Weight change increases the odds of psychological distress in middle age: bidirectional analyses from the Whitehall II Study

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Abstract

Background. Mood disorders and adiposity are major public health challenges. Few studies have investigated the bidirectional association of weight and waist circumference (WC) change with psychological distress in middle age, while taking into account the potential U-shape of the association. The aim of this study was to examine the bidirectional association between psychological distress and categorical change in objectively measured weight and WC.

Methods. We analysed repeated measures (up to 17 522 person-observations in adjusted analyses) of psychological distress, weight and WC from the Whitehall II cohort. Participants were recruited at age 35–55 and 67% male. Psychological distress was assessed using the General Health Questionnaire. We used random-effects regressions to model the association between weight and WC changes and psychological distress, with and without a 5-year lag period.

Results. Psychological distress was associated with weight and WC gain over the subsequent 5 years but not the second 5-year period. Weight gain and loss were associated with increased odds for incident psychological distress in models with and without time-lag [odds ratio (OR) for incident psychological distress after 5-year time-lag: loss 1.20, 95% confidence interval (CI) 1.00–1.43; gain>5% 1.20, 95% CI 1.02–1.40]. WC changes were only associated with psychological distress in models without time-lag (OR for incident psychological distress: loss 1.29, 95% CI 1.02–1.64; gain>5% 1.33, 95% CI 1.11–1.58).

Conclusions. Weight gain and loss increase the odds for psychological distress compared with stable weight over subsequent 10 years. In contrast, the association between psychological distress and subsequent weight and WC changes was limited to the first 5 years of follow-up.

Introduction

Mental health and obesity are two major public health challenges in the European region and Western world (WHO, 2015, 2017). An estimated one in three Europeans suffer from symptoms of depression and anxiety at least once in their lifetime, and in the UK, prevalence peaks at middle age (Spiers et al., 2011; Steel et al., 2014). The prevalence of overweight and obesity also peaks in middle age, at which more than half of adults in developed countries are either overweight or obese (Ng et al., 2014).

The nature of the association between obesity and psychological distress is unclear; it could be driven by adiposity increasing the risk of psychological distress, or by psychological distress increasing the risk of obesity. Both pathways may operate (Luppino et al., 2010). Studies using an instrumental-variable design have not been able to clarify the dominant direction of the association. As there are no known single-nucleotide polymorphisms for psychological distress, a study used maternal mental health as an instrumental variable for offspring adolescent depression. Findings suggest that adolescent depression was a causal predictor of adult obesity, but not the opposite (Hamer et al., 2016). In contrast, two Mendelian randomization studies support adiposity as a cause of depression and psychological distress (Kivimaki et al., 2011; Jokela et al., 2012). Nevertheless, the nature of the obesity–psychological distress association could differ by age, and there could be common underlying factors that predispose individuals to both conditions (Luppino et al., 2010; Kivimaki et al., 2011; Jokela et al., 2012).

While many studies including middle-aged and older adults found that depression prospectively increases weight and waist circumference (WC) (Forman-Hoffman et al., 2007; Sutin and Zonderman, 2012; Brumpton et al., 2013; Lasserre et al., 2014; Singh et al., 2014; de Wit et al., 2015; Fezeu et al., 2015; Gibson-Smith et al., 2016), studies looking at categorical change (e.g. a change in weight status) also found associations with weight loss, suggesting a U-shaped association (Forman-Hoffman et al., 2007; de Wit et al., 2015; Gibson-Smith et al., 2016). Similarly, studies that have looked at the association in the direction from weight changes to depressive symptoms have found both positive and negative associations such
that weight gain and weight loss are associated with increased depressive symptoms (Forman-Hoffman et al., 2007; Jackson et al., 2014; Khalaila and Litwin, 2014; Singh et al., 2014); although in some studies the associations depended on covariates or differed by sex (Forman-Hoffman et al., 2007; Jackson et al., 2014; Singh et al., 2014).

Based on the current evidence, we hypothesized that the prospective relationship between adiposity and psychological distress is both bidirectional and U-shaped. From a public health point of view, establishing the temporal sequence and nature of this relationship in middle age could inform policy makers about targets and timing of interventions and monitoring to reduce the risk for either weight change or mental health issues and thereby increase chances for successful ageing (Brunner et al., 2014; Singh-Manoux et al., 2014).

Time-lagged analyses help to disentangle temporal sequences of events and shed light on the direction of cause and effect. To our knowledge, two studies in middle-aged adults have investigated the association in this way (Forman-Hoffman et al., 2007; Singh et al., 2014). However, they were both based on self-reported weight, which could be particularly sensitive to misreporting as participants would require to have tracked their weight for a long period of time (Forman-Hoffman et al., 2007; Gorber et al., 2007; Singh et al., 2014). In the light of inconclusive evidence from instrumental analyses and the methodological limitations in studies using time-lagged models, we firstly aim to investigate the bidirectional association of objectively measured weight and WC changes with psychological distress in a cohort of middle-aged British men and women. Secondly, we aim to establish the temporal sequence using time-lagged models in both directions.

