Promoting weight loss and psychological well-being in patients with obesity: A sequential combination of behavioural lifestyle intervention and well-being therapy

Promoting Weight Loss and Psychological Well-being in Patients with Obesity: A Sequential Combination of Behavioral Lifestyle Intervention and Well-Being Therapy

Running Title: Promoting Weight Loss and Well-Being in Obesity

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Key Practitioner Message

1. Both treatments (WBT following BLI versus BLI alone) were associated with significant weight loss, up to a 12-month follow-up.
2. Only the addition of WBT was linked to greater improvements in depressive symptoms, autonomy, personal growth, and global well-being.
3. WBT may have enduring effects that reduce vulnerability to depression in patients with obesity.

Behavioral lifestyle interventions focused on diet and physical activity are a cornerstone for the treatment of obesity. However, their effects vary substantially across individuals in terms of magnitude and durability. Personalized approaches that target psychological well-being may be promising to facilitate healthy behaviors and sustained weight loss. This preliminary study aimed to explore whether the sequential combination of behavioral lifestyle intervention (BLI) and Well-Being Therapy (WBT) may result in more favorable outcomes than BLI alone in promoting weight loss (primary outcome) and improving psychological well-being, distress, dietary behaviors, and physical activity (secondary outcomes). 83 patients with obesity were randomly assigned to BLI/WBT (N= 38) or BLI group (N= 45). BLI group received a 12-week behavioral weight loss program, whereas BLI/WBT group received the same program followed by an additional 4-week WBT, adapted for group interventions. Data were collected at pre-treatment (baseline, T1), at the end of BLI/WBT (T2), and at 6-month (T3) and 12-month (T4) follow-ups. There was a significant weight loss in both treatment groups at T2, T3, and T4. BLI/WBT group showed greater improvements in depressive symptoms at T3 and T4, in autonomy at T2, personal growth at T4, and global well-being at T4 compared with BLI group. WBT yielded no additional effect on weight loss. However, the secondary outcomes indicate that WBT may have enduring effects that reduce vulnerability to psychological distress in patients with obesity. In order to confirm these preliminary findings and explore whether a more intensive and individualized WBT can foster sustained weight loss, future studies are needed.

*Keywords***:** lifestyle; obesity; psychological well-being; weight loss; Well-Being Therapy

1 INTRODUCTION

Obesity designates an excessive fat deposition that is commonly defined as having a Body Mass Index (BMI) of 30 kg/m^2 or greater in adults (World Health Organization, 2020). The worldwide prevalence of adult obesity is steadily growing and reached 13% in 2016 (World Health Organization, 2020), which presents a major challenge to global health. Individuals with obesity are vulnerable to various chronic medical complications, including type 2 diabetes (Haslam & James, 2005), hypertension, cardiovascular disease, sleep apnea (Young, Skatrud, & Peppard, 2004), and cancer (Wadden & Bary, 2019), thereby leading to a decrease in life expectancy (Whitlock et al., 2009) and high healthcare burden (Tannous et al., 2021).

Comprehensive lifestyle interventions involving dieting, physical activity, and behavioral strategies (e.g., stimulus control, goal setting, and problem solving) are considered first-line treatments for weight management (Wadden & Bary, 2019; Kushner, 2014; Paccosi, Cresci, Pala, Rotella, & Parenti, 2020). Nonetheless, treatment responses vary substantially across individuals in terms of magnitude and durability (Webb & Wadden, 2017). In most cases, short-term weight loss is usually followed by a weight-loss plateau and complete weight regain within five years (Hall & Kahan, 2018; Look AHEAD Research Group, 2014).

Previous studies have suggested that unbalanced levels of psychological well-being and high psychological distress are associated with poor weight reduction (Elfhag & Rössner, 2005; Pameira et al., 2010; Swencionis et al., 2013; Sawer et., al, 2019; Zhu et al., 2022). By contrast, sustained weight loss is positively correlated with resilience, self-efficacy, autonomy, and overall psychological well-being and stability (Elfhag & Rössner, 2005; Pameira et al., 2010; Shin et al., 2011; Gorin, Powers, Koestner, Wing, & Raynor, 2014). Although it has been argued that enduring lifestyle changes can only be achieved with a personalized approach that targets psychological well-being (Guidi, Rafanelli, & Fava, 2018a), little is known about

whether addressing psychological well-being in patients with obesity could help to improve their weight outcomes (Iturbe, Echeburúa, & Maiz, 2021).

Well-Being Therapy (WBT; Fava, 2016; Guidi & Fava, 2021) is an innovative, manualized, short-term psychotherapeutic strategy based on self-monitoring of instances of well-being using a structured diary, cognitive restructuring of interfering thoughts and behaviors, and homework assignments (Fava, 2016). It is aimed at the pursuit of euthymia, a trans-diagnostic construct that refers to the lack of affective disturbances, and the presence of positive affect and balanced psychological well-being (Fava & Guidi, 2020; Guidi & Fava, 2020). This latter refers to the balance and integration of psychic forces underlying psychological well-being (flexibility), a unifying outlook on life that guides actions and feelings for shaping the future accordingly (consistency), and resistance to stress (resilience and anxiety/frustration tolerance) according to Jahoda's (1958) model. It can be differentiated from positive psychology interventions on the basis of the following features: a) patients are encouraged to identify episodes of well-being that recently occurred and to set them in a situational context with the use of a structured diary; b) once the instances of well-being are recognized, the patient learns to identify thoughts and/or behaviors leading to premature interruption of well-being; c) homework assignments that elicit psychological well-being and, particularly, optimal experiences are prescribed; d) monitoring of the diary allows the therapist to discover specific impairments or, conversely, excessive levels of well-being dimensions (environmental mastery, personal growth, purpose in life, autonomy, self-acceptance and positive relations with others); e) patients are not simply encouraged to pursue the highest possible levels of psychological well-being, but to obtain an optimal balanced functioning, i.e., euthymia (Fava, 2016; Fava & Guidi, 2020). The patient thus becomes able to readily identify moments of well-being, to be aware of interruptions to well-being feelings (interfering thoughts and/or behaviors), and to apply cognitive behavioral techniques to address these interruptions and pursue optimal experiences.

WBT has been validated with Randomized Controlled Trials (RCTs) in different clinical settings (Fava & Guidi, 2020; Guidi & Fava, 2021; Benasi et al., 2022), including relapse prevention in depression (Fava, Rafanelli, Cazzaro, Conti, & Grandi, 1998; Fava et al., 2004) and depression associated with Acute Coronary Syndromes (Rafanelli et al., 2020). Preliminary data suggested the potential role of WBT in managing the challenges associated with chronic medical conditions and promoting healthy behaviors (Guidi et al., 2018a; Rafanelli et al., 2020).

As suggested by Fava (2016), WBT can be reduced to four sessions as an adjuvant to other therapies, particularly in combination with cognitive-behavioral therapy, with promising findings (Rafanelli et al., 2020; Benasi et al., 2022). We thus adapted the WBT protocol (Fava, 2016) for a short, small-group format. The present study was primarily designed to evaluate the efficacy of a sequential combination of behavioral lifestyle and well-being interventions (BLI/WBT group) on weight loss (i.e., changes in kilograms, BMI, and a reduction of at least 5% from initial body weight) in patients with obesity (primary outcome). Secondary aims included the evaluation of the efficacy of BLI/WBT on psychological well-being and distress, dietary behaviors, and physical activity (secondary outcomes). Lastly, the feasibility and acceptability of WBT were examined.

