ORIGINAL ARTICLE

Depressive Symptoms and Change in Abdominal Obesity in Older Persons

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Context: Depression has been hypothesized to result in abdominal obesity through the accumulation of visceral fat. No large study has tested this hypothesis longitudinally.

Objective: To examine whether depressive symptoms predict an increase in abdominal obesity in a large population-based sample of well-functioning older persons.

Design: The Health, Aging, and Body Composition Study, an ongoing prospective cohort study with 5 years of follow-up.

Setting: Community-dwelling older persons residing in the areas surrounding Pittsburgh, Pennsylvania, and Memphis, Tennessee.

Participants: A total of 2088 well-functioning white and black persons aged 70 to 79 years.

Main Outcome Measures: Baseline depression was defined as a Center for Epidemiological Studies Depression score of 16 or higher. At baseline and after 5 years, overall obesity measures included body mass index (calculated as weight in kilograms divided by height in meters squared) and percentage of body fat (measured by dual-energy x-ray absorptiometry). Abdominal obesity measures included waist circumference, sagittal diameter, and visceral fat (measured by computed tomography).

Results: After adjustment for sociodemographics, lifestyle, diseases, and overall obesity, baseline depression was associated with a 5-year increase in sagittal diameter ($\beta = .054$; $P = .01$) and visceral fat ($\beta = .080$; $P = .001$).

Conclusions: This study shows that depressive symptoms result in an increase in abdominal obesity independent of overall obesity, suggesting that there may be specific pathophysiological mechanisms that link depression with visceral fat accumulation. These results might also help explain why depression increases the risk of diabetes and cardiovascular disease.

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DEPRESSION IS COMMON IN later life. Clinically relevant depressive symptoms are present in 10% to 15% of the older population.[1] According to the World Health Organization, depression is one of the leading disorders causing disability and will be the second most important cause of disability worldwide in 2020.[2] Depression has been associated with the onset of diabetes, cardiovascular disease (CVD), and cardiac mortality.[3-6] To better prevent occurrence of these major disabling and life-threatening diseases, more insight into underlying mechanisms relating depression to these disorders is needed.

Neuroendocrine disturbances found in depressed persons include dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and hypothalamic-pituitary-gonadal axis, indicated by high levels of cortisol[7,8] and low levels of sex-steroid hormones,[9] respectively. In addition, high levels of inflammatory markers have been observed in persons who report clinically relevant depressive symptoms.[10] Similar abnormalities have been identified in persons with abdominal obesity.[11,12] Consequently, Björntorp[13] hypothesized that chronic stress and/or depression results in abdominal obesity through long-term activation of the HPA axis. Björntorp argued that elevated cortisol, particularly when combined with low sex-steroid hormones, causes fat to accumulate in visceral adipose tissue. This might be owing to specific properties of visceral fat such as a high density of glucocorticoid receptors.[14] Excess visceral fat, as indicated by abdominal obesity, subsequently has been found to predict diabetes, CVD, and mortality to a greater degree than overall obesity.[15-18]

Until now, no large study has longitudinally tested the hypothesis that depressive symptoms lead to an increase in visceral fat. Some cross-sectional studies report an association between abdominal obesity and depression[19-24] independent of overall obesity. One prospective study found that 29 patients with major depression had a larger increase in visceral fat than 17 persons without depression.[25]

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The present study investigates the longitudinal association between depressive symptoms at baseline and 5-year changes in abdominal obesity in a large community sample of older persons. We hypothesize that depressive symptoms at baseline will predict an increase in abdominal obesity over time and that this association is specific to abdominal obesity compared with overall obesity.

