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Research paper

Association of mental health and negative life events with weight change in patients with overweight: A cohort study

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ABSTRACT

Background: It is unclear to what extent mental health and negative life events (NLEs) contribute to weight change in patients with overweight. This study aimed to evaluate the association of anxiety, depression, NLEs and quality of life (QoL) with weight change over ten years in middle-aged individuals with overweight.
Methods: Population-based cohort study of 2889 middle-aged men and women with a body mass index ≥27 kg/m^2. Relative weight change over ten years was defined as weight loss (≤− 5 %), stable weight (between >− 5 % and <5 %) or weight gain (≥5 %). At baseline, participants reported anxiety symptoms, depressive symptoms, recent (last year) and distant (lifetime) NLEs, and a mental component summary of QoL. With multinomial logistic regression adjusting for potential confounding, we examined the association of mental health and NLEs with weight change after a median (25th, 75th percentiles) follow-up of 9.7 (9.0–10.5) years.
Results: In 51 % participants weight was stable, 33 % participants lost weight and 17 % gained weight. Mild (odds ratio 1.36; 95 % confidence interval 1.05–1.75), and moderate to very severe depressive symptoms (1.43; 0.97–2.12) and four or more distant NLEs (1.35; 1.10–1.67) were associated with weight gain. Anxiety symptoms, the mental component summary of QoL were not associated with either weight gain or weight loss.
Limitations: Due to the observational design residual confounding cannot be excluded.
Conclusion: Our study suggests that depressive symptoms or having experienced distant NLEs are associated with weight gain over time in middle-aged individuals with overweight. These subgroups might benefit from proactive attention from their health care providers.

1. Introduction

Obesity has become a worldwide and rapidly growing public health problem. In 2016 worldwide, >1.9 billion adults were overweight. Of these over 650 million were obese (WHO, 2021). In 2022, 50.2 % of the Dutch adult population were overweight or obese (RIVM, 2023). Care for patients with obesity should be optimized to control this pandemic more effectively. Weight loss, or maintaining a stable weight, in patients with obesity contributes to achieving health benefits (Moore et al., 2005). In contrast, weight gain yields an increased risk of the development of co-morbidities and mortality (de Mutsert et al., 2014; Guh et al., 2009; Must et al., 1999; Verkouter et al., 2019). To reduce the burden of obesity on society, it is important to know which potentially modifiable factors (e.g., psychological and sociological factors) contribute to weight change in patients with obesity.

Studies have suggested that weight change might partly be attributed to mental health problems as many studies showed associations between, for example, depression and anxiety, and obesity (Alshehri et al., 2019; Baldofski et al., 2019; de Wit et al., 2009; Gariepy et al., 2010; Ma et al., 2017). It is also known that negative life events (NLEs) (e.g., death of first degree relative, major financial crisis) and deterioration of quality of life (QoL) are associated with obesity (Kolotkin and Andersen, 2017; Wardle et al., 2011). It is unclear to what extent these factors play a role in weight change in people who already have overweight or obesity. Studies that examined the association between anxiety, depression, experiencing NLEs and the mental domain of QoL and

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Table 1
Baseline characteristics.

