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Excess Body Weight and Colorectal Cancer Survival: The Multiethnic Cohort

Gertraud Maskarinec^a, Brook E. Harmon^b, Melissa A. Little^c, Nicholas J. Ollberding^d, Laurence N. Kolonel^a, Brian E. Henderson^e, Loic Le Marchand^a, and Lynne R. Wilkens^a

^aUniversity of Hawaii Cancer Center, 701 Ilalo Street, Honolulu, HI

^bUniversity of Memphis School of Public Health, 200 Robison Hall, Memphis, TN

^cUniversity of Tennessee Health Science Center, Memphis, TN

^dDivision of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

^eUniversity of Southern California, Health Sciences Campus, Los Angeles, CA

Abstract

Purpose—Excess body weight is a risk factor for colorectal cancer (CRC) and may also adversely affect survival in CRC patients.

Methods—This study examined the relation of body mass index (BMI), which was self-reported at cohort entry and after 5.7 ± 0.8 years, with CRC-specific and all-cause survival among 4,204 incident cases of invasive CRC in the Multiethnic Cohort (MEC). Cox regression analysis with age as time metric and BMI as time-varying exposure was applied to estimate hazard ratios (HR) and 95% confidence intervals (CIs) while adjusting for relevant covariates.

Results—Over 6.0 ± 4.7 years of follow-up, 1,976 all-cause and 1,095 CRC-specific deaths were recorded. The mean time interval between cohort entry and diagnosis was 7.6 ± 4.7 years. No association with CRC-specific survival was detected in men ($HR_{5\text{units}} = 0.94$; 95% CI 0.84–1.04) or women ($HR_{5\text{units}} = 0.98$; 95% CI 0.89–1.08). In men, all-cause survival also showed no relation with BMI ($HR_{5\text{unit}} = 0.97$; 95% CI 0.90–1.06), whereas it was reduced in women ($HR_{5\text{units}} = 1.10$; 95% CI 1.03–1.18). Interactions of BMI with ethnicity were only significant for obesity. Obese Latino and overweight Native Hawaiian men as well as overweight African American women, experienced significantly better CRC-specific survival than whites. Overweight Japanese men and African American women had better all-cause survival and obese Latino women had the lowest all-cause survival ($HR_{\text{obese}} = 1.74$; 95% CI 1.08–2.80).

Conclusions—This analysis detected little evidence for an adverse effect of excess body weight on CRC-specific survival, but all-cause survival was reduced in women. These findings suggest that adiposity may be less important for CRC survival than as an etiologic factor.

Contact Info: Gertraud Maskarinec, MD, PhD, University of Hawaii Cancer Center, 701 Ilalo Street, Honolulu, HI 96813, Phone: (808) 586-3074, gertraud@cc.hawaii.edu.

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Keywords

Colorectal cancer; obesity; survival; ethnicity

Introduction

Colorectal cancer (CRC) is the fourth most commonly diagnosed malignancy and the second leading cause of cancer-related death in the United States [1]. To date, the majority of epidemiologic studies on modifiable lifestyle factors affecting CRC have assessed the association with incidence. Physical inactivity [2], diet [3, 4], alcohol intake [5], and smoking [6] have all been associated with CRC risk. In particular, a higher risk has been reported with increasing body size, as measured by body mass index (BMI); this association appears to be stronger among men than women [7, 8]. While mortality rates from CRC have been declining [1], little is known about the role of modifiable lifestyle factors in relation to CRC survival. Evidence from several meta-analyses indicates that excess body weight may adversely affect survival in CRC patients, but the timing of BMI assessment is important [9–12]. When assessed before diagnosis, obesity, but not overweight, predicts worse survival in many studies, whereas excess body weight assessed at or after diagnosis shows no association or even a protective effect [10–12]. Findings from population-based prospective cohorts that measured BMI at the time of recruitment many years before diagnosis are inconsistent [13–18]; CRC-specific survival was reduced among those with higher BMI in two investigations [15, 18], all-cause survival was lower in four studies [14, 15, 17, 18], and two reports found no significant associations [13, 16]. Given the strong correlation between BMI before and after diagnosis, it is a challenge to disentangle whether pre- or post-diagnostic is more important for survival [10, 12]. The association of BMI with CRC-specific survival is even less clear when different ethnic groups are examined. No previous studies have looked at BMI and CRC-specific survival by ethnicity, but when excess BMI and survival from all causes was assessed, weaker associations were seen among African Americans and Latino men as compared to whites [19–21]. Although it is uncertain when an optimal BMI is most beneficial, the current study examined the relation of self-reported BMI measured closest to death, as well as BMI assessed before diagnosis, with CRC-specific and all-cause survival among CRC cases in the Multiethnic Cohort (MEC).