METHODS

STUDY POPULATION

Data are from 3075 well-functioning white and black men and women aged 70 to 79 years enrolled in the Health, Aging, and Body Composition (Health ABC) study, an ongoing prospective cohort study. Participants were recruited in 1997 and 1998 from a sample of white and black Medicare-eligible beneficiaries residing in the areas surrounding Pittsburgh, Pennsylvania, and Memphis, Tennessee. Race was self-identified and black persons were oversampled to examine race differences. Subjects were eligible if they reported no difficulty walking for a quarter of a mile, walking up 10 steps, or performing activities of daily living. Subjects were ineligible if they had severe difficulty communicating, had active cancer treatment in the past 3 years, had plans to move out of the area, or were participating in a randomized trial of a lifestyle intervention. All participants signed an informed written consent form approved by the institutional review boards of the clinical sites. In the present study, persons with missing baseline data on depressive symptoms and/or obesity were excluded (n=26). In addition, persons without obesity data at the 5-year assessment in 2002 and 2003 were excluded (n=961; 375 persons had died, 13 were lost to follow-up, 63 did not participate that year, and 510 were assessed by phone interview only), leaving 2088 persons for the present analysis. Included persons (n=2088) were younger (73.4 vs 74.1 years at baseline; $P<.001$); more often women (52.7% vs 48.9%; $P=.05$), white (63.6% vs 47.2%; $P<.001$), and college educated (46.7% vs 32.8%; $P<.001$); and had lower rates of depression at baseline (4.0% vs 6.2%; $P=.007$) than excluded persons (n=987).

DEPRESSIVE SYMPTOMS

During the baseline interview, depressive symptoms were measured with the 20-item Center for Epidemiologic Studies Depression (CES-D) scale assessing depressive symptoms in the previous week.[26] This scale, ranging from 0 to 60, has been widely used in older populations and has been shown to be a valid and reliable instrument for elderly persons.[27] In our study the internal consistency was high (Cronbach $\alpha=0.81$). A score of 16 or higher, the usual cut-off, identified persons with clinically relevant depressive symptoms. Although this definition does not reflect a psychiatric diagnosis of depression, for convenience in this article we will refer to this cut-off measure as *depression*. In addition, the CES-D 10-item version, which has shown good predictive accuracy when compared with the 20-item CES-D scale,[28] was administered at follow-up after 2, 3, 4, and 5 years. For sensitivity analyses, depressed persons were subdivided into persons who were only depressed at baseline (single depression) and those who also had depression at at least 1 follow-up assessment (CES-D $\geq$ 10; persistent or recurrent depression).

OBESITY

All obesity measures were assessed at the clinic visit at baseline and after 5 years.

Overall Obesity

Body weight was measured on a standard balance beam scale to the nearest 0.1 kg. Height was measured barefoot using a wall-mounted stadiometer to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight in kilograms divided by the height in meters squared. Total mass (grams) and total fat mass (grams) were determined via a whole-body dual energy x-ray absorptiometry scan using fan beam technology (QDR4500A; Hologic, Waltham, Massachusetts). The percentage of body fat was defined as (total fat mass/total mass) $\times$ 100; when total mass was missing, weight (grams) was used instead.

Abdominal Obesity

Computed tomographic (CT) scanning was performed at the level between the fourth and fifth lumbar vertebrae to measure visceral fat (centimeters squared) using a Somatom Plus 4 (Siemens, Erlangen, Germany) or a Picker PQ 2000S (Marconi Medical Systems, Cleveland, Ohio) scanner in Memphis and a 9800 Advantage scanner (General Electric, Milwaukee, Wisconsin) in Pittsburgh. The scans were conducted at 120 kilovolt (peak) (kVp) and 200 to 250 mA/s at a slice thickness of 10 mm. Areas were calculated by multiplying the number of pixels of a given tissue type by the pixel area using IDL development software (Research Systems Inc, Boulder, Colorado). Visceral fat was manually distinguished from abdominal subcutaneous fat by tracing along the fascial plane defining the internal abdominal wall. Quality of repositioning on CT scans between baseline and the 5-year assessment was rated, incorporating abdominal level and anatomical landmarks. In addition to the continuous measure of 5-year change in visceral fat, a categorical measure was constructed defining loss, no change, or gain of visceral fat. A cut-off of 30% change in visceral fat was selected because this approximated 1 SD in the visceral fat–change score. Besides the direct CT measure of visceral fat, some anthropometric measures were assessed. Maximum sagittal diameter (centimeters), the distance between the abdomen and back, was derived from the CT scans. Waist circumference (centimeters) was measured at the largest abdominal circumference to the nearest 0.1 cm using a flexible plastic tape measure.

