Anthropometric Measures, Body Mass Index, and Pancreatic Cancer

A Pooled Analysis From the Pancreatic Cancer Cohort Consortium (PanScan)

Alan A. Arslan, MD; Kathy J. Helzlsouer, MD, MHS; Charles Kooperberg, PhD; Xiao-Ou Shu, MD, PhD; Emily Steplowski, BS; H. Bas Bueno-de-Mesquita, MD, PhD, MPH; Charles S. Fuchs, MD, MPH; Myron D. Gross, PhD; Eric J. Jacobs, PhD; Andrea Z. LaCroix, PhD; Gloria M. Petersen, PhD; Rachael Z. Stolzenberg-Solomon, PhD, MPH; Wei Zheng, MD, PhD; Demetrius Albanes, MD; Laufey Amundadottir, PhD; William R. Bamlet, MS; Aurelio Barricarte, MD, PhD; Sheila A. Bingham, PhD†; Heiner Boeing, PhD, MSPH; Marie-Christine Boutron-Ruault, MD, PhD; Julie E. Buring, ScD; Stephen J. Chanock, MD; Sandra Clipp, MPH, MA; J. Michael Gaziano, MD, MPH; Edward L. Giovannucci, MD, ScD; Susan E. Hankinson, ScD; Patricia Hartge, ScD, MA; Robert N. Hoover, MD, ScD; David J. Hunter, ScD; Amy Hutchinson, MS; Kevin B. Jacobs, PhD; Peter Kraft, PhD; Shannon M. Lynch, MPH; Jonas Manjer, MD, PhD; JoAnn E. Manson, MD, DrPH; Anne McTiernan, MD, PhD; Robert R. McWilliams, MD; Julie B. Mendelsohn, JD, MPH; Dominique S. Michaud, ScD; Domenico Palli, MD; Thomas E. Rohan, MD, PhD; Nadia Slimani, MSc, PhD; Gilles Thomas, MD, PhD; Anne Tjønneland, PhD, DMSc; Geoffrey S. Tobias, BS; Dimitrios Trichopoulos, MD, PhD; Jarmo Virtamo, MD, PhD; Brian M. Wolpin, MD, MPH; Kai Yu, PhD; Anne Zeleniuch-Jacquotte, MD, MS; Alpa V. Patel, PhD

Background: Obesity has been proposed as a risk factor for pancreatic cancer.

Methods: Pooled data were analyzed from the National Cancer Institute Pancreatic Cancer Cohort Consortium (PanScan) to study the association between prediagnostic anthropometric measures and risk of pancreatic cancer. PanScan applied a nested case-control study design and included 2170 cases and 2209 control subjects. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using unconditional logistic regression for cohort-specific quartiles of body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]), weight, height, waist circumference, and waist to hip ratio as well as conventional BMI categories (underweight, <18.5; normal weight, 18.5-24.9; overweight, 25.0-29.9; obese, 30.0-34.9; and severely obese, ≥35.0). Models were adjusted for potential confounders.

Results: In all of the participants, a positive association between increasing BMI and risk of pancreatic cancer was observed (adjusted OR for the highest vs lowest BMI quartile, 1.33; 95% CI, 1.12-1.58; $P_{trend} < .001$). In men, the adjusted OR for pancreatic cancer for the highest vs lowest quartile of BMI was 1.33 (95% CI, 1.04-1.69; $P_{trend} < .03$), and in women it was 1.34 (95% CI, 1.05-1.70; $P_{trend} = .01$). Increased waist to hip ratio was associated with increased risk of pancreatic cancer in women (adjusted OR for the highest vs lowest quartile, 1.87; 95% CI, 1.31-2.69; $P_{trend} = .003$) but less so in men.

Conclusions: These findings provide strong support for a positive association between BMI and pancreatic cancer risk. In addition, centralized fat distribution may increase pancreatic cancer risk, especially in women.

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Pancreatic adenocarcinoma is the fourth leading cause of cancer death in the United States[1] and is responsible for about 227 000 deaths per year worldwide.[2] Because of the lack of effective screening tests for pancreatic cancer, it is often diagnosed at an advanced stage, contributing to a 5-year survival rate that is less than 5%.[3] The incidence of pancreatic cancer is higher in men than in women, and in the United States, it is higher in blacks than in whites.[3] Smoking, diabetes mellitus, and a family history of pancreatic cancer are known risk factors,[4,5] but these factors do not account for all the cases of pancreatic cancer.

Obesity and high body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) have been proposed as additional risk factors for pancreatic cancer. Prospective studies have yielded conflicting results concerning the association between BMI and risk of pancreatic cancer. Most prospective epidemiological studies[6-15] have found that a high BMI and a lack of physical activity are associated with an increased risk of pancreatic cancer incidence or mortality, independent of a history of diabetes mellitus. However, several prospective studies have not confirmed a significant role of BMI in pancreatic cancer[16-23] or have found that effect of BMI varied according to smoking status[24,25] or sex.[26-28]

Author Affiliations are listed at the end of this article.
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Table 1. Characteristics of the 13 Cohorts Included in the PanScan Pooled Analysis

Cohort	Center	Location	Enrollment Years[a]	Follow-up, Mean, y	Race, %[b]	Age Range, y	Available Anthropometric Data	Cases/ Controls, No. (n=2170/2209)	Matching
Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study[29]	National Cancer Institute, National Institute for Health and Welfare	Finland	1985-1988	11.8	100 White	57-85	BMI	210/211	Race, age at randomization (1-5 y), month, year of baseline blood collection (+30 d)
CLUE II[30]	Johns Hopkins Bloomberg School of Public Health	US	1989	8.3	100 White	42-94	BMI	83/83	Race, sex, age
Cancer Prevention Study II[31]	American Cancer Society	US	1992-1993	10.0	97.6 White, 1.2 black, 0.6 Asian, 0.6 other	64-90	BMI	165/165	Race, self-reported ethnicity, sex, date of birth (±6 mo), DNA source (blood or buccal), DNA sample provided during the same season and year
European Prospective Investigation Into Cancer and Nutrition (EPIC)[32]	International Agency for Research on Cancer and Imperial College London	Europe	1992-2000 (varied by center)	6.8	100 White	37-84	BMI[c], WHR[d]	440/459	Sex, center, age at recruitment (±1 mo), date of blood donation (±1 mo), time of blood collection (±1 h), hours between blood collection and last food or drinks (<3, 3-6, >6)
Health Professionals Follow-up Study[33]	Harvard University	US	1986	12.7	100 White	55-87	BMI, WHR	55/55	Race, sex, year of birth (±5 y), smoking status (never/former/current), fasting status, month and hour of blood collection
Mayo Clinic study[34]	Mayo Clinic	US	2000-2006	0	99.3 White, 0.5 black, 0.3 Asian	39-86	BMI	400/400	Clinic-based controls, frequency matched to cases on age, race, sex, and residence
New York University Women's Health Study[35]	New York University	US	1985-1991	11.6	76.7 White, 7.7 other, 15.4 missing	48-82	BMI, WHR	13/13	Age at enrollment (±6 mo), date of enrollment (±3 mo), menopausal status at enrollment, race/ethnicity
Nurses' Health Study[36]	Harvard University	US	1976-2003	21.6	85.2 White, 1.1 other, 13.6 missing	47-80	BMI, WHR	88/88	Race, sex, year of birth (±5 y), smoking status (never/former/current), fasting status, month and hour of blood collection
Physicians' Health Study[37]	Brigham and Women's Hospital	US	1982-1983	13.6	61.2 White, 1.6 black, 37.1 missing	49-88	BMI	62/62	Race, year of birth (±5 y), smoking status (never/former/current) fasting status, month and hour of blood collection
Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial[38]	National Cancer Institute	US	1993-2001	6.2	90.9 White, 4.7 Asian, 3.2 black, 1.2 other	56-84	BMI	253/271	Race, sex, ethnicity, center, frequency samples by calendar year of birth (5-y blocks), broad categories of race, source of DNA (blood or buccal), study arm; for the intervention arm, additionally stratified sample by age
Shanghai Men's and Women's Health Studies[39,40]	Vanderbilt University	China	1996 (F) 2001 (M)	3.6	100 Asian	43-77	BMI, WHR	78/79	Race, ethnicity, sex, year of birth (<2 y), menopausal status at baseline, date of sample collection (<30 d), time of sample collection (AM/PM), time after the last meal (<2 h)
Women's Health Initiative[41]	Women's Health Initiative Clinical Centers	US	1992-1998	3.8	85.5 White, 7.4 black, 4.2 Asian, 1.8 other, 1.0 missing	53-88	BMI, WHR	283/283	Sex, center, race, ethnicity, age at screening, enrollment date, study component, hysterectomy status, menopausal status
Women's Health Study[42]	Harvard University	US	1992-1993	5.1	95 White, 2.5 black, 2.5 missing	47-82	BMI	40/40	Race, year of birth (±5 y), smoking status (never/former/current), fasting status, month and hour of blood collection

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); EPIC, European Prospective Investigation Into Cancer and Nutrition; PanScan, Pancreatic Cancer Cohort Consortium; WHR, waist to hip ratio.

