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 3,648 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.
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 greater 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)

| Variable                        | No. of participants | BMI < 18.5 (No) | BMI 18.5–24.9 (Yes) | BMI ≥ 25.0 (No) | Waist circumference | Hip circumference | Waist–hip ratio | Vigorous physical activity ** |
|---------------------------------|---------------------|-----------------|---------------------|-----------------|--------------------|-------------------|-----------------|-----------------------------|
| Age at baseline, mean, yr       | 113 279             | 887             | 46 669              | 65 723          | 33 570             | 79 709            | 58 706          |                             |
| Sex                             |                     |                 |                     |                 | 54 573             |                   | 48 365          |                             |
| Female                          | 69                  | 53               | 62                  | 62              | 62                 | 62                | 62              | 62                          |
| Male                            | 31                  | 47               | 66                  | 60              | 58                 | 58                | 28              | 80                          |
| Marital status                  |                     |                 |                     |                 | 69                 | 73                | 71              |                             |
| Married or common law           | 55                  | 67               | 75                  | 69              | 71                 | 72                | 61              | 80                          |
| Not married                     | 45                  | 33               | 25                  | 31              | 29                 | 28                | 39              | 20                          |
| Postgraduate education          |                     |                 |                     |                 | 77                 | 73                | 73              |                             |
| No                              | 72                  | 72               | 76                  | 73              | 73                 | 75                | 73              | 77                          |
| Yes                             | 28                  | 28               | 24                  | 23              | 27                 | 25                | 25              | 27                          |
| Ethnicity                       |                     |                 |                     |                 | 94                 | 94                | 94              |                             |
| White                           | 96                  | 95               | 94                  | 95              | 94                 | 94                | 94              | 94                          |
| Nonwhite                        | 4                   | 5                | 5                   | 6               | 5                  | 6                 | 6               | 5                           |
| BMI < 18.5 (not recommended)    |                     |                 |                     |                 | 0                  | 1                 | 1               | 0                           |
| BMI 18.5–24.9 (recommended)     |                     |                 |                     |                 | 7                  | 56                | 65              | 16                          |
| BMI ≥ 25.0 (not recommended)    |                     |                 |                     |                 | 93                 | 43                | 34              | 84                          |
| Waist circumference within recommended guideline‡ |                 |                 |                     |                 | 47                 | 54                | 13              | 42                          |
| No                              | 5                   | 5                | 5                   | 0               | 1                  | 1                 | 0               | 0                           |
| Yes                             | 95                  | 95               | 53                  | 7               | 54                 | 13                | 42              | 37                          |

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 colleagues18 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-reports20 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)

| Variable                          | Levels within recommended guidelines, %† | BMI < 18.5 (No) | BMI 18.5–24.9 (Yes) | BMI ≥ 25.0 (No) | Waist circumference‡ | Hip circumference§ | Waist–hip ratio¶ | Vigorous physical activity** |
|----------------------------------|------------------------------------------|----------------|---------------------|----------------|---------------------|---------------------|------------------|--------------------------|
| 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 guideline¶|                                          |                |                     |                |                     |                     |                  |                          |
| No                               |                                          | 74             | 60                  | 30             | 19                  | 53                  | 45               | 40                       | —                        | —                        | 40                       | 45                       |
| Yes                              |                                          | 26             | 40                  | 70             | 81                  | 47                  | 55               | 60                       | —                        | —                        | 60                       | 55                       |
| Physical activity level 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 104 cm 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.
likelihood-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 | Adjusted for age and sex† | Model 1‡ | Model 1 plus BMI§ | Model 1 plus waist circumference¶ | Model 1 plus BMI and hip circumference** |
|---|
| BMI | 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) | 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) |
| < 80 (men) | 1 330 | 47 815 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | — | 1.00 (ref) |
| 64–79 (women) | 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) |
| 80–93 (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) |
| 8–9 (women) | 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) |
| ≥ 110 (women) | 12 5 | 3 583 | 1.09 (0.90–1.31) | 1.16 (0.96–1.41) | — | 0.78 (0.62–0.98) | — |
| p_trend | < 0.001 | < 0.001 | < 0.001 | — | < 0.001 |
| Hip circumference, cm | | | | | | |
| < 86 (women) | 55 | 1 254 | 1.53 (1.16–2.02) | 1.24 (0.93–1.66) | — | 1.27 (0.95–1.70) | — |
| < 87 (men) | 1 511 | 46 622 | 1.00 (ref) | 1.00 (ref) | — | 1.00 (ref) | — |
| 86–99 (women) | 1 105 (men) | 31 334 | 0.88 (0.81–0.96) | 0.94 (0.86–1.03) | — | 0.85 (0.77–0.94) | — |
| 100–106 (men) | 107–119 (men) | 3 486 | 1.05 (0.97–1.14) | 1.10 (1.01–1.20) | — | 0.86 (0.77–0.97) | — |
| ≥ 125 (women) | 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 | — | — |
(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 hip circumference. Additional adjustment for BMI category and created inverse associations in positive association with COPD both before the 2 intermediate BMI categories.