Methods
Study population
We used data from the Whitehall II cohort study that started in 1985–88. With a response rate of 73%, the initial sample included 10,308 individuals between 35 and 55 years old. From 1985 to 2013, participants were followed up via questionnaire and visited the clinic screenings (Knüppel et al., 2005). The present study has been approved by Joint UCL/UCLH Committee on the Ethics of Human Research and participants have been asked to provide informed consent at every follow-up.

Measures
Relative changes in weight and WC
Weight was measured without shoes and clothing to the nearest 0.1 kg on Soehnle electronic scales every 5 years from 1985–88 to 2012–13. WC was measured by trained staff every 5 years from 1991–93 to 2012–13. Relative change per 5 years was calculated in log percentages \[L\% = 100 \times \log_e(x_{t+1}/x_t),\] where \(x_t\) and \(x_{t+1}\) are measurements at time \(t\) and \(t+1\) (Tornqvist et al., 1985) and transformed back to actual percentages for analysis and presentation. Weight/WC loss, moderate and heavy gain were defined as relative change of \(<-3\), \(\geq 3\) and \(>5\)% respectively (Stevens et al., 2006). Due to the small number of participants losing between \(-3\)% and \(-5\)% of initial weight, this and the more extreme loss group were combined.

Groups of changers were compared with the stable group, defined as those staying within 3% of their baseline weight or WC.

Psychological distress
Psychological distress was measured with the 30-item General Health Questionnaire (GHQ) and defined as scoring \(\geq 5\), based on receiver operating characteristic analysis (Stansfeld and Marmot, 1992; Head et al., 2013). The GHQ is a screening questionnaire for non-psychotic psychological distress and elicits depressive and anxiety symptoms such as having lost sleep over worry, or feeling unhappy or depressed (Goldberg, 1972; Stansfeld et al., 2002). GHQ caseness has in some studies been described as a common mental disorder (Kivimäki et al., 2014; Knüppel et al., 2017). The cut-off has been found to have good sensitivity (86.4%) and specificity (87.2%) to measure any mental disorder when compared with a clinical interview in a subsample of the study cohort (Head et al., 2013). In sensitivity analyses, associations using higher cut-off scores of \(\geq 6\), \(\geq 8\), \(\geq 10\) were also investigated.

Other variables of interest
Covariates were chosen based on literature review and restricted to variables available at data collection phases with psychological distress and weight data. The following covariates were assessed: sex, age, ethnicity (White, South Asian, Black), marital status, (married/cohabiting, single/divorced/widowed), last employment grade level within the civil service (high, intermediate, low), smoking (never, former, current), alcohol intake (none: \(\leq 1\) unit/week, moderate, heavy: \(>14\) units/week), self-reported physical activity (vigorous, moderate and non/mild) (Kumari et al., 2004), sleep duration (five categories from \(\leq 5\) to \(>9\) h/day), baseline body mass index class (BMI) (normal: \(<25\) kg/m\(^2\), overweight, obese: \(\geq 30\) kg/m\(^2\)), weight (kg) or WC (cm), when modelling WC change, diabetes and cardiovascular disease (coronary heart disease and stroke, CVD) based on self-report, clinical examination, Hospital Episode Statistics data or general practitioners contact; information on cancer was based on cancer registration data (Marmot and Brunner, 2005); other longstanding illnesses were self-reported and coded as yes, no or missing; menopausal status was assessed by a question on the age when menstrual bleeding stopped.

Intake of antidepressants, anxiety and antipsychotic medication was self-reported at all phases after phase 4 (1995–99), and from phase 1 (1985–88) to 4 (1995–99) medication intake or current treatment was assumed when doctor diagnosis of depression or anxiety was reported.

Statistical analysis
We used 5-year cycles of weight/WC and GHQ data across the 25 years of observation, reflecting the time interval between research clinic screenings (Knüppel et al., 2017). The observed associations were pooled across these four 5-year cycles (Figure S1). We modelled the association of psychological distress and subsequent relative weight/WC change with a mean number of cycles of 2.1 and 1.6 per individual participant, and relative weight/WC change and subsequent incident psychological distress using multinomial and binomial random-effects logistic regression with a mean number of cycles of 2.5 and 2.0, respectively. This allowed us to model simultaneously, for all cycles combined, the association between the exposure at baseline (\(t_0\)) with the outcome at end of the cycle (\(t_1\), 5 years later; \(t_2\), 10 years later), while accounting for within- and between-individual differences (Twisk, 2004). Table S1 depicts the included phases for analyses with and without a time-lag period. As WC was not measured at phase 1 (1985–88),
only phases 3 (1991–94) to 11 (2012–13) could be included, resulting in three cycles per analysis direction (Figure S1).

