Body size and physical activity in relation to incidence of chronic obstructive pulmonary disease

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Abstract

Background: Limited evidence suggests that adiposity and lack of physical activity may increase the risk of chronic obstructive pulmonary disease (COPD). We investigated the relation of body size and physical activity with incidence of COPD.

Methods: We obtained data on anthropometric measurements and physical activity from 113 279 participants in the National Institutes of Health–AARP Diet and Health Study who reported no diagnosis of COPD at baseline (1995–1996). We estimated associations between these measurements and subsequent diagnosis of COPD between 1996 and 2006, with extensive adjustment for smoking and other potentially confounding variables.

Results: Participants reported 3648 new COPD diagnoses during follow-up. The incidence of COPD was higher in both severely obese (body mass index [BMI] ≥ 35) and underweight (BMI < 18.5) participants, but after adjustment for waist circumference, only underweight remained positively associated with COPD (relative risk [RR] 1.56, 95% confidence interval [CI] 1.15–2.11). Larger waist circumference (highest v. normal categories, adjusted RR 1.72, 95% CI 1.37–2.16) and higher waist–hip ratio (highest v. normal categories, adjusted RR 1.46, 95% CI 1.23–1.73) were also positively associated with COPD. In contrast, hip circumference (highest v. normal categories, adjusted RR 0.78, 95% CI 0.62–0.98) and physical activity (≥ 5 v. 0 times/wk, adjusted RR 0.71, 95% CI 0.63–0.79) were inversely associated with COPD.

Interpretation: Obesity, in particular abdominal adiposity, was associated with an increased risk of COPD, and increased hip circumference and physical activity were associated with a decreased risk of COPD. These findings suggest that following guidelines for a healthy body weight, body shape and physical activity decrease the risk of COPD.

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Chronic obstructive pulmonary disease (COPD) is a progressive, irreversible condition that severely affects quality of life[1] and ability to work.[2] Direct and indirect annual costs of COPD, including inpatient and outpatient care, medication and loss of productivity, sum to $50 billion in the United States[3] and €39 billion (about US$50 billion) in Europe.[4]

Chronic obstructive pulmonary disease may be prevented by avoidance of tobacco smoke, occupational dust and other environmental air pollution.[5] Body mass index (BMI) and physical activity are established correlates of disease progression among patients with COPD,[6,7] but data relating body size or physical activity to incident COPD are sparse. The few studies available are based on small samples and show inverse relations of both BMI[8,9] and physical activity[10,11] to incidence of COPD. Data are lacking regarding waist or hip circumference in relation to COPD incidence. We therefore examined BMI, waist circumference, hip circumference, waist–hip ratio and physical activity in relation to incidence of COPD in a large cohort of women and men in the US.

Methods

Study cohort and follow-up

The National Institutes of Health (NIH)–AARP Diet and Health Study[12] was originally designed to prospectively investigate dietary and lifestyle factors in relation to the development of cancer in a large US cohort of men and women aged 50 to 70 years at baseline in 1995–1996. Participants were recruited from among members of the AARP in 6 states (California, Florida, Pennsylvania, New Jersey, North Carolina and Louisiana) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). The NIH-AARP Diet and Health Study involved a large number of AARP members and cancer registries certified to have at least 90% completeness of case ascertainment. The study also included both rural and metropolitan areas, and geographic areas with large minority populations. The 3.5 million members who were invited to participate were sampled uniformly from the age distribution of 50 to 70 years. A total of 566 398 AARP members joined the study by returning a 16-page baseline questionnaire (avail-

able at http://dietandhealth.cancer.gov/resource) in 1995–1996, thereby expressing informed consent. Of those, 334 894 participants replied to a second questionnaire (available at http://dietandhealth.cancer.gov/resource) sent 6 months later to all respondents of the baseline questionnaire. A follow-up questionnaire (available at http://dietandhealth.cancer.gov/resource) was sent between 2004 and 2006 to all 475 297 nondeceased participants who had completed the baseline questionnaire and was completed by 318 449 participants.

Our analytic cohort comprised 113 279 participants who reported no history of COPD, cancer or heart disease at baseline, and who provided complete self-reported information on anthropometric measurements, physical activity, smoking and COPD incidence during follow-up. The distributions of age, sex and ethnicity of the analytic cohort are comparable to those of the overall cohort of the NIH-AARP Diet and Health Study (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.140025/-/DC1). However, because a history of COPD, cancer or heart disease is positively associated with adiposity, current smoking and low socioeconomic status, the analytic cohort had an anticipated slightly lower average BMI, a greater proportion of people who had never smoked and a great proportion of people who had completed postgraduate education than the overall cohort. Cohort follow-up, as estimated by the comprehensiveness of cancer and mortality ascertainment, is more than 93% complete.[13,14]

Ethics

The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the US National Cancer Institute.

Table 1 (part 1 of 2): Age-standardized* baseline characteristics by body mass index, waist circumference, hip circumference, waist–hip ratio and vigorous physical activity (NIH-AARP Diet and Health Study, 1995–1996)

	Levels within recommended guidelines, %†										
	BMI			Waist circumference‡		Hip circumference§		Waist–hip ratio¶		Vigorous physical activity**	
Variable	< 18.5 (No)	18.5–24.9 (Yes)	≥ 25.0 (No)	No	Yes	< Median	≥ Median	No	Yes	No	Yes
No. of participants	887	46 669	65 723	33 570	79 709	58 706	54 573	48 365	64 914	54 685	58 594
Age at baseline, mean, yr	63	63	62	63	62	62	62	62	63	62	63
Sex											
Female	69	53	34	46	40	42	42	72	20	45	39
Male	31	47	66	54	60	58	58	28	80	55	61
Marital status											
Married or common law	55	67	75	69	73	71	72	61	80	69	74
Not married	45	33	25	31	27	29	28	39	20	31	26
Postgraduate education											
No	72	72	76	77	73	73	75	75	73	77	71
Yes	28	28	24	23	27	27	25	25	27	23	29
Ethnicity											
White	96	95	94	95	94	94	95	94	95	94	95
Nonwhite	4	5	6	5	6	6	5	6	5	6	5
BMI											
< 18.5 (not recommended)	—	—	—	0	1	1	0	1	0	1	1
18.5–24.9 (recommended)	—	—	—	7	56	65	16	58	28	36	46
≥ 25.0 (not recommended)	—	—	—	93	43	34	84	41	72	63	53
Waist circumference within recommended guideline‡											
No	5	5	47	—	—	7	54	13	42	37	23
Yes	95	95	53	—	—	93	46	87	58	63	77