Characteristics	Total population	Men (53.0 %)	Women (47.0 %)
Participants, n	2889	1530	1359
Age (years)	56.0 (5.9)	56.3 (6.0)	55.7 (5.8)
Baseline BMI (kg/m^2)	30.3 (28.6–32.9)	29.9 (28.4–32.1)	30.9 (28.9–33.7)
Baseline waist circumference (cm)	105.5 (10.2)	108.6 (9.0)	102.0 (10.3)
Total body fat (%)	37.8 (29.3–44.0)	29.6 (26.8–32.9)	44.1 (41.7–46.7)
Tobacco smoking (%)			
Never	33.2	30.0	36.8
Former	52.9	52.6	53.3
Current	13.9	17.5	9.9
Alcohol consumption (g/day)	10.4 (2.1–22.8)	16.8 (5.2–30.4)	4.9 (1.0–15.0)
Educational level (% high)	40.5	43.8	36.6
Ethnicity (% Caucasian)	96.7	97.1	96.2
Physical activity (metabolic equivalent of task hours per week)	27.0 (14.0–47.0)	28.0 (13.9–49.5)	26.0 (14.0–45.0)
Energy intake (kJ/day)	9680 (3276)	10,581 (3361)	8665 (2857)
Use of psychotropic drugs (%)	9.6	6.6	12.9
Co-morbidity			
Diabetes (%)	7.0	7.8	6.0
Cardiovascular disease (%)	6.9	9.2	4.4
Median BAI score range 0–63	3 (1–7)	2 (0–5)	4 (2–9)
Low (%)	97.9	98.2	97.4
Moderate and high (%)	2.1	1.8	2.6
Median IDS-SR 30 range 0–84	8 (5–14)	7 (4–12)	11 (7–17)
None (%)	72.3	81.0	62.6
Mild (%)	20.9	13.5	29.1
Moderate to very severe (%)	6.8	5.4	8.3
Median score recent NLEs range 0–12	0 (0–1)	0 (0–1)	0 (0–1)
<1 recent NLE (%)	54.1	56.6	51.3
≥1 recent NLEs (%)	45.9	43.4	48.7
Median score distant NLEs range 0–12	3 (2–5)	3 (2–4)	4 (2–5)
<4 distant NLEs (%)	53.1	58.2	47.4
≥4 distant NLEs (%)	46.9	41.8	52.6
Median MCS of the SF-36 range 0–100	54.2 (49.1–57.3)	54.8 (50.5–57.6)	53.7 (46.7–57.0)
Low (%)	28.0	23.3	33.3
High (%)	72.0	76.7	66.7

Normally distributed data shown as mean and standard deviation (SD), skewed distributed data shown as median (25th, 75th percentiles) and categorical data are shown as percentage BMI: body mass index, BAI: Beck Anxiety Inventory, IDS-SR30: Inventory of Depressive Symptomatology, NLEs: Negative Life Events, MCS: Mental Component Summary, SF-36: Short Form Health Survey-36.
Missing values: total body fat n = 13, educational level n = 19, ethnicity n = 2, physical activity n = 40, tobacco smoking n = 1, diabetes n = 28, cardiovascular disease n = 9, BAI n = 3, IDS-SR n = 3, recent NLEs n = 6, distant NLEs n = 6, MCS n = 24.

change in body weight, have shown diverse findings (Brumpton et al., 2013; Luppino et al., 2010; Mehlig et al., 2020; Sahle et al., 2019; Sahle et al., 2020). For anxiety, one study with a follow-up of 11 years showed an association with weight gain, while another study over 5 years follow-up did not find this association (Brumpton et al., 2013; Sahle et al., 2019). Regarding depression, different longitudinal studies have observed a positive association between depression and weight gain, including Brumpton et al. with a follow-up of 11 years (Brumpton et al., 2013), a meta-analysis of 15 studies with varying follow-up durations (Luppino et al., 2010), and Sahle et al. with a follow-up of 5 years (Sahle et al., 2019). Evidence concerning experiencing negative life events and weight gain is limited. Only one longitudinal study with a follow-up of 13 years investigated specifically the association between life events and weight gain, they found a positive association with weight gain (Mehlig et al., 2020). Finally, it is unclear if a deterioration in QoL is associated