In the first set of analyses, we modelled the association of psychological distress with a relative 5-year weight and WC change (Table 1). In a non-lag model, prevalent psychological distress at each baseline \((t_0)\) was modelled to predict a 5-year change in weight/WC \((t_1−t_0)\), and in a lag model, the same psychological distress prevalence \((t_0)\) was modelled to predict a 5-year change after a 5-year time-lag \((t_2−t_1)\). Secondly, we modelled the association of a 5-year change in weight and WC and incident psychological distress (Table 1). Incident psychological distress was defined as those having psychological distress, among those who did not have psychological distress at baseline \((t_0)\). In a non-lag model, 5-year change in weight/WC \((t_1−t_0)\) was used to predict incident psychological distress at the cycle when the change was recorded \((t_1)\), and in a lag-model, incident psychological distress after 5 years \((t_2)\) (Table 1, Table S1).

Participants with missing information on ethnicity or ethnicity other than White/South Asian/Black were excluded from analyses. To control for selection bias for the four sets of analyses, the analytical sample was restricted to participants who had three consecutive measures of GHQ and two consecutive measures of weight or WC change. For example, participants with data on weight change from phase 3 (1991–94) to 5 (1997–99), 7 (2002–04) and 9 (2007–09). Finally, participants who became GHQ cases 5 years later were compared on the basis whether they had lost or gained weight following the approach used by Gibson-Smith et al. (Gibson-Smith et al., 2016).

### Results

At phases 1 (1985–88), 3 (1991–94), 5 (1997–99), 7 (2002–04), 9 (2007–09) and 11 (2012–13), the prevalence proportion of psychological distress was 26.8, 21.6, 21.5, 19.9, 14.3 and 16.3% of the eligible sample.

Table 2 shows the comparison of psychological distress cases and non-cases at phase 3. Psychological distress prevalence was higher in younger participants, women, unmarried participants, those who smoked, were less physically active, slept for \(<7\) h/day and those with obesity. Associations were similar at the following phases; non-white ethnicity, lower grade level and CVD were significantly associated with higher psychological distress prevalence at phases 5 (1997–99) and 7 (2002–04) (not depicted). From phase 3 (1991–94) to 5 (1997–99), 11.2% lost weight, 14.6% gained a large amount (>5%) of weight and 53.7% heavily gained weight following the approach used by Gibson-Smith et al. (Gibson-Smith et al., 2016).

### Table 1. Mode of analyses by direction, exposure and outcome

| Direction                      | Exposure                                      | Outcome                                                                 |
|--------------------------------|-----------------------------------------------|-------------------------------------------------------------------------|
| Psychological distress to weight change | Prevalent psychological distress year 0 \((t_0)\) | Relative weight change across 0 to 5 years \((t_1−t_0)\)              |
| Weight change to psychological distress | Relative weight change across 0–5 years \((t_1−t_0)\) | Psychological distress at 5 years \((t_1)\), excluding those with psychological distress at 0 years \((t_0)\); referred to as incident |

Factors, health behaviours, sleep duration and baseline health status (CVD, diabetes and cancer). To investigate the role of health status over the course of follow-up, health status at follow-up \((t_1)\) was administered in time-lagged models. In sensitivity analyses, main analyses were repeated (a) excluding participants with unknown or intake of antidepressants, antipsychotic or anxiety medication at each baseline to account for confounding by treatment of mood disorders; and (b) additionally adjusted for longstanding illnesses in sensitivity analyses, to investigate whether other diseases could confound associations. A posteriori several sensitivity analyses were added: (c) using different cut-off points for GHQ caseness; (d) adjusting additionally for menopausal status and change in status; (e) an analysis for the association of 5-year change in weight and incident psychological distress which excluded participants who had lost weight and reported intentional weight loss based on the question ‘Are you on a slimming diet now?’ in a Food Frequency Questionnaire administered at phases 5 (1997–99), 7 (2002–04) and 9 (2007–09). Finally, participants who became GHQ cases 5 years later were compared on the basis whether they had lost or gained weight following the approach used by Gibson-Smith et al. (Gibson-Smith et al., 2016).
Table 2. Cross-sectional associations between psychological distress and covariates at phase 3 (1991–94)