A greater weight loss in the group receiving the BLI/WBT than in the group receiving the behavioral lifestyle intervention alone (BLI), at the end of BLI/WBT and at 6-month and 12-month follow-ups was expected. We also hypothesized that the combination of BLI/WBT would outperform BLI in a) improving psychological well-being and distress and b) promoting dietary behaviors and physical activity, at the end of BLI/WBT, at 6-month and 12-month follow-ups.

2 METHODS

2.1 Design and procedure

The randomized controlled trial (RCT) was carried out between September 2018 and March 2021 at the *Center of Metabolism Diseases and Clinical Dietetics* of IRCCS *Sant'Orsola Hospital* in Bologna. Assessment and treatments (e.g., BLI and WBT) were administered by a panel of well-trained clinicians. Given the nature of the treatment, only the assessors were blind to group allocation. The study has been approved by the local Ethics Committee.

Participants were consecutively recruited from succeeding groups of patients scheduled for an interdisciplinary behavioral lifestyle intervention (with 4 subsequent waves) at the same clinic, between September 2018 and November 2019. Individuals interested in participating in the study were screened for eligibility and provided written informed consent for study participation. During the first three months, all participants received the behavioral lifestyle intervention, and those who completed it (with a minimum of 50% attendance) were randomly assigned to either BLI/WBT or BLI group using an online computer program (www.randomizer.org). Patients in BLI/WBT group received additional 4-weekly sessions of WBT, while those in the BLI group only received treatment as usual (TAU). Data were collected for each participant through questionnaires and interviews at baseline (T1), the end of BLI/WBT (T2), and at 6-month (T3) and 12-month (T4) follow-ups.

2.2 Eligibility

Patients had to meet the following criteria to be included in the study: a) diagnosis of obesity (BMI ≥ 30), b) aged ≥18 years, and c) willing to participate in the study.

Exclusion criteria were: a) presence of a severe psychiatric illness (i.e. psychotic and bipolar disorders) and/or cognitive deficit; b) insufficient knowledge of Italian; c) pregnancy, d) bariatric surgery, e) weight loss medications, and/or f) participation in another psycho-behavioral intervention for modifying dieting and/or physical activity or trail during the past

year or within 12 months from the beginning of the study; g) attending less than 6 sessions of the behavioral lifestyle intervention.

2.3 Treatments

Behavioral lifestyle intervention (BLI): the program was administered by a multidisciplinary team including physicians, dieticians, and a psychologist. It included 12 two-hour weekly sessions held in a group setting (with a maximum of 20 participants). The main components of this program included general therapeutic education about obesity (sessions 1 and 11), lifestyle education on diet and physical activity (sessions 3-10), and psychoeducation regarding motivation and maintenance of a healthy lifestyle (sessions 2 and 12). In the first session, a physician provided an overview of obesity, including its definition, etiological factors, and complications. The second session was focused on encouraging patients to initiate lifestyle changes. The psychologist explained the stages of change and discussed the pros and drawbacks of changing their lifestyle with the patients using a decisional balance sheet (Prochaska & DiClemente, 1983). The following 8 sessions were dedicated to lifestyle education concerning diet and physical activity. Initially, a dietician taught the patients the fundamentals of healthy eating, which were mostly based on the Mediterranean diet model, and encouraged them to make qualitative changes. Next, participants were taught how to utilize a structured diary, in which they were requested to record their daily calorie intake (through a written list of meals with caloric content) and expenditure (i.e., basal metabolic rate and physical activity). Furthermore, they were instructed on how to bank calories on a weekly basis, allowing for compensation between days, in order to manage calories in a flexible manner. A physician led the penultimate session, which was devoted to therapeutic education on bariatric surgery. During the final session, a psychologist worked with participants on how to identify prodromes of crisis (such as the distinction between slip and relapse) related to weight regain and to employ

problem-solving approaches, in order to promote and maintain healthy eating habits and physical exercise.

Well-Being Therapy (WBT): Participants in the experimental group received four additional weekly sessions delivered by a well-trained psychologist supervised by a certified WBT specialist. All sessions lasted about two hours and were administered in a group setting. Each group included from 8 to maximum 10 participants. During the sessions, they were coached on how to self-monitor their daily episodes of well-being - especially those associated with their engagement in a lifestyle change - using a structured diary (first session). Participants were then encouraged to discuss their well-being experiences during group sessions, focusing on dysfunctional thoughts/beliefs interrupting them and fostering the identification of alternative and more functional thoughts (second session). Starting from the second session, the psychologist taught participants how to promote well-being situations through the assignment of behavioral exercises between sessions. Finally, during the third and fourth sessions, the psychologist introduced and discussed relevant dimensions of psychological well-being (Fava, 2016) that were associated with patients' experiences reported during treatment, and encouraged group discussions on functional strategies to promote balanced levels of psychological well-being.

Treatment as usual (TAU): The treatment as usual involved recommendations for weight management, including diet, physical activity, and physician-prescribed medication for other comorbidities.

2.4 Assessment

Measures were performed at pre-treatment (baseline, T1), at the end of BLI/WBT (T2), at 6- (T3) and 12-month (T4) follow-ups after the intervention. Data on age, gender, education, employment status, living condition, cigarette smoking, alcohol use, and medical history (i.e.,

cardiovascular diseases, hypertension, diabetes, hypercholesterolemia, psychiatric disorders), were collected at baseline.

Weight. Body weight was measured to the nearest 0.1 kg on a standard balance beam scale with participants in lightweight clothing. Stadiometer was used to measure height to the nearest 1.0 cm with participants standing without shoes. Both body weight and height were used to calculate BMI. Clinically significant weight loss (CWL) was defined as at least a 5% weight loss from the initial body weight.

Psychological well-being. The short version of Psychological Well-Being scales (PWB; Ryff & Keyes, 1995) contains 42 self-rating items that assess 6 dimensions of psychological well-being: self-acceptance, positive relations with others, autonomy, environmental mastery, purpose in life, and personal growth. On a 6-point Likert scale, respondents were asked to indicate how much they agreed with each statement (from 1= strongly disagree to 6= strongly agree). Subtotal scores for each dimension were computed independently with a range from 7 to 42. Higher scores imply higher levels of psychological well-being. In addition, the global well-being scale of Psycho-Social Index (PSI; Piolanti et al., 2016; Sonino & Fava, 1998) was used to assess the global level of psychological well-being. It includes 7 self-rated items, where 6 items investigate general well-being with yes/no answers, and one item evaluates quality of life on a *Likert* scale ranging from 4 (excellent) to 1 (awful).