Patients and Methods

Study population

The MEC is an ethnically diverse prospective cohort designed to investigate the association of lifestyle and genetic factors with the incidence of cancer. The design and implementation of the MEC have been described elsewhere [22]. Briefly, over 215,000 men and women aged 45–75 years at recruitment and residing in Hawaii or California (primarily Los Angeles County) were enrolled into the cohort between 1993 and 1996. To obtain a multiethnic sample of whites, African Americans, Native Hawaiians, Japanese Americans, and Latinos, a population-based sampling frame utilized drivers' license files, supplemented with voter registration lists and Health Care Financing Administration (Medicare) files. The Institutional Review Boards at the University of Hawaii and the University of Southern

California approved the study protocol. Incident colon and rectal cancer cases were identified through regular linkages with the Los Angeles County Cancer Surveillance Program, the State of California Cancer Registry, and the statewide Hawaii Tumor Registry, all part of the NCI's Surveillance, Epidemiology, and End Results (SEER) program. Dates and causes of death were identified by routine linkages with California and Hawaii vital record and the National Death Index databases. Complete case and/or death ascertainment was available up to December 31, 2010. Among participants of the five major ethnic groups who did not have previous self-reported or registry-detected diagnosis of colon or rectal cancer at cohort entry, and were therefore eligible for inclusion in this analysis, 4,832 newly diagnosed invasive CRC cases were identified from cohort entry until the end of 2010. After exclusions (272 not adenocarcinoma, 179 invalid diet, 1 no follow-up time, 69 missing BMI at cohort entry, 166 with BMI <18.5 kg/m²), the final dataset included 4,204 cohort members.

Data Collection

At cohort entry, participants completed a self-administered, 26-page questionnaire (Qx1) that collected self-reported demographic characteristics, height and body weight, medical history, family history of colon and rectal cancer, physical activity, and a dietary history using a validated food frequency questionnaire (FFQ). The FFQ asked participants their average frequency of consumption and serving sizes of over 180 food items during the last year. A calibration study indicated acceptable correlations between FFQ and 24-hour recall based dietary data for all sex-ethnic groups [23]. Dietary intakes were calculated using a food composition table. Alcohol consumption was classified into 3 categories: <1 drink/month, 1 drink/month but <1 drink/day, and 1 drink/day. Fiber and red meat (processed and unprocessed) intake was assessed as grams per 1,000 kcal/day. Physical activity was classified into <0.5 vs. 0.5 hours spent per day in moderate or vigorous activities. Ethnicity was based on self-report and was classified as: white, African American, Native Hawaiian, Japanese American, Latino, and other. Family history of colon or rectal cancer included a self-report of the cancer in the participant's natural father, mother, or full siblings. Education was coded as high school or less, vocational school or some college, and undergraduate/graduate degree. Cigarette smoking was classified as never, past, or current and pack-years were computed. Based on questions about aspirin or other pain medication but not acetaminophen, NSAID use was coded as ever (at least twice per week for 1 month or longer) or never.

Between 1999 and 2002, approximately 85% of eligible MEC members completed a brief follow-up questionnaire (Qx2) that updated information on medical history and self-reported body weight. Tumor characteristics were available from the SEER-based cancer registries in Hawaii and Los Angeles and included stage at diagnosis and first course of treatment, but no information on recurrence.

The self-reported height and weight measures from both questionnaires were used to calculate BMI. BMI was modeled as a continuous variable (per 5 kg/m²) to test for linear trends and as categories to obtain estimates for overweight (25–29.9 kg/m²) and obesity (>30 kg/m²) with normal weight (18.5–<25 kg/m²) as the reference group. The obese group

was further divided into modest ($30 < 35 \text{ kg/m}^2$) and extreme obesity ($\geq 35 \text{ kg/m}^2$). In a comparison against values from the drivers' license files, the Qx1 measures showed excellent correlations of >0.90 for most sex-ethnic groups [24]. In a small subset of white and Japanese MEC participants who were invited for clinic visits, under-reporting of BMI by self-report was only 0.67 kg/m^2 although the bias was greater for heavier than lean women [25].

