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Review article

Non-pharmacological interventions for preventing weight gain in patients with first episode schizophrenia or bipolar disorder: A systematic review.

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ABSTRACT

Weight gain is a side effect of antipsychotic medication and highly prevalent in people with schizophrenia or bipolar disorder, increasing their overall cardio-metabolic risk. We conducted a systematic review on non-pharmacological interventions for preventing/reducing weight gain or increase in waist-circumference in young, newly diagnosed patients with schizophrenia or bipolar disorder. We searched major electronic databases from inception to 04/2019 on RCTs, pre- and post-test studies, and non-randomized controlled clinical trials. From a potential of 2963 hits, eight studies met the inclusion criteria (n = 438, mean age of 18.8 (13–45) years). The interventions comprised supervised and individually adjusted aerobic exercise activities (5 studies), individual lifestyle counselling vs. control condition (2 RCTs), and dietetic counselling and practical training of cooking and shopping (1 study). Physical activity and practical dietetic interventions seem to be more efficient than lifestyle counselling. However, the results shall be taken with caution due to the non-randomized designs and other methodologically deficits in the majority of the included studies.

1. Introduction

Patients with schizophrenia or bipolar disorder have a 15–20 years shorter life-expectancy compared with the general population (Laursen, 2011; Laursen et al., 2014; Nordentoft et al., 2013). Although there is a high risk of suicide among patients with bipolar disorder and schizophrenia (Miller and Bauer, 2014; Palmer et al., 2005) mounting evidence suggests that the increased mortality is primarily due to death from natural causes, in particular cardiovascular disease (CVD) (Ringen et al., 2014; Walker et al., 2015; Hayes et al., 2015; Correll et al., 2017). The metabolic syndrome (MetS), defined as abdominal obesity, raised triglycerides, reduced high density lipoprotein (HDL) cholesterol, elevated blood pressure or raised plasma glucose, significantly increases the risk of CVD as well as type-2-diabetes (T2D) (Alberti et al., 2006; Mottillo et al., 2010). Both MetS and cardio-metabolic abnormalities are highly prevalent in patients with schizophrenia or bipolar disorder compared to the general population (Vancampfort et al., 2015c; Vancampfort et al., 2013a; Vancampfort et al., 2013b; Vancampfort et al., 2015b; Mitchell et al., 2011). According to The International Diabetes Federation abdominal obesity is the most significant, single risk factor for development of MetS and T2D, therefore preventing weight gain, in particular abdominal obesity, is essential for decreasing the overall cardio-metabolic risk and premature mortality (Alberti et al., 2007). Mounting evidence confirms that weight gain is one of the most significant side-effects of antipsychotic medication (AP) (Allison and Casey, 2001; De Hert et al., 2012; Foley and Morley, 2011) and weight gain occurs after short-time exposure to AP (Perez-Iglesias et al., 2014; Maayan and Correll, 2011; Alvarez-Jimenez et al., 2008a). Further, preventing weight gain seems to be essential for patients as weight gain decreases adherence with treatment as well as the overall quality of life (Dayabandara et al., 2017). Thus, as presented by a recent Lancet Psychiatric Commision interventions targeting the first episode period are of critical importance for preventing further downstream adverse events (Firth et al., 2019).

To date, pharmacological interventions, comprising use of metformin or other statins, or switching to agents with lesser tendency to cause weight gain, as well as non-pharmacological interventions have been investigated to reduce weight gain (Alvarez-Jimenez et al., 2008b; Dayabandara et al., 2017; de Silva et al., 2016; Caemmerer et al.,

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2012). Non-pharmacological interventions have proven to be effective in reducing weight in obese patients with severe mental illness (Caemmerer et al., 2012; Naslund et al., 2017), yet in the recent CHANGE-study this was not confirmed (Speyer et al., 2016; Jakobsen et al., 2017). Preventing obesity is far more efficient than treating the long-term consequences and it can be strongly argued to prescribe life style interventions to patients with schizophrenia or bipolar disorder regardless of metabolic health (Firth et al., 2019). However, very few studies have reported on interventions in relation to young first-episode patients with schizophrenia (FEP) or bipolar disorder (BD) and to the best of our knowledge, no prior systematic review on this topic exists.

Thus, the objectives of this review was to identify and evaluate the effectiveness of non-pharmacological lifestyle interventions for preventing and reducing weight gain in young, first-episode patients with schizophrenia or bipolar disorder.

2. Methods

This systematic review followed the PRISMA reporting guidelines. A protocol for the review was registered at PROSPERO International prospective register of systematic reviews in December 2018: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=117600

2.1. Search procedure

A health research librarian identified studies by performing a systematic literature search in PubMed, EMBASE, Scopus, PsycInfo and Cochrane bibliographic databases from their inception to February 2019. An updated search was performed in March 2019. In addition, the reference lists of included articles were reviewed and so were the citations received by them.

