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Lifestyle interventions targeting dietary habits and exercise in bipolar disorder: a systematic review

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Abstract

Background—Bipolar disorder (BD) is a serious mental illness associated with a high risk of medical comorbidities, long-term disability and premature death. This systematic review examined the current literature on therapeutic interventions targeting nutrition and physical activity in BD and collecting health-related measures such as mood and course of illness.

Methods—Scopus (all databases), Pubmed and Ovid Medline were systematically searched with no language or year restrictions, up to June 2015, for studies focusing on lifestyle interventions in BD. Search terms were related to *bipolar disorder*, *nutrition*, *physical activity*, *wellbeing*, *psychosocial interventions* and *course of illness*. We hand searched content pages of Bipolar

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Contributors

Drs Bauer, Galvez, Hamilton and Meyer designed the protocol, conducted the systematic review and co-wrote the manuscript. Drs Balanzá-Martínez, Zunta-Soares and Soares reviewed and proofread the final version of the manuscript. All authors have approved the final article.

Conflict of Interest

Drs Bauer, Galvez, Hamilton, Meyer and Zunta-Soares do not have any relevant conflicts of interest to disclose with respect to this manuscript.

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Disorders and Journal of Affective Disorders and checked references of relevant reviews and dissertations to identify additional papers.

Results—After applying inclusion and exclusion criteria to identified hits, this literature search retrieved six papers. Overall findings point towards a beneficial role of lifestyle interventions on mood, weight, blood pressure, lipid profile, physical activity and overall wellbeing. Methodological limitations include small sample size, gender ratio imbalance, inconsistencies in terms of laboratory measures, and lack of randomized control trials and absence of follow-up and longitudinal studies to determine the benefits of these factors on clinical and functional outcomes over time

Conclusions—Lifestyle interventions in BD targeting nutrition, exercise, wellbeing alongside beliefs, coping strategies and attitudes towards health show promise in reducing the risk of comorbid ailments in BD. There is still a strong need for studies a) developing interventions which are informed by the patient's input and b) examining the effectiveness of such interventions targeting general wellness using well-controlled trials.

Keywords

Bipolar Disorder; Physical activity; Nutrition; wellbeing; psychosocial intervention; lifestyle intervention

Introduction

Bipolar Disorder (BD) is a chronic and recurrent mental illness with a 3% to 5% lifetime prevalence (Cerimele et al., 2014, Merikangas et al., 2007) and is considered one of the leading causes of years of disability adjusted life years (DALYs) as well as years lived with a disability (YLDs) in young adults (Murray and Lopez, 1997). Alongside mood and cognitive deficits (Bora et al., 2009) BD is associated with a high incidence of medical conditions such as overweight/obesity, type 2 diabetes (T2D), cardiovascular disease (CVD), and stroke (Galvez et al., 2014, McIntyre et al., 2005, McIntyre et al., 2004, Prieto et al., 2014, Sharma et al., 2014, Sylvia et al., 2015). Furthermore, these medical conditions might negatively impact the course of the illness. For example, comorbid T2D is associated with an increased risk of recurrent episodes, frequent hospitalizations, suicidality, and poor response to conventional mood stabilizers in BD (Calkin et al., 2009, Gomes et al., 2010, Kim et al., 2009). Obesity appears to be a risk factor for relapse to depression as shown by the high number of obese patients experiencing a depressive recurrence (Fagiolini et al., 2003). In BD suboptimal dietary patterns (Kilbourne et al., 2007, Sylvia et al., 2014, Sylvia et al., 2011) and physical inactivity have been correlated with low self-efficacy and high incidence of medical comorbidities (Vancampfort et al., 2013).

Unhealthy lifestyle habits such as smoking, substance/alcohol misuse, poor dietary choices, and sedentary life (Kemp et al., 2010, Sylvia, Nierenberg, 2011) contribute to the development and severity of the physical ailments and clinical symptoms in BD (Sylvia et al., 2013a). It becomes apparent that these maladaptive behaviors contribute to poor health outcomes and reduce cost-effectiveness of therapeutic interventions in BD (Elmslie et al., 2001, Fagiolini et al., 2008, Hong et al., 2011, Sylvia et al., 2013b).

Current literature suggests that a better understanding of the attitudes and beliefs of BD patients towards food and exercise would assist health professionals in developing better targeted psychosocial interventions that induce lifestyle changes (Ussher et al., 2007, Van Citters et al., 2010). Although research supporting the potential effectiveness of increased physical activity (Daumit et al., 2013) and optimal nutrition control (Davison and Kaplan, 2011, 2012) is growing (Sarris et al., 2015), the question remains as to whether combining interventions aiming to change lifestyle behaviors as part of a multimodal psychosocial treatment in BD is feasible. Thus, we systematically reviewed the existing literature on interventions targeting diet and exercise in patients with BD which collected information on the physical and emotional health of participants as the result of the intervention.

