

RESEARCH ARTICLE

Improvement in mood symptoms after post-bariatric surgery among people with obesity: A systematic review and meta-analysis

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Abstract

Aims: We aimed to examine if bariatric surgery was associated with a reduction in the prevalence of depressive and anxiety symptoms among people with obesity.

Materials and Methods: We pooled data from 49 studies involving 11,255 people with obesity who underwent bariatric surgery. The study outcomes were the prevalence of depressive and anxiety symptoms among these patients pre- and post-surgery.

Results: There was a significant reduction in body mass index (BMI) post-operatively (pooled $d+$: -13.3 kg/m^2 [95% confidence interval [CI] 15.19, -11.47], $p < 0.001$). The pooled proportion of patients with anxiety symptoms reduced from 24.5% pre-operatively to 16.9% post-operatively, with an odds ratio (OR) of 0.58 (95% CI 0.51, 0.67, $p < 0.001$). The reduction remained significant in women aged ≥ 40 years and irrespective of post-operative BMI. There were significant reductions in Hospital Anxiety and Depression Score (HADS) (anxiety component) by 0.64 (pooled $d+$: -0.64 [95% CI -1.06 , -0.22], $p = 0.003$) and Generalized Anxiety Disorder Assessment-7 score by 0.54 (pooled $d+$: -0.54 [95% CI -0.64 , -0.44], $p < 0.001$). The pooled proportion of depressive symptoms reduced from 34.7% pre-operatively to 20.4% post-operatively, with an OR of 0.49 (95% CI 0.37, 0.65, $p < 0.001$). The reduction remained significant irrespective of patient's age and post-operative BMI. There were also significant reductions in HADS score (depressive component) (pooled $d+$: -1.34 [95% CI -1.93 , -0.76], $p < 0.001$), Beck's Depression Inventory score (pooled $d+$: -1.04 [95% CI -1.46 , -0.63], $p < 0.001$) and Patient Health Questionnaire-9 score (pooled $d+$: -1.11 [95% CI -1.21 , -1.01], $p < 0.001$).

Conclusion: Bariatric surgery was associated with significant reduction in the prevalence and severity of depressive and anxiety symptoms among people with obesity.

Abbreviations: 5HT2C, 5-Hydroxytryptamine 2C receptor; BDI, Beck's Depression Inventory; BMI, body mass index; DSM-V, Diagnostic and Statistical Manual of Mental Disorders 5th edition; HADS, Hospital Anxiety and Depression Score; HRQOL, Health-Related Quality of Life; NB, naltrexone/bupropion; NOS, Newcastle-Ottawa Scoring; OR, odds ratio; U.S. FDA, United States Food & Drug Administration; WHO, World Health Organization.

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KEYWORDS

anxiety symptoms, depressive symptoms, mental health, metabolic surgery, obesity

1 | INTRODUCTION

Obesity is a chronic, relapsing and progressive disease with excessive subcutaneous or visceral fat accumulation, leading to adverse health effects.¹ The prevalence of obesity has been increasing globally, in part due to rapid modernization and industrialization.^{2,3} In 2016, the World Health Organization (WHO) estimated that more than 1.9 billion adults aged 18 years and older are overweight, of whom 650 million have obesity. Obesity has a negative effect on overall health as it increases the risk for type 2 diabetes mellitus, coronary artery disease, musculoskeletal disorders and cancers.⁴

Obesity can be linked to psychosocial dysfunction and social disabilities related to stigmatization.⁵ Over the past few decades, there has been an increasing amount of evidence that shows a bidirectional association between mental illnesses and obesity.^{6–8} Depression and anxiety are the common mood disorders that frequently co-exist with obesity, although the association is stronger with depression (odds ratio [OR] 1.21–5.80) than anxiety (OR 1.27–1.40), as reported in 15 studies on obesity and depression and 4 studies on obesity and anxiety.⁶ A meta-analysis of 14 cross-sectional studies reported that obesity had an OR of 1.4 for anxiety.⁹ There are several hypotheses regarding the close link between obesity and depression. Leptin dysregulation in people with obesity has been implicated as a risk factor to develop depressive symptoms via its involvement in the amygdala and hippocampal neurogenesis and neuroplasticity.¹⁰ Systemic and neuro-inflammation, via an increased release of pro-inflammatory cytokines, have been implicated as potential mediators that link obesity and adiposity with depression.¹¹ Other mechanisms include neuroendocrine dysregulation of the hypothalamic–pituitary–adrenal axis and alterations of peripheral cortisol metabolism, which also contribute to insulin resistance in people with obesity, leading to cardiometabolic diseases.¹²

The pathogenesis of obesity involves not just a sustained positive calorie balance, but also a change of a body weight set point, which explains the tendency of people with obesity to regain lost weight over time.¹³ Bariatric surgery is an effective therapeutic intervention for severe obesity to reduce substantial body weight, and improve or even induce remission of common co-existing medical conditions, including type 2 diabetes mellitus, hyperlipidaemia and hypertension.^{14–17} The most common type of bariatric surgery performed worldwide is Roux-en-Y gastric bypass, although in the last 2 years, the number of sleeve gastrectomy recorded is greater than Roux-en-Y gastric bypass.¹⁸ Structurally, bariatric surgery reduces caloric intake by modifying the anatomy of the gastrointestinal tract via either restrictive or malabsorptive effects. Functionally, it also reduces appetite and improves insulin sensitivity, mediated by incretin hormones such as glucagon-like peptide-1 (GLP-1) and pancreatic peptide YY (PYY).¹⁹

Compared to non-surgical methods, people with obesity and type 2 diabetes who underwent bariatric surgery achieved greater weight loss, remission rates in diabetes and dyslipidemia 5 years post-surgery, as reported in a population-based propensity score-matched cohort study.¹⁷ A randomized control trial at the University of Pittsburgh reported that bariatric surgeries were more effective than lifestyle interventions for people with obesity and type 2 diabetes mellitus, and were associated with a 19%–30% remission rate in diabetes mellitus.²⁰ In a retrospective case-control study in Canada, bariatric surgery conferred an 89% relative risk reduction in mortality and a 53% relative risk reduction of psychiatric disorders after 5 years.²¹ Currently, bariatric surgery is recommended for patients with Class III obesity (defined as body mass index [BMI] ≥ 40 kg/m²) or Class II obesity (BMI ≥ 35 –40 kg/m²) with comorbidities.^{22,23}

We aimed to systematically review the literature and examine if bariatric surgery was associated with a reduction in the prevalence and severity of depressive and anxiety symptoms among people with obesity. We also examined if these changes were modified by the age of the subjects and their post-operative BMI.

