Introduction

Obesity is common in schizophrenia, particularly in younger patients\(^1\), the cause of which may be attributable to many factors such as a genetic predisposition, lifestyle factors including diet and physical inactivity, and medication side effects\(^2\). 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\(^3\).

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\(^1, 2, 4\). 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\(^2\).

Weight management is affected in turn by lifestyle factors, as people with schizophrenia tend to be less physically active. 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\(^2\). Weight management is important to ensure that the benefits of antipsychotic medications are not outweighed by the increased risk of physical disease\(^5\).

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 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version 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\(^6\). 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\(^7\) 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).

Results

We found fifteen systematic reviews that met our inclusion criteria.1-5, 8-17.

• Moderate to high quality evidence suggests a medium-sized benefit of behavioural therapies, including cognitive behavioural therapy, psycho-education, and nutritional counselling for weight reduction, the prevention of weight gain, reducing waist circumference, and improving triglycerides, fasting glucose and insulin.

• The largest benefits were reported for weight gain prevention, individual therapies and psycho-education, particularly those that incorporated both a diet and exercise strategy.
Alvarez-Jimenez M, Hetrick SE, Gonzalez-Blanch C, Gleeson JF, McGorry PD

Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials

British Journal of Psychiatry 2008; 193(2): 101-107
View review abstract online

Comparison
Lifestyle interventions (cognitive behavioural therapy [CBT] or nutritional counselling [psychoeducation, diet and exercise]) vs. treatment as usual.

Summary of evidence
Moderate to high quality evidence (large samples, consistent, direct, unable to assess precision) suggests both CBT and nutritional counselling are effective for weight reduction and prevention of weight gain.

Weight reduction and prevention of weight gain

A significant effect favouring behavioural interventions combined over standard care for weight reduction or prevention of weight gain;

10 RCTs, N = 482, WMD = -2.56kg, 95%CI -3.20 to -1.92, p < 0.00001, I² = 29.8%, p = 0.18

Subgroup analysis shows similar effects for CBT and nutritional counselling (p = 0.14);

CBT: 6 RCTs, N = 308, WMD = -2.98kg, 95%CI -2.14 to -1.30, p < 0.00001, I² = 45.6%, p = 0.10
Nutritional counselling: 4 RCTs, N = 174, WMD = -3.12kg, 95%CI -4.10 to -2.14, p < 0.00001, I² = 0%, p = 0.74

Subgroup analysis shows similar effects for group therapy and individual therapy (p = 0.20);

Group: 5 RCTs, N = 274, WMD = -2.09kg, 95%CI -3.05 to -1.13, p < 0.001, I² = 56.8%, p = 0.06
Individual: 5 RCTs, N = 208, WMD = -2.94kg, 95%CI -3.79 to -2.08, p < 0.00001, I² = 0%, p = 0.79

Subgroup analysis showed similar effects of behavioural interventions for the prevention of weight gain or weight reduction (p = 0.29);

Prevention: 4 RCTs, N = 182, WMD = -3.05kg, 95%CI -4.16 to -1.94, p < 0.00001, I² = 0%, p = 0.72
Weight reduction: 6 RCTs, N = 300, WMD = -2.32kg, 95%CI -3.10 to -1.54, p < 0.00001, I² = 51%, p = 0.007
Behavioural therapies for weight gain

Subgroup analysis shows similar effects for recent onset psychosis vs. chronic schizophrenia (p > 0.05);

Recent onset: 1 RCT, N = 61, WMD = -2.80kg, 95%CI -4.93 to -0.67, p = 0.01
Chronic: 9 RCTs, N = 421, WMD = -2.54kg, 95%CI -3.20 to -1.87, p < 0.00001, I² = 36.5%, p = 0.13

Consistency in results
Consistent, apart from weight reduction and group therapy subgroup analyses.

Precision in results
Unable to assess (not standardised).

Directness of results
Direct

Bonfioli E, Berti L, Goss C, Muraro F, Burti L

Health promotion lifestyle interventions for weight management in psychosis: a systematic review and meta-analysis of randomised controlled trials

BMC Psychiatry 2012; 12: 78
View review abstract online

Comparison
Lifestyle interventions (CBT, psycho-education, diet/exercise plan) vs. treatment as usual.

Summary of evidence
Moderate to high quality evidence (large samples, consistent, direct, unable to assess precision) suggests benefits of lifestyle therapies for weight reduction and prevention of weight gain. The largest benefits were reported for weight gain prevention, individual therapies and psycho-education, particularly those that incorporated a diet and exercise strategy.