Statistical analysis

To evaluate the association of BMI with overall and CRC-specific death, we computed multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CI) using Cox proportional hazards models. Age was used as the time metric, so that each person's observation started at the age at diagnosis and ended at the age of death or the age at the closure date for analysis of 12/31/2010. For CRC-specific death, death due to other causes was also censored. Note that this results in risk sets of similar aged women created at each death age. BMI was treated as a time-varying exposure. The most recently available value of BMI is used in each risk set. Any ages between entry, i.e., CRC diagnosis, and Qx2 were assigned the BMI value at cohort entry, while any ages after Qx2 were assigned the BMI value at Qx2. That is, BMI at cohort entry was modeled at each risk set for participants who never completed or died before Qx2, and BMI at Qx2 was modeled at each risk set for participants who were diagnosed after Qx2. For participants who were diagnosed prior to Qx2, completed Qx2, and died or were censored after Qx2, both BMI at Qx1 and Qx2 were modeled: BMI at Qx1 was modeled for risk sets prior to the age at Qx2 and BMI at Qx2 was modeled for risk sets after the age at Qx2. While unlikely because the median time between Qx2 and death was 6.1 ± 3.1 years, weight loss before death could have biased our results. To understand the extent of any bias, a sensitivity analysis was performed only using BMI at baseline.

The following covariates (Table 1) were included into the models as potential confounders based on previous publications and on survival analyses for other cancers within the MEC [26, 27]: ethnicity, age at CRC diagnosis in 5-year age groups, education, family history of CRC, alcohol use, smoking status and number of pack-years, physical activity, SEER tumor stage, radiation treatment, chemotherapy treatment, and NSAID use, as well as red meat intake and fiber intake as log-transformed (with 1 added to allow for zero intake) continuous variables ($\text{g}/1000 \text{ kcal}$). For covariates with missing values, i.e., education, smoking status, physical activity, NSAID use, tumor stage, treatment variables, a missing category was created. Self-reported hypertension, stroke, heart disease, and stroke from Qx1 were used to create an indicator variable for comorbidity (0, 1, or 2+).

All analyses were stratified by sex, ethnic group, subsite (colon and rectal), and stage at diagnosis. We examined potential interactions of BMI with sex and with ethnicity on survival using a global Wald test of the cross-product terms. For the categorical analysis, separate interaction terms for the variables indicating overweight and obese status were included in the models. As sensitivity analyses, models were repeated with minimal adjustment, using only BMI at Qx1, including the comorbidity variable, and excluding the person-time contributed by cases diagnosed within 3 years of cohort entry or Qx2 to account

for possible weight loss before the CRC diagnosis. All analyses were conducted in SAS 9.2 (SAS Institute, Cary, NC), using two-tailed tests with significance set at $p < 0.05$.

Results

A total of 4,204 CRC cases among participants in the MEC were included in the analysis (Table 1). The mean follow-up time for all cases was 6.0 ± 4.7 years with 1,976 deaths due to all-causes and 1,095 deaths due to CRC. More CRC cases occurred in men than women (2,258 and 1,946 cases) and the largest number of cases was diagnosed among Japanese participants (1,441 cases). Among all cases, 38% were normal weight, 40% overweight, and 22% obese (15% modest and 7% extreme obesity). More women than men were obese (27% and 18%) and the prevalence was higher in African Americans and Native Hawaiians (35% and 42%) than in the other ethnic groups. A total of 3,080 (73%) participants had a valid BMI value at Qx2 approximately 5.7 ± 0.8 years after cohort entry. When the two BMI values were compared, 78% of the participants remained in the same BMI category and only $< 1\%$ changed by two categories. The mean time interval between data collection and diagnosis was 7.6 ± 4.7 for Qx1 and 2.5 ± 4.5 years for Qx2. The percentage of participants in each obesity category was similar across CRC stages at diagnosis. Receipt of chemotherapy did not differ significantly by BMI status ($p = 0.18$); it was 32% for normal weight, 32% for overweight, 28% for obese participants.

Given statistically significant interactions between sex and continuous BMI for all-cause survival ($p_{\text{interaction}} = 0.01$), all analyses were stratified by sex. In the overall models, CRC-specific survival differed to a small degree by ethnic group ($p = 0.08$ for men and $p = 0.03$ for women). As compared to whites, the respective HRs for CRC-specific survival in Japanese men and women were 0.76 (95% CI 0.60–0.96) and 0.72 (95% CI 0.53–0.98), but survival for the other ethnic groups did not differ from whites. Japanese men and women also showed better all-cause survival ($p = 0.003$ in men and $p = 0.12$ in women) with respective HRs of 0.69 (95% CI 0.55–0.87) and 0.83 (95% CI 0.70–0.99).

