Associations of A Body Shape Index (ABSI) with Cancer Incidence, All-Cause, and at 23 Sites—Findings from the UK Biobank Prospective Cohort Study

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ABSTRACT

Background: Few studies have explored the emerging adiposity marker A Body Shape Index (ABSI) with cancer risk. This study investigated the associations between ABSI and the incidence of cancer at 23 sites and all cancer combined.

Methods: Data from 442,610 participants from the UK Biobank prospective study were included in this study. ABSI was used as the exposure. Incidence of cancer at 23 sites was the outcome. Cox proportional hazard models were performed to explore the association of ABSI, and combined ABSI and body mass index (BMI) with cancer risk, after adjusting for multiple testing.

Results: 36,961 individuals developed cancer during the 8.8 years median follow-up. In multivariable analyses, participants in the highest tertile of ABSI had higher risk of lung [HR, 1.58; 95% confidence interval (CI), 1.44–1.74], liver (HR, 1.45; 95% CI, 1.18–1.77), esophagus (HR, 1.32; 95% CI, 1.12–1.57), colorectal (HR, 1.19; 95% CI, 1.10–1.28), and breast (HR, 1.05; 95% CI, 1.04–1.17) cancers, and all cancers combined (HR, 1.11; 95% CI, 1.08–1.14) compared with the lowest tertile. These associations remained significant after adjustment for BMI. When ABSI was combined with BMI, participants in the highest ABSI who also had a BMI $\geq$ 25 kg/m^2 were at higher risk of uterus, esophagus, liver, stomach, colorectal, and breast cancers, as well as all cancers combined, compared with those in the lowest ABSI tertile with a normal BMI.

Conclusions: ABSI is associated with an increased risk of five cancers as well as all cancers combined, independently of BMI.

Impact: ABSI is a useful marker for adiposity. However, cancer risk prediction improves with the combination of BMI.

Introduction

Obesity is a major risk factor for many noncommunicable diseases, including cancer (1). Recent reports suggest that excess adiposity is linked to a higher risk of 13 cancers (2), including colorectal, postmenopausal breast, esophageal, pancreatic, liver, endometrial, kidney, oral, pharyngeal/laryngeal, stomach cardia, gallbladder, ovarian, and advanced prostate cancer (3). However, most of the evidence supporting these associations has been derived using body mass index (BMI) as the adiposity marker (4). Although BMI is a measure of general adiposity, it does not provide any information on body fat distribution (5). This is important as body fat distribution, particularly the accumulation of fat in central depots, is a risk factor for several noncommunicable diseases independent of general obesity, with limited evidence for other markers that may have even stronger associations with health outcomes (6, 7).

A new adiposity index that considers both overall and central adiposity, called A Body Shape Index (ABSI), may overcome some limitations related to either using overall or central adiposity markers independently to explore the association with cancer risk (8, 9). Recent evidence suggests that ABSI predicts all-cause mortality independent of BMI in U.S. and European study populations (8, 10). Harding and colleagues (11) reported a sex-specific association between ABSI and five cancer outcomes (overall, prostate, colorectal, postmenopausal breast cancer, and a joint outcome called obesity-related cancers) in a pooled analysis of 11 Australian cohorts including 70,458 participants. From these cancers, only overall and colorectal cancer were associated with higher ABSI. However, due to the pooled data across studies, the authors could not adjust for key confounding factors including physical activity, diet, alcohol, and hormone replacement therapy (11). A study conducted in 143,901 American women showed that ABSI was associated with a higher risk of colorectal and kidney cancers (12). In contrast, among 27,474 Swedish residents (16,669 women and 10,805 men), ABSI was associated with rectal but not colon cancer in men but not women (13). Therefore, the available evidence for associations between ABSI and cancer risk is restricted to few cancer sites, mainly colorectal and breast cancer, with limited evidence for other cancer sites related to adiposity. Moreover, current evidence is conflicting, which could be explained by the lack of adjustment for key confounding factors, cohort heterogeneity, and small sample size (11, 13). In addition, it is not known whether these associations differ between men and women, or whether such associations are independent of

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BMI, or whether ABSI and BMI act together to influence cancer risk. To address these limitations, the current study aims firstly to investigate the associations between ABSI and incidence of cancer at 23 sites and all cancers combined and, secondly, to investigate the combined associations of ABSI and BMI with cancer risk.

Materials and Methods

Study design

UK Biobank recruited more than 500,000 participants (aged between 37 and 73 years, 56.3% were women) between 2006 and 2010 (14). Participants attended one of 22 assessment centers across England, Scotland, and Wales, where they completed a self-administered, touch-screen questionnaire, a face-to-face interview, and provided biological samples (15, 16). The outcomes used in this study were incidence of invasive cancers at 23 sites and four subgroups for colorectal cancer, as well as all cancers combined. Of the 23 cancers, 17 were relevant to both men and women, two were specific to men (testicular and prostate), and four were specific to women (breast, uterine, cervical, and ovarian).

Participant follow-up

Date of death was obtained from death certificates held by the National Health Service Information Centre (England and Wales) and the National Health Service Central Register Scotland (Scotland). Date and cause of hospital admissions were obtained through record linkage to Health Episode Statistics (England and Wales) and Scottish Morbidity Records (Scotland). Detailed information about the linkage procedures can be found at http://content.digital.nhs.uk/services. At the time of analysis, mortality data were available up to June 1, 2020. Mortality analyses were therefore censored at this date or the date of death, whichever occurred first. Hospital admission data were available until March 31, 2017 for Scotland and Wales and until June 1, 2020 for England, resulting in analyses of incident outcomes being censored at these dates or the date of relevant hospitalization or death, whichever occurred first. We defined incident cancer as fatal or nonfatal events. The International Classification of Diseases, 10th revision (ICD-10) was used to define the following 23 cancers sites and four subgroups for colorectal cancer: all cancers combined [C00-C97, excluding nonmelanoma skin cancer (C44)], head and neck (C00-C14), esophagus (C15), stomach (C16), colorectal (C18, C19, and C20), colon proximal (C 18.0–18.4), colon distal (C18.5, C18.7), colon (C18.0), rectum (C19-C20), liver (C22), gallbladder (C23-24), pancreas (C25), lung (C33-34), malignant melanoma (C43), breast (C50), uterus (C54-C55), cervix (C53), ovary (C56), prostate (C61), testis (C62), kidney (C64-C65), bladder (C67), brain (C70–72), thyroid (C73), Hodgkin lymphoma (C81), non–Hodgkin lymphoma (C82-C86, C96), multiple myeloma (C88–90), and leukemia (C91-C95).

Exposure

Anthropometric measurements, including body weight, height, and waist circumference (WC), were collected at baseline by trained staff using standardized protocols (17). Height was measured to the nearest centimeter, using a Seca 202 stadiometer, and body weight to the nearest 0.1 kg, using the Tanita BC-418 body composition analyzer. BMI was calculated as weight (kg) divided by height (m) squared and classified into the following categories: underweight (<18.5 kg/m^2), normal weight (18.5 to <25 kg/m^2), overweight (25 to <30 kg/m^2), or obese (≥30 kg/m^2; ref. 18). WC was measured at the natural indent (or umbilicus if the natural indent could not be observed) in 500,366 individuals. ABSI was calculated using the formula ABSI = WC/(BMI$^{2/3}$ × height$^{1/2}$; ref. 8) and standardized by sex [expressed as 1-standard deviation (SD)].