[a] Enrollment years refers to years of study included in this nested case-control study. Some studies have ongoing recruitment.

[b] Due to rounding percentages do not total 100.

[c] In the EPIC, BMI correction for differences in clothing for people with direct measurements of weight or prediction of BMI from self-reports for the Oxford health-conscious group.

[d] In the EPIC, the WHR was available in the EPIC–International Agency for Research on Cancer and the EPIC-Denmark subcohorts.

The objective of the present study was to examine the association between BMI, other anthropometric factors, and pancreatic cancer risk by pooling data from nested case-control studies included in the National Cancer Institute (NCI) Pancreatic Cancer Cohort Consortium (PanScan). With 2170 cases, this is one of the largest analyses to date of BMI and pancreatic cancer.

METHODS

STUDY POPULATION

PanScan is an initiative that was funded jointly by the NCI's Division of Cancer Control and Population Sciences and the Division of Cancer Epidemiology and Genetics in 2006. PanScan includes investigators from 12 prospective epidemiological cohorts and 1 case-control study and was created to identify genetic markers of susceptibility through a genome-wide association scan and to investigate environmental, lifestyle, and genetic causes of pancreatic cancer.

Studies in the pooled analysis included the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC)[29]; CLUE II[30]; Cancer Prevention Study II (CPS II)[31]; European Prospective Investigation Into Cancer and Nutrition (EPIC)[32]; the Health Professionals Follow-up Study[33]; the Mayo Clinic study[34]; the New York University Women's Health Study,[35] the Nurses' Health Study[36]; the Physicians' Health Study[37]; the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial[38]; Shanghai Men's and Women's Health Studies (SMWHS)[39,40]; the Women's Health Initiative [41]; and the Women's Health Study.[42] A total of 2170 cases and 2209 controls were eligible for the present study (**Table 1**).

CASE ASCERTAINMENT AND DATA COLLECTION

Cases included all incident primary pancreatic adenocarcinoma (*International Classification of Diseases for Oncology, Third Edition,* codes C25.0-C25.3 and C25.7-C25.9). Endocrine pancreatic tumors (*International Classification of Diseases for Oncology, Third Edition,* code C25.4, histologic types 8150, 8151, 8153, 8155, 8240, and 8246) were excluded because the etiology of these cancers is thought to be different from that of exocrine tumors, which account for most pancreatic tumors. Case ascertainment varied among studies but included linking participants to cancer registries and national death indices and self-report and next-of-kin reports. Most cases were histologically confirmed (ATBC, CLUE II, EPIC, New York University Women's Health Study, SMWHS, and the Women's Health Initiative) or were confirmed through cancer registries (ATBC, CPS II, EPIC, and SMWHS), death certificates (CPS II and EPIC), or review of medical records by medical personnel (ATBC; CPS II; EPIC; Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; and SMWHS).

Controls were incidence density sampled with a 1:1 control to case ratio and were alive and cancer free on the date of diagnosis of the matched case. At a minimum, controls were matched to cases on calendar year of birth (±5 years), sex, race, and ethnicity. Some cohorts used more stringent matching on age and, in addition, on other relevant factors (for comparisons of blood levels of analytes of interest), such as age at baseline or age at blood collection (±5 years), date and time of day of blood collection, fasting blood collection, and length of follow-up (Table 1).

Data on anthropometric measures, demographics, and possible confounders were collected through self-administered written questionnaires or in-person interviews. Detailed descriptions of data collection methods have been published previously by the individual studies.[29,30,32,33,35-44] From each study, baseline information on BMI, weight, height, waist circumference, waist to hip ratio (WHR), history of cigarette smoking, sex, age, race, family history of pancreatic cancer, alcohol consumption, pancreatitis, and history of diabetes mellitus was requested. Individual data sets were checked for consistency with previously published results. Forty cases and 46 controls had missing data on BMI, resulting in 2130 cases and 2163 controls available for the main analyses.

The Special Studies Institutional Review Board of the NCI approved the pooled PanScan. Each study also was approved by its local institutional review board.

Table 2. Participant Characteristics: the PanScan

Characteristic	No. (%)[a] Cases (n=2170)	No. (%)[a] Controls (n=2209)	*P* Value (χ^2)
Sex, No. (%)			
Male	1059 (48.8)	1080 (48.9)	.95
Female	1111 (51.2)	1129 (51.1)	
Race, No. (%)			
White	1979 (91.2)	2046 (92.6)	.30
Black	35 (1.6)	34 (1.5)	
Asian	104 (4.8)	108 (4.9)	
Other	11 (0.5)	8 (0.4)	
Unknown	41 (1.9)	13 (0.6)	
Age, y, No. (%)			
<55	150 (6.9)	119 (5.4)	<.05
55-59	188 (8.7)	154 (7.0)	
60-64	338 (15.6)	325 (14.7)	
65-69	443 (20.4)	473 (21.4)	
70-74	491 (22.6)	552 (25.0)	
75-79	368 (17.0)	399 (18.1)	
≥80	192 (8.8)	187 (8.5)	
Cigarette smoking status, No. (%)[a]			
Never smoker	829 (39.0)	970 (44.5)	<.001
Former smoker	767 (36.1)	812 (37.3)	
Current smoker	530 (24.9)	397 (18.2)	
Diabetes mellitus, No. (%)[b]			
No	1762 (86.0)	1973 (92.6)	<.001
Yes	288 (14.0)	157 (7.4)	
History of pancreatitis, No. (%)[b]			
No	862 (88.8)	963 (99.6)	<.001
Yes	109 (11.2)	4 (0.4)	
Family history of pancreatic cancer, No. (%)[a]			
No	1107 (93.3)	1162 (96.4)	<.006
Yes	76 (6.4)	43 (3.6)	
Age at diagnosis of pancreatic cancer, y			
Mean (SD)	68.3 (8.8)	NA	NA
Median (range)	69 (37-93)	NA	
Lag time between diagnosis and enrollment, y			
Mean (SD)	6.3 (5.7)	NA	NA
Median (range)	6.0 (0-28)	NA	

Abbreviations: NA, not applicable; PanScan, Pancreatic Cancer Cohort Consortium.
[a] Because of rounding percentages do not total 100.
[b] Data were missing for smoking status (44 cases and 30 controls), diabetes mellitus status (120 cases and 79 controls), history of pancreatitis (1199 cases and 1242 controls), and family history of pancreatic cancer (987 cases and 1004 controls).