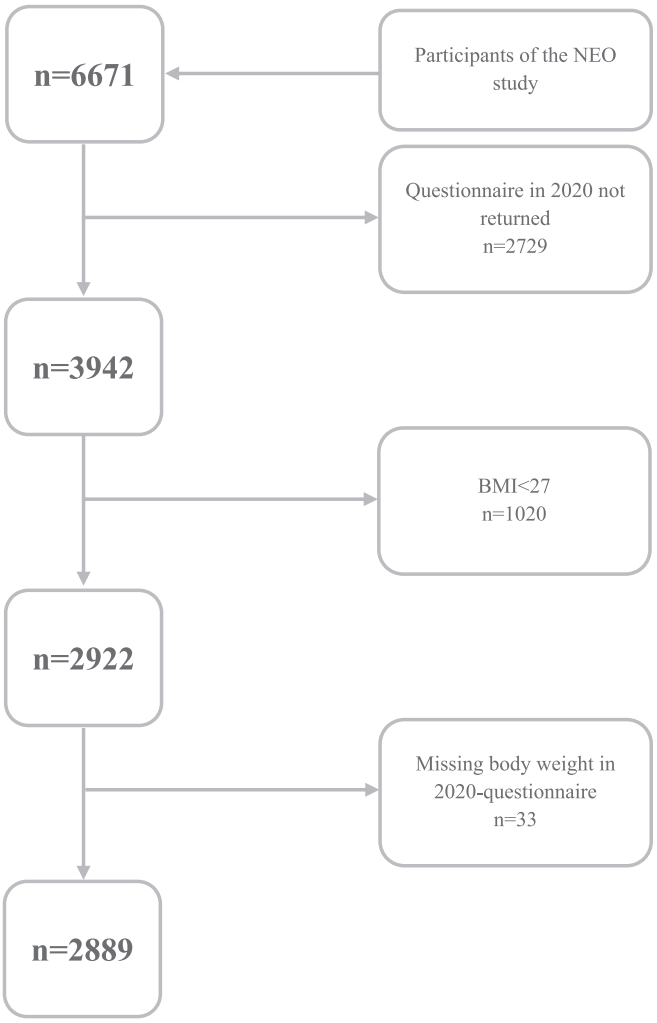

Fig. 1. Flowchart of participants with exclusion criteria.

with weight gain. Literature shows different results for the physical, mental and social health domains of QoL and weight change. When focusing on the mental health domain of QoL and weight gain, mainly no association was found over a follow-up of 11 years (Sahle et al., 2020).

Patients with mental health problems constitute a heterogeneous population. In order to identify high-risk patients for weight gain, especially in those with obesity it is important to know to what extent mental health problems are related to weight change in this population.

Therefore, the aim of this study was to investigate the associations of mental health problems (anxiety, depression, mental health domain in quality of life) and negative life events (recent and distant), with weight change over 10-year follow-up in middle-aged individuals with overweight.

2. Methods

2.1. Study design and study population

The Netherlands Epidemiology of Obesity (NEO) study is a population-based cohort study of 6671 individuals. Inclusion criteria for participating the NEO study were men and women aged between 45 and 65 years with a self-reported body mass index (BMI) of 27 kg/m^2 or higher, living in the greater area of Leiden (in the West of the Netherlands). In addition, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited, irrespective of their BMI.