There was no significant association between continuous BMI and CRC-specific ($\text{HR}_{5\text{units}} = 0.94$; 95% CI 0.84–1.04) or all-cause survival ($\text{HR}_{5\text{units}} = 0.97$; 95% CI 0.90–1.06) for all men combined (Table 2). For CRC-specific survival, the interaction term of continuous BMI with ethnicity was not statistically significant ($p_{\text{interaction}} = 0.20$), but ethnicity modified the association with obesity ($p_{\text{interaction}} = 0.04$). Latino men experienced better CRC-specific survival with higher BMIs ($\text{HR}_{5\text{units}} = 0.68$; 95% CI 0.52–0.88), in particular among obese men ($\text{HR}_{\text{obese}} = 0.43$; 95% CI 0.24–0.79) than whites. Overweight Native Hawaiian men showed better CRC-specific survival ($\text{HR}_{\text{overwt}} = 0.48$; 95% CI 0.13–0.76) and overweight Japanese men had better all-cause survival ($\text{HR}_{\text{overwt}} = 0.79$; 95% CI 0.63–0.98) in comparison to white men.

In women (Table 3), no statistically significant association between continuous BMI and CRC-specific survival ($\text{HR}_{5\text{units}} = 0.98$; 95% CI 0.89–1.08) was detected, but all-cause survival per 5 units of BMI was significantly lower ($\text{HR}_{5\text{units}} = 1.10$; 95% CI 1.03–1.18). For CRC-specific survival, the interaction term of continuous BMI with ethnicity was not statistically significant ($p_{\text{interaction}} = 0.34$) and the interaction with obesity was borderline

($p_{\text{interaction}}=0.08$). On the other hand, the interaction between ethnicity and obesity was significant ($p=0.03$) for all-cause survival. Better CRC-specific and all-cause survival was observed in overweight African American women with respective HRs of 0.55 (95% CI 0.35–0.86) and 0.70 (95% CI 0.49–0.99), as compared to white women. Although not statistically significant, worse all-cause survival in the range of 9–29% per 5 units BMI was seen for all non-white women but Japanese; all-cause survival was particularly low in obese Latinas ($\text{HR}_{\text{obese}}=1.74$; 95% CI 1.08–2.80).

After stratification of the obese group into modest and extreme obesity, no difference in survival was detected. The respective HRs for men were 0.97 (95% CI 0.74–1.26) and 0.98 (95% CI 0.61–1.55) and for women 0.89 (95% CI 0.66–1.18) and 0.94 (95% CI 0.66–1.35). When only BMI at Qx1 was modeled, the findings did not change substantially. In men, the respective HRs for CRC-specific and all-cause survival were 0.96 (95% CI 0.87–1.07) and 1.00 (95% CI 0.93–1.09) per 5 BMI units. In women, the HR for CRC-specific mortality remained null ($\text{HR}=1.00$; 95% CI 0.91–1.11), whereas all-cause survival was reduced ($\text{HR}=1.12$; 95% CI 1.04–1.20). Stratification by stage of disease at diagnosis showed a significant protective effect of higher BMI in men but not women with localized disease; the respective HRs for men and women per 5 units BMI were $\text{HR}_{5\text{units}}=0.69$ (95% CI 0.49–0.96) and $\text{HR}_{5\text{units}}=1.00$ (95% CI 0.78–1.28) for CRC-specific survival. No significant associations were detected for regional and distant disease.

Crude models with only age and ethnicity as covariates also showed no significant association with excess weight (data not shown). Exclusion of person-years contributed by CRC patients diagnosed within 3 years of Qx1 or Qx2 did not materially change the findings. The respective HRs for continuous BMI and CRC-specific survival in men and women were 0.91 (95% CI 0.78–1.06) and 0.97 (95% CI 0.86–1.08). Similarly, the HRs for all-cause survival were 0.96 (95% CI 0.87–1.09) and 1.10 (95% CI 1.02–1.20).

Including the comorbidity indicator did not change the null findings for CRC-specific survival among men and women (data not shown). For all causes of death, reporting one or more pre-existing conditions reduced survival significantly; the association with BMI was unchanged in men and attenuated in women ($\text{HR}_{5\text{units}}=1.07$; 95% CI 1.00–1.15). After stratification by subsite, the HRs in overweight men were 0.90 (95% CI 0.72–1.13) for colon and 1.20 (95% CI 0.84–1.72) for rectum. The respective values for obese men were 0.94 (95% CI 0.70–1.26) and 0.80 (95% CI 0.48–1.36). Also, no difference by subsite was detected among women; the HRs for colon were 0.90 (95% CI 0.69–1.16) and 0.83 (95% CI 0.61–1.11) and for rectum 0.80 (95% CI 0.44–1.44) and 1.53 (95% CI 0.78–2.98).