STATISTICAL ANALYSIS

Odds ratios (ORs) and 95% confidence intervals (95% CIs) for pancreatic cancer risk were calculated using unconditional logistic regression, adjusting for cohort, age (categorical), sex,

Table 3. Baseline Anthropometric Characteristics by Sex: the PanScan[a]

Characteristic	Women		Men	
	Cases (n=1111)	Controls (n=1129)	Cases (n=1059)	Controls (n=1080)
BMI source, No. (%)				
Self-reported	533 (48)	518 (46)	544 (51)	559 (52)
Measured	384 (35)	396 (35)	250 (24)	251 (23)
Adjusted	178 (16)	187 (17)	241 (23)	252 (23)
Unknown	16 (1)	28 (2)	24 (2)	18 (2)
BMI				
Mean (SD)	26.8 (5.3)	26.2 (4.9)	27.0 (4.1)	26.7 (3.9)
Median (range)	25.8 (14.0-67.5)	25.4 (15.0-54.6)	26.6 (16.8-53.4)	26.3 (15.4-51.5)
BMI, cohort- and sex-specific quartiles, No. (%)				
Q1 (low)	251 (23)	286 (25)	251 (24)	285 (26)
Q2	257 (23)	269 (24)	247 (23)	257 (24)
Q3	273 (25)	279 (25)	251 (24)	261 (24)
Q4 (high)	314 (28)	267 (24)	286 (27)	259 (24)
Unknown	16 (1)	28 (2)	24 (2)	18 (2)
BMI category, No. (%)				
Underweight, <18.5	14 (1)	21 (2)	5 (0.5)	4 (0.4)
Normal weight, 18.5-24.9	445 (40)	507 (45)	327 (31)	356 (33)
Overweight, 25.0-29.9	381 (34)	339 (30)	505 (48)	524 (49)
Obese, 30.0-34.9	175 (16)	175 (16)	153 (14)	141 (13)
Severely obese, ≥35.0	80 (7)	59 (5)	45 (4)	37 (3)
Unknown	16 (1)	28 (2)	24 (2)	18 (2)
Weight source, No. (%)				
Self-reported	537 (48)	526 (47)	622 (59)	626 (58)
Measured	561 (51)	581 (51)	428 (40)	440 (41)
Unknown	13 (1)	22 (2)	9 (.09)	14 (1)
Weight, kg				
Mean (SD)	70.0 (14.7)	68.5 (13.5)	83.8 (14.6)	82.7 (13.3)
Median (range)	67.5 (41.4-167.5)	66.5 (38.0-134.1)	81.9 (43.9-172.4)	81.0 (48.0-171.0)
Weight, cohort- and sex-specific quartiles, No. (%)				
Q1 (low)	270 (24)	291 (26)	260 (25)	292 (27)
Q2	244 (22)	284 (25)	253 (24)	257 (24)
Q3	286 (26)	274 (24)	237 (22)	262 (24)
Q4 (high)	298 (27)	258 (23)	300 (28)	255 (24)
Unknown	13 (1)	22 (2)	9 (.09)	14 (1)
Height source, No. (%)				
Self-reported	541 (49)	536 (47)	613 (58)	629 (58)
Measured	560 (50)	581 (51)	428 (40)	441 (41)
Unknown	10 (1)	12 (1)	18 (2)	10 (1)
Height, cm				
Mean (SD)	162 (6.6)	162 (6.8)	176 (7.0)	176 (6.8)
Median (range)	162 (132-184)	163 (140-198)	176 (136-199)	176 (152-201)
Height, cohort- and sex-specific quartiles, No. (%)				
Q1 (low)	349 (31)	340 (30)	290 (27)	309 (29)
Q2	251 (23)	266 (24)	300 (28)	305 (28)
Q3	256 (23)	272 (24)	249 (24)	251 (23)
Q4 (high)	245 (22)	239 (21)	202 (19)	205 (19)
Unknown	10 (1)	12 (1)	18 (2)	10 (1)
Waist circumference at baseline, cm				
Mean (SD)	83.4 (16.4)	81.4 (14.8)	96.2 (10.8)	96.8 (9.6)
Median (range)	83.3 (38.1-129.0)	80.0 (38.1-134.0)	96.0 (64.0-144.8)	96.0 (65.2-131.0)
Unknown, No.	515	523	836	846
Waist-hip ratio				
Mean (SD)	0.83 (0.09)	0.82 (0.09)	0.95 (0.06)	0.95 (0.06)
Median (range)	0.82 (0.43-1.25)	0.80 (0.65-1.73)	0.95 (0.76-1.12)	0.95 (0.78-1.15)
Unknown, No.	577	586	836	846

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); PanScan, Pancreatic Cancer Cohort Consortium.
[a]Because of rounding percentages do not total 100.

BMI source (self-reported vs measured), and smoking (never, former, or current) (model 1). Several multivariate models were assessed to control the effects of potential confounders. Model 2 was additionally adjusted for diabetes mellitus history (yes or no). In model 3, cases diagnosed in the first 2 years of follow-up were excluded to address the possibility of an effect of early undiagnosed disease. In model 4, current smokers (at baseline) were excluded, and in model 5, cases diagnosed in the first 2 years of follow-up and current smokers were excluded. Furthermore, models including waist circumference and WHR were additionally adjusted for height to remove extraneous variation due to body size. No adjustment was made for family history of pancreatic cancer because few cohorts had this information. Trend tests were conducted using cohort-specific

Table 4. Risk of Pancreatic Cancer According to Baseline Anthropometric Factors in All the Study Participants: the PanScan

Characteristic	Cases (n=2095)	Controls (n=2141)	OR (95% CI) Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]
BMI, cohort-specific quartiles							
Q1	500	563	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	496	523	1.09 (0.92-1.30)	1.09 (0.92-1.31)	1.09 (0.90-1.33)	1.12 (0.91-1.36)	1.04 (0.82-1.32)
Q3	515	534	1.13 (0.95-1.34)	1.08 (0.90-1.29)	1.13 (0.93-1.38)	1.11 (0.91-1.35)	1.03 (0.81-1.31)
Q4	584	521	1.33 (1.12-1.58)[f]	1.21 (1.01-1.44)[f]	1.29 (1.06-1.57)[f]	1.43 (1.18-1.74)[f]	1.39 (1.10-1.77)[f]
P value for trend			<.001[f]	.049[f]	.008[f]	<.001[f]	.004[f]
BMI categories							
Underweight, <18.5	19	24	0.83 (0.45-1.55)	0.84 (0.44-1.59)	0.65 (0.31-1.35)	0.71 (0.33-1.50)	0.48 (0.18-1.24)
Normal weight, 18.5 to 24.9	759	854	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Overweight, 25.0 to 29.9	868	853	1.18 (1.03-1.35)[f]	1.15 (1.00-1.33)[f]	1.22 (1.04-1.42)[f]	1.19 (1.02-1.40)[f]	1.15 (0.95-1.39)
Obese, 30.0 to 34.9	325	315	1.20 (1.00-1.44)[f]	1.13 (0.93-1.37)	1.22 (0.98-1.51)	1.25 (1.02-1.55)[f]	1.28 (0.99-1.67)
Severely obese, ≥35.0	124	95	1.55 (1.16-2.07)[f]	1.26 (0.93-1.71)	1.32 (0.94-1.87)	1.62 (1.19-2.21)[f]	1.53 (0.99-2.36)
P value for trend			<.001[f]	.047[f]	.008[f]	<.001[f]	.003[f]
Weight, cohort-specific quartiles, kg							
Q1	522	575	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	485	530	1.03 (0.86-1.22)	1.02 (0.85-1.22)	1.06 (0.87-1.29)	1.01 (0.83-1.23)	1.02 (0.80-1.29)
Q3	512	528	1.10 (0.92-1.30)	1.08 (0.91-1.29)	1.10 (0.90-1.34)	1.15 (0.95-1.40)	1.10 (0.87-1.40)
Q4	576	508	1.30 (1.09-1.54)[f]	1.19 (1.00-1.42)[f]	1.34 (1.10-1.63)[f]	1.32 (1.09-1.60)[f]	1.34 (1.05-1.71)[f]
P value for trend			.002[f]	.04[f]	.003[f]	.002[f]	.01[f]
Height, cohort-specific quartiles, cm							
Q1	622	635	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	543	556	0.98 (0.83-1.16)	0.99 (0.84-1.18)	1.01 (0.84-1.23)	0.96 (0.79-1.15)	0.92 (0.73-1.17)
Q3	495	514	0.98 (0.83-1.16)	1.00 (0.84-1.18)	1.04 (0.86-1.27)	0.94 (0.78-1.13)	0.96 (0.76-1.21)
Q4	435	436	0.99 (0.83-1.18)	1.02 (0.85-1.22)	1.06 (0.87-1.30)	0.95 (0.78-1.16)	0.93 (0.72-1.18)
P value for trend			.93	.81	.41	.58	.65
Waist circumference, cohort-specific quartiles, cm[g]							
Q1	215	224	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	172	208	0.87 (0.66-1.15)	0.89 (0.67-1.18)	0.82 (0.61-1.10)	0.88 (0.65-1.20)	0.82 (0.58-1.16)
Q3	200	198	1.10 (0.83-1.45)	1.08 (0.81-1.44)	1.04 (0.77-1.40)	1.09 (0.81-1.47)	1.05 (0.75-1.48)
Q4	225	200	1.23 (0.94-1.62)	1.21 (0.91-1.60)	1.21 (0.90-1.61)	1.20 (0.89-1.61)	1.14 (0.81-1.59)
P value for trend			.04[f]	.09	.07	.10	.22
Waist-hip ratio, cohort-specific quartiles[g]							
Q1	186	206	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	172	196	1.01 (0.75-1.35)	1.07 (0.79-1.44)	1.01 (0.74-1.37)	1.07 (0.79-1.47)	1.05 (0.74-1.49)
Q3	167	207	0.90 (0.67-1.21)	0.88 (0.65-1.19)	0.89 (0.65-1.22)	0.87 (0.63-1.20)	0.87 (0.60-1.24)
Q4	225	158	1.71 (1.27-2.30)[f]	1.69 (1.24-2.30)[f]	1.62 (1.18-2.22)[f]	1.83 (1.32-2.53)[f]	1.57 (1.09-2.26)[f]
P value for trend			.001[f]	.004[f]	.007[f]	.001[f]	.06