2 | MATERIALS AND METHODS

2.1 | Data sources and extraction

We performed a systematic search of all English-language medical literature published from inception till March 2020 using PubMed, CINAHL and Ovid using the following MESH headings: ‘psycho\$', ‘depression’, ‘anxiety’, ‘mood disorders’, ‘mental health’, ‘bariatric surgery’ and ‘weight loss surgery’. We also looked into references of the selected papers. When the papers were not available or information of the study cohort was inadequate, we attempted to contact the respective authors via email to obtain the full paper and more detailed data. To be included in the analysis, studies had to fulfil the following criteria: (i) recruited subjects fulfilled criteria for bariatric surgery, that is, BMI ≥ 40 kg/m² or BMI ≥ 35 kg/m² with comorbidities, (ii) reported the proportion of depressive or anxiety symptoms both pre- and post-operatively, and/or (iii) reported the scores of validated questionnaires for mood disorder pre- and post-operatively. Studies were excluded if subjects recruited had other concurrent medical illnesses or diseases which might affect the results, or only reported results on health-related quality of life (HRQOL). Review articles, posters, abstracts and thesis were also excluded. The titles and abstracts obtained through the electronic search were screened followed by the analysis of the full-text articles by two independent reviewers (HHL and HSL). All duplicates were removed. Data such as age, gender ratio, sample size, types of

surgery performed, duration of follow-up, as well as pre- and post-operative data (BMI, the proportion of depressive and anxiety symptoms, and the scores of various assessment tools for mood disorders of interest) were documented using a standardized data extraction form. Wherever data were not provided numerically, they would be read off graphs. Data from eligible studies were extracted by HHL, and all extracted data were reviewed by AY.

2.2 | Quality assessment

HHL and HSL independently assessed the quality of the methodology and reporting of the studies using the Newcastle-Ottawa Scoring (NOS) Scale. Any discrepancies were resolved by the third reviewer (LLL). The NOS scale was developed to assess the quality of non-randomized case-control studies for interpretation of meta-analysis results. It uses a 'star system' which judges the studies in three broad categories, namely the selection of study group, group comparability and ascertainment for the outcome of interest (exposure). In the original NOS Scale for case-control studies, each study can be awarded a maximum of one star for each numbered item (four in the Selection category and three in the Exposure category) and a maximum of two stars in the Comparability category. For the adapted NOS Scale for cross-sectional studies, each study can be awarded a maximum of five stars in the Selection category, two stars for the Comparability category and three stars for the Outcome category. Both scales have a maximum score of 10.

2.3 | Statistical analysis

2.3.1 | Qualitative

All abstracted information was tabulated. A qualitative meta-analysis was conducted to summarize, compare and contrast the abstracted data.

2.3.2 | Quantitative

All data analyses were performed using Stats Direct (version 2.7.9). The presence of heterogeneity between the trials was tested using the *I*-squared (I^2) statistic. I^2 of more than 40% indicated a significant heterogeneity. If the I^2 was significant, we pooled the data by using random effects model (DerSimonian-Laird); if not, we pooled the data by using fixed effects model (Hedges-Olkin). We also assessed publication bias with the Begg-Mazumdar and Egger test. For dichotomous data, namely the respective proportion of patients with anxiety and depressive symptoms, the pooled OR with 95% confidence intervals (CI) were estimated based on the random effects model. If the mean and standard deviation (SD) of continuous outcomes were presented in the original articles, we analysed them by using the effect size meta-analysis and presented the results as

weighted mean difference with 95% CI. The risk of developing adverse effects after bariatric surgery was reported as a proportional rate with 95% CI.

2.4 | Assessment tools for screening of mood disorders

2.4.1 | Hospital Anxiety and Depression Score

This validated questionnaire comprises seven questions for anxiety symptoms and seven questions for depressive symptoms, rated on a 4-point severity scale. The maximum score for each subscale is 21. A total Hospital Anxiety and Depression Score (HADS) score of ≥ 11 indicates a definitive case.^{24,25}

2.4.2 | Beck's Depression Inventory

This validated and widely used 21-item self-administered questionnaire evaluates the severity of depressive symptoms on a 4-point scale. The score ranges from 0 to 63. In non-clinical populations, a score of >20 indicates the presence of depressive symptoms, requiring further psychiatric evaluation.

2.4.3 | Generalized Anxiety Disorder Assessment-7

The Generalized Anxiety Disorder Assessment (GAD-7) is a seven-item validated instrument that is used to assess the severity of generalized anxiety disorder. Each item asks the individual to rate the severity of his/her symptoms in the past 2 weeks. The total score ranges from 0 to 21. A score of 5, 10 and 15 represents the cut-off point for mild, moderate and severe anxiety symptoms, respectively. Further evaluation is recommended if the total score is 10 or more.

2.4.4 | Patient Health Questionnaire-9

The Patient Health Questionnaire (PHQ) is a diagnostic tool for eight mental disorders. The PHQ-9 is a self-administered nine-item depression module from the full version of PHQ. Each item asks the individual to mark the presence of depressive symptoms in the past 2 weeks. The total score ranges from 0 to 27. A score of 5, 10, 15 and 20 represents mild, moderate, moderately severe and severe depressive symptoms, respectively.