BASELINE CHARACTERISTICS

Sociodemographic characteristics included age, sex, race (white, black), site (Pittsburgh, Memphis), and education (less than high school, high school, postsecondary education). We also assessed lifestyle characteristics known to be related to both abdominal obesity and depression: smoking status (nonsmoker, former, or current), current alcohol consumption (0-1 vs $\geq$2 drinks per day), and physical activity (sum of weight training, high- and medium-intensity exercise, aerobic dance, [exercise] walking, and stair climbing [in kilocalories per week]). Presence of baseline diabetes and CVD (including stroke or transient ischemic attack, myocardial infarction, angina pectoris, percutaneous transluminal coronary angioplasty, or coronary artery bypass grafting) were adjudicated using standardized algorithms considering various sources of information: self-report, medication use, oral glucose tolerance testing, and medical claims data from the former Health Care Financing Administration. The number of other chronic diseases was mainly based on self-report and included congestive heart failure, peripheral arterial disease, cancer, lung disease, osteoarthritis, osteoporosis, gastrointestinal disease, prostate disease, thyroid disease, Parkinson disease, and kidney disease. In addition, all medications regularly taken in the 2 weeks before baseline were recorded and coded according to the Iowa Drug

Information System (IDIS).[29] From this inventory, the total number of prescription medications taken was calculated. In addition, use of antidepressant medication was ascertained, which included monoamine oxidase inhibitors (IDIS code 281605), tricyclic or tetracyclic antidepressants (IDIS code 281606), selective serotonin reuptake inhibitors (IDIS code 281607), and other antidepressants (IDIS code 281604), regardless of reason. Other psychoactive medication included antipsychotic (phenothiazines, IDIS code 281609; butyrophenones, IDIS code 282610; other, IDIS code 281608) and anxiolytic (benzodiazepines, barbiturates, other, IDIS code 2824) medication.

STATISTICAL ANALYSIS

Sample characteristics were compared between depressed and nondepressed persons using χ^2 statistics for dichotomous and categorical variables and independent *t* tests for continuous variables. Because some of the obesity measures differ greatly between men and women, sex-adjusted means were presented based on analyses of covariance. Paired-sample *t* tests were performed to assess whether 5-year changes in obesity were statistically significant. To evaluate the association between depressive symptoms at baseline (both continuous as well as dichotomous) and 5-year change in abdominal obesity, linear regression analyses were conducted with abdominal obesity change scores as the outcome. For comparison, associations between depressive symptoms and overall obesity were also presented. Covariates were a priori selected and initial analyses were adjusted for the corresponding baseline obesity measure and sociodemographic variables (sex, age, race, site, and education). Next, to assess whether results were independent of baseline overall obesity, abdominal obesity analyses were additionally adjusted for BMI. Finally, because lifestyle, abdominal obesity–related diseases, and general health status might partly explain the association between abdominal obesity and depression, we examined their role by additionally adjusting analyses for smoking, alcohol consumption, physical activity, prevalent diabetes, prevalent CVD, number of other chronic diseases, and number of prescription medications taken.

Because depression has also been associated with weight loss,[30,31] it is possible that a U-shaped association exists between depression and change in visceral fat, with depression being associated with both gain and loss of visceral fat. Therefore, it was checked whether baseline depression was also associated with a decrease in visceral fat distinct from a potential increase in visceral fat. For this purpose, an adjusted multinomial logistic regression analysis was performed using categories of visceral fat change (loss, no change, gain) as the outcome. By choosing the no change group as the reference category, this analysis gives 2 odds ratios, one assessing the risk of losing visceral fat when depressed at baseline, and one assessing the risk of gaining visceral fat when depressed at baseline. Furthermore, to verify that the association between depression and visceral fat was independent of change in BMI, a linear regression analysis was performed with change in visceral fat as the outcome, adjusted for change in BMI. In addition, it was tested whether an interaction existed with change in BMI to assess whether the relationship between depression and change in visceral fat was consistent across the whole range from weight loss and weight stability to weight gain.

Because sex differences in the relationships between depression, abdominal obesity, and CVD have been observed[3,18] and because fat distribution differs across sex and race, all analyses were repeated including sex × depression and sex-specific race × depression interaction terms to test whether findings were consistent across sex and race. For graphing purposes, adjusted mean 5-year changes in abdominal obesity were calculated using analyses of covariance. Finally, because a significant proportion of persons enrolled at baseline did not have a clinic visit after 5 years, leaving the most healthy persons for analysis, missing values at follow-up were multiply imputed. Multiple imputation was established by Multivariate Imputation by Chained Equations[32] using *R*-statistical software. Obesity follow-up measures were only imputed if depression and the corresponding obesity measure at baseline were not missing. Missing follow-up obesity values were 5 times imputed by predictive mean matching using information from all available covariates (sex, age, race, site, education, smoking status, alcohol consumption, physical activity, prevalent diabetes, prevalent CVD, number of other chronic diseases, number of prescription medications taken, antidepressant medication, other psychoactive medication), predictors (CES-D score; depression, yes or no; persistent depression, yes or no), the corresponding baseline obesity measure, BMI and change in BMI for abdominal obesity measures, and visceral fat and change in visceral fat for overall obesity measures. Fully adjusted (including adjustment for yes or no imputed value) linear regression analyses that associated depression with change in obesity were conducted on each of the 5 newly created data sets and the results were pooled.