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; OR, odds ratio; PanScan, Pancreatic Cancer Cohort Consortium.

[a] Adjusted for cohort, age (categorical), sex, anthropometric factor source (self-reported or measured), and smoking (never, former, or current).

[b] Adjusted for cohort, age (categorical), sex, anthropometric factor source (self-reported or measured), smoking (never, former, and current), and diabetes mellitus history (no or yes).

[c] Adjusted for cohort, age (categorical), sex, anthropometric factor source (self-reported vs measured), and smoking (never, former, or current) and excluding the first 2 years of follow-up.

[d] Adjusted for cohort, age (categorical), sex, and anthropometric factor source (self-reported or measured) and excluding current and former smokers.

[e] Adjusted for cohort, age (categorical), sex, and anthropometric factor source (self-reported or measured) and excluding the first 2 years of follow-up, current and former smokers, and people with diabetes mellitus.

[f] Statistically significant.

[g] Models for waist circumference and waist to hip ratio were additionally adjusted for height.

quartiles of BMI, weight, height, waist circumference, and WHR as well as descriptive BMI categories (underweight, <18.5; normal weight, 18.5-24.9; overweight, 25.0-29.9; obese, 30.0-34.9; and severely obese, ≥35.0). To test for heterogeneity, BMI quartile categories were modeled as a continuous variable, and the risk estimates and standard errors from the cohort-specific models were used to generate the Q statistic.

The association between BMI and time of onset for pancreatic cancer was also examined using logistic regression modeling. Differences in time of onset were examined for normal vs overweight vs obese categories of BMI and in a combined category of overweight and obese. The analyses were conducted using a software program (SAS version 9.1.3; SAS Institute Inc, Cary, North Carolina).

RESULTS

The study included 2170 pancreatic cancer cases and 2209 controls aged 37 to 94 years (Table 1). Of the 2170 pancreatic cancer cases, 1059 were men and 1111 were women. Cases and controls were similar for age and racial distribution (**Table 2**). Most participants were white, and 86% of the study population was 60 years or older. Compared with controls, cases had a higher prevalence of current smoking (18% and 25%), diabetes mellitus (7% and 14%), history of pancreatitis (0.4% and 11%), and family history of pancreatic cancer (4% and 6%) based on data from

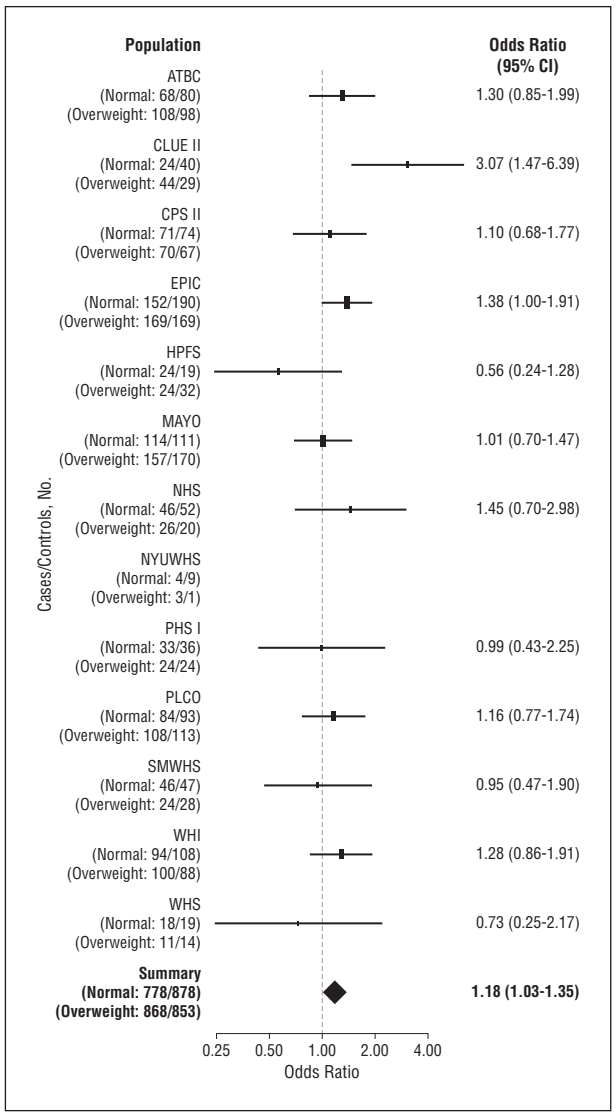

Figure 1. Risk estimates for pancreatic cancer associated with body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) by study for overweight people (BMI, 25 to <30) compared with normal-weight people (BMI, <25). ATBC indicates Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; CI, confidence interval; CLUE II CPS II, Cancer Prevention Study II; EPIC, European Prospective Investigation Into Cancer and Nutrition; HPFS, Health Professionals Follow-up Study; MAYO, Mayo Clinic study; NHS, Nurses' Health Study; NYUWHS, New York University Women's Health Study; PHSI, Physicians' Health Study; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; SMWHS, Shanghai Men's and Women's Health Studies; WHI, Women's Health Initiative; and WHS, Women's Health Study.

