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Obesity and Onset of Significant Depressive symptoms:

Results from a community-based cohort of older men and women

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Abstract

Objective—Although several cross-sectional studies have linked obesity and depression, less is known about their longitudinal association and about the relative influence of obesity subtypes. We prospectively examined whether (abdominal) obesity increased the risk of onset of depression in a population-based sample of older persons.

Method—Participants were 2540 non-depressed well-functioning white and black persons, aged 70–79 years, enrolled in the Health ABC Study, an ongoing prospective community-based cohort study. Overall obesity was assessed by body mass index and percent body fat (measured by dual energy x-ray absorptiometry), whereas abdominal obesity measures included waist circumference, sagittal diameter, and visceral fat (measured by computer tomography). Onset of significant depressive symptoms was defined as a Center for Epidemiological Studies Depression 10-item score ≥ 10 at any annual follow-up over 5 years and/or new antidepressant medication use. Persistent depression was defined as depression at two consecutive follow-up visits.

Results—Over 5 years, significant depressive symptoms emerged in 23.7% of initially non-depressed persons. In men, both overall (BMI: HR per SD increase=1.20, 95%CI=1.03–1.40) and abdominal obesity (visceral fat: HR per SD increase=1.19, 95%CI=1.07–1.33) predicted onset of depressive symptoms after adjustment for sociodemographics. When BMI and visceral fat were adjusted for each other, only visceral fat was significantly associated with depression onset (HR=1.18, 95%CI=1.04–1.34). Stronger associations were found for persistent depressive symptoms. No associations were found in women.

Conclusion—This study shows that obesity, in particular visceral fat, increases the risk of onset of significant depressive symptoms in men. These results suggest that specific mechanisms might relate visceral fat to the onset of depression.

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Keywords

(abdominal) obesity; visceral fat; depression; older persons; longitudinal

INTRODUCTION

In a recent systematic review of epidemiological studies Atlantis and Baker[1] concluded there is a weak level of evidence that obesity increases the incidence of depression, predominantly based on cross-sectional studies[2–4]. The prevalence of overweight and obesity is increasing worldwide at an alarming rate[5]. In the US, obesity is prevalent among almost one third of the general population, and another third is overweight[6]. Overweight and obesity are associated with a multitude of health risks, including increased risks of diabetes and cardiovascular disease (CVD)[7;8]. This combination of high prevalence and poor outcomes makes obesity a major public health concern with implications for depression outcomes as well. At this moment, however, depression guidelines do not consider obesity as a major comorbidity of depression. Before obesity comorbidity can be incorporated in depression treatment, it is important to gain more knowledge of the direction, specifics, and strength of the association between obesity and depression.

Longitudinal studies that examine the direction of the association between depression and obesity are relatively sparse, mostly conducted among adolescents, and show mixed results. Recently, we showed that depression is associated with an increase in obesity over time[9]. Conversely, one study showed that obesity was associated with subsequent depression[10], but this was not confirmed in another study[11]. In addition, sex inconsistencies in the obesity-depression relationship have been found[1–3;11;12]. Furthermore, different subtypes of obesity exist and the location of excess fat storage may be an important determinant of subsequent health risks. Excess fat in the visceral region has been found to be a stronger predictor of diabetes and CVD than overall obesity[13;14]. Longitudinal studies on the association between abdominal obesity and depression are even more sparse.

The present study investigated prospectively whether obesity predicted the onset of significant depressive symptoms in an older sample of initially non-depressed persons. In addition, it was examined whether the association between obesity and onset of depressive symptoms was consistent for men and women, and whether type of obesity (overall vs. abdominal) influenced the obesity-depression link.

METHODS AND MATERIALS

Study Population

The Health, Aging, and Body Composition (ABC) study is an ongoing prospective cohort study among 3075 well-functioning white and black men and women, aged 70–79 years. The Health ABC study was designed to prospectively investigate (changes in) body composition and weight-related health outcomes, in an aging population. Participants were recruited in 1997/98 from a random sample of white and black Medicare-eligible beneficiaries residing in the areas surrounding Pittsburgh PA and Memphis TN. Eligible subjects reported no difficulty with walking a 1/4 mile, walking up 10 steps, or performing activities of daily living. Subjects were ineligible if they had severe difficulty communicating, active cancer treatment in the past three years, or plans to move away. After complete description of the study all participants signed an informed written consent, approved by the institutional review boards of the clinical sites. For the present study, only persons free of depression at baseline were selected (N=2802). Of these, persons without data on baseline BMI or visceral fat (N=104) or with no follow-up data on depressive

