Weight gain in antipsychotic-naive patients: a review and meta-analysis

Tarricone I, Ferrari Gozzi B, Serretti A, Grieco D, Berardi D

CRD summary
This review concluded that weight gain associated with first exposure to antipsychotic drugs occurred rapidly in the first few weeks and continued during the following months. The authors’ conclusions were broadly in line with the evidence presented, but variation within the review and limitations in the review methods suggest that the findings should be applied with caution.

Authors’ objectives
To assess the amount of weight gain in patients exposed to antipsychotic drugs for the first time.

Searching
MEDLINE, PsycINFO, EMBASE and the Cochrane Library were searched from 1997 to July 2008. Search terms were reported. Reference lists of retrieved articles and review articles were also searched. Only studies published in English were included.

Study selection
Studies of antipsychotic-naive patients (aged over 15 years) treated with antipsychotic drugs, without any other medication to reduce weight gain, were eligible for the review. Eligible studies had to report changes in weight and/or body mass index (BMI) during treatment. No inclusion criteria were reported for study design, although case reports were excluded.

Participants in included studies were mainly patients with first-episode schizophrenia or schizophreniform disorder who were treated with a wide range of antipsychotic drugs. Participants mean baseline BMI ranged from 19.4 to 24.9 and weight from 48.5 to 69.4kg (where reported); most were treated as in-patients. Participants in some studies received dietary or exercise interventions to limit weight gain. Study duration ranged from four weeks to 2.5 years (most commonly four to 10 weeks).

Two reviewers selected studies for the review.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
For studies that reported weight gain in patients treated with different drugs, data were extracted to calculate a mean weight change for the whole sample. For studies that reported a mean weight change without a standard deviation (SD), the standard deviation was calculated from the standard deviation weighted mean in studies that did report it. It appeared that a similar procedure was followed for studies that reported on changes in BMI.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
A notional control group with the same number of participants and a mean weight gain of 0kg was created for each study. The control group standard deviation was the weighted mean standard deviation of all the studies included in the analysis. The weighted mean difference (WMD) between treatment and ‘control’ groups and associated 95% confidence interval (CI) were calculated. Pooled weighted mean differences were calculated by meta-analysis using a fixed-effect model. Heterogeneity between studies was assessed by the $\chi^2$ test.

Subgroup analyses included studies with a follow-up at 12 weeks or less, studies without co-therapy, studies with out-patients and patients with physical co-morbidity, and studies not sponsored by pharmaceutical companies. Studies were
also analysed by follow-up duration (four to eight weeks; 10 to 12 weeks; 24 to 48 weeks).

Publication bias was assessed using funnel plots and Egger's test.

**Results of the review**

Eleven studies reported in 12 publications were included in the review (n appears to be 734 patients treated with antipsychotic drugs). Four studies were randomised controlled trials and two had control groups of healthy people. One study was double-blinded.

Antipsychotic drug treatment was associated with significant increases in BMI (WMD 1.97, 95% CI 1.81 to 2.1; nine studies) and weight (WMD 4.85kg, 95% CI 4.23 to 5.47; eight studies) at the last available follow-up. Statistical heterogeneity was highly significant in both analyses ($\chi^2=241.3$, $I^2=96.7\%$ for BMI; $\chi^2=76.9$ for weight).

Significant heterogeneity was also found in most subgroup analyses (results reported in the paper). Studies lasting 24 to 48 weeks showed a significant BMI gain (WMD 3.87, 95% CI 3.48 to 4.26; three studies), without significant heterogeneity. Weight gain was directly correlated with duration of antipsychotic drug treatment.

Funnel plot asymmetry was present in some analyses, but Egger's test did not suggest significant publication bias.

**Authors' conclusions**

Weight gain associated with first exposure to antipsychotic drug treatment occurred rapidly in the first few weeks and continued during the following months.

**CRD commentary**

Inclusion criteria for participants, interventions and outcomes were clear. Inclusion criteria for study designs were not stated, but it appeared that all study types except case reports were included; this seemed appropriate for a review of an adverse effect. The authors searched a range of relevant sources, but restrictions by language and publication status meant that some relevant studies could have been missed. Publication bias was assessed using standard methods. Two reviewers selected studies for the review, minimising risk of errors and bias. It was not reported whether similar methods were used for data extraction.

The authors did not assess the quality of the included studies, which meant that their reliability was uncertain. Studies were pooled by meta-analysis; statistical and clinical heterogeneity were explored. Significant statistical heterogeneity was present in most analyses, which suggested that meta-analysis was possibly not appropriate. As noted by the authors, the method used to analyse the data, i.e. creation of a notional control group, could have inflated the statistical significance of the results. The clinical heterogeneity of the included studies meant that generalisability across drugs and settings was uncertain.

The authors’ conclusions were broadly in line with the evidence presented and results of other reviews, but the limitations suggest that the findings should be applied with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that clinicians should monitor weight in patients treated with antipsychotic drugs from the outset and continue monitoring for as long as treatment continues.

**Research:** The authors did not state any implications for further research.

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