2.5 | Results

Our initial search identified a total of 3471 articles with 1701 articles from PubMed, 461 articles from CINAHL and 1309 articles from

Ovid. After screening of titles, abstracts and full texts, followed by elimination of duplicate publications, 103 articles were identified. Among these, 61 articles were further excluded: 42 did not include comparative data pre- and post-operatively; 11 due to incomplete data; 1 due to overlap cohort.

2.6 | Data synthesis

A total of 11,255 subjects from 49 articles were included in the present meta-analysis (Figure 1). All were prospective studies, except for one cross-sectional²⁶ and three retrospective study design.²⁷⁻²⁹ Roux-en-Y gastric bypass was performed in 31 studies, biliopancreatic diversion in 4, gastric banding in 24, sleeve gastrectomy in 15 and vertical gastropasty in 7. A total of 24 studies examined the proportion of anxiety symptoms and 28 studies compared the proportion of depressive symptoms pre- and post-surgery. Eight studies compared HADS (anxiety component), three examined GAD-7 scores and two reported SCL90R scores pre- and post-surgery. Twelve studies compared Beck's Depression Inventory (BDI) scores, nine examined HADS (depression component), five reported PHQ-9 scores and two compared SCL90R scores pre- and post-surgery. The baseline characteristics of all studies are described in Table 1. The sample size ranged between 21 and 3045. For prospective

studies, the duration of follow-up ranged between 3 and 120 months, with a mean of 34.0 months.

The pooled mean \pm SD age of the subjects was 40.3 ± 8.0 years. In the entire cohort, 79.4% were women. There was a significant reduction of BMI from 47.4 ± 3.2 kg/m² at baseline to 34.5 ± 4.5 kg/m² post-operatively, with a pooled $d+$ of -13.3 kg/m² (95% CI -15.19 , -11.47 , $p < 0.001$).

2.7 | Meta-analysis

2.7.1 | Anxiety symptoms

The proportion of patients with anxiety symptoms, the types of scoring system used, and their scores pre- and post-operatively are shown in Table S1. At baseline, the pooled proportion of patients with anxiety symptoms was 24.5% (95% CI 0.19, 0.31), which reduced to 16.9% (95% CI 0.12, 0.22) during the post-operative period, with an OR of 0.58 (95% CI 0.51, 0.67, $p < 0.001$) (Figure 2A). Furthermore, there was a significant reduction in the HADS score (anxiety component), from a mean baseline score of 7.66 ± 0.99 to 6.16 ± 1.18 during the post-operative period, with a pooled $d+$ of -0.64 (95% CI -1.06 , -0.22 , $p = 0.003$) (Figure 2B). Similarly, there was a significant reduction in the GAD-7 score, from