symptoms (N=151) were excluded, leaving 2547 persons for the present analyses. Excluded persons were more often men (57.6% vs. 48.6%, p=.006), black (52.2% vs. 40.6%, p<.001), less educated (35.7% vs. 43.6% with postsecondary education; p<.001), had more often onset of depressive symptoms (33.7% vs. 23.9%, p=.03) and had a lower (sex-adjusted) percent body fat (33.7% vs. 35.1%, p=.002) than included persons, but did not differ in age or other obesity measures.

Significant depressive symptoms

During the baseline interview and at follow-up (after 2, 3, 4, and 5 years), depressive symptoms were measured with the Center for Epidemiologic Studies Depression (CES-D) scale 10-item version, assessing depressive symptoms in the previous week[15]. The original 20-item CES-D scale has been widely used in older populations and has been shown to be a valid and reliable instrument (100% sensitivity and 88% specificity for detecting a major depressive disorder in the older population)[16], but the 10-item subset of the CES-D, ranging from 0–30, has shown good predictive accuracy when compared to the 20-item CES-D scale[17]. In addition, at baseline and at follow-up (after 1, 2, 4 and 5 years) all medications regularly taken in the past 2 weeks were recorded and coded according to the Iowa Drug Information System (IDIS)[18]. Antidepressant use included monoamine oxidase inhibitors (281605), tri/tetracyclic antidepressants (281606), selective serotonin reuptake inhibitors (281607), and other antidepressants (281604) with depression or mood disorder as self-reported reason. Persons with antidepressant use or a CES-D-10 score ≥ 10 (compares to the commonly used cut-off of ≥16 on CES-D-20 [17]) at baseline were excluded from the analyses. For the present analyses, onset of significant depressive symptoms was defined as having a CES-D-10 score ≥ 10 on any of the follow-up assessments and/or new antidepressant medication use during follow-up. To identify the onset of more chronic depressive symptoms, persistent depressive symptoms was defined as depressive symptoms at two consecutive follow-up visits. For sensitivity analyses two alternative definitions of depressive symptoms were constructed: one based on CES-D-10 scores only (since antidepressant medications are sometimes used in the treatment of obesity), and another incorporated an additional requirement of a minimum increase of 3 points on the CES-D-10 (to assure an actual onset of depressive symptoms and not just a crossing of the cut-off point).

Obesity

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. BMI was calculated as body weight (kg) divided by the square of height (m^2). BMI categories were constructed to indicate normal weight (BMI < 25), overweight (BMI: 25–30), and obesity (BMI ≥ 30). Percent body fat was determined via a whole body dual energy x-ray absorptiometry (DXA) scan (for details see [9]).

Abdominal obesity—Computer tomography (CT) scanning was performed at the level between the fourth and fifth lumbar vertebrae (L4–L5) to measure visceral fat (cm^2), as described in [9]. Next to this continuous measure of visceral fat, sex-specific quartiles of visceral fat were constructed and a dichotomous visceral fat variable compared persons in the highest quartile to persons in quartiles 1 to 3. In addition to this direct CT measure of visceral fat, some anthropometric measures were assessed. Maximum sagittal diameter (cm), the distance between the abdomen and back, was derived from the CT scans. Waist circumference (cm) was measured at the largest abdominal circumference to the nearest 0.1 cm using a flexible plastic tape measure.

Covariates

Covariates were a priori selected on the basis of previously reported associations with both obesity and depression. Sociodemographic characteristics included age, sex, site (Pittsburgh, Memphis), race (white, black), marital status (yes or no currently married) and education (less than high school, high school, postsecondary). Lifestyle characteristics were also assessed: smoking status (non-, former, or current), current alcohol use (yes or no > 1 drink per day) and physical activity (sum of weight training, high and medium intensity exercise, aerobic dance, (exercise) walking, and stair climbing (in kcal/week)). As both (abdominal) obesity and depression have consistently been associated with CVD and diabetes, these diseases were specifically addressed. Presence of baseline diabetes and CVD (including stroke, myocardial infarction, angina pectoris, coronary angioplasty or coronary artery bypass grafting) was adjudicated using standardized algorithms considering various sources of information: self-report, medication use, clinical examination findings, and medical claims data from the former Health Care Financing Administration. Identification of incident diabetes and new CVD events during follow-up additionally included hospitalization records assessed according to set algorithms. Also, we included two indicators for general health status. 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's disease, and kidney disease. In addition, all medications regularly taken in the past two weeks before baseline were recorded and coded according to the Iowa Drug Information System (IDIS)[18]. From this inventory, the total number of prescription medication taken was calculated.