Discussion

This analysis within a large population-based multiethnic cohort of CRC patients detected little evidence for an adverse effect of excess body weight, either as measured prior to death or prior to diagnosis, on CRC-specific survival, in fact protective associations with higher BMI were seen in Latino and Native Hawaiian men, as well as in African American women. Conversely, a 10% lower all-cause survival per 5 units of BMI was found in women but not in men; the adverse prognosis was most pronounced in obese Latino women. Adding an

indicator variable for pre-existing conditions attenuated the HR for all-cause survival in women; this suggests that the lower survival is partially due to the impact of BMI on comorbid conditions rather than on CRC-specific survival. Several sensitivity analyses did not indicate that the null findings were due to subsite, stage at diagnosis, or weight change before diagnosis.

These results partly agree with reports from six large prospective cohorts, the most appropriate comparison in terms of study design, which assessed BMI years before diagnosis and followed the cases 4–12 years [13–18]. Only the Cancer Prevention Study-II Nutrition Cohort [15] and the European Prospective Investigation into Cancer and Nutrition study [18] reported positive associations; the respective HRs were 1.35 and 1.26, for prediagnostic obesity with CRC-specific survival. For all-cause deaths, these two cohorts, the Iowa Women's Health Study [14], and the National Institutes of Health-AARP Diet and Health study [17] reported HRs between 1.19 and 1.45 among obese participants. The Melbourne Collaborative Cohort Study [13] and the Women's Health Initiative [16] found no adverse prognosis in relation to higher prediagnostic BMI. None of the population-based cohorts detected associations of prediagnostic overweight (BMI 25–29.9 kg/m²) with CRC-specific or all-cause mortality. Our results were similar to another cohort that reported elevated all-cause mortality in women, but not men [17]. Three recent meta-analyses have explored the question of excess body weight on CRC outcomes; they included between 16 and 32 studies each; many of the investigations were based on CRC patients identified through cancer registries or patient cohorts [10–12]. Heterogeneity across studies was detected and primarily attributed to the timing of BMI assessment; obesity but not overweight before diagnosis more likely predicted worse survival in the range of 10–20%, whereas a high BMI after diagnosis showed primarily null or protective associations [10–12].

As in this study, weaker adverse associations between high BMI and all-cause mortality have been reported for African Americans and Latinos [19–21], but these population-based studies examined deaths within the entire cohort and not just among CRC patients. Our finding of better survival among Japanese Americans than whites agrees with previous reports from Hawaii [28] and Asians within SEER registries [29]. The protective effects of excess BMI in Latinos, African Americans, and Native Hawaiians may be the result of chance or a number of possible biases [10]. As documented repeatedly, individuals with moderate overweight appear to have a survival advantage over leaner adults in population-based studies [30]. Nutritional status, intentional vs. unintentional weight loss, and the possibility of a J-shaped relation between BMI and survival may be responsible for this observation [10]. To our knowledge no survival studies have been conducted in Japanese CRC cases. However, obesity and weight gain were associated with CRC mortality in women, but not men, within a Japanese cohort of healthy individuals [31] though this may reflect the influence of excess BMI on CRC incidence and not on survival [10].

Strengths of the current study are the large number of cases across a variety of ethnic groups, the wide range in BMI across ethnic groups, the population-based recruitment resulting in a representative group of cases, and the relatively long follow-up. In addition, a large proportion of the study population provided a BMI measure 6 years after cohort entry,

which allowed modeling of BMI as a time dependent exposure to reflect changes in body weight. It is unlikely that the findings are biased due to changes in body weight close to diagnosis as excluding cases diagnosed within 3 years of BMI assessment and limiting analysis to pre-diagnostic BMI did not alter the risk estimates. In contrast to patient cohorts, our study population was not susceptible to immortality bias [10]. It is not likely that reverse causation due to unintentional weight loss [10, 12] biased the findings as excluding cases diagnosed within the first 3 years and modeling only BMI at cohort entry did not change the results.