RESULTS

SAMPLE CHARACTERISTICS

At baseline, the mean (SD) age of the participants was 73.4 (2.8) years, 52.7% were women, and 36.4% were black. Depression was present in 4.0% of participants and the mean (SD) BMI was 27.3 (4.7). Women had a greater percentage of body fat than men (40.5% vs 29.5%) but had less visceral fat (130.7 cm^2 vs 157.4 cm^2). Overall, 5-year changes in obesity were small, although some increases in obesity were seen in men while decreases in abdominal obesity were observed in women, especially in visceral fat (–11.4 cm^2), consistent with earlier reported findings in this older sample.[33] Visceral fat correlated more strongly with waist circumference (Pearson $r=0.63$) and sagittal diameter (Pearson $r=0.75$) than with BMI (Pearson $r=0.54$). **Table 1** shows the sample characteristics for persons with and without depression. Persons with baseline depression were less educated, had more chronic diseases, and were taking more prescription medication. Depressed persons had slightly higher sex-adjusted percentages of body fat at baseline (35.2% vs 36.6%; $P=.02$) and showed a larger sex-adjusted 5-year increase in sagittal diameter (0.2 cm vs 0.9 cm; $P=.007$) and visceral fat (–7.1 cm^2 vs 9.0 cm^2; $P=.001$) than nondepressed persons.

BASELINE DEPRESSIVE SYMPTOMS AND 5-YEAR CHANGE IN ABDOMINAL OBESITY

Table 2 describes the results of adjusted linear regression analyses assessing the association between baseline CES-D score (continuous) and depression (CES-D ≥ 16) with 5-year changes in obesity measures. No significant associations were found for the continuous CES-D score or the depression variable with 5-year changes in overall obesity (BMI or percentage of body fat). In contrast, after full adjustment for covariates, baseline de-

Table 1. Sample Characteristics

Characteristic	CES-D < 16 (n=2004)	CES-D ≥ 16 (n=84)	*P* Value[a]
Sociodemographic variables, %			
Mean (SD) age, y	73.4 (2.8)	73.6 (2.9)	.50
Black	36.3	38.1	.74
Memphis site	50.0	42.9	.20
Education			
<High school	21.6	27.4	.05
High school	31.2	36.9	
Postsecondary	47.2	35.7	
Lifestyle variables, %			
Current smoker	7.7	11.9	.16
>1 Alcoholic drink per day	7.3	7.1	.96
Mean (SD) physical activity, kcal/wk	1177 (2023)	1118 (2615)	.80
Somatic comorbidities, %			
Prevalent diabetes	20.9	17.9	.50
Prevalent cardiovascular disease	21.1	25.0	.39
Mean (SD) No. of other chronic diseases	1.2 (1.0)	1.5 (1.1)	.02
Mean (SD) No. of prescription medications	3.0 (2.4)	4.2 (3.4)	.002
Depression variables, %			
Mean (SD) baseline CES-D score, 0-60	3.8 (3.7)	20.9 (5.3)	<.001
Baseline antidepressant use	5.0	13.1	.001
Baseline other psychoactive medication use	6.3	22.6	<.001
Obesity variables			
Mean (SD) overall obesity			
BMI	27.3 (4.7)	27.9 (4.7)	.28
Percentage of body fat	35.2 (5.2)	36.6 (5.2)	.02
5-y Change in BMI	−0.0 (1.8)	0.2 (2.2)	.18
5-y Change in percentage of body fat	0.4 (2.7)[b]	0.3 (2.7)	.78
Mean (SD) abdominal obesity			
Waist circumference, cm	99.3 (12.2)	100.7 (12.2)	.29
Sagittal diameter, cm	23.5 (3.3)	23.5 (3.3)	.87
Visceral fat, cm^2	142.8 (64.7)	155.7 (64.7)	.08
5-y Change in waist circumference, cm	−0.8 (9.3)[b]	0.9 (9.3)	.09
5-y Change in sagittal diameter, cm	0.2 (2.1)[b]	0.9 (2.1)[b]	.007
5-y Change in visceral fat, cm^2	−7.1 (40.4)[b]	9.0 (40.4)	.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CES-D, Center for Epidemiological Studies Depression scale.