(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 (pinteraction = 0.07), waist circumference (pinteraction = 0.6), waist–hip ratio (pinteraction = 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     | 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)            | 28         | 1 271 | 0.89 (0.61–1.29)          | 0.85 (0.58–1.25) | —                 |                                   |                                        |
| < 0.82 (men)              | 1 201      | 47 687| 1.00 (ref)                | 1.00 (ref) | —                 |                                   |                                        |
| 0.67–0.78 (women)         | 944        | 28 581| 1.32 (1.21–1.43)          | 1.18 (1.08–1.30) | —                 |                                   |                                        |
| 0.82–0.92 (men)           | 1 303      | 32 397| 1.59 (1.47–1.72)          | 1.29 (1.18–1.40) | —                 |                                   |                                        |
| ≥ 0.96 (women)            | 172        | 3 343 | 2.12 (1.80–2.49)          | 1.46 (1.23–1.73) | —                 |                                   |                                        |
| ≥ 1.07 (men)              |            |       |                           |          |                   |                                   |                                        |
| pinteraction              |            |       | < 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)                 |                                        |
| pinteraction              |            |       | < 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, 0.1–1.49, 1.50–29.9, 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).
§Adjusted for BMI (< 18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, ≥ 35.0).
¶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)

| 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    | 0.002         | 0.3        | 0.4           |

*Interaction < 0.001

**BMI analysis 2**

| Variable                      | COPD cases | RR (95% CI)§ | COPD cases | RR (95% CI)§ | COPD cases | RR (95% CI)§ |
|-------------------------------|------------|---------------|------------|---------------|------------|---------------|
| **Waist circumference analysis 1, cm††** |            |               |            |               |            |               |
| < 64 (women)                  | 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) |
| < 80 (men)                    | 214        | 1.00 (ref)    | 314        | 1.00 (ref)    | 200        | 1.00 (ref)    | 602        | 1.00 (ref)    |
| 64–79 (women) 80–93 (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) |
| 80–87 (women) 94–101 (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) |
| 88–110 (women) 102–117 (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           |

*Interaction = 0.004

**Waist circumference analysis 2, cm‡‡**

| Variable                      | COPD cases | RR (95% CI)§ | COPD cases | RR (95% CI)§ | COPD cases | RR (95% CI)§ |
|-------------------------------|------------|---------------|------------|---------------|------------|---------------|
| < 64 (women)                  | 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) |
| < 80 (men)                    | 214        | 1.00 (ref)    | 314        | 1.00 (ref)    | 200        | 1.00 (ref)    | 602        | 1.00 (ref)    |
| 64–79 (women) 80–93 (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) |
| 80–87 (women) 94–101 (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) |
| 88–109 (women) 102–117 (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         |

*Interaction = 0.007

Continued
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 ($p_{\text{interaction}} = 0.008$). The relations of BMI, body shape and physical activity to COPD did not vary by ethnicity or educational achievement (all $p_{\text{interaction}} \geq 0.1$).

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

| Variable                                      | Smoking status | COPD cases | COPD cases | COPD cases | COPD cases |
|-----------------------------------------------|----------------|------------|------------|------------|------------|
|                                               | Never n = 47 874 | (95% CI)§ | (95% CI)§ | (95% CI)§ | (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) |
| $p_{\text{trend}}$                             | 0.7            | 0.4        | 0.001      | 0.02       |
| $p_{\text{interaction}} = 0.01$                |                |            |            |            |            |
| 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) |
| $p_{\text{trend}}$                             | 0.002          | < 0.001    | < 0.001    | 0.02       |
| $p_{\text{interaction}} < 0.001$               |                |            |            |            |            |
| 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) |
| $p_{\text{trend}}$                             | 0.07           | < 0.001    | < 0.001    | < 0.001    |            |
| $p_{\text{interaction}} = 0.7$                 |                |            |            |            |            |

Continued
BMI and COPD were seen among participants who had never smoked ($p_{\text{trend}} < 0.001$) and those who had smoked in the distant past ($p_{\text{trend}} = 0.02$), but not among participants who had smoked in the recent past ($p_{\text{trend}} = 0.3$) or those who currently smoked ($p_{\text{trend}} = 0.4$). 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 ($p_{\text{trend}} < 0.001$).