|                           | No psychological distress ($n = 3542$) | Psychological distress ($n = 984$) | $p$  |
|---------------------------|----------------------------------------|-----------------------------------|------|
|                           | Mean/n ± S.D./%                         | Mean/n ± S.D./%                   |      |
| Age                       | 50.0 ±6.1                              | 48.9 ±6.6                         | <0.001|
| Sex                       |                                        |                                   |      |
| Women                     | 944 (26.7)                             | 350 (35.6)                        | <0.001|
| Ethnic group              |                                        |                                   | 0.97 |
| White                     | 3303 (93.3)                            | 918 (93.3)                        |      |
| South Asian               | 155 (4.4)                              | 44 (4.5)                          |      |
| Black                     | 84 (2.4)                               | 22 (2.2)                          |      |
| Marital status            |                                        |                                   | <0.001|
| Married/cohabiting        | 2804 (79.3)                            | 719 (73.1)                        |      |
| Single/divorced/widowed   | 734 (20.7)                             | 264 (26.9)                        |      |
| Last grade level in Civil service† |                                   |                                   | 0.37 |
| Highest                   | 1509 (42.6)                            | 398 (40.4)                        |      |
| Moderate                  | 1607 (45.4)                            | 471 (47.9)                        |      |
| Lowest                    | 426 (12.0)                             | 115 (11.7)                        |      |
| Smoking                   |                                        |                                   | 0.023|
| Never-smoker              | 1690 (50.2)                            | 439 (46.8)                        |      |
| Ex-smoker                 | 1308 (38.8)                            | 368 (39.2)                        |      |
| Current smoker            | 371 (11.0)                             | 132 (14.1)                        |      |
| Physical activity         |                                        |                                   | <0.001|
| Non/mild                  | 1202 (33.9)                            | 410 (41.7)                        |      |
| Moderate                  | 1611 (45.5)                            | 423 (43.0)                        |      |
| Vigorous                  | 729 (20.6)                             | 151 (15.4)                        |      |
| Alcohol consumption       |                                        |                                   | 0.22 |
| None                      | 718 (20.3)                             | 222 (22.6)                        |      |
| Moderate                  | 1939 (54.8)                            | 512 (52.0)                        |      |
| Heavy                     | 881 (24.9)                             | 250 (25.4)                        |      |
| Sleep duration            |                                        |                                   | <0.001|
| <7 h/day                  | 811 (22.9)                             | 281 (28.6)                        |      |
| ≥7 h/day                  | 2729 (77.1)                            | 703 (71.4)                        |      |
| Weight status (derived using body mass index) |                                   |                                   | 0.032|
| Normal weight <25 kg/m²   | 1856 (53.6)                            | 524 (55.0)                        |      |
| Overweight 25–30 kg/m²    | 1345 (38.8)                            | 336 (35.3)                        |      |
| Obese >30 kg/m²           | 262 (7.6)                              | 92 (9.7)                          |      |
| Diabetes                  | 80 (2.3)                               | 22 (2.2)                          | 0.97 |
| CVD                       | 87 (2.5)                               | 29 (2.9)                          | 0.39 |
| Cancer                    | 35 (1.0)                               | 8 (0.8)                           | 0.62 |
| Weight change             |                                        |                                   | <0.001|
| Loss (>−3%)               | 398 (11.5)                             | 98 (10.3)                         |      |
| Stable (±3%)              | 1317 (38.0)                            | 322 (33.7)                        |      |
| Gain (>3% to ≤5%)         | 527 (15.2)                             | 119 (12.5)                        |      |
| High Gain (>5%)           | 1225 (35.3)                            | 416 (43.6)                        |      |

(Continued)
0.018, fully adjusted models], and there was no difference after additionally adjusted for any longstanding illnesses. When the analysis was based on a 5-year time-lag, baseline psychological distress was not associated with subsequent weight changes (Table 2).

Compared with person-observations in the stable weight group, participants with gains above 5% of their baseline body weight from 0 to 5 years and losses above 3% had increased odds for incident psychological distress at 5 years and at 10 years (Table 4). This association was independent of baseline socio-demographic factors, health behaviours, weight, BMI class and disease. The associations of weight gain and loss with incident psychological distress at 10 years were marginally attenuated when adjusted for disease at 5 years ($p = 0.054$) and stayed statistically significant when additionally adjusted for longstanding illnesses at baseline and 5 years ($p = 0.041$). Excluding participants taking antidepressants, antipsychotic or anxiety medication at baseline marginally attenuated the association of high weight gain and incident psychological distress 5 years later in fully adjusted models (OR 1.15, 95% CI 0.99–1.33, $p = 0.061$) and the association of weight loss with subsequent incident psychological distress at 10 years (OR 1.19, 95% CI 0.99–1.42, $p = 0.068$, in fully adjusted models).

In sensitivity analyses using cut-off points of 6, 8 and 10 for psychological distress results were generally replicated showing similar ORs at different cut-offs. However, with smaller numbers of participants being classified as psychologically distressed, the association between weight change and psychological distress after a 5-year time lag did not reach statistical significance (see Table S4–S9 for associations with weight change).