Continued

Assessment of anthropometric measurements and physical activity

Participants were instructed to measure their weight, height, and waist and hip circumferences. Anthropometric information from self-reported measurements is valid.[15,16]

We defined BMI categories according to the World Health Organization (WHO) classification,[17] and waist circumference categories according to the classifications proposed by Lean and colleagues[18] and the WHO.[19] We used the second lowest categories of BMI, waist circumference, hip circumference and waist–hip ratio as reference groups. The physical activity variable was based on validated self-reports[20] of frequency of vigorous physical activity at home or work, or for exercise.

Ascertainment of COPD cases

Participants indicated incidence of COPD between 1996 and 2006 using self-reported questionnaires. Self-reported COPD diagnoses are highly specific, although they tend to underascertain cases.[21,22]

Statistical analysis

We investigated BMI, waist and hip circumferences, waist–hip ratio and physical activity in relation to COPD incidence using relative risks (RRs) estimated as odds ratios and 95% confidence intervals (CIs) obtained from multivariable logistic regression, with additional adjustment for age, sex, marital status, education, ethnicity, alcohol intake, smoking status, smoking intensity, history of type 2 diabetes mellitus and height. Effect modification was assessed by like-

Table 1 (part 2 of 2): Age-standardized* baseline characteristics by body mass index, waist circumference, hip circumference, waist–hip ratio and vigorous physical activity (NIH-AARP Diet and Health Study, 1995–1996)

	Levels within recommended guidelines, %†										
	BMI			Waist circumference‡		Hip circumference§		Waist–hip ratio¶		Vigorous physical activity**	
Variable	< 18.5 (No)	18.5–24.9 (Yes)	≥ 25.0 (No)	No	Yes	< Median	≥ Median	No	Yes	No	Yes
Hip circumference§											
< Median	87	82	30	12	69	—	—	55	50	46	57
≥ Median	13	18	70	88	31	—	—	45	50	54	43
Waist–hip ratio within recommended guideline¶											
No	74	60	30	19	53	45	40	—	—	40	45
Yes	26	40	70	81	47	55	60	—	—	60	55
Physical activity level within recommended guideline**											
No	42	42	53	59	44	43	54	46	50	—	—
Yes	58	58	47	41	56	57	46	54	50	—	—
Smoking status											
Never	47	46	40	39	43	43	42	49	38	43	43
Distant past††	30	35	42	40	39	38	40	33	42	36	42
Recent past‡‡	7	8	11	13	9	9	11	9	11	10	9
Current	16	11	7	8	9	10	7	9	9	11	6
Alcohol intake, g/d, mean	12	12	14	13	13	13	13	9	16	13	13
History of type 2 diabetes mellitus											
No	97	97	93	92	96	96	94	97	93	95	95
Yes	3	3	7	8	4	4	6	3	7	5	5

BMI = body mass index, NIH = National Institutes of Health.
*Using direct standardization to the baseline age distribution of the cohort.
†Unless stated otherwise.
‡Recommended guideline for waist circumference was defined as less than 88 cm (women) or less than 102 cm (men).
§There is no World Health Organization recommendation for hip circumference. Thus, the dichotomous cut-off was defined by the sex-specific median. The median hip circumference was 102 cm in men and in women.
¶Recommended guideline for waist–hip ratio was defined as < 0.85 (women) or < 0.90 (men).
**Vigorous physical activity was defined as ≥ 20 minutes of exercise that was sufficient to increase breathing, increase heart rate or work up a sweat. Recommended guideline was defined as engaging in vigorous physical activity ≥ 3 times per week.
††Distant past defined as ≥ 10 years ago.
‡‡Recent past defined as < 10 years ago.

lihood-ratio tests. All p values correspond to 2-sided tests at the 5% significance level.

Results

Distribution of risk factors at baseline

Participants whose BMI, waist circumference, waist–hip ratio or physical activity levels fell within the recommended categories tended to have a higher level of education than those whose levels did not meet recommended guidelines. In addition, BMI was inversely associated with never having smoked and current smoking, whereas it was positively related to past smoking. In contrast, participants who met the recommendations for waist circumference were slightly more likely to currently smoke than those who did not meet the recommendations (Table 1).

Multivariate analyses of anthropometric measurements and physical activity in relation to COPD

Overweight and class 1 obesity were unrelated to COPD (Table 2). However, class 2 to 3 obesity

Table 2 (part 1 of 2): Relative risk of chronic obstructive pulmonary disease in relation to body mass index, waist circumference, hip circumference, waist–hip ratio and physical activity (NIH-AARP Diet and Health Study, 1996–2006)