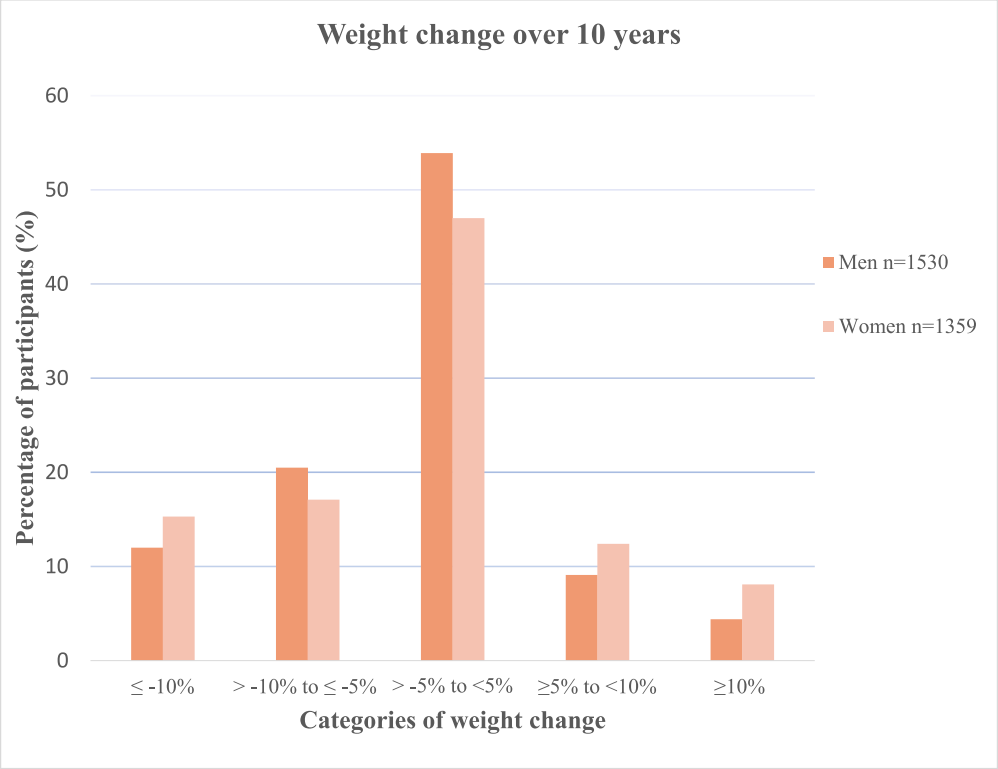

Fig. 2. Distribution of weight change over 10 years in 1530 men and 1359 women of middle age with overweight.

Participants were invited to a baseline visit between September 2008 and September 2012 at the NEO study center of the Leiden University Medical Center (LUMC) after an overnight fast. Prior to the study visit, participants completed several questionnaires at home to report demographic, lifestyle and clinical information, in addition to questions on mental health and NLEs. Participants came to the research site in the morning to undergo several baseline measurements including anthropometric measurements and blood sampling. The study design and population have been described in detail elsewhere (de Mutsert et al., 2013). The Medical Ethical Committee of the LUMC approved the design of the study. All participants gave their written informed consent.

During the COVID-19 outbreak a questionnaire was sent in June and July 2020 to 6356 participants of the baseline participants to report COVID-19 related symptoms. In this 2020-questionnaire, demographic, lifestyle and clinical information including body weight were reported. Due to unavailability of an email/home address in the Netherlands, death, or no permission for follow-up research, the questionnaire was not sent to the other 315 of the total 6671 participants. The response rate of the 2020-questionnaire was 62 % (n = 3942).

2.2. Data collection

2.2.1. Assessment of mental health and negative life events at baseline

Mental health and NLEs were assessed by self-reported questionnaires at baseline. For analysis purposes and better interpretation side-by-side we dichotomized each questionnaire, except for depression which was divided into three categories.

2.2.1.1. Anxiety symptoms. The Beck Anxiety Inventory (BAI) questionnaire measures clinical anxiety (range 0–63) (Beck et al., 1988). A score of 0–21 represents low anxiety (reference category), a score of 22–35 represents moderate anxiety and a score of ≥36 represents potentially concerning levels of anxiety. For analysis purposes and due to the relatively small sample size in the moderate and high subcategories, we merged them into "moderate to high". Cronbach's alpha in the present study was 0.88.

2.2.1.2. Depressive symptoms. The Inventory of Depressive Symptomatology – Self Rated (IDS-SR30) is a 30-item self-reported questionnaire, that represents the severity of depressive complaints and symptoms (range 0–84) over a period of the past seven days. Scores are rated as follows: 0–13 "no depressive mood" (reference category), 14–25 "mild depressive mood", 26–38 "moderate depressive mood", 39–48 "severe depressive mood" and 49–84 "very severe depressive mood" (Rush et al., 1996). For analysis purposes and due to the relatively small sample size in moderate, severe and very severe sub-categories, were merged into "moderate to very severe depressive mood" (scores 39–84). Cronbach's alpha in the present study was 0.84.