Weight reduction and prevention of weight gain

A significant effect favouring health prevention/lifestyle therapies over treatment as usual for BMI reduction:

13 RCTs, N = 583, MD = -0.98kg/m², 95%CI -1.31 to -0.65kg/m², p < 0.001, I² = 30%, p = 0.14

Larger effects were reported for weight gain prevention than weight loss;
Behavioural therapies for weight gain

Weight gain prevention: 4 RCTs, N = 201, MD = -1.09, 95%CI -1.51 to -0.68, p < 0.05, I² = 0%
Weight loss: 9 RCTs, N = 382, MD = -0.86, 95%CI -1.38 to -0.33, p < 0.05, I² = 49%

Larger effects were reported for individual therapies than group therapies;
Individual intervention: 4 RCTs, N = 191, MD = -1.20, 95%CI -1.57 to -0.83, p < 0.05, I² = 8%
Group intervention: 9 RCTs, N = 392, MD = -0.70, 95%CI -1.24 to -0.15, p < 0.05, I² = 37%

Larger effects were reported for psycho-education than CBT;
Psycho-education: 8 RCTs, N = 345, MD = -1.28, 95%CI -1.64 to -0.93, p < 0.05, I² = 0%
CBT: 5 RCTs, N = 238, MD = -0.66, 95%CI -1.15 to -0.16, p < 0.05, I² = 41%

Larger effects were reported for physical activity than no physical activity;
Physical activity: 4 RCTs, N = 183, MD = -1.22, 95%CI -1.59 to -0.85, p < 0.05, I² = 2%
No physical activity: 9 RCTs, N = 400, MD = -0.75, 95%CI -1.22 to -0.85, p < 0.05, I² = 27%

Larger effects were reported for diet plans than no diet plans;
Diet: 3 RCTs, N = 122, MD = -1.31, 95%CI -1.78 to -0.83, p < 0.05, I² = 21%
No diet: 10 RCTs, N = 461, MD = -0.80, 95%CI -1.19 to -0.42, p < 0.05, I² = 20%

No differences were reported between first-episode and chronic patients;
First-episode psychosis: 1 RCT, N = 61, MD = -0.99, 95%CI -1.71 to -0.27, p < 0.05, I² = NA
Chronic: 11 RCTs, N = 488, MD = -0.92, 95%CI -1.34 to -0.49, p < 0.05, I² = 39%

<table>
<thead>
<tr>
<th>Consistency in results</th>
<th>Consistent where applicable.</th>
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<tbody>
<tr>
<td>Precision in results</td>
<td>Unable to assess, not standardised.</td>
</tr>
<tr>
<td>Directness of results</td>
<td>Direct</td>
</tr>
</tbody>
</table>

Bruins J, Jorg F, Bruggeman R, Slooff C, Corpeleijn E, Pijnenborg M

The effects of lifestyle interventions on (long-term) weight management, cardiometabolic risk and depressive symptoms in people with psychotic disorders: a meta-analysis
**Behavioural therapies for weight gain**

**PLoS ONE 2014; 9(12): e112276**

View review abstract online

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Lifestyle interventions (diet, exercise, education) vs. treatment as usual.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary of evidence</strong></td>
<td>Moderate to high quality evidence (large samples, direct, precise, inconsistent) suggests benefits of lifestyle interventions for weight reduction, prevention of weight gain, waist circumference, triglycerides, fasting glucose and insulin. The largest benefits were reported for weight gain prevention and individual therapies.</td>
</tr>
</tbody>
</table>

**Weight loss or prevention of weight gain**

- A significant, medium-sized effect favouring lifestyle interventions over treatment as usual for:
  - **Weight loss or weight gain prevention**: 24 RCTs, N = 1,464, SMD = -0.63, 95%CI -0.84 to -0.42, $p < 0.00001$, $I^2 = 70\%$, $p < 0.00001$
  - **Waist circumference**: 10 RCTs, N = 705, SMD = -0.37, 95%CI -0.60 to -0.13, $p = 0.002$, $I^2 = 56\%$
  - Subgroup analyses including only high quality studies ($k = 4$), or studies with long-term follow up ($k = 7$, 2-6 months follow-up), found similar results for weight loss and weight gain prevention, but a non-significant effect size for waist circumference.

  Larger effects were reported for weight gain prevention than weight loss:
  - **Weight gain prevention**: 8 RCTs, N = 411, SMD = -0.84, 95%CI -1.28 to -0.40, $p = 0.0002$, $I^2 = 76\%$, $p = 0.0001$
  - **Weight loss**: 16 RCTs, N = 1,053, SMD = -0.52, 95%CI -0.72 to -0.31, $p < 0.00001$, $I^2 = 55\%$, $p = 0.004$

  Larger effects were reported for individual therapies than group therapies:
  - **Individual intervention**: 5 RCTs, N = 201, SMD = -0.67, 95%CI -1.04 to -0.30, $p = 0.0004$, $I^2 = 35\%$, $p = 0.19$
  - **Group intervention**: 10 RCTs, N = 560, SMD = -0.36, 95%CI -0.60 to -0.13, $p = 0.002$, $I^2 = 42\%$, $p = 0.08$