Variable	COPD cases	*N*	Relative risk (95% CI)*				
			Adjusted for age and sex†	Model 1‡	Model 1 plus BMI§	Model 1 plus waist circumference¶	Model 1 plus BMI and hip circumference**
BMI							
< 18.5	54	887	1.76 (1.33–2.33)	1.50 (1.12–2.03)	—	1.56 (1.15–2.11)	—
18.5–24.9	1 552	46 669	1.00 (ref)	1.00 (ref)	—	1.00 (ref)	—
25.0–29.9	1 393	47 856	0.95 (0.88–1.02)	0.94 (0.87–1.02)	—	0.83 (0.76–0.91)	—
30.0–34.9	505	14 386	1.14 (1.03–1.26)	1.11 (1.00–1.24)	—	0.87 (0.76–0.99)	—
≥ 35.0	144	3 481	1.30 (1.09–1.55)	1.36 (1.13–1.63)	—	1.00 (0.80–1.24)	—
p_{trend}			0.04	0.03	—	0.04	—
Waist circumference, cm							
< 64 (women) < 80 (men)	35	1 110	1.09 (0.78–1.54)	1.13 (0.79–1.61)	1.03 (0.72–1.47)	—	0.99 (0.69–1.42)
64–79 (women) 80–93 (men)	1 330	47 815	1.00 (ref)	1.00 (ref)	1.00 (ref)	—	1.00 (ref)
80–87 (women) 94–101 (men)	937	30 784	1.08 (0.99–1.18)	1.02 (0.93–1.11)	1.10 (1.00–1.20)	—	1.14 (1.03–1.26)
88–109 (women) 102–117 (men)	1 185	30 188	1.36 (1.26–1.48)	1.22 (1.12–1.33)	1.36 (1.22–1.52)	—	1.44 (1.28–1.63)
≥ 110 (women) ≥ 118 (men)	161	3 382	1.76 (1.48–2.08)	1.47 (1.23–1.75)	1.55 (1.25–1.92)	—	1.72 (1.37–2.16)
p_{trend}			< 0.001	< 0.001	< 0.001	—	< 0.001
Hip circumference, cm							
< 86 (women) < 87 (men)	55	1 254	1.53 (1.16–2.02)	1.24 (0.93–1.66)	—	1.27 (0.95–1.70)	—
86–99 (women) 87–100 (men)	1 511	46 622	1.00 (ref)	1.00 (ref)	—	1.00 (ref)	—
100–105 (women) 101–106 (men)	876	31 334	0.88 (0.81–0.96)	0.94 (0.86–1.03)	—	0.85 (0.77–0.94)	—
106–124 (women) 107–119 (men)	1 081	30 486	1.05 (0.97–1.14)	1.10 (1.01–1.20)	—	0.86 (0.77–0.97)	—
≥ 125 (women) ≥ 120 (men)	125	3 583	1.09 (0.90–1.31)	1.16 (0.96–1.41)	—	0.78 (0.62–0.98)	—
p_{trend}			0.6	0.04	—	0.001	—

Continued

(RR 1.36, 95% CI 1.13–1.63) and underweight (RR 1.50, 95% CI 1.12–2.03) were positively associated with COPD. Additional adjustment for waist circumference attenuated COPD risk in the top BMI category and created inverse associations in the 2 intermediate BMI categories.

The highest waist circumference had a positive association with COPD both before (RR 1.47, 95% CI 1.23–1.75) and after (RR 1.55, 95% CI 1.25–1.92) adjustment for BMI (Table 2). The relation strengthened after additional adjustment for hip circumference (RR 1.72, 95% CI 1.37–2.16). In contrast, the group with the lowest waist circumference showed no association with COPD. The highest hip circumference had an inverse relation to COPD (RR 0.78, 95% CI 0.62–0.98). A positive association was observed between high waist–hip ratio and COPD (RR 1.46, 95% CI 1.23–1.73). A high level of physical activity was associated with a decreased risk of COPD (RR 0.71, 95% CI 0.63–0.79). These relations remained materially unchanged after exclusion of the first 5 years of follow-up (data not shown).

Multivariate analyses stratified by sex, ethnicity, education and smoking status

Sex did not modify the relations of BMI ($p_{interaction}$ = 0.07), waist circumference ($p_{interaction}$ = 0.6), waist–hip ratio ($p_{interaction}$ = 0.5) or physical activity

Table 2 (part 2 of 2): Relative risk of chronic obstructive pulmonary disease in relation to body mass index, waist circumference, hip circumference, waist–hip ratio and physical activity (NIH-AARP Diet and Health Study, 1996–2006)

Variable	COPD cases	*N*	Relative risk (95% CI)*				
			Adjusted for age and sex†	Model 1‡	Model 1 plus BMI§	Model 1 plus waist circumference¶	Model 1 plus BMI and hip circumference**
Waist–hip ratio							
< 0.67 (women) < 0.82 (men)	28	1 271	0.89 (0.61–1.29)	0.85 (0.58–1.25)	—	—	—
0.67–0.78 (women) 0.82–0.92 (men)	1 201	47 687	1.00 (ref)	1.00 (ref)	—	—	—
0.79–0.83 (women) 0.93–0.96 (men)	944	28 581	1.32 (1.21–1.43)	1.18 (1.08–1.30)	—	—	—
0.84–0.95 (women) 0.97–1.06 (men)	1 303	32 397	1.59 (1.47–1.72)	1.29 (1.18–1.40)	—	—	—
≥ 0.96 (women) ≥ 1.07 (men)	172	3 343	2.12 (1.80–2.49)	1.46 (1.23–1.73)	—	—	—
p_{trend}			< 0.001	< 0.001	—	—	—
Physical activity, times/wk							
0	757	14 442	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	—
< 1	564	14 731	0.76 (0.68–0.85)	0.84 (0.75–0.95)	0.85 (0.76–0.95)	0.85 (0.76–0.96)	—
1–2	829	25 512	0.64 (0.58–0.71)	0.79 (0.71–0.88)	0.80 (0.72–0.89)	0.81 (0.73–0.90)	—
3–4	900	33 969	0.51 (0.46–0.56)	0.71 (0.64–0.79)	0.73 (0.65–0.80)	0.74 (0.66–0.82)	—
≥ 5	598	24 625	0.47 (0.42–0.52)	0.67 (0.60–0.75)	0.68 (0.61–0.77)	0.71 (0.63–0.79)	—
p_{trend}			< 0.001	< 0.001	< 0.001	< 0.001	—