[a] Based on χ^2 test for dichotomous and categorical variables and on independent *t* test for continuous variables; for obesity variables, sex-adjusted means and standard deviations are presented based on analyses of covariance.

[b] Paired-sample *t* test indicated statistically significant 5-y increase or decrease in (abdominal) obesity; $P \leq .001$.

pression was associated with increases in sagittal diameter (β = .054; *P* = .01) and visceral fat (β = .080; *P* = .001) with a trend for an increase in waist circumference (β = .031, *P* = .08). For the continuous CES-D score these associations were still consistent but somewhat attenuated (waist circumference β = .026, *P* = .15; sagittal diameter β = .037, *P* = .10; visceral fat β = .042, *P* = .07).

ROLE OF WEIGHT CHANGE

To check whether depressive symptoms were also associated with a loss in abdominal obesity, an adjusted multinomial logistic regression analysis was performed using visceral fat change categories (≥30% loss, no change, ≥30% gain) as the outcome. Persons with baseline depression had odds of 0.43 (95% CI, 0.18-1.04; *P* = .06; ie, a decreased risk) to lose visceral fat and odds of 2.06 (95% CI, 1.04-4.05; *P* = .04; ie, an increased risk) to gain visceral fat compared with having no change in visceral fat, indicating a linear association between baseline depression and change in visceral fat. To verify that the association between depression and visceral fat was independent of change in BMI, the association between depression and visceral fat, as reported in Table 2, was additionally adjusted for change in BMI. The relationship between depression and change in visceral fat remained statistically significant (β = .050; *P* = .009). Furthermore, no interaction between depression and change in BMI in the association with visceral fat was found (*P* = .95).

SEX AND RACE DIFFERENCES

To examine whether associations between depression and abdominal obesity were consistent across sex and race, sex × depression and sex-specific race × depression interaction terms were included in the fully adjusted models assessing the association between depression and change in abdominal obesity as described in Table 2. A significant sex × depression interaction (*P* = .03) was found for change in visceral fat only. No race interactions were found for men (all *P* > .20), but in women, trends for race × depression interactions in predicting 5-year change in abdominal obe-

Table 2. Baseline Depressive Symptoms and 5-Year Change in Obesity

	Overall Obesity				Abdominal Obesity					
	BMI (n=2088)		Percentage of Body Fat (n=1944)		Waist Circumference (n=2067)		Sagittal Diameter (n=1885)		Visceral Fat (n=1752)	
	β	*P* Value	β	*P* Value	β	*P* Value	β	*P* Value	β	*P* Value
Continuous CES-D score										
Sociodemographics[a]	.037	.09	.012	.59	.028	.16	.048	.04	.045	.06
+Overall obesity[b]					.032	.07	.044	.05	.045	.05
+Lifestyle and diseases[c]	.035	.11	.007	.76	.026	.15	.037	.10	.042	.08
Depression (CES-D ≥ 16)										
Sociodemographics[a]	.033	.13	.003	.88	.034	.08	.061	.006	.079	.001
+Overall obesity[b]					.034	.05	.057	.008	.079	.001
+Lifestyle and diseases[c]	.030	.18	−.002	.94	.031	.08	.054	.01	.080	.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CES-D, Center for Epidemiological Studies Depression scale.

[a] Linear regression analyses adjusted for corresponding baseline obesity measure, sex, age, race, site, and education.

[b] Previous model plus baseline BMI for abdominal obesity measures.