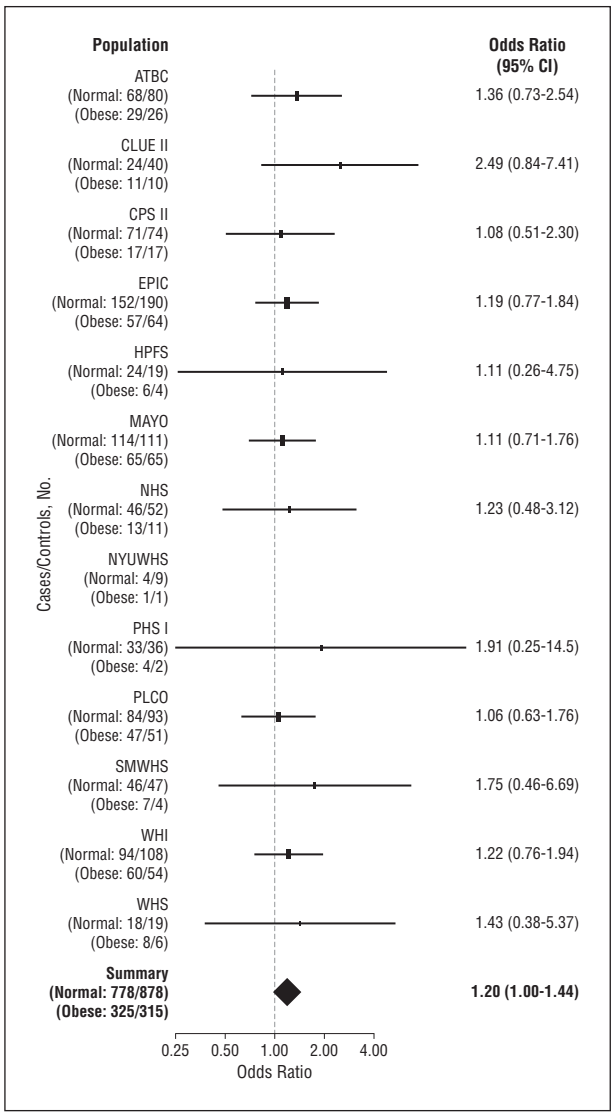

Figure 2. Risk estimates for pancreatic cancer associated with body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) by study for obese people (30 to <35) compared with normal-weight people (<25). See the legend for Figure 1 for an explanation of the abbreviations.

cohorts with available information. The average age at pancreatic cancer onset in cases was 68.3 years, and the average lag time between cohort enrollment and diagnosis of pancreatic cancer in cases was 6.3 years.

Table 3 describes baseline anthropometric characteristics of cases and controls. Weight, height, and corresponding BMI were self-reported in approximately 50% of participants, measured in 29%, and measured and subsequently adjusted for difference in clothing in approximately 20%. Thirty-six percent of cases and 39% of controls had BMI in the normal range, 41% of cases and 39% of controls were overweight, and 21% of cases and 19% of controls were obese (Table 3). Cases had slightly higher mean weight compared with controls (76.8 and 75.5 kg) and a larger mean waist circumference (86.9 and 85.7 cm). Mean WHR and height were similar.

Table 4 displays ORs and 95% CIs for pancreatic cancer according to baseline anthropometric factors for all individuals in the study. In all of the participants, a positive association between increasing BMI and risk of pancreatic cancer was observed (adjusted OR for the highest vs lowest BMI quartile, 1.33; 95% CI, 1.12-1.58; $P_{\text{trend}} < .001$ in model 1). Statistically significant trends of increasing risk of pancreatic cancer with increasing BMI (both quartiles and clinical categories) were observed in all 5 models analyzed.

The figures demonstrate the individual study results (model 1) and pooled risk estimates for overweight (**Figure 1**), obese (**Figure 2**), and severely obese individuals (**Figure 3**). Further adjustment for diabetes mellitus history (model 2) resulted in attenuation of risk estimates compared with model 1, but *P* values for trend were statistically significant for BMI quartiles and categories

(Table 4). In addition, waist circumference and WHR were positively associated with risk of pancreatic cancer in all participants with top vs bottom quartile ORs of 1.23 (95% CI, 0.94-1.62) and 1.71 (95% CI, 1.27-2.30), respectively (Table 4). Stratification by BMI source (self-reported vs measured) resulted in similar risk estimates: ORs (95% CIs) for obese vs normal-weight BMI were 1.24 (0.92-1.68) for measured BMI and 1.21 (0.95-1.53) for self-reported BMI. The OR per BMI increase of 5 was 1.13 (95% CI, 1.11-1.14).

The risk estimates did not change significantly in the sensitivity analysis excluding the Mayo Clinic case-control study (data not shown); therefore, we decided to include the Mayo participants in the final analyses. There was no evidence of significant heterogeneity between different cohorts for the BMI–pancreatic cancer results ($P_{\text{heterogeneity}}$=.36).

Table 5 and **Table 6** provide ORs and 95% CIs for pancreatic cancer in men and women, respectively. In men, the adjusted risk estimate (model 1) for the top vs bottom quartile of BMI was 1.33 (95% CI, 1.04-1.69). Higher risk estimates were observed after the exclusion of current smokers (model 4). In men who never smoked, there was a significant trend of increasing risk with increasing BMI (P_{trend}=.007) with the top vs bottom quartile (OR, 1.51; 95% CI, 1.13-2.03). Height, waist circumference, and WHR ratio were not significantly associated with pancreatic cancer in men (Table 5).

In women, statistically significant trends of increasing risk of pancreatic cancer with increasing BMI were observed overall (model 1) and after the exclusion of cases diagnosed in the first 2 years of follow-up (model 3) or current and former smokers (model 4) (Table 6). Compared with normal-weight BMI (model 1), the ORs for pancreatic cancer were 1.31 (95% CI=1.07-1.60) for overweight women and 1.61 (95% CI, 1.12-2.33; P_{trend}=.003) for severely obese women. Increasing waist circumference and WHR were significantly associated with pancreatic cancer risk in women. Compared with the reference group, women in the highest quartile of WHR had an OR of 1.87 (95% CI, 1.31-2.69) after adjustment for cohort, age, BMI source, and smoking status. Inclusion of BMI (categorical) and WHR (quartiles) in the same model suggested that the effect of increasing WHR is stronger (P=.006) compared with that of BMI categories (P=.44) after adjustment for cohort, age, sex, BMI source, smoking, and diabetes mellitus history.

We did not observe clinically meaningful differences in time of onset for pancreatic cancer between normal-weight and overweight/obese individuals. Overweight and obese individuals together were diagnosed approximately 4 months earlier than were normal-weight individuals (data not shown). When comparing obese individuals only with normal-weight individuals, obese participants were diagnosed on average approximately 1 year earlier than were normal-weight individuals, and the difference was significant (P=.03).

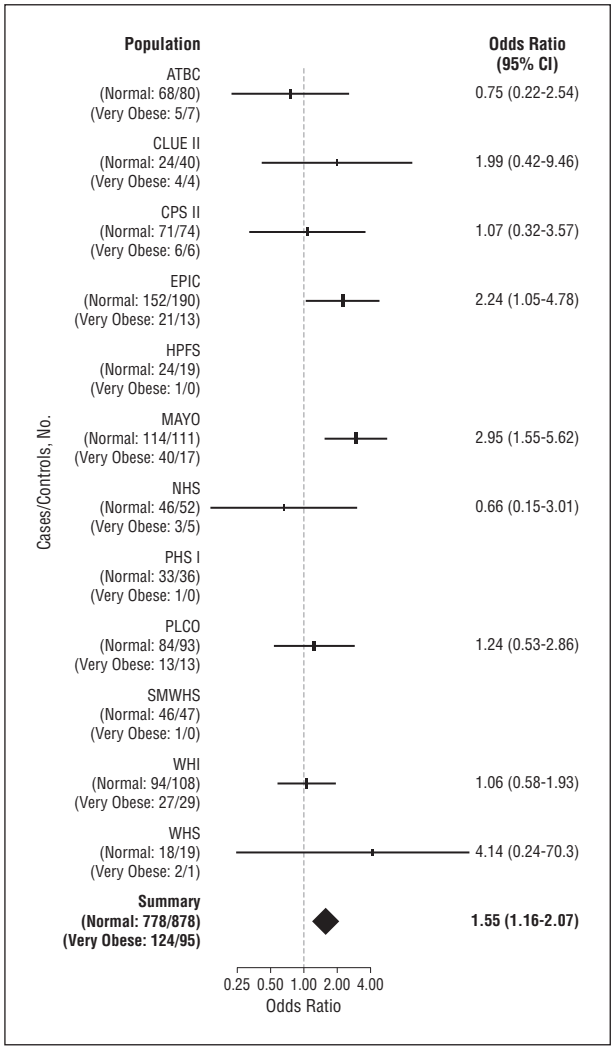

Figure 3. Risk estimates for pancreatic cancer associated with body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) by study for severely obese people (>35) compared with normal-weight people (<25). See the legend for Figure 1 for an explanation of the abbreviations.