2.2.1.3. Negative life events. The list of threatening experiences questionnaire is an instrument to score negative life events developed by Brugha (Brugha et al., 1985; Brugha and Cragg, 1990; Rosmalen et al., 2012). This questionnaire consists of 12 categories of common life events with considerable long-term contextual threat. The list of threatening experiences questionnaire has shown good test-retest reliability and high interrater agreement (Brugha and Cragg, 1990). Every question addresses a particular life-threatening event and when answered positively, results in one point. The total score ranges from 0 to 12. A score of 0 means no life event has been reported. We calculated the score for recent NLEs defined as any event experienced in the last year before baseline and distant NLEs defined as any event experienced more than one year ago before baseline. Both time frames can have a score from 0 to 12. We categorized the recent and distant NLEs in two groups based on the median of each variable (the median for recent NLEs was zero events, the median for distant NLEs was three events). Concerning recent NLEs, a score of 0 represents "no recent NLEs" (reference category) and a score of 1–12 represents "one or more recent NLEs". For distant NLEs, a score of 0–3 represents "fewer than four NLEs" (reference category) and a score of 4–12 represents "four or more distant NLEs".

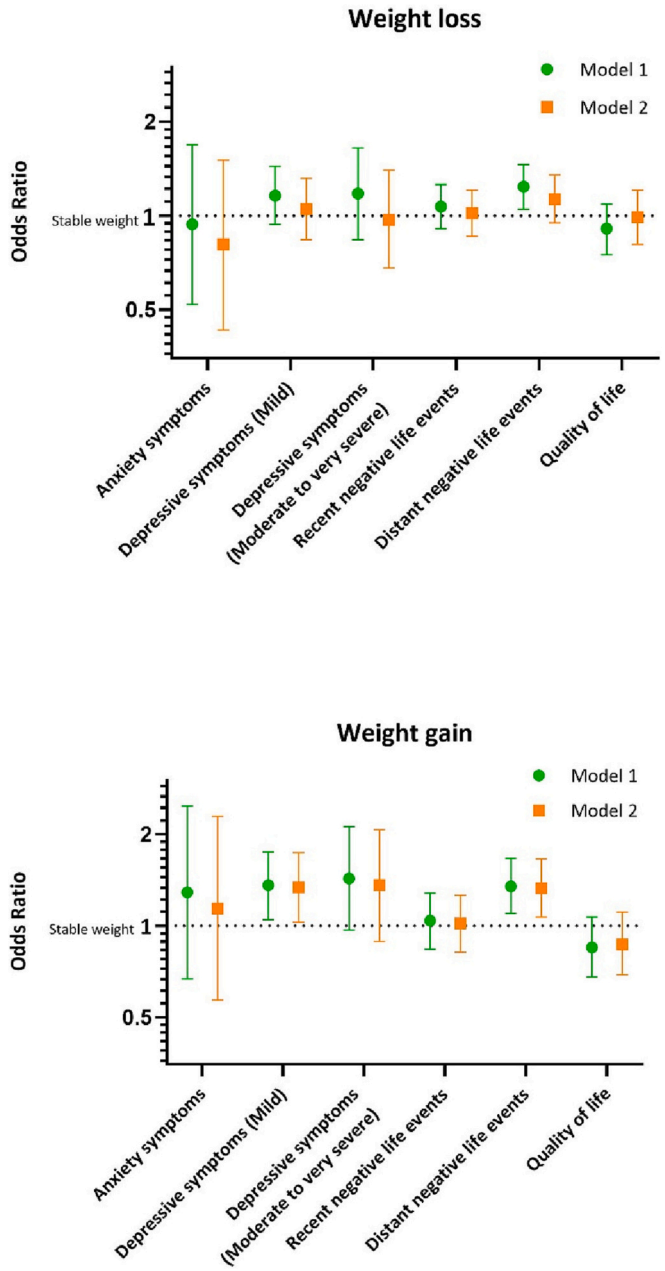

Fig. 3. Results of multinomial logistic regression analysis of the association between mental health, negative life events and weight change after 10 years (n = 2889).
The categories "low anxiety", "no depressive mood", "no recent negative life events", "fewer than four distant negative life events", and "low mental component summary" of quality of life were set as the reference categories.
Model 1 adjusted for age and sex.
Model 2 adjusted for age, sex, the use of psychotropic drugs, BMI at baseline, educational level, tobacco smoking, alcohol consumption, physical activity, energy intake, ethnicity, diabetes and cardiovascular disease.

