting a probable increased risk associated with adult weight gain [1]. Our findings from both the incidence and mortality analyses confirmed this association.

We did not find a significant association between BMI in early adulthood and risk of colorectal cancer in women and men. This is consistent with the findings from the Nurses’ Health study [31], the Iowa Women’s Health Study [32], and a recent cohort study from

Scotland [27]. However, three previous studies33-35 in men found that higher BMI at late adolescence or early adulthood was associated with increased risk of colon cancer. Our study, along with the previous studies, suggests that the association of body size in young adulthood and colorectal cancer risk is more complicated and may differ according to gender and site (colon or rectum). Future studies will be needed to elucidate this.

Endometrial cancer is one of the cancers with strong links to body fatness [1]. Previous studies showed no evidence of effect modification by menopause status [1]. BMI or weight as a young adult has been shown to be positively associated with risk of endometrial cancer in later life by both cohort [36, 37] and case-control [38-40] studies. Besides confirming the previous findings, our study further found that BMI in early adulthood and subsequent weight gain may be independent risk factors for endometrial cancer.

Our study was limited by relatively small sample sizes for the less common cancer types. Also, there was potential for recall error from the self-reported weight at age 25. This error was unlikely to be related to case status given the prospective design, but the resulting non-differential misclassification may have attenuated the associations. We did not have information on tumor stage, grade and histology as well as receptor status for breast cancer, thus were not able to evaluate the association by subtypes for specific cancers.

In summary, our study provides evidence that BMI at age 25 may influence risk of cancer later in life in females independent of subsequent weight change, with the association being especially strong for endometrial cancer. Our study also showed that more weight gain from age 25 to later adulthood was associated with higher risk of post-menopausal breast cancer and endometrial cancer in females and higher risk of colorectal cancer in males independent of BMI at age 25. This study supports the importance of avoiding excess weight during young adulthood and weight gain through adulthood as they may independently contribute to increases in cancer risk in later life.

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References

1. AICR/WCRF. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. AICR; Washington DC: 2007.
2. U.S. Department of Health and Human Services CfDCaP, National Center for Health Statistics., Health, United States. With Special Feature on the Health of Young Adults. 2008. 2009.
3. The ARIC investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol. 1989; 129:687–702. [PubMed: 2646917]