BMI = body mass index, CI = confidence interval, COPD = chronic obstructive pulmonary disease, NIH = National Institutes of Health.
*Unless stated otherwise.
†Adjusted for age (5-year groups) and sex (female, male).
‡Adjusted for age (5-year groups), sex (female, male), marital status (married or common law, never married, separated, divorced, widowed), education (high school or less than high school, vocational training or some college, college education, postgraduate education), ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, other ethnic background), alcohol intake (0, 0.1–14.9, 15.0–29.9, 30.0–59.9, ≥ 60 g/d), 31 combinations of smoking status (currently smoking, stopped smoking within the last 12 months, stopped smoking 1–4 years ago, stopped smoking 5–9 years ago, stopped smoking ≥ 10 years ago, never smoked) and smoking intensity (never smoked: 0 cigarettes/d; ever smoked: 1–10, 11–20, 21–30, 31–40, 41–60, ≥ 61 cigarettes/d), history of type 2 diabetes mellitus (no, yes) and height (sex-specific quintiles). The BMI, waist circumference and waist–hip ratio analyses were additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk).
§Additionally adjusted for BMI (< 18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, ≥ 35.0).
¶Additionally adjusted for waist circumference (women: < 64, 64–79, 80–87, 88–109, ≥ 110 cm; men: < 80, 80–93, 94–101, 102–117, ≥ 118 cm).
**Additionally adjusted for BMI (< 18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, ≥ 35.0) and hip circumference (women: < 86, 86–99, 100–105, 106–124, ≥ 125 cm; men: < 87, 87–100, 101–106, 107–119, ≥ 120 cm).

Table 3 (part 1 of 3): Multivariate-adjusted* relative risk of chronic obstructive pulmonary disease in relation to body mass index, waist circumference, hip circumference, waist–hip ratio and physical activity, stratified by smoking status (NIH-AARP Diet and Health Study, 1996–2006)

	Smoking status							
	Never *n* = 47 874		Distant past† *n* = 44 228		Recent past‡ *n* = 11 207		Current *n* = 9 970	
Variable	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§
BMI analysis 1¶								
< 18.5	11	2.17 (1.17–4.02)	8	1.34 (0.65–2.74)	4	1.00 (0.35–2.82)	31	1.50 (0.99–2.28)
18.5–24.9	220	1.00 (ref)	344	1.00 (ref)	266	1.00 (ref)	722	1.00 (ref)
25.0–29.9	250	1.41 (1.17–1.70)	427	1.00 (0.86–1.16)	313	0.85 (0.71–1.02)	403	0.76 (0.66–0.87)
30.0–34.9	91	1.55 (1.21–2.00)	176	1.26 (1.04–1.53)	103	0.80 (0.62–1.02)	135	1.00 (0.81–1.23)
≥ 35.0	31	1.75 (1.18–2.58)	44	1.35 (0.97–1.87)	35	1.06 (0.72–1.56)	34	1.49 (1.01–2.21)
p_{trend}		< 0.001		0.02		0.3		0.4
$p_{interaction}$ < 0.001								
BMI analysis 2**								
< 18.5	11	2.30 (1.22–4.32)	8	1.28 (0.62–2.65)	4	1.15 (0.40–3.27)	31	1.54 (1.01–2.35)
18.5–24.9	220	1.00 (ref)	344	1.00 (ref)	266	1.00 (ref)	722	1.00 (ref)
25.0–29.9	250	1.28 (1.03–1.60)	427	0.88 (0.74–1.04)	313	0.65 (0.53–0.80)	403	0.72 (0.62–0.85)
30.0–34.9	91	1.26 (0.92–1.74)	176	0.99 (0.77–1.26)	103	0.51 (0.37–0.68)	135	0.87 (0.67–1.13)
≥ 35.0	31	1.36 (0.86–2.17)	44	1.00 (0.68–1.49)	35	0.62 (0.39–0.98)	34	1.19 (0.75–1.86)
p_{trend}		0.3		0.9		<0.001		0.08
$p_{interaction}$ < 0.001								
Waist circumference analysis 1, cm††								
< 64 (women) < 80 (men)	5	0.84 (0.35–2.06)	11	2.08 (1.12–3.86)	2	0.56 (0.13–2.30)	17	1.00 (0.59–1.68)
64–79 (women) 80–93 (men)	214	1.00 (ref)	314	1.00 (ref)	200	1.00 (ref)	602	1.00 (ref)
80–87 (women) 94–101 (men)	146	1.07 (0.87–1.33)	274	1.16 (0.98–1.37)	187	1.03 (0.83–1.27)	330	0.90 (0.78–1.05)
88–110 (women) 102–117 (men)	215	1.49 (1.22–1.81)	349	1.35 (1.15–1.58)	289	1.30 (1.07–1.59)	332	0.95 (0.82–1.11)
≥ 110 (women) ≥ 118 (men)	23	1.69 (1.08–2.63)	51	1.58 (1.16–2.16)	43	1.32 (0.92–1.89)	44	1.48 (1.04–2.11)
p_{trend}		< 0.001		< 0.001		0.002		0.5
$p_{interaction}$ = 0.004								
Waist circumference analysis 2, cm‡‡								
< 64 (women) < 80 (men)	5	0.74 (0.30–1.83)	11	1.84 (0.98–3.45)	2	0.45 (0.11–1.92)	17	0.89 (0.53–1.52)
64–79 (women) 80–93 (men)	214	1.00 (ref)	314	1.00 (ref)	200	1.00 (ref)	602	1.00 (ref)
80–87 (women) 94–101 (men)	146	1.00 (0.78–1.28)	274	1.25 (1.04–1.51)	187	1.34 (1.06–1.69)	330	1.04 (0.89–1.23)
88–109 (women) 102–117 (men)	215	1.30 (0.98–1.73)	349	1.45 (1.15–1.82)	289	2.12 (1.62–2.78)	332	1.22 (0.98–1.51)
≥ 110 (women) ≥ 118 (men)	23	1.56 (0.90–2.72)	51	1.64 (1.10–2.47)	43	2.49 (1.55–3.99)	44	1.73 (1.12–2.68)
p_{trend}		0.04		0.007		< 0.001		0.007
$p_{interaction}$ = 0.007								

Continued

($p_{interaction}$ = 0.3) to COPD. In contrast, the relation of hip circumference to COPD was more pronounced among women than men. The RRs for increasing hip circumference categories in women were 1.76, 1.0 (ref.), 0.98, 0.92 and 0.67. The corresponding values in men were 1.07, 1.0 (ref.), 0.73, 0.77 and 0.80 ($p_{interaction}$ = 0.008). The relations of BMI, body shape and physical activity to COPD did not vary by ethnicity or educational achievement (all $p_{interaction} \geq 0.1$).