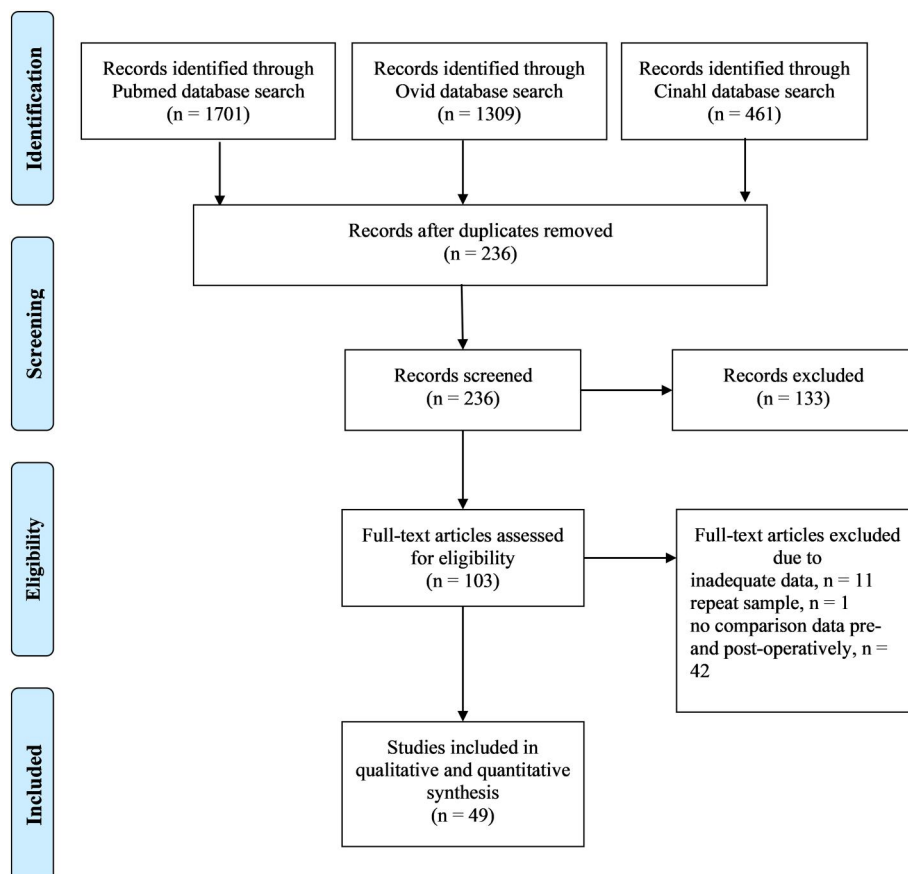


FIGURE 1 Study design

TABLE 1 Baseline demographic

Reference	Site	Study type	Sample size, <i>n</i>	Age, mean \pm SD, median (range)	Female: male, <i>n</i>	Type of surgery	Duration of study, months	NOS score
Gertler 1986	Australia	Prospective	20	37.2 (24–52)	0:20	RYGB, GP, GG, NA VG		7
Gertler 1986	Australia	Prospective	133	34.9 (18–60)	133:0	RYGB, GP, GG, NA VG		7
Waters 1991	USA	Prospective	157	36.3 (19–67)	132:25	RYGB	36	7
Maddi 2001	USA	Prospective	52	38.4 (19–56)	46:6		12	8
Dixon 2003	Australia	Prospective	487	41.2 \pm 9.7	414:73	GB	48	7
Mamplekou 2005	Greece	Prospective	59	37.7 \pm 10.7	45:14	VG	24	7
Burgmer 2007	Germany	Prospective	149	38.8 \pm 10.3	102:47	GB, VG	24	8
Karlsson 2007	Sweden	Prospective	655	47.0 \pm 5.7		RYGB, GB, VG	120	8
Nickel 2007	Germany, Austria	Prospective	21	38.0 \pm 9.5	50:0	GB	72	7
Scholtz 2007	UK	Prospective	29	39.0 \pm 9.0	28:1	GB	60	8
Schowalter 2008	Germany	Prospective	248	38.5 \pm 10.1	200:48	GB	67	8
Andersen 2010	Norway	Prospective	50	37.9 \pm 7.9	28:22	BPD	24	8
Kruseman 2010	Switzerland	Prospective	141	40.0 \pm 10.0	80:0	RYGB	96	7
Thonney 2010	Switzerland	Prospective	43	39.2 \pm 1.4	43:0	RYGB	24	9
Assimakopoulos 2011	Greece	Prospective	59	36.0 (18–56)	59:0	RYGB, BPD, SG	12	7
Lier 2011	Norway	Prospective	127	41.3 \pm 10.3	94:33	RYGB	12	8
Strain 2011	USA	Retrospective	77	52.3 \pm 12.7	54:23	SG	24.6	6
Zwaan 2011	Germany	Prospective	107	37.5 \pm 9.7	75:32	RYGB, GB	36	8
Jarvholm 2012	Sweden	Prospective	37	16.6 \pm 1.3	25:12	RYGB	3	8
Ortega 2012	Spain	Prospective	60	44.1 \pm 10.9	46:14	RYGB	12	7
Rutledge 2012	USA	Prospective	55	52.5 \pm 7.4	17:38	RYGB, GB	60	8
Sysko 2012	USA	Prospective	101	15.8 \pm 1.1	73:28	GB	12	7
Lier 2013	Norway	Prospective	127	41.3 \pm 10.3	125:44	RYGB	12	8
Burgmer 2014	Germany	Prospective	148	38.8 \pm 10.2	101:47	GB, VG	96	8
Castellini 2014	Italy	Prospective	83	45.3 \pm 10.1	75:8	RYGB, BPD, GB	12	7
Hayden 2014	Australia	Prospective	204	45.2 \pm 11.5	168:36	GB	24	8
Ivezaj 2014	USA	Prospective	107	42.7 \pm 10.5	94:13	GB	12	7
Matini 2014	Iran	Prospective	67	36.8 \pm 8.5	55:12	RYGB	6	9
Mitchell 2014	USA	Prospective	2146	46.0 (18–76)	1685:461	RYGB, GB, SG, BPD	36	7
Strain 2014	USA	Prospective	105	43.5 \pm 10.8	76:29	RYGB, BPD, GB, SG	24	7
Tae 2014	Brazil	Prospective	32	41.0 \pm 11.6	32:0		10	8
Booth 2015	UK	Prospective	3045	45.9 \pm 10.2	2406:639	RYGB, GB, SG	96	7
Herpertz 2015	Germany	Prospective	152	39.1 \pm 10.3	102:50	GB, VG	108	8

(Continues)

TABLE 1 (Continued)

Reference	Site	Study type	Sample size, <i>n</i>	Age, mean \pm SD, median (range)	Female: male, <i>n</i>	Type of surgery	Duration of study, months	NOS score
Sockalingam 2015	USA	Prospective	164	43.5 \pm 9.7	133:31	RYGB, SG	12	7
White 2015	USA	Prospective	357	43.7 \pm 10.0	307:50	RYGB	24	7
Jarvholm 2016	Sweden	Prospective	82	16.8 \pm 1.2	57:25	RYGB	24	8
Kalarchian 2016	USA	Prospective	165	46.0 (21-68)	135:30	RYGB, GB@	36	8
Mack 2016	Germany	Prospective	75	45.2 \pm 11.6	48:27	SG	48	9
Efferdinger 2017	Austria	Prospective	45	44.1 \pm 13.3	34:11	RYGB, SG	6	7
Osterhues 2017	Germany	Cross-sectional	192	40.7 \pm 11.4	136:56	RYGB, SG, GB	19	8
Sockalingam 2017	Canada	Prospective	156	45.2 \pm 9.3	126:30	RYGB, SG	24	7
Alabi 2018	Mexico	Retrospective	73	38.1 \pm 9.1	56:17	GB	12	8
Ho 2018	Canada	Retrospective	365	44.7 \pm 10.0	292:73	RYGB, SG	12	8
Hunsaker 2018	USA	Prospective	139	19.2 \pm 1.3	162:40	RYGB, SG, GB	24	8
Monte 2018	USA	Prospective	59	51.0 \pm 13.0	51:8	SG	6	8
Pinto-Bastos 2018	Portugal	Prospective	122	42.8 \pm 11.4	108:14	RYGB, SG	6	7
Pinto-Bastos 2018	Portugal	Prospective	116	47.9 \pm 9.2	107:9		6	7
Ribeiro 2018	Brazil	Prospective	281	40.7 \pm 9.8	225:56	RYGB	60	6
Kalarchian 2019	USA	Prospective	104	45.0 (21-68)	84:20	RYGB, GB	60	8
Kalarchian 2019	USA	Prospective	69	47.0 (40-54)	58:11		60	8
Hawkins 2020	Canada	Prospective	190	44.5 \pm 10.6	156:34	RYGB, SG	12	7

Abbreviations: BPD, biliopancreatic diversion; GB, gastric banding; GG, gastrogastrostomy; GP, gastric partitioning; NA, not available; RYGP, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; VG, vertical gastroplasty.

a mean baseline score of 5.29 ± 0.34 to 3.0 ± 0.64 post-operatively, with a pooled $d+$ of -0.54 (95% CI $-0.64, -0.44, p < 0.001$).