Statistical Analyses

Because sex differences in the relationship between obesity and depression have been observed[3;12] and since men and women differ in body composition, all analyses were presented for men and women separately and sex-interaction effects were tested for statistical significance. Sample characteristics were compared between persons with and without onset of depressive symptoms during follow-up using chi-square test for dichotomous and categorical variables and independent t-test for continuous variables. Risk of onset of ([non]persistent) depressive symptoms according to different measures of baseline obesity (overall and abdominal) was assessed using Cox regression analyses and the proportional hazards assumption was examined. The assumption of linearity was assessed by checking improvement of model fit after inclusion of a quadratic term for each corresponding obesity measure respectively. Presence of multicollinearity was assessed by means of the Variance Inflation Factor (VIF) when all covariates were included in the same model. To be able to compare Hazard Ratios (HR) across obesity measures, HR's with 95% confidence intervals (CI) were expressed per standard deviation (SD) increase. For comparability across sub samples, sex-weighted SD's were used. Analyses were adjusted for baseline CES-D-10 score, sex, age, race, site, marital status and education. Because fat distribution differs between Whites and Blacks, all analyses were repeated including race-interaction terms, to test whether findings were consistent across race.

To examine whether associations between obesity and onset of significant depressive symptoms could be explained by lifestyle or disease differences at baseline, the above described Cox regression analyses were additionally adjusted for smoking, alcohol use, physical activity, prevalent and incident diabetes and CVD, number of other chronic diseases and number of prescription medication taken. In order to compare the independent effects of overall and abdominal obesity, the associations between overall obesity measures and onset of depressive symptoms were adjusted for visceral fat and the associations between abdominal obesity measures and onset of depression were adjusted for BMI.

Finally, the risk of (persistent) depressive symptoms onset was plotted for men and women across BMI categories and for men and women with high vs. normal visceral fat mass and onset rates of depressive symptoms were calculated (in percent per year). In addition, population attributable risks (PAR) of obesity (BMI ≥ 30) and high visceral fat (≥ 194 cm^2) in men were calculated. PAR describes the percentage by which the onset rate of (persistent) depressive symptoms could be reduced when the risk factor would be completely eliminated. The following equation was used: PAR = p(HR-1) / (1+ p(HR-1)), where p is the prevalence of the risk factor in the population at risk[19].

RESULTS

The mean age of the participants was 73.6 (SD=2.9) years, 51.4% were women and 40.6% were black. During a mean follow-up of 4.3 (SD=1.1) years, significant depressive symptoms emerged in 23.9% (N=609) of the initially non-depressed sample and significant persistent depressive symptoms in 7.8% (N=198). Men experienced more diabetes and CVD, but women had a higher rate of onset of depressive symptoms. The mean BMI was comparable between men and women, however women had a higher percent body fat (40.7% vs. 29.3%) than men, but had less visceral fat (132.2 vs. 155.2 cm^2). Visceral fat correlated more strongly with waist circumference (Pearson's r = 0.65) and sagittal diameter (Pearson's r = 0.75) than with BMI (Pearson's r = 0.56). Table 1 shows sample characteristics for persons with and without onset of depressive symptoms during follow-up for men and women separately.