**Cardiometabolic parameters**

- A significant, small effect favouring lifestyle interventions over treatment as usual for:
  - **Triglycerides**: 8 RCTs, N = 659, SMD = -0.27, 95%CI -0.49 to -0.04, $p = 0.02$, $I^2 = 51\%$
  - **Fasting glucose**: 8 RCTs, N = 688, SMD = -0.24, 95%CI -0.32 to -0.10, $p = 0.001$, $I^2 = 0\%$
  - **Insulin**: 6 RCTs, N = 481, SMD = -0.28, 95%CI -0.56 to -0.01, $p = 0.04$, $I^2 = 52\%$
  - Subgroup analysis including only high quality studies ($k = 3$) resulted in a non-significant effect size
No differences were reported for:

- Total cholesterol: 7 RCTs, N = 590, SMD = -0.27, 95%CI -0.59 to 0.05, p = 0.10, I² = 72%
- HDL-cholesterol: 8 RCTs, N = 627, SMD = 0.28, 95%CI -0.16 to 0.73, p = 0.21, I² = 91%
- LDL-cholesterol: 5 RCTs, N = 517, SMD = -0.27, 95%CI -0.75 to 0.22, p = 0.28, I² = 87%
- Systolic blood pressure: 7 RCTs, N = 615, SMD = -0.22, 95%CI -0.49 to 0.05, p = 0.10, I² = 60%
- Diastolic blood pressure: 3 RCTs, N = 171, SMD = -0.08, 95%CI -0.57 to 0.41, p = 0.74, I² = 64%

Consistency in results

Inconsistent, apart from individual interventions and fasting glucose.

Precision in results

Precise

Directness of results

Direct

Cabassa LJ, Ezell JM, Lewis-Fernandez R

Lifestyle interventions for adults with serious mental illness: A systematic literature review

Psychiatric Services 2010; 61(8): 774-782

View review abstract online

Comparison

Lifestyle interventions (information on diet and calorie intake, exercise and health promotion) in group or individual settings vs. treatment as usual.

Summary of evidence

Moderate to low quality evidence (large sample, unable to assess consistency or precision, direct) suggests no significant benefit of educational programs for weight loss or metabolic outcomes.

Weight loss

12 studies (N = 425: 3 single-group studies; 3 quasi-experimental; 6 RCT) examined educational interventions for weight loss in people with schizophrenia spectrum disorders.

Only 6 of these studies (N = 264: 1 single-group, 2 quasi and 3 RCT) found significant benefits of the intervention for mean weight change at end of treatment.

3 studies (N = 145) reported significant benefits of educational interventions for reducing blood pressure; 1 study (N = 18) reported significant benefits for reducing blood glucose levels; and 1
study (N = 51) reported benefits for reducing haemoglobin A1C levels.  
1 study (N = 57) reported more reductions in triglyceride levels in those receiving education, and two studies (N = 108) reported reductions in waist circumference.

<table>
<thead>
<tr>
<th>Consistency in results</th>
<th>No measure of consistency is reported.</th>
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<td>Precision in results</td>
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</tr>
<tr>
<td>Directness of results</td>
<td>Direct</td>
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</tbody>
</table>

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**Caemmerer J, Correll CU, Maayan L**

**Acute and maintenance effects of non-pharmacologic interventions for antipsychotic associated weight gain and metabolic abnormalities: A meta-analytic comparison of randomized controlled trials**

*Schizophrenia Research* 2012; 140: 159-168  
[View review abstract online](#)

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Lifestyle interventions (CBT, nutritional education, exercise) vs. control conditions.</th>
</tr>
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<tbody>
<tr>
<td>Summary of evidence</td>
<td>Moderate quality evidence (medium-sized samples, indirect, some inconsistencies, unable to assess precision) suggests benefits of lifestyle interventions for weight reduction, prevention of weight gain, smaller waist circumference, less body fat, triglycerides, glucose, insulin, total and LDL-cholesterol.</td>
</tr>
</tbody>
</table>

**Weight loss and weight gain prevention**

*significant effect favouring lifestyle interventions over control conditions for;*

- Weight loss or weight gain prevention; 14 RCTs, N = 741, WMD = -3.12kg, 95%CI -4.03 to -2.21, \( p < 0.0001 \), \( I^2 = 42\%

  - Percent body fat: 3 RCTs, N = 83, WMD = -2.82%, 95%CI -5.35 to -0.30, \( p = 0.03 \), \( I^2 = 0\%

  - Waist circumference: 6 RCTs, N = 349, WMD = -3.58cm, 95%CI -5.51 to -1.66, \( p = 0.03 \), \( I^2 = 65\%

- Weight gain >7%: 3 RCTs, N = 126, 29.7% vs. 61.3%, RR = 0.52, 95%CI 0.35 to 0.78, \( p = 0.002 \), \( I^2 = 67\%

  - Subgroup analyses found effect sizes were significant in outpatient trials (k = 12), but not in inpatient (k = 3) or mixed samples (k = 2). No differences in effect sizes were found according to; follow up period (k = 5), CBT (k = 6) vs. nutritional and/or exercise interventions (k = 11), trial
Behavioural therapies for weight gain

duration ≤3 months (k = 9) vs. trial duration >3 months (k = 8), prevention trials (interventions initiated within 4 weeks of starting antipsychotics, N = 6) vs. intervention trials (interventions initiated after antipsychotic weight gain had occurred, N = 11), individual interventions (N = 5) vs. group interventions (N = 12).