Psychological distress. Symptom Questionnaire (SQ; Benasi, Fava, & Rafanelli, 2020; Kellner, 1987) is a self-rating tool for measuring psychological distress over a one-week period. SQ consists of 92 items with dichotomous answers (i.e., Yes/No or True/False) resulting in four main domains: depression, anxiety, somatization, and hostility/irritability. Higher scores indicate greater psychological distress. Moreover, the global psychological distress scale of PSI (Piolanti et al., 2016; Sonino & Fava, 1998) was used to assess the global severity of psychological distress. This is a 15-item scale that assesses the presence of symptoms of

anxiety, hostility/irritability, depression, somatization, and sleep disturbances. Participants were asked to self-rate how much they had suffered from these symptoms on a scale ranging from 0 (not at all) to 3 (a great deal). The presence of major depression was measured with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders - 5th edition (SCID-5-CV; First, Williams, Karg, & Spitzer, 2016). Finally, demoralization, a prolonged psychological state characterized by feelings of being unable to cope with a problem, hopelessness, and helplessness, was evaluated with the semi-structured interview for the Diagnostic Criteria for Psychosomatic Research (DCPR; Fava et al., 1995; Rafanelli et al., 2003).

Dietary behaviors and physical activity. GOSPEL questionnaire (Giannuzzi et al., 2008) is a self-administered survey to quantify diet habits and physical activity levels over a 6-month period. The instrument, which was named after the GOSPEL study on cardiovascular diseases (Giannuzzi et al., 2008), includes ten items addressing adherence to Mediterranean diet (e.g., vegetables, fish, butter), on a scale ranging from 1 (never or rarely) to 4 (every day), which provide a Mediterranean diet score ranging from 0 (worst) to 30 (best). Three additional items measure eating behaviors based on how often respondent routinely eats slowly and with no urgency, with a scale ranging from 1 (never) to 4 (always); scores on each item are summed up to provide a score ranging from 0 (worst habits) to 9 (best habits). Physical activity is measured through eight items: 5 assess how frequently respondents engage in particular physical activities (e.g., stair climbing, walking, and going to the gym), on a range from 1 (never or seldom) to 4 (every day); 2 explore the involvement of other physical activities with yes/no response options; 1 assesses the overall self-perceived level of physical activity on a scale from 4 (very high) to 1 (poor). Scores on each of these items are added to provide a total physical activity score ranging from 0 (least active) to 20 (most active).

2.5 Statistical Analyses

We calculated the sample size a priori for repeated measures ANOVA (within-between interaction) using G*Power 3.1. The outcomes showed that at least 36 cases were required to achieve a power of 0.80 to detect a small-to-medium effect size (f= 0.2), between 2 groups with 4 repeated assessments, at an alpha level of 0.05 (two-tailed). With a 30% drop-out rate anticipated, a minimum of 52 subjects would have been acceptable.

Data were analyzed using the Statistical Package for Social Science (SPSS, version 24). Multiple imputation procedures were performed for dealing with missing data with 25 imputations as suggested by Austin, White, Lee, and van Buuren (2021). Samples were compared at baseline using Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables.

We performed an intention-to-treat (ITT) analysis using generalized estimated equations (GGE) to evaluate mean treatment differences between (BLI/WBT group vs. BLI group) and within groups at the end of BLI/WBT and at 6- and 12-month follow-ups adjusted for their respective baseline and demographic data, which were significantly different between groups (Zeger, Liang, & Albert, 1988). GEE is a robust approach that allows for modeling the dependency of measurements within the same subject to provide greater precision than an analysis of covariance (Hanley, Negassa, Edwardes, & Forrester, 2003). The working correlation structure was assumed to be exchangeable and estimates were adjusted by the number of nonredundant parameters. For binary variables (major depression and demoralization), the differences were computed as odds ratios. Effect sizes for continuous outcomes were estimated using Cohen's *d* calculated as estimated marginal mean divided by pooled standardized deviation.

Given the constant value at baseline, logistic regression instead of generalized estimated equations was employed to analyze the rate of clinically relevant weight loss adjusted for

baseline BMI and demographic variables that showed significant group differences. Statistical significance level was set at a *p*-value ≤ 0.05, two-tailed.

3 RESULTS

3.1 Feasibility

Patients flow is presented in Figure 1, according to Consolidated Standards of Reporting Trials (CONSORT). 147 patients were screened for eligibility: 9 patients declined to participate due to no interest, no time, and lack of transportation; 34 patients did not attend the screening meeting without providing any explanation; one patient was excluded due to a BMI < 30. Before randomization, further 20 participants were excluded from the study. Reasons for exclusion were a high number of absences (> 6 sessions) from behavioral lifestyle intervention (N= 12) and consent withdrawal after baseline assessment (N= 4) or before randomization, without giving any feedback (N= 4). There were not statistically significant differences in socio-demographic characteristics between these individuals and those enrolled in the study.

A total of 83 subjects were enrolled for randomization: 38 were allocated to BLI/WBT group and 45 to BLI group. Three participants (7.8%) in BLI/WBT group discontinued the intervention because of lack of time. Overall, 13 participants (34.2%) in BLI/WBT group and 25 participants (55.6%) in BLI group were lost to follow-ups. The main reasons for drop-out included lack of time. In addition, 8 patients were excluded after T2, since they joined another psycho-behavioral intervention for promoting dieting and/or physical activity.

3.2 Sample characteristics

Sample characteristics are displayed in Table 1. BLI/WBT and BLI groups were comparable in terms of gender, education, medical history, smoking habit, and alcohol drinking. BLI/WBT

group has a higher age and a lower employment rate compared to BLI group. Cardiovascular diseases were the most prevalent comorbidity, followed by hypertension. The prevalence of major depression and demoralization at baseline was 18.4% and 39.5%, respectively, in BLI/WBT group and 24.4% and 40.0%, respectively, in BLI group. The mean baseline BMI was 37.7±6.7 in BLI/WBT group and 36.7±4.1 in BLI group (Table 2).

3.3 Primary outcomes

Primary and secondary outcomes from ITT analysis are presented in Table 2, Table 3, Table 4, and Figure 2. There were no significant between-group differences in body weight change in kg at T2 (β= -2.31, d=-0.12, p>0.05), T3 (β= -0.98, d=-0.05, p>0.05), and T4 (β= -1.94, d=-0.10, p>0.05) compared to T1. Both groups reduced body weight significantly at T2 (BLI/WBT: β= -6.24, d=-0.27, p<0.01; BLI: β= -3.93, d=-0.31, p<0.05), T3 (BLI/WBT: β= -5.44, d=-0.25, p<0.01; BLI: β= -4.47, d=-0.36, p<0.05) and T4 (BLI/WBT: β= -6.14, d=-0.33, p<0.01; BLI: β= -4.20, d=-0.35, p<0.05). Consistent with the body weight in kg, no between-group differences were detected in BMI at all the measurement points. A significant BMI decrease was observed in both groups at T2, T3, and T4.

Similarly, the effect of group allocation on the rate of clinically relevant weight loss was not significant at any measurement points (T2: odds ratio (OR)= 1.12, p>0.05; T3: OR= 0.77, p>0.05; T3: OR= 0.44, p>0.05). At T2, 39.5% of participants in BLI/WBT group and 35.6% of participants in BLI group achieved clinically relevant weight loss; at T3, 42.1% in BLI/WBT group and 46.7% in BLI group; at T4, 31.6% in BLI/WBT group and 44.4% in BLI group.