When we sub-analysed the cohort of women ≥ 40 years of age, the reduction in the proportion of patients with anxiety symptoms remained significant, with a baseline proportion of 27.9% to 15.7% after bariatric surgery. The OR was 0.47 (95% CI 0.40, 0.55, $p < 0.001$). As for women < 40 years of age, the proportion of patients with anxiety symptoms reduced from 20.5% at baseline to 18.7% postoperatively, but this did not achieve statistical significance with an OR of 0.94 (95% CI 0.75, 1.18, $p = 0.663$).

We also attempted to analyse if a lower BMI achieved post-operatively would affect the proportion of patients with anxiety symptoms. Using a cut-off BMI of 35 kg/m^2 , the proportion of patients with anxiety symptoms and post-operative BMI of $\geq 35 \text{ kg/m}^2$ reduced from 25.4% at baseline to 20.9% post-operatively, with an OR of 0.72 (95% CI 0.60, 0.86, $p = 0.0003$). Similarly, the proportion of patients with anxiety symptoms and post-operative BMI of $< 35 \text{ kg/m}^2$ reduced from 33.3% at baseline to 21.3% post-operatively, with an OR of 0.39 (95% CI 0.30, 0.52, $p < 0.001$).

2.7.2 | Depressive symptoms

The proportion of patients with depressive symptoms, the types of scoring system used, and their scores pre- and post-operatively are shown in Table S2. At baseline, the pooled proportion of depressive symptoms was 34.7% (95% CI 0.29, 0.41), which reduced to 20.4% (95% CI 0.16, 0.25) post-operatively, with an OR of 0.49 (95% CI 0.37, 0.65, $p < 0.001$) (Figure 3A). Furthermore, there was a significant reduction in the HADS score (depression component), from 7.49 ± 0.88 at baseline to 4.36 ± 1.01 post-operatively, with a pooled $d+$ of -1.34 (95% CI $-1.93, -0.76, p < 0.001$) (Figure 3B). The BDI score also significantly reduced from 13.46 ± 3.77 at baseline to 8.12 ± 3.29 post-operatively, with a pooled $d+$ of -1.04 (95% CI $-1.46, -0.63, p < 0.001$) (Figure 3C). Similarly, the PHQ-9 score showed a significant reduction from 9.60 ± 0.07 at baseline to 4.01 ± 0.98 post-operatively, with a pooled $d+$ of -1.11 (95% CI $-1.21, -1.01, p < 0.001$).

When we sub-analysed the cohort of women ≥ 40 years of age, the reduction of proportion of patients with depressive symptoms