Table 2 shows the results of Cox regression analyses assessing the risk of onset of significant depressive symptoms according to baseline obesity among non-depressed persons at baseline. In the total sample, no associations were found for overall obesity measures, but sagittal diameter (HR per SD (3.4 cm) increase = 1.11, 95%CI=1.02–1.20) and visceral fat (HR per SD (65.5 cm^2) increase = 1.10, 95%CI=1.02–1.20) predicted onset of depressive symptoms after adjustment for sociodemographics. Sex-stratified analyses showed that both overall and abdominal obesity increased the risk of onset of depressive symptoms in men. For instance, risk of depressive symptoms increased by 20% for each SD (4.6) increase in BMI (HR=1.20, 95%CI=1.03–1.40) and by 19% for each SD (65.5 cm2) increase in visceral fat (HR=1.19, 95%CI=1.07–1.33) (Table 2). No associations were found in women. When tested, obesity by sex interactions were found (BMI: p=.04, percent body fat: p=.03, waist circumference: p=.04, sagittal diameter: p=.04, visceral fat: p=.06). No significant obesity by race interactions were observed among men and women (all p >.20). Similar results were found when the definition of the onset of depressive symptoms was determined without data on new antidepressant use (N with depression: 553) or when an additional requirement of a minimum 3 point increase on the CES-D-10 was incorporated (N with depression: 593). Persons with significant depressive symptoms at follow-up (based on CES-D-10), increased from a mean baseline CES-D-10 score of 3.7 (SD=2.6) to a mean CES-D-10 score of 12.4 (SD=2.8) during their depressed episode. As can be seen in Table 2, additional adjustment for smoking, alcohol use, physical activity, prevalent and incident diabetes and CVD, number of other chronic diseases and number of prescription medication taken did not change the results in any meaningful way.

Next, to assess the effect of abdominal obesity versus overall obesity, the associations between overall obesity measures and onset of significant depressive symptoms were adjusted for visceral fat and were found to be no longer significant in men (e.g. for BMI: HR=1.10, 95%CI=0.93–1.32; Table 2). Alternatively, when associations between abdominal obesity and onset of depressive symptoms in men were adjusted for BMI, the associations remained similar (e.g. for visceral fat: HR=1.18, 95%CI=1.04–1.34; Table 2). Table 3 presents fully adjusted models (with and without adjustment for obesity) with onset of non-

persistent depressive symptoms and persistent depressive symptoms as the outcome. Although associations of abdominal obesity with onset of non-persistent depressive symptoms were found, obesity was more strongly associated with the more chronic indicator of depressive symptoms in men; in women associations remained absent. When tested, no indications of non-linearity or multicollinearity were found (all quadratic terms p>.05; all VIF<2).

To graphically illustrate the association between obesity and significant depressive symptoms onset, the cumulative onset of (persistent) depressive symptoms over time adjusted for sociodemographics, lifestyle, and diseases was plotted for men and women across BMI categories (Figure 1A&C) and for men and women with normal (Q1–Q3) and high (Q4) visceral fat (Figure 1B&D). In addition, unadjusted depressive symptoms onset rates across groups are presented in the Figures. Among men, obese men (BMI > 30) were at the highest risk for onset of depressive symptoms, which was statistically significant for persistent depressive symptoms (HR=2.03, 95%CI=1.06–3.89). Men with high visceral fat (≥ 194 cm^2) had a 1.33 increased risk (95%CI=1.00–1.77) of becoming depressed and a 2.04 increased risk (95%CI=1.25–3.34) of becoming persistently depressed compared to men with visceral fat < 194 cm^2. As can be seen from Figure 1, men with high visceral fat were at an equal risk of becoming depressed than women in general. In fact, the unadjusted hazard ratio of depressive symptoms onset for women compared to men was 1.38 (95%CI=1.17–1.62) and 1.62 (95%CI=1.22–2.16) for onset of persistent depressive symptoms, which is equal to or even lower than the hazard ratio of onset of (persistent) depressive symptoms due to high visceral fat in men. High BMI or visceral fat did not increase the risk of becoming depressed in women. Finally, the population attributable risks of BMI > 30 and high visceral fat adjusted for sociodemographics, lifestyle and diseases were calculated for men and found to be 7% and 8% respectively, for onset of depressive symptoms, and 17% and 19%, for onset of persistent depressive symptoms. This suggests that in the entire older male population, 19% of all new cases with persistent depressive symptoms were related to having high visceral fat mass.

DISCUSSION

This study examined whether obesity was associated with onset of significant depressive symptoms in a large community-based sample of older, initially non-depressed, persons during 5 years of follow-up. The results showed that in men but not in women obesity increased the risk of onset of significant depressive symptoms. Specifically, abdominal obesity appeared to be associated with the onset of depressive symptoms, independent of and more consistently than overall obesity. Men with high visceral fat had a more than 2-fold increased risk of becoming persistently depressed compared to men with normal amounts of visceral fat. Moreover, results showed that in men almost 10% of depressive symptoms onset and 20% of persistent depressive symptoms onset was related to having high visceral fat.