3.4 Secondary outcomes

Psychological distress. In terms of symptoms of depression as assessed with SQ, significant differences between groups were observed at T3 (β= -2.13, d=-0.52, p<0.05) and T4 (β=-1.80,

d=-0.44, p<0.05) while not at T2. Compared to baseline, the adjusted mean level of depression increased by 0.85 (d=0.17, p>0.05) in BLI group and decreased by 1.28 (d=-0.34, p<0.05) in BLI/WBT group at T3. At T4, the level of depression significantly increased in BLI group (β= 2.21, d=0.50, p<0.001), whereas did not significantly change in BLI/WBT group (β= 0.42, d=0.12, p>0.05).

No between-group differences were observed in SQ subscales of anxiety, somatic symptoms, and hostility/irritability at any measurement point.

As to major depression and demoralization, the groups did not differ from each other, and no changes were observed in either group at any measurement point.

As to PSI score of global distress, no significant differences between groups were found at any measurement points.

Psychological well-being. At T2, BLI/WBT group showed a significantly greater increase (β= 2.75, d=0.41, p<0.05) in the levels of PWB autonomy compared to BLI group. At T3 and T4, however, between-group differences in autonomy were no longer significant. There was no difference between groups concerning the levels of PWB personal growth at T2 and T3. However, at T4, a significantly greater improvement (β= 2.56, d=0.45, p<0.05) was observed in BLI/WBT group in comparison with BLI group. Groups did not differ from each other in any of the other subscales of PWB at any measurement point.

Concerning the global well-being of PSI, the groups differed from each other significantly at T2 (β= 0.71, d=0.36, p<0.05) while not at T3 and T4. Compared to T1, the adjusted mean level of global well-being increased by 0.36 (d=0.20) in BLI/WBT group and decreased by 0.34(d=-0.19) in BLI group at T2, although statistical significance was not reached (both *p*-values > 0.5).

Dietary behaviors and physical activity. No between-group differences were observed in physical activity, diet, and eating behavior at any measurement points.

4 DISCUSSION

In this RCT, the efficacy of a sequential combination of behavioral lifestyle and a modified version of WBT on weight loss compared to the behavioral lifestyle intervention alone was tested in obesity. The trial included independent randomization, manualized treatment administered by an interdisciplinary team, single-blinded assessment, and a combination of self- and observer-rated assessments. This is in line with the methodological recommendations for clinical trials provided by Guidi et al. (2018b). Given the low treatment discontinuation rate, this modified version of WBT for a group format is feasible and highly accepted in patients with obesity.

The findings of the present study did not support our primary hypothesis. The combination of BLI/WBT did not outperform BLI in promoting weight loss. However, there were considerable limitations in the approach that we tested. A 4-session WBT is suggested to follow cognitive-behavioral therapy (CBT) (Fava, 2016), whereas the comprehensive lifestyle program in the present study did not involve the self-monitoring of emotions as in CBT. Four sessions of WBT delivered in a group format may be sub-optimal compared to the 8-12 individualized sessions that are recommended (Fava, 2016). Indeed, the participants in the present study had just got to know the basics of the therapy and how it works.

Both BLI/WBT and BLI groups were associated with significant weight loss at post-WBT intervention, and at 6-month and 12-month follow-ups. These findings are in line with those of previous studies on comprehensive lifestyle interventions that consisted of diet, physical activity, and behavioral treatment (Look AHEAD Research Group, 2014; Shaw, O'Rourke, Del Mar, & Kenardy, 2005). It has been suggested that this treatment modality can produce a modest reduction in initial body weight at short and mid-term follow-ups (6-12 months) (Wadden & Bary, 2019). On the same vein, according to group allocation, no significant difference about

dietary behaviors and physical activity, which represent the central determinants of weight reduction (Brownell, 1999), was found.

As to secondary outcomes, the sequential combination of the lifestyle and WBT showed significantly greater improvements in depressive symptoms at both 6-month and 12-month follow-ups compared to the lifestyle intervention alone. These results indicate that WBT may reduce vulnerability to depression among patients with obesity. This interpretation is in line with the clinical application of WBT in relapse prevention for depression (Fava et al., 2004; Fava, 2016). Indeed, the importance of psychological distress has been increasingly acknowledged in obesity. For example, a meta-analytic review of longitudinal studies concluded that individuals with obesity were 1.55 times more likely to develop depression (Luppino et al., 2010). Moreover, anxiety and depression disorders can exert a negative impact on treatment outcomes and worsen obesity conditions (de Zwaan et al., 2011; Hryhorczuk, Sharma, & Fulton, 2013). The finding from the present study may shed light on the use of WBT to prevent psychological comorbidities (e.g., depression) of obesity.

As to major depression and demoralization, there were no changes in either group. Although considerable data have suggested the benefit of weight loss for depression, the studies have high methodological variability, in particular, the difference in defining depression (as continuous or categorical), which may lead to mixed results. Our findings suggest that treatments focused on lifestyle modifications may not be sufficient to deal with major depression and demoralization, and additional strategies for treating these conditions are needed.

As to psychological well-being, the sequential combination of BLI and WBT produced significantly greater improvements in PWB autonomy and the PSI global well-being at the end of treatment, compared to the lifestyle intervention alone. The PWB autonomy evaluates the extent to which a person thinks and acts according to his/her own personal convictions (Ryff,

2014). In a previous investigation, a pronounced increase in autonomy predicted poor weight outcomes following a comprehensive lifestyle intervention (Zhu et al., 2022). Both exceedingly high and low levels of autonomy may entail maladaptive thoughts and beliefs (e.g., the weight outcome is totally under one's control or it is impossible to manage one's weight without the aid of clinicians) that can be detrimental to one's functioning (Fava 2016; Fava & Guidi, 2020; Gostoli et al., 2021; Zhu et al., 2022). Hence, it is reasonable to assume that the balance of autonomy could vary across different stages of change, in particular, between those of pre-maintenance and maintenance, which usually mark a transition from supervised to unsupervised weight loss. Compared with pre-maintenance, during maintenance stage, a higher level of autonomy would be beneficial to reach a balanced state. On the contrary, the optimal level of autonomy in the phase of maintenance could be excessive for the other stages, potentially hampering behavioral change. Preliminary findings highlighted the beneficial effects of WBT – administered *prior* to lifestyle intervention – on greater self-reported physical activity and reduction of lypidic level (Benasi et al., 2022). Future studies exploring the clinical implications of WBT across different stages of change using various sequential designs (e.g., implementing WBT either before BLI – in order to improve motivation to behavioral change – or after BLI – to support healthy behaviors maintance), are needed.

WBT was also linked with a greater increase in personal growth in comparison with BLI group at the 12-month follow-up. Personal growth pertains to the extent to which people experience their life as a growing and expanding process (Ryff & Keyes, 1995). Individuals with optimal levels of personal growth could see improvements in their lives and behaviors, whereas those with low levels would have a sense of stagnation and lose interest in their life. Consistent with previous studies, this finding lends support to personal growth as a protective factor against psychological distress that helps people to be resilient to stress (e.g., weight regain, the pandemic) (Danitz, Orsillo, Beard, & Björgvinsson, 2018; Kim et al., 2021).