Systematic search

To systematically identify and review studies investigating the notion of interventions in BD targeting dietary habits and physical activity which examined health-related outcomes such as mood and course of illness, we searched Pubmed, Ovid Medline and Scopus (all databases) with no language or year restrictions, up to June 2015, for articles containing the words *bipolar, depression, mania, mood* cross-referenced with *nutrition, food, obesity, diet, hunger, eating* and/or *weight, physical activity, sedentary, exercise, dietary and lifestyle, functioning, trial, intervention, therapy, adjunct, psychosocial, longitudinal, prospective, follow-up, coping, outcome, and course of illness*. Based on existing guidelines for conducting systematic reviews (including The Cochrane Guidelines for Systematic Reviews of Health Promotion and Public Health) (Armstrong R et al., 2007, Booth et al., 2011, Greenhalgh and Peacock, 2005) we additionally hand searched content pages of key journals in psychiatry which usually publish research about treatments for BD (*Bipolar Disorders* and *Journal of Affective Disorders*) to yield articles that would not have been otherwise detected.

Abstracts were used to screen papers, and in cases where this information was not provided in abstracts, full texts were obtained. Review papers and dissertations were excluded but we checked reference lists to identify potential additional literature. We did not include studies that did not focus on an intervention targeting nutrition and exercise. Studies assessing the broader effects of psychotherapy and medication on clinical outcomes in BD were discarded. Inclusion was restricted to studies with a) clinical populations with a diagnosis of BD (regardless of subtypes) and b) diagnoses were based on formal diagnostic criteria such as DSM (e.g. ideally using instruments such as the SCID or WMH-CIDI-10). We only included studies which had specified their samples as being individuals with BD. Studies were excluded if they focused on a) using animal models, b) clinical populations with neurological diseases; c) cardiovascular diseases when this was the primary inclusion criteria to take part in the lifestyle intervention study c) children aged <13 because there are additional factors to be considered in preadolescent samples, or d) pregnant or lactating mothers. During pregnancy and lactation, a number of physiological changes take place and this physiological state and the interventions targeting this specific group are likely to be different. Given our specific interest in nutrition and physical activity, we considered studies associated with circadian rhythms and interventions targeting sleep quality in BD as falling outside the scope of the review. All data were extracted by two single, non-blinded,

reviewers (IB & TDM) to determine if studies met inclusion criteria. All papers identified were published in English. The details of the search strategy are depicted in Figure 1.

Lifestyle intervention programs currently used in bipolar disorder

Characteristics of the included studies

Studies retrieved as part of the current review are presented in Table 1. Sample sizes ranged from one to 116. Participants' ages ranged from 28.87 (SD=7.86) to 60 (SD=6.7) years. Overall, males outweighed females, with the number of women in the studies ranged from two to ten. Only three studies used a randomized control trial (RCT) design, and the duration of the interventions varied from 12 weeks to 24 months. Studies included a variety of outcome measures such as body mass index (BMI), mood, estimates of autonomic functioning (e.g. blood pressure), inflammation (e.g. C-reactive protein), glucose levels, sleep quality, quality of life, exercise, thoughts and beliefs towards food and weight loss.

Findings of the included studies

In this section we will first present the results from the RCTs and proceed by describing less well controlled or treatment development studies.

Gillhoff and colleagues tested the effects of a 5-month multimodal lifestyle intervention on BMI compared with standard care (Gillhoff et al., 2010). This intervention included three modules focusing on nutrition, motivation, and physical activity. Using a randomized controlled design the authors tested 50 participants with BD prior to and following the intervention. Participants were assessed again four months after the end of the intervention (month 11). The primary finding of this study was a significant decrease in BMI in the treatment group compared to the control group. Looking at potential predictors, it emerged that this decrease was only observed in females and not in males. The authors speculated that women might be more driven to lose weight compared to men and therefore may have been more motivated to adhere to the intervention. Furthermore, given that participants were medicated it is possible that some medications may have interfered with the efforts to lose weight. There were no changes in cardiovascular and metabolic measures over time. In sum, this study provided evidence of the feasibility and efficacy of a multimodal lifestyle intervention targeting BMI decrease in a medium-sized sample of individuals with BD over a period of 5 months. This seems to be the first RCT in this field.

Kilbourne and colleagues also conducted a RCT in the field of lifestyle management in BD and reported positive effects of an intervention involving patient self-management on physical health called 'Life Goals Collaborative Care' (LGCC) compared to treatment as usual. This trial collected physiological measures such as blood pressure parameters and non-fasting total cholesterol, and wellness measures such as self-reported physical health-related quality of life in patients with BD at risk for CVD (Kilbourne et al., 2013). LGCC is based on a chronic care model that aims to help individuals set their personal wellness goals by enhancing collaboration among health care providers, patients and community services. The LGCC includes self-management sessions to assist patients with goal setting and management of mental health symptoms. Educational sessions focus on the individual's symptom profile; potential symptom triggers, the link between lifestyle and mental health,

and helps individuals identify appropriate coping responses. These sessions address issues related to co-occurring illnesses affecting quality of life, e.g. CVD, diabetes, anxiety disorders, and substance use disorders, along with positive lifestyle changes in areas such as nutrition, exercise, and sleep to support wellness. In the maintenance sessions, a health specialist discusses with participants their progress toward goals and recurring challenges and provides ongoing motivation for goal attainment. As part of this intervention participants received a workbook to review or reinforce what was learned. In Kilbourne et al.'s study LGCC led to reduced systolic and diastolic blood pressure and decreased severity of manic symptoms, but did not lead to a reduction of primary metabolic parameters of interest such as cholesterol and triglycerides levels, and BMI. Nevertheless, in the LGCC condition the patients' overall health-related quality of life was rated as significantly higher compared to that reported in individuals receiving treatment as usual. The current findings provide first evidence of the feasibility of an intervention targeting comorbid ailments in patients with BD. The self-management component of the LGCC model may be crucial in helping patients to develop symptom coping strategies and reassert a sense of control over the illness. The interpretation of these findings is, however, limited by the lack of positive findings in terms of blood tests and BMI, the open-label nature of the design and the absence of monitoring of treatment adherence. Despite these limitations, the LGCC model is a promising candidate for integrated psychosocial interventions searching to improve general health outcomes in BD.