[c] Previous model plus smoking, alcohol consumption, physical activity, prevalent diabetes, prevalent cardiovascular disease, number of other chronic diseases, and number of prescription medications taken.

sity were found for waist circumference ($P=.06$), sagittal diameter ($P=.09$), and visceral fat ($P=.08$). Because race interactions were found in women only, subsequent analyses were stratified by sex and race. Depression rates across sex × race groups were as follows: white men (n=683), 3.5%; white women (n=645), 4.3%; black men (n=304), 3.3%; and black women (n=456), 4.8%. Stratification showed that the association between depression and 5-year change in visceral fat was generally consistent across sex and race with the exception of black women (white men $\beta=.154$, $P<.001$; white women $\beta=.078$, $P=.05$; black men $\beta=.121$, $P=.06$; black women $\beta=-.029$, $P=.54$). To graph these findings for all abdominal obesity measures, adjusted mean 5-year changes in abdominal obesity were calculated for persons with and without baseline depression using analyses of covariance stratified by sex and race (**Figure**). The Figure shows that baseline depression was associated with an increase in abdominal obesity, while persons without depression showed a much smaller increase or even a decrease in abdominal obesity over 5 years. This finding was consistent across all abdominal obesity measures and across sex and race, with the exception of black women.

ADDITIONAL ANALYSES

To assess the robustness of our findings, a set of sensitivity analyses was conducted. First, the association between depression and change in abdominal obesity was assessed in persons with a single depression at baseline (n=17) and in those with persistent/recurrent depression (n=67). These analyses showed rather consistent associations for both depression groups (waist circumference $\beta=.016$, $P=.36$ and $\beta=.027$, $P=.13$; sagittal diameter $\beta=.028$, $P=.21$ and $\beta=.047$, $P=.03$; visceral fat $\beta=.070$, $P=.002$ and $\beta=.055$, $P=.02$, respectively). To ensure that associations between depression and increase in abdominal fat were not due to antidepressant use, the analyses described in Table 2 were additionally adjusted for antidepressant use, which did not change the results in any meaningful way. Similar results were also found when adjusting for other psychoactive medications. Also, when persons with a low quality of repositioning on the CT scans (n=84) were excluded from the analyses, associations with increases in visceral fat were comparable. Finally, to include all persons with baseline obesity data and to check the potential effect of selective drop-out, analyses were conducted after multiple imputation for missing values. When repeating the fully adjusted analyses described in Table 2, associations between depression and change in abdominal obesity largely remained (waist circumference n=3038, $\beta=.021$, $P=.27$; sagittal diameter n=2998, $\beta=.041$, $P=.03$; visceral fat n=2931, $\beta=0.073$, $P<.001$).

COMMENT

This study examined whether depressive symptoms could predict an increase in abdominal obesity over time in a large community-based sample of older persons. As hypothesized, depressed persons showed a significantly greater increase in abdominal obesity over 5 years, especially in visceral fat, than nondepressed persons. Such an association was not found for an increase in overall obesity and also appeared to be independent of changes in overall obesity, suggesting that depressive symptoms are rather specifically associated with fat gain in the visceral region.

To our knowledge, this is the first study to examine the association between depressive symptoms and increases in abdominal obesity over time in a large cohort. Our results are consistent with a study by Weber-Hamann et al[25] that showed a larger accumulation of visceral fat mass over time in 29 depressed patients compared with 17 controls. Most studies so far have assessed the association between abdominal obesity and depression cross-sectionally, using either anthropometric measures alone or CT measures in relatively small study

samples.[19-24] Most of these studies showed a positive relationship between depression and abdominal obesity, although one large epidemiological study could not demonstrate an association between waist circumference and depression.[34] In our study, associations with waist circumference were also weaker than those with visceral fat, possibly owing to the fact that waist circumference is only an indirect measure of visceral fat and is determined by both abdominal subcutaneous and visceral fat mass. Also, measuring waist circumference might be less precise than CT scanning. Stronger associations were found for sagittal diameter, which is considered a better indicator of visceral fat than waist circumference in older persons.[35] Our results indeed show a higher correlation of sagittal diameter (r=0.75) than waist circumference (r=0.63) with visceral fat. Most pronounced, however, were the associations with visceral fat, which is in line with our hypothesis that depressive symptoms contribute to an accumulation of visceral fat specifically.