Given the preliminary nature of the study, present findings should be interpreted within the context of some limitations. Firstly, the study was mono-centric with a limited sample size that may lead to bias (Bellomo, Warrillow, & Reade, 2009). Thus, future studies are needed to confirm these preliminary findings in a large sample multi-center trial. Second, as some of the patients had signed up for the behavioral lifestyle intervention a few months before the program started, they might have started dieting and exercising on their own. It is unknown whether this had an impact on the current study findings. Third, due to its ease of use in a busy clinical setting, a self-rated questionnaire was used to assess food and physical activity (Prince et al., 2008). As a result, it could be likely that diet and exercise scores do not correspond to their actual levels. Fourth, data regarding medical history were self-reported by the participants. This – on one hand – does not allow us to determine the criteria used to make diagnoses and – on the other hand – could have made medical anamnesis less reliable (Kelstrup, Juillerat, & Korzenik, 2014). Fifth, we used a group format for administering WBT, which is not the preferred modality (Fava, 2016), and consisted of only 4 sessions. Sixth, since there was no form of active psychotherapeutic control group, it is difficult to determine whether the results were determined by WBT or may reflect non-specific psychological ingredients that apply to group psychotherapy (Guidi et al., 2018b). Seventh, the effects of medication or psychotherapy possibly administered to certain participants to treat depression during the study could represent unmeasured confounders. Lastly, although WBT aims to promote euthymia, we did not measure euthymia directly using a self-rating questionnaire, such as the Euthymia Scale (Fava & Bech, 2016; Carrozzino, Svicher, Patierno, Berrocal, & Cosci, 2019) or the Clinical Interview for Euthymia (Fava & Guidi, 2020).

Even though there were no direct effects on weight (primary hypothesis) and health behaviors such as diet and physical activity (secondary hypothesis), the results from the current study can provide preliminary evidence that well-being modulation geared to euthymia may be

beneficial for the management of psychological distress in obesity. In particular, the secondary outcomes indicate that WBT may mitigate one's vulnerability to depressive symptoms that may exacerbate obesity (Hryhorczuk et al., 2013) and hamper weight loss (Elfhag & Rössner, 2005). This finding highlights the potential use of a modified form of WBT to prevent psychological comorbidities (e.g., depression) of obesity. As WBT was feasible and acceptable in patients with obesity, it might be a valuable add-on component to comprehensive lifestyle intervention. Future studies including a valid measure of euthymia and exploring whether a more intense and individualized WBT protocol (with a higher number of sessions, as well as varied sequential designs) could entail effects on weight loss, are needed.

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Table 1. Sample characteristics at baseline in each group.

	BLI/WBT (n=38)	BLI (n=45)	
			p^a
Age (y), *Mean±SD*	57.9±10.9	53.4±9.8	**.022**
Female sex, *n*(%)	29(76.3)	36(80.0)	.685
Education, *n(%)*			.213
Middle school or lower	8(21.1)	15(33.3)	
High school or higher	30(78.9)	30(66.7)	
Employed, *n*(%)	17(44.7)	30(66.7)	**.045**
Living alone, *n*(%)	10(26.3)	10(22.2)	.664
Cardiovascular diseases, *n*(%)	26(68.4)	24(53.3)	.162
Diabetes, *n*(%)	14(36.8)	13(28.9)	.441
Hypertension, *n*(%)	23(60.5)	21(46.7)	.149
Hypercholesterolemia, *n*(%)	20(52.6)	16(35.6)	.118
Lifetime psychiatric disorders	6(15.8)	9(20.0)	.619
Current smoking, *n*(%)	1(2.6)	3(6.7)	.392
Current alcohol drinking, *n*(%)	9(23.7)	13(29.5)	.550
Scheduled for 6-month follow-up before lockdown, *n*(%)	18(47.4)	17(37.8)	.378
Scheduled for 12-month follow-up before lockdown, *n*(%)	6(15.8)	9(20)	.619

Note. Bold: *p*-value ≤ .05; BLI: Behavioral lifestyle intervention; WBT: Well-being Therapy; GOSPEL scale for lifestyle characteristics; PWB= Psychological well-being scale; PSI= Psychosocial index; SQ= Symptom questionnaire; [a] Chi-square tests for categorical variables and Mann-Whitney U tests for continuous variables.

Table 2. Body weight, BMI, clinically relevant weight loss rate, and the secondary outcomes at different measurement points (baseline - T1, end of the BLI/WBT intervention - T2, 6-month post-intervention follow-up - T3, 12-month post-intervention follow-up - T4) in each group for intention-to-treat analyses.

	BLI/WBT (n=38)				BLI (n=45)			
	T1	T2	T3	T4	T1	T2	T3	T4
Primary outcomes								
Body weight	100.2±23.8	93.9±22.5	94.7±20.4	94.0±10.6	99.2±13.9	95.2±11.4	94.7±11.0	95.0±9.4
BMI	37.7±6.7	35.4±6.0	35.7±5.5	35.8±4.4	36.7±4.1	35.3±3.6	35.2±4.0	35.3±4.0
Clinically relevant weight loss, *n (%)*	0 (0)	15 (39.5)	16 (42.1)	12 (31.6)	0 (0)	16 (35.6)	21 (46.7)	20 (44.4)
Secondary outcomes								
SQ								
Anxiety	6.2±4.0	5.2±4.2	5.7±5.0	6.2±3.6	6.7±4.9	7.2±5.6	7.6±5.3	8.3±4.1
Depression	6.6±3.3	5.5±4.1	5.3±4.1	7.0±3.5	6.3±4.7	6.7±5.4	7.2±5.2	8.5±4.1
Somatic symptoms	10.1±5.4	8.4±5.3	9.8±4.5	11.4±4.6	10.0±5.6	9.6±5.8	10.7±5.1	11.8±4.2
Hostility/Irritability	6.2±4.4	4.6±4.4	4.3±4.2	4.7±3.4	6.2±5.5	5.9±5.2	5.6±5.3	6.2±4.5
Major Depression, *n(%)*	7(18.4)	5(13.2)	8(21.1)	11(28.9)	11(24.4)	18(40.0)	17(37.8)	12(26.7)
Demoralization, *n(%)*	15(39.5)	12(31.6)	9(23.7)	18(47.4)	18(40.0)	22(48.9)	20(44.4)	27(60.0)
PWB								
Autonomy	29.2±6.2	31.9±6.6	31.9±4.7	29.1±8.3	31.1±7.0	31.1±6.3	31.3±5.8	30.1±4.5
Environmental mastery	29.4±5.5	31.1±6.6	31.3±5.8	30.0±4.7	27.4±6.6	28.7±7.5	28.2±6.6	27.5±5.1
Personal growth	31.4±6.0	32.2±6.0	32.8±4.4	32.1±5.2	31.7±5.4	32.3±5.5	32.0±4.7	29.8±4.3
Positive relationship	31.6±6.5	31.5±5.5	32.6±5.1	31.9±4.7	31.0±6.6	32.1±5.8	32.8±5.8	32.0±4.8
Purpose of life	28.2±5.5	29.3±5.0	29.6±4.0	27.9±4.9	28.1±4.9	29.4±4.4	28.4±3.5	27.5±3.5
Self-acceptance	27.9±6.6	29.4±6.5	30.0±5.4	29.0±5.2	25.3±6.6	26.9±7.2	27.5±6.4	26.0±5.8
PSI								
Global distress	11.5±7.4	8.5±6.0	9.9±5.6	12.0±6.1	12.6±8.2	9.9±7.4	13.0±7.4	13.9±6.7
Global well-being	6.6±2.0	6.9±1.6	6.7±1.8	6.8±1.4	6.6±1.9	6.3±1.7	6.4±1.8	6.2±1.6
GOSPEL								
Physical activities	4.0±2.6	5.5±3.1	5.2±3.0	4.6±2.5	4.6±2.5	6.4±2.4	5.6±2.2	5.0±1.8