Frank et al. recently published a RCT in a sample of BD-I patients with a BMI above 25. The authors aimed to compare the efficacy of an integrated risk reduction intervention (IRRI) to a control condition. The control condition included psychiatric care with medical monitoring (PCMM) for a 6-month period. Both IRRI and PCMM involved psychiatric treatment, assessment and symptom monitoring conducted by a psychiatric nurse. In addition the IRRI included lifestyle coaching. Psychiatric treatment was offered throughout the intervention and medication was continuously monitored and adjusted to reduce metabolic side effects. As part of the nursing management the nurse met with patients once a month, and mediated and coordinated the communication between the patient, the psychiatrist, the primary physician, and the lifestyle coach. The lifestyle coach helped patients to develop, implement and maintain behavioral changes pertaining to sleep, food intake, social rhythms, mood, and overall functioning. Further the coach encouraged patients to identify health risk and find strategies to optimize physical and mental health. Overall, participants were heavily involved in the therapy and could choose their primary therapy goals (e.g. weight loss or exercise). A mixed effect model was used to determine the effects of a range of physiological and clinical measures on the BMI following each intervention. After 6 months IRRI was associated with a decrease in BMI. Three physiological measures related to inflammation and neuroendocrinological functioning (C-reactive protein, total cholesterol, instability of total sleep time) led to a faster decrease in BMI (Frank et al., 2014). This study shows that an intervention focusing on developing relevant and individualized therapeutic goals leads to beneficial lifestyle changes positively affecting physiological measures and the BMI. This study also indicates that BD patients can learn strategies to counteract the effects of medication on weight and metabolism in general.

Although not a controlled study, we felt that at this stage of the research it is important to also present data from treatment development studies. Goldstein et al. (Goldstein et al., 2011) presented a case study focusing on the outcome of a brief motivational intervention for a medicated 15-year old boy suffering from BD I disorder and with a BMI of 24. This manualized intervention involved five sessions over a 3 month period. Sessions 1, 3, and 5 were delivered in person at weeks 1, 4–5, and 8–10, while the other sessions were conducted over the (15-minute phone consultations at weeks 2 and 6). Primary outcome measures were the BMI trajectory and behaviors in relation to the intake of sweet beverages and fast food, interactions during family meals, exposure to media, and frequency of physical activity. The relative importance and confidence of the patient in his ability to change his lifestyle behaviors were also recorded. By week 11 the patient showed a decrease in BMI, increased energy and exercise levels, lower levels of depression and improved sleep. This finding suggests that a short motivational intervention has the potential to reduce weight associated with psychotropic medication. Further, in this case the patient's father was involved in the treatment (e.g. patient walked with his dad). This suggests that the support of family members may increase the chances of success of such therapeutic interventions, at least in younger patients. In sum, making patients aware of the relationship between mood, medication, lifestyle and behavior may be necessary for the maintenance of the benefits observed during the intervention.

Another study reported findings from a pilot intervention program adopting a Nutrition/ weight loss, Exercise, and Wellness treatment (NEW Tx) in BD individuals. This treatment comprised three modules. The first module focuses on weight loss and nutritional health. The second module aims at engaging individuals in regular physical activities. The third module targets negative thinking styles associated with lifestyle changes in patients with BD by including cognitive restructuring techniques and problem solving strategies to support long-term adherence to healthy lifestyle choices in terms of nutrition, physical activity, sleep, substance and alcohol use. The NEW Tx was administered in twelve 60-minute group sessions over 14 weeks (Sylvia, Nierenberg, 2011). The authors initially administered the NEW Tx to four participants and then administered a revised version of their program to six more participants. Revisions included the addition of Cognitive Behavioral Therapy (CBT) skills to the wellness module, more cognitive restructuring and goal-setting tasks as a group activity. Overall the authors reported greater gains following the revised Tx intervention. However, retention was lower in the second group. While one could view the small sample size and revising the manual during the course of the intervention as methodological limitations, one has to keep in mind that the goal of the study was to describe the development of the treatment. It is however worth mentioning that the educational level of the participants was rather high and that a high percentage of individuals was employed (67% in Group II). Furthermore, only weight and waist circumference were assessed in this treatment development study. A second study by the same authors used the NEW Tx in five adults with BD. However, this time it was a 20-week, individual CBT-based treatment comprising the three modules described in the previous study (Sylvia, Salcedo, 2013b). The authors reported that the overall attendance rate was high (85%), and that by the end of the program, participants made better food choices (e.g. higher vegetable and lower sugar intake), exercised more and reported lower depressive symptoms. Furthermore, their clinical

profile in terms of blood pressure, cholesterol and glucose levels improved over the duration of the study. Based on the findings of these two trials, the NEW Tx appears to be a successful example of lifestyle intervention for patients with BD. More importantly this intervention was shown to be feasible and the majority of the participants rated it as highly satisfactory. Not surprisingly in this early stage of the research, methodological limitations were the small sample size, the lack of a control group, the assignment to interventions based on self-motivation, and the lack of a follow-up to determine whether acute changes were maintained over time.