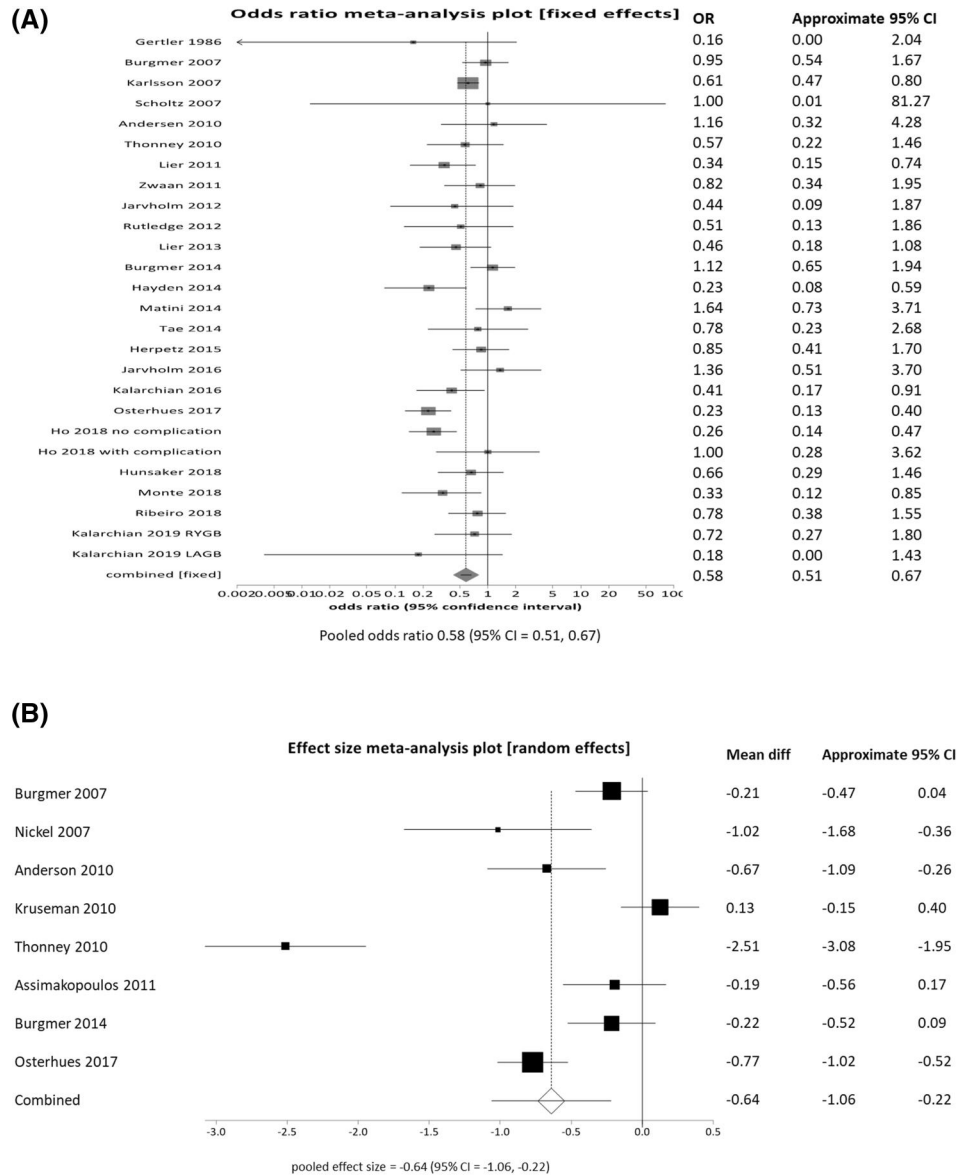


FIGURE 2 (A) Proportion of patients with anxiety symptoms pre- and post-bariatric surgery (by fixed effects meta-analysis). Pooled odds ratio (Mantel-Haenszel, Robins-Breslow-Greenland) = 0.58 (95% CI 0.51, 0.67), $I^2 = 64.8\%$ (95% CI 50.7, 66.4), $p < 0.0001$. (B) Mean Hospital Anxiety and Depression scores (anxiety component) among patients with anxiety symptoms pre- and post-bariatric surgery (by random effects meta-analysis). Pooled $d+$ (DerSimonian-Laird) = -0.64 (95% CI -1.06, -0.22), $I^2 = 91.8\%$ (95% CI 86.8, 94.4), $p = 0.003$

remained significant, with a baseline proportion of 36.2% to 19.2% post-operatively, with an OR of 0.43 (95% CI 0.29, 0.63, $p < 0.001$). As for women <40 years of age, the proportion of patients with depressive symptoms reduced from 32.5% at baseline to 23.2% post-operatively, with an OR of 0.60 (95% CI 0.47, 0.77, $p < 0.001$).

We also attempted to analyse if a lower BMI achieved post-operatively would affect the proportion of patients with depressive symptoms. Using a cut-off BMI of 35 kg/m², the proportion of patients with depressive symptoms and post-operative BMI of ≥ 35 kg/m² reduced from 29.1% at baseline to 17.5% post-operatively, with an OR of 0.54 (95% CI 0.45, 0.66, $p < 0.001$). Similarly, the proportion of patients with depressive symptoms and post-operative BMI of

<35 kg/m² reduced from 46.6% at baseline to 21.4% post-operatively, with an OR of 0.29 (95% CI 0.13, 0.65, $p = 0.002$).

3 | DISCUSSION

The present meta-analysis of 49 studies reported a decreasing proportion of people with obesity experiencing either depressive symptoms (from 34.7% to 20.4%, OR 0.49) or anxiety symptoms (from 24.5% to 16.9%, OR 0.58) after bariatric surgery. We also showed that the severity of anxiety (measured by HADS and GAD-7) and depressive symptoms (measured by HADS, BDI and PHQ-9) generally reduced after bariatric surgery.