There were also several limitations. Weight change may have occurred for many participants after completion of the two questionnaires and this weight may be important for survival. Only clinical trials or well-designed prognostic cohorts are able to look at weight change after diagnosis and confounding by disease progression and co-morbidities [32]. Because the BMI in this cohort was obtained through self-reports, under-reporting, in particular among overweight and obese individuals, may have occurred despite documentation in a small MEC sample that under-reporting was low [25]. However, the fact that previous analyses within the MEC detected associations of self-reported BMI with survival for other cancer sites [26, 27] provides confidence in the accuracy of self-reported weight. Measured vs. self-reported BMI did also not constitute a major determinant of outcomes in previous studies [10, 12]. Given that BMI is not a good measure to classify lean vs. fat tissue, the availability of other anthropometric measures, such as waist circumference, would have been desirable. Therefore, the current findings might have been biased towards the null. Emerging research that shows that visceral adiposity is higher in Asians than whites highlights the problems with BMI as a measure of adiposity [33, 34]. Confounding due to insufficient clinical information may have obscured any underlying relations [10]. Information on treatment and follow-up was limited to what is provided by the SEER registries, i.e., only the first course of treatment and no information on recurrence. Underdosing of obese patients has been described as a problem affecting treatment outcomes, but could not be assessed due to lack of detailed chemotherapy information [35]. On the other hand, equal proportions of cases across BMI categories received chemotherapy. Residual confounding due to covariates with crude classification, e.g., NSAID use, or changes in risk factors during the time after cohort entry, an issue in all prospective studies, may be present. Also, the lack of information on socioeconomic status (SES) is a problem as higher BMI is more likely to be associated with lower SES, which may affect treatment and adherence to treatment and, thus, death and recurrence [29]. The California Accuracy of Cancer Mortality study indicated that misclassification of the underlying cause of death is a particular concern for CRC as it may lead to overestimation of cause-specific survival [36]. Adjusting for foods and nutrients other than red meat and fiber was beyond the objective of this paper, but these foods are frequently identified as risk factors in etiologic studies [3].

The fact that CRC survival showed little consistent association with BMI status is surprising in light of the relatively consistent evidence for adverse outcomes in overweight and obese breast cancer survivors [37], the higher risk to develop CRC in obese individuals [7, 8], and the hypothesized influence of chronic inflammation on CRC survival [28, 38]. It is possible that the adverse effects of excess body weight are obscured because not all obese patients may be in an inflammatory state and detrimental effects of body weight may only occur in

patients with chronic inflammation as suggested by a report from Hawaii [28]. Participants in the highest quintile of C-reactive protein (CRP) experienced approximately 50% lower survival, but excess BMI was not associated with survival [28]. Also, signs of systemic inflammatory response were independent predictors of poor outcome in patients receiving adjuvant 5-FU-based chemotherapy [39]. In addition, CRC patients with diabetes, another condition associated with chronic inflammation, had higher all-cause mortality than patients without diabetes [40]. Therefore, it is possible that only patients with excess body weight who also suffer from a state of chronic inflammation, information that was not available for the current analysis, are more likely to experience adverse outcomes related to obesity.

In this relatively large population of cohort participants with CRC, no consistent association of BMI with CRC-specific survival was detected although weak associations in both directions were seen in some sex and ethnic subgroups. The lower all-cause survival observed in women with higher BMI may reflect the adverse effects of obesity on health as documented by the elevated cardiovascular, but not CRC-specific, mortality in the AARP cohort [17]. These findings suggest that adiposity may be less important for CRC survival than as an etiologic risk factor and indicate that caution is warranted when transferring findings from risk to survival studies [10]. The time of BMI assessment appears to be crucial. Whereas adiposity assessed many years before diagnosis predicts lower CRC survival in some, this relation is substantially weaker or non-existent for post-diagnosis, probably due to selection bias in clinical cohorts [10–12]. Ideally, repeated measurement of adiposity over time and assessment of chronic inflammatory status will be included in future studies to identify patients who may benefit from weight control interventions.

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Table 1

Characteristics of the study population by Body Mass Index (BMI)