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 ($p_{\text{trend}} = 0.001$) and who currently smoked ($p_{\text{trend}} = 0.02$). 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 ($p_{\text{trend}} = 0.07$), particularly after adjustment for waist circumference ($p_{\text{trend}} = 0.3$).

**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 ($p_{\text{interaction}} < 0.001$).
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 ($p_{\text{interaction}} = 0.004$) than among those with a low level of physical activity ($p_{\text{interaction}} = 0.06$).

**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 ($\geq 110$ cm in women or $\geq 118$ 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) | $p_{\text{interaction}}$ |
|---|---|---|---|
| **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 $\geq 30.0$ | | | | | |
| 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 $\geq 30.0$ | | | | | |
| 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
Data have been lacking regarding the relations of waist circumference, hip circumference and waist–hip ratio to COPD incidence. One cohort study\(^5\) 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\(^6\) 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.\(^7\) 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. Data regarding obese values of BMI in COPD incidence are limited to 2 small 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, air pollution or occupational dust, which damage the lung through oxidative stress, chronic local inflammation and disturbed tissue repair. Increased local abdominal and overall fat depots increase local and systemic inflammation, 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. 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.

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, 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 and chronic inflammation, factors that promote COPD. In addition, physical activity improves processes of lung repair and reduces obesity. 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.

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. 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, but reporting is not affected by sex, age, BMI, socioeconomic status, smoking or comorbidities, which suggests that any potential misclassification of COPD status in our study would have biased results toward the null hypothesis. 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, 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 or lack of physical activity 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.45

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.