4. Stevens J, Truesdale KP, McClain JE, Cai J. The definition of weight maintenance. Int J Obes (Lond). 2006; 30:391–9. [PubMed: 16302013]
5. Colditz GA, Giovannucci E, Rimm EB, Stampfer MJ, Rosner B, Speizer FE, Gordis E, Willett WC. Alcohol intake in relation to diet and obesity in women and men. Am J Clin Nutr. 1991; 54:49–55. [PubMed: 2058587]
6. Schoenborn, CA.; Adams, PF.; Barnes, PM.; Vickerie, JL.; Schiller, JS. Vital and health statistics Series 10, Data from the National Health Survey. 2004. Health behaviors of adults: United States, 1999-2001; p. 1-79.
7. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. Am J Clin Nutr. 1982; 36:936–42. [PubMed: 7137077]
8. Mink PJ, Shahar E, Rosamond WD, Alberg AJ, Folsom AR. Serum insulin and glucose levels and breast cancer incidence: the atherosclerosis risk in communities study. Am J Epidemiol. 2002; 156:349–52. [PubMed: 12181105]
9. Ahmed RL, Schmitz KH, Anderson KE, Rosamond WD, Folsom AR. The metabolic syndrome and risk of incident colorectal cancer. Cancer. 2006; 107:28–36. [PubMed: 16721800]
10. Cheung N, Shankar A, Klein R, Folsom AR, Couper DJ, Wong TY. Age-related macular degeneration and cancer mortality in the atherosclerosis risk in communities study. Archives of ophthalmology. 2007; 125:1241–7. [PubMed: 17846365]
11. Ruder EH, Dorgan JF, Kranz S, Kris-Etherton PM, Hartman TJ. Examining breast cancer growth and lifestyle risk factors: early life, childhood, and adolescence. Clin Breast Cancer. 2008; 8:334–42. [PubMed: 18757260]
12. Le Marchand L, Kolonel LN, Earle ME, Mi MP. Body size at different periods of life and breast cancer risk. Am J Epidemiol. 1988; 128:137–52. [PubMed: 3381822]
13. Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter DJ, Manson JE, Hennekens CH, Rosner B, Speizer FE, Willett WC. Dual effects of weight and weight gain on breast cancer risk. JAMA. 1997; 278:1407–11. [PubMed: 9355998]
14. Trentham-Dietz A, Newcomb PA, Storer BE, Longnecker MP, Baron J, Greenberg ER, Willett WC. Body size and risk of breast cancer. Am J Epidemiol. 1997; 145:1011–9. [PubMed: 9169910]
15. Peacock SL, White E, Daling JR, Voigt LF, Malone KE. Relation between obesity and breast cancer in young women. Am J Epidemiol. 1999; 149:339–46. [PubMed: 10025476]
16. Hirose K, Tajima K, Hamajima N, Takezaki T, Inoue M, Kuroishi T, Miura S, Tokudome S. Effect of body size on breast-cancer risk among Japanese women. Int J Cancer. 1999; 80:349–55. [PubMed: 9935173]
17. Weiderpass E, Braaten T, Magnusson C, Kumle M, Vainio H, Lund E, Adami HO. A prospective study of body size in different periods of life and risk of premenopausal breast cancer. Cancer Epidemiol Biomarkers Prev. 2004; 13:1121–7. [PubMed: 15247122]
18. Michels KB, Terry KL, Willett WC. Longitudinal study on the role of body size in premenopausal breast cancer. Arch Intern Med. 2006; 166:2395–402. [PubMed: 17130395]
19. Coates RJ, Uhler RJ, Hall HI, Potischman N, Brinton LA, Ballard-Barbash R, Gammon MD, Brogan DR, Daling JR, Malone KE, Schoenberg JB, Swanson CA. Risk of breast cancer in young women in relation to body size and weight gain in adolescence and early adulthood. Br J Cancer. 1999; 81:167–74. [PubMed: 10487629]
20. Ahlgren M, Melbye M, Wohlfahrt J, Sorensen TI. Growth patterns and the risk of breast cancer in women. N Engl J Med. 2004; 351:1619–26. [PubMed: 15483280]
21. De Stavola BL, dos Santos Silva I, McCormack V, Hardy RJ, Kuh DJ, Wadsworth ME. Childhood growth and breast cancer. Am J Epidemiol. 2004; 159:671–82. [PubMed: 15033645]
22. Harris HR, Tamimi RM, Willett WC, Hankinson SE, Michels KB. Body size across the life course, mammographic density, and risk of breast cancer. Am J Epidemiol. 2011; 174:909–18. [PubMed: 21911827]
23. Suzuki R, Iwasaki M, Inoue M, Sasazuki S, Sawada N, Yamaji T, Shimazu T, Tsugane S. Alcohol consumption-associated breast cancer incidence and potential effect modifiers: the Japan Public Health Center-based Prospective Study. Int J Cancer. 2010; 127:685–95. [PubMed: 19960437]
24. Brinton LA, Swanson CA. Height and weight at various ages and risk of breast cancer. Ann Epidemiol. 1992; 2:597–609. [PubMed: 1342311]