BMI category (kg/m ²)	18.5 to <25			25 to <30			30		
	All	No.	%	No.	%	No.	No.	%	%
Number of cases	4,204	1,591	37.8	1,674	39.8	939	22.3		
Number of deaths	1,976	738	37.4	795	40.2	443	22.4		
Number of CRC deaths	1,095	420	38.4	437	39.9	238	21.7		
Sex									
Male	2,258	807	35.7	1,042	46.2	409	18.1		
Female	1,946	784	40.3	632	32.5	530	27.2		
Age at baseline, years									
<55	586	179	30.6	199	34.0	208	35.4		
55 to <65	1,206	390	32.3	495	41.1	321	26.6		
65 to <75	1,937	797	41.1	802	41.4	338	17.5		
75	475	225	47.4	178	37.5	72	15.1		
Age at diagnosis, years									
<55	155	47	30.3	51	32.9	57	36.8		
55 to <65	747	231	30.9	286	38.3	230	30.8		
65 to <75	1,610	569	35.3	672	41.7	369	22.8		
75	1,692	744	44.0	665	39.3	283	16.7		
Ethnicity									
White	840	329	39.2	327	38.9	184	21.9		
African American	842	193	22.9	357	42.4	292	34.7		
Native Hawaiian	276	56	20.3	105	38.0	115	41.7		
Japanese	1,441	800	55.5	506	35.1	135	9.4		
Latino	805	213	26.5	379	47.1	213	26.4		
Education ^a , years									
12	2,018	722	35.8	801	39.7	495	24.5		
13–15	1,205	482	40.0	465	38.6	258	21.4		
16	940	377	40.1	387	41.2	176	18.7		
BMI at Qx2, kg/m ²									
18.5 to <25	1,159	956	82.5	184	15.9	19	1.6		
25 to <30	1,237	195	15.8	908	73.4	134	10.8		
>30	684	5	0.7	147	21.5	532	77.8		
Did not participate	1,124	435	–	435	–	254	–		
Smoking status ^b									
Never	1,594	663	41.6	560	35.1	371	23.3		
Past	1,915	621	32.4	842	44.0	452	23.6		

BMI category (kg/m ²)	All	18.5 to <25		25 to <30		30	
		No.	%	No.	%	No.	%
Current	654	293	44.8	256	39.1	105	16.1
Alcohol intake, drinks	2,240	820	36.6	867	38.7	553	24.7
<1 /mo	1,057	387	36.6	435	41.2	235	22.2
1+/mo- <1/day	907	384	42.3	372	41.0	151	16.7
1+/day	2,411	977	40.5	986	40.9	448	18.6
Physical activity ^c							
30 min/day	441	169	38.3	171	38.8	101	22.9
Yes							
Family history of CRC ^d							
Yes	2,033	668	32.9	814	40.0	551	27.1
Ever NSAID ^e							
Yes	1,854	703	37.9	735	39.6	416	22.4
Stage of disease ^f							
Local	1,605	610	38.0	645	40.2	350	21.8
Regional	647	247	38.2	258	39.9	142	22.0
Distant							
Yes	374	149	39.8	152	40.6	73	19.5
Radiation therapy ^g							
Yes	1,298	507	39.1	529	40.8	262	20.2
Chemotherapy ^h							
Yes							
Fiber intake (g/1000 kcal/day) ⁱ		23.8	14.0	24.7	14.7	25.7	16.9
Red meat intake (g/1000 kcal/day) ⁱ		24.5	15.5	28.1	16.1	30.1	16.1

^a 41 missing^b 41 missing^c 78 missing^d 611 missing^e 173 missing^f 98 missing^g 13 missing^h 110 missingⁱ Means and std

Table 2

Survival for Colorectal Cancer Patients by BMI category and Ethnic Group in Men^a

		CRC Deaths				All-Cause Deaths			
		18.5 to <25	25 to <30	30	Per 5 kg/m ²	18.5 to <25	25 to <30	30	Per 5 kg/m ²
All men	No. of deaths Person-years	222	284	111		425	506	200	
		4,344	5,932	2,121		4,344	5,932	2,121	
	HR	1	0.98	0.94	0.94	1	0.91	0.94	0.97
	95% CI		(0.81–1.17)	(0.73–1.20)	(0.84–1.04)		(0.79–1.04)	(0.78–1.12)	(0.90–1.06)
Interaction by ethnicity ^b		P _{interaction}	0.42	0.04	0.20	P _{interaction}	0.17	0.15	0.15
White	No. of deaths Person-years	41	61	27		82	99	48	
		814	1,121	464		814	1,121	464	
	HR	1	1.37	1.74	1.13	1	0.84	1.20	1.00
	95% CI		(0.87–2.17)	(0.96–3.15)	(0.87–1.47)		(0.60–1.17)	(0.77–1.81)	(0.83–1.21)
African American	No. of deaths Person-years	34	49	31		50	91	56	
		439	782	438		439	782	438	
	HR	1	1.15	0.92	0.95	1	1.31	1.19	1.15
	95% CI		(0.66–2.02)	(0.50–1.72)	(0.72–1.26)		(0.88–1.96)	(0.76–1.86)	(0.96–1.38)
Japanese	No. of deaths Person-years	93	88	19		209	159	24	
		2,237	2,333	385		2,237	2,333	385	
	HR	1	0.91	1.28	0.98	1	0.79	0.83	0.87
	95% CI		(0.66–1.24)	(0.74–2.20)	(0.78–1.23)		(0.63–0.98)	(0.53–1.29)	(0.73–1.04)
Hawaiian	No. of deaths Person-years	10	12	16		16	30	31	
		159	397	279		159	397	279	
	HR	1	0.48	0.61	0.77	1	0.90	1.58	1.11
	95% CI		(0.13–0.76)	(0.17–2.13)	(0.49–1.20)		(0.40–1.99)	(0.70–3.55)	(0.85–1.45)
Latino	No. of deaths Person-years	44	74	18		68	127	41	
		695	1,299	555		695	1,299	555	
	HR	1	0.81	0.43	0.68	1	0.95	0.73	0.84