Smoking significantly modified the associations of BMI, waist circumference, hip circumference and waist–hip ratio (all $p_{interaction} \leq 0.01$), but not physical activity ($p_{interaction}$ = 0.7) with COPD (Table 3).

Significant positive associations between

Table 3 (part 2 of 3): Multivariate-adjusted* relative risk of chronic obstructive pulmonary disease in relation to body mass index, waist circumference, hip circumference, waist–hip ratio and physical activity, stratified by smoking status (NIH-AARP Diet and Health Study, 1996–2006)

	Smoking status							
	Never *n* = 47 874		Distant past† *n* = 44 228		Recent past‡ *n* = 11 207		Current *n* = 9 970	
Variable	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§
Hip circumference, cm§§								
< 86 (women) < 87 (men)	5	1.32 (0.53–3.25)	15	1.77 (1.04–3.01)	8	1.17 (0.56–2.45)	27	1.03 (0.67–1.56)
86–99 (women) 87–100 (men)	212	1.00 (ref)	345	1.00 (ref)	257	1.00 (ref)	697	1.00 (ref)
100–105 (women) 101–106 (men)	145	0.99 (0.78–1.25)	261	0.89 (0.74–1.07)	185	0.73 (0.59–0.91)	285	0.82 (0.70–0.97)
106–124 (women) 107–119 (men)	219	1.08 (0.83–1.40)	335	0.99 (0.81–1.22)	240	0.66 (0.52–0.85)	287	0.77 (0.63–0.95)
≥ 125 (women) ≥ 120 (men)	22	0.81 (0.48–1.39)	43	0.95 (0.64–1.40)	31	0.57 (0.35–0.91)	29	0.76 (0.48–1.21)
p_{trend}		0.7		0.4		0.001		0.02
$p_{interaction}$ = 0.01								
Waist–hip ratio¶¶								
< 0.67 (women) < 0.82 (men)	5	0.78 (0.32–1.90)	8	1.07 (0.52–2.17)	1	0.19 (0.03–1.37)	14	1.02 (0.57–1.80)
0.67–0.78 (women) 0.82–0.92 (men)	230	1.00 (ref)	317	1.00 (ref)	186	1.00 (ref)	468	1.00 (ref)
0.79–0.83 (women) 0.93–0.96 (men)	148	1.14 (0.92–1.40)	255	1.20 (1.02–1.42)	181	1.34 (1.08–1.65)	360	1.22 (1.05–1.41)
0.84–0.95 (women) 0.97–1.06 (men)	202	1.39 (1.15–1.69)	376	1.50 (1.28–1.74)	316	1.68 (1.39–2.03)	409	1.07 (0.92–1.23)
≥ 0.96 (women) ≥ 1.07 (men)	18	1.36 (0.84–2.22)	43	1.65 (1.19–2.29)	37	1.68 (1.16–2.44)	74	1.52 (1.15–2.00)
p_{trend}		0.002		< 0.001		< 0.001		0.02
$p_{interaction}$ < 0.001								
Physical activity analysis 1, times/wk								
0	105	1.00 (ref)	146	1.00 (ref)	135	1.00 (ref)	371	1.00 (ref)
< 1	74	0.80 (0.59–1.09)	135	0.93 (0.73–1.18)	116	0.94 (0.72–1.22)	239	0.77 (0.65–0.93)
1–2	151	0.93 (0.72–1.20)	212	0.84 (0.67–1.04)	167	0.83 (0.65–1.06)	299	0.69 (0.59–0.82)
3–4	152	0.72 (0.56–0.92)	300	0.78 (0.64–0.96)	188	0.73 (0.58–0.93)	260	0.67 (0.56–0.80)
≥ 5	121	0.81 (0.62–1.06)	206	0.68 (0.55–0.85)	115	0.64 (0.49–0.83)	156	0.65 (0.53–0.80)
p_{trend}		0.07		< 0.001		< 0.001		< 0.001
$p_{interaction}$ = 0.7								

Continued

Table 3 (part 3 of 3): Multivariate-adjusted* relative risk of chronic obstructive pulmonary disease in relation to body mass index, waist circumference, hip circumference, waist–hip ratio and physical activity, stratified by smoking status (NIH-AARP Diet and Health Study, 1996–2006)

	Smoking status							
	Never *n* = 47 874		Distant past† *n* = 44 228		Recent past‡ *n* = 11 207		Current *n* = 9 970	
Variable	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§	COPD cases	RR (95% CI)§
Physical activity analysis 2, times/wk* **								
0	105	1.00 (ref)	146	1.00 (ref)	135	1.00 (ref)	371	1.00 (ref)
< 1	74	0.82 (0.60–1.11)	135	0.94 (0.74–1.19)	116	0.95 (0.73–1.23)	239	0.78 (0.65–0.93)
1–2	151	0.97 (0.75–1.25)	212	0.86 (0.69–1.07)	167	0.85 (0.67–1.08)	299	0.70 (0.59–0.82)
3–4	152	0.77 (0.60–0.99)	300	0.82 (0.67–1.01)	188	0.77 (0.60–0.97)	260	0.67 (0.56–0.80)
≥ 5	121	0.89 (0.68–1.17)	206	0.73 (0.59–0.91)	115	0.68 (0.52–0.88)	156	0.65 (0.53–0.80)
p_{trend}		0.3		0.004		0.001		< 0.001
$p_{interaction} = 0.7$								