Discussion

To date only a small number of published studies have focused on lifestyle interventions in BD. The papers reviewed here provide preliminary evidence that multimodal lifestyle interventions targeting diet, physical activity, self-motivation, and beliefs surrounding wellbeing are feasible and efficacious in individuals with BD. Furthermore, a successful psychosocial management of BD should challenge the individuals' potential negative view towards their health and improve their knowledge about modifiable medical risk factors. Thus, seeking to control or ameliorate medical risk factors and change maladaptive or unhealthy behaviors appear to be core components of an effective lifestyle intervention (Depp et al., 2008).

Several methodological challenges must be taken into account when trying to implement a multi-modal intervention in BD. First, there is a dearth of empirical data about the mechanisms underlying the establishment of maladaptive routines and disruption of dietary habits and physical activity in BD patients and whether they are the same or differ from those in the general population. Second, research has not yet elucidated how to initiate and maintain healthy levels of physical activity among BD patients presenting with maladaptive behavioral patterns. For instance, it has been hypothesized that one reason for the reluctance in initiating physical activity observed in patients with BD may be due to the focus of the health professionals on the health benefits of exercise rather than on the individuals' value of the benefits of physical activity (Vancampfort et al., 2015).

An important research question that arose while reviewing the current literature was related to who should be leading such lifestyle intervention programs. It could be expected that a multidisciplinary team involving psychologists, psychiatrists, nutritionists, and experts in sports medicines, lifestyle coaches, dieticians and fitness trainers would maximize compliance and long-term outcomes of the program. However, feasibility and implementation of such a multidisciplinary treatment have yet to be established. It is also unclear whether group therapy would be more or less beneficial than individual therapy. While a group can provide encouragement, helpful information and non-judgmental support, some individuals may feel intimidated and overwhelmed as they would compare themselves to their peers and feel they are not able to change their lifestyles. A group setting also leaves less room to work on individual goals, especially if these are quite different (e.g. decreasing sedentary behavior versus eating more healthy) Further, it has yet to be established whether patients would prefer and/or benefit from programs which integrate specific BD related modules with changing lifestyles or which solely focus on improving health and global

functioning. Another important debate relates to the advantages and disadvantages of heterogeneous (i.e. mixed groups) and homogeneous groups (i.e. only patients with BD). While the latter promotes social cohesion and increases feelings of safety because participants share the same mental illness, the former makes individuals realize that concerns about health and lifestyle are struggles of all people in all circumstances. This realization may help individuals to focus on their commitment to make changes to their lives.

Future studies should consider using predictive and meditational analyses that would help to learn about variables that moderate lifestyle interventions. For instance Jewell et al. found that adolescents with BD were less likely than their counterparts to exercise on a regular basis (Jewell et al., 2015). However incidental exercise was as prevalent as in healthy individuals. These findings may suggest that individuals with BD may benefit from external planning or strategies to help them implement and maintain optimal exercise levels. Such approach would help personalize interventions and possibly improve long-term clinical outcomes.

Notably, all studies, except those by Kilbourne et and Sylvia et al. (Kilbourne, Goodrich, 2013, Sylvia, Nierenberg, 2011) considered weight or BMI as a primary outcome variable. As highlighted by Belanger et al.'s review (Bélanger et al., 2013) even a modest weight loss can reduce the risk of developing CVD as it can lead to reduced blood sugar level and heart rate fluctuations. However, even weight maintenance, with no weight loss, can be viewed as contributing to individuals' health. Thus, one should consider other factors such as blood pressure, lipid levels, blood glucose levels, and especially quality of life and psychological variables that may affect the individuals' behavior in response to a weight loss program.

Not surprisingly, given the stage of the research in this area, only three of the six studies included in this systematic review used a randomized control design, which is often considered the gold standard for effectiveness research. Future studies should therefore consider including quality assurance checklists to enable effectiveness claims (Nover and Jackson, 2013). However, other designs such as single case experimental designs are an option as well at this stage (Kazdin, 2011) Another limitation of the current studies is the absence of questionnaires that reliably assess dietary habits and physical activity possibly due to the lack of available validated and standardized batteries collecting such measures (Janney et al., 2014). For instance, self-rated measures of physical activity are not fully reliable as patients may either forget to report or report wrong measures of frequency, duration, and/or intensity of physical activity (Soundy et al., 2014). Further, food frequency questionnaires may provide more accurate estimates of intake distributions but may not be designed to collect relevant information such as food perceptions and beliefs and social settings surrounding eating occasions. Thus, different types of assessment methods may be combined to improve accuracy and facilitate interpretation of the individual's lifestyle habits.

In conclusion, considering the patients' expertise in relation to helpful and unhelpful strategies, there is a strong need for studies a) developing interventions which are informed by the patient's needs and shaped by their priorities; and b) examining the effectiveness of

such interventions targeting general wellness (e.g. dietary lifestyle, physical activity, and setting of realistic goals). Health-related psychosocial interventions in BD should move beyond treatment adherence and adopt a multi-modal harm reduction strategy. Such a shift would help both patients and health professionals to jointly modify and decrease the occurrence of unhealthy behaviors. In this sense, a specific multi-modal intervention promoting a healthy lifestyle and focusing on behavioral changes in terms of physical activity and dietary habits may result in improved long-term management of BD. Challenging maladaptive patterns of behavior is a complex process that requires multiple steps including both effective techniques to induce healthy lifestyle changes, boost the patients' readiness for change and awareness of the risks associated with current behaviors and lifestyle. Such approach is likely to increase the likelihood that individuals with BD adopt and maintain healthy behaviors, thus reducing the risk of long-term medical consequences and ultimately improving quality of life and functional outcomes.

