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Evaluating associations between metabolic health, obesity and depressive symptoms: a prospective analysis of data from the English Longitudinal Study of Ageing (ELSA) with a 2-year follow-up

Natasha Slater, Charlotte Rowley, Rebecca Hayley Venables, Simon White, Martin Frisher

School of Pharmacy, Keele University, Keele, UK

Correspondence to
Natasha Slater;
n.slater@keele.ac.uk

ABSTRACT

Objectives Conflicting results have been reported when the associations between metabolic health, obesity and depression were examined previously. The primary aim of this study was to determine whether metabolic health or obesity are independently associated with depressive symptoms, among a representative sample of older people living in England. Independent associations between covariates and depression were also examined.

Design Prospective study with a 2-year follow-up.

Setting The English Longitudinal Study of Ageing Wave 6 (2012–2013) and Wave 7 (2014–2015).

Participants 6804 participants aged older than 50 years.

Data Analysis Multivariate models were used to determine whether metabolic health or obesity are independently associated with depressive symptoms at 2-year follow-up. Unadjusted and adjusted ORs with corresponding 95% CI were calculated; the adjusted ORs took account of baseline depression, gender, age, wealth, obesity and poor metabolic health.

Results Before adjusting for covariates, poor metabolic health was associated with depressive symptoms at 2-year follow-up (OR 1.24; 95% CI, 1.07 to 1.44, p<0.01). After adjusting for covariates, the association was no longer statistically significant (OR 1.17; 95% CI, 0.99 to 1.38, p=0.07). Similarly, obesity was associated with depressive symptoms at 2-year follow-up before adjusting for covariates (OR 1.54; 95% CI, 1.33 to 1.79, p<0.01). However, after adjusting for covariates the association between obesity and depressive symptoms at 2-year follow-up became statistically insignificant (OR 1.19; 95% CI, 1.00 to 1.41, p=0.06). The strongest predictors for future depression were baseline depression (OR 10.59; 95% CI, 8.90 to 12.53, p<0.01) and lower wealth (OR 3.23; 95% CI, 2.44 to 4.35, p<0.01).

Conclusion Neither poor metabolic health nor obesity were associated with a risk of depressive symptoms at 2-year follow-up, after adjusting for covariates. As wealth inequalities continue to rise across England, the risk of depressive symptoms at 2-year follow-up is likely to be elevated in individuals living in the lower wealth quintiles.

Strengths and limitations of this study

► A representative sample (*n*=6804) of older people living in England provided data for this prospective analysis.

► Standardised data collection methods and validated data collection tools were used to obtain data for the English Longitudinal Study of Ageing Wave 6 and Wave 7.

► All multivariate models were adjusted for baseline depression, gender, age, wealth, obesity and poor metabolic health to reduce the impact of confounders.

► Participants were required to truthfully and accurately recall information about their mood to prevent study bias.

INTRODUCTION

Obesity and depression are significant public health issues in the UK. At present 26% of adults are classified as obese (defined as a body mass index of $30\,\text{kg/m}^2$ or above), and this percentage is anticipated to rise in future years.[1] Obesity is associated with adverse outcomes including the development of cardiovascular diseases, type 2 diabetes and other potentially life-threatening conditions.[2] However, further research is needed to determine whether obesity is associated with psychological conditions, particularly depression, because this condition is now the leading cause of disability and ill health within the UK.[3]

Inconsistent findings have been reported when the association between obesity and depression has been examined previously. Conclusions drawn from early studies suggested that there was no association

between obesity and depression.[4] However, Crisp and McGuiness[5] reported an inverse association between obesity and depression in men, while other studies have shown that obesity is positively associated with depressive symptoms in women only.[6 7] Participant characteristics (age and gender) and sample sizes vary significantly in the aforementioned studies, which may offer some explanation for the differing results. To address this limitation, a large-scale study involving a representative sample of the population is required.