Additional adjustment for menopausal status and change in status did not change the conclusions but associations between weight loss (OR 1.28, 95% CI 1.04–1.57) and gain (OR 1.29, 95% CI 1.06–1.59) and incident psychological distress after a 5-year time lag period were slightly stronger.

Sensitivity analysis excluding participants who lost weight and reported to be on a weight loss diet in a subgroup with available data did not change the association with incident psychological distress (OR 1.28, 95% CI 1.04–1.57) and gain (OR 1.29, 95% CI 1.06–1.59) and incident psychological distress after a 5-year time lag period were slightly stronger.

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**Table 2.** Short-term (0–5 years) and long-term (5–10 years) effect of prevalent psychological distress on subsequent weight change

| Waist change         | No psychological distress ($n = 3542$) | Psychological distress ($n = 984$) | $p$ |
|----------------------|---------------------------------------|-----------------------------------|-----|
|                      | Mean/n ± S.D./%                        | Mean/n ± S.D./%                   |     |
| Loss (−3%)           | 192 (6.3)                             | 47 (5.5)                          | 0.028 |
| Stable (±3%)         | 821 (26.8)                            | 196 (23.0)                        |     |
| Gain (>3% to ≤5%)    | 445 (14.5)                            | 113 (13.3)                        |     |
| High gain (>5%)      | 1608 (52.4)                           | 496 (58.2)                        |     |

**Table 3.** Short-term (0–5 years) and long-term (5–10 years) effect of prevalent psychological distress on subsequent weight change

| Outcome: weight change | Non-time-lagged model (0–5 years change) | 5-year time-lagged model (5–10 years change)$^{c}$ |
|-----------------------|------------------------------------------|-----------------------------------------------|
| Person-obs.           | 3030                                     | 3737                                         |
| Psychological distress cases | 586                                      | 794                                        |
| OR$^{a}$ (95% CI)     | 0.93 (0.84–1.04)                         | 0.98 (0.89–1.09)                             |
| OR$^{b}$ (95% CI)     | 1.07 (0.96–1.20)                         | 0.96 (0.85–1.08)                             |
| OR$^{d}$ (95% CI)     | 1.30 (1.20–1.44)                         | 1.27 (1.16–1.39)                             |

$^{a}$Odds ratios from base model adjusted for age, sex and ethnicity.
$^{b}$Odds ratios from fully adjusted model: additionally adjusted for marital status, last grade level in civil service, smoking, alcohol intake, physical activity, BMI, weight, diabetes, cardiovascular disease, cancer at baseline.
$^{c}$Weight change is lagged 5 years after psychological distress assessment (at 0 years).
$^{d}$Odds ratios additionally adjusted for diabetes, cardiovascular disease, cancer at 5 years.
time-lag (OR 1.04, 95% CI 0.93–1.16) compared with odds for keeping WC stable. WC loss was associated with increased odds for incident psychological distress at 5 years (OR 1.29, 95% CI 1.02–1.64), but no significant increase at 10 years (OR 1.08, 95% CI 0.83–1.39) and similarly WC gain was associated with an increased odds for incident psychological distress at 5 years (OR 1.33, 95% CI 1.11–1.58) but not at 10 years (OR 1.08, 95% CI 0.90–1.31). There was no association of WC loss with incident psychological distress when participants taking antidepressants, antipsychotic or anxiety medication at baseline were excluded (OR 1.26, 95% CI 0.99–1.60, p = 0.065, in models adjusted for age, sex and ethnicity). Additionally, adjusting for any longstanding illnesses did not change results.

There was no evidence for interaction by sex or cycle in any of the modes of analysis. There was an interaction with age (p = 0.028) for the association between psychological distress and weight loss, suggesting that baseline psychological distress was mainly associated with decreased odds for weight loss in the younger participants.

Both weight loss and weight gain were shown to have an adverse effect on the long-term likelihood of new psychological distress. We compared participants who lost weight and became psychological distress cases 5 years later with those who gained weight and became psychological distress cases 5 years later (Table 5). People with new psychological distress at follow-up weight and became psychological distress cases 5 years later who lost weight on average lost 6.1% (S.D. 3.4) of their initial distress. We compared participants who

Discussion

This was the first study to investigate the bidirectional association of psychological distress and objectively measured weight and WC changes in middle-aged adults using time-lagged analyses. Our findings confirmed the hypothesis of bidirectional associations between psychological distress and relative change in weight and WC short term. The association between prevalent psychological distress and relative change in weight and WC showed a linear trend, while both loss and gain >5% of weight and WC increased the odds of incident psychological distress. When the first 5 years of follow-up were excluded from analysis, weight changes continued to predict incident psychological distress, while the effect of psychological distress on weight change was restricted to the first 5 years. The findings suggest an association in the direction of weight changes to psychological distress.