**Cardiometabolic parameters**

* A significant, small effect favouring lifestyle interventions over control conditions for;  
  - Triglycerides: 4 RCTs, N = 253, WMD = -61.68mg/dL, 95%CI -92.77 to -30.59, p = 0.0001, I² = 0%
  - Glucose: 6 RCTs, N = 348, WMD = -5.79mg/dL, 95%CI -9.73 to -1.86, p = 0.004, I² = 58%
  - Insulin: 3 RCTs, N = 150, WMD = -4.93ulU/mL, 95%CI -7.64 to -2.23, p = 0.0004, I² = 0%
  - Total cholesterol: 5 RCTs, N = 273, WMD = -20.98mg/dL, 95%CI -33.78 to -8.19, p = 0.001, I² = 41%
  - LDL-cholesterol: 3 RCTs, N = 200, WMD = -22.06mg/dL, 95%CI -37.80 to -6.32, p = 0.006, I² = 58%

* No differences were reported for;  
  - HDL-cholesterol: 4 RCTs, N = 220, WMD = 2.89mg/dL, 95%CI -5.67 to 11.45, p = 0.51, I² = 85%
  - Systolic blood pressure: 2 RCTs, N = 128, WMD = -3.88, 95%CI -8.79 to 1.03, p = 0.12, I² = 0%

* Leaving the study early  
  - No differences were reported in rates of leaving the study early;  
    15 RCTs, N = 858, RR = 1.03, 95%CI 0.68 to 1.56, p = 0.88, I² = 30%

**Consistency in results**

Consistent, apart from weight circumference, weight gain >7%, glucose, LDL- and HDL-cholesterol.

**Precision in results**

Unable to assess (not standardised measure).

**Directness of results**

Indirect (control conditions combined).

**Das C, Mendez G, Jagasia S, Labbate LA**

Second-generation antipsychotic use in schizophrenia and associated weight gain: a critical review and meta-analysis of behavioral and pharmacologic treatments


[View review abstract online]
**Behavioural therapies for weight gain**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Behavioural therapies plus treatment as usual vs. treatment as usual.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Low quality evidence (small samples, unable to assess consistency or precision, direct) is unable to determine the benefits of behavioural interventions for weight management.</td>
</tr>
</tbody>
</table>

**Weight management**

**Nutrition and exercise counselling**

1 study (N = 48) compared intensive nutrition and exercise counselling with standard diet and exercise in community outpatients, and found the counselling intervention had greater weight loss over 12 weeks (4.1kg vs. 1.4kg) but no differences in quality of life or long term differences. 2 outpatient studies (N not reported) found maintenance of weight loss 3-12 months after the end of the interventions, however 2 additional studies (N not reported) did not find any weight maintenance at follow up.

1 study (N = 53) compared a normal diet with a low-calorie diet and exercise in inpatients, and found greater weight loss in the intervention group over 6 months (4.1kg vs. 0.9kg).

**Nutrition counselling alone**

1 small study (N = 22) compared a Weight Watchers program with TAU, and showed mean weight loss of 2.3kg compared to no change in the control group over 10 weeks but did not reach statistical significance.

**Group nutrition and exercise counselling**

1 study (N = 57) of diabetic patients compared group counselling with TAU over 24 weeks, and found mean weight loss of 2.3kg compared to weight gain of 2.7kg in the control group.

Another study (N = 70) compared an educational intervention with TAU over 6 months and found weight maintenance in the intervention group, while the control group gained 4.5kg.

**Cognitive behavioural therapy (CBT)**

1 study (N = 61) compared weekly CBT over 3 months with a single information session, and found mean weight loss of 4.1kg compared to weight gain of 2.1kg in the control group.

**CBT plus nutritional counselling**

1 study (N = 72) compared the intervention with TAU over 14 weeks, and found no significant difference in weight loss (1.9kg vs. 1.1kg respectively).

1 study (N = 51) compared the intervention with TAU over 1 year, and found mean loss of 3.2kg compared to weight gain of 3.2kg in the control group.

**Consistency in results**

No measure of consistency is reported.

**Precision in results**

No measure of precision is reported.
### Behavioural therapies for weight gain

**Directness of results**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Behavioural therapy interventions for reducing antipsychotic-induced weight gain.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Low quality evidence (small samples, direct, unable to assess precision or consistency) is unable to determine the benefits of a diet and exercise plan, token economy, or problem solving for weight loss.</td>
</tr>
</tbody>
</table>

**Reduction of weight gain**

8/8 studies (N = 142) reported weight loss following intervention;

Four studies were a pre-post design, three were quasi-experimental (not randomised) and one was a randomised trial. Intervention duration ranged from 8-72 weeks.