References
1. Arne M, Janson C, Janson S, et al. Physical activity and quality of life in subjects with chronic disease: chronic obstructive pulmonary disease compared with rheumatoid arthritis and diabetes mellitus. Scand J Prim Health Care 2009;27:141-7.
2. Fletcher MJ, Upton J, Taylor-Fishwick J, et al. COPD uncovered: an international survey on the impact of chronic obstructive pulmonary disease (COPD) on a working age population. BMC Public Health 2011;11:612.
3. Morbidity and mortality: 2012 chartbook on cardiovascular, lung and blood diseases. Bethesda (MD): National Institutes of Health, National Heart, Lung and Blood Institute; 2012. Available: www.nhlbi.nih.gov/resources/docs/cht-book.htm (accessed 2013 July 11).
4. Chronic obstructive pulmonary disease. In: European lung white book. Lausanne (Switzerland): European Respiratory Society and European Lung Foundation; 2003: 34-43. Available: http://dev.eursn.org/268-white-book.htm (accessed 2013 July 11).
5. Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet 2012;379:1341-51.
6. Franssen FM, O’Donnell DE, Goossens GH, et al. Obesity and COPD. Thorax 2008;63:1110-7.
7. Gimeno-Santos E, Frei A, Steurer-Stey C, et al. Determinants and outcomes of physical activity in patients with COPD: a systematic review. Thorax 2014 Feb 20 [Epub of print].
8. Zhou Y, Wang D, Liu S, et al. The association between BMI and COPD: the results of two population-based studies in Guangzhou, China. COPD 2013;10:567-72.
9. Harik-Khan R, Fleg JL, Wise RA. Body mass index and the risk of COPD. Chest 2002;121:370-6.
10. Garcia-Aymerich J, Lange P, Benet M, et al. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. Am J Respir Crit Care Med 2007;175:458-63.
11. Hirayama F, Lee AH, Hirama T. Life-long physical activity involvement reduces the risk of chronic obstructive pulmonary disease: a case-control study in Japan. J Phys Act Health 2010;7:622-6.
12. Schatzkin A, Subar AF, Thompson FE, et al. Design and serendipity in establishing a large cohort with wide dietary intake distributions: the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol 2001;154:1119-25.
13. Hill ME. Rosenwaike I. The Social Security Administration’s Death Master File: the completeness of death reporting at older ages. Soc Secur Bull 2001–2002;64:45-51.
14. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax Nationwide Death Search. Am J Epidemiol 1994;140:1016-9.
15. McMannis MA, Van Dam RM, Hu FB. Comparison of self-reported and measured BMI as correlates of disease markers in US adults. Obesity (Silver Spring) 2007;15:188-96.
16. Rimm EB, Stampfer MJ, Colditz GA, et al. Validity of self-reported waist and hip circumferences in men and women. Epidemiology 1990;1:466-73.
17. Waist circumference and waist-hip ratio: report of a WHO expert consultation Geneva, 8–11 December 2008. Geneva (Switzerland): World Health Organization; 2011. Available: http://whqlibdoc.who.int/publications/2011/9789241501491_eng.pdf (accessed 2013 Feb 5).
18. Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. BMJ 1995;311:158-61.
19. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:1-253.
20. Marshall AL, Smith BJ, Bauman AE, et al. Reliability and validity of a brief physical activity assessment for use by family doctors. Br J Sports Med 2005;39:294-7.
21. Muggah E, Graves E, Bennett C, et al. Ascertainment of chronic diseases using population health data: a comparison of health administrative data and patient self-report. BMC Public Health 2013:13:16.
22. Hill K, Goldstein RS, Guyatt GH, et al. Prevalence and under-diagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. CMAJ 2010;182:673-8.
23. Rossi AP, Watson NL, Newman AB, et al. Effects of body composition and adipose tissue distribution on respiratory function in elderly men and women: the health, aging, and body composition study. J Gerontol A Biol Sci Med Sci 2011;66:801-8.
24. Rossi A, Fantin F, Di Francesco V, et al. Body composition and pulmonary function in the elderly: a 7-year longitudinal study. Int J Obes (Lond) 2008;32:1423-30.
25. Lokek A, Lange P, Scharling H, et al. Developing COPD: a 25 year follow up study of the general population. Thorax 2000;55:199-203.
26. Eisner MD, Balmes J, Katz PP, et al. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease, Environ Health 2005;4:7.
27. Lindgren A, Stroh E, Montemeyer P, et al. Traffic-related air pollution associated with prevalence of asthma and COPD/chronic bronchitis. A cross-sectional study in Southern Sweden. Int J Health Geogr 2009;8:2.
28. Blanc PD, Jih-Jih C, Truong L, et al. Occupational exposures and the risk of COPD: dusty trades revisited. Thorax 2009;64:6-12.
29. Watson RA, Pride NB, Thomas EL, et al. Relation between trunk volume and reduction of total lung capacity in obese men. J Appl Physiol 2012;112:118-26.
30. Flegal KM, Shepherd JA, Looker AC, et al. Comparisons of percentage body fat, body mass index, waist circumference, and waist to hip ratio as correlates of body composition studied in men and women. Am J Clin Nutr 2009;89:500-8.
31. Karastergiou K, Mohamed-Ali V. The autocrine and paracrine roles of adipokines. Mol Cell Endocrinol 2010;318:69-78.
32. Koemen TB, Stienstra R, van Tijt LJ, et al. The inflammomaome and caspase-1 activation: a new mechanism underlying increased inflammatory activity in human visceral adipose tissue. Endocrinology 2011;152:3769-78.
33. Wannamethee SG, Shaper AG, Whincup PH. Body fat distribution, body composition, and respiratory function in elderly men. Am J Clin Nutr 2005;82:996-1003.
34. Hu FB. Obesity epidemiology. Oxford (UK): Oxford University Press; 2008.
35. Miyazuki H, Oh-ishi S, Ookayama T, et al. Strenuous endurance training in humans reduces oxidative stress following exhausting exercise. Eur J Appl Physiol 2001;84:1-6.
36. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. J Am Coll Cardiol 2005;45:1563-9.
37. Toledo AC, Magalhaes RM, Hizume DC, et al. Aerobic exercise training in humans reduces oxidative stress following exhausting exercise. Eur J Appl Physiol 2009;109:254-64.
38. Wing RR. Physical activity in the treatment of the adulthood overweight and obesity: current evidence and research issues. Med Sci Sports Exerc 1999;31:5457-52.
39. Wata H, Wadschi B, Meyer T, et al. Physical activity in patients with COPD. Eur Respir J 2009;33:626-72.
40. Hvidsten SC, Storesund L, Wentzel-Larsen T, et al. Prevalence and predictors of undiagnosed chronic obstructive pulmonary dis-
ease in a Norwegian adult general population. Clin Respir J 2010; 4:13-21.

41. Barr RG, Herbstman J, Speizer FE, et al. Validation of self-reported chronic obstructive pulmonary disease in a cohort study of nurses. Am J Epidemiol 2002;155:965-71.

42. van den Borst B, Gosker HR, Schols AM. Central fat and peripheral muscle: partners in crime in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2013;187:8-13.

43. Mannino DM, Reichert MM, Davis KJ. Lung function decline and outcomes in an adult population. Am J Respir Crit Care Med 2006;173:985-90.

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