Although depression has been associated with weight loss,[30,31] our results show an increase in visceral fat in persons with depressive symptoms, even in this aging population where decreases in fat mass are common.[36] We found no evidence that depression would result in a loss of visceral fat. In fact, we found that depression was negatively associated with a loss of visceral fat, indicating that depression is linearly linked with the accumulation of visceral fat and no U-shaped association exists. Furthermore, depression appeared to be specifically associated with abdominal obesity stronger than and independent of overall obesity. Associations between depressive symptoms and overall obesity were not found, and adjusting abdominal obesity analyses for baseline BMI did not influence findings. We additionally adjusted for change in BMI, which was partly an overadjustment because changes in BMI also reflect changes in visceral fat. However, despite this relatively strict adjustment, the relationship between depression and change in visceral fat remained. Moreover, our results showed that across the whole range of weight change, an association existed between depression and visceral fat, suggesting that even in persons who lost weight, visceral fat was preferentially retained in those with depression. The finding that associations were specific for abdominal obesity is in line with other studies showing that abdominal obesity, more than overall obesity, is associated with poor health outcomes such as diabetes, CVD, and mortality.[15-18] Because both depression and diabetes and CVD appear to be specifically associated with excess visceral fat, this could help explain the frequently found increased risk of diabetes and CVD in depressed persons.

Our results indicate that depression predicts increases in abdominal obesity in all but black women. Reasons for this exception are not entirely clear. One explanation may be that the black women in this older sample experienced a relatively large decrease in visceral fat, which might have obscured the association between depressive symptoms and the accumulation of visceral fat. Alternatively, this could have been a chance finding due to small sample sizes after stratification by sex and race. However, expected associations were found for the other 3 sex × race groups. Future research should explore sex and race differences further in younger samples.

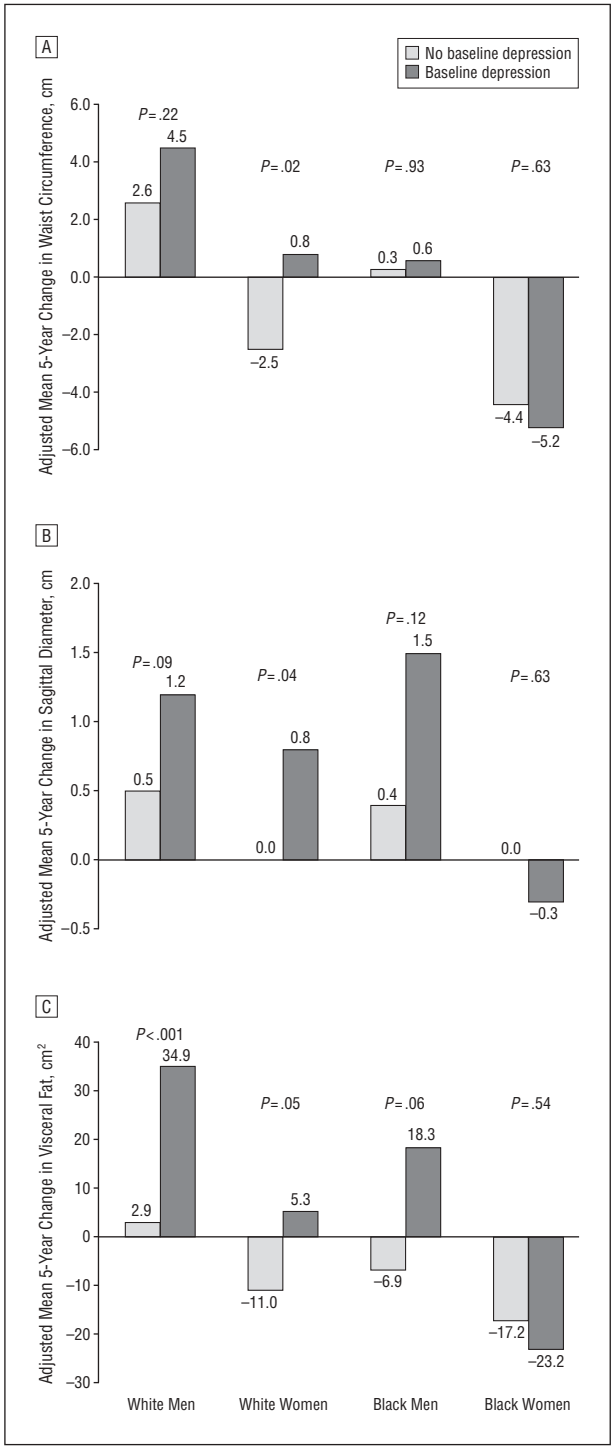

Figure. Adjusted mean 5-year changes in abdominal obesity according to baseline depression across sex and race groups, measured by waist circumference (A; overall P=.08), sagittal diameter (B; overall P=.01), and visceral fat (C; overall P=.001); adjusted for corresponding baseline abdominal obesity measure, age, site, education, body mass index (calculated as weight in kilograms divided by height in meters squared), smoking, alcohol consumption, physical activity, prevalent diabetes, prevalent cardiovascular disease, number of other chronic diseases, and number of prescription medications taken.