Few studies have prospectively examined the association between obesity and the risk of future depression, as previous studies have been predominantly cross-sectional.[8] Findings from the existing prospective studies were evaluated in a meta-analysis. Pooled ORs showed that obesity significantly increased an individual's risk of developing depression during follow-up (OR 1.55, 95% CI; 1.22 to 1.98, p<0.01), in both men and women.[9] Meta-analytic data was adjusted for age and gender; however, there may be other confounding factors involved in this association.[9]

Metabolic health has been identified as a potential confounder in the association between obesity and the risk of future depression in several studies.[10 11] Partial support for this finding is provided from analyses conducted on eight cohort studies.[12] Jokela *et al*[12] reported that obese individuals with poor metabolic health were 23% more likely to experience depression, compared with obese individuals with a favourable metabolic profile; however, the risk of depression for the latter group remained elevated when compared with non-obese individuals who had good metabolic health.[12] Furthermore, findings from a prospective cohort study with 16-year follow-up showed that metabolic health was a better predictor of future depression, compared with obesity.[13] No association between metabolic health and depression has been reported in other studies. Various definitions of metabolic health exist within the literature, which may offer some explanation for the differing study findings; however, further research into the relationship between metabolic health, obesity and depression is required.[14]

The primary aim of this study was to determine whether metabolic health or obesity are independently associated with depressive symptoms at 2-year follow-up, using the latest data from the English Longitudinal Study of Ageing (ELSA). In addition, we determined whether the covariates used in our analyses were independently associated with depressive symptoms at follow-up.

METHOD
Sample and participants
A prospective study was conducted using Wave 6 and Wave 7 data gathered from ELSA. Since inception in 2002, ELSA has gathered socio-economic, lifestyle and health data from a representative sample of the English population, who are older than 50 years. Every 2 years, a new 'wave' of ELSA data are collected.[15] This study used data collected between 2012 and 2013 (Wave 6) as baseline

data. Data collected between 2014 and 2015 (Wave 7) was used for follow-up. Overall, 6804 participants successfully provided data in both Wave 6 and Wave 7, and this group are the focus of the current study (online supplementary material figure 1).[15]

Patient and public involvement
No patients were involved in the development of the research question, study design or data interpretation in this study.

ELSA wave data are anonymised and freely accessible from the UK Data Service.[16]

Data collection
Three methods of data collection were utilised during ELSA Wave 6: a paper-based questionnaire, a face-to-face interview and a nurse interview. In Wave 7, the nurse interview did not take place; instead, data was collected during a face-to-face interview and using a paper-based questionnaire.

Face-to-face interviews
In both Wave 6 and Wave 7, face-to-face interviews were conducted by trained interviewers at the participant's residential address. The interviewers recorded demographic information for each participant, in addition to asking the participants questions about their physical and mental health status. To determine whether participants were experiencing depressive symptoms, they were asked to answer eight questions which had been adapted from the Center for Epidemiologic Studies Depression (CES-D) Scale.[17] One point was awarded for each depressed answer given. Each participant received a total score between 0 and 8. In accordance with previous studies, a score ≥4 was used to define participants with elevated depressive symptoms.[10 18]

The interviewers also asked the participants to provide information about everyone who resided within their property, including information about their financial situation, employment status, assets and whether they were in receipt of any benefits. Participants were allocated to one of five wealth quintiles, with quintile 1 being the poorest and quintile 5 being the wealthiest. Wealth quintiles refer to household wealth (financial assets, physical assets and housing wealth) but not pension wealth.[19] Wealth was calculated less debts and included the value of owner-occupied housing (less mortgage); all assets held in bank accounts in England; the value of any business properties or holiday homes (less mortgage) and the value of physical assets such as antiques, artwork and jewellery.[20]