Note: BMI = body mass index, CI = confidence interval, COPD = chronic obstructive pulmonary disease, NIH = National Institutes of Health, RR = relative risk.
*Adjusted for age (5-year groups), sex (female, male), marital status (married or common law, never married, separated, divorced, widowed), education (high school or less than high school, vocational training or some college, college education, postgraduate education), ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, other ethnic background), alcohol intake (0, 0.1–14.9, 15.0–29.9, 30.0–59.9, ≥ 60 g/d), history of type 2 diabetes mellitus (no, yes) and height (sex-specific quintiles). Analyses involving participants who formerly and currently smoked were additionally adjusted for those of the 30 combinations of smoking status (currently smoking, stopped smoking within the last 12 months, stopped smoking 1–4 years ago, stopped smoking 5–9 years ago, stopped smoking ≥ 10 years ago, never smoked) and smoking intensity (never smoked: 0 cigarettes per day; ever smoked: 1–10, 11–20, 21–30, 31–40, 41–60, ≥ 61 cigarettes/d) applicable to the smoking stratum. See footnotes ¶ to *** for additional exposure-specific adjustment factors.
†Distant past defined as ≥ 10 years ago.
‡Recent past defined as < 10 years ago.
§Unless stated otherwise.
¶BMI analysis 1 was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk).
**BMI analysis 2 was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk) and waist circumference (women: < 64, 64–79, 80–87, 88–109, ≥ 110 cm; men: < 79, 79–93, 94–101, 102–116, ≥ 117 cm).
††Waist circumference analysis 1 was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk).
‡‡Waist circumference analysis 2 was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk), hip circumference (women: < 86,86–99,100–105, 106–124, ≥ 125 cm; men: < 87, 87–100, 101–106, 107–119, ≥ 120 cm) and BMI (< 18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, ≥ 35.0).
§§The hip circumference analysis was additionally adjusted for waist circumference (women: < 64, 64–79, 80–87, 88–107, ≥ 108 cm; men: < 79, 79–93, 94–101, 102–116, ≥ 117 cm).
¶¶The waist–hip–ratio analysis was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk).
***Physical activity analysis 2 was additionally adjusted for waist circumference (women: < 64, 64–79, 80–87, 88–107, ≥ 108 cm; men: < 79, 79–93, 94–101, 102–116, ≥ 117 cm).

BMI and COPD were seen among participants who had never smoked ($p_{trend} < 0.001$) and those who had smoked in the distant past ($p_{trend} = 0.02$), but not among participants who had smoked in the recent past ($p_{trend} = 0.3$) or those who currently smoked ($p_{trend} = 0.4$). Underweight was significantly associated with COPD only among participants who had never smoked. After additional adjustment for waist circumference, the risk estimates for high BMI in relation to COPD were decreased in all smoking strata, and BMI was inversely associated with COPD among those who had smoked in the recent past ($p_{trend} < 0.001$).

Waist circumference showed significant positive associations with COPD in all smoking strata. In contrast, the inverse relation of hip circumference to COPD was apparent only among those who had smoked in the recent past ($p_{trend} = 0.001$) and who currently smoked ($p_{trend} = 0.02$). Low hip circumference was positively associated with COPD among those who had smoked in the distant past. Waist–hip ratio was positively associated with COPD in all smoking groups. Physical activity was inversely related to COPD in all smoking strata, although the association was not significant among those who had never smoked ($p_{trend} = 0.07$), particularly after adjustment for waist circumference ($p_{trend} = 0.3$).

Multivariate analyses of the combination of BMI and waist circumference by smoking status

In the entire analytic cohort, the risk of COPD was increased among overweight or obese participants only if they had a large waist circumference (Table 4). That pattern was particularly evident among those who had never smoked and, to a certain degree, among those who had smoked in the distant past. The pattern was not apparent among participants who had smoked in the recent past or who currently smoked ($p_{interaction} < 0.001$).

We further stratified the joint analyses of BMI and waist circumference by level of physical activity (Table 4). Among those who had never smoked, the previously observed pattern of increased COPD risk among overweight and obese participants with a large waist circumference was seen both for those with high and low levels of physical activity. Smoking status affected the joint relations of BMI and waist circumference more strongly among those with a high level of physical activity ($p_{interaction} = 0.004$) than among those with a low level of physical activity ($p_{interaction} = 0.06$).

Interpretation

The primary findings from this large, prospective study of middle-aged to older women and men in the US are that total and abdominal obesity were associated with an increased risk of COPD. Participants with a large waist circumference (≥ 110 cm in women or ≥ 118 cm in men) had a 72% increased risk of COPD. A secondary finding is that underweight was related to a 56% increased risk of COPD. In contrast, increased hip circumference and physical activity were associated with a decrease in COPD risk by up to 29%.