Several studies indicated that obesity and depression are associated[2–4]. However, as concluded by Atlantis and Baker[1] in their systematic review on obesity and depression, few studies have investigated the temporal direction of this association. Our findings correspond to a study by Roberts et al.[10] which showed among persons aged 50+ that obesity at baseline was associated with an increased risk of depression 5 years later. Our results additionally showed that associations with depressive symptoms appear to be more consistently related to abdominal obesity than to overall obesity. The association between depressive symptoms and overall obesity in men was not consistently found after adjustment for visceral fat, while the association with visceral fat remained after controlling for BMI. At least, these results show that abdominal obesity has an additional effect on depressive symptoms onset above

the influence of overall obesity. These results are in line with other studies showing that in particular abdominal obesity, more than overall obesity, is associated with poor health outcomes, such as diabetes and CVD[13;14].

To our knowledge, the current study was the first to test and demonstrate that abdominal obesity increases the risk of onset of significant depressive symptoms in men. This evidence should be considered together with other recent longitudinal results which illustrates that – the other way around – depressive symptoms also lead to increases in abdominal obesity over 5 years[9]. The fact that abdominal obesity and depressive symptoms are found to be reciprocally associated, indicates that the two are strongly intertwined and suggests that a vicious cycle might exist. The bidirectional relationship between abdominal obesity and depressive symptoms further indicates that when trying to break this vicious cycle, treatment of either obesity or depression cannot be given in isolation and comorbidity between these two should be taken into consideration.

How might abdominal obesity increase the risk of incident depression? First, a poor self-image or perceived stigma of an obese person might induce depression[20]. Also, binge-eating behavior, not uncommon in obese persons, has been associated with major depressive disorder[21]. These mechanisms are probably true for overall obesity as well as and not specific for abdominal obesity. Poor lifestyle behaviors might lead to both abdominal obesity and depression. However, in our analyses adjustment for lifestyle behaviors did not influence results much. In addition, diseases related to abdominal obesity such as diabetes and CVD have been associated with depression[22;23] and might be responsible for the association between abdominal obesity and depression. In our study, adjustment for prevalent as well as incident diabetes and CVD did not affect the relationship between abdominal obesity and depressive symptoms onset, suggesting that such an association does exist rather independently of diabetes and CVD. Other pathophysiological explanations may exist. Studies have shown that visceral fat produces cytokines in higher amount than subcutaneous fat[24]. High levels of cytokines such as TNF-alpha, IL-6, and C-reactive protein have been found both in visceral obesity[25] and depression[26]. In addition, the mechanisms discussed above (poor lifestyle, more diabetes and CVD, and inflammation in obese persons) might all induce vascular damage and are therefore in line with the vascular depression hypothesis, which states that vascular damage in the brain might predispose, precipitate, or perpetuate depression in the elderly[27]. Also, a dysregulation of the hypothalamic-pituitary-adrenal axis[28;29] and sex steroid hormones[30;31] have been found to be involved in both abdominal obesity and depression, and could be linking mechanisms.

The link between abdominal obesity and significant depressive symptoms was restricted to men. A reason for this could be due to the fact that men have more visceral fat than women. If the amount of visceral fat is important for negative health effects to emerge, than men will be more at risk to experience such negative health effects. In addition, this is an aging population in which losses of (visceral) fat over time are not uncommon especially in women[32], which might leave women at a smaller risk of visceral fat to cause poor health. Another explanation might be that in women the relative contribution of visceral fat to depression onset is small due to a larger influence of competing risk factors. For instance, insufficient social support and stressful life events have been found to pose a greater risk for depression among women compared to men[33;34]. Although previous cross-sectional studies that examined sex differences predominantly showed stronger results for women in the association between overall obesity and depression[3;12], one study reported an association between depression and abdominal obesity only in men[2]. Future research should explore these sex differences further in younger samples to eliminate counteracting effects of aging.

Our study has some limitations. We did not have well-defined DSM-IV-based depression diagnoses. However, the CES-D is a commonly used scale to assess clinically significant depressive symptoms. In addition, since we had no information on history of depression, depressive symptoms onset might represent recurrence of an earlier depression in life. Therefore, results do not necessarily indicate incidence of a first depression episode in life, which is less common in later life, but do reflect a new occurrence of depressive symptoms during later life. Our study also had some important strengths including a large sample with longitudinal assessments of depressive symptoms. In addition, DXA and CT scans were performed, which assess total and visceral fat stores directly and we were able to compare them with more commonly used anthropometric measures.