25. Barnes-Josiah D, Potter JD, Sellers TA, Himes JH. Early body size and subsequent weight gain as predictors of breast cancer incidence (Iowa, United States). Cancer Causes Control. 1995; 6:112–8. [PubMed: 7749050]
26. Wenten M, Gilliland FD, Baumgartner K, Samet JM. Associations of weight, weight change, and body mass with breast cancer risk in Hispanic and non-Hispanic white women. Ann Epidemiol. 2002; 12:435–4. [PubMed: 12160603]
27. Burton A, Martin R, Galobardes B, Davey Smith G, Jeffreys M. Young adulthood body mass index and risk of cancer in later adulthood: historical cohort study. Cancer Causes Control. 2010; 21:2069–77. [PubMed: 20680433]
28. Radimer K, Siskind V, Bain C, Schofield F. Relation between anthropometric indicators and risk of breast cancer among Australian women. Am J Epidemiol. 1993; 138:77–89. [PubMed: 8342532]
29. Frisch RE. Body fat, puberty and fertility. Biol Rev Camb Philos Soc. 1984; 59:161–88. [PubMed: 6375750]
30. Kodama H. Problems of Underweight in Young Females and Pregnant Women in Japan. JMAJ. 2010; 53:285–9.
31. Chute CG, Willett WC, Colditz GA, Stampfer MJ, Baron JA, Rosner B, Speizer FE. A prospective study of body mass, height, and smoking on the risk of colorectal cancer in women. Cancer Causes Control. 1991; 2:117–24. [PubMed: 1873436]
32. Oxentenko AS, Bardia A, Vierkant RA, Wang AH, Anderson KE, Campbell PT, Sellers TA, Folsom AR, Cerhan JR, Limburg PJ. Body size and incident colorectal cancer: a prospective study of older women. Cancer Prev Res (Phila). 2010; 3:1608–20. [PubMed: 20719902]
33. Lee IM, Paffenbarger RS Jr. Quetelet's index and risk of colon cancer in college alumni. J Natl Cancer Inst. 1992; 84:1326–31. [PubMed: 1495102]
34. Le Marchand L, Wilkens LR, Mi MP. Obesity in youth and middle age and risk of colorectal cancer in men. Cancer Causes Control. 1992; 3:349–54. [PubMed: 1617122]
35. Levi Z, Kark JD, Barchana M, Liphshitz I, Zavdi O, Tzur D, Derazne E, Furman M, Niv Y, Gordon B, Afek A, Shamiss A. Measured body mass index in adolescence and the incidence of colorectal cancer in a cohort of 1.1 million males. Cancer Epidemiol Biomarkers Prev. 2011; 20:2524–31. [PubMed: 22056504]
36. Terry P, Baron JA, Weiderpass E, Yuen J, Lichtenstein P, Nyren O. Lifestyle and endometrial cancer risk: a cohort study from the Swedish Twin Registry. Int J Cancer. 1999; 82:38–42. [PubMed: 10360818]
37. Schouten LJ, Goldbohm RA, van den Brandt PA. Anthropometry, physical activity, and endometrial cancer risk: results from the Netherlands Cohort Study. J Natl Cancer Inst. 2004; 96:1635–8. [PubMed: 15523093]
38. Xu WH, Xiang YB, Zheng W, Zhang X, Ruan ZX, Cheng JR, Gao YT, Shu XO. Weight history and risk of endometrial cancer among Chinese women. Int J Epidemiol. 2006; 35:159–66. [PubMed: 16258056]
39. Lu L, Risch H, Irwin ML, Mayne ST, Cartmel B, Schwartz P, Rutherford T, Yu H. Long-term overweight and weight gain in early adulthood in association with risk of endometrial cancer. Int J Cancer. 2011; 129:1237–43. [PubMed: 21387312]
40. Win AK, Dowty JG, Antill YC, English DR, Baron JA, Young JP, Giles GG, Southey MC, Winship I, Lipton L, Parry S, Thibodeau SN, et al. Body mass index in early adulthood and endometrial cancer risk for mismatch repair gene mutation carriers. Obstet Gynecol. 2011; 117:899–905. [PubMed: 21422863]

Brief description: Obesity later in adulthood, resulting from obesity at early adulthood and/or the subsequent weight gain, is associated with risks of many cancers. This study examined the cancer risks associated with BMI at early adulthood and subsequent weight change separately. We found that BMI at age 25 and the subsequent weight gain were independently associated with cancer risk in later life, supporting the importance of avoiding excess weight during young adulthood and weight gain through adulthood.

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Table 1

Descriptive characteristics of analysis sample by gender and BMI category at age 25, ARIC