Interventions included calorie restricted diets; exercise programs; token therapies; cognitive behavioural therapy; other behavioural therapy incorporating problem solving, goal setting and social support; and Weight Watchers programs.

A greater degree of weight loss was associated with programs incorporating multiple elements, such as calorie restriction combined with behavioural therapy.

Applicability of results to community settings was questioned as 7/8 studies were conducted in hospital settings; authors also report a high risk of bias in all studies (performance, selection and detection biases).

**Consistency in results**

No measure of consistency is reported, results appear consistent.

**Precision in results**

No measure of precision is reported.

**Directness of results**

Direct
## Behavioural therapies for weight gain

**Faulkner G, Cohn T, Remington G**

**Interventions to reduce weight gain in schizophrenia**

Cochrane Database of Systematic Reviews 2007; (1): CD005148

[View review abstract online](#)

<table>
<thead>
<tr>
<th>Comparison 1</th>
<th>Cognitive behavioural therapy (CBT) vs. standard care for prevention of weight gain.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Moderate to low quality evidence (small samples, consistent, direct, unable to assess precision) suggests CBT may be more effective than standard care for preventing weight gain.</td>
</tr>
</tbody>
</table>

### Prevention of weight gain

- **Significant effect favouring CBT for preventing weight gain at six month follow up;**
  - 2 RCTs, N = 89, WMD -4.87kg, 95%CI -7.1 to -2.6, *p* = 0.000019, I² = 15%, *p* = 0.28

- **Significant effect favouring CBT for preventing BMI increase at six month follow up;**
  - 2 RCTs, N = 89, WMD -1.52BMI, 95%CI -2.25 to -0.79, *p* = 0.000044, I² = 2%, *p* = 0.31

- **Significant effect favouring CBT for preventing waist circumference increases at six month follow up;**
  - 1 RCT, N = 34, WMD -5.50cm, 95%CI -8.21 to -2.79, *p* = 0.000071

- **Significant effect favouring CBT for preventing weight increases of 7% by 12 weeks;**
  - 1 RCT, N = 34, WMD = 0.20, 95%CI 0.07 to 0.64, *p* = 0.0067

### Global state

**Measured by CGI**

- **Significant effect favouring CBT for better body image;**
  - 1 RCT, N = 34, WMD 1.10, 95%CI 0.29 to 1.91, *p* = 0.0081

  - *No significant differences for quality of life;*  
    - 1 RCT, N = 34, WMD = 0.90, 95%CI -0.04 to 1.84, *p* = 0.061

  - *No significant differences for improvement in health;*  
    - 1 RCT, N = 34, WMD = 0.90, 95%CI -0.01 to 1.81, *p* = 0.051

### Leaving the study early

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NeuRA

Behavioural therapies for antipsychotic induced weight gain

May 2016

Margaret Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

To donate, phone 1800 888 019 or visit www.neura.edu.au/donate/schizophrenia
## Behavioural therapies for weight gain

No significant differences for study attrition at six month follow up;
1 RCT, N = 34, RR 1.91, 95%CI 0.68 to 5.42, \( p = 0.22 \), NNT 5

Overall compliance was reported to be 92%

<table>
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<td>Directness of results</td>
<td>Direct</td>
</tr>
<tr>
<td>Comparison 2</td>
<td>CBT vs. standard care for the reduction of weight gain.</td>
</tr>
</tbody>
</table>

### Summary of evidence

Moderate to low quality evidence (small sample, consistent, direct, unable to assess precision) suggests CBT may be more effective than standard care for reducing weight gain.

### Reduction of weight gain

**Significant effect favouring CBT for reducing weight gain;**
3 RCTs, N = 129, WMD -1.69kg, 95%CI -2.77 to -0.61, \( p = 0.0022 \), \( I^2 = 0\% \), \( p = 0.41 \)

**Significant effect favouring CBT for reduction in BMI;**
3 RCTs, N = 129, WMD -0.66, 95%CI -1.06 to -0.25, \( p = 0.0015 \), \( I^2 = 0\% \), \( p = 0.51 \)

No significant differences for waist-to-hip circumference ratio;
1 RCT, N = 15, WMD -0.02, 95%CI -0.06 to 0.02, \( p = 0.33 \)

### Satisfaction with service

Measured by CSQ-8

**Significant effect favouring CBT for overall satisfaction with service;**
1 RCT, N = 71, WMD 2.30, 95%CI 0.9 to 3.7, \( p = 0.0012 \)

### Mental state

Measured by PANSS

No significant differences for mental state;
1 RCT, N = 71, WMD 3.00, 95%CI -6.23 to 12.23, \( p = 0.52 \)

### Global state

Measured by CGI
No significant differences for global state;
1 RCT, N = 72, RR 0.86, 95% CI 0.6 to 1.2, p = 0.36