Nurse interview
Demographic information for each participant was also collected during the nurse interview in Wave 6. Subsequent stages of the nurse interview involved participants having their blood pressure, pulse rate, lung function and grip strength measured, in addition to providing hair samples and fasting blood samples. Fasting blood test results and blood pressure readings were analysed

to determine a participant's metabolic health status. In this study, a participant with two or more metabolic risk factors was described as having poor metabolic health. The following were defined as metabolic risk factors: glycated haemoglobin greater than 6.0% (42 mmol/mol); C-reactive protein greater than or equal to 3 mg/L; high-density lipoprotein less than 1.03 mmol/L for men or less than 1.30 mmol/L for women; triglycerides greater than or equal to 1.7 mmol/L and blood pressure readings greater than 130/85 mm Hg.[10]

The nurse interviewer also recorded a number of anthropometric measurements including height, weight and waist circumference for each participant. Using a participant's weight and height values, it was possible to calculate their body mass index (BMI). A participant was classified as obese if their calculated BMI was $\geq 30 \, \text{kg/m}^2$.

Data analysis

Descriptive statistics were used initially to summarise the prevalence of depressive symptoms among participants. These data were subsequently stratified according to participant demographics and X^2 tests were performed. Multivariate models were used to determine whether metabolic health or obesity are independently associated with depressive symptoms at 2-year follow-up (Wave 7). The minimum sample size required for our multivariate models was 319.[21] Unadjusted and adjusted odds ratios with corresponding 95% CI for the risk of depressive symptoms at 2-year follow-up were calculated. Following the main analysis, a secondary analysis was conducted excluding cases with depressive symptoms at Wave 6. The following factors were covariates: baseline depression, gender, age, wealth, obesity and poor metabolic health. Missing data was coded as 'missing' and presented as a separate category in the multivariate models. All p values generated from the models were considered to be statistically significant if p<0.05. Analyses were undertaken using SPSS V.24.0.

RESULTS
Participant characteristics

Overall, 6804 participants successfully provided data in both Wave 6 and Wave 7. Baseline participant characteristics are presented in table 1. The mean age of the participants was 67.6 years, 44.5% (n=3030/6804) of the participants were male and 12.8% (n=872/6804) of the participants had elevated depressive symptoms at baseline. At follow-up (Wave 7), 12.5% (n=851/6804) of the participants had elevated depressive symptoms (table 1). Baseline data were stratified according to participant characteristics, including gender, age, metabolic health status and BMI. The prevalence of depressive symptoms was higher among females (15.1%), compared with males (9.2%) at Wave 7 (table 1). Results from the X^2 statistical test showed an association between gender and depressive symptoms ($\chi^2(1)=53.26$, p<0.01). There was also a significant association between age and depressive symptoms

($\chi^2(3)=36.24$, p<0.01). A greater proportion of individuals with poor metabolic health (13.6%) had elevated depressive symptoms at Wave 7, compared with participants with good metabolic health (11.2%) (table 1). The association between metabolic health and depressive symptoms was significant ($\chi^2(1)=8.48$, p<0.01). Similarly, there was a significant association between obesity (BMI $\geq 30 \, \text{kg/m}^2$) and depressive symptoms ($\chi^2(2)=32.63$, p<0.01).

Examining the association between poor metabolic health and the risk of depressive symptoms at 2-year follow-up (Wave 7)

The unadjusted logistical regression analysis showed that participants with poor metabolic health were 24.0% more likely to experience depressive symptoms at 2-year follow-up, compared with those with good metabolic health. This finding was statistically significant (p<0.01) (table 2). The OR for the risk of depressive symptoms at

Table 1 Wave 6 participant characteristics and associated depressive symptoms at Wave 7 (n=6804)