	Women (N=7,569)				Men (N=6,332)			
	Underweight (N=649)	**Normal (N=5821)**	**Overweight (N=792)**	**Obese (N=307)**	**Underweight (N=124)**	**Normal (N=3929)**	**Overweight (N=1878)**	**Obese (N=401)**
Age at baseline (years, mean [SD])	53.4 (5.9)	53.7 (5.7)	53.6 (5.7)	53.3 (5.7)	54.2 (6.0)	54.6 (5.8)	54.1 (5.7)	53.4 (5.7)
BMI at age 25 (kg/m^2, mean [SD])	17.5 (0.9)	21.4 (1.6)	26.8 (1.4)	34.5 (4.6)	17.4 (1.4)	22.4 (1.7)	26.9 (1.3)	32.6 (2.6)
Weight change (lbs, mean [SD])	39.8 (30.1)	33.0 (28.3)	37.9 (36.4)	15.6 (44.9)	49.5 (31.8)	26.1 (23.2)	17.0 (25.7)	3.0 (36.3)
Weight change (%, mean [SD])	38.8 (29.2)	26.5 (22.5)	24.9 (23.7)	9.2 (22.6)	42.1 (31.1)	17.5 (15.8)	9.4 (14.0)	1.6 (16.0)
Height at baseline (cm, mean [SD])	163.8 (6.1)	162.3 (5.8)	160.8 (6.6)	161.2 (6.7)	178.4 (6.8)	176.0 (6.6)	176.0 (6.6)	176.1 (6.6)
African American (%)	36.2	27.1	40.0	48.5	41.9	22.5	19.5	27.7
Field center (%)								
Forsyth County, NC	29.0	26.1	17.1	13.4	37.1	27.2	23.5	25.4
Jackson, MS	32.7	23.8	36.5	44.3	38.7	19.5	17.5	22.7
Minneapolis, MN	16.2	25.9	17.6	12.1	8.9	25.7	32.9	27.9
Washington County, MD	22.2	24.2	28.9	30.3	15.3	27.6	26.1	23.9
Education (%)								
Basic education or 0-yr education	25.7	20.8	31.9	43.3	34.7	25.2	19.1	24.2
Intermediate education	39.8	45.6	44.7	38.1	30.7	35.8	37.4	38.4
Advanced education	34.5	33.6	23.4	18.6	34.7	39.0	43.5	37.4
Smoking status at age 25 (%)								
Non-smoker	51.3	62.6	68.1	68.7	29.0	34.5	37.7	39.7
Smoker	48.7	37.4	31.9	31.3	71.0	65.5	62.4	60.4
Smoking status (%)								
Never	42.7	54.1	57.2	59.6	20.2	27.5	30.4	29.4
Former	23.7	22.4	19.1	21.2	43.6	44.3	44.5	41.9
Current	33.6	23.5	23.7	19.2	36.3	28.2	25.1	28.7
Drinking status (%)								
Never/rare	54.7	55.2	62.5	63.8	26.6	25.6	25.8	27.2
Former	17.1	14.8	19.7	24.4	27.4	22.1	21.9	26.7
Current light	7.2	9.5	6.8	4.2	8.1	9.5	10.9	8.2
Current moderate	9.9	9.7	4.9	2.3	18.6	25.5	23.4	24.2

	Women (N=7,569)				Men (N=6,332)			
	Underweight (N=649)	**Normal (N=5821)**	**Overweight (N=792)**	**Obese (N=307)**	**Underweight (N=124)**	**Normal (N=3929)**	**Overweight (N=1878)**	**Obese (N=401)**
Current heavy	11.1	10.8	6.1	5.2	19.4	17.3	17.9	13.7
Sports at leisure time (%)								
Low (tertile 1)	49.9	45.0	54.3	58.3	49.2	35.9	33.1	36.2
Medium (tertile 2)	28.8	31.4	28.0	27.7	26.6	29.8	28.7	33.9
High (tertile 3)	21.3	23.6	17.7	14.0	24.2	34.3	38.2	29.9

Table 2

Association between BMI at age 25 and incident cancer with and without adjusting for weight change from age 25 to baseline, ARIC, 1987-2006 [1,2]