In collaboration the team and the research librarian developed an appropriate search strategy combining medical subject headings (MESH), EMTREE headings and thesaurus term with natural language terms, using the following key-words: (“first episode” OR FEP OR “newly diagnosed” OR naîve OR “early onset” OR “early intervention” OR “early psychosis” OR “adolescent*” OR “young adult*) AND (”schizoaffective OR schizophr* OR psychosis OR psychotic OR “affective disorder” OR bipolar OR “severe mental illness” OR ”serious mental illness” OR mania OR “manic disorder” OR “cyclothymic disorder”) in combination with (“weight gain” OR overweight OR “body weight” OR “weight change*” OR obesity OR “body mass index” OR BMI OR “waist circumference”) AND (diet OR nutrition OR “physical activity” OR exercise* OR “physical training” OR psychoeducation OR "psycho education" OR coaching OR mentoring OR lifestyle OR “life style” OR prevention OR “health promotion” OR counseling OR “health education” OR “physical health” OR “behavioural intervention” OR “behavioral intervention” OR “behavior therapy” OR “behavior therapy” OR “patient compliance” OR “weight reduction program” OR “weight loss program”). The search was restricted to English and Nordic languages and duplicates were removed using EndNote.

2.2. Inclusion criteria

In accordance with the PRISMA reporting guidelines the participants, interventions, comparisons, outcomes, and study design criteria were used to assess study eligibility:

Participants: Young patients with first-episode ICD-10 or DSM-IV diagnosed schizophrenia or bipolar disorder aged between 15–25 years; including studies in which the mean age of participants was <25 years.

Interventions: Any non-pharmacological interventions aiming at preventing or reducing weight gain or increase in waist-circumference, including exercise or physical activity, nutritional interventions, behavioural counselling, motivational interviewing or Cognitive Behavioural Therapy (CBT).

Comparators: All usual-care or wait list conditions were considered eligible.

Outcomes: The outcome measures had to be changes in kilograms, body mass index (BMI), or centimetres in waist circumference (WC), respectively.

Study design: Included study designs were randomized controlled trials (RCT), pre- and post-test studies without a control group, and non-randomized controlled clinical trials in which the experimental and the control intervention were of similar duration.

2.3. Study selection and data extraction

The selection of studies was conducted in two stages. In the first stage *Title* and *Abstract* of each reference was screened by two independent reviewers (LN, SL) against the criteria mentioned above. In stage two the full text of the included articles was screened for eligibility by the two reviewers, independently; disagreements were solved through discussions or by consulting a third author (BS).

Two reviewers (LN, SL) independently extracted relevant data from the included studies, including study design, characteristics of participants, intervention approach, the nature of the intervention, counselling, diet, nutritional counselling or other, intervention format, duration of intervention, description of comparison intervention. Any conflicts of extraction were resolved through discussion or by consulting a third reviewer (BS).

2.4. Risk of bias assessment

The quality of the included studies was evaluated using the ROBINS-I risk of bias assessment tool for non-randomized studies of interventions (Schunemann et al., 2018; Sterne et al., 2016) and for RCTs the RoB −2 (Higgins et al., 2016). The quality assessment of studies included confounding and selection of participants for the study, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported results. Two authors (LN, SL) independently assessed the risk of bias in the included studies; any disagreements were resolved through discussion or consulting of a third author (BS).

3. Results

3.1. Search results and flow of studies through the review

A total of 2960 records were identified in the databases; three additional studies were identified through reference and citation searching. After the first review of title and abstract, 67 full-text articles were screened of which eight studies were identified and included in the review (Abdel-Baki et al., 2013; Curtis et al., 2016; Curtis et al., 2018; Detke et al., 2016; Firth et al., 2018; Lovell et al., 2014; Nuechterlein et al., 2016; Teasdale et al., 2015). Fig 1 presents the flow of studies through the review.

3.2. Characteristics of included trials

Across the eight included studies, three included patients with FEP and five included a mixture of patients with FEP and BD with a mean age of 18.8 (13–45) years and 36.0% females. The length of follow-up differed from 10 weeks to two years. Non-pharmacological interventions were provided for 286 out of 438 patients with FEP; descriptions of articles are presented in Table 1.

Four (Curtis et al., 2016; Detke et al., 2016; Lovell et al., 2014; Nuechterlein et al., 2016) of the included studies were controlled studies of which two were RCTs (Detke et al., 2016; Lovell et al., 2014) whereas the remaining four were prospective pre and post test studies (Abdel-Baki et al., 2013; Curtis et al., 2018; Firth et al., 2018; Teasdale et al., 2015). The mean number of participants was 154 (range