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References

- Armstrong, RWE.; Jackson, N.; Oliver, S.; Popay, J.; Shepherd, J.; Petticrew, M.; Anderson, L.; Bailie, RBG.; Hawe, P.; Kristjansson, E.; Naccarella, L.; Norris, S.; Pienaar, E.; Roberts, H.; Rogers, WSA.; Thomas, Hf. Guidelines Report prepared for the Health Promotion and Public Health Taskforce of Cochrane Health Promotion and Public Health Field. Melbourne University; Australia: 2007. Systematic reviews of health promotion and public health interventions.
- Bélangier M-È, Provencher MD, Shriqui C. Efficacité des programmes de modifications des habitudes de vie pour la gestion de poids des personnes avec des troubles psychiatriques. *Santé mentale au Québec*. 2013; 38:103–18. [PubMed: 24336992]
- Booth, A.; Papaioannou, D.; Sutton, A. Systematic approaches to a successful literature review. Sage; 2011.
- Bora E, Yucel M, Pantelis C. Cognitive endophenotypes of bipolar disorder: a meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. *Journal of affective disorders*. 2009; 113:1–20. [PubMed: 18684514]
- Calkin C, Van De Velde C, R ži ková M, Slaney C, Garnham J, Hajek T, et al. Can body mass index help predict outcome in patients with bipolar disorder? *Bipolar disorders*. 2009; 11:650–6. [PubMed: 19689507]
- Cerimele JM, Chwastiak LA, Dodson S, Katon WJ. The prevalence of bipolar disorder in general primary care samples: a systematic review. *General hospital psychiatry*. 2014; 36:19–25. [PubMed: 24144521]
- Daumit GL, Dickerson FB, Wang N-Y, Dalcin A, Jerome GJ, Anderson CA, et al. A behavioral weight-loss intervention in persons with serious mental illness. *New England Journal of Medicine*. 2013; 368:1594–602. [PubMed: 23517118]
- Davison KM, Kaplan BJ. Vitamin and mineral intakes in adults with mood disorders: comparisons to nutrition standards and associations with sociodemographic and clinical variables. *Journal of the American College of Nutrition*. 2011; 30:547–58. [PubMed: 22331690]
- Davison KM, Kaplan BJ. Food intake and blood cholesterol levels of community-based adults with mood disorders. *BMC psychiatry*. 2012; 12:10. [PubMed: 22333556]

- Depp CA, Moore DJ, Patterson TL, Lebowitz BD, Jeste DV. Psychosocial interventions and medication adherence in bipolar disorder. *Dialogues in clinical neuroscience*. 2008; 10:239. [PubMed: 18689293]
- Elmslie JL, Mann JI, Silverstone JT, Williams SM, Romans SE. Determinants of overweight and obesity in patients with bipolar disorder. *The Journal of clinical psychiatry*. 2001; 62:486–91. quiz 92–3. [PubMed: 11465534]
- Fagiolini A, Chengappa KR, Soreca I, Chang J. Bipolar Disorder and the Metabolic Syndrome. *CNS drugs*. 2008; 22:655–69. [PubMed: 18601304]
- Fagiolini A, Kupfer DJ, Houck PR, Novick DM, Frank E. Obesity as a correlate of outcome in patients with bipolar I disorder. *American Journal of Psychiatry*. 2003; 160:112–7. [PubMed: 12505809]
- Frank E, Wallace ML, Hall M, Hasler B, Levenson JC, Janney CA, et al. An Integrated Risk Reduction Intervention can reduce body mass index in individuals being treated for bipolar I disorder: results from a randomized trial. *Bipolar disorders*. 2014
- Galvez JF, Bauer IE, Sanches M, Wu HE, Hamilton JE, Mwangi B, et al. Shared clinical associations between obesity and impulsivity in rapid cycling bipolar disorder: a systematic review. *Journal of affective disorders*. 2014; 168:306–13. [PubMed: 25086289]
- Gillhoff K, Gaab J, Emini L, Maroni C, Tholuck J, Greil W. Effects of a multimodal lifestyle intervention on body mass index in patients with bipolar disorder: a randomized controlled trial. *Primary care companion to the Journal of clinical psychiatry*. 2010; 12
- Goldstein TR, Goldstein BI, Mantz MB, Bailey B, Douaihy A. A brief motivational intervention for preventing medication-associated weight gain among youth with bipolar disorder: treatment development and case report. *Journal of child and adolescent psychopharmacology*. 2011; 21:275–80. [PubMed: 21663430]
- Gomes F, Telo DF, Souza HP, Nicolau JC, Halpern A, Serrano CV Jr. Obesity and coronary artery disease: role of vascular inflammation. *Arquivos brasileiros de cardiologia*. 2010; 94:273–9. [PubMed: 20730253]
- Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. *Bmj*. 2005; 331:1064–5. [PubMed: 16230312]
- Hong J, Reed C, Novick D, Haro JM, Aguado J. Clinical and economic consequences of medication nonadherence in the treatment of patients with a manic/mixed episode of bipolar disorder: Results from the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) Study. *Psychiatry research*. 2011; 190:110–4. [PubMed: 21571375]
- Janney CA, Fagiolini A, Swartz HA, Jakicic JM, Holleman RG, Richardson CR. Are adults with bipolar disorder active? Objectively measured physical activity and sedentary behavior using accelerometry. *Journal of affective disorders*. 2014; 152:498–504. [PubMed: 24095103]
- Jewell L, Abtan R, Scavone A, Timmins V, Swampillai B, Goldstein BI. Preliminary evidence of disparities in physical activity among adolescents with bipolar disorder. *Mental Health and Physical Activity*. 2015; 8:62–7.
- Kazdin, AE. *Single-case research designs: Methods for clinical and applied settings*. Oxford University Press; 2011.
- Kemp DE, Gao K, Chan PK, Ganocy SJ, Findling RL, Calabrese JR. Medical comorbidity in bipolar disorder: relationship between illnesses of the endocrine/metabolic system and treatment outcome. *Bipolar disorders*. 2010; 12:404–13. [PubMed: 20636638]
- Kilbourne AM, Goodrich DE, Lai Z, Post EP, Schumacher K, Nord KM, et al. Randomized Controlled Trial to Reduce Cardiovascular Disease Risk for Patients with Bipolar Disorder: the Self-Management Addressing Heart Risk Trial (SMAHRT). *The Journal of clinical psychiatry*. 2013; 74:e655. [PubMed: 23945460]
- Kilbourne AM, Rofey DL, McCarthy JF, Post EP, Welsh D, Blow FC. Nutrition and exercise behavior among patients with bipolar disorder. *Bipolar Disorders*. 2007; 9:443–52. [PubMed: 17680914]
- Kim B, Kim S, McIntyre RS, Park HJ, Kim SY, Joo YH. Correlates of metabolic abnormalities in bipolar I disorder at initiation of acute phase treatment. *Psychiatry investigation*. 2009; 6:78–84. [PubMed: 20046379]