In all, our findings indicate that the strength of the association between abdominal obesity and depressive symptoms is of both clinical and public health relevance. Men with visceral fat levels in the highest quartile (≥194 cm^2) had almost 35% more chance of becoming depressed over 5 years than men with normal amounts of visceral fat. The risk of becoming persistently depressed was more than 2-fold for men with high visceral fat. We found that the size of this effect was at least equal to the difference in the onset rate of depressive symptoms between men and women. A 35–40% increased risk of incident depression for women vs. men is comparable to what has been found in other studies among older persons[35], and is normally considered to be an important predictor for depression onset. In contrast to sex, however, high visceral fat is potentially modifiable and it is tempting to consider the possibility that weight reduction might reduce the onset of new depressive symptoms. Future research should investigate whether visceral fat reduction indeed can prevent onset of depressive symptoms.

In conclusion, our results suggest that, in older men, obesity relates to the onset of significant depressive symptoms. Abdominal obesity appears to be more consistently associated with depressive symptoms onset than overall obesity or at least shows an additional effect above overall obesity. These findings strengthen the idea that specific properties of visceral fat might give rise to depression. The impact of the association between abdominal obesity and onset of significant depressive symptoms on public mental health seems to be of great enough importance to warrant additional research that confirms our findings and explores underlying mechanisms. When known, this might have direct implications for depression treatment and prevention.

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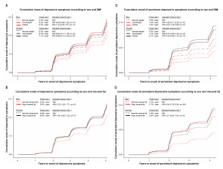

Figure 1.
Cumulative onset of significant depressive symptoms according to sex and **A**) BMI categories; **B**) visceral fat status; cumulative onset of persistent depression according to sex and **C**) BMI categories; **D**) visceral fat status; in Figures C and D persons with non-persistent depressive symptoms were excluded from the analyses. [a] Unadjusted rates; [b] Based on Cox regression analyses adjusted for baseline CES-D-10 score, age, race, site, marital status, educational level, smoking, alcohol use, physical activity, prevalent diabetes or CVD, incident diabetes, new CVD events, number of other chronic diseases, number of prescription medication taken.

Table 1

Sample characteristics

	MEN			WOMEN		
	No depressive symptoms during follow-up (N=988)	**Depressive symptoms during follow-up (N=250)**	**p***	**No depressive symptoms during follow-up (N=950)**	**Depressive symptoms during follow-up (N=359)**	**p***
Sociodemographic variables						
Age (years), mean (SD)	73.6 (2.9)	73.9 (2.8)	.22	73.5 (2.9)	73.5 (2.9)	.90
Black, %	33.7	44.0	.002	43.9	48.7	.12
Memphis site, %	47.1	52.4	.13	49.4	53.2	.22
Married, %	73.0	65.6	.02	39.7	39.6	.97
Educational level, %			<.001			<.001
Less than high school	22.9	35.6		19.8	28.1	
High school	26.5	21.6		38.2	42.6	
Postsecondary	50.6	42.8		42.0	29.2	
Lifestyle variables						
Smoking, %			.87			.28
Never	30.9	29.2		56.8	61.6	
Former	59.2	60.4		34.5	30.1	
Current	9.9	10.4		8.6	8.4	
> 1 alcoholic drink / day, %	12.9	8.8	.08	3.7	2.8	.43
Physical activity (kcal/week), mean (SD)	1539 (2514)	1215 (1879)	.02	743 (1240)	649 (1309)	.23
Health & disease variables						
Prevalent cardiovascular disease, %	28.1	29.2	.74	16.9	23.7	.005
Prevalent diabetes, %	25.7	28.4	.39	17.9	24.8	.005
New cardiovascular event during follow-up, %	16.5	11.6	.06	8.4	9.5	.55
Incident diabetes during follow-up, %	4.6	5.2	.67	4.9	2.8	.09
Number of other chronic diseases, mean (SD)	1.4 (1.0)	1.5 (1.1)	.24	0.9 (0.9)	1.2 (1.0)	<.001
Number of prescription medication taken, mean (SD)	2.8 (2.4)	3.2 (2.7)	.02	3.0 (2.5)	3.8 (2.8)	<.001
Depression-related variables						
Baseline CES-D-10 score (0–30), mean (SD)	1.9 (2.1)	3.5 (2.6)	<.001	2.3 (2.3)	3.8 (2.6)	<.001