Covariates

Age, sex, ethnicity, income, education, smoking status, diet (intake of fruits and vegetables, red and processed meat, and oily fish), and alcohol intake (daily, 2–4 times a week, once or twice a week, 1–3 times a month, special occasions, and never; this categorical variable was inserted into the model as an ordinal variable), and health-related variables were self-reported at the baseline assessment (17). Townsend area deprivation index was derived from the postcode of residence using aggregated data on unemployment, car- and homeownership, and household overcrowding (19). Physician-diagnosed medical conditions were self-reported at baseline. These health conditions were used to derive a multi-morbidity count, including 43 health conditions (20–22). Physical activity levels over a typical week were self-reported using the International Physical Activity Questionnaire, and reported as metabolic equivalent of task (MET) per week (23). Time spent in discretionary sedentary behaviors was derived from the questionnaire and included time spent in front of a television or computer or leisure time driving. Pack years adult smoking as a proportion of life span was derived as pack years divided by the number of years between the participant's age at recruitment and the age of 16. Further details of these measurements can be found in the UK Biobank online protocol (http://www.ukbiobank.ac.uk).

Ethics

All participants provided written informed consent before enrolment in the study, which was conducted in accordance with the Declaration of Helsinki. The study was approved by the NHS National Research Ethics Service (Ref: 11/NW/0382).

Statistical analyses

Descriptive characteristics of the cohort are presented by tertiles of ABSI standardized by sex. Continuous variables are presented as means and SD, and categorical variables as frequencies and percentages. Correlations between ABSI and other anthropometric measurements (body height and weight, BMI, WC, and body fat in kg) were analyzed using Pearson correlation coefficient.

Cox proportional hazard models were used to investigate the associations between ABSI, expressed both as sex-specific tertiles and per 1-SD (1-SD was equivalent to 0.04 ABSI for men, 0.05 ABSI for women), and incidence of cancer at 23 sites and all cancers combined. Risk estimates were reported as HRs and 95% confidence intervals (CI). Duration of follow-up was used as the time-varying covariate. In addition, to reduce the potential for reverse causality, landmark analysis was performed with follow-up commencing 2 years after recruitment.

Analyses were adjusted hierarchically using three statistical models: Model 1 was adjusted for sociodemographic variables only (age, sex, deprivation, ethnicity, education, income); Model 2 was adjusted for Model 1 variables plus lifestyle factors [pack years adult smoking, diet (alcohol, fruits and vegetables, red and processed meat, and oily fish), physical activity, and sedentary time]; and Model 3 was adjusted for Model 2 variables plus multi-morbidity. Additional health-related covariates were included in Model 3 for cancers at specific sites i.e., diabetes for pancreatic, thyroid, and colorectal cancer, aspirin for colorectal cancer and age of menarche, hormonal replacement and contraceptive use for female cancers (breast, ovarian, cervical, and uterine cancer). Model 4 included all covariates in Model 3 plus BMI. In addition, the associations of ABSI with esophageal, head and neck,

and lung cancer were stratified by smoking status (never, former, and current). For breast cancer, the analyses were repeated stratified by menopausal status (premenopausal and postmenopausal).

To investigate the combined effect of ABSI and BMI, four categories were derived: low ABSI and normal weight (reference category); low ABSI and overweight/obese; high ABSI and normal weight; and high ABSI and overweight/obese. High ABSI was defined as above the median value (0.079 for men, 0.074 for women). The analyses were repeated based on obese rather than overweight/obese.

Finally, because of potentially inflated type-I errors due to multiple tests, all analyses were corrected for multiple testing using Holm method (24), which performs similarly to Bonferroni method while retaining higher statistical power (25). The multiple testing corrected P value is denoted as P_{adj}. All analyses were performed using R Statistical Software, version 3.6.2, with the package survival.

Data availability

Data are available upon request from UK Biobank (www.ukbiobank.ac.uk).

Results

After excluding 41,406 (8.3%) participants with a prevalent cancer diagnosis at baseline, 16,250 (3.2%) with missing data for exposures and covariates, and 2,226 (0.4%) participants who were classified as underweight, this study included 442,610 participants who were followed-up for 8.8 years [interquartile range (IQR), 7.9–9.6] for cancer incidence, after excluding the first 2 years of follow-up. Over this period, 39,961 incident cancers were recorded (Supplementary Fig. S1).

The characteristics of participants by sex-specific tertiles of ABSI are shown in **Table 1**. In summary, 53.7% of the study population were women, 94.6% were of white European background, and the mean age was 56.3 years (range: 38–73 years). Those in the highest tertile for ABSI were older, had lower income and education, and higher deprivation. They were also more likely to be current smokers, have multi-morbidity, and be less physically active. There were no differences in dietary intake (specifically fruits and vegetables, red and processed meat, and oily fish) or alcohol consumption (**Table 1**). ABSI correlated weakly with BMI ($r = 0.12$, $P < 0.001$; Supplementary Fig. S2).

The associations between sex-specific tertiles of ABSI and cancer risk at 23 sites are presented in **Table 2**. For the minimally adjusted model (Model 1: adjusted for sociodemographic variables), there were significant associations between the highest tertile of ABSI and cancer at six sites: lung (HR, 1.75; 95% CI, 1.59–1.92), liver (HR, 1.64; 95% CI, 1.34–2.00), esophagus (HR, 1.42; 95% CI, 1.20–1.68), kidney (HR, 1.31; 95% CI, 1.13–1.52), colorectal (HR, 1.21; 95% CI, 1.12–1.31; driven by proximal and colon), and breast (HR, 1.11; 95% CI, 1.05–1.18) and for all cancers combined (HR, 1.14; 95% CI, 1.11–1.17). When the analyses were further adjusted for lifestyle factors (Model 2), the same cancer sites remained significantly associated with ABSI (lung, liver, esophagus, kidney, colorectal, and breast cancer) as well as all cancers combined. Further adjustment for health-related covariates (Model 3) revealed similar significant associations for lung (HR, 1.58; 95% CI, 1.44–1.74), liver (HR, 1.45; 95% CI, 1.18–1.77), esophagus (HR, 1.32; 95% CI, 1.12–1.57), colorectal (HR, 1.19; 95% CI, 1.10–1.28), breast (HR, 1.05; 95% CI, 1.04–1.17), and all cancers combined (HR, 1.11; 95% CI, 1.08–1.14; **Table 2**). These associations remained significant for lung (HR, 1.61; 95% CI, 1.47–1.77), liver (HR, 1.42; 95% CI, 1.17–1.74), esophagus (HR, 1.30; 95% CI, 1.10–1.54), colorectal (HR, 1.18; 95% CI, 1.09–1.27), all cancers combined (HR, 1.10; 95% CI, 1.06–1.27), but the association with breast cancer was attenuated (HR, 1.09; 95% CI, 1.03–1.16; $P_{adj} = 0.117$) when the analysis was adjusted for BMI (Supplementary Table S1). When ABSI was standardized and expressed per 1-SD increment, there was a higher risk of esophageal, liver, lung, colorectal, and breast cancer with higher ABSI, as shown in **Fig. 1** and Supplementary Table S2. There was no strong evidence to suggest nonlinear associations (Supplementary Fig. S3).

When analyses for lung, head and neck, and esophageal cancer were stratified by smoking status, there was evidence of interaction for lung ($P_{interaction} = 0.0083$) and head and neck cancers ($P_{interaction} = 0.0032$; **Fig. 2**). The association of ABSI (lowest vs. highest tertile) and lung cancer was observed in ex-smokers (HR, 1.34; 95% CI, 1.17–1.55) and current smokers (HR, 1.50; 95% CI, 1.28–1.76), but not in those who had never smoked (HR, 1.17; 95% CI, 0.93–1.47). A higher risk of head and neck cancer with increased ABSI was observed in current smokers only (HR, 1.54; 95% CI, 1.07–2.22). A similar pattern was observed for esophageal cancer, although the interaction was not significant (HR for current smokers, 1.51; 95% CI, 1.01–2.26). There was no evidence of interaction between ABSI and menopausal status for breast cancer ($P_{interaction} = 0.0743$). Only postmenopausal women in the highest tertile for ABSI had a greater risk of breast cancer (HR, 1.15; 95% CI, 1.07–1.25; Supplementary Table S3).