- McIntyre RS, Konarski JZ, Misener VL, Kennedy SH. Bipolar disorder and diabetes mellitus: epidemiology, etiology, and treatment implications. *Annals of Clinical Psychiatry*. 2005; 17:83–93. [PubMed: 16075661]
- McIntyre RS, Konarski JZ, Yatham LN. Comorbidity in bipolar disorder: a framework for rational treatment selection. *Human Psychopharmacology: Clinical and Experimental*. 2004; 19:369–86. [PubMed: 15303241]
- Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Archives of general psychiatry*. 2007; 64:543–52. [PubMed: 17485606]
- Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. 2009; 6:e1000097. [PubMed: 19621072]
- Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *The Lancet*. 1997; 349:1498–504.
- Nover C, Jackson SS. Primary care-based educational interventions to decrease risk factors for metabolic syndrome for adults with major psychotic and/or affective disorders: a systematic review. *Systematic reviews*. 2013; 2:116. [PubMed: 24369749]
- Prieto M, Cuéllar-Barboza A, Bobo W, Roger V, Bellivier F, Leboyer M, et al. Risk of myocardial infarction and stroke in bipolar disorder: a systematic review and exploratory meta-analysis. *Acta Psychiatrica Scandinavica*. 2014; 130:342–53. [PubMed: 24850482]
- Sarris J, Logan AC, Akbaraly TN, Amminger GP, Balanzá-Martínez V, Freeman MP, et al. Nutritional medicine as mainstream in psychiatry. *The Lancet Psychiatry*. 2015; 2:271–4. [PubMed: 26359904]
- Sharma AN, Bauer IE, Sanches M, Galvez JF, Zunta-Soares GB, Quevedo J, et al. Common biological mechanisms between bipolar disorder and type 2 diabetes: focus on inflammation. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2014; 54:289–98. [PubMed: 24969830]
- Soundy A, Roskell C, Stubbs B, Vancampfort D. Selection, use and psychometric properties of physical activity measures to assess individuals with severe mental illness: a narrative synthesis. *Archives of psychiatric nursing*. 2014; 28:135–51. [PubMed: 24673789]
- Sylvia, LG.; Iosifescu, D.; Friedman, ES.; Bernstein, EE.; Bowden, CL.; Ketter, TA., et al. Use of treatment services in a comparative effectiveness study of bipolar disorder. 2014.
- Sylvia LG, Nierenberg AA, Stange JP, Peckham AD, Deckersbach T. Development of an integrated psychosocial treatment to address the medical burden associated with bipolar disorder. *Journal of psychiatric practice*. 2011; 17:224. [PubMed: 21587004]
- Sylvia LG, Peters AT, Deckersbach T, Nierenberg AA. Nutrient-based therapies for bipolar disorder: a systematic review. *Psychother Psychosom*. 2013a; 82:10–9. [PubMed: 23147067]
- Sylvia LG, Salcedo S, Bernstein EE, Baek JH, Nierenberg AA, Deckersbach T. Nutrition, Exercise, and Wellness Treatment in bipolar disorder: proof of concept for a consolidated intervention. *International journal of bipolar disorders*. 2013b; 1:1–7. [PubMed: 25505668]
- Sylvia LG, Shelton RC, Kemp DE, Bernstein EE, Friedman ES, Brody BD, et al. Medical burden in bipolar disorder: findings from the Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder study (Bipolar CHOICE). *Bipolar disorders*. 2015; 17:212–23. [PubMed: 25130321]
- Ussher M, Stanbury L, Cheeseman V, Faulkner G. Physical activity preferences and perceived barriers to activity among persons with severe mental illness in the United Kingdom. *Psychiatric services*. 2007; 58:405–8. [PubMed: 17325117]
- Van Citters AD, Pratt SI, Jue K, Williams G, Miller PT, Xie H, et al. A pilot evaluation of the In SHAPE individualized health promotion intervention for adults with mental illness. *Community mental health journal*. 2010; 46:540–52. [PubMed: 20012197]
- Vancampfort D, Correll CU, Probst M, Sienaert P, Wyckaert S, De Herdt A, et al. A review of physical activity correlates in patients with bipolar disorder. *Journal of affective disorders*. 2013; 145:285–91. [PubMed: 22889526]