BMI at age 25 by cancer type	Women				Men			
	Number of cases	HR (95% CI)			Number of cases	HR (95% CI)		
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3
Any cancer								
Underweight	95	0.86(0.69, 1.06)	0.84(0.68, 1.04)	0.83(0.67, 1.03)	35	1.27(0.90, 1.78)	1.26(0.89, 1.77)	1.27(0.90, 1.79)
Normal	987	1	1	1	924	1	1	1
Overweight	123	0.98(0.81, 1.19)	0.98(0.81, 1.18)	0.99(0.82, 1.20)	455	1.11(0.99, 1.24)	1.11(0.99, 1.25)	1.10(0.98, 1.23)
Obese	47	1.11(0.82, 1.49)	1.12(0.83, 1.51)	1.19(0.88, 1.62)	85	1.13(0.90, 1.41)	1.14(0.91, 1.42)	1.10(0.87, 1.39)
Linear (5 kg/m^2)	1252	1.07(0.99, 1.16)	**1.08(1.00, 1.16)**	**1.10(1.02, 1.20)**	1499	1.05(0.98, 1.14)	1.06(0.98, 1.14)	1.04(0.96, 1.13)
Obesity-related w/o breast cancer								
Underweight	19	0.76(0.47, 1.21)	0.76(0.47, 1.21)	0.75(0.47, 1.20)	4	0.79(0.29, 2.14)	0.79 (0.29 −2.14)	0.76(0.28, 2.05)
Normal	225		1	1	170	1	1	1
Overweight	40	1.32(0.94, 1.86)	1.33(0.94, 1.87)	1.37(0.97, 1.94)	70	0.91(0.69, 1.20)	0.91 (0.69, 1.20)	0.95(0.71, 1.27)
Obese	17	1.62(0.99, 2.68)	**1.65(1.00, 2.73)**	**1.95(1.16, 3.27)**	21	1.47(0.93, 2.32)	1.46 (0.92, 2.30)	1.57(0.97, 2.53)
Linear (5 kg/m^2)	301	**1.28(1.13, 1.46)**	**1.28(1.13, 1.46)**	**1.38(1.20, 1.59)**	265	1.09(0.92, 1.30)	1.09 (0.92, 1.30)	1.15(0.95, 1.39)
Post-menopausal breast cancer[3]								
Underweight	22	0.61 (0.39, 0.94)	0.58(0.37, 0.92)	0.57(0.36, 0.90)				
Normal	310	1	1	1				
Overweight	30	0.78 (0.54, 1.14)	0.78(0.53, 1.14)	0.80(0.55, 1.17)				
Obese	10	0.80 (0.42, 1.50)	0.79(0.42, 1.49)	0.87(0.45, 1.66)				
Linear (5 kg/m^2)	372	N/A	N/A	N/A				
Colorectal cancer								
Underweight	10	0.75 (0.39, 1.44)	0.74(0.39, 1.42)	0.73(0.38, 1.40)	3	1.03 (0.33, 3.28)	1.05(0.33, 3.35)	1.00(0.31, 3.18)
Normal	114	1	1	1	96	1	1	1
Overweight	18	1.12 (0.68, 1.86)	1.15(0.69, 1.90)	1.19(0.72, 1.98)	40	0.92 (0.64, 1.34)	0.92(0.63, 1.33)	0.96(0.66, 1.41)
Obese	5	0.88 (0.36, 2.17)	0.91(0.37, 2.25)	1.10(0.44, 2.78)	12	1.52 (0.83, 2.78)	1.54(0.84, 2.81)	1.65(0.87, 3.11)
Linear (5 kg/m^2)	147	0.99 (0.79, 1.25)	1.01(0.80, 1.26)	1.06(0.84, 1.35)	151	1.14 (0.91, 1.44)	1.14(0.91, 1.44)	1.21(0.94, 1.55)
Endometrial cancer								

BMI at age 25 by cancer type	Women				Men			
	Number of cases	HR (95% CI)			Number of cases	HR (95% CI)		
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3
Underweight	5	1.07 (0.42, 2.70)	1.14(0.45, 2.89)	1.15(0.46, 2.93)				
Normal	50	1	1	1				
Overweight/Obese	23	**2.76 (1.66, 4.60)**	**2.79(1.67, 4.68)**	**2.87(1.70, 4.84)**				
Linear (5 kg/m^2)	78	**1.63 (1.37, 1.93)**	**1.69(1.40, 2.03)**	**1.83(1.47, 2.26)**				

*1*Model 1 was adjusted for race-center, age, education, height and smoking status at age 25. For post-menopausal breast, obesity-related and endometrial cancer, age at menarche (continuous) was further adjusted. Model 2 was adjusted for covariates at model 1, plus cigarette smoking status, alcohol consumption, physical activity at baseline. Age at menopause (<50, ≥50, missing) or menopause status at baseline was further adjusted for post-menopausal breast, obesity-related and endometrial cancer. Model 3 was adjusted for covariates at model 2, plus weight change percentage from age 25 to baseline.

*2*HR for linear BMI at age 25 was noted as N/A if a linear association was not supported by comparing the nested models using likelihood ratio tests.

*3*The baseline visit for post-menopausal breast cancer was the first visit at which the participant self-reported reaching menopause.