The associations between categories of ABSI (lower and higher) and of BMI (normal and BMI ≥25 kg/m^2) with risk of cancer are presented in **Table 3**. Compared with participants in the lower ABSI and normal BMI category (reference), those with higher ABSI and BMI ≥25 kg/m^2 had higher cancer risk at six sites (uterus, esophagus, kidney, stomach, colorectal, and breast). The magnitude of the associations ranged from 1.14 for all cancers combined to 2.28 for uterine cancer (**Table 3**). Similar results were found for higher ABSI in people with obesity (Supplementary Table S4).

Discussion

Our study provides evidence for associations between ABSI and the risk of three cancers sites. After adjusting for a wide range of confounding factors and for multiple testing, higher ABSI was associated with higher risk of liver, lung, colorectal cancer, and all cancers combined. Importantly, there was a weak correlation between ABSI and BMI, and the associations with ABSI were independent of BMI. Since ABSI is an independent predictor of body fat (26) and, specifically, of visceral adipose tissue, these findings suggest that higher abdominal fat mass may exacerbate risk of liver, lung, and colorectal cancer independent of body weight (27). We also found that having a higher ABSI and being overweight or obese (defined as BMI ≥25 kg/m^2) was associated with a greater risk of cancer at seven sites, including uterus, esophagus, liver, stomach, kidney, colorectal, and breast. This suggests–for the first time—that cancer risk could be better stratified by using both BMI and ABSI. Therefore, the combination of both markers may be a useful approach for identifying those at greatest cancer risk and for targeting cancer prevention interventions in public health and clinical practice.

Three previous studies have investigated associations between ABSI and overall, colorectal, prostate, breast, endometrial, and renal cancers. Using data on 16,669 women and 10,805 men from the Malmo Diet and Cancer study in Sweden, who were followed-up for 22 years, Andreasson and colleagues (13) reported that 1-SD higher ABSI was associated with a 21% higher risk of colorectal cancer in men in a crude model (HR, 1.21; 95% CI, 1.10–1.33). However, this was attenuated (HR, 1.13; 95% CI, 1.03–1.25) when BMI was included as a covariate. Similar results were reported for rectal cancer (HR, 1.16; 95% CI, 1.00–1.36) but not colon cancer (HR, 1.11; 95% CI, 0.98–1.26). Andreasson

Table 1. Cohort characteristics by tertiles of sex-specific ABSI.

	Low	Middle	High	Overall
Sociodemographic				
N	150,390 (34.0%)	147,751 (33.4%)	144,469 (32.6%)	442,610
Sex, % (*n*)				
Females	82,788 (55.0%)	78,599 (53.2%)	76,381 (52.9%)	237,768 (53.7%)
Males	67,602 (45.0%)	69,152 (46.8%)	68,088 (47.1%)	204,842 (46.3%)
Age, mean (SD)	54.2 (8.2)	56.3 (7.8)	58.4 (7.6)	56.3 (8.1)
Income, % (*n*)				
Less than £18,000	22,570 (15.0%)	26,777 (18.1%)	34,413 (23.8%)	83,760 (18.9%)
£18,000 to 30,999	30,523 (20.3%)	32,293 (21.9%)	33,298 (23.0%)	96,114 (21.7%)
£31,000 to 51,999	36,845 (24.5%)	34,332 (23.2%)	29,608 (20.5%)	100,785 (22.8%)
£52,000 to 100,000	32,354 (21.5%)	27,149 (18.4%)	20,331 (14.1%)	79,834 (18.0%)
Greater than £100,000	9,182 (6.1%)	7,248 (4.9%)	4,772 (3.3%)	21,202 (4.8%)
Do not know/prefer not to answer	18,916 (12.6%)	19,952 (13.5%)	22,047 (15.3%)	60,915 (13.8%)
Education, % (*n*)				
CSEs or equivalent/NVQ or HND or HNC or equivalent	18,291 (12.2%)	18,016 (12.2%)	17,109 (11.8%)	53,416 (12.1%)
O levels/GCSEs or equivalent	32,731 (21.8%)	31,501 (21.3%)	29,901 (20.7%)	94,133 (21.3%)
A levels/AS levels or equivalent	18,235 (12.1%)	16,772 (11.4%)	14,874 (10.3%)	49,881 (11.3%)
College or university degree	61,384 (40.8%)	56,749 (38.4%)	49,951 (34.6%)	168,084 (38.0%)
Do not know/prefer not to answer	19,749 (13.1%)	24,713 (16.7%)	32,634 (22.6%)	77,096 (17.4%)
Townsend deprivation index, % (*n*)				
Lowest deprivation	53,503 (35.6%)	50,739 (34.3%)	45,440 (31.5%)	149,682 (33.8%)
Middle deprivation	50,855 (33.8%)	49,990 (33.8%)	47,527 (32.9%)	148,372 (33.5%)
Highest deprivation	46,032 (30.6%)	47,022 (31.8%)	51,502 (35.6%)	144,556 (32.7%)
Ethnicity, % (*n*)				
White	142,785 (94.9%)	140,525 (95.1%)	135,479 (93.8%)	418,789 (94.6%)
Mixed	2,263 (1.5%)	2,096 (1.4%)	2,227 (1.5%)	6,586 (1.5%)
South Asian	1,804 (1.2%)	2,510 (1.7%)	4,421 (3.1%)	8,735 (2.0%)
Black	3,067 (2.0%)	2,126 (1.4%)	1,922 (1.3%)	7,115 (1.6%)
Chinese	471 (0.3%)	494 (0.3%)	420 (0.3%)	1,385 (0.3%)
Anthropometrics				
ABSI cut-off, men: mean (min–max)	0.075 (0.032–0.077)	0.080 (0.078–0.081)	0.084 (0.082–0.124)	
ABSI cut-off, women: mean (min–max)	0.068 (0.041–0.071)	0.074 (0.072–0.075)	0.080 (0.076–0.143)	
Height (m): mean (SD)	1.68 (0.09)	1.690 (0.09)	1.69 (0.09)	1.69 (0.09)
Weight (kg): mean (SD)	76.3 (15.40)	78.4 (15.82)	80.0 (16.01)	78.2 (15.81)
Waist (cm): mean (SD)	83.2 (11.55)	90.4 (11.90)	97.7 (12.44)	90.3 (13.35)
Body fat (%): mean (SD)	29.7 (8.61)	31.4 (8.30)	33.1 (8.23)	31.4 (8.50)
BMI (kg/m^2): mean (SD)	26.8 (4.60)	27.5 (4.70)	28.1 (4.81)	27.5 (4.73)
Lifestyle				
Smoking, % (*n*)				
Never	90,320 (60.1%)	81,688 (55.3%)	72,580 (50.2%)	244,588 (55.3%)
Ex-smoker	46,518 (30.9%)	51,291 (34.7%)	54,313 (37.6%)	152,122 (34.4%)
Current	13,552 (9.0%)	14,772 (10.0%)	17,576 (12.2%)	45,900 (10.4%)
Alcohol intake, % (*n*)				
Never	10,380 (6.9%)	10,488 (7.1%)	13,353 (9.2%)	34,221 (7.7%)
Special occasions only	15,933 (10.6%)	16,007 (10.8%)	17,924 (12.4%)	49,864 (11.3%)
1–3 times a month	17,706 (11.8%)	16,281 (11.0%)	15,505 (10.7%)	49,492 (11.2%)
Once or twice a week	41,731 (27.7%)	38,498 (26.1%)	34,849 (24.1%)	115,078 (26.0%)
3–4 times a week	37,152 (24.7%)	35,595 (24.1%)	30,900 (21.4%)	103,647 (23.4%)
Daily or almost daily	27,488 (18.3%)	30,882 (20.9%)	31,938 (22.1%)	90,308 (20.4%)
Fruit and vegetable intake (portion/day)	2.0 (0.83)	2.0 (0.83)	1.9 (0.83)	2.0 (0.83)
Red meat (portion/week)	2.0 (1.42)	2.1 (1.43)	2.2 (1.49)	2.1 (1.44)
Processed meat (portion/week)	1.8 (1.05)	1.9 (1.06)	1.9 (1.07)	1.9 (1.06)
Oily fish (portion/week)	1.7 (0.92)	1.6 (0.92)	1.6 (0.93)	1.6 (0.93)
Total discretionary sedentary behavior (h/day): mean (SD)	4.9 (2.22)	5.0 (2.26)	5.2 (2.35)	5.0 (2.28)
Total physical activity (MET-h/week): mean (SD)	127.5 (131.6)	117.5 (126.4)	110.3 (123.0)	118.8 (127.4)
Health	29,607 (19.7%)	38,177 (25.8%)	47,774 (33.1%)	115,558 (26.1%)
Aspirin, % (*n*)				
No	138,085 (91.8%)	132,163 (89.4%)	125,494 (86.9%)	395,742 (89.4%)
Yes	12,305 (8.2%)	15,588 (10.6%)	18,975 (13.1%)	46,868 (10.6%)
No. of long-term conditions, % (*n*)				
No illness	66,759 (44.4%)	55,628 (37.6%)	43,072 (29.8%)	165,459 (37.4%)
1+ illness	83,631 (55.6%)	92,123 (62.4%)	101,397 (70.2%)	277,151 (62.6%)

Note: Data are presented as number of participants and their percentage (%) for categorical variables. Continuous variables are presented as mean and SD. Data available for 442,614 participants.

Abbreviations: AS, advanced subsidiary; CSE, certificate of secondary education; GCSE, general certificate of secondary education; HNC, higher national certificate; HND, higher national diploma; NVQ, national vocational qualification.

Table 2. Associations of sex-specific tertiles of ABSI with cancer by site, subsite, and overall.

Cancer sites	Low ABSI (Ref.)	Middle ABSI	P_{adj}	High ABSI	P_{adj}	HR for trend	*P* for trend
Model 1							
All cancer combined[a]	1.00 (Ref.)	1.05 (1.03–1.08)	**0.002**	1.14 (1.11–1.17)	<**0.001**	1.07 (1.05–1.08)	<**0.001**
Head & neck	1.00 (Ref.)	0.96 (0.81–1.15)	1.000	1.16 (0.98–1.38)	1.000	1.08 (1.00–1.18)	0.938
Esophagus	1.00 (Ref.)	1.21 (1.02–1.44)	0.873	1.42 (1.20–1.68)	**0.001**	1.19 (1.10–1.29)	**0.001**
Stomach	1.00 (Ref.)	1.07 (0.88–1.29)	1.000	1.22 (1.01–1.46)	0.687	1.11 (1.01–1.21)	0.591
Colorectal	1.00 (Ref.)	1.07 (0.99–1.16)	1.000	1.21 (1.12–1.31)	<**0.001**	1.10 (1.06–1.15)	<**0.001**
Colon	1.00 (Ref.)	1.04 (0.94–1.14)	1.000	1.20 (1.10–1.31)	**0.001**	1.10 (1.05–1.15)	**0.001**
Proximal	1.00 (Ref.)	1.16 (1.02–1.32)	0.661	1.23 (1.09–1.40)	**0.029**	1.11 (1.04–1.18)	**0.034**
Distal	1.00 (Ref.)	0.96 (0.83–1.10)	1.000	1.18 (1.03–1.34)	0.401	1.09 (1.02–1.17)	0.223
Rectum	1.00 (Ref.)	1.05 (0.93–1.17)	1.000	1.15 (1.02–1.28)	0.401	1.07 (1.01–1.13)	0.318
Liver	1.00 (Ref.)	1.27 (1.03–1.57)	0.739	1.64 (1.34–2.00)	<**0.001**	1.28 (1.16–1.41)	<**0.001**
Gallbladder	1.00 (Ref.)	1.23 (0.92–1.64)	1.000	1.21 (0.91–1.62)	1.000	1.09 (0.95–1.26)	1.000
Pancreas	1.00 (Ref.)	1.01 (0.87–1.18)	1.000	1.01 (0.87–1.17)	1.000	1.00 (0.93–1.08)	1.000
Lung	1.00 (Ref.)	1.35 (1.22–1.49)	<**0.001**	1.75 (1.59–1.92)	<**0.001**	1.32 (1.26–1.38)	<**0.001**
Melanoma	1.00 (Ref.)	0.89 (0.80–0.99)	1.000	0.89 (0.79–0.99)	0.670	0.94 (0.89–1.00)	1.000
Breast	1.00 (Ref.)	1.06 (1.00–1.12)	1.000	1.11 (1.05–1.18)	**0.010**	1.06 (1.02–1.09)	**0.010**
Uterus	1.00 (Ref.)	1.03 (0.88–1.19)	1.000	1.09 (0.94–1.26)	1.000	1.05 (0.97–1.13)	1.000
Cervix	1.00 (Ref.)	1.09 (0.68–1.76)	1.000	1.09 (0.67–1.76)	1.000	1.04 (0.82–1.32)	1.000
Ovary	1.00 (Ref.)	1.11 (0.94–1.32)	1.000	1.07 (0.90–1.26)	1.000	1.03 (0.95–1.12)	1.000
Prostate	1.00 (Ref.)	0.99 (0.93–1.05)	1.000	0.96 (0.90–1.01)	1.000	0.98 (0.95–1.01)	1.000
Testis	1.00 (Ref.)	0.75 (0.42–1.33)	1.000	0.81 (0.44–1.47)	1.000	0.89 (0.65–1.20)	1.000
Kidney	1.00 (Ref.)	1.19 (1.02–1.38)	0.765	1.31 (1.13–1.52)	**0.009**	1.14 (1.06–1.23)	**0.009**
Bladder	1.00 (Ref.)	1.08 (0.97–1.22)	1.000	1.08 (0.97–1.21)	1.000	1.04 (0.98–1.10)	1.000
Brain	1.00 (Ref.)	0.92 (0.77–1.11)	1.000	0.95 (0.79–1.14)	1.000	0.98 (0.89–1.07)	0.591
Thyroid	1.00 (Ref.)	1.33 (0.98–1.79)	1.000	1.41 (1.04–1.90)	0.573	1.18 (1.02–1.37)	<**0.001**
Non–Hodgkin lymphoma	1.00 (Ref.)	1.02 (0.91–1.16)	1.000	1.02 (0.91–1.15)	1.000	1.01 (0.95–1.07)	1.000
Hodgkin lymphoma	1.00 (Ref.)	1.53 (0.98–2.40)	1.000	1.39 (0.88–2.20)	1.000	1.16 (0.93–1.44)	1.000
Multiple myeloma	1.00 (Ref.)	1.04 (0.88–1.23)	1.000	1.04 (0.88–1.22)	1.000	1.02 (0.94–1.10)	1.000
Leukemia	1.00 (Ref.)	0.99 (0.85–1.15)	1.000	1.10 (0.95–1.27)	1.000	1.05 (0.98–1.13)	1.000
Model 2							
All cancer combined[a]	1.00 (Ref.)	**1.05 (1.02–1.08)**	**0.017**	**1.12 (1.09–1.15)**	<**0.001**	**1.06 (1.04–1.07)**	<**0.001**
Head & neck	1.00 (Ref.)	0.95 (0.80–1.14)	1.000	1.14 (0.96–1.36)	1.000	1.07 (0.99–1.17)	1.000
Esophagus	1.00 (Ref.)	1.20 (1.00–1.42)	1.000	**1.37 (1.16–1.63)**	**0.006**	**1.17 (1.08–1.27)**	**0.005**
Stomach	1.00 (Ref.)	1.06 (0.87–1.28)	1.000	1.17 (0.97–1.41)	1.000	1.08 (0.99–1.19)	1.000
Colorectal	1.00 (Ref.)	1.06 (0.98–1.15)	1.000	**1.19 (1.10–1.28)**	<**0.001**	**1.09 (1.05–1.13)**	<**0.001**
Colon	1.00 (Ref.)	1.03 (0.93–1.12)	1.000	**1.18 (1.08–1.29)**	**0.009**	**1.09 (1.04–1.14)**	**0.005**
Proximal	1.00 (Ref.)	1.15 (1.01–1.31)	1.000	1.20 (1.06–1.36)	0.108	1.09 (1.03–1.16)	0.130
Distal	1.00 (Ref.)	0.95 (0.82–1.09)	1.000	1.16 (1.01–1.33)	0.664	1.09 (1.01–1.16)	0.392
Rectum	1.00 (Ref.)	1.03 (0.92–1.16)	1.000	1.12 (1.00–1.26)	0.878	1.06 (1.00–1.12)	0.731
Liver	1.00 (Ref.)	1.25 (1.01–1.54)	1.000	**1.56 (1.28–1.90)**	<**0.001**	**1.25 (1.13–1.37)**	<**0.001**
Gallbladder	1.00 (Ref.)	1.23 (0.92–1.64)	1.000	1.21 (0.91–1.61)	1.000	1.09 (0.95–1.25)	1.000
Pancreas	1.00 (Ref.)	1.01 (0.87–1.17)	1.000	1.00 (0.86–1.15)	1.000	1.00 (0.93–1.07)	1.000
Lung	1.00 (Ref.)	**1.31 (1.19–1.45)**	<**0.001**	**1.63 (1.49–1.79)**	<**0.001**	**1.27 (1.22–1.33)**	<**0.001**
Melanoma	1.00 (Ref.)	0.89 (0.80–1.00)	1.000	0.89 (0.80–1.00)	0.878	**1.05 (1.02–1.08)**	**0.033**
Breast	1.00 (Ref.)	1.05 (0.99–1.12)	1.000	**1.10 (1.04–1.17)**	**0.035**	1.03 (0.96–1.11)	1.000
Uterus	1.00 (Ref.)	1.02 (0.88–1.18)	1.000	1.06 (0.91–1.23)	1.000	1.04 (0.82–1.31)	1.000
Cervix	1.00 (Ref.)	1.09 (0.68–1.76)	1.000	1.07 (0.66–1.74)	1.000	1.04 (0.95–1.13)	1.000
Ovary	1.00 (Ref.)	1.12 (0.95–1.32)	1.000	1.08 (0.91–1.28)	1.000	0.98 (0.95–1.01)	1.000
Prostate	1.00 (Ref.)	0.99 (0.93–1.05)	1.000	0.96 (0.90–1.02)	1.000	0.89 (0.66–1.21)	1.000
Testis	1.00 (Ref.)	0.76 (0.42–1.34)	1.000	0.82 (0.45–1.50)	1.000	1.12 (1.04–1.21)	0.052
Kidney	1.00 (Ref.)	1.17 (1.01–1.36)	1.000	**1.27 (1.09–1.47)**	**0.046**	1.03 (0.97–1.09)	1.000
Bladder	1.00 (Ref.)	1.07 (0.96–1.21)	1.000	1.07 (0.95–1.20)	1.000	0.98 (0.89–1.07)	1.000
Brain	1.00 (Ref.)	0.93 (0.77–1.11)	1.000	0.96 (0.80–1.15)	1.000	1.19 (1.02–1.38)	0.505
Thyroid	1.00 (Ref.)	1.34 (1.00–1.81)	1.000	1.42 (1.05–1.93)	0.510	0.94 (0.89–1.00)	0.852
Non–Hodgkin	1.00 (Ref.)	1.02 (0.91–1.15)	1.000	1.01 (0.89–1.14)	1.000	1.00 (0.95–1.06)	1.000
Hodgkin	1.00 (Ref.)	1.51 (0.96–2.37)	1.000	1.32 (0.83–2.09)	1.000	1.12 (0.90–1.40)	1.000
Multiple myeloma	1.00 (Ref.)	1.04 (0.88–1.23)	1.000	1.04 (0.88–1.22)	1.000	1.02 (0.94–1.10)	1.000
Leukemia	1.00 (Ref.)	0.99 (0.85–1.15)	1.000	1.09 (0.95–1.27)	1.000	1.05 (0.98–1.13)	1.000

(Continued on the following page)

Table 2. Associations of sex-specific tertiles of ABSI with cancer by site, subsite, and overall. (Cont'd)

Cancer sites	Low ABSI (Ref.)	Middle ABSI	P_{adj}	High ABSI	P_{adj}	HR for trend	*P* for trend
Model 3							
All cancer combined[a]	1.00 (Ref.)	**1.04 (1.02–1.07)**	**0.049**	**1.11 (1.08–1.14)**	**<0.001**	**1.05 (1.04–1.07)**	**<0.001**
Head & neck	1.00 (Ref.)	0.95 (0.80–1.13)	1.000	1.12 (0.95–1.33)	1.000	1.07 (0.98–1.16)	1.000
Esophagus	1.00 (Ref.)	1.18 (0.99–1.40)	1.000	**1.32 (1.12–1.57)**	**0.032**	**1.15 (1.06–1.25)**	**0.030**
Stomach	1.00 (Ref.)	1.05 (0.87–1.28)	1.000	1.17 (0.97–1.40)	1.000	1.08 (0.99–1.19)	1.000
Colorectal	1.00 (Ref.)	1.06 (0.98–1.15)	1.000	**1.19 (1.10–1.28)**	**<0.001**	**1.09 (1.05–1.14)**	**<0.001**
Colon	1.00 (Ref.)	1.02 (0.93–1.12)	1.000	**1.18 (1.07–1.29)**	**0.011**	**1.09 (1.04–1.14)**	**0.006**
Proximal	1.00 (Ref.)	1.15 (1.01–1.31)	1.000	1.20 (1.05–1.36)	0.136	1.09 (1.02–1.16)	0.163
Distal	1.00 (Ref.)	0.95 (0.83–1.09)	1.000	1.17 (1.02–1.33)	0.568	1.09 (1.02–1.17)	0.318
Rectum	1.00 (Ref.)	1.04 (0.92–1.16)	1.000	1.13 (1.01–1.27)	0.701	1.07 (1.01–1.13)	0.580
Liver	1.00 (Ref.)	1.21 (0.98–1.49)	1.000	**1.45 (1.18–1.77)**	**0.009**	**1.20 (1.09–1.32)**	**0.006**
Gallbladder	1.00 (Ref.)	1.23 (0.92–1.64)	1.000	1.20 (0.90–1.61)	1.000	1.09 (0.94–1.25)	1.000
Pancreas	1.00 (Ref.)	1.00 (0.86–1.16)	1.000	0.98 (0.85–1.14)	1.000	0.99 (0.92–1.07)	1.000
Lung	1.00 (Ref.)	**1.30 (1.18–1.44)**	**<0.001**	**1.58 (1.44–1.74)**	**<0.001**	**1.25 (1.20–1.31)**	**<0.001**
Melanoma	1.00 (Ref.)	0.89 (0.80–0.99)	1.000	0.89 (0.80–1.00)	0.938	**1.05 (1.02–1.08)**	**0.033**
Breast	1.00 (Ref.)	1.05 (0.99–1.12)	1.000	**1.10 (1.04–1.17)**	**0.034**	1.02 (0.95–1.10)	1.000
Uterus	1.00 (Ref.)	1.01 (0.87–1.18)	1.000	1.05 (0.90–1.22)	1.000	1.04 (0.82–1.32)	1.000
Cervix	1.00 (Ref.)	1.10 (0.68–1.77)	1.000	1.09 (0.67–1.77)	1.000	1.03 (0.95–1.12)	1.000
Ovary	1.00 (Ref.)	1.12 (0.94–1.32)	1.000	1.07 (0.90–1.27)	1.000	0.98 (0.95–1.01)	1.000
Prostate	1.00 (Ref.)	0.99 (0.93–1.05)	1.000	0.97 (0.91–1.02)	1.000	0.89 (0.65–1.21)	1.000
Testis	1.00 (Ref.)	0.75 (0.42–1.34)	1.000	0.81 (0.44–1.48)	1.000	1.10 (1.02–1.18)	0.280
Kidney	1.00 (Ref.)	1.15 (0.99–1.34)	1.000	1.22 (1.05–1.41)	0.245	1.02 (0.96–1.08)	1.000
Bladder	1.00 (Ref.)	1.07 (0.95–1.20)	1.000	1.04 (0.93–1.17)	1.000	0.98 (0.89–1.07)	1.000
Brain	1.00 (Ref.)	0.93 (0.77–1.11)	1.000	0.96 (0.80–1.15)	1.000	1.17 (1.01–1.36)	0.801
Thyroid	1.00 (Ref.)	1.33 (0.98–1.79)	1.000	1.38 (1.02–1.88)	0.771	0.94 (0.89–1.00)	0.912
Non–Hodgkin	1.00 (Ref.)	1.02 (0.90–1.15)	1.000	0.99 (0.88–1.12)	1.000	1.00 (0.94–1.06)	1.000
Hodgkin	1.00 (Ref.)	1.47 (0.94–2.30)	1.000	1.23 (0.77–1.96)	1.000	1.09 (0.87–1.35)	1.000
Multiple myeloma	1.00 (Ref.)	1.04 (0.88–1.23)	1.000	1.03 (0.87–1.21)	1.000	1.01 (0.93–1.10)	1.000
Leukemia	1.00 (Ref.)	0.99 (0.85–1.15)	1.000	1.09 (0.94–1.26)	1.000	1.05 (0.97–1.13)	1.000

Note: Data presented as HRs and their 95% CIs. Analyses were adjusted for: Model 1: age, sex, deprivation, ethnicity, education, income. Model 2: Model 1 plus smoking, dietary intake (alcohol, fruits and vegetables, red and processed meat, and oily fish), physical activity, and sedentary time. Model 3: Model 2, plus multi-morbidity. In addition, analyses were adjusted for diabetes for investigation of pancreatic, thyroid, and colorectal cancer; aspirin for colorectal cancer; and age at menarche, hormonal replacement, and contraceptive use for breast, ovary, cervix, and uterus cancer.

[a]All invasive cancers, excluding nonmelanoma skin cancer. P_{adj} indicates the *P* value corrected for multiple testing using Holm method.

and colleagues (13) reported that while ABSI was associated with higher risk of colorectal and of rectal cancer in women in the crude model, these associations disappeared when the analyses were adjusted for other anthropometric markers. Although our analyses were not stratified by sex, we found that 1-SD higher (sex-specific) ABSI was associated with increased risk of cancer in the colorectum and, separately, proximal and distal colon and rectum, with HR ranging from 7% to 8% per 1-SD higher ABSI when no multiple testing correction was applied. Differences in the magnitude of the association between our study and those reported by Andreasson and colleagues (13), may be explained by the comprehensive adjustments included in our study, but also by sex differences if the associations for women were, as reported by Andreasson and colleagues (13), weaker than those observed for men. However, when our analyses were corrected for multiple testing, only colorectal, colon, and proximal colon cancer risk remained associated with ABSI; such corrections were not included in the Andreasson and colleagues study. Another study that pooled data from 11 Australian cohorts, covering 79,458 participants, investigated the association of six adiposity markers, including ABSI, and incidence of overall, colorectal, prostate, breast (in postmenopausal women), and obesity-related cancers (11). Among these Australians, 1-SD higher ABSI was associated with a 3% and 10% higher risk of all-cause and colorectal cancer in men, respectively, and 4% and 9%, respectively, in women, with no associations, reported for postmenopausal breast cancer, prostate cancer, or obesity-related cancers (11). These risk estimates are similar to those observed in our study for overall and colorectal cancer, but differ for breast cancer in postmenopausal women. In the Women's Health Initiative study, which included 143,901 postmenopausal women from the United States, there was no association of ABSI with breast or endometrial cancer (12). However, for colorectal and kidney cancers, those participants in the highest quintile for ABSI had a 50% and 78% higher risk compared with those in the lowest quintile, respectively. However, their study did not assess whether these associations with ABSI were independent of BMI. We observed an association between ABSI and colorectal cancer but no association between ABSI and kidney cancer, in analyses of the whole cohort.

In our study, higher ABSI was associated with greater risk of lung cancer, in agreement with that reported by Ardesh and colleagues (28). However, when stratified by smoking status, these associations were evident in only former smokers and current smokers.

There are plausible biological mechanisms that could explain the association between ABSI, a visceral and overall adiposity marker, and cancer risk. Some of the potential mechanisms may be related to inflammation-induced adiposity (29, 30), and the resulting increase in adipokines, circulating cytokines, and chemokines (31). This could facilitate a tumor microenvironment, which is critical in the initiation and progression of cancer (29). Adiposity could also generate systemic

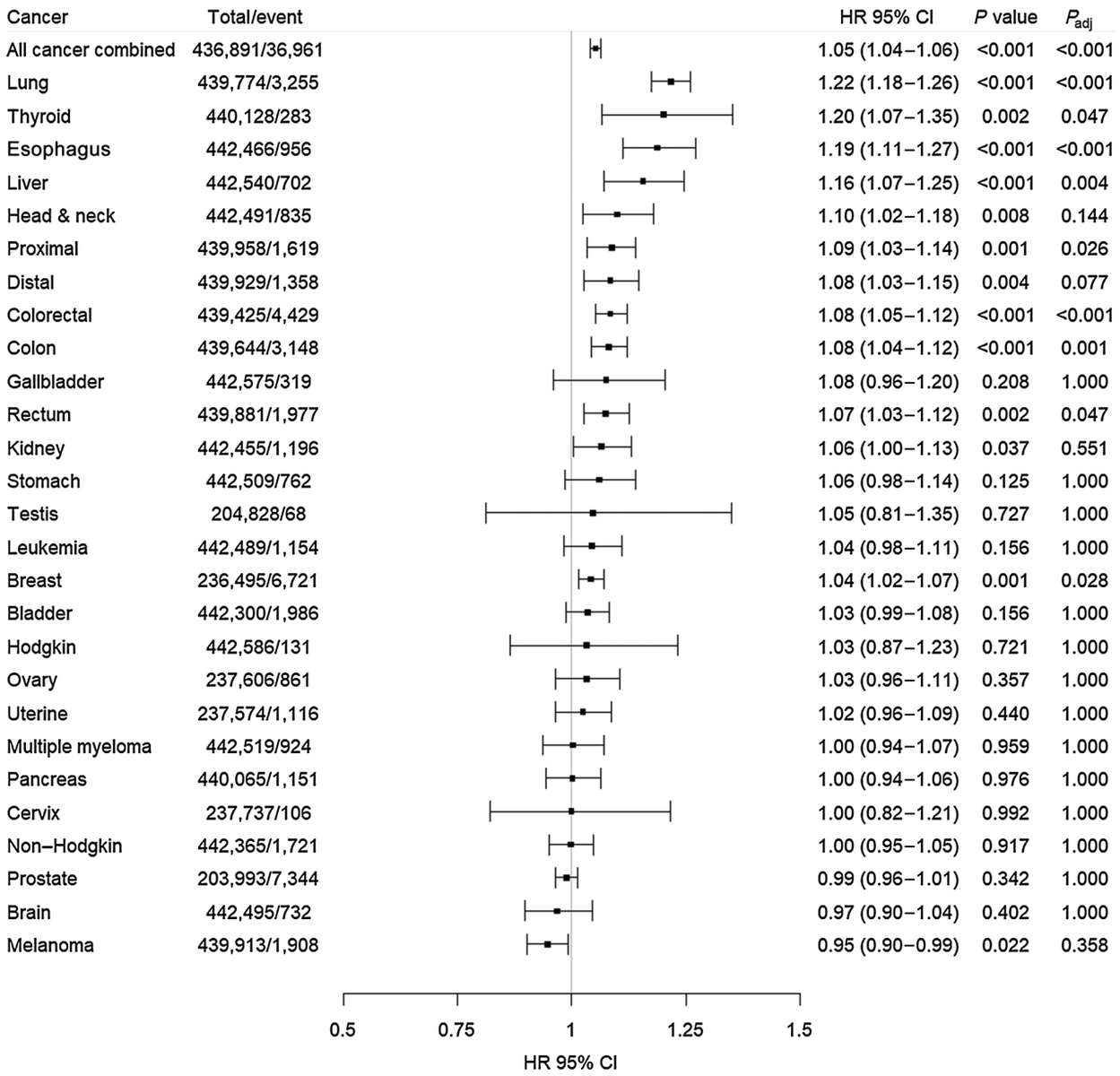

Figure 1.

Forest plot for the association of 1-SD higher ABSI with incidence cancer at 23 sites and all cancer combined. Data presented as HRs and their 95% CIs. Analyses were adjusted for age, sex, deprivation, ethnicity, education, income, smoking, dietary intake (alcohol, fruits and vegetables, red and processed meat, and oily fish), physical activity, and sedentary time, and multi-morbidity (Model 3). In addition, analyses were adjusted for diabetes for investigation of pancreas, thyroid, and colorectal cancer; aspirin for colorectal cancer; and age at menarche, hormonal replacement, and contraceptive use for breast, ovary, cervix, and uterus cancer. P_{adj} indicates the *P* value corrected for multiple testing using Holm method.

metabolic dysregulation—increased insulin, dyslipidemia, glycemia, oxidative stress, and insulin growth factor-1 (29, 30, 32)—which have been associated with cancer, especially the latter (33–36).

Clinical implications

The findings of this study have important clinical implications. They provide evidence that ABSI is associated with increased risk of cancer at several sites, with an increase in prediction potential when combined with BMI. Both measures are feasible and economically viable to be included in routine clinical practice.

Strengths and limitations

UK Biobank is not a fully representative sample of the UK adult population and so we should be cautious in generalizing findings to the general population. However, relative risks derived from the UK Biobank are consistent with those from more representative population cohorts (37). The adiposity exposures were measured by trained staff using standardized protocols, which minimizes the chance of measurement error and misclassification. However, there are several limitations that should be taken into account. Because some cancers lead to weight loss, reverse causation is a concern in

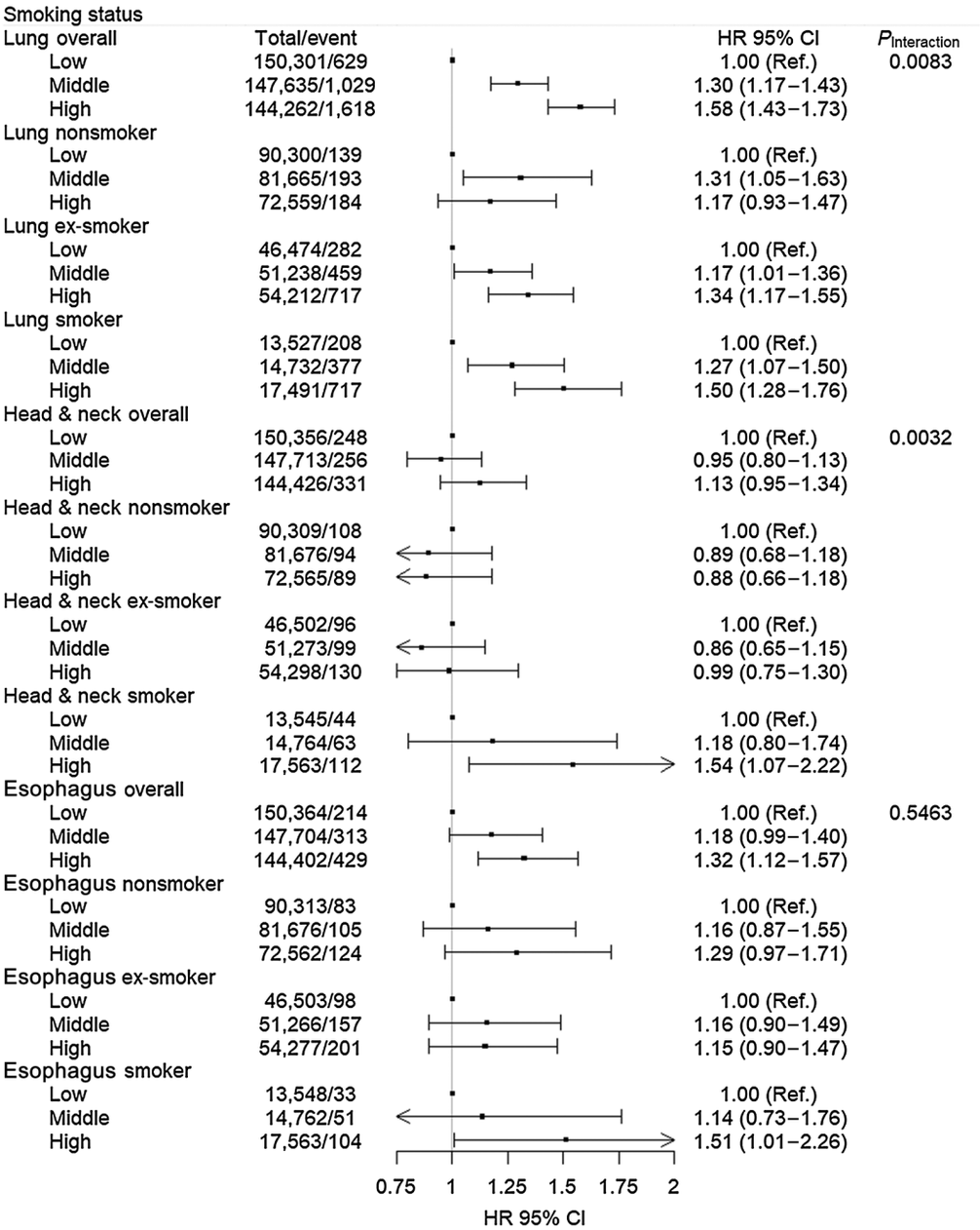

Figure 2.

Sensitivity analysis for the association between tertiles of ABSI with esophagus, head and neck, and lung cancer risk by smoking status. Data presented as HRs and their 95% CIs. Analyses were adjusted for age, sex, deprivation, education, income, ethnicity, dietary intake (alcohol, fruits and vegetables, red and processed meat, and oily fish), physical activity and sedentary time, and multi-morbidity (Model 3). The $P_{interaction}$ indicates significant differences on the associations between ABSI and cancer risk across smoking categories.

prospective cohort studies investigating the association between adiposity and cancer. Therefore, to minimize potential reverse causation, we excluded all cancers present at baseline and those diagnosed within the first 2 years of follow-up. Residual confounding remains possible despite our comprehensive adjustment scheme. Less than 5% of participants were excluded due to missing exposure and covariate data. However, since none of the covariates that we included have more than 5% of missingness, it does not seem that using other handling methods could affect our conclusions (38). Another limitation to consider is related to the joint association between ABSI and BMI or WC as we were unable to stratify WC or BMI into more categories. Therefore, future studies should investigate the joint association of these adiposity markers in overweight and obese individuals separately.

Table 3. Association of ABSI combined with BMI (normal versus BMI ≥25) with incidence of cancer, by site, subsite, and all cancers combined.

Cancer site	1. Lower ABSI, BMI normal		2. Lower ABSI, BMI overweight		3. Higher ABSI, BMI normal		4. Higher ABSI, BMI overweight	
All cancers combined[a]	82,079/5,364	1.00 (Ref.)	139,881/10,896	1.06 (1.03–1.10)	61,515/5,115	1.05 (1.01–1.09)	153,418/15,586	**1.14 (1.11–1.18)**
Head & neck	82,952/149	1.00 (Ref.)	141,505/225	0.69 (0.56–0.85)	62,339/146	1.07 (0.85–1.35)	155,697/315	0.76 (0.62–0.93)
Esophagus	82,960/78	1.00 (Ref.)	141,510/276	1.43 (1.11–1.84)	62,335/113	1.37 (1.02–1.82)	155,663/489	**1.72 (1.34–2.20)**
Stomach	82,960/67	1.00 (Ref.)	141,518/240	1.53 (1.16–2.01)	62,351/90	1.28 (0.93–1.75)	155,682/365	**1.60 (1.22–2.09)**
Colorectal	82,560/586	1.00 (Ref.)	140,627/1,258	1.11 (1.00–1.22)	61,972/583	1.06 (0.95–1.19)	154,268/2,002	**1.30 (1.18–1.43)**
Colon	82,592/406	1.00 (Ref.)	140,691/902	1.17 (1.03–1.31)	62,006/408	1.07 (0.93–1.23)	154,357/1,432	**1.35 (1.20–1.51)**
Proximal	82,627/220	1.00 (Ref.)	140,775/451	1.09 (0.93–1.29)	62,052/202	0.97 (0.80–1.18)	154,506/746	**1.29 (1.10–1.51)**
Distal	82,623/160	1.00 (Ref.)	140,775/416	1.36 (1.13–1.64)	62,051/171	1.16 (0.93–1.44)	154,482/611	**1.51 (1.26–1.81)**
Rectum	82,609/260	1.00 (Ref.)	140,760/565	1.08 (0.93–1.25)	62,039/268	1.10 (0.93–1.31)	154,475/884	**1.26 (1.09–1.46)**
Liver	82,962/67	1.00 (Ref.)	141,522/187	1.18 (0.89–1.57)	62,352/87	1.22 (0.88–1.68)	155,706/361	1.47 (1.12–1.93)
Gallbladder	82,970/45	1.00 (Ref.)	141,529/97	1.12 (0.78–1.60)	62,355/31	0.73 (0.46–1.15)	155,723/146	1.20 (0.85–1.71)
Pancreas	82,632/161	1.00 (Ref.)	140,818/350	1.06 (0.88–1.29)	62,076/139	0.87 (0.69–1.09)	154,541/501	1.04 (0.86–1.26)
Lung	82,601/375	1.00 (Ref.)	140,753/706	0.80 (0.71–0.91)	61,999/610	**1.49 (1.31–1.69)**	154,423/1,564	1.11 (0.99–1.25)
Melanoma	82,591/342	1.00 (Ref.)	66,580/1,939	**1.19 (1.11–1.28)**	37,846/1,050	1.10 (1.01–1.19)	76,396/2,380	**1.22 (1.14–1.31)**
Breast	55,673/1,352	1.00 (Ref.)	66,897/369	**2.14 (1.75–2.61)**	38,004/107	1.04 (0.81–1.35)	76,743/505	**2.28 (1.87–2.77)**
Uterus	55,930/135	1.00 (Ref.)	66,947/34	1.24 (0.72–2.13)	38,021/9	0.53 (0.25–1.16)	76,815/40	1.18 (0.69–2.04)
Cervix	55,954/23	1.00 (Ref.)	66,910/220	0.99 (0.81–1.21)	38,005/139	1.05 (0.84–1.32)	76,771/330	1.15 (0.95–1.39)
Ovary	55,920/172	1.00 (Ref.)	74,333/2,385	1.00 (0.92–1.08)	24,213/930	0.94 (0.85–1.03)	78,533/3,155	0.96 (0.89–1.04)
Prostate	26,916/874	1.00 (Ref.)	74,582/30	1.11 (0.54–2.30)	24,331/5	0.65 (0.22–1.91)	78,903/23	0.95 (0.44–2.05)
Testis	27,014/10	1.00 (Ref.)	141,496/360	1.40 (1.13–1.73)	62,338/132	1.16 (0.90–1.49)	155,663/590	**1.61 (1.31–1.99)**
Kidney	82,960/114	1.00 (Ref.)	141,446/589	1.05 (0.90–1.22)	62,308/238	0.95 (0.79–1.13)	155,597/928	1.11 (0.96–1.30)
Bladder	82,951/231	1.00 (Ref.)	141,508/238	1.13 (0.90–1.42)	62,337/95	0.97 (0.74–1.28)	155,692/286	1.09 (0.86–1.36)
Brain	82,960/113	1.00 (Ref.)	140,824/79	1.17 (0.80–1.70)	62,078/34	1.05 (0.67–1.65)	154,589/126	1.59 (1.11–2.28)
Thyroid	82,639/44	1.00 (Ref.)	140,757/619	1.03 (0.90–1.18)	62,055/237	0.83 (0.71–0.99)	154,512/710	0.97 (0.85–1.11)
Non–Hodgkin lymphoma	82,931/264	1.00 (Ref.)	141,508/353	1.24 (1.02–1.52)	62,344/163	1.20 (0.95–1.50)	155,688/498	1.26 (1.03–1.53)
Hodgkin lymphoma	82,969/18	1.00 (Ref.)	141,469/511	1.00 (0.86–1.16)	62,325/231	0.93 (0.78–1.11)	155,642/715	1.02 (0.88–1.18)
Multiple myeloma	82,958/138	1.00 (Ref.)	141,536/43	1.06 (0.61–1.87)	62,356/19	1.15 (0.60–2.21)	155,727/51	0.93 (0.53–1.64)
Leukemia	82,951/140	1.00 (Ref.)	141,518/270	1.02 (0.83–1.26)	62,349/102	0.78 (0.60–1.01)	155,696/414	1.15 (0.94–1.41)

Note: Data presented as HRs and their 95% CIs. Analyses were adjusted for: Model 1: age, sex, deprivation, ethnicity, education, income. Model 2: Model 1 plus smoking, dietary intake (alcohol, fruits and vegetables, red and processed meat, and oily fish), physical activity, and sedentary time. Model 3: Model 2, plus multi-morbidity. In addition, analyses were adjusted for diabetes for investigation of pancreas, thyroid, and colorectal cancer; aspirin for colorectal cancer; and age at menarche, hormonal replacement, and contraceptive use for breast, ovary, cervix, and uterus cancer.
[a]All invasive cancers, excluding nonmelanoma skin cancer.

Conclusion

In conclusion, ABSI was associated with increased risk of liver, lung, colorectal, and postmenopausal breast cancers as well as all cancers combined, independent of BMI. This provides evidence that body shape, in addition to body weight, is an important risk factor for these cancers. Furthermore, the combination of higher ABSI with raised BMI was associated with elevated risk of cancers of the uterus, esophagus, liver, stomach, kidney, colorectum, and breast. The combination of both markers may be a useful approach for identifying those at greatest cancer risk and for targeting cancer prevention interventions in public health and clinical practice.

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Authors' Contributions

S. Parra-Soto: Conceptualization, formal analysis, methodology, writing–original draft, writing–review and editing. **F.C. Malcomson:** Conceptualization, formal analysis, methodology, writing–original draft, writing–review and editing. **F.K. Ho:** Conceptualization, resources, writing–review and editing. **J.P. Pell:** Data curation, supervision, project administration, writing–review and editing. **L. Sharp:** Conceptualization, methodology, writing–original draft, writing–review and editing. **J.C. Mathers:** Conceptualization, validation, methodology, writing–original draft, writing–review and editing. **C. Celis-Morales:** Conceptualization, resources, data curation, formal analysis, supervision, funding acquisition, validation, investigation, writing–original draft, writing–review and editing.

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