Participant characteristics	Depressive symptoms (Wave 7) (Center for Epidemiologic Studies Depression Scale 4+)	
	No (0–3) (n=5953) (%)	Yes (≥4) (n=851) (%)
All participants (n=6804)	87.5	12.5
Gender		
Male (n=3030)	90.8	9.2
Female (n=3774)	84.9	15.1
Age		
50–59 years (n=1492)	85.4	14.6
60–69 years (n=2720)	90.0	10.0
70–84 years (n=2313)	86.6	13.4
85+ years (n=279)	81.7	18.3
Metabolic Health		
Good metabolic health (n=3123)	88.8	11.2
Poor metabolic health (n=3681)	86.4	13.6
Body Mass Index (BMI)		
Non-obese (BMI<30 kg/m²) (n=4737)	89.0	11.0
Obese (BMI≥30 kg/m²) (n=2058)	84.0	16.0
Missing BMI data (n=9)		
Baseline Depression (Wave 6)		
Baseline depression (n=872)	50.8	49.2
No baseline depression (n=5932)	92.9	7.1
Wealth		
Wealth quintile 1 (poorest) (n=1005)	76.4	23.6
Wealth quintile 2 (n=1214)	81.7	18.3
Wealth quintile 3 (n=1372)	88.6	11.4
Wealth quintile 4 (n=1464)	91.4	8.6
Wealth quintile 5 (wealthiest) (n=1619)	94.4	5.6
Missing wealth data (n=130)		

Table 2 The association between poor metabolic health and the risk of depressive symptoms at 2-year follow-up (Wave 7) (n=6804)

Independent variable	OR	95% CI for OR		P value
		Lower	Upper	
Metabolic health	1.24	1.07	1.44	<0.01
Metabolic health Adjusted for obesity	1.17	1.01	1.35	0.04
Metabolic health Adjusted for obesity and baseline depression (Wave 6)	1.19	1.01	1.40	0.04
Metabolic health Adjusted for obesity, baseline depression (Wave 6), gender, age and wealth	1.17	0.99	1.38	0.07

2-year follow-up reduced to 1.17 (1.01 to 1.35, p=0.04), after the model was adjusted for obesity. The OR for the risk of depressive symptoms at 2-year follow-up was 1.19 (1.01 to 1.40, p=0.04), after the model was adjusted for obesity and baseline depression (table 2). After adjusting for participant characteristics and baseline depression, the OR for the risk of depressive symptoms at 2-year follow-up decreased to 1.17 (0.99 to 1.38, p=0.07) (table 2). The latter finding was not statistically significant.

Examining the association between obesity and the risk of depressive symptoms at 2-year follow-up (Wave 7)

The unadjusted logistical regression analysis showed that obese participants were 54.0% more likely to experience depressive symptoms at 2-year follow-up, compared with participants who had a BMI $<30\,\text{kg/m}^2$ (table 3). This finding was statistically significant (p<0.01) (table 3). The OR for the risk of depressive symptoms at 2-year follow-up reduced to 1.50 (1.29 to 1.75, p<0.01), after adjusting for poor metabolic health (table 3). The OR for the risk of depressive symptoms at 2-year follow-up decreased further to 1.32 (1.11 to 1.56, p<0.01), after adjustments for poor metabolic health and baseline depression were made (table 3). After adjusting for participant characteristics and baseline depression the OR for the risk of depressive symptoms at 2-year follow-up was 1.19 (1.00 to 1.41, p=0.06) (table 3). The latter finding was not statistically significant.

Examining the associations between gender, age, wealth, baseline depression (Wave 6) and the risk of depressive symptoms at 2-year follow-up (Wave 7)

Results showed that females were 48.0% more likely to experience depressive symptoms at 2-year follow-up compared with males (table 4). This finding was statistically significant (p<0.01) (table 4). The association between age and depression was examined. The adjusted OR for the risk of depressive symptoms at 2-year follow-up was 0.91 (0.73 to 1.13, p=0.38) in participants aged between 60 and 69 years (table 4). This value increased to 1.27 (1.02 to 1.58, p=0.03) in participants aged between 70 and 84 years (table 4). For participants older than 85 years, the adjusted OR increased further to 1.43 (0.97 to 2.11, p=0.07) (table 4). Most findings, in relation to age, were not statistically significant. The association between wealth and depression was also examined. The adjusted OR for the risk of depressive symptoms at follow-up reduced from 0.80 (0.63 to 1.02, p=0.07) in wealth quintile 2 to 0.31 (0.23 to 0.41, p<0.01) in wealth quintile 5 (table 4). This suggests that individuals in the higher wealth quintiles are less likely to experience depressive symptoms at 2-year follow-up, compared with individuals in the lower wealth quintiles. Finally, the association between baseline depression and future depression was examined. The adjusted OR for the risk of depressive symptoms at 2-year follow-up was 10.59 (8.90 to 12.53, p<0.01).

Table 3 The association between obesity and the risk of depressive symptoms at 2-year follow-up (Wave 7) (n=6804)

Independent variable	OR	95% CI for OR		P value
		Lower	Upper	
Obesity	1.54	1.33	1.79	<0.01
Obesity Adjusted for poor metabolic health	1.50	1.29	1.75	<0.01
Obesity Adjusted for poor metabolic health and baseline depression (Wave 6)	1.32	1.11	1.56	<0.01
Obesity Adjusted for poor metabolic health, baseline depression (Wave 6), gender, age and wealth	1.19	1.00	1.41	0.06

Table 4   The association between the independent variables and the risk of depressive symptoms at 2-year follow-up (Wave 7) (n=6804)

Independent variables	Adjusted OR	95% CI for OR		P value
		Lower	Upper	
Gender				
Male (Reference) (n=3030)	1			
Female (n=3774)	1.48	1.25	1.75	<0.01
Age				
50–59 years (Reference) (n=1492)	1			
60–69 years (n=2720)	0.91	0.73	1.13	0.38
70–84 years (n=2313)	1.27	1.02	1.58	0.03
85+ years (n=279)	1.43	0.97	2.11	0.07
Wealth				
Wealth quintile 1 (poorest) (Reference) (n=1005)	1			
Wealth quintile 2 (n=1214)	0.80	0.63	1.02	0.07
Wealth quintile 3 (n=1372)	0.50	0.39	0.64	<0.01
Wealth quintile 4 (n=1464)	0.43	0.33	0.56	<0.01
Wealth quintile 5 (wealthiest) (n=1619)	0.31	0.23	0.41	<0.01
Missing wealth data (n=130)				
Baseline depression (Wave 6)				
Baseline depression (n=872)	10.59	8.90	12.53	<0.01
No baseline depression (n=5932)				

Adjusted for obesity, poor metabolic health, baseline depression (Wave 6), gender, age and wealth.

DISCUSSION

This study evaluated the associations between metabolic health, obesity and depressive symptoms. Initially, the unadjusted logistical regression model showed that poor metabolic health was associated with depressive symptoms at 2-year follow-up; however, after adjusting for covariates, including baseline depression, obesity, gender, age and wealth, this finding was no longer statistically significant, and the previously elevated adjusted ORs diminished. Similar findings were generated when the association between obesity and depressive symptoms was examined. The unadjusted logistical regression model initially showed that obesity was associated with depressive symptoms at 2-year follow-up, but after adjusting for covariates, the finding became statistically insignificant.

Our findings are different to those reported in previous studies. Studies which report an association between metabolic health, obesity and depression often attribute the association to biological changes. For example, obesity is commonly associated with metabolic abnormalities such as insulin resistance and raised inflammatory markers, and previous research has shown that these abnormalities are independently associated with the development of depression.[22–24] Another explanation offered for the association is that poor metabolic health and obesity have both been linked to a reduction in serotonergic activity in the brain, thus increasing the likelihood of depression.[25 26] However, the biological mechanisms underlying the association are complex and not fully understood.

To our knowledge, only one prospective study has been conducted previously to determine 'whether the association of obesity with depressive symptoms is dependent on the individual's metabolic health', using ELSA data.[10] Hamer et al[10] created four participant models: 'metabolically healthy non-obese', 'metabolically unhealthy non-obese', 'metabolically healthy obese' and 'metabolically unhealthy obese'. Using participants in the 'metabolically healthy non-obese' group as controls, the adjusted ORs showed that 'metabolically unhealthy obese' participants were 50% more likely to experience depression at follow-up. For 'metabolically unhealthy non-obese' participants, the likelihood of experiencing depression at follow-up was 44%. This value reduced to 38% for 'metabolically healthy obese' participants.[10] Based on their findings, the authors concluded that 'the association between obesity and risk of depression symptoms appears to be partly dependent on metabolic health'.[10] However, in this study, we found that neither poor metabolic health nor obesity are associated with a risk of depressive symptoms at 2-year follow-up. It is possible that a period effect may have contributed towards the differing findings because Hamer et al[10] analysed ELSA data gathered between 2004 and 2007, and this study analysed ELSA data gathered between 2012 to 2015; however, the time frame between the two studies is relatively short.[27] Another possible explanation for the differing findings is that Hamer et al[10] identified medical factors as confounders, whereas this

study included wealth, in addition to medical factors as confounders.

This study shows that lower wealth, along with baseline depression, are strong predictors for the risk of depressive symptoms at 2-year follow-up. Patten et al[28] support our wealth finding, concluding that an increased prevalence of major depression was associated with lower personal wealth. Similarly, Martikainen et al[29] analysed data collected during the Whitehall II study and reported that depression was most common among individuals in the lowest wealth categories, after adjusting for age and ill health at baseline. This finding is important because wealth inequalities are continuing to rise across England; therefore, the risk of experiencing depressive symptoms at 2-year follow-up is likely to be elevated in individuals living in the lower wealth quintiles.[30]

Our multivariate model was also used to determine whether gender or age were independently associated with a risk of depressive symptoms at 2-year follow-up. Findings showed that females were more likely to experience depressive symptoms at 2-year follow-up compared with males. This finding was statistically significant ($p<0.01$) and consistent with the existing literature.[31–33] Albert[31] suggests that 'biological sex differences' are fundamentally responsible for the differing prevalence of depression between males and females, but the author also acknowledges that further research is necessary to develop our understanding about this complex finding. While a critical review by Piccinelli and Wilkinson[33] identified that a lack of social integration, reduced social support and an increased vulnerability to adverse life events were social factors, which may potentially contribute towards a higher incidence of depression among females.

Individuals older than 70 years were at least 27.0% more likely to experience depressive symptoms at 2-year follow-up compared with individuals aged between 50 and 59 years. Findings also showed that participants aged between 60 and 69 years were 9.0% less likely to experience depressive symptoms at 2-year follow-up, compared with individuals aged between 50 and 59 years. This U-shaped curve in depression prevalence has been reported previously by Blanchflower and Oswald.[34] An explanation for this finding could be that retirement is beneficial for an individual's mental well-being.[35]

The size and representativeness of our sample are the primary strengths of this study, and therefore, our findings are generalisable to the English population, who are aged over 50 years. Standardised data collection methods and validated data collection tools were used to obtain data for ELSA, for example the CES-D was used to gather data about depressive symptoms. The CES-D scale requires participants to accurately and truthfully recall information about their depressive symptoms to prevent study bias.[36] The cause of depressive symptoms is often multifactorial, and although many covariates were used in the analyses to minimise study bias, there may be other contributory factors which have not been examined in ELSA, and thus, these factors could have influenced our findings. While this study indicated that neither metabolic health nor obesity predict depressive symptoms at 2-year follow-up, there could nevertheless be associations which are obscured by the study design. As the study only included respondents aged older than 50 years, it is possible that metabolic health and/or obesity could predict depression earlier in the life course.

CONCLUSION

This study has identified that neither poor metabolic health nor obesity are associated with a risk of depressive symptoms at 2-year follow-up. Findings from this study also showed that baseline depression and lower wealth are strong predictors for the risk of depressive symptoms at 2-year follow-up. Previous research has predominantly identified medical factors as confounders; however, this study highlights the importance of considering wealth, in addition to medical factors, as confounders in future research.

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