Table 4 (part 1 of 2): Multivariate-adjusted* relative risk of chronic obstructive pulmonary disease in relation to combinations of body mass index, waist circumference and physical activity in the entire analytic cohort and stratified by smoking status (NIH-AARP Diet and Health Study, 1996–2006)

Combination† of BMI, waist circumference and physical activity	RR (95% CI) for entire analytic cohort	Smoking status; RR (95% CI)				$p_{interaction}$
		Never	Distant past‡	Recent past§	Current	
Entire analytic cohort¶						< 0.001
BMI 18.5–24.9						
Small waist circumference**	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Large waist circumference††	1.13 (0.93–1.38)	1.17 (0.70–1.95)	1.48 (1.01–2.16)	1.15 (0.76–1.73)	0.91 (0.66–1.26)	
BMI 25.0–29.9						
Small waist circumference**	0.84 (0.76–0.92)	1.11 (0.90–1.38)	0.91 (0.77–1.07)	0.72 (0.58–0.89)	0.75 (0.64–0.87)	
Large waist circumference††	1.12 (1.01–1.23)	1.60 (1.27–2.01)	1.19 (0.99–1.43)	1.15 (0.94–1.42)	0.83 (0.69–0.99)	
BMI ≥ 30.0						
Small waist circumference**	0.87 (0.70–1.10)	1.29 (0.78–2.12)	1.13 (0.78–1.63)	0.54 (0.31–0.94)	0.72 (0.47–1.11)	
Large waist circumference††	1.21 (1.09–1.34)	1.65 (1.32–2.08)	1.33 (1.11–1.60)	0.93 (0.74–1.17)	1.12 (0.93–1.36)	
Participants with a high level of physical activity‡‡						0.004
BMI 18.5–24.9						
Small waist circumference**	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Large waist circumference††	1.05 (0.75–1.46)	1.33 (0.61– 2.87)	1.18 (0.63–2.19)	1.35 (0.72–2.54)	0.65 (0.34–1.23)	
BMI 25.0–29.9						
Small waist circumference**	0.91 (0.80–1.04)	1.17 (0.86– 1.58)	0.99 (0.79–1.23)	0.81 (0.59–1.09)	0.78 (0.60–1.01)	
Large waist circumference††	1.17 (1.00–1.36)	1.78 (1.27–2.50)	1.24 (0.95–1.62)	1.27 (0.92–1.74)	0.65 (0.45–0.93)	
BMI ≥ 30.0						
Small waist circumference**	0.84 (0.59–1.21)	1.31 (0.61–2.83)	1.12 (0.66–1.92)	0.44 (0.16–1.22)	0.60 (0.27–1.32)	
Large waist circumference††	1.33 (1.12–1.58)	1.50 (1.01–2.23)	1.73 (1.33–2.24)	1.00 (0.69–1.47)	1.03 (0.69–1.54)	

Continued

Table 4 (part 2 of 2): Multivariate-adjusted* relative risk of chronic obstructive pulmonary disease in relation to combinations of body mass index, waist circumference and physical activity in the entire analytic cohort and stratified by smoking status (NIH-AARP Diet and Health Study, 1996–2006)

Combination† of BMI, waist circumference and physical activity	RR (95% CI) for entire analytic cohort	Smoking status; RR (95% CI)				$p_{interaction}$
		Never	Distant past‡	Recent past§	Current	
Participants with a low level of physical activity§§						0.06
BMI 18.5–24.9						
Small waist circumference**	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Large waist circumference††	1.18 (0.93–1.51)	1.07 (0.54–2.13)	1.70 (1.05–2.76)	1.02 (0.59–1.75)	1.07 (0.73–1.55)	
BMI 25.0–29.9						
Small waist circumference**	0.78 (0.69–0.88)	1.06 (0.78–1.44)	0.82 (0.64–1.05)	0.64 (0.48–0.86)	0.73 (0.60–0.89)	
Large waist circumference††	1.09 (0.96–1.23)	1.50 (1.10–2.04)	1.13 (0.87–1.46)	1.06 (0.81–1.39)	0.91 (0.74–1.12)	
BMI ≥ 30.0						
Small waist circumference**	0.90 (0.67–1.19)	1.28 (0.66–2.46)	1.10 (0.67–1.82)	0.58 (0.30–1.12)	0.80 (0.47–1.34)	
Large waist circumference††	1.16 (1.02–1.31)	1.74 (1.30–2.32)	1.11 (0.86–1.42)	0.88 (0.66–1.16)	1.18 (0.95–1.47)	

Note: CI = confidence interval, NIH = National Institutes of Health, RR = relative risk.
*Adjusted for age (5-year groups), sex (female, male), marital status (married or common law, never married, separated, divorced, widowed), education (high school or less than high school, vocational training or some college, college education, postgraduate education), ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, other ethnic background), alcohol intake (0, 0.1–14.9, 15.0–29.9, 30.0–59.9, ≥ 60 g/d), history of type 2 diabetes mellitus (no, yes) and height (sex-specific quintiles). Analyses involving participants who formerly and currently smoked were additionally adjusted for those of the 30 combinations of smoking status (currently smoking, stopped smoking within the last 12 months, stopped smoking 1–4 years ago, stopped smoking 5–9 years ago, stopped smoking ≥ 10 years ago, never smoked) and smoking intensity (never smoked: 0 cigarettes per day; ever smoked: 1–10, 11–20, 21–30, 31–40, 41–60, ≥ 61 cigarettes/d) applicable to the smoking stratum.
†Underweight participants (BMI < 18.5, *n* = 887) were excluded from the analysis because of a lack of cases in underweight participants with a waist circumference of ≥ 88 cm (women) and ≥ 102 cm (men). For similar reasons, participants with a waist circumference of < 64 cm (women) or < 80 cm (men) were excluded (*n* = 984).
‡Distant past defined as ≥ 10 years ago.
§Recent past defined as < 10 years ago.
¶The multivariate analysis was additionally adjusted for physical activity (0, < 1, 1–2, 3–4, ≥ 5 times/wk).
**A small waist circumference was defined as a waist circumference of < 88 cm (women) and < 102 cm (men).
††A large waist circumference was defined as a waist circumference of ≥ 88 cm (women) and ≥ 102 cm (men).
‡‡A high level of physical activity was defined as engaging in vigorous physical activity ≥ 3 times/wk.
§§A low level of physical activity was defined as engaging in vigorous physical activity < 3 times/wk.

Data have been lacking regarding the relations of waist circumference, hip circumference and waist–hip ratio to COPD incidence. One cohort study[23] of visceral fat and respiratory function did not exclude patients with COPD at baseline, so the relation of visceral fat to COPD incidence could not be established. Another cohort study[24] observed that a decline in respiratory function during follow-up was associated with a gain in visceral fat mass during follow-up but was not able to discern whether the gain in visceral fat mass was the cause or the consequence of the decline in respiratory function.