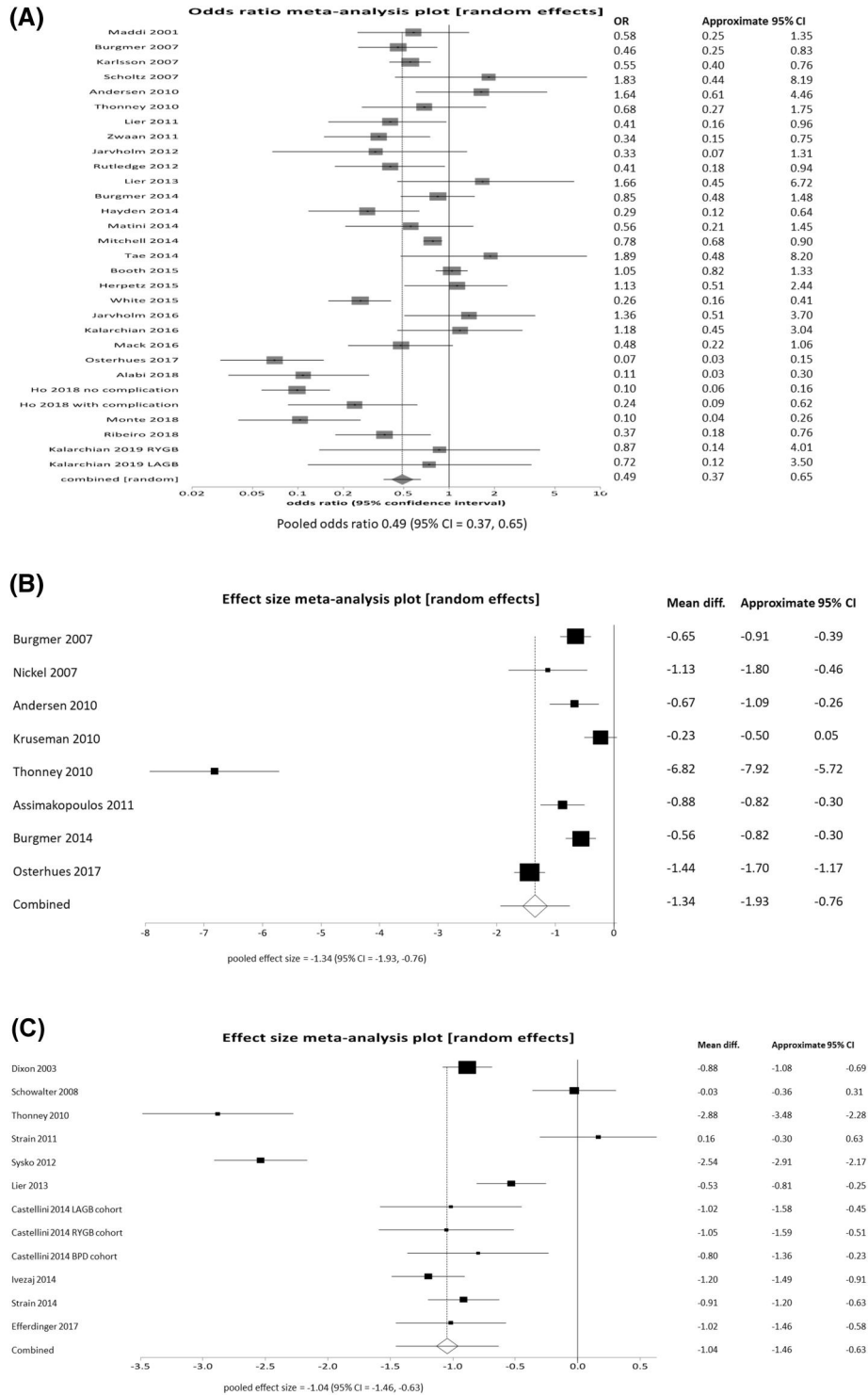


FIGURE 3 (A) Proportion of patients with depressive symptoms pre- and post-bariatric surgery (by random effects meta-analysis). Pooled odds ratio (DerSimonian-Laird) = 0.49 (95% CI 0.37, 0.65), $I^2 = 86%$ (95% CI 81.3, 89.0), $p < 0.0001$. (B) Mean Hospital Anxiety and Depression scores (depression component) among patients with depressive symptoms pre- and post-bariatric surgery (by random effects meta-analysis). Pooled $d+$ (DerSimonian-Laird) = -1.34 (95% CI -1.93, -0.76), $I^2 = 95.6%$ (95% CI 93.8, 96.7), $p < 0.0001$. (C) Mean Beck's Depression Inventory scores among patients with depressive symptoms pre- and post-bariatric surgery (by random effects meta-analysis). Pooled $d+$ (DerSimonian-Laird) = -1.04 (95% CI -1.46, -0.63), $I^2 = 93.7%$ (95% CI 91.2, 95.2), $p < 0.0001$

In concordance with prior studies that examined mood disorders related to bariatric surgery, our findings give credence to the benefits of bariatric surgery in improving depressive and anxiety symptoms, at

least for the first 3 years post-surgery.³⁰⁻³⁵ A meta-analysis of 68 studies reported that 19% of people seeking or undergoing bariatric surgery suffered from clinically diagnosed depression, and the post-

operative prevalence of depression decreased by 8%–74%, whereas the severity of depressive symptoms reduced by 40%–70%.³² In another systematic review of 14 studies, comprising 12 prospective cohorts and 2 time-controlled longitudinal trials, 13 reported significant improvements of depressive symptoms and 8 reported improvements in anxiety symptoms after 2–3 years of bariatric surgery.³⁴ A systematic review of 48 studies examined the effects of bariatric surgery on depressive and anxiety symptoms at incremental post-operative intervals, and concluded these symptoms decreased for most patients in the first 3 post-operative years.³⁵ While the prior review had described the post-bariatric surgery improvements of anxiety and depressive symptoms to a similar effect,^{32,34,35} our analysis is the first to objectively report the pooled strength of these associations.

Patients who undergo bariatric surgery constitute a vulnerable and often overlooked population, with many of these patients having mood symptoms. Data from a Brazilian study reported that 45% and 58% of patients had either depressive or anxiety symptoms, respectively, prior to bariatric surgery.³⁰ Apart from improvements in their primary medical conditions, avoidance of stigma and social embarrassment is often cited as a driving force for patients opting for this intervention.^{36,37} Stigma is often borne of self-loathing and is bolstered by the perception of others. This may influence a patient's decision to seek surgery as a means of losing weight. Depressive and anxiety symptoms, often a corollary of stigma associated with obesity, are common among patients pre- and post-bariatric surgery.^{38,39} The present meta-analysis demonstrates that overall, bariatric surgery plays a role in reducing the prevalence and severity of these symptoms, on top of the well-proven metabolic benefits. It will be interesting to further explore the factors that mediate these improvements.

In our exploratory analysis, patients who achieved post-operative BMI <35 kg/m², when compared to those with a post-operative BMI above this threshold, had larger relative risk reductions in both anxiety (71% vs. 46%) and depressive (61% vs. 28%) symptoms. This suggests that lower post-operative BMI is associated with better improvements in rates of depressive and anxiety symptoms. Similarly, the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study found that improvements in depressive symptoms were positively correlated with a reductions in BMI.³¹ Another study in Germany reported that the presence of post-operative depressive disorder was associated with lower degree of weight loss at 24–36 months follow-up.⁴⁰ Among younger women with obesity, bariatric surgery may not significantly reduce rates of anxiety symptoms. In our analysis, when sub-analysed according to women below or above the age of 40 years, the post-bariatric surgery reduction of the prevalence of depressive and anxiety symptoms remained clinically significant, except in younger women aged <40 years with anxiety symptoms. This is in keeping with the fact that the prevalence of anxiety symptoms is higher among women and reduces with advancing age.^{41–43} Previous studies have also found that anxiety symptoms are more impervious to improvements after bariatric surgery compared to depressive symptoms.³⁵ While interesting, we

acknowledge that the present findings are based on analysis around arbitrary cut-off points of BMI and age in the pooled cohort, and these may not necessarily represent significant thresholds in real-world conditions.