Diet	17.8±2.4	19.0±2.5	18.5±2.4	17.1±2.5	17.2±3.1	18.7±2.5	18.1±2.5	17.2±1.8
Eeating behavior	4.8±2.0	6.1±1.5	5.7±1.5	5.7±1.5	4.5±2.2	5.6±2.0	5.8±1.7	5.6±1.6

Note. BLI: Behavioral lifestyle intervention; WBT: Well-Being Therapy; SQ= Symptom questionnaire; PWB= Psychological well-being scale; PSI= Psychosocial index; GOSPEL= GOSPEL scale for lifestyle characteristics

Table 3. Between-group differences and 95% Wald confidence intervals for the primary and secondary outcomes from intention-to-treat analyses.

Variables	Group difference T1/T2		Group difference T1/T3		Group difference T1/T4	
	β (95%CI)	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***
Primary outcomes						
Body weight	-2.31(-7.71 to 3.09)	-0.12	-0.98(-6.37 to 4.42)	-0.05	-1.94(-7.34 to 3.46)	-0.10
BMI	-0.95(-2.79 to 0.89)	-0.17	-0.45(-2.29 to 1.39)	-0.08	-0.59(-2.43 to 1.25)	-0.11
CWL[1,2], *n(%)*	1.12(0.43 to 2.92)	—	0.77(0.29 to 2.00)	—	0.44(0.15 to 1.30)	—
Secondary outcomes						
SQ						
Anxiety	-1.52(-3.20 to 0.17)	-0.34	-1.41(-3.10 to 0.27)	-0.31	-1.59(-3.27 to 0.10)	-0.35
Depression	-1.44(-3.08 to 0.20)	-0.35	**-2.13(-3.76 to -0.49)***	-0.52	**-1.80(-3.44 to -0.16)***	-0.44
Somatic symptoms	-1.20(-3.00 to 0.59)	-0.22	-0.91(-2.70 to 0.89)	-0.17	-0.44(-2.23 to 1.36)	-0.08
Hostility/Irritability	-1.29(-3.03 to 0.45)	-0.26	-1.34(-3.08 to 0.40)	-0.27	-1.44(-3.18 to 0.30)	-0.29
Major Depression[1], *n(%)*	0.21(0.04 to 1.16)	—	0.51(0.10 to 2.56)	—	1.89(0.38 to 9.34)	—
Demoralization[1], *n(%)*	0.44(0.12 to 1.68)	—	0.34(0.09 to 1.36)	—	0.57(0.15 to 2.12)	—
PWB						
Autonomy	**2.75(0.22 to 5.27)***	0.41	2.50(-0.03 to 5.02)	0.38	0.97(-1.56 to 3.50)	0.15
Environmental mastery	0.44(-1.61 to 2.49)	0.07	1.24(-0.81 to 3.29)	0.20	0.57(-1.48 to 2.62)	0.09
Personal growth	0.18(-2.00 to 2.36)	0.03	1.08(-1.11 to 3.26)	0.19	**2.56(0.38 to 4.74)***	0.45
Positive relationship	-1.26(-3.28 to 0.77)	-0.19	-0.78(-2.80 to 1.25)	-0.12	-0.67(-2.70 to 1.35)	-0.10
Purpose of life	-0.13(-2.07 to 1.81)	-0.03	1.08(-0.86 to 3.01)	0.21	0.32(-1.62 to 2.25)	0.06
Self-acceptance	-0.06(-2.22 to 2.11)	-0.01	-0.08 (-2.24 to 2.09)	-0.01	0.35(-1.82 to 2.51)	0.05
PSI						
Global distress	-0.27(-2.91 to 2.37)	-0.03	-2.06(-4.70 to 0.58)	-0.26	-0.86(-3.50 to 1.78)	-0.11
Global well-being	**0.71(0.02 to 1.39)***	0.36	0.36(-0.33 to 1.04)	0.18	0.67(-0.01 to 1.36)	0.34
GOSPEL						
Physical activities	-0.29(-1.29 to 0.71)	-0.11	0.15(-0.85 to 1.15)	0.06	0.12(-0.88 to 1.12)	0.05
Diet	-0.20(-1.37 to 0.98)	-0.07	-0.12(-1.29 to 1.06)	-0.04	-0.68(-1.86 to 0.50)	-0.24
Eeating behavior	0.27(-0.43 to 0.98)	0.13	-0.35(-1.05 to 0.36)	-0.17	-0.07(-0.77 to 0.64)	-0.03

Note. All the values were adjusted for age, employment status, and baseline. BLI group and T1 were set as the referents. Bold*: *p*-value ≤ .05; Bold**: *p*-value < .01; Bold***: *p*-value < 0.001; CWL: Clinically significant weight loss; SQ= Symptom questionnaire; PWB= Psychological well-being scale; PSI= Psychosocial index; GOSPEL= GOSPEL scale for lifestyle characteristics; T1= baseline, T2= end of the BLI/WBT intervention, T3=6-month post-intervention follow-up, T4= 12-month post-intervention follow-up. [1] Odds ratios were computed as regression coefficients for each variable; [2] No time effects per group computed as data were analyzed with logistic regression instead of generalized estimating equations due to constant values at baseline.

Table 4. Within-group effects and 95% Wald confidence intervals for the primary and secondary outcomes from intention-to-treat analyses.