Effect of psychological distress on subsequent weight and WC changes

The association between psychological distress and increases in weight and WC in non-lagged models was consistent with previous literature (Forman-Hoffman et al., 2007; Lasserre et al., 2014; Singh et al., 2014; Gibson-Smith et al., 2016). We did not find a positive association between psychological distress and weight loss in the main analysis as observed by others (de Wit et al., 2015; Gibson-Smith et al., 2016). In fact, when including an age interaction and excluding participants with antidepressant, antipsychotic or anxiety medication intake, which might have a pharmacological effect on adiposity, psychological distress was associated with reduced odds of weight loss compared with those not reporting distress, which was stronger at younger ages.

The null association between psychological distress and weight changes in time-lagged models contrasts results of previous studies using this method. Forman-Hoffman et al., 2007 and Singh et al., 2014 found prevalent depression to be associated with a 2-year weight loss and gain in women after a 2-year time-lag and a 3-year weight gain after a 3-year time-lag, respectively (Forman-Hoffman et al., 2007; Singh et al., 2014). This discrepancy could be due to the longer period between weight measures

Table 4. Short-term (0–5 years) and long-term (5–10 years) effect of weight change on subsequent incident psychological distress

| Outcome: incident psychological distress | Non-time-lagged model (at 5 years) | 5-year time-lagged model (at 10 years)* |
|----------------------------------------|-----------------------------------|----------------------------------------|
| Person-obs. | Cases | ORb (95% CI) | ORc (95% CI) | ORd (95% CI) | Cases | ORb (95% CI) | ORc (95% CI) | ORd (95% CI) |
| Loss (>-3%) | 2444 | 322 | 1.21 (1.03–1.42) | 1.19 (1.01–1.40) | 322 | 1.21 (1.01–1.44) | 1.20 (1.00–1.43) | 1.19 (1.00–1.42) |
| Stable (±3%) | 6072 | 715 | Ref. | Ref. | 713 | Ref. | Ref. | Ref. |
| Gain (>3% to ≤5%) | 1824 | 230 | 0.98 (0.82–1.18) | 0.98 (0.82–1.27) | 230 | 1.02 (0.84–1.24) | 1.02 (0.84–1.24) | 1.02 (0.84–1.24) |
| High gain (>5%) | 3239 | 519 | 1.18 (1.02–1.36) | 1.17 (1.01–1.35) | 500 | 1.19 (1.04–1.42) | 1.20 (1.02–1.40) | 1.19 (1.02–1.39) |

*aThe incident psychological distress is lagged 5 years after weight change (from 0 to 5 years).
*bOdds ratios from base model adjusted for age, sex and ethnicity.
*cOdds ratios from fully adjusted model: additionally adjusted for marital status, last grade level in civil service, smoking, alcohol intake, physical activity, BMI, weight, diabetes, cardiovascular disease, cancer at baseline.
*dOdds ratios additionally adjusted for diabetes, cardiovascular disease, cancer at 5 years.
Table 5. Comparison of person-observations of participants who lost $>−3\%$ weight and person-observations of participants who gained $>5\%$ weight and suffered from psychological distress psychological distress 5 years later (at 10 years)