	MEN			WOMEN		
	No depressive symptoms during follow-up (N=988)	**Depressive symptoms during follow-up (N=250)**	**p***	**No depressive symptoms during follow-up (N=950)**	**Depressive symptoms during follow-up (N=359)**	**p***
Onset of persistent depressive symptoms, %	*NA*	30.0	*NA*	*NA*	34.3	*NA*
Obesity variables						
Overall obesity						
Body mass index (kg/m^2), mean (SD)	27.0 (3.7)	27.5 (4.3)	.09	27.7 (5.4)	27.9 (5.4)	.52
Percent body fat, mean (SD)	29.2 (4.7)	29.7 (5.4)	.14	40.7 (5.6)	40.6 (5.9)	.87
Abdominal obesity						
Waist circumference (cm), mean (SD)	100.7 (10.3)	102.3 (11.3)	.04	97.9 (13.4)	99.0 (13.8)	.22
Sagittal diameter (cm), mean (SD)	23.6 (3.2)	24.2 (3.5)	.01	23.4 (3.5)	23.6 (3.5)	.28
Visceral fat (cm^2), mean (SD)	153.0 (68.8)	163.8 (78.7)	.05	131.8 (61.1)	133.4 (59.9)	.66

*based on chi-square test for dichotomous and categorical variables and independent t-test for continuous variables.

Table 2

Risk (per SD increase [e]) of onset of significant depressive symptoms among initially non-depressed persons according to baseline obesity

	Unadjusted risk[a]			*Risk adjusted for sociodemographics*[b]			*Risk additionally adjusted for lifestyle and diseases*[c]			*Risk additionally adjusted for obesity*[d]		
	HR	**95% CI**	**p**	**HR**	**95% CI**	**p**	**HR**	**95% CI**	**p**	**HR**	**95% CI**	**p**
TOTAL *(N=2547)*												
Overall obesity												
BMI	1.06	0.99–1.15	.11	1.04	0.96–1.12	.32	1.02	0.94–1.10	.71	0.96	0.87–1.06	.41
Percent body fat	1.03	0.95–1.12	.42	1.04	0.96–1.13	.34	1.02	0.94–1.11	.58	0.98	0.89–1.08	.68
Abdominal obesity												
Waist circumference	1.11	1.03–1.20	.01	1.08	0.99–1.17	.07	1.05	0.97–1.14	.27	1.10	0.95–1.27	.19
Sagittal diameter	1.14	1.05–1.23	.002	1.11	1.02–1.20	.02	1.08	0.99–1.17	.09	1.23	1.05–1.43	.01
Visceral fat	1.10	1.02–1.19	.02	1.10	1.02–1.20	.02	1.07	0.99–1.17	.09	1.10	0.99–1.22	.06
MEN (*N=1238)*												
Overall obesity												
BMI	1.18	1.01–1.37	.03	1.20	1.03–1.40	.02	1.18	1.01–1.37	.04	1.10	0.93–1.32	.27
Percent body fat	1.14	0.99–1.31	.08	1.19	1.03–1.36	.02	1.15	1.00–1.33	.05	1.10	0.94–1.28	.22
Abdominal obesity												
Waist circumference	1.20	1.04–1.39	.01	1.23	1.06–1.42	.006	1.20	1.04–1.39	.01	1.26	1.04–1.52	.02
Sagittal diameter	1.24	1.09–1.40	.001	1.24	1.08–1.41	.001	1.21	1.06–1.38	.004	1.31	1.11–1.56	.002
Visceral fat	1.16	1.04–1.29	.01	1.19	1.07–1.33	.002	1.17	1.04–1.31	.009	1.18	1.04–1.34	.009
WOMEN (*N=1309)*												
Overall obesity												
BMI	1.03	0.94–1.12	.54	0.99	0.91–1.08	.84	0.97	0.88–1.06	.47	0.93	0.83–1.03	.16
Percent body fat	0.99	0.90–1.09	.82	0.97	0.88–1.07	.55	0.96	0.87–1.06	.45	0.93	0.84–1.04	.20
Abdominal obesity												
Waist circumference	1.07	0.98–1.18	.14	1.02	0.92–1.12	.74	0.99	0.90–1.09	.80	1.04	0.89–1.21	.66
Sagittal diameter	1.08	0.98–1.20	.13	1.03	0.93–1.15	.53	1.00	0.90–1.11	.98	1.12	0.93–1.34	.23
Visceral fat	1.05	0.94–1.18	.37	1.03	0.92–1.15	.64	1.00	0.89–1.12	.93	1.02	0.88–1.17	.83