Leaving the study early

No significant differences for study attrition;
3 RCTs, N = 137, RR 0.13 CI -0.01 to 0.3, p = 0.079, I² = 70%, p = 0.03

<table>
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</tbody>
</table>


The Effectiveness of Lifestyle Interventions to Reduce Cardiovascular Risk in Patients with Severe Mental Disorders: Meta-Analysis of Intervention Studies

Community Mental Health Journal 2014; 50: 81-95
View review abstract online

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Lifestyle interventions vs. control conditions. Samples primarily included people with schizophrenia spectrum disorders.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Moderate to low quality evidence (medium-sized samples, indirect, mostly inconsistent, unable to assess precision) suggests benefits of lifestyle interventions for lower BMI and waist circumference, and better triglyceride, glucose, and cholesterol.</td>
</tr>
</tbody>
</table>

Weight measures

A significant effect favouring lifestyle interventions over control conditions for;
BMI at 3 months: 15 studies (mixed design), N = 739, WMD = -1.16kg/m², 95% CI -1.72 to -0.58, p < 0.05, I² = 92.7%, p < 0.001
Behavourial therapies for weight gain

<table>
<thead>
<tr>
<th>Cardiometabolic parameters</th>
</tr>
</thead>
</table>

A significant effect favouring lifestyle interventions over control conditions for:

**Glucose**
- at 3 months: 3 studies (mixed design), N = 281, WMD = -5.58mg/dL, 95%CI -9.63 to -1.53, p < 0.05, I² = 91.2%, p < 0.001
- at 6 months: 2 studies (mixed design), N = 163, WMD = -3.62mg/dL, 95%CI -11.30 to -4.06, p < 0.05, I² = 92.4%, p < 0.001
- at 12 months: 2 studies (mixed design), N = 184, WMD = -9.32mg/dL, 95%CI -13.30 to -5.34, p < 0.05, I² = 69.5%, p = 0.070

**Triglycerides**
- at 3 months: 3 studies (mixed design), N = 179, WMD = -24.64mg/dL, 95%CI -48.24 to -1.04, p < 0.05, I² = 71.8%, p = 0.029
- at 6 months: 2 studies (mixed design), N = 163, WMD = -44.85mg/dL, 95%CI -76.83 to -12.87, p < 0.05, I² = 86.7%, p = 0.006
- at 12 months: 2 studies (mixed design), N = 184, WMD = -38.04mg/dL, 95%CI -75.28 to -0.80, p < 0.05, I² = 92.2%, p < 0.001

**Total cholesterol**
- at 3 months: 4 studies (mixed design), N = 205, WMD = -8.32mg/dL, 95%CI -14.57 to -2.08, p < 0.05, I² = 63.5%, p = 0.042
- at 6 months: 2 studies (mixed design), N = 163, WMD = -15.66mg/dL, 95%CI -25.64 to -5.68, p < 0.05, I² = 89.7%, p = 0.002
- at 12 months: 1 study, N = 110, WMD = -31.32mg/dL, 95%CI -33.98 to -28.66, p < 0.05

No consistent differences in results according to study quality. No publication bias.

**Consistency in results**
- Inconsistent apart from BMI and waist circumference at 6 months.

**Precision in results**
- Unable to assess (not standardised).
Behavioural therapies for weight gain

**Directness of results** | Indirect (control conditions combined).

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**Loh C, Meyer JM, Leckband SG**

*A comprehensive review of behavioral interventions for weight management in schizophrenia*


[View review abstract online](#)

**Comparison** | Behavioural interventions vs. either treatment as usual or no control group.

**Summary of evidence** | Moderate to low quality evidence (large samples, direct, unable to assess precision, data appears inconsistent) suggests behavioural intervention may result in weight loss.

**Weight loss**

- 23 studies (N = 701); 4 case studies, 9 pre-post studies, 3 RCT, 7 non-randomised controlled studies;
- 6/10 controlled studies reported significant weight loss in patients receiving behavioural intervention when compared to controls (treatment duration range 4 weeks to 6 months), one study also showed a significant prevention of weight gain compared to controls.
- 9/13 non-controlled studies reported weight loss following behavioural intervention (treatment duration range 6 weeks to 18 months).

**Consistency in results** | Studies appear inconsistent.

**Precision in results** | No measure of precision is reported.

**Directness of results** | Direct

---

**Lowe T, Lubos E**

*Effectiveness of weight management interventions for people with serious mental illness who receive treatment with atypical antipsychotic medications. A literature review*
Behavioural therapies for weight gain


Comparison 1

<table>
<thead>
<tr>
<th>Comparison 1</th>
<th>Educational therapies, including behavioural interventions and cognitive-behavioural therapy for reducing weight gain following olanzapine vs. various comparison groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Low quality evidence (small samples, direct, unable to assess precision, appears inconsistent) is unable to determine the benefits of educational therapies for weight loss.</td>
</tr>
</tbody>
</table>

Weight loss

*Four studies measured the effectiveness of psycho-education therapies for reducing weight gained during olanzapine administration;*

1 RCT, N = 72, used behavioural therapy involving a manual, incorporating a food diary, exercise planner, diet tips and weight loss techniques, compared to treatment as usual. Treatment lasted 14 weeks and showed significant weight loss in both groups, though greater in the intervention group.