Table 3

Association between BMI at age 25 and cancer mortality with and without adjusting for weight change from age 25 to baseline, ARIC, 1987-2009 [1,2]

BMI at age 25 by cancer type	Women				Men			
	Number of deaths	HR (95% CI)			Number of deaths	HR (95% CI)		
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3
Any cancer								
Underweight	52	1.13(0.84, 1.51)	1.09(0.82, 1.47)	1.07(0.80, 1.44)	12	0.90(0.51, 1.61)	0.87(0.49, 1.55)	0.88(0.49, 1.57)
Normal	386	1	1	1	421	1	1	1
Overweight	52	1.02(0.76, 1.37)	1.03(0.77, 1.38)	1.05(0.78, 1.41)	191	1.06(0.89, 1.26)	1.06(0.89, 1.26)	1.03(0.86, 1.23)
Obese	17	0.99(0.61, 1.61)	1.04(0.64, 1.70)	1.10(0.66, 1.82)	42	**1.39(1.01, 1.91)**	**1.42(1.03, 1.96)**	1.32(0.94, 1.84)
Linear (5kg/m^2)	507	1.02(0.90, 1.15)	1.04(0.92, 1.17)	1.06(0.94, 1.21)	666	1.08(0.97, 1.21)	1.09(0.97, 1.22)	1.05(0.93, 1.19)
Obesity-related w/o breast cancer								
Underweight	8	0.94(0.45, 1.95)	0.92(0.44, 1.92)	0.91(0.44, 1.91)	1	0.39(0.05, 2.80)	0.36(0.05, 2.63)	0.35(0.05, 2.56)
Normal	74	1	1	1	88	1	1	1
Overweight	12	1.23(0.66, 2.29)	1.23(0.66, 2.28)	1.27(0.68, 2.37)	30	0.76(0.50, 1.16)	0.77(0.51, 1.17)	0.78(0.51, 1.20)
Obese	4	1.23(0.45, 3.41)	1.28(0.46, 3.55)	1.52(0.53, 4.32)	14	**2.01(1.14, 3.55)**	**1.99(1.13, 3.53)**	**2.06(1.12, 3.78)**
Linear (5kg/m^2)	98	N/A	N/A	N/A	133	N/A	N/A	N/A
Post-menopausal breast cancer[3]								
Underweight	4	1.17(0.41, 3.38)	1.22(0.42, 3.53)	1.16(0.40, 3.37)				
Normal	28	1	1	1				
Overweight/obese	4	0.74(0.25, 2.13)	0.71(0.25, 2.06)	0.74(0.25, 2.19)				
Linear (5kg/m^2)	36	0.90(0.55, 1.48)	0.88(0.53, 1.45)	0.90(0.54, 1.51)				
Colorectal cancer								
Underweight	3	0.75(0.23, 2.48)	0.76(0.23, 2.50)	0.72(0.22, 2.38)	1	1.13(0.15, 8.37)	0.99(0.13, 7.36)	1.00(0.13, 7.50)
Normal	33	1	1	1	32	1	1	1
Overweight/obese	5	0.93(0.36, 2.43)	0.91(0.35, 2.37)	1.08(0.41, 2.81)	21	1.30(0.75, 2.26)	1.28(0.73, 2.23)	1.24(0.70, 2.22)
Linear (5kg/m^2)	41	0.91(0.56, 1.48)	0.90(0.56, 1.46)	1.02(0.61, 1.70)	54	1.39(0.96, 2.01)	1.40(0.97, 2.04)	1.41(0.95, 2.11)
Endometrial cancer								
Underweight	0	--	--	--				
Normal	3	1	1	1				

BMI at age 25 by cancer type	Women				Men			
	Number of deaths	HR (95% CI)			Number of deaths	HR (95% CI)		
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3
Overweight/Obese	1	2.05(0.18, 23.26)	2.08(0.18, 24.44)	1.17(0.05, 27.72)				
Linear (5kg/m^2)	4	**3.39(1.59, 7.21)**	**4.44(1.61, 12.31)**	**4.97(1.08, 22.90)**				

*1*Model 1 was adjusted for race-center, age, education, height and smoking status at age 25. For post-menopausal breast, obesity-related and endometrial cancer, age at menarche (continuous) was further adjusted. Model 2 was adjusted for covariates at model 1, plus cigarette smoking status, alcohol consumption, physical activity at baseline. Age at menopause (<50, ≥50, missing) or menopause status at baseline was further adjusted for post-menopausal breast, obesity-related and endometrial cancer. Model 3 was adjusted for covariates at model 2, plus weight change percentage from age 25 to baseline.

