Weight gain as an adverse effect of some commonly prescribed drugs: a systematic review

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CRD summary
This review provided evidence of the weight gain potential of some common 'obesogenic' drugs used in the treatment of chronic disease. Several possible sources of potential error and bias were identified in the review, but the authors' conclusