OPEN ACCESS

WHO guidelines on waist circumference and physical activity and their joint association with cancer risk

Patricia Bohmann ,[1] Michael J Stein ,[1] Amina Amadou,[2,3] Hansjörg Baurecht,[1] Béatrice Fervers,[2,3] Emma Fontvieille,[4] Heinz Freisling,[4] Christine Friedenreich,[5,6] Julian Konzok,[1] Laia Peruchet-Noray,[4,7] Michael F Leitzmann,[1] Anja M Sedlmeier,[1,8,9] Andrea Weber[1]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bjsports-2024-108708).

For numbered affiliations see end of article.

Correspondence to
Patricia Bohmann;
patricia.bohmann@ukr.de

PB and MJS are joint first authors.

Accepted 22 November 2024

ABSTRACT

Objective Low body fat and high physical activity levels are key lifestyle factors in cancer prevention, but the interplay of abdominal obesity and physical activity on cancer risk remains unknown. We explored individual and joint associations of waist circumference and physical activity with cancer risk.

Methods Using UK Biobank data (n=315 457), we categorised individuals according to WHO guideline thresholds for waist circumference and self-reported physical activity levels. Multivariable-adjusted Cox regression was used to estimate HRs and 95% CIs of total cancer. The reference group comprised individuals with recommended levels of waist circumference (<88 cm for women and <102 cm for men) and physical activity (>10 metabolic equivalent of task hours/week). Furthermore, we estimated the proportion of cancers attributable to abdominal obesity and insufficient physical activity.

Results During a median follow-up period of 11 years (3 321 486 person-years), 29 710 participants developed any type of cancer. Participants not meeting the WHO guideline on waist circumference had increased cancer risk, even when sufficiently physically active according to the WHO (HR 1.11, 95% CI 1.08 to 1.15). Similarly, individuals not achieving the WHO guideline for physical activity showed an elevated risk, even if they were abdominally lean (HR 1.04, 95% CI 1.01 to 1.07). Not adhering to either guideline yielded the strongest increase in risk (HR 1.15, 95% CI 1.11 to 1.19). We estimated that abdominal obesity coupled with insufficient physical activity could account for 2.0% of UK Biobank cancer cases.

Conclusion Adherence to both WHO guidelines for waist circumference and physical activity is essential for cancer prevention; meeting just one of these guidelines is insufficient.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Abdominal obesity is associated with an increased risk of cancer, while physical activity is related to reduced cancer risk. However, whether individuals with abdominal obesity can decrease their cancer risk by being physically active is unknown. Likewise, whether physically inactive individuals have lower cancer risk if they are abdominally lean has not been previously examined.

WHAT THIS STUDY ADDS

⇒ Our study provides novel insights into the joint association of waist circumference and physical activity with cancer risk. We found that abdominal obesity and insufficient physical activity were distinct risk factors for cancer. Specifically, achieving the WHO guideline for waist circumference showed benefits but failed to nullify the elevated cancer risk associated with insufficient physical activity. Similarly, meeting the WHO guideline for physical activity attenuated but did not eliminate the increased risk of cancer related to abdominal obesity. The most favourable scenario in terms of cancer prevention was observed for individuals who met the guidelines for both abdominal leanness and physical activity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Meeting international guidelines for both waist circumference and physical activity is important for cancer prevention.

INTRODUCTION

Abdominal obesity and physical inactivity have reached epidemic proportions, with over 40% of the global population living with central obesity[1] and nearly 30% not meeting physical activity guidelines.[2] Both abdominal obesity and physical inactivity are modifiable key risk factors for cancer.[3–5] Obesity and physical activity are possibly linked to cancer development through shared biological pathways such as metabolic hormones, insulin sensitivity, endogenous sex steroids and chronic inflammation,[6] as well as genetic factors common to both.[7]

Epidemiological studies have traditionally focused on general obesity, measured by body mass index (BMI) and physical activity in relation to cancer risk. Some of these investigations have shown that high levels of physical activity can mitigate the increased cancer risk associated with elevated BMI,[8–10] whereas other studies have not demonstrated such a counterbalancing physical activity effect.[11–13] Importantly, the reliance on BMI as a primary indicator of obesity in these studies overlooks critical aspects of body composition. Waist circumference may be a more relevant anthropometric indicator of cancer risk than BMI

Check for updates

To cite: Bohmann P, Stein MJ, Amadou A, *et al*. *Br J Sports Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjsports-2024-108708

because abdominal obesity is more strongly associated with fundamental aetiological mechanisms linked to cancer, such as insulin resistance, compared with general obesity.[6]

Despite the purported advantages of using waist circumference as a cancer risk indicator, no study has yet examined the joint associations of abdominal obesity and physical activity with total cancer risk. Specifically, it remains unknown whether individuals with abdominal obesity can reduce their cancer risk by being physically active. Similarly, the question of whether individuals who are physically active have a lower risk of cancer, even when they exhibit abdominal obesity, has not been investigated.

Therefore, our study explores the combined relations of abdominal obesity and physical activity with total cancer risk. We used established WHO guidelines for waist circumference and physical activity to effectively communicate public health recommendations.

METHODS

Study population and data collection

UK Biobank is a prospective cohort that recruited over 500 000 UK participants aged 40–69 years during 2006–2010. The study collected sociodemographic, lifestyle and phenotypic information. Assessments included touchscreen questionnaires, interviews, physical and functional measurements, and biological samples.[14]

Of the 502 356 participants, those underweight (BMI<18.5 kg/m^2, n=2626), with prevalent cancer other than non-melanoma skin cancer (n=36 691), or missing covariate (n=84 416) or exposure (waist circumference and/or self-reported physical activity; n=62 876) data were excluded. Additionally, implausible low waist circumference values were excluded at the 0.1th percentile (n=290), resulting in an analytical sample of 315 457 participants (online supplemental file S1).

During the baseline visit, clinical staff measured waist circumference in centimetres at the smallest part of the trunk, or the belly button, during exhalation.[15] Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) Short Form,[16] capturing weekly frequency and daily duration (minimum 10 min) of walking, moderate and vigorous physical activity during the previous 4 weeks. Following the IPAQ evaluation protocol,[16] metabolic equivalent of task (MET) values from the Ainsworth *et al* compendium[17] for moderate (4.0 METs) and vigorous (8.0 METs) activities were multiplied by their frequency and duration to obtain combined MET-hours per week (MET-hours/week) of physical activity. Additionally, we used physical activity from 7-day accelerometry in a UK Biobank subset (n=72 097).[18] Moderate-to-vigorous physical activity from accelerometry was previously derived using machine learning algorithms, trained on a labelled dataset of 152 individuals who wore an accelerometer and a wearable camera and completed a time-use diary in free-living conditions.[19]

We categorised participants based on WHO thresholds for abdominal obesity (>88 cm for women and >102 cm for men)[20] and sufficient physical activity levels (>10 MET-hours/week; 4 METs multiplied by 150 min and divided by 60 min),[21] resulting in four analysis groups: (1) abdominal leanness and sufficient physical activity (reference), (2) abdominal leanness and insufficient physical activity, (3) abdominal obesity and sufficient physical activity and (4) abdominal obesity and insufficient physical activity.

Cohort follow-up and ascertainment of cancer cases

Participants' vital status was determined through linkage with routine healthcare data and national death registries.[22] Follow-up began at the assessment date and ended at the date of cancer diagnosis, date of complete follow-up (February 2020 for England/Wales, January 2021 for Scotland),[23] loss to follow-up or date of death, whichever occurred first. The endpoint was any type of first primary malignant cancer (other than non-melanoma skin cancer) (online supplemental file S2).

Covariates

We identified potential confounding variables using evidence-derived directed acyclic graphs[24] (online supplemental file S3). We stratified by age at baseline (10-year increments), sex and study centre. Further, we adjusted for self-reported socioeconomic status (Townsend index), diet (healthy diet score, 0–7 scale),[25] sedentary behaviour (hours; sum of daily time spent watching television, using the computer in leisure and driving), measured height (cm) and hand grip strength (kg) (as continuous variables); self-reported education level (college/university degree; higher national diploma, A-level, other professional qualifications; general certificate of secondary education, O-level or none), smoking (never, former and current) and alcohol use (never, former and current) (as categorical variables); registry-obtained diabetes and/or cardiovascular disease (classification in online supplemental file S4), self-reported family history of cancer, and screening for bowel, breast, and prostate cancer (as binary variables). For female-specific cancers, we adjusted for menopausal status, oral contraceptive use, hysterectomy, hormone replacement therapy (as binary variables); age at menarche and number of births (as continuous variables). Covariate data were assessed at baseline, except for diabetes and cardiovascular disease status, which were obtained from registries up until the baseline date.

Statistical analysis

We performed Cox proportional hazards regression, with age as the underlying time metric,[26] to estimate HRs and corresponding 95% CIs for waist circumference and physical activity (in mutually adjusted models), and the combination of waist circumference and physical activity in relation to cancer. We used abdominal leanness and sufficient physical activity (and the combination of both) as the reference group, assuming that it had the lowest risk.[27] We tested for multiplicative interaction between categorised waist circumference and physical activity in relation to cancer using Wald tests. Proportional hazards assumptions were checked using Schoenfeld residuals and visual inspection.

We conducted the following sensitivity analyses to test the robustness of our results. We addressed reverse causation by excluding participants who developed cancer within the first 2 or 5 follow-up years. We assessed associations based on accelerometer-derived physical activity to confirm the validity of our results. We multiplied the weekly proportion of time spent in moderate-to-vigorous physical activity with 10 080 min (resulting from 7 days×24 hours×60 min) to assess the accelerometer-derived threshold of 150 min of moderate-to-vigorous physical activity. We assessed potential sex differences by stratifying the analysis by sex, examined potential smoking-related residual confounding by restricting the analysis to never-smokers and considered alcohol use intensity (grams per day) in place of its respective status variable. In an additional sensitivity analysis, we focused on obesity-related[28] and physical inactivity-related[29] cancers, including oesophageal (adenocarcinoma;

International Classification of Diseases, 10th Revision (ICD-10): C15; histology: 8140–8145, 8210–8260, 8323), colon (C18), liver (C22), breast (postmenopausal; C50) and endometrial (C54.1) cancers. We also verified the stability of our results by assessing mean values and SD across sex-standardised and age-standardised tertiles of waist circumference and physical activity and examined their relations to cancer risk. Furthermore, we assessed the association between continuous physical activity, stratified by abdominal obesity and cancer risk, as well as the association between continuous waist circumference, stratified by physical activity recommendations and cancer risk. To assess the influence of missing values, we conducted multiple imputation using chained equations (10 datasets with 5 iterations each).[30] Furthermore, we estimated the proportion of UK Biobank cancers potentially preventable if all participants avoided abdominal obesity and were physically active (population attributable fraction, PAF), assuming these factors are causally related to cancer. PAFs were estimated using Levin's formula.[31]

Cox regression was conducted using the rms package.[32] All data processing and statistical analyses were performed using R V.4.2.3.[33] All p values were based on two-sided tests with a 0.05 significance level.

Patient and public involvement

Patients or the public were not involved in the conceptualisation, analysis or interpretation of this study.

Equity, diversity and inclusion statement

The author list includes both early-career researchers and senior scientists, with more women than men on the team. The study population varied in terms of age, gender and demographics. However, ethnic groups other than predominantly white and marginalised communities are under-represented.

RESULTS

Our analytical cohort comprised 315 457 individuals (48.1% women) aged 56.1±8.2 years at baseline. We inspected waist circumference and physical activity according to participant characteristics to assess the potential for confounding (table 1). The group defined by abdominal leanness and a sufficient activity level exhibited a healthier lifestyle, marked by better dietary habits and lower rates of sedentary behaviour and smoking, compared with the group with abdominal obesity and insufficient physical activity. Group-specific average values for waist circumference and physical activity are provided in online supplemental file S5.

During 10.9 years of follow-up (3 321 486 person-years), 29 710 participants developed any type of primary malignant cancer. Compared with the reference group of participants without abdominal obesity (defined as those with a waist circumference <88 cm for women and <102 cm for men), those with abdominal obesity had an increased risk of total cancer (HR 1.11, 95% CI 1.09 to 1.14). Similarly, insufficient (defined as

Table 1 Characteristics of UK Biobank participants at baseline between 2006 and 2010 (n=315 457)

Characteristic	Abdominal leanness		Abdominal obesity	
	Sufficient physical activity n=147 502	Insufficient physical activity n=78 310	Sufficient physical activity n=46 580	Insufficient physical activity n=43 065
Sex				
Women	67 952 (46%)	37 124 (47%)	24 384 (52%)	22 208 (52%)
Men	79 550 (54%)	41 186 (53%)	22 196 (48%)	20 857 (48%)
Age (years)	55.7 (8.4)	55.4 (8.0)	57.5 (7.9)	56.7 (7.7)
Physical activity (MET-hours/week)	43.0 (35.8)	3.3 (3.1)	40.3 (34.6)	2.7 (3.0)
Waist circumference (cm)	84.6 (9.6)	85.6 (9.7)	103.6 (9.9)	105.4 (10.9)
Maximum grip strength (kg)	35.0 (11.3)	33.8 (11.2)	33.5 (11.7)	32.7 (11.6)
Townsend index of deprivation	−1.6 (2.9)	−1.6 (3.0)	−1.2 (3.1)	−1.1 (3.1)
Education				
College or university	56 914 (39%)	32 335 (41%)	13 167 (28%)	13 351 (31%)
A/AS, NVQ/HND/HNC or equivalent, other professional qualification	34 252 (23%)	17 968 (23%)	11 630 (25%)	10 384 (24%)
O/GCSE, CSE or equivalent	37 908 (26%)	19 508 (25%)	13 067 (28%)	11 971 (28%)
None of the above	18 428 (12%)	8499 (11%)	8716 (19%)	7359 (17%)
Sedentary behaviour (hours/day)	4.2 (2.4)	4.4 (2.6)	5.0 (2.6)	5.3 (2.8)
Healthy diet score	3.8 (1.4)	3.4 (1.4)	3.6 (1.3)	3.3 (1.4)
Smoking status				
Never	84 487 (57%)	45 253 (58%)	23 383 (50%)	21 470 (50%)
Former	49 630 (34%)	24 339 (31%)	19 058 (41%)	16 903 (39%)
Current	13 385 (9.1%)	8718 (11%)	4139 (8.9%)	4692 (11%)
Alcohol drinking status				
Never	4499 (3.1%)	2874 (3.7%)	1997 (4.3%)	2093 (4.9%)
Former	3998 (2.7%)	2388 (3.0%)	1718 (3.7%)	1835 (4.3%)
Current	139 005 (94%)	73 048 (93%)	42 865 (92%)	39 137 (91%)
Prevalent cardiometabolic disease				
No	136 148 (92%)	71 161 (91%)	38 781 (83%)	34 582 (80%)
Yes	11 354 (7.7%)	7149 (9.1%)	7799 (17%)	8483 (20%)

A, advanced; AS, advanced subsidiary; CSE, certificate of secondary education; GCSE, general certificate of education; HND, higher national diploma; HNE, higher national education; MET-hours/week, metabolic equivalent of task hours per week; NVQ, national vocational qualification; O, ordinary levels.

Table 2 HRs and 95% CIs of total cancer according to WHO guidelines on waist circumference and physical activity

Group	HR (95% CI) for crude model	HR (95% CI) for full model	Events/person-years
Abdominal leanness			
Sufficient physical activity	1.0	1.0	12 950/1 559 862.3
Insufficient physical activity	1.06 (1.03 to 1.09)	1.04 (1.01 to 1.07)	7098/829 190.2
Abdominal obesity			
Sufficient physical activity	1.16 (1.12 to 1.20)	1.11 (1.08 to 1.15)	4983/484 818.0
Insufficient physical activity	1.22 (1.18 to 1.26)	1.15 (1.11 to 1.19)	4679/447 615.2

The crude model is adjusted for age, sex and study centre. The full model is adjusted for age, sex, study centre, standing height, grip strength, cardiometabolic diseases, ethnicity, education, alcohol status, smoking status, Townsend index, healthy diet score, sedentary behaviour, cancer screening (bowel, breast and prostate), family history of cancer, hormone replace therapy and oral contraceptive medication intake, menopausal status, age menarche, number of births given and age hysterectomy.

<10 MET-hours/week) versus sufficient physical activity was associated with an increased cancer risk (HR 1.05, 95% CI 1.02 to 1.07).

The joint associations of abdominal obesity and insufficient physical activity with total cancer risk are shown in table 2. Cancer risk was higher for individuals with abdominal obesity, regardless of their physical activity levels, with HRs of 1.11 (95% CI 1.08 to 1.15) for sufficiently physically active and 1.15 (95% CI 1.11 to 1.19) for insufficiently physically active individuals, compared with those who were abdominally lean and sufficiently active. Furthermore, cancer risk for abdominally lean individuals with insufficient physical activity, compared with their sufficiently active counterparts, was also slightly increased, with an HR of 1.04 (95% CI 1.01 to 1.07).

Results comparing abdominally obese and insufficiently physically active individuals to their lean and sufficiently active counterparts remained consistent in sensitivity analyses. These included analyses that excluded the first 2 years of follow-up (HR 1.16, 95% CI 1.12 to 1.21), and the first 5 years of follow-up (HR 1.20, 95% CI 1.14 to 1.25); analyses that used accelerometry-based data for physical activity instead of questionnaire data (HR 1.22, 95% CI 1.10 to 1.36); analyses limited to never-smokers (HR 1.18, 95% CI 1.12 to 1.25) (figure 1); analyses using alcohol use intensity (HR 1.13, 95% CI 1.08 to 1.17) (online supplemental file S6); and sex-stratified analyses (women: HR 1.25, 95% CI 1.18 to 1.32; men: HR 1.08, 95% CI 1.03 to 1.13) (online supplemental file S7). We found no multiplicative interaction between waist circumference and physical activity associated with the risk of cancer (p for interaction=0.80).

To verify the robustness of our results using different cut points, we also classified individuals according to age-standardised and sex-standardised tertiles of waist circumference and physical activity (average values given in online supplemental file S8). Compared with those with a low waist circumference and high levels of physical activity, total cancer risk was 1.03 (95% CI 0.98 to 1.08) for individuals with both low waist circumference and low levels of physical activity, 1.13 (95% CI 1.07 to 1.19) for participants with high waist circumference and high levels of physical activity, and 1.18 (95% CI 1.12 to 1.23) for those with high waist circumference and low levels of physical activity (online supplemental file S9). Additionally, physical activity showed a linear inverse dose-response association with cancer risk among abdominally lean individuals, which was slightly attenuated for individuals with abdominal obesity. Waist circumference was linearly positively associated with cancer risk, irrespective of physical activity levels (online supplemental file S10).

We investigated total cancer risk with imputed covariate data, and the results remained consistent (online supplemental file S11).

When focusing on obesity-related and physical inactivity-related cancers, results were more pronounced. Compared with abdominally lean and sufficiently physically active individuals, HRs were 1.38 (95% CI 1.30 to 1.47) for abdominally obese and sufficiently active and 1.48 (95% CI 1.39 to 1.58) for abdominally obese and insufficiently active individuals (table 3).

In the UK Biobank, 13.7% of participants were both abdominally obese and insufficiently physically active. We estimated that the presence of abdominal obesity coupled with insufficient physical activity accounted for 2.0% (1.5%–2.5%) of total

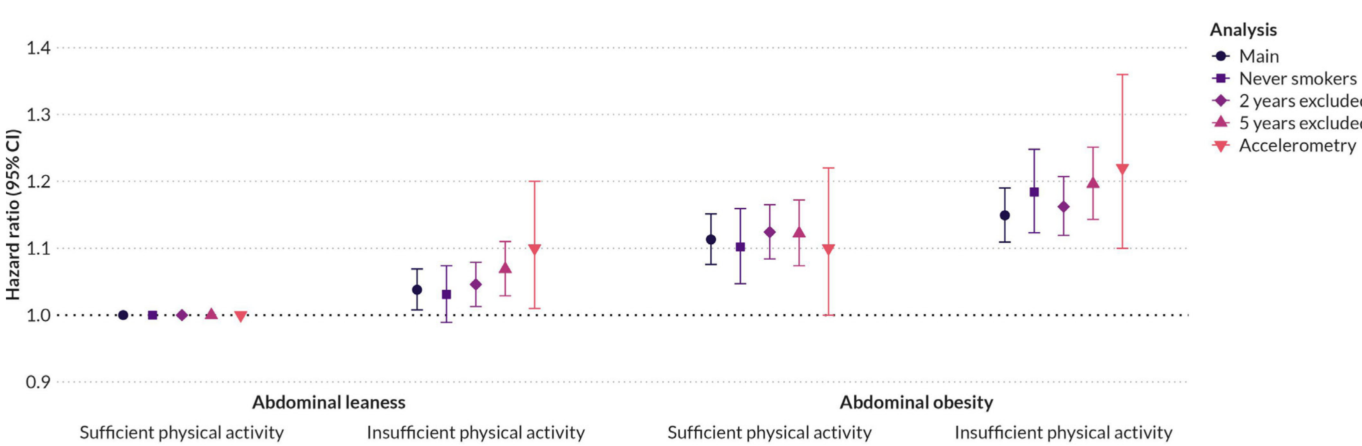

Figure 1 HRs and 95% CIs of total cancer according to WHO guidelines on waist circumference and physical activity across several analyses: main analysis, analysis limited to never smokers, analysis excluding the initial 2 years of follow-up, analysis excluding the initial 5 years of follow-up and analysis based on accelerometer-based physical activity.

Table 3 HRs and 95% CIs of obesity-related and physical inactivity-related cancer according to WHO guidelines on waist circumference and physical activity

Group	HR (95% CI) for crude model	HR (95% CI) for full model	Events/person-years
Abdominal leanness			
Sufficient physical activity	1.0	1.0	3017/1 600 895.0
Insufficient physical activity	1.11 (1.04 to 1.17)	1.08 (1.01 to 1.14)	1721/850 545.9
Abdominal obesity			
Sufficient physical activity	1.44 (1.35 to 1.53)	1.38 (1.30 to 1.47)	1611/497 760.9
Insufficient physical activity	1.59 (1.49 to 1.69)	1.48 (1.39 to 1.58)	1532/459 348.1

The crude model is adjusted for age, sex and study centre. The full model is adjusted for age, sex, study centre, standing height, grip strength, cardiometabolic diseases, ethnicity, education, alcohol status, smoking status, Townsend index, healthy diet score, sedentary behaviour, cancer screening (bowel, breast and prostate), family history of cancer, hormone replace therapy and oral contraceptive medication intake, menopausal status, age menarche, number of births given and age hysterectomy.

cancer and 6.1% (5.0%–7.3%) of obesity-related and physical inactivity-related cancers (online supplemental file S12).

DISCUSSION

To the best of our knowledge, this study is the first to examine the joint relations of abdominal obesity and insufficient physical activity to risk of cancer. We found that not meeting the WHO guideline on waist circumference was associated with an 11% increased risk of cancer, while non-adherence to the WHO guideline for physical activity was related to a 5% increased cancer risk. Notably, being sufficiently physically active according to the WHO guideline did not eliminate the heightened risk of cancer associated with abdominal obesity, nor did a waist circumference below the WHO thresholds fully offset the elevated cancer risk related to insufficient physical activity, though it did attenuate the association. Combined non-adherence to both guidelines led to a 15% elevated cancer risk. We estimated that such non-adherence could account for 2% of total cancer cases. Our findings underscore the importance of meeting WHO guidelines for both waist circumference and physical activity to mitigate cancer risk.

Previous research indicates that not meeting the international guidelines on waist circumference is linked to an increased overall cancer risk. Specifically, men with abdominal obesity, defined by the WHO as a waist circumference above 102 cm, had a 22% greater total cancer risk compared with those without abdominal obesity. Similarly, women exceeding 88 cm for waist circumference demonstrated a 17% elevated risk of cancer.[3] Beyond abdominal obesity, general obesity, defined by BMI, is also associated with an increased total cancer risk.[34]

Epidemiological studies have reported that following international physical activity guidelines is associated with decreased cancer risk.[6 35] Specifically, a meta-analysis indicated a 7% reduction in overall cancer risk for individuals who met the WHO guideline of >10 MET-hours/week, compared with those who did not meet the guideline.[36] Additionally, a large pooled study that defined the recommended level of physical activity as 7.5–15 MET-hours/week found that this level of physical activity was associated with a lower risk of 7 out of 15 investigated cancer types (breast, endometrial, kidney, myeloma, liver, non-Hodgkin's lymphoma (women only), colon (men only)).[37]

No study has examined the joint association of waist circumference and physical activity on total cancer. However, previous investigations of individual cancer sites have consistently shown that individuals with the combination of elevated anthropometric measures (primarily measured using BMI) and low physical activity exhibit the highest cancer risk.[9 12] This association was observed, for example, in pancreatic cancer where individuals with a BMI>30 kg/m^2 and low levels of physical activity (categorised in tertiles) had a higher risk compared with those with a BMI<25 kg/m^2 and high physical activity.[9] Similarly, physically inactive (<15 MET-hours/week) and overweight women (BMI>25 kg/m^2) had a higher risk of developing endometrial cancer compared with active (>15MET-hours/week), normal-weight (BMI<25 kg/m^2) women.[12] Conversely, those with a healthy weight who engage in high levels of physical activity show the greatest cancer risk reduction.[8] Moreover, in research examining different types of cancer, no interactive relation between physical activity and obesity was identified.[8 13]

Plausible biological pathways that link excess body fat and physical inactivity to cancer include insulin resistance, metabolic hormones, chronic inflammation and increased levels of circulating sex hormones, factors exacerbated by obesity but potentially mitigated by physical activity.[6 38] For instance, the link between insulin resistance and obesity, particularly abdominal fat, is well established.[6] Moreover, various types of physical activity have been shown to reduce body weight[39] and waist circumference,[40] as well as enhance insulin sensitivity.[39 40] Other potential pathways, such as DNA methylation, telomere length, oxidative stress, immune function and the gut microbiome, may not require the simultaneous presence of both obesity and insufficient physical activity. For example, alterations in DNA methylation or telomere length induced by physical activity can influence cancer risk without the concurrent loss of abdominal fat.[38]

Research and policy implications

Our study echoes critical public health messages and aligns with previous research on diverse health outcomes.[41–44] Maintaining a healthy weight throughout life and engaging in regular physical activity are pivotal in reducing cancer risk.[21 45 46] Our findings underscore the importance of adhering to guidelines regarding both waist circumference and physical activity to minimise the risk of developing cancer. In circumstances where adherence to both guidelines proves impractical, following the guidelines for abdominal obesity may be superior. Enabling individuals to achieve WHO guidelines for waist circumference and physical activity requires not only individual lifestyle changes but also systemic changes at political and societal levels. Policy interventions targeting the obesogenic environment should encompass multiple domains, including the food industry and urban planning, to promote access to healthy dietary choices and opportunities for physical activity. Public awareness campaigns on healthy lifestyles should be integrated into educational institutions.[45]

Strengths and limitations

To the best of our knowledge, no epidemiological study has previously examined waist circumference and physical activity simultaneously in relation to total cancer. An asset of our study is our utilisation of objective data on waist circumference and physical activity, which minimised measurement errors. Also, using waist circumference as a measure of abdominal obesity circumvented possible limitations of BMI since physical activity can decrease waist circumference without causing weight loss, a change not captured by BMI.[47] An additional advantage of our study is its long follow-up period, which led to large numbers of cases and enabled several sub-analyses. For example, we investigated the potential for reverse causation by excluding the first 2 and 5 years of follow-up.

However, relying solely on baseline exposure data limits the analysis by not accounting for temporal changes in anthropometric measures and physical activity levels. Also, our study's reliance on European participants somewhat limits its generalisability, further compounded by the UK Biobank's low response rate and potential susceptibility to selection bias, which may be reflected in the relatively high levels of physical activity observed.[48]

CONCLUSION

In summary, our analysis suggests distinct relations of waist circumference and physical inactivity to cancer. Notably, a high waist circumference was linked to increased cancer risk, and physical activity failed to nullify the heightened cancer risk associated with abdominal obesity. Likewise, insufficient physical activity was associated with enhanced cancer risk, even among those without abdominal obesity, though the risk was less pronounced. The group with the lowest cancer risk consisted of individuals who were both abdominally lean and sufficiently physically active. Our findings underscore the critical importance of adhering to both public health recommendations—maintaining a lean waistline and engaging in regular physical activity—as essential strategies for reducing cancer risk.

Author affiliations
[1]Department of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany
[2]Department of Prevention Cancer Environment, Centre Léon Bérard, Lyon, France
[3]Radiation: Defense, Health, Environment, INSERM Unit U1296, Lyon, France
[4]Nutrition and Metabolism Branch, International Agency for Research on Cancer, Lyon, France
[5]Department of Cancer Epidemiology and Prevention Research, Alberta Health Services, Calgary, Alberta, Canada
[6]Departments of Oncology and Community Health Sciences, University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada
[7]Department of Clinical Sciences, University of Barcelona Faculty of Medicine and Health Sciences, Barcelona, Spain
[8]Center for Translational Oncology, University Hospital Regensburg, Regensburg, Germany
[9]Bavarian Cancer Research Center (BZKF), Regensburg, Germany

Correction notice This article has been corrected since it published Online First. Affiliations 1 and 3 have been corrected.

X Michael J Stein @MichaelJStein

Acknowledgements UK Biobank is an open-access resource. Bona fide researchers can apply to use the UK Biobank dataset by registering and applying at http://ukbiobank.ac.uk/register-apply/. This research has been conducted using the UK Biobank Resource under Application Number 55870. We are grateful to the participants and those involved in building the resource. This work uses data provided by patients and collected by the NHS as part of their care and support, therefore, for the data linkage we want to acknowledge NHS England (Copyright (2023), NHS England. Reused with the permission of the NHS England (and/or UK Biobank). All rights reserved). This research used data assets made available by National Safe Haven as part of the Data and Connectivity National Core Study, led by Health Data Research UK in partnership with the Office for National Statistics and funded by UK Research and Innovation (research which commenced between 1 October 2020 and 31 March 2021 grant ref MC_PC_20029; 1 April 2021–30 September 2022 grant ref MC_PC_20058).

Contributors PB and MJS contributed equally to this paper, had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Study design: PB, MJS; Acquisition, analysis or interpretation of the data: PB, MJS, AW, HB, AMS, MFL, JK, HF, CF, BF, EF, LP-N, AA; Manuscript writing: PB, MJS and MFL; Critical revision of the manuscript for important intellectual content: AW, AMS, HB, JK, MFL, HF, CF, BF and AA. PB and MJS are the study guarantors. AMS and AW shared last authorship.

Funding Funding for IIG_FULL_2021_027 was obtained from World Cancer Research Fund (WCRF UK), as part of the World Cancer Research Fund International grant programme. This study was supported by the French National Cancer Institute (l'Institut National du Cancer, INCA_16824), the German Research Foundation (BA 5459/2-1). The UK Biobank was supported by the Wellcome Trust, Medical Research Council, Department of Health, Scottish government and Northwest Regional Development Agency. It has also had funding from the Welsh Assembly government and British Heart Foundation. The research was designed, conducted, analysed, and interpreted by the authors entirely independently of these funding sources. The funder had no role in study design, data acquisition and analysis, decision to publish, or preparation of the manuscript.

Disclaimer Where authors are identified as personnel of the International Agency for Research on Cancer/WHO, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/WHO.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and UK Biobank has approval from the North West Multi-centre Research Ethics Committee (MREC) as a Research Tissue Bank (RTB) approval. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The data that support the findings of this study are available from the UK Biobank but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Researchers will need to apply to access the UK Biobank database at the following link: https://www.ukbiobank.ac.uk/enable-your-research/apply-for-access.

ORCID iDs
Patricia Bohmann http://orcid.org/0000-0002-0931-8651
Michael J Stein http://orcid.org/0000-0002-1120-1751

REFERENCES

1 Wong MCS, Huang J, Wang J, *et al*. Global, regional and time-trend prevalence of central obesity: a systematic review and meta-analysis of 13.2 million subjects. *Eur J Epidemiol* 2020;35:673–83.
2 Guthold R, Stevens GA, Riley LM, *et al*. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1·9 million participants. *Lancet Glob Health* 2018;6:e1077–86.
3 Barberio AM, Alareeki A, Viner B, *et al*. Central body fatness is a stronger predictor of cancer risk than overall body size. *Nat Commun* 2019;10:383.
4 Recalde M, Davila-Batista V, Díaz Y, *et al*. Body mass index and waist circumference in relation to the risk of 26 types of cancer: a prospective cohort study of 3.5 million adults in Spain. *BMC Med* 2021;19:10.
5 Moore SC, Lee I-M, Weiderpass E, *et al*. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. *JAMA Intern Med* 2016;176:816–25.

6 Friedenreich CM, Ryder-Burbidge C, McNeil J. Physical activity, obesity and sedentary behavior in cancer etiology: epidemiologic evidence and biologic mechanisms. *Mol Oncol* 2021;15:790–800.
7 Schnurr TM, Stallknecht BM, Sørensen TIA, *et al*. Evidence for shared genetics between physical activity, sedentary behaviour and adiposity-related traits. *Obes Rev* 2021;22:e13182.
8 Sun M, Bjørge T, Teleka S, *et al*. Interaction of leisure-time physical activity with body mass index on the risk of obesity-related cancers: A pooled study. *Int J Cancer* 2022;151:859–68.
9 Michaud DS, Giovannucci E, Willett WC, *et al*. Physical activity, obesity, height, and the risk of pancreatic cancer. *JAMA* 2001;286:921–9.
10 Patel AV, Feigelson HS, Talbot JT, *et al*. The role of body weight in the relationship between physical activity and endometrial cancer: results from a large cohort of US women. *Int J Cancer* 2008;123:1877–82.
11 Maliniak ML, Gapstur SM, McCullough LE, *et al*. Joint associations of physical activity and body mass index with the risk of established excess body fatness-related cancers among postmenopausal women. *Cancer Causes Control* 2021;32:127–38.
12 Conroy MB, Sattelmair JR, Cook NR, *et al*. Physical activity, adiposity, and risk of endometrial cancer. *Cancer Causes Control* 2009;20:1107–15.
13 Nunez C, Clausen J, Jensen MT, *et al*. Main and interactive effects of physical activity, fitness and body mass in the prevention of cancer from the Copenhagen Male Study. *Sci Rep* 2018;8:11780.
14 Sudlow C, Gallacher J, Allen N, *et al*. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;12:e1001779.
15 UK Biobank. Anthropometric measurements at ukb assessment centres. 2023. Available: https://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=146620 [Accessed 18 Oct 2023].
16 IPAQ Research Committee. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) - Short and Long Forms, 2023. Available: https://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=540 [Accessed 18 Oct 2023].
17 Ainsworth BE, Haskell WL, Herrmann SD, *et al*. 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc* 2011;43:1575–81.
18 Doherty A, Jackson D, Hammerla N, *et al*. Large Scale Population Assessment of Physical Activity Using Wrist Worn Accelerometers: The UK Biobank Study. *PLoS ONE* 2017;12:e0169649.
19 Walmsley R, Chan S, Smith-Byrne K, *et al*. Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease. *Br J Sports Med* 2022;56:1008–17.
20 World Health Organization. Waist circumference and waist-hip ratio: report of a who expert consultation. Geneva, 2011. Available: https://iris.who.int/handle/10665/44583 [accessed 05 Jan 2024]
21 Bull FC, Al-Ansari SS, Biddle S, *et al*. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020;54:1451–62.
22 Trehearne A. Genetics, lifestyle and environment. UK Biobank is an open access resource following the lives of 500,000 participants to improve the health of future generations. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2016;59:361–7.
23 UK Biobank. Data providers and dates of data availability, Available: https://biobank.ndph.ox.ac.uk/showcase/exinfo.cgi?src=Data_providers_and_dates [Accessed 19 Oct 2023].
24 VanderWeele TJ. Principles of confounder selection. *Eur J Epidemiol* 2019;34:211–9.
25 Lourida I, Hannon E, Littlejohns TJ, *et al*. Association of Lifestyle and Genetic Risk With Incidence of Dementia. *JAMA* 2019;322:430–7.
26 Harrell FE. Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. Springer International Publishing, 2015.
27 Knol MJ, VanderWeele TJ, Groenwold RHH, *et al*. Estimating measures of interaction on an additive scale for preventive exposures. *Eur J Epidemiol* 2011;26:433–8.
28 World Cancer Research Fund/American Institute for Cancer Research. Continuous update project. espert report 2018. body fatnes and weight gain and the risk of cancer. Available: https://www.wcrf.org/research-policy/global-cancer-update-programme/
29 World Cancer Research Fund/American Institute for Cancer Research. Continuous update project expert report 2018. physical activity and the risk of cancer. Available: https://www.wcrf.org/research-policy/global-cancer-update-programme/
30 van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw* 2011;45:1–67.
31 Lin CK, Chen ST. Estimation and application of population attributable fraction in ecological studies. *Env Health* 2019;18:52.
32 Harrell FE. Rms: regression modeling strategies. 2022. Available: https://cran.r-project.org/web/packages/rms/index.html [Accessed 29 Sep 2023].
33 R Core Team. R: a language and environment for statistical computing. 2022. Available: https://www.r-project.org/ [Accessed 29 Sep 2023].
34 Pan SY, Johnson KC, Ugnat A-M, *et al*. Association of obesity and cancer risk in Canada. *Am J Epidemiol* 2004;159:259–68.
35 McTiernan A, Friedenreich CM, Katzmarzyk PT, *et al*. Physical Activity in Cancer Prevention and Survival: A Systematic Review. *Med Sci Sports Exerc* 2019;51:1252–61.
36 Liu L, Shi Y, Li T, *et al*. Leisure time physical activity and cancer risk: evaluation of the WHO's recommendation based on 126 high-quality epidemiological studies. *Br J Sports Med* 2016;50:372–8.
37 Matthews CE, Moore SC, Arem H, *et al*. Amount and Intensity of Leisure-Time Physical Activity and Lower Cancer Risk. *J Clin Oncol* 2020;38:686–97.
38 Neilson HK, Conroy SM, Friedenreich CM. The Influence of Energetic Factors on Biomarkers of Postmenopausal Breast Cancer Risk. *Curr Nutr Rep* 2014;3:22–34.
39 Jelleyman C, Yates T, O'Donovan G, *et al*. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obes Rev* 2015;16:942–61.
40 Armstrong A, Jungbluth Rodriguez K, Sabag A, *et al*. Effect of aerobic exercise on waist circumference in adults with overweight or obesity: A systematic review and meta-analysis. *Obes Rev* 2022;23:e13446.
41 Tarp J, Fagerland MW, Dalene KE, *et al*. Device-measured physical activity, adiposity and mortality: a harmonised meta-analysis of eight prospective cohort studies. *Br J Sports Med* 2022;56:725–32.
42 Sanchez-Lastra MA, Ding D, Dalene K-E, *et al*. Physical Activity and Mortality Across Levels of Adiposity: A Prospective Cohort Study From the UK Biobank. *Mayo Clin Proc* 2021;96:105–19.
43 Pharr JR, Coughenour CA, Bungum TJ. An assessment of the relationship of physical activity, obesity, and chronic diseases/conditions between active/obese and sedentary/normal weight American women in a national sample. *Public Health (Fairfax)* 2018;156:117–23.
44 Loprinzi P, Smit E, Lee H, *et al*. The "fit but fat" paradigm addressed using accelerometer-determined physical activity data. *N Am J Med Sci* 2014;6:295–301.
45 WCRF/IARC. Diet, nutrition, physical activity and cancer: a global perspective. continuous update project expert report. 2018.
46 Recalde M, Pistillo A, Davila-Batista V, *et al*. Longitudinal body mass index and cancer risk: a cohort study of 2.6 million Catalan adults. *Nat Commun* 2023;14:3816.
47 Giovannucci E. A framework to understand diet, physical activity, body weight, and cancer risk. *Cancer Causes Control* 2018;29:1–6.
48 Fry A, Littlejohns TJ, Sudlow C, *et al*. Comparison of Sociodemographic and Health-Related Characteristics of UK Biobank Participants With Those of the General Population. *Am J Epidemiol* 2017;186:1026–34.