1 mixed method study, N = 93, used a discussion group intervention with weekly weigh-ins and motivational topics. No control group was used. Study length was over four years and at two years 81.2% of participants had lost over 7% of their initial body weight.

2 RCTs, N = 65, used cognitive-behavioural approaches compared to standard care. Both were 12 weeks duration and both found more weight loss in the intervention group, though this did not reach statistical significance. However one study had a small sample and the other had high attrition.

Consistency in results

Studies appear inconsistent.

Precision in results

No measure of precision is reported.

Directness of results

Direct

Comparison 2

<table>
<thead>
<tr>
<th>Comparison 2</th>
<th>Dietary intervention and exercise strategies for reducing weight gain following olanzapine vs. various comparison groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary of evidence</td>
<td>Low quality evidence (small samples, direct, unable to assess precision, appears inconsistent) is unable to determine the benefits of diet and exercise therapies for weight loss.</td>
</tr>
</tbody>
</table>

Weight loss
Behavioural therapies for weight gain

Four studies measured the effectiveness of dietary intervention and exercise therapies for reducing weight gained during olanzapine administration;

1 descriptive study, N = 22, used a manualised programme of diet counselling and exercise. There was no control group. Treatment lasted 48 weeks and patients showed an average weight loss of 6kg.

1 RCT, N = 56, followed a reduced calorie and increased exercise regime for 26 weeks compared to standard care alone. Although high attrition was reported, patients showed an average weight loss of 4.2kg.

1 RCT, N = 21, followed a Weight Watchers programme of diet and exercise, for 10 weeks compared to standard care alone. Patients reported an average weight loss of 5.1lbs.

1 RCT, N = 31, followed a regime of weight control, nutrition education, exercise and behavioural interventions for 52 weeks compared to standard care alone. Patients reported an average 3% loss of body weight.

Consistency in results | Studies appear inconsistent.
--- | ---
Precision in results | No measure of precision is reported.
Directness of results | Direct

Strassnig M, Ganguli R

Weight loss interventions for people with schizophrenia

Clinical schizophrenia and related psychoses 2007; 1: 43-53
View review abstract online

Comparison | Behavioural interventions (duration ranged from 10 weeks to 1.5 years) for weight loss.
--- | ---
Summary of evidence | Moderate to low quality evidence (small to medium-sized samples, unable to assess precision, appears consistent, direct) suggests behavioural interventions may result in weight loss.

Weight loss

Greater weight loss was reported following behavioural therapies (cognitive therapy, diet education, weight watchers, motivational counseling, exercise) in 7 of 9 studies. One RCT (N = 51) reported prevention of weight gain compared to controls, and one trial (N = 31) reported no weight change.
Behavioural therapies for weight gain

Consistency in results | Appears consistent.
Precision in results | No measure of precision is reported.
Directness of results | Direct


Cardiometabolic effects of physical activity interventions for people with schizophrenia

View review abstract online

Comparison | Physical activity (duration ranged from 10 sessions to 52 weeks, frequency 1-7 times per week) with or without diet counselling, for reducing weight and improving cardiometabolic outcomes.

Summary of evidence | Moderate to low quality evidence (small to medium-sized samples, unable to assess precision, appears consistent, direct) suggests that physical activity showed some benefits for weight loss and preventing weight gain, and when combined with diet counselling, may also have cardiometabolic benefits.

Weight loss

13 studies (1 case study, six quasi-experimental, 6 RCTs) examined the effectiveness of physical activity interventions;

Interventions largely included aerobic exercise; 5 studies also included additional resistance training. The intensity of the interventions varied widely.

All studies found moderate levels of weight loss, ranging from 2-7%. One study also reported effective prevention of weight gain. 5-10% improvements were reported in cardiovascular fitness.

Without clinical maintenance, program attendances rates were poor, with dropout rates as high as 90% in 1 study (N = 10). Poor motivation and medication side-effects were the most commonly cited reason for non-attendance.

Greater adherence correlated with reduced depressive symptoms (1 study, N = 13). Greater attendance was also related to levels of weight loss (4 studies, N = 265).

Cardiometabolic outcomes
2 quasi-experimental studies (N = 24) found reductions in both systolic and diastolic blood pressure over 12-24 weeks, most notably in hypertensive participants.

2 studies (N = 70) found non-significant reductions of hyperglycaemia (fasting glucose concentration) and one study (N = 128) reported significant blood glucose reductions.

Physical activity combined with diet counselling was found to reduce insulin resistance (1 study, N = 128) and fasting blood insulin concentrations (2 studies, N = 181).