|                           | Participants with weight loss ($<−3\%$) and psychological distress ($n = 337$) | Participants with high weight gain ($>5\%$) and psychological distress ($n = 528$) |   |   |
|---------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|---|---|
|                           | Mean/n ± S.D./(%)                                                 | Mean/n ± S.D./(%)                                                 | $p$ |
| Baseline characteristics   |                                                                 |                                                                 |   |   |
| Women                     | 121 (35.9)                                                      | 189 (35.8)                                                      | 0.98 |   |
| Age                       | 55.1 ±9.4                                                      | 47.7 ±8.10                                                      | <0.001 |   |
| Smoking                   |                                                                 |                                                                 |   |   |
| Never-smoker              | 173 (52.1)                                                      | 277 (53.6)                                                      |   |   |
| Ex-smoker                 | 126 (37.5)                                                      | 170 (32.9)                                                      |   |   |
| Current smoker            | 35 (10.4)                                                       | 70 (13.5)                                                       | 0.23 |   |
| Physical activity         |                                                                 |                                                                 |   |   |
| Non/mild                  | 133 (40.1)                                                      | 191 (36.5)                                                      |   |   |
| Moderate                  | 154 (46.4)                                                      | 228 (43.6)                                                      |   |   |
| Vigorous                  | 45 (13.6)                                                       | 104 (19.9)                                                      | 0.058 |   |
| Alcohol consumption       |                                                                 |                                                                 |   |   |
| None                      | 79 (23.7)                                                       | 111 (21.3)                                                      |   |   |
| Moderate                  | 155 (46.6)                                                      | 273 (52.4)                                                      |   |   |
| Heavy                     | 99 (29.7)                                                       | 137 (26.3)                                                      | 0.25 |   |
| Sleep duration            |                                                                 |                                                                 |   |   |
| <7 h/day                  | 111 (33.0)                                                      | 166 (31.4)                                                      |   |   |
| ≥7 h/day                  | 225 (67.0)                                                      | 362 (68.6)                                                      | 0.49 |   |
| Disease status at baseline: |                                                               |                                                                 |   |   |
| CVD                       | 22 (6.5)                                                        | 24 (4.6)                                                        | 0.21 |   |
| Diabetes                  | 26 (7.7)                                                        | 17 (3.2)                                                        | 0.003 |   |
| Diabetes (self-reported)  | 15 (4.4)                                                        | 11 (2.1)                                                        | 0.047 |   |
| Cancer                    | 13 (3.9)                                                        | 6 (1.1)                                                         | 0.008 |   |
| Disease status at end of weight change |                                                               |                                                                 |   |   |
| CVD                       | 39 (11.6)                                                      | 39 (7.4)                                                        | 0.035 |   |
| Diabetes                  | 40 (11.9)                                                      | 24 (4.6)                                                        | <0.001 |   |
| Cancer                    | 20 (5.9)                                                        | 19 (3.6)                                                        | 0.11 |   |
| Measures of adiposity     |                                                                 |                                                                 |   |   |
| Baseline BMI class        |                                                                 |                                                                 |   |   |
| Normal                    | 148 (44.2)                                                      | 291 (55.4)                                                      |   |   |
| Overweight                | 132 (39.4)                                                      | 185 (35.2)                                                      |   |   |
| Obese                     | 55 (16.4)                                                       | 49 (9.3)                                                        | <0.001 |   |
| Weight loss in next 5 years | 78 (23.1)                                                      | 112 (21.2)                                                      | 0.16 |   |
| Weight gain in next 5 years | 146 (43.3)                                                      | 205 (38.8)                                                      | 0.073 |   |
| Psychological distress details |                                                               |                                                                 |   |   |
| Psychological distress at end of weight gain | 123 (36.5)                                                      | 181 (34.3)                                                      | 0.51 |   |
| Intake of antidepressants, antipsychotic or anxiety medication |   |   |   |   |
| At baseline               | 15 (4.5)                                                        | 19 (3.6)                                                        | 0.53 |   |
(Continued)
and lag length in our study (5 years compared with 2 and 3 years). It is possible that mood disorders only have a short-term effect on weight changes. This association could be explained by dysregulations of the hypothalamic–pituitary–adrenal axis (Peckett et al., 2011; Stetter and Miller, 2011) or adverse effects on health behaviours, such as physical activity (Azevedo Da Silva et al., 2012).

**Effect of weight and WC changes on incident psychological distress**

We found a robust association between weight and WC change (from 0 to 5 years) on odds of an incident psychological distress at 5 years. This finding was in line with previous results from prospective studies (Forman-Hoffman et al., 2007; Jackson et al., 2014; Khalaila and Litwin, 2014; Singh et al., 2014). However, some previous findings depended on adjustment for other factors, and in one study, the association with weight gain was restricted to men (Forman-Hoffman et al., 2007; Khalaila and Litwin, 2014; Singh et al., 2014).

Weight gain and weight loss (from 0 to 5 years) also increased the chances for mood disorders after a 5-year time-lag (incident psychological distress at 10 years) in models adjusted for covariates at baseline. Although our results differed from the fully adjusted time-lagged models reported by Singh et al. (2014) and Forman-Hoffman et al. (2007), they are in line with their unadjusted results (Forman-Hoffman et al., 2007; Singh et al., 2014). In contrast to our analyses, Singh et al. (2014) and Forman-Hoffman et al. (2007) adjusted for covariates at baseline and time-varying factors in fully adjusted models. This could have led to overadjustment as time-varying factors may have collinear associations or act as mediators. In addition, the difference to our findings might be due to the use of self-reported weight. Under-reporting of weight could have resulted in misclassification of participants to the stable weight group, thereby underestimating the true association (Gorber et al., 2007).

The association between weight gain and increased chance of incident mood disorder could be explained by biological and psychological mechanisms. Inflammatory markers have been shown to increase with weight gain and elevated marker levels have been found to be associated with increased risk for psychological distress (Fransson et al., 2010; Kivimäki et al., 2014). Furthermore, weight gain may prompt experiences and perception of weight discrimination, which have been found to explain about 40% of the association of obesity and psychological well-being (Jackson et al., 2015).

