TECHNICAL COMMENTARY

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Therapies for weight gain

Introduction

Being overweight is common in people with a serious mental illness, the cause of which may be attributable to lifestyle factors such as poor diet and physical inactivity and also due to medication side effects. Weight gain is a well-documented side effect of many antipsychotic medications, particularly the newer second-generation medications. This could in part be a result of the wide mode of action of antipsychotic drugs, including disruption of metabolic pathways.

Excessive weight gain is a serious health concern, it is associated not only with reduced quality of life and social stigma but can affect treatment adherence and increase morbidity (both physical and psychological) and mortality. Obesity is reported to double the risk of all-cause mortality, as well as related diseases such as coronary heart disease, stroke, and type-2 diabetes.

Pharmacological strategies are at best only moderately effective for weight management, thus the ideal non-pharmacological strategies for weight management should combine diet, exercise and psychological/behavioural components. Weight management is important to ensure that the benefits of medications are not outweighed by the increased risk of physical disease.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with bipolar or related disorders. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. When multiple copies of review topics were found, the most recent and/or comprehensive review was included. Reviews with pooled data are given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group[2] approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention, or other matter under review, are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise, and direct with low associated risks (see end of table for an explanation of these terms).

The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

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Results

We found two systematic reviews that met our inclusion criteria[3, 4].

- Moderate to high quality evidence suggests lifestyle interventions are effective for weight reduction in people with severe mental illness.
- Moderate to low quality evidence suggests lifestyle interventions reduce body mass index and may also improve depressive mood.

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Bauer IE, Galvez JF, Hamilton JE, Balanza-Martinez V, Zunta-Soares GB, Soares JC, Meyer TD

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

Journal of Psychiatric Research 2016; 74: 1-7

View review abstract online

Comparison	**Lifestyle interventions targeting nutrition, physical activity and wellness in people with bipolar disorder (3-24 months).**
Summary of evidence	**Moderate to low quality evidence (small samples, appears consistent, indirect, unable to assess precision) suggests lifestyle interventions reduce body mass index and may also improve depressive mood.**

All outcomes

1 RCT (N = 114) assessed lifestyle coaching vs. a risk reduction intervention and found lifestyle coaching reduced BMI and that C-reactive protein levels, total cholesterol levels, and instability of total sleep time all modulated the rate of BMI decrease (direction of modulation is not reported).

1 RCT (N = 50) assessed a lifestyle intervention targeting nutrition and physical activity vs. a control group and found the lifestyle intervention reduced BMI in women but not men, with no effects on cardiovascular or metabolic parameters.

1 RCT (N = 116) assessed four weekly self management sessions followed by client tailored strategies to improve interaction with a health provider vs. enhanced usual care and found reduced systolic and diastolic blood pressure and reduced manic symptoms.

1 Treatment Development Study (N = 10) assessed a nutrition, weight loss, exercise, and wellness treatment in 12, 60-minute group sessions over 14 weeks (no controls) and found improved quality of life, less depressive symptoms, and weight loss.

1 pilot study (N = 5) assessed an 18 session, 20-week individual Cognitive Behavioural Therapy aimed at nutrition, physical activity and wellness and found decreases in weight, cholesterol, tryglicerides, daily calorie and sugar intake, higher vegetable intake, weekly exercise duration tripled, and depressive symptoms and functioning improved.

1 case study (N = 1) assessed a brief motivational intervention over three 45-minute sessions in person and two 15-minute phone conversations, and found decreased BMI, sustained mood improvement, and increased sleep and physical activity.

Consistency in results‡	Appears consistent.
Precision in results§	Unable to assess (no data reported).
Directness of results‖	Indirect; mixed interventions.

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Naslund JA, Whiteman KL, McHugo GJ, Aschbrenner KA, Marsch LA, Bartels SJ

Lifestyle interventions for weight loss among overweight and obese adults with serious mental illness: A systematic review and meta-analysis

General Hospital Psychiatry 2017; 47: 83-102

View review abstract online

Comparison	**Lifestyle interventions targeting weight reduction in people with severe mental illness (22% with bipolar disorder) vs. treatment as usual or other interventions.** **Lifestyle interventions include behavioural interventions and interventions targeting self-monitoring, dietary changes, nutrition education, fitness, exercise, or physical activity.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistency, precise, indirect) suggests lifestyle interventions are effective for weight reduction in people with severe mental illness.**
Weight reduction	
Lifestyle interventions showed significant, small effects of greater weight reduction than controls; ≤6months: 10 RCTs, N = 778, SMD = -0.20, 95%CI -0.34 to -0.05, $p < 0.05$, $I^2 = 90\%$ ≥12months: 6 RCTs, N = 1,075, SMD = -0.24, 95%CI -0.36 to -0.12, $I^2 = 0\%$	
Consistency in results	Inconsistent for short-term assessment, consistent for longer term.
Precision in results	Precise
Directness of results	Indirect; mixed intervention and control conditions.

Explanation of acronyms

BMI = body mass index, CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), RCT = randomised controlled trial, SMD = standardised mean difference, vs. = versus

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[5].

† Different effect measures are reported by different reviews.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large effect[5].

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[6]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time

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period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may be considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[5];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[7].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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