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All-Cause Deaths				
18.5 to <25	25 to <30	30	Per 5 kg/m ²	95% CI
	(0.53–1.24)	(0.24–0.79)	(0.52–0.88)	(0.69–1.01)
CRC Deaths				
18.5 to <25	25 to <30	30	Per 5 kg/m ²	95% CI
	(0.53–1.24)	(0.24–0.79)	(0.52–0.88)	(0.69–1.01)

^a Hazard ratios (HR) and 95% confidence intervals (95% CI) obtained by Cox regression and adjusted for age at diagnosis, ethnicity, smoking status, pack-years, physical activity, education, stage at diagnosis, radiation treatment, chemotherapy, NSAID use, family history of colorectal cancer, intake of alcohol, fiber, and red meat.

^b Interactions were examined by a global Wald test.

Table 3

Survival for Colorectal Cancer Patients by BMI category and Ethnic Group in Women^a

		CRC Deaths				All-Cause Deaths			
		18.5 to <25	25 to <30	30	Per 5 kg/m ²	18.5 to <25	25 to <30	30	Per 5 kg/m ²
All women	No. of deaths Person-years	198	153	127		313	289	243	
		4,482	3,423	2,863		4,482	3,423	2,863	
	HR	1	0.91	0.88	0.98	1	1.01	1.12	1.10
	95% CI		(0.72–1.15)	(0.68–1.14)	(0.89–1.08)		(0.84–1.20)	(0.93–1.36)	(1.03–1.18)
Interaction by ethnicity ^b		P _{interaction}		0.19	0.34	0.08		0.03	0.17
White	No. of deaths Person-years	43	26	21		73	58	41	
		1,010	665	487		1,010	665	487	
	HR	1	0.97	0.82	1.08	1	1.17	0.97	1.15
	95% CI		(0.56–1.68)	(0.42–1.61)	(0.86–1.36)		(0.80–1.70)	(0.61–1.53)	(0.99–1.35)
African American	No. of deaths Person-years	45	55	54		59	101	116	
		501	1,027	1,010		501	1,027	1,010	
	HR	1	0.55	0.71	0.98	1	0.70	1.05	1.11
	95% CI		(0.35–0.86)	(0.46–1.10)	(0.82–1.16)		(0.49–0.99)	(0.75–1.47)	(0.98–1.26)
Japanese	No. of deaths Person-years	81	26	12		139	43	15	
		2,340	895	417		2,340	895	417	
	HR	1	1.26	0.80	1.00	1	0.98	0.63	0.92
	95% CI		(0.78–2.03)	(0.38–1.68)	(0.78–1.27)		(0.67–1.42)	(0.34–1.18)	(0.75–1.13)
Hawaiian	No. of deaths Person-years	7	12	9		10	20	18	
		150	220	331		150	220	331	
	HR	1	0.53	0.39	0.79	1	1.15	1.10	1.29
	95% CI		(0.10–2.86)	(0.08–1.80)	(0.45–1.40)		(0.42–3.17)	(0.39–3.14)	(0.94–1.76)
Latino	No. of deaths Person-years	22	34	31		32	67	53	
		481	616	618		481	616	618	
	HR	1	1.15	1.37	1.04	1	1.51	1.74	1.09

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95% CI	CRC Deaths			All-Cause Deaths			Per 5 kg/m ²
	18.5 to <25	25 to <30	30	18.5 to <25	25 to <30	30	
		(0.64–2.06)	(0.74–2.55)		(0.96–2.39)	(1.08–2.80)	(0.95–1.25)

^a Hazard ratios (HR) and 95% confidence intervals (95% CI) obtained by Cox regression and adjusted for age at diagnosis, ethnicity, smoking status, pack-years, physical activity, education, stage at diagnosis, radiation treatment, chemotherapy, NSAID use, family history of colorectal cancer, intake of alcohol, fiber, and red meat.

^b Interactions were examined by a global Wald test.