2.2.1.4. Quality of life. The Short Form Health Survey (SF-36) measures the QoL (Dutch translation) (Aaronson et al., 1998; Ware and Sherbourne, 1992). The questionnaire contains 36 items on the domains: physical, mental and social health: divided over 8 subcategories: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. In addition to this score, a sub score can be calculated for every subcategory, but also a physical component summary and a mental component summary can be calculated (Ware and Sherbourne, 1992). In this study we will focus on the mental component summary, as this study focuses on mental health. This score ranges between 0 and 100. A higher score represents a better mental health experience. The score is categorized in two groups with cut off value of 50: a "low mental component summary" (reference category) ranges from 0 to 50.0 and a "high mental component summary" ranges from 50.01 to 100. Cronbach's alpha in the present study for the mental component summary (14 items from the SF-36 included) was 0.90.

2.2.2. Assessment of weight change during follow-up

Body weight at baseline was measured by the Tanita impedance balance (TBF-310, Tanita International Division, UK) without shoes and 1 kg was subtracted to correct for weight of clothing. Body weight was self-reported in the 2020-questionnaire. Relative weight change (%) was calculated by subtracting measured baseline weight from the self-reported weight in the 2020-questionnaire divided by measured baseline weight and multiplied by 100.

2.2.3. Covariates at baseline

At baseline, participants reported their date of birth, ethnicity, educational level (as a proxy for the socioeconomic status), tobacco smoking status and alcohol consumption. Also, participants reported the frequency and duration of their usual physical activity during leisure time in the short questionnaire to assess health-enhancing physical activity (SQUASH), which was expressed in hours per week of metabolic equivalents (de Hollander et al., 2012; Wendel-Vos et al., 2003). Energy intake (kJ/day) and alcohol consumption (g/day) were estimated by a food frequency questionnaire (Siebelink et al., 2011). The presence of cardiovascular disease was based on self-reported pre-existing cardiovascular disease such as myocardial infarction, angina, congestive heart failure, stroke, or peripheral vascular disease. The presence of diabetes mellitus type I or diabetes mellitus type II was based on the use of antidiabetic drugs or self-report. For the use of medication (including psychotropic drugs: N05A (antipsychotics), N05B (anxiolytics), N05CD (benzodiazepine derivates), N05CF (benzodiazepine related drugs), N06A (antidepressant use including use of tricyclic antidepressants and selective serotonin reuptake inhibitors)), participants were asked to bring all medications that they have been using for the last month to the NEO study center. Research nurses recorded prescribed and self-medication based on Anatomical Therapeutic Chemical Classification System (ATC). Finally, anthropometric measurements were assessed at baseline. Body height was measured with a vertically fixed, calibrated tape measure. Total body fat was estimated by Tanita bioelectrical impedance balance (TBF-310, Tanita International Division, UK). BMI was calculated by dividing the weight by the height squared (kg/m^2). Waist circumference was measured with a measuring tape placed midway horizontally between the lower costal margin and the iliac crest.

2.3. Statistical analysis

Baseline characteristics of the study population were summarized as mean (SD), median (25th, 75th percentiles) or as percentage (Table 1). First, we categorized relative weight change during 10 years into 3 categories: weight loss (≤− 5 %), stable weight (between >− 5 % and <5 %) based on the influence of normal fluctuations on body weight and weight gain (≥5 %) (Fazzino et al., 2019). We performed multinominal logistic regression to examine the associations of anxiety symptoms, depressive symptoms, NLEs and mental component summary of QoL with weight change over 10 years of follow-up. The first model was adjusted for age and sex (model 1); the second model for age, sex, use of psychotropic drugs, BMI at baseline, educational level, ethnicity, tobacco smoking status, alcohol consumption, physical activity, energy intake and pre-existing diabetes and cardiovascular disease (model 2). Lastly, we repeated all analyses stratified by sex. All statistical analyses were performed with SPSS statistical software (version 25, IBM

Corporation, Armonk, NY).