*2*HR for linear BMI at age 25 was noted as N/A if a linear association was not supported by comparing the nested models using likelihood ratio tests.

*3*The baseline visit for post-menopausal breast cancer was the first visit at which the participant self-reported reaching menopause.

Table 4

Association between weight change from age 25 to baseline and incident cancer with and without adjusting for BMI at age 25, ARIC, 1987-2006 [1,2]

	Women			Men		
		HR (95% CI)			HR (95% CI)	
Weight change by cancer type	Number of cases	Model 1	Model 2	Number of cases	Model 1	Model 2
Any cancer						
< −3%	61	0.95(0.67, 1.35)	0.93(0.65, 1.32)	190	1.14(0.93, 1.41)	1.12(0.91, 1.39)
−3 to <3%	67	1	1	170	1	1
3 to <10%	135	1.05(0.78, 1.40)	1.05(0.78, 1.41)	295	1.07(0.88, 1.29)	1.07(0.89, 1.30)
10+%	989	1.12(0.87, 1.44)	1.14(0.89, 1.46)	844	1.00(0.85, 1.18)	1.01(0.86, 1.20)
Linear (5%)	1252	N/A	N/A	1499	N/A	N/A
Obesity-related w/o breast cancer						
< −3%	10	0.59(0.27, 1.28)	0.51(0.23, 1.12)	30	1.19(0.71, 2.01)	1.13(0.67, 1.91)
−3 to <3%	18	1	1	27	1	1
3 to <10%	32	0.93(0.52, 1.66)	0.96(0.54, 1.72)	44	1.00(0.62, 1.62)	1.01(0.63, 1.64)
10+%	241	0.94(0.58, 1.52)	1.00(0.62, 1.63)	164	1.25(0.83, 1.89)	1.29(0.85, 1.96)
Linear (5%)	301	**1.03(1.01, 1.05)**	**1.04(1.02, 1.07)**	265	1.03(0.99, 1.06)	**1.04(1.00, 1.08)**
Post-menopausal breast cancer[3]						
< −3%	15	0.76(0.39, 1.48)	0.78(0.40, 1.55)			
−3 to <3%	20	1	1			
3 to <10%	40	1.00(0.58, 1.71)	0.99(0.58, 1.70)			
10+%	297	1.07(0.68, 1.70)	1.09(0.69, 1.73)			
Linear (5%)	372	**1.04(1.02, 1.06)**	**1.05(1.02, 1.07)**			
Colorectal cancer						
< −3%	4	0.61(0.18, 2.08)	0.59(0.17, 2.05)	18	1.62(0.78, 3.36)	1.53(0.73, 3.20)
−3 to <3%	7	1	1	12	1	1
3 to <10%	16	1.23(0.51, 2.99)	1.24(0.51, 3.03)	26	1.34(0.67, 2.65)	1.35(0.68, 2.68)
10+%	120	1.21(0.56, 2.61)	1.25(0.58, 2.70)	95	1.60(0.88, 2.94)	1.65(0.90, 3.05)
Linear (5%)	147	N/A	N/A	151	1.04(0.99, 1.08)	**1.05(1.00, 1.10)**
Endometrial cancer						
< −3%	3	0.59(0.15, 2.38)	0.43(0.11, 1.77)			

Weight change by cancer type	Women			Men		
	Number of cases	HR (95% CI)		Number of cases	HR (95% CI)	
		Model 1	Model 2		Model 1	Model 2
−3 to <3%	6	1	1			
3 to <10%	10	0.85(0.31, 2.34)	0.90(0.33, 2.48)			
10+%	59	0.69(0.30, 1.62)	0.75(0.32, 1.76)			
Linear (5%)	78	**1.07(1.03, 1.13)**	**1.09(1.04, 1.14)**			

[1] Model 1 was adjusted for race-center, age, education, height and smoking status at age 25, and cigarette smoking status, alcohol consumption and physical activity at baseline. For post-menopausal breast, obesity-related and endometrial cancer, age at menarche, age at menopause or menopause status at baseline was further adjusted. Model 2 was adjusted for covariates at model 1, plus BMI at age 25.