Vancampfort D, Madou T, Moens H, De Backer T, Vanhalst P, Helon C, et al. Could autonomous motivation hold the key to successfully implementing lifestyle changes in affective disorders? A multicentre cross sectional study. *Psychiatry research*. 2015

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Highlights

- BD is associated with medical comorbidities and long-term disability
- Lifestyle interventions are feasible and efficacious in individuals with BD
- Lifestyle interventions may improve long-term management of BD
- Psychosocial interventions should adopt a multi-modal harm reduction strategy
- Lifestyle interventions should be informed by the patient's needs and priorities

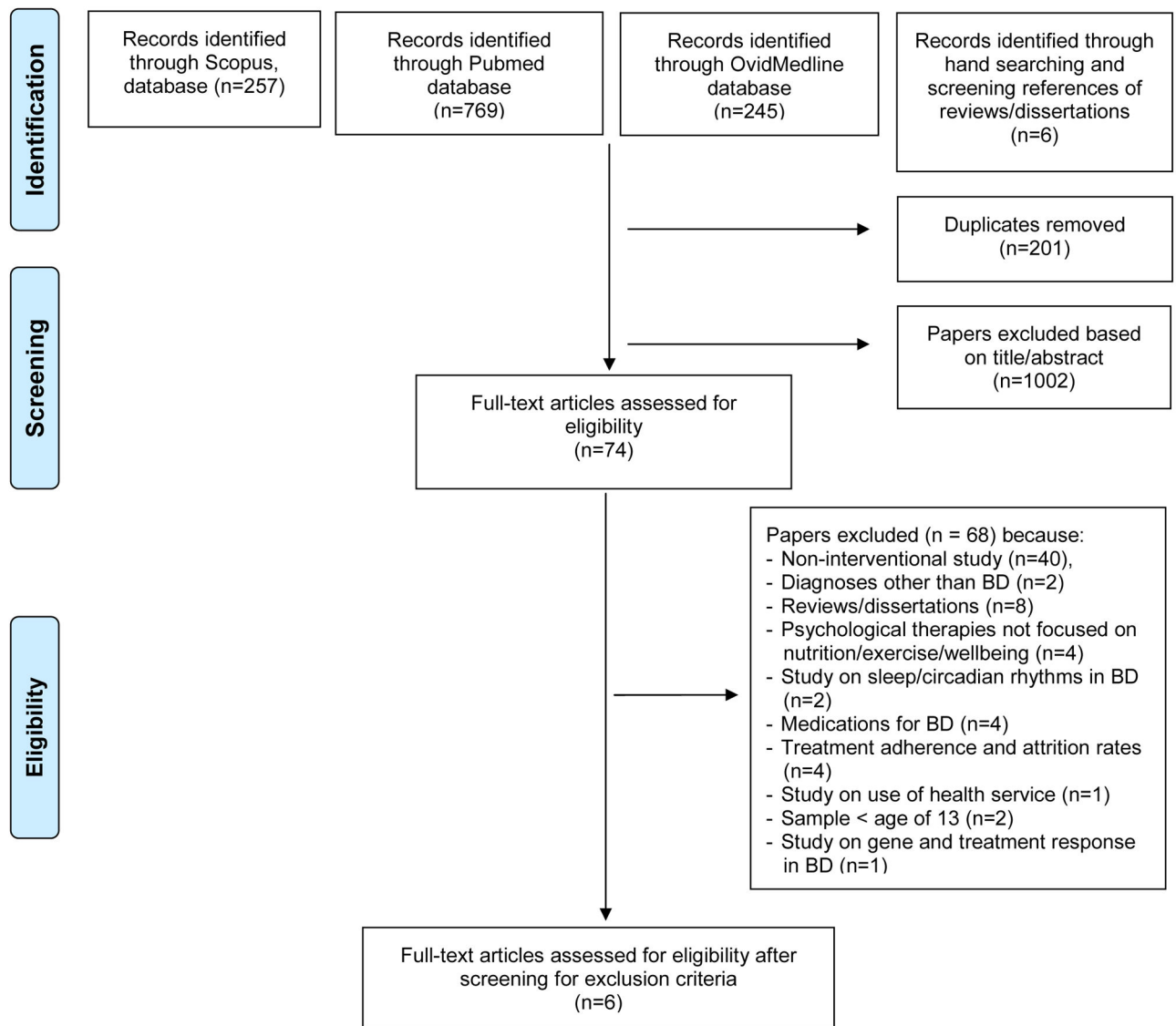


Figure 1. Filtering process used to select the studies investigating lifestyle interventions (including those targeting nutrition and exercise) in bipolar disorder
 PRISMA flowchart (Moher, 2009) showing the filtering process used to select studies investigating the effects of dietary habits, exercise and wellbeing interventions in BD.