COMMENT

The results of this large pooled set of studies support the hypothesis that obesity is associated with an increased risk of pancreatic cancer. The present findings are consistent with most previous epidemiological studies that found a positive association between BMI and pancreatic cancer risk[45] and support the conclusion from a recent review panel from the World Cancer Research Fund[45] that the strength of the evidence supporting an association between obesity and pancreatic cancer is convincing.

Previous studies that did not observe a positive association between BMI and pancreatic cancer were often limited by the use of proxy respondents[46-49] or by inadequate statistical power to examine associations at BMI levels that correspond with obesity (<10 cases with BMI >30.0).[7,10,17,50] Controversy regarding the role of smoking in the BMI and pancreatic cancer relationship still remains. Many previous studies[7,47,48,50] that did not observe an association with obesity did not properly control for smoking history. It is possible that residual confounding due to improper adjustment for smoking history may have biased the association between BMI and pancreatic cancer toward the null. When stratifying on smoking status, some previous studies found that the relationship be-

Table 5. Risk of Pancreatic Cancer According to Baseline Anthropometric Factors in Men: the PanScan

Characteristic	Cases (n=1031)	Controls (n=1055)	OR (95% CI) Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]
BMI, cohort- and sex-specific quartiles							
Q1	251	283	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	247	256	1.13 (0.88-1.45)	1.15 (0.89-1.48)	1.09 (0.82-1.45)	1.20 (0.89-1.63)	1.01 (0.70-1.47)
Q3	249	259	1.12 (0.88-1.44)	1.07 (0.83-1.38)	1.04 (0.78-1.38)	1.12 (0.83-1.52)	0.88 (0.60-1.29)
Q4	284	257	1.33 (1.04-1.69)[f]	1.23 (0.96-1.58)	1.22 (0.92-1.62)	1.51 (1.13-2.03)[f]	1.27 (0.88-1.84)
P value for trend			<.03[f]	.16	.19	.007[f]	.21
BMI categories							
Underweight, <18.5	5	4	1.45 (0.37-5.68)	1.89 (0.42-8.48)	0.90 (0.14-5.60)	0.92 (0.15-5.66)	0.73 (0.06-8.33)
Normal weight, 18.5-24.9	326	354	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Overweight, 25.0 to 29.9	503	520	1.09 (0.89-1.33)	1.06 (0.86-1.30)	1.08 (0.87-1.35)	1.08 (0.85-1.38)	0.96 (0.71-1.29)
Obese, 30.0-34.9	152	141	1.23 (0.93-1.63)	1.13 (0.85-1.51)	1.21 (0.87-1.68)	1.26 (0.89-1.77)	1.29 (0.82-2.03)
Severely obese, ≥35.0	45	36	1.48 (0.92-2.39)	1.26 (0.77-2.06)	1.07 (0.58-1.97)	1.65 (0.96-2.84)	0.90 (0.40-2.02)
P value for trend			.07	.33	.32	.047[f]	.54
Weight, cohort- and sex-specific quartiles, kg							
Q1	257	290	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	250	254	1.14 (0.89-1.46)	1.12 (0.87-1.44)	1.28 (0.96-1.69)	1.10 (0.82-1.49)	1.29 (0.89-1.87)
Q3	233	259	1.05 (0.82-1.34)	1.04 (0.81-1.35)	1.03 (0.77-1.38)	1.12 (0.83-1.51)	1.06 (0.72-1.56)
Q4	291	252	1.36 (1.07-1.74)[f]	1.27 (0.99-1.63)	1.42 (1.07-1.88)[f]	1.43 (1.07-1.91)[f]	1.36 (0.93-1.98)
P value for trend			.02[f]	.09	.046[f]	.01[f]	.21
Height, cohort- and sex-specific quartiles, cm							
Q1	284	305	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	298	301	1.05 (0.83-1.32)	1.08 (0.85-1.37)	1.13 (0.87-1.48)	1.05 (0.79-1.38)	1.10 (0.78-1.57)
Q3	247	249	1.07 (0.84-1.37)	1.08 (0.85-1.39)	1.15 (0.87-1.52)	1.00 (0.75-1.34)	0.90 (0.63-1.30)
Q4	202	200	1.05 (0.81-1.36)	1.08 (0.83-1.41)	1.19 (0.88-1.60)	1.02 (0.74-1.41)	1.04 (0.69-1.56)
P value for trend			.63	.54	.23	.92	.98
Waist circumference, cohort- and sex-specific quartiles[g]							
Q1	68	62	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	55	65	0.79 (0.47-1.34)	0.78 (0.45-1.34)	0.82 (0.47-1.42)	0.94 (0.50-1.74)	0.96 (0.49-1.88)
Q3	47	50	1.04 (0.60-1.80)	0.98 (0.55-1.76)	0.98 (0.54-1.78)	1.05 (0.55-2.01)	0.84 (0.40-1.74)
Q4	52	53	1.04 (0.61-1.79)	1.11 (0.63-1.96)	1.02 (0.58-1.80)	1.09 (0.58-2.06)	1.08 (0.55-2.14)
P value for trend			.72	.61	.84	.72	.86
Waist-hip ratio, cohort- and sex-specific quartiles[g]							
Q1	67	63	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	52	65	0.76 (0.45-1.29)	0.83 (0.47-1.44)	0.79 (0.45-1.38)	0.74 (0.40-1.38)	0.76 (0.39-1.48)
Q3	41	53	0.80 (0.46-1.39)	0.78 (0.43-1.40)	0.78 (0.44-1.41)	0.76 (0.39-1.46)	0.64 (0.31-1.35)
Q4	62	49	1.41 (0.83-2.40)	1.46 (0.83-2.56)	1.39 (0.79-2.44)	1.57 (0.85-2.89)	1.50 (0.77-2.93)
P value for trend			.20	.19	.24	.12	.29

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; OR, odds ratio; PanScan, Pancreatic Cancer Cohort Consortium.

[a] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), and smoking (never, former, or current).

[b] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), smoking (never, former, or current), and diabetes mellitus history (no or yes).

[c] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), and smoking (never, former, or current) and excluding the first 2 years of follow-up.

[d] Adjusted for cohort, age (categorical), and anthropometric factor source (self-reported or measured) and excluding current and former smokers.

[e] Adjusted for cohort, age (categorical), and anthropometric factor source (self-reported or measured) and excluding the first 2 years of follow-up, current and former smokers, and people with diabetes mellitus.

[f] Statistically significant.

[g] Models for waist circumference and waist to hip ratio were additionally adjusted for height.

tween BMI and pancreatic cancer was strongest in never smokers.[24,25] The present findings are consistent with previous reports that the association between BMI and pancreatic cancer is stronger in nonsmokers (adjusted OR for BMI ≥30, 1.37; 95% CI, 1.06-1.78) than in smokers (adjusted OR for BMI ≥30, 1.14; 95% CI, 0.91-1.78).

Unlike a recent study[51] in which the authors reported that individuals who were overweight or obese from age 20 to 49 years had earlier onset of pancreatic cancer compared with those with normal body weight, we did not find a substantial difference in age at diagnosis between normal-weight and the combined group of overweight and obese individuals.