[2] HR for linear percent weight change was noted as N/A if a linear association was not supported by comparing the nested models using likelihood ratio tests.

[3] The baseline visit for post-menopausal breast cancer was the first visit at which the participant self-reported reaching menopause.

Table 5

Association between weight change from age 25 to baseline and cancer mortality with and without adjusting for BMI at age 25, ARIC, 1987-2009 [1,2]

	Women			Men		
		HR (95% CI)			HR (95% CI)	
Weight change by cancer type	Number of deaths	Model 1	Model 2	Number of deaths	Model 1	Model 2
Any cancer						
< −3%	28	1.08(0.62, 1.86)	1.06(0.61, 1.84)	105	**1.34(1.00, 1.81)**	1.31(0.97, 1.77)
−3 to <3%	25	1	1	75	1	1
3 to <10%	51	1.07(0.66, 1.73)	1.08(0.67, 1.74)	114	0.94(0.70, 1.26)	0.95(0.71, 1.27)
10+%	403	1.25(0.83, 1.88)	1.25(0.83, 1.88)	372	1.00(0.78, 1.29)	1.03(0.80, 1.32)
Linear (5%)	507	**1.02(1.00, 1.04)**	**1.02(1.00, 1.04)**	666	0.99(0.96, 1.01)	0.99(0.97, 1.02)
Obesity-related w/o breast cancer						
< −3%	3	0.53(0.13, 2.13)	0.49(0.12, 2.00)	16	0.95(0.48, 1.89)	0.88(0.44, 1.76)
−3 to <3%	6	1	1	17	1	1
3 to <10%	11	0.93(0.34, 2.52)	0.95(0.35, 2.57)	20	0.71(0.37, 1.35)	0.72(0.38, 1.38)
10+%	78	0.95(0.41, 2.22)	0.99(0.42, 2.31)	80	0.91(0.54, 1.55)	0.96(0.56, 1.64)
Linear (5%)	98	1.00(0.95, 1.04)	1.00(0.96, 1.05)	133	1.00(0.95, 1.06)	1.02(0.96, 1.08)
Post-menopausal breast cancer[3]						
< −3%	2	1.75(0.16, 19.47)	1.80(0.16, 20.35)			
−3 to <3%	1	1	1			
3 to <10%	1	0.50(0.03, 7.98)	0.48(0.03, 7.74)			
10+%	32	1.87(0.25, 13.89)	1.77(0.24, 13.27)			
Linear (5%)	36	**1.08(1.01, 1.14)**	**1.08(1.01, 1.15)**			
Colorectal cancer						
< −3%	0	--	--	8	1.27(0.44, 3.67)	1.14(0.39, 3.34)
−3 to <3%	1	1	1	6	1	1
3 to <10%	5	2.52(0.29, 21.59)	2.51(0.29, 21.60)	10	1.05(0.38, 2.90)	1.10(0.40, 3.05)
10+%	35	2.71(0.37, 20.03)	2.72(0.37, 20.15)	30	0.98(0.40, 2.37)	1.13(0.46, 2.79)
Linear (5%)	41	**1.07(1.00, 1.14)**	**1.07(1.00, 1.14)**	54	0.97(0.89, 1.05)	0.99(0.90, 1.08)
Endometrial cancer						
< −3%	2	--	--			

Weight change by cancer type	Women			Men		
	Number of deaths	HR (95% CI)		Number of deaths	HR (95% CI)	
		Model 1	Model 2		Model 1	Model 2
−3 to <3%	0	1	1			
3+%	2	--	--			
Linear (5%)	4	N/A	N/A			

[1] Model 1 was adjusted for race-center, age, education, height and smoking status at age 25, and cigarette smoking status, alcohol consumption and physical activity at baseline. For post-menopausal breast, obesity-related and endometrial cancer, age at menarche, age at menopause or menopause status at baseline was further adjusted. Model 2 was adjusted for covariates at model 1, plus BMI at age 25.

[2] HR for linear percent weight change was noted as N/A if a linear association was not supported by comparing the nested models using likelihood ratio tests.

[3] The baseline visit for post-menopausal breast cancer was the first visit at which the participant self-reported reaching menopause.