2 studies found no significant differences in levels of total serum cholesterol (N = 65), but some reductions were found in triglyceride levels in 2 studies (N = 65) but not in a third (N = 6). Reduced ratio of low density to high density lipoproteins was also reported in 1 study (N = 48).

### Consistency in results
Appears consistent.

### Precision in results
No measure of precision is reported.

### Directness of results
Direct

---

**Verhaeghe N, De Maeseneer J, Maes L, Van Heeringen C, Annemans L**

Effectiveness and cost-effectiveness of lifestyle interventions on physical activity and eating habits in persons with severe mental disorders: a systematic review


*View review abstract online*

### Comparison

Behavioural or educational therapies plus treatment as usual vs. treatment as usual for weight loss or preventing weight gain.

*Note: all patients were treated with atypical antipsychotics.*

### Summary of evidence

Low quality evidence (small individual samples, unable to assess consistency or precision, direct) is unable to determine the benefit of behavioural interventions for weight management.

### Weight management

14 studies compared behavioural or psycho-educational interventions for weight loss/maintenance;

*Pre-post baseline measures;*

11 studies reported weight loss compared to baseline in the *intervention* group, of which 5 studies were statistically significant. 2 studies found non-significant increases of weight and 1 found
Behavioural therapies for weight gain

significant increases. 11 studies also reported a decrease in mean BMI (five studies significant). 2 studies found mean increases in BMI in the intervention group compared to baseline.

4 of 14 studies found weight loss compared to baseline in the control group, while the other 10 studies reported weight gain. 4 of 14 studies found mean BMI reduction compared to baseline in the control group, while the other 10 studies reported increases in BMI.

Between-group differences post-intervention;

The difference between groups in weight change was significant in 9/14 studies, with greater reductions in the intervention group (mean difference -1.96kg vs. +1.77kg). 5/14 studies showed no significant difference.

The difference between groups in BMI was significant in 8/14 studies, with greater reductions in the intervention group (mean difference -0.87 vs. +0.64). 3/14 studies showed no significant difference.

The maintenance of weight loss at follow up was unclear, with 1 study reporting reversal of weight loss, 1 maintaining stable weight and 1 study further reducing weight over 2-3 months post-treatment.

<table>
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<tr>
<td>Directness of results</td>
<td>Direct</td>
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</tbody>
</table>

Werneke U, Taylor D, Sanders TAB, Wessely S

Behavioural management of antipsychotic-induced weight gain: A review


View review abstract online

Comparison | Behavioural interventions for adult obesity following antipsychotic administration.

Summary of evidence | Low quality evidence (small samples, direct, unable to assess precision, data appears inconsistent) is unable to determine the effectiveness of behavioural therapies for weight loss.

Weight loss
5 studies measured the effectiveness of behavioural intervention for reducing weight gained during antipsychotic administration;

1 pre-post intervention, N = 22, used a Weight Watchers programme of diet and exercise for 10 weekly group sessions. Weight loss was reported more in men, mean 3.3kg. Weight increases were reported in 3 of 4 women patients.

1 pre-post intervention, N = 22 (no control group), used a 5 minute education on diet and exercise during outpatient visits for seven months study duration, and reported a mean weight increase of 2.4kg.

1 pre-post intervention, N = 6 (no control group), used diet and exercise counselling as part of a cognitive behavioural therapy incorporating 7-9 individual sessions and 10 group sessions, for 32 week study duration. Mean BMI was reported to decrease by 4.5kg/m².

1 intervention study, N = 49 (using a historical control group) applied full medical and psychiatric care as well as low calorie monitored diet, nutritional education and supportive care. Weight gain was reported in 30% of patients and 71% of controls, which was a significant difference (p < 0.01).

1 retrospective case-note review, N = 122 (no control group), considered a paradigm including weight monitoring, food diaries, nutritional advice, education, exercise classes and group support, for a study duration up to 6 years. Quantitative data was not reported but overall group difference was significant, p < 0.003.

<table>
<thead>
<tr>
<th>Consistency in results</th>
<th>Studies appear inconsistent.</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

Explanation of acronyms

CI = Confidence Interval, \( d \) = Cohen’s \( d \) and \( g \) = Hedges’ \( g \) = standardised mean differences, \( I^2 \) = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), \( k \) = number of studies, \( kg \) = kilogram, \( lbs \) = pounds, \( N \) = number of participants, \( p \) = statistical probability of obtaining that result (\( p < 0.05 \) generally regarded as significant), \( Q \) = \( Q \) statistic (chi-square) for the test of heterogeneity, \( RCT \) = randomised controlled trial, vs. = versus, \( \chi^2 \) = chi-square.
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.

† 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.

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. InOR 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 unforeseen 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
Behavioural therapies for weight gain

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 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. I² 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. I² can be calculated from Q (chi-square) for the test of heterogeneity with the following formula18:

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

§ 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 relaxed20.

‖ 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.
References