Table 1

Description of basic features of the identified studies looking interventions focusing on changing lifestyle habits in individuals with bipolar disorder

Citation	n	Age	Gender (n females)	BMI/weight (kg)	Design	Duration	Intervention type	Outcome measures	Findings
Frank et al. 2015 (<i>Bipolar Disorder</i>)	n=56: Psychiatric care with medical monitoring - PCMMO; n=58: Risk Reduction Intervention - IRR)	41.4 (±9.7) 41.8 (±9.5)	-----	>25	RCT	6 months	PCMM: psychiatric treatment, assessment, and referral by a psychiatric nurse IRR: psychiatric treatment, assessment, medical monitoring, and lifestyle coaching	<ul style="list-style-type: none"> BMI C-reactive protein (CRP) Cholesterol Sleep Alcohol Anxiety Exercise 	<ul style="list-style-type: none"> BMI reduction CRP, sleep, and cholesterol modulate rate of BMI decrease
Gillhoff et al. 2015 (<i>Prim Care Companion J Clin Psychiatry</i>)	n=26: Intervention Group n=24; Control Group	48.1 (±11.5) 48.9 (±12)	13 10	28.4 (±4.5) 28.4 (±3.5)	RCT	5 months Plus follow-up at 4 months	Lifestyle Intervention targeting Lifestyle, Nutrition and Physical Activity	<ul style="list-style-type: none"> BMI Body weight Blood markers (e.g. lipids, cholesterol, glucose levels) Waist conference 	<ul style="list-style-type: none"> Significant and lasting decrease in BMI (observable in women, not men) No effect on cardiovascular and metabolic parameters
Goldstein et al. 2011 (<i>J Child Adolesc Psychopharmacol</i>)	n=1	15 y	0	24	Case study	3 months	Brief Motivational intervention (MI): 4 session MI (3×45-minute sessions in person and 2×15-minute phone conversations)	<ul style="list-style-type: none"> BMI Behaviors with intake of sweet beverages, fast food meals, media time per day, physical activity, dinners with parents Mood Energy levels Motivation 	<ul style="list-style-type: none"> Decrease in BMI sustained mood improvement in mood and sleep, and increased physical activity
Kilbourne et al. 2013 (<i>J Clin Psychiatry</i>)	n=57: Life Goals Collaborative Care (LGCC); n=59: Enhanced Usual Care)	53.1 (±10.6) 52.4 (±9.2)	10 10	>30	RCT	24 months	LGCC: 4 weekly self-management sessions followed by client tailored strategies to improve interaction with health provider	<ul style="list-style-type: none"> Blood pressure Cholesterol levels QoL (12-item Short Form Health Survey) 	<ul style="list-style-type: none"> LGCC reduced systolic and diastolic blood pressure and reduced manic

Citation	n	Age	Gender (n females)	BMI/weight (kg)	Design	Duration	Intervention type	Outcome measures	Findings
Sylvia et al. 2011 (<i>J Psychia Res</i>)	n=4: Group I, n=6: Group II – after revising intervention)	60 (± 6.7) 50.2 (±10.2)	3 2	86.7kg	TDS	14 weeks	New Nutrition/ weight loss, Exercise, and Wellness treatment (NEW Tx) administered in twelve 60- minute group session over 14 weeks	<ul style="list-style-type: none"> • PAR-Q • MINI Plus • CGI-BP • PWBS • LIFE-RIFT • QoL • Exercise Questionnai re 	symptoms compared with usual care ER et al Participants of Group II showed <ul style="list-style-type: none"> • improved quality of life, • less depressive symptoms • weight loss
Sylvia et al. 2013 (<i>Int J Bipolar Disord</i>)	n=5	44 (±16)	3	-----	Phlot	20 week	18-session, 20-week individual Cognitive Behavioral Therapy [3 modules: nutrition, physical activity, wellness (new TX)]	<ul style="list-style-type: none"> • Weight • Lipid, cholesterol, glucose, exercise levels • Mood symptoms and illness severity (MADRS, YM RS, CGI-BP) • LIFE-RIFT 	<ul style="list-style-type: none"> • Decrease in weight, cholesterol, triglycerides, daily calorie and sugar intake • Higher vegetable intake • Weekly exercise duration tripled • Depressive and functioning improved

Notes: Beck Depression Inventory (BDI-II); Body Mass Index (BMI); Clinical Global Impressions Scale-Bipolar Version (CGI-BP), The Range of Impaired Functioning Tool (LIFE-RIFT), Mini International Neuropsychiatric Interview (MINI Plus), Montgomery Asberg Depression Rating Scale (MADRS), Physical Activity Readiness Questionnaire (PAR-Q), Psychological Well-Being (PWBS), Quality of Life (QoL), Randomized Controlled Trial (RCT); Range of Impaired Functioning Tool (LIFE-RIFT), Treatment Development Study (TDS); Young Mania Rating Scale (YMRS)