In this study, BMI was assessed between ages 37 and 94 years, and overweight or obese individuals were diagnosed a mean of 4 months earlier than were normal-weight individuals. The study by Li et al,[51] using a hospital-based case-control study design, found that overweight or obese patients aged 20 to 49 years had a median age at pancreatic cancer onset 2 to 6 years earlier than that of normal-

Table 6. Risk of Pancreatic Cancer According to Baseline Anthropometric Factors in Women: the PanScan

Characteristic	Cases (n=1064)	Controls (n=1086)	OR (95% CI) Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]
BMI, cohort- and sex-specific quartiles							
Q1	249	280	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	249	267	1.07 (0.83-1.36)	1.06 (0.82-1.36)	1.11 (0.84-1.48)	1.07 (0.82-1.39)	1.08 (0.79-1.47)
Q3	266	275	1.13 (0.89-1.44)	1.08 (0.85-1.39)	1.24 (0.94-1.64)	1.10 (0.85-1.43)	1.16 (0.85-1.57)
Q4	300	264	1.34 (1.05-1.70)[f]	1.19 (0.93-1.53)	1.37 (1.03-1.81)[f]	1.39 (1.08-1.80)[f]	1.52 (1.11-2.10)[f]
P value for trend			.01[f]	.17	.02[f]	.008[f]	.007[f]
BMI categories							
Underweight, <18.5	14	20	0.75 (0.37-1.51)	0.72 (0.35-1.48)	0.65 (0.29-1.44)	0.68 (0.29-1.55)	0.45 (0.16-1.29)
Normal weight, 18.5-24.9	433	500	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Overweight, 25.0-29.9	365	333	1.31 (1.07-1.60)[f]	1.27 (1.03-1.55)[f]	1.40 (1.12-1.76)[f]	1.30 (1.05-1.61)[f]	1.34 (1.04-1.72)[f]
Obese, 30.0-34.9	173	174	1.19 (0.93-1.54)	1.12 (0.87-1.46)	1.23 (0.92-1.64)	1.25 (0.96-1.63)	1.29 (0.93-1.79)
Severely obese, ≥35.0	79	59	1.61 (1.12-2.33)[f]	1.29 (0.88-1.89)	1.50 (0.98-2.30)	1.65 (1.13-2.40)[f]	1.98 (1.17-3.36)[f]
P value for trend			.003[f]	.08	.01[f]	.002[f]	.001[f]
Weight, cohort- and sex-specific quartiles, kg							
Q1	265	285	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	235	276	0.92 (0.72-1.18)	0.93 (0.73-1.20)	0.89 (0.67-1.18)	0.94 (0.72-1.21)	0.86 (0.62-1.18)
Q3	279	269	1.14 (0.90-1.46)	1.12 (0.87-1.43)	1.16 (0.88-1.52)	1.18 (0.91-1.52)	1.14 (0.84-1.54)
Q4	285	256	1.23 (0.96-1.56)	1.12 (0.87-1.44)	1.27 (0.96-1.68)	1.24 (0.96-1.61)	1.34 (0.98-1.84)
P value for trend			.03[f]	.22	.03[f]	.03[f]	.02[f]
Height, cohort- and sex-specific quartiles, cm							
Q1	338	330	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	245	255	0.91 (0.72-1.16)	0.89 (0.70-1.14)	0.89 (0.67-1.17)	0.89 (0.69-1.15)	0.79 (0.57-1.09)
Q3	248	265	0.89 (0.71-1.13)	0.92 (0.72-1.17)	0.95 (0.73-1.24)	0.89 (0.69-1.14)	0.98 (0.73-1.32)
Q4	233	236	0.92 (0.72-1.17)	0.95 (0.74-1.21)	0.95 (0.72-1.25)	0.89 (0.69-1.16)	0.85 (0.63-1.16)
P value for trend			.45	.69	.80	.38	.52
Waist circumference, cohort- and sex-specific quartiles[g]							
Q1	147	162	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	117	143	0.89 (0.64-1.25)	0.92 (0.66-1.30)	0.81 (0.56-1.16)	0.85 (0.60-1.22)	0.77 (0.51-1.14)
Q3	153	148	1.14 (0.83-1.58)	1.14 (0.82-1.58)	1.08 (0.76-1.54)	1.12 (0.80-1.57)	1.14 (0.77-1.68)
Q4	173	147	1.31 (0.95-1.80)	1.26 (0.91-1.75)	1.28 (0.91-1.80)	1.24 (0.88-1.73)	1.17 (0.79-1.73)
P value for trend			.04[f]	.09	.06	.10	.19
Waist-hip ratio, cohort- and sex-specific quartiles[g]							
Q1	119	143	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Q2	120	131	1.14 (0.80-1.63)	1.21 (0.84-1.74)	1.15 (0.78-1.68)	1.20 (0.83-1.75)	1.20 (0.80-1.82)
Q3	126	154	0.96 (0.67-1.36)	0.94 (0.66-1.34)	0.96 (0.66-1.39)	0.92 (0.63-1.33)	0.97 (0.64-1.47)
Q4	163	109	1.87 (1.31-2.69)[f]	1.85 (1.27-2.69)[f]	1.77 (1.20-2.61)[f]	1.95 (1.33-2.86)[f]	1.61 (1.03-2.50)[f]
P value for trend			.003[f]	.008[f]	.01[f]	.005[f]	.11

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; OR, odds ratio; PanScan, Pancreatic Cancer Cohort Consortium.

[a] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), and smoking (never, former, or current).

[b] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), smoking (never, former, or current), and diabetes mellitus history (no or yes).

[c] Adjusted for cohort, age (categorical), anthropometric factor source (self-reported or measured), and smoking (never, former, or current) and excluding the first 2 years of follow-up.

[d] Adjusted for cohort, age (categorical), and anthropometric factor source (self-reported or measured) and excluding current and former smokers.

[e] Adjusted for cohort, age (categorical), and anthropometric factor source (self-reported or measured) and excluding the first 2 years of follow-up, current and former smokers, and people with diabetes mellitus.

[f] Statistically significant.

[g] Models for waist circumference and waist to hip ratio were additionally adjusted for height.

weight patients. However, these differences were based on BMI as recalled from early adulthood and may have been subject to recall bias. Nevertheless, as suggested by Li et al,[51] obesity at younger ages might have a more profound effect on risk and age at onset of pancreatic cancer than would obesity at older ages.

There are established biologic pathways to support a relationship between excess body weight and the development of pancreatic cancer. Body fatness has a direct linear relationship with insulin production and is related to the development of insulin resistance.[52] Furthermore, insulin resistance and abnormal glucose metabolism, even in the absence of diabetes mellitus, is associated with pancreatic cancer risk.[8,53,54] In vitro studies have also shown that insulin has growth-promoting effects in the pancreas.[55] A hyperinsulinemic state allows increased insulin to pass through the pancreas and trigger mitotic activity.[8,53,56] In addition, excess insulin can also downregulate insulinlike growth factor I–binding proteins, which would result in more bioavailable insulinlike growth factor I, which

has been associated with cell proliferation and pancreatic cancer risk.[54,57]

The results of this study also support a specific role of central adiposity in pancreatic cancer risk, especially in women. In addition to general body fatness, there is a direct linear relationship between intra-abdominal fat deposits, insulin production, and the development of insulin resistance.[52]

The present study has several strengths, including the very large sample size, the wide range of BMI, and the ability to control for most known or suspected pancreatic cancer risk factors. In addition, the study population was largely a nested sample from various prospective cohort studies so that BMI was measured before pancreatic cancer diagnosis, thus reducing differential reporting of past exposure information. Limitations include the use of some self-reported exposure information; however, adjusting for source of exposure information (self-reported or measured) did not alter the association. Another potential limitation is the wide range of lag periods between BMI measurement (collected at baseline for each cohort) and the date of diagnosis; however, sensitivity analyses examining this lag time by excluding the first 2 years of follow-up did not change the point estimates appreciably, thus arguing against an effect of prediagnostic disease-related changes in anthropometric measures (reverse causation). Participating cohorts had different coding systems for physical activity that were not readily comparable; therefore, we could not assess whether the association between BMI and pancreatic cancer varies by level of physical activity. To address potential residual confounding by smoking, we performed the analyses in never smokers and found a slightly stronger association between BMI and pancreatic risk. Last, only a few cohorts had data available on waist and hip circumference so that there was limited statistical power to examine these relationships.

In summary, the results of this study provide additional evidence that obesity is associated with increased risk of pancreatic cancer. In addition, the association between waist circumference and pancreatic cancer risk, especially in women, suggests a possible association with the distribution of body fat. These findings, along with those from previous studies, strongly support the role of obesity in pancreatic cancer development.