On the other hand, several studies have reported less favourable long-term mental health outcomes post-bariatric surgery. In the LABS-2 cohort, the initial improvement of depressive symptoms was not sustained beyond the first post-operative year.³¹ A study in Israel showed that despite successful weight loss and improvements in physical domains of HRQOL, measures of general mental health, neuroticism, sense of control and fear of intimacy improved in the first year, but subsequently deteriorated 10 years post-bariatric surgery.⁴⁴ An increase in the rates of depression and self-harm post-bariatric surgery has also been reported, but it was more common in patients with prior history of depression and self-harm.^{45,46} The notion of a 'psychological honeymoon' period of 3-year post-bariatric surgery has been proposed, after which, many studies have reported rebounds in anxiety, depressive symptoms and binge eating disorder.³⁵ Besides, bariatric surgery has been shown to reduce bioavailability of antidepressants, which may contribute to relapse or deterioration of mood disorders post-operatively.⁴⁷ In the present analysis, the mean follow-up duration of post-bariatric surgery was 34 months, which might not be sufficient to determine its long-term effects on mood symptoms.

It is interesting to note that the mental health benefits from weight reduction are not confined to bariatric surgery per se. Studies on several anti-obesity medications have shown similar results. Lorcaserin, a selective serotonin (5HT_{2C}) receptor agonist, used as an adjunct to diet and exercise, can significantly reduce body weight in people with either overweight or obesity.^{48–51} In addition to cardiometabolic benefits, patients have reported improvements in HRQOL, which was mediated by BMI reduction and improvement of depressive symptoms.^{51,52} Due to reports of increased incidence of cancer, lorcaserin has since been withdrawn by the United States Food and Drug Administration (US FDA). Prolonged-release Naltrexone/Bupropion (NB), another central nervous-system-acting medication, has been used as an adjunct therapy for weight reduction. In a post-hoc analysis of five randomized placebo-controlled clinical trials, NB-treated patients had lower rates of depressive psychiatric adverse events compared to placebo.⁵³ Recently, liraglutide, a GLP-1 receptor agonist, has been widely used for weight reduction and glucose control with positive cardiometabolic and renal outcomes.^{54,55} In a retrospective study of 29 patients with co-existing psychiatric disorders (bipolar or major depressive disorder) and obesity previously failing other lifestyle interventions, liraglutide was well tolerated, showed good weight reduction, and did not worsen psychiatric symptoms.⁵⁶ As most anti-obesity medications involve neurohormonal changes, it is unclear whether this mediates mood changes among people with obesity. While previous reports have indicated that anti-obesity medications are effective in preventing weight regain post-bariatric surgery,^{57,58} limited data exist on whether these benefits also include mental health outcomes.

Last but not least, the advent of the global COVID-19 pandemic has affected mood symptoms among people with obesity. A cross-sectional study among both pre- and post-bariatric surgery patients during the lockdown period in Italy showed increased measures of anxiety and depressive symptoms, along with poorer dietary compliance. The findings were similar in both pre- and post-operative patients, suggesting a consistent psychological effect on all people with either current or past history of obesity.⁵⁹ Increased visceral adiposity is also a risk factor for worse clinical outcomes and increased need for intensive care among patients with COVID-19.⁶⁰

Our study has a few limitations. As only English-language publications were included, this may have introduced elements of selection bias. Second, most included studies mainly comprised women subjects, who are known to have a higher risk of anxiety and depressive symptoms than men. Third, we were not able to compare the effects of bariatric surgery on mental health in subjects with or without diabetes due to limited data availability. We also could not further analyse the outcomes based on the different types of bariatric surgery as most studies did not report breakdown of different mood disorders according to surgical methods. It was also not feasible to distinguish changes in mental health at different follow-up periods in the present analysis. As the assessment tools (HADS and BDI) in the included studies were measurements of symptomatology rather than clinical diagnosis by a certified mental health professional (defined by either formal interview methods or DSM-V criteria), the present results may be more representative of symptom burden rather than actual rates of diagnoses of depression and anxiety disorders. Lastly, the scales used in the present analysis included questions on somatic symptoms such as reduced energy levels (HADS and PHQ-9), restlessness (GAD-7 and HADS), sleep problems (PHQ-9), among others, which may be indistinguishable from physical symptoms associated with obesity. Therefore, we cannot rule out the possibility that the reported improvements post-operatively may be contributed by mitigation of physical symptoms of obesity, rather than amelioration of mood symptoms.

4 | CONCLUSION

The present meta-analysis adds to the body of evidence that bariatric surgery is associated with improvements in the prevalence and severity of depressive and anxiety symptoms, at least up to 3 years. Lower post-bariatric surgery BMI is associated with lower rates of depressive and anxiety symptoms. Bariatric surgery may be less effective in reducing rates of anxiety symptoms among younger women with obesity.

In light of these findings, comprehensive pre-operative psychological assessments should be emphasized for all patients opting for bariatric surgery. This is essential, not only to improve the screening and timely treatment for mood symptoms, but also to better understand the long-term effect of bariatric surgery on different subsets of patients. Due to the possible symptom recurrence in the subsequent years after bariatric surgery, ongoing psychological support should be

offered to these patients during the post-operative period to sustain improvements in mental health outcomes. Future studies should be designed to confirm the role of post-operative BMI, age and sex as mediators for improvements in depressive and anxiety symptoms post-bariatric surgery. Indeed, novel research is also needed to determine whether co-administration of anti-obesity medications in people undergoing bariatric surgery improves mental health outcomes.

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CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

ETHICS STATEMENT

Ethics approval and consent to participate.

AUTHOR CONTRIBUTIONS

Huai Heng Loh and Huai Seng Loh designed the conception of the study. Huai Heng Loh and Lee-Ling Lim acquired the data. Anne Yee analysed and interpreted the data. Huai Heng Loh, Benedict Francis and Quan Hziung Lim drafted the manuscript. Lee-Ling Lim revised the manuscript. All authors agreed on the order in which their names will be listed on the manuscript and agreed to be accountable for all aspects of the work.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

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