What are the mechanisms by which depression may promote visceral fat accumulation? As suggested by Björntorp,[13] stress activates the HPA axis, which leads to an accumulation of visceral fat. Studies show that chronic stress and de-

pression are, at least in a subset of patients, associated with a dysregulation of the HPA axis and elevated concentrations of cortisol.[7,8] Visceral fat is highly sensitive to cortisol owing to a high density of glucocorticoid receptors.[14] Cortisol promotes the accumulation of visceral fat by activating lipoprotein lipase and inhibiting lipid mobilization.[13] Indeed, it has been shown that hypercortisolemic depression is associated with abdominal obesity.[20,37] Moreover, these effects might be most pronounced when levels of sex steroid hormones, which have been found to reduce visceral fat mass and have a lipid-mobilizing effect,[13,38] are low, as has been observed in late-life depression.[9] Further, depression has been linked to high levels of inflammatory markers,[10] which can activate the HPA axis[39] and therefore result in visceral obesity. Moreover, as described by Gold and Chrousos,[40] even in persons with nonhypercortisolemic atypical depression, owing to overeating, a cycling of weight gain and loss occurring throughout recurrent episodes of depression could preferentially distribute weight to visceral fat areas. An alternative explanation for why depression may lead to abdominal obesity is that depressed persons have an unhealthier lifestyle. Although we adjusted our analyses for some lifestyle behaviors (smoking, alcohol consumption, and physical activity), it is possible that depressed persons have a poorer dietary pattern. However, a poor diet in itself would likely lead to an increase in both overall and abdominal obesity.[41] In combination with a hyperactive HPA axis, however, it is possible that excess caloric intake is preponderantly stored into visceral fat depots.[42] In addition, somatic comorbidities of depressed persons could have led to the increase in visceral fat, although our results were little affected by adjustment for diabetes, CVD, and general health status. Furthermore, weight gain in depressed persons has been associated with the use of antidepressants.[43] However, in our study antidepressant use was not associated with increases in (abdominal) obesity, and therefore our findings cannot be the result of antidepressant use.

The link between depressive symptoms and increased abdominal obesity was stronger for the dichotomous indicator of depression than for the continuous CES-D score, suggesting that a certain amount of distress is needed before visceral fat starts to accumulate. On the other hand, we did not find evidence that the association between depression and an increase in abdominal obesity was specific for persons with persistent/recurrent depression compared with persons with a single depression episode at baseline. However, most persons depressed at baseline did have an additional episode of depression during follow-up and it is possible that persons only depressed at baseline did experience additional depressive episodes between annual assessments.

Our study has some limitations. We did not have well-accepted criterion-based psychiatric diagnoses of depression. However, the CES-D is a commonly used scale to measure clinically relevant depressive symptoms. Our results might have been even stronger for persons with a diagnosis of major depressive disorder. Further, our sample showed low levels of depressive symptomatology at baseline and this aging population exhibited little change or even decrease in obesity, making it more difficult to detect associations with increases in obesity. Possibly, associations may be even stronger in a middle-aged population were visceral fat tends to increase over time. In addition, after 5 years of follow-up, there was drop-out owing to mortality and nonresponse, likely resulting in a relatively healthy sample, which could have led to an underestimation of the association between depression and change in abdominal obesity. On the other hand, studying the most healthy had the advantage that associations found were less likely confounded by somatic comorbidities. When missing values of persons without 5-year follow-up data were imputed, thereby including the less healthy, associations between depression and increase in abdominal obesity largely remained. Our study also has some important strengths, including use of a large community-based cohort followed up for several years with repeated dual-energy x-ray absorptiometry and CT scans, which provide more direct assessments of total and visceral fat stores as well as the more commonly used anthropometric measures.

Our longitudinal results suggest that clinically relevant depressive symptoms give rise to an increase in abdominal obesity, in particular visceral fat, which seems to be stronger than and independent of overall obesity. Because of this specific accumulation of visceral fat, these results clearly suggest that there may be certain underlying pathophysiological mechanisms, plausibly involving the HPA axis, which link depression with visceral fat. This could also help explain why depression is often followed by diabetes or CVD. Future research should further disentangle these mechanisms because this will yield important information for prevention or treatment of depression-related health consequences.

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