Variables	Time effect in BLI/WBT group T1/T2		Time effect in BLI group T1/T2		Time effect in BLI/WBT group T1/T3		Time effect in BLI group T1/T3		Time effect in BLI/WBT group T1/T4		Time effect in BLT group T1/T4	
	β (95%CI)	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***	**β (95%CI)**	**Cohen's *d***
Primary outcomes												
Body weight	**-6.24(-10.21 to-2.26)****	-0.27	**-3.93(-7.58 to -0.27)***	-0.31	**-5.44(-9.42 to -1.47)****	-0.25	**-4.47(-8.12 to -0.81)***	-0.36	**-6.14(-10.12 to -2.17)****	-0.33	**-4.20(-7.58 to -0.55)***	-0.35
BMI	**-2.34(-3.69 to -0.99)****	-0.37	**-1.39(-2.63 to -0.15)***	-0.36	**-1.99(-3.34 to -0.64)****	-0.32	**-1.54(-2.79 to -0.30)***	-0.38	**-1.97(-3.33 to -0.62)****	-0.35	**-1.38(-2.63 to -0.14)***	-0.34
CWL[1,2], *n(%)*	—	—	—	—	—	—	—	—	—	—	—	—
Secondary outcomes												
SQ												
Anxiety	-1.04(-2.28 to 0.20)	-0.25	0.48(-0.66 to 1.62)	0.09	-0.50(-1.74 to 0.74)	-0.11	0.91(-0.23 to 2.05)	0.18	-0.04(-1.28 to 1.20)	-0.01	**1.56(0.41 to 2.70)****	0.35
Depression	-1.07(-2.28 to 0.14)	-0.29	0.37(-0.72 to 1.48)	0.07	**-1.28(-2.48 to -0.07)***	-0.34	0.85(-0.26 to1.96)	0.17	0.42(-0.79 to 1.62)	0.12	**2.21(1.11 to 3.32)*****	0.50
Somatic symptoms	**-1.65(-2.97 to -0.33)***	-0.31	-0.44(-1.66 to 0.77)	-0.08	-0.25(-1.57 to 1.07)	-0.05	0.66(-0.56 to 1.87)	0.12	**1.34(0.02 to 2.66)***	0.27	**1.78(0.56 to 3.00)****	0.36
Hostility/Irritability	**-1.53(-2.81 to -0.25)***	-0.35	0.24(-1.42 to 0.93)	0.04	**-1.89(-3.17 to -0.61)****	-0.44	-0.55(-1.72 to 0.63)	-0.10	**-1.43(-2.71 to -0.15)***	-0.36	0.02(-1.16 to 1.19)	0.00
Major Depression[1], *n(%)*	0.59(0.15 to 2.28)	—	2.79(1.00 to 7.77)	—	1.25(0.36 to 4.36)	—	2.45(0.88 to 6.86)	—	2.23(0.68 to 7.34)	—	1.18(0.41 to 3.44)	—
Demoralization[1], *n(%)*	0.67(0.25 to 1.82)	—	1.52(0.63 to 3.70)	—	0.43(0.15 to 1.21)	—	1.24(0.51 to 3.01)	—	1.46(0.55 to 3.84)	—	2.56(1.05 to 6.28)	—
PWB												
Autonomy	**2.69(0.83 to 4.55)****	0.42	-0.05(-1.76 to 1.66)	-0.01	**2.68(0.82 to 4.54)****	0.49	0.19(-1.52 to 1.90)	0.03	-0.10(-1.96 to 1.76)	-0.01	-1.07(-2.78 to 0.64)	-0.18

Environmental mastery	**1.70(0.20 to 3.21)***	0.28	1.27(-0.12 to 2.65)	0.18	**1.99(0.48 to 3.50)***	0.35	0.75(-0.64 to 2.14)	0.11	0.66(-0.85 to 2.17)	0.13	0.09(-1.30 to 1.47)	0.02
Personal growth	0.81(-0.79 to 2.42)	0.14	0.64(-0.84 to 2.11)	0.12	1.44(-0.16 to 3.05)	0.27	0.37(-1.11 to 1.84)	0.07	0.72(-0.88 to 2.33)	0.13	**-1.84(-3.31 to -0.36)***	-0.38
Positive relationship	-0.17(-1.66 to 1.33)	-0.03	1.09(-0.28 to 2.46)	0.18	0.98(-0.51 to 2.47)	0.17	**1.76(0.39 to 3.13)***	0.28	0.33(-1.17 to 1.82)	0.06	1.00(-0.37 to 2.37)	0.17
Purpose of life	1.15(-0.28 to 2.57)	0.22	1.28(-0.04 to 2.59)	0.27	1.40(-0.03 to 2.83)	0.29	0.32(-0.99 to 1.63)	0.08	-0.28(-1.70 to 1.15)	-0.05	-0.59(-1.90 to 0.72)	-0.14
Self-acceptance	1.53(-0.07 to 3.12)	0.23	**1.58(0.12 to 3.05)***	0.23	**2.08(0.48 to 3.67)***	0.34	**2.15(0.69 to 3.62)****	0.33	1.05(-0.54 to 2.65)	0.18	0.70(-0.76 to 2.17)	0.11
PSI												
Global distress	**-2.96(-4.91 to -1.02)****	-0.44	**-2.70(-4.48 to -0.91)****	-0.35	-1.61(-3.55 to 0.33)	-0.25	0.45(-1.34 to 2.24)	0.06	0.50(-1.44 to 2.44)	0.07	-0.47(-3.35 to 2.40)	-0.06
Global well-being	0.36(-0.14 to 0.87)	0.20	-0.34(-0.81 to 0.12)	-0.19	0.20(-0.30 to 0.71)	0.11	-0.15(-0.62 to 0.31)	-0.08	0.29(-0.22 to 0.79)	0.17	-0.39(-0.85 to 0.08)	-0.22
GOSPEL												
Physical activities	**1.52(0.78 to 2.26)*****	0.53	**1.81(1.13 to 2.49)*****	0.74	**1.20(0.46 to 1.94)****	0.43	**1.05(0.37 to 1.73)****	0.45	0.57(-0.16 to 1.31)	0.22	0.45(-0.22 to 1.13)	0.21
Diet	**1.27(0.40 to 2.13)****	0.52	**1.46(0.67 to 2.26)*****	0.52	0.69(-0.17 to 1.56)	0.29	**0.81(0.01 to 1.61)***	0.29	-0.71(-1.58 to 0.15)	-0.29	-0.03(-0.83 to 0.76)	-0.01
Eeating behavior	**1.31(0.79 to 1.83)*****	0.74	**1.04(0.57 to 1.52)*****	0.49	**0.92(0.41 to 1.44)*****	0.52	**1.27(0.79 to 1.75)*****	0.65	**0.99(0.47 to 1.51)*****	0.56	**1.05(0.58 to 1.53)*****	0.55

Note. All the values were adjusted for age, employment status, and baseline; BLI group and T1 were set as the referents; Bold*: *p*-value ≤ .05; Bold**: *p*-value < .01; Bold***: *p*-value < 0.001; BLI: Behavioral lifestyle intervention; WBT: Well-being therapy; CWL: Clinically significant weight loss; SQ= Symptom questionnaire; PWB= Psychological well-being scale; PSI= Psychosocial index; GOSPEL= GOSPEL scale for lifestyle characteristics; T1= baseline, T2= end of the BLI/WBT intervention,, T3=6-month post-intervention follow-up; T4= 12-month post-intervention follow-up. [1] Odds ratios were computed as regression coefficients for each variable; [2] No time effects per group computed as data were analyzed with logistic regression instead of generalized estimating equations due to constant values at baseline.

Figure 1. CONSORT patient flow chart.