[a] Based on Cox regression analyses adjusted for sex (total sample only);

[b] additionally adjusted for baseline CES-D-10 score, age, race, site, marital status and educational level;

[c] additionally adjusted for smoking, alcohol use, physical activity, prevalent diabetes or CVD, incident diabetes, new CVD events, number of other chronic diseases and number of prescription medication taken;

[d] additionally adjusted for visceral fat (overall obesity only) and BMI (abdominal obesity only);

[e] Per SD increase: 4.6 for BMI, 5.3% for percent body fat, 12.0 cm for waist circumference, 3.4 cm for sagittal diameter, and 65.5 cm^2 for visceral fat.

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Table 3

Risk [a] (per SD increase [b]) of onset of significant non-persistent and persistent depressive symptoms among initially non-depressed persons according to baseline obesity

	Non-persistent depressive symptoms *(N: Men:175; Women:236)*						Persistent depressive symptoms *(N: Men:75; Women:123)*					
	Risk adjusted for lifestyle and diseases[a]			*Risk additionally adjusted for obesity*[b]			*Risk adjusted for lifestyle and diseases*[a]			*Risk additionally adjusted for obesity*[b]		
	HR	**95% CI**	**p**	**HR**	**95% CI**	**p**	**HR**	**95% CI**	**p**	**HR**	**95% CI**	**p**
MEN (*N=1238)*												
Overall obesity												
BMI	1.07	0.89–1.29	.49	1.03	0.83–1.28	.76	1.50	1.13–1.98	.005	1.29	0.94–1.76	.12
Percent body fat	1.05	0.89–1.25	.54	1.03	0.85–1.24	.76	1.50	1.16–1.95	.002	1.37	1.04–1.82	.03
Abdominal obesity												
Waist circumference	1.12	0.94–1.34	.20	1.23	0.99–1.54	.07	1.46	1.12–1.92	.006	1.41	1.01–1.96	.05
Sagittal diameter	1.14	0.97–1.33	.11	1.27	1.04–1.56	.02	1.43	1.12–1.83	.004	1.47	1.08–2.01	.01
Visceral fat	1.08	0.94–1.25	.27	1.10	0.94–1.29	.22	1.40	1.17–1.68	<.001	1.42	1.17–1.73	<.001
WOMEN (*N=1309)*												
Overall obesity												
BMI	0.96	0.86–1.07	.47	0.94	0.82–1.07	.35	0.96	0.81–1.12	.58	0.86	0.72–1.04	.12
Percent body fat	0.95	0.84–1.07	.40	0.93	0.82–1.07	.31	0.98	0.82–1.16	.80	0.91	0.76–1.11	.35
Abdominal obesity												
Waist circumference	1.00	0.88–1.12	.96	1.10	0.91–1.34	.32	0.94	0.80–1.11	.47	0.90	0.69–1.18	.45
Sagittal diameter	1.00	0.87–1.14	.95	1.17	0.93–1.46	.18	0.99	0.82–1.19	.88	1.03	0.74–1.42	.87
Visceral fat	0.97	0.84–1.12	.64	0.99	0.84–1.18	.94	1.02	0.84–1.23	.86	1.05	0.83–1.32	.71

[a] Based on Cox regression analyses adjusted for baseline CES-D-10 score, age, race, site, marital status, educational level, smoking, alcohol use, physical activity, prevalent diabetes or CVD, incident diabetes, new CVD events, number of other chronic diseases and number of prescription medication taken;

[b] additionally adjusted for visceral fat (overall obesity only) and BMI (abdominal obesity only).

[b] Per SD increase: 4.6 for BMI, 5.3% for percent body fat, 12.0 cm for waist circumference, 3.4 cm for sagittal diameter, and 65.5 cm^2 for visceral fat; persons with persistent depressive symptoms were excluded from the analyses on non-persistent depressive symptoms and persons with non-persistent depressive symptoms were excluded from the analyses on persistent depressive symptoms.