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Author Affiliations: Departments of Obstetrics and Gynecology (Dr Arslan) and Environmental Medicine (Drs Arslan and Zeleniuch-Jacquotte), New York University School of Medicine, and New York University Cancer Institute, New York (Drs Arslan and Zeleniuch-Jacquotte); Prevention and Research Center, Mercy Medical Center, Baltimore, Maryland (Dr Helzlsouer); Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington (Drs Kooperberg, LaCroix, and McTiernan); Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center and Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, Tennessee (Drs Shu and Zheng); Information Management Services, Silver Spring, Maryland (Ms Steplowski); National Institute for Public Health and the Environment, Bilthoven, the Netherlands (Dr Bueno-de-Mesquita); Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, the Netherlands (Dr Bueno-de-Mesquita); Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts (Drs Fuchs and Wolpin); Channing Laboratory (Drs Fuchs, Giovannucci, Hankinson, Hunter, and Wolpin), Divisions of Preventive Medicine and Aging (Dr Buring), and Physicians' Health Study, Divisions of Aging, Cardiovascular Medicine, and Preventive Medicine (Dr Gaziano), Department of Medicine (Dr Manson), Brigham and Women's Hospital and Harvard Medical School, Boston; Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis (Dr Gross); Department of Epidemiology, American Cancer Society, Atlanta, Georgia (Drs E. J. Jacobs and Patel); Department of Health Sciences Research (Dr Petersen and Mr Bamlet) and Department of Oncology, College of Medicine (Dr McWilliams), Mayo Clinic, Rochester, Minnesota; Division of Cancer Epidemiology and Genetics (Drs Stolzenberg-Solomon, Albanes, Amundadottir, Chanock, Hartge, Hoover, K. B. Jacobs, Mendelsohn, Thomas, and Yu, and Ms Hutchinson and Mr Tobias) and Laboratory of Translational Genomics, Division of Cancer Epidemiology and Genetics (Drs Amundadottir and Chanock), and Division of Cancer Control and Population Sciences (Ms Lynch), National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland; Public Health Institute of Navarra, Pamplona, Spain (Dr Barricarte); CIBER Epidemiología y Salud Pública, Barcelona, Spain (Dr Barricarte); MRC Centre for Nutrition and Cancer, University of Cambridge, Cambridge, England (Dr Bingham); German Institute of Human Nutrition, Potsdam-Rehbrüecke, Nuthetal, Germany (Dr Boeing); Institut National de la Santé et de la Recherche Médicale and Institut Gustave Roussy, Villejuif, France (Dr Boutron-Ruault); Department of Ambulatory Care and Prevention, Harvard Medical School (Dr Buring); George W. Comstock Center for Public Health Research and Prevention, Hagerstown, Maryland (Ms Clipp); Massachusetts Veterans Epidemiology Research and Information Center, Veterans Affairs Boston Healthcare System (Dr Gaziano); Departments of Nutrition (Dr Giovannucci), Epidemiology (Drs Giovannucci, Hankinson, Hunter, Kraft, Manson, and Trichopoulos), and Biostatistics (Dr Kraft), Harvard School of Public Health; Core Genotyping Facility, Advanced Technology Program, SAIC-Frederick Inc, NCI-Frederick, Frederick, Maryland (Ms Hutchinson and Dr K. B. Jacobs); Bioinformed Consulting Services LLC, Gaithersburg, Maryland (Dr K. B. Jacobs); Department of Surgery, Malmö University Hospital, Malmö, Sweden (Dr Manjer); Division of Epidemiology, Public Health and Primary Care, Imperial College, London, England (Dr Michaud); Molecular and Nutritional Epidemiology Unit, Cancer Research and Prevention Institute, Florence, Italy (Dr Palli); Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York (Dr Rohan); International Agency for Research on Cancer, Lyon, France (Dr Slimani); Diet, Cancer, and Health, Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark (Dr Tjønneland); Department of Hygiene and Epidemiology, University of Athens Medical School, Athens, Greece (Dr Trichopoulos); and Department of Chronic

Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland (Dr Virtamo).
Correspondence: Alan A. Arslan, MD, Department of Obstetrics and Gynecology, New York University School of Medicine, 550 First Ave, TH-528, New York, NY 10016 (alan.arslan@nyumc.org).
Author Contributions: Dr Arslan had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses. *Study concept and design:* Kooperberg, Shu, Bueno-de-Mesquita, Fuchs, Stolzenberg-Solomon, Zheng, Amundadottir, Barricarte, Bingham, Chanock, Hartge, Hoover, K. B. Jacobs, Manson, McTiernan, Mendelsohn, Palli, Slimani, Tjønneland, and Tobias. *Acquisition of data:* Helzlsouer, Kooperberg, Shu, Bueno-de-Mesquita, Fuchs, E. J. Jacobs, LaCroix, Petersen, Stolzenberg-Solomon, Albanes, Bamlet, Barricarte, Boeing, Buring, Clipp, Gaziano, Giovannucci, Hankinson, Hartge, Hoover, Hunter, Hutchinson, K. B. Jacobs, Lynch, Manson, McWilliams, Michaud, Palli, Thomas, Tjønneland, Trichopoulos, Virtamo, Wolpin, and Zeleniuch-Jacquotte. *Analysis and interpretation of data:* Arslan, Helzlsouer, Kooperberg, Shu, Steplowski, Fuchs, Gross, E. J. Jacobs, Boutron-Ruault, Giovannucci, Hankinson, Hartge, K. B. Jacobs, Kraft, Manjer, Rohan, Trichopoulos, Yu, and Patel. *Drafting of the manuscript:* Arslan, Helzlsouer, Kooperberg, and Patel. *Critical revision of the manuscript for important intellectual content:* Arslan, Helzlsouer, Kooperberg, Shu, Steplowski, Bueno-de-Mesquita, Fuchs, Gross, E. J. Jacobs, LaCroix, Petersen, Stolzenberg-Solomon, Zheng, Albanes, Amundadottir, Bamlet, Barricarte, Bingham, Boeing, Boutron-Ruault, Buring, Chanock, Clipp, Gaziano, Giovannucci, Hankinson, Hartge, Hunter, Hutchinson, K. B. Jacobs, Kraft, Lynch, Manson, McTiernan, McWilliams, Mendelsohn, Michaud, Palli, Rohan, Slimani, Thomas, Tjønneland, Tobias, Trichopoulos, Virtamo, Wolpin, Yu, and Zeleniuch-Jacquotte. *Statistical analysis:* Kooperberg, Shu, E. J. Jacobs, Bamlet, Hunter, K. B. Jacobs, Manjer, and Yu. *Obtained funding:* Shu, Bueno-de-Mesquita, Fuchs, Petersen, Stolzenberg-Solomon, Albanes, Boeing, Gaziano, Giovannucci, Hoover, Kraft, Lynch, Palli, Tjønneland, Trichopoulos, and Zeleniuch-Jacquotte. *Administrative, technical, and material support:* Arslan, Kooperberg, Steplowski, Fuchs, Gross, Petersen, Zheng, Albanes, Amundadottir, Bingham, Boeing, Chanock, Clipp, Gaziano, Hartge, Hunter, K. B. Jacobs, Lynch, Manjer, Manson, Mendelsohn, Slimani, Thomas, Tobias, Trichopoulos, and Virtamo. *Study supervision:* Arslan, Helzlsouer, Kooperberg, Bueno-de-Mesquita, Hankinson, Hartge, and Hoover.
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PanScan Writing Committee Members: Alan A. Arslan, MD; Kathy J. Helzlsouer, MD, MHS; Charles Kooperberg, PhD; Xiao-Ou Shu, MD, PhD; Emily Steplowski, BS; and Alpa V. Patel, PhD.
Steering Committee Members: Alan A. Arslan, MD; Kathy J. Helzlsouer, MD, MHS; H. Bas Bueno-de-Mesquita, MD, PhD, MPH; Charles S. Fuchs, MD, MPH; Myron D. Gross, PhD; Eric J. Jacobs, PhD; Andrea Z. LaCroix, PhD; Gloria M. Petersen, PhD; Rachael Z. Stolzenberg-Solomon, PhD, MPH; and Wei Zheng, MD, PhD.
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