3. Results

3.1. Characteristics of the study population

For the present analysis we included the subset of participants who completed the 2020-questionnaire (n = 3942) and of those we excluded participants who had a BMI < 27 kg/m^2 at baseline (n = 1020). Data on self-reported weight in 2020 were missing in 33 participants, resulting in a total study population for the present study of n = 2889 (Fig. 1). Median (25th, 75th percentiles) time from baseline to follow-up was 9.7 (9.0–10.5) years. Responders to the 2020-questionnaire included in our analysis (n = 2889) used fewer psychotropic drugs (9.6 % vs. 14.7 %), had fewer depressive symptoms (no depressive symptoms 72.3 % vs. 63.8 %) and had fewer anxiety symptoms (low anxiety 97.7 % vs. 95.8 %) than non-responders to the 2020-questionnaire (n = 2729) (Supplementary Table 1). Baseline characteristics of the 2889 participants are shown in Table 1. More participants lost weight (32.5 %) than gained weight (16.8 %). Half of the participants (50.7 %) had a stable weight (Fig. 2). Weight gain was more often seen in women (20.5 %) than in men (13.5 %).

3.2. Mental health, negative life events and weight change at middle age

Regarding anxiety symptoms, there was no association between a moderate or high score on the BAI and weight loss and weight gain (Fig. 3). For the depressive symptoms, a mild or moderate to very severe score on the IDS-SR30 was associated with weight gain over 10 years at middle age. After adjustment for potential confounding including the use of psychotropic drugs and BMI at baseline (model 2), participants with a mild score (odds ratio (OR) 1.34; 95 % confidence interval (CI) = 1.03–1.74) showed an increased risk of weight gain compared with participants with a low IDS-SR30. Participants with a moderate to very severe score (OR 1.36; 95 % CI = 0.89–2.07) also showed an increased risk of weight gain compared with participants with a low IDS-SR30, though this association was not significant. Regarding NLEs, participants who had experienced four or more distant NLEs had a higher risk of weight gain than participants who experienced fewer than four distant NLEs (OR 1.33; 95 % CI = 1.07–1.66), after adjustment for potential confounding (model 2). Furthermore, having experienced four or more distant NLEs was also associated with weight loss compared with experiencing fewer than four distant NLEs (OR 1.24; 95 % CI = 1.05–1.46), which association attenuated after adjustment for potential confounders (OR 1.13; 95 % CI = 0.95–1.35). Having experienced recent NLEs was not associated with either weight loss or weight gain over time. Regarding QoL, there was no association between a high score of the mental component summary of QoL and both weight loss and weight gain.

In the sex-stratified analysis of the association between mental health and NLEs with weight loss and weight gain, direction and strength of the effect sizes were similar for men and women, except for the association of anxiety: compared with a low score on the BAI the OR of weight gain was 1.73 (95 CI% = 0.60–4.97) for men with a moderate or high score on the BAI, and 0.77 (95 CI% = 0.29–2.04) for women (model 2, Supplementary Fig. 1).

4. Discussion

In this population-based cohort study of 2889 middle-aged overweight individuals with ten years follow-up, about half of the participants maintained a stable weight, almost a third of the participants lost weight, and less than a quarter gained weight. Depressive symptoms at baseline were associated with weight gain. In addition, the association between distant NLEs and weight change was U-shaped, with both an increased risk of weight gain and weight loss. Anxiety symptoms, recent NLEs, and the mental component summary of QoL were not associated with weight changes.

Results from previous studies on anxiety symptoms and weight gain are inconsistent. Several studies with varying follow-up durations of 11, 19 and 40 years have shown, in contrast to our results, a positive association between anxiety and weight gain (Brumpton et al., 2013; Gaysina et al., 2011; Kivimäki et al., 2009). However, other studies with a shorter follow-up duration of 2 respectively 5 years showed no association (de Wit et al., 2015; Sahle et al., 2019). This inconsistency can be explained by the heterogeneity among these studies such as variation in duration of follow-up, participants characteristics (e.g., age), affective disorders in broad sense (depression and anxiety were merged), and the severity of anxiety symptoms. Patients with anxiety symptoms are also heterogenous population according to severity, subtype, age of onset, and chronicity. Mechanisms of anxiety pathways and weight change might differ between patients. The results of the present study can also possibly be explained by the small sample size, since only 2 % of the participants experienced anxiety symptoms.