In addition, the large size of our prospective study provided substantial power to evaluate BMI and physical activity in relation to COPD risk, as well as to examine potential differential associations according to smoking status, a major determinant of COPD.[5] Previous data on BMI and COPD incidence are limited to 2 small studies.[8,9] One prospective study from China[8] reported an increased risk of COPD among people with BMI values less than 18.5 (RR 2.88, 95% CI 1.06–7.85) compared with BMI values of 18.5 or greater. In contrast, when modelling BMI as a continuous variable, a significant positive association between BMI and COPD was observed in that study[8] (RR [per 1-unit BMI increase] 1.14, 95% CI 1.02–1.26). One retrospective US study[9] observed an increased risk of COPD among people with BMI values below 24.3 (RR 2.76, 95% CI 1.15–6.59) compared with BMI values of 26.6 or greater. Data regarding obese values of BMI in relation to COPD were not presented in those studies.[8,9] Inverse associations between physical activity and risk of COPD have been previously reported from a Danish cohort[10] and a Japanese case–control study.[11]

Chronic obstructive pulmonary disease is thought to be caused by toxic particles inhaled from tobacco smoke,[25,26] air pollution[27] or occupational dust,[28] which damage the lung through oxidative stress, chronic local inflammation and disturbed tissue repair.[5] Increased local,[29] abdominal[29] and overall fat depots[30] increase local and systemic inflammation,[31] thus potentially stimulating COPD-related processes in the lung.

We observed a stronger positive relation with abdominal body fat than with total body fat and COPD. In particular, overweight as measured by BMI emerged as a significant predictor of increased risk of COPD only among those with a large waist circumference. Visceral fat depots may play a greater role in the development of COPD than overall or subcutaneous fat depots because visceral fat depots produce more proinflammatory cytokines.[32] One cross-sectional analysis involving people without COPD found that waist circumference and waist–hip ratio were inversely associated with lung function, whereas BMI was unrelated to lung function.[33]

In our study, increased waist circumference and waist–hip ratio were robust predictors of COPD in participants who had never smoked and who had ever smoked, the latter of whom are at increased COPD risk. By comparison, the relations of BMI to COPD were inconsistent across smoking strata, which may have been due to strong residual confounding by smoking.

Underweight BMI was positively associated with COPD both before and after adjustment for waist circumference. Because underweight BMI adjusted for waist circumference represents an indirect marker of low muscularity, particularly in the elderly,[34] we suspect that low muscularity is positively associated with development of COPD. Similarly, if hip circumference adjusted for waist circumference represented an indirect marker of gluteal muscularity, our finding of an inverse association between hip circumference and COPD suggests that large gluteal muscularity protects against COPD.

Engaging in physical activity 5 or more times per week was associated with a 29% decreased risk of COPD. Relevant biologic mechanisms are speculative, but they include physical activity–induced reductions in oxidative stress[35] and chronic inflammation,[36] factors that promote COPD. In addition, physical activity improves processes of lung repair[37] and reduces obesity.[38] In our study, the inverse effect estimates for physical activity were strongest among those who currently smoked, and they became progressively less pronounced across strata of those who smoked in the recent past, distant past and never. Residual confounding by smoking is one possible explanation for this constellation of findings. Also, the inverse association between physical activity and COPD may have been susceptible to reverse causation because lung damage in COPD reduces exercise capacity.[39]

Limitations and strengths

Limitations of our study include potential measurement errors due to self-reported anthropometric and physical activity variables. However, validation studies of assessments of anthropometric variables and physical activity comparable to those used in our study indicate that our measurements are reasonably reliable and valid.[15,16,20] Moreover, because the data regarding anthropometry and physical activity were collected before COPD diagnosis, any measurement errors would have weakened, not strengthened, the associations.

Another potential limitation of our study is the absence of spirometry data to confirm COPD. Self-reported COPD diagnoses have imperfect validity,[21,22] but reporting is not affected by sex, age, BMI, socioeconomic status, smoking or comorbidities,[40] which suggests that any potential misclassification of COPD status in our study would have biased results toward the null hypothesis.[41] Also, our results for BMI and physical activity in relation to COPD are broadly consistent with previous data from studies that used spirometry-based definitions of COPD,[8–11] which suggests that our findings are not merely an artifact of COPD misclassification at baseline or follow-up.

It is possible that our findings were affected by protopathic bias induced by excessive visceral fat[42] or lack of physical activity[7] increasing the rate of progression of subclinical COPD.

A further potential limitation is the predominantly white sample. However, we observed no effect variation by ethnicity.

Strengths of our study include the large sample size, which yielded precise risk estimates and allowed for extensive stratification by smoking status. Detailed anthropometric assessments allowed us to discern the independent and joint effects of abdominal and overall adiposity on COPD risk. Our prospective study design largely precluded recall and selection biases. Specific care was taken to adjust for a broad range of potential confounding variables. We reduced the potential for reverse causation by excluding participants with pre-existing chronic diseases at baseline and excluding the first 5 years of follow-up in a sensitivity analy-

sis. Concern remains regarding reverse causation because the induction time for development of clinically relevant COPD exceeds our follow-up period.[43]

Conclusion

We found that obesity, in particular abdominal obesity, represents an important risk factor for incidence of COPD. We also noted that underweight was positively related to COPD, an association we suspect is at least partly attributable to the effects of low muscularity. By comparison, large hip circumference and increased physical activity levels were related to decreased COPD risk. Our findings suggest that next to smoking cessation and the prevention of smoking initiation, meeting guidelines for body weight, body shape and physical activity level may represent important individual and public health opportunities to decrease the risk of COPD. Physicians should encourage their patients to adhere to these guidelines as a means of preventing chronic diseases in general and possibly COPD in particular.

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