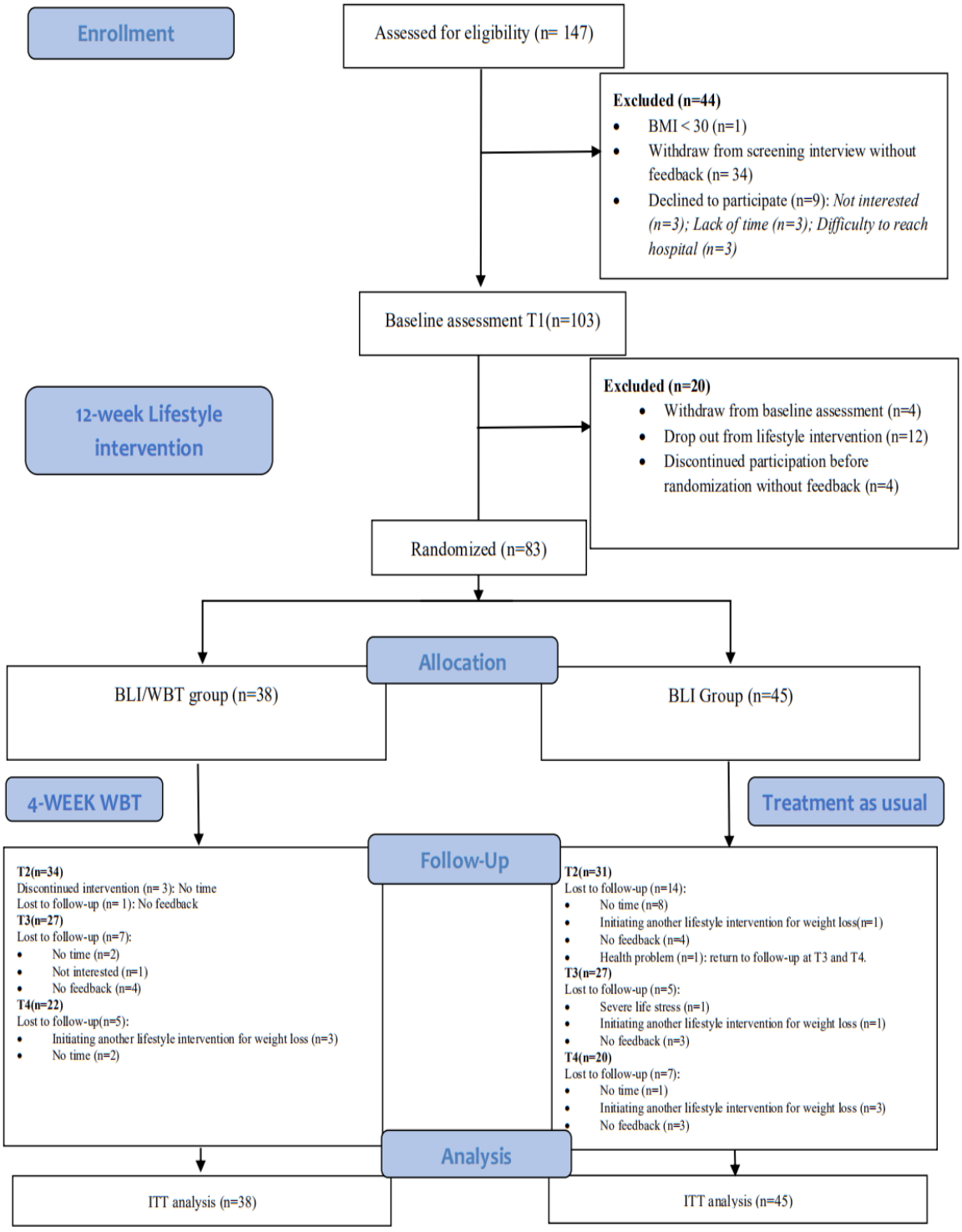
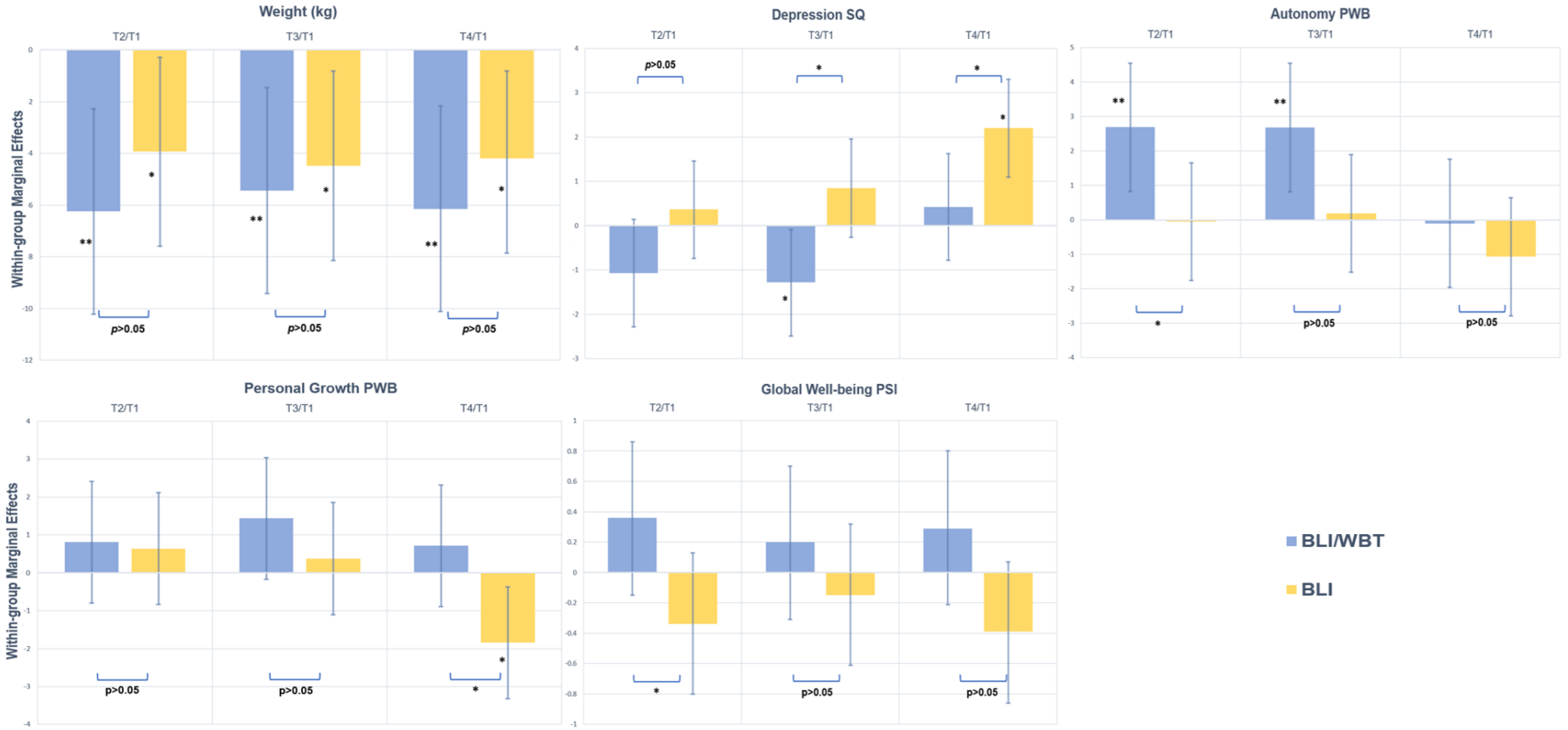


Figure 2. Within-group marginal effects for select primary and secondary outcomes.



Note. All the values were adjusted for age, employment status, and baseline. *: p-value ≤ .05; **: p-value < .01; ***: p-value < 0.001; BLI: Behavioral lifestyle intervention; WBT: Well-being intervention; SQ= Symptom questionnaire; PWB= Psychological well-being scale; PSI= Psychosocial index; T1= baseline, T2= end of the 16-week intervention, T3=6-month post-intervention follow-up; T4= 12-month post-intervention follow-up.