Concerning depressive symptoms, in line with our results other longitudinal studies with varying follow-up durations have also observed a positive association between depression and weight gain over time (Brumpton et al., 2013; de Wit et al., 2015; Luppino et al., 2010; Sahle et al., 2019; Singh et al., 2014). Alterations in systems involved in homeostatic adjustments (hypothalamic-pituitary-axis activation, immune-inflammatory activation, neuroendocrine regulators of energy metabolism including leptin and insulin and microbiome) which are directly associated with adiposity levels in the body might explain this association (Milaneschi et al., 2019). Behavioral mechanisms (low motivation, low energy level, physical inactivity and overconsumption of energy-dense food) have also been suggested (Yu, 2017). Especially vegetative depressive symptoms (such as pain, change in appetite and weight, gastrointestinal symptoms and arousal related symptoms), and not mood and cognitive symptoms of depression, lead to a higher BMI (Alshehri et al., 2019; Baldofski et al., 2019).

NLEs have been shown to be associated with obesity over a follow-up time of 13 years (Mehlig et al., 2020). This might be explained by the fact that experiencing NLEs increases stress levels (Geiker et al., 2018). Stress might cause weight gain due to metabolic (hypothalamic-pituitary-axis activation) and behavioral changes (eating behavior) (Geiker et al., 2018; Wardle et al., 2011). The most remarkable finding in our study is the association between distant NLEs with both weight gain and weight loss. This might be due to the fact that distant NLEs are heterogeneous and experienced in different ways, giving rise to different reactions and stress levels, which may then in turn be associated with either weight gain or weight loss.

Regarding QoL, in line with our study, one study also observed that the mental domain of QoL was not associated with weight change over a 11-year period (Sahle et al., 2020). In contrast, another study with a follow-up duration of 5 years, that did not account for a wide range of lifestyle factors as confounders, did show a relationship between the mental domain of QoL and weight gain (Cameron et al., 2012). Since our study and Sahle et al. (Sahle et al., 2020) are both longitudinal studies with a longer period of follow-up, a clear association of the mental domain of QoL with weight change seems unlikely.

Some methodological issues should be considered. The most important strengths of the present study include the large sample size, the prospective study design, the long follow-up period and the availability of the different aspects of mental health. However, this study also has some limitations. First, we calculated weight change using self-reported weight in the 2020-questionnaire. Previous studies have shown that self-reported weight often is lower than objectively measured body weight (Connor Gorber et al., 2007), which may have led to an underestimation of weight gain and an overestimation of weight loss. This would have resulted in an underestimation of the associations with weight gain, and an overestimation of relations with weight loss. Second, although we adjusted for a large number of confounding factors

in the models, due to the observational nature of the study residual confounding may still be present. Third, the non-responders to the follow-up questionnaire slightly differed from our study population. Non-responders more often used psychotropic drugs, and more often reported anxiety and depressive symptoms when entering the study. If these non-responders would have had different weight change patterns this may have influenced our results. Lastly, it must be noted that the majority of this population-based study is white, and that in this study we selected middle-aged participants with overweight. Therefore, our findings apply to a middle-aged white population with overweight and should be confirmed in other groups.

In conclusion, depressive symptoms and distant NLEs were associated with weight gain over time in middle-aged men and women with overweight. Since most mental health professionals and primary care physicians will learn about this kind of symptoms and events from their patients, it might be worthwhile to pay proactive attention to this subgroup of patients. In many countries, somatic and psychological health care is still separated. Optimized cooperation between psychosocial and somatic health care providers might be beneficial for patients with overweight and mental health problems.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.05.001.

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Ethical approval

The Medical Ethical Committee of the Leiden University Medical Center (LUMC) approved the design of the study (P08.109).

CRediT authorship contribution statement

WH, DM, PP, FL, RM contributed to the conception and design of the study. WH performed the statistical analysis. WH, PP, DM wrote the first draft of the manuscript. DM, PP, RM, MN, BE, FR critically revised the manuscript. All authors contributed to manuscript revision, read, and approved the final version of the manuscript.

Declaration of competing interest

None.

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