We tested several potential alternative explanations for the association of weight loss and subsequent psychological distress. We additionally adjusted for health status at 5 years to investigate whether the association was driven by a change in health status over follow-up; while results lost statistical significance the estimates were only marginally attenuated. Our finding was in line with the findings by Jackson et al. (2014) who found that the association between weight loss and depressed mood could not be explained by changes in health and major life events (Jackson et al., 2014). We excluded participants with intake of antidepressants, antipsychotic or anxiety medication and found small differences in associations. In sensitivity analyses, we tested whether the association was driven by unintentional weight loss. We could not show a difference in the association, suggesting that the association might be independent of weight loss intention. Additional adjustments for longstanding illnesses, menopausal status and status change also did not change the conclusions.

Results from weight loss trials show that lifestyle interventions can improve mood. But the null association between weight loss and depression symptoms within groups suggests that the effect is not fully due to weight loss itself (Fabricatore et al., 2011). Outside of a controlled environment, the difficulties surrounding the attainment of weight loss could motivate unhealthy behaviours and negative thoughts (Jackson et al., 2014). Compared with a general population, those who are successfully losing weight have been shown to have more depressive symptoms, concerns about health and body shape, engage in binge eating and unhealthy dieting practices (Feller et al., 2015). We compared those with incident psychological distress at 10 years that had gained weight to those who had lost weight to elucidate whether they had specific characteristics. Those who lost weight and got depressed were sicker, older and more overweight than those who gained weight. We found little difference in reported

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### Table 5. (Continued.)

| Outcome GHQ | Participants with weight loss (<−3%) and psychological distress (n=337) | Participants with high weight gain (>5%) and psychological distress (n=528) |
|-------------|-------------------------------------------------|-------------------------------------------------|
|             | Mean/n ± s.d./ (%) | Mean/n ± s.d./ (%) | p     |
| At end of weight change | 16 (4.8) | 32 (4.8) | 0.41 |
| At outcome | 35 (10.4) | 44 (8.4) | 0.31 |
| GHQ score at outcome | 10.9 ± 5.9 | 10.7 ± 5.7 | 0.72 |
| Have you recently: | | | |
| Question 14 – felt constantly under strain? | 207 (61.6) | 358 (67.8) | 0.062 |
| Question 17 – been able to enjoy your normal day-to-day activities? | 189 (56.1) | 259 (49.2) | 0.047 |
| Question 18 – been taking things hard? | 153 (45.8) | 208 (39.4) | 0.063 |
| Question 25 – felt that life is entirely hopeless? | 59 (17.5) | 66 (12.5) | 0.041 |

*a*Reverse scored.
symptoms of psychological distress, although a few answers could point to that those who lost weight could have severe symptoms with a severe effect on daily life. Further research is warranted to elucidate the prospective effect of weight loss on mood outside of controlled trial settings.

Limitations

Limitations need to be considered in the interpretation of our results. Our study was based on a non-representative cohort, which might reduce generalizability of results. For example, the prevalence of obesity in this study (8.0%) was lower than reported in the Health Survey for England in 1993 (13.6%) (Zaninotto et al., 2009). Nevertheless, hazard ratios produced in the Whitehall II study have been found to be similar when investigating associations between common risk factors for CVD and CVD risk to those from representative cohorts even though disease incidence and prevalence of exposures differed (Batty et al., 2014). Representativeness is further affected by attrition with healthier participants being more likely to remain and be included in this research (Jokela et al., 2011).

Mental health was assessed using a population screening tool which may have led to some misclassification of participants. However, the GHQ at a cut-off of 5 was found to be a sensitive and specific measure for any mental disorder in this cohort (Head et al., 2013). Further, sensitivity analyses using higher cut points produced similar associations. Psychological distress has been found to be recurrent in 36% of cases in Whitehall II; it cannot be ruled out that associations might differ by number of case-ness episodes (Jokela et al., 2011). Moreover, the 5-year period between screening phases could not be investigated.

Despite the wide range of covariates included in the models, residual confounding could still be present. Hypothetically, there may be pleiotropic genetic predisposition for both psychological distress and higher or lower adiposity. Furthermore, use of antidepressants, antipsychotic or anxiety medication could not be directly identified in data collection up to phase 4 and was inferred from self-reported doctor diagnoses of depression and anxiety.

Finally, the relatively long period between screening phases did not fully allow for the role of short-term changes in weight, WC and psychological distress to be investigated.

The present study examined bidirectional associations between psychological distress and adiposity across 10 years. In mid-life, it appears there are long-term adverse effects of weight loss and substantive weight gain, over 5%, on psychological distress. Conversely, low mood was associated with weight and WC gain in the short term (0–5 years), but this effect was not evident in the longer term. Our findings suggest that monitoring of weight changes in both directions could help identify persons at risk of mood disturbances in middle age. Interventions encouraging the maintenance of weight could have a protective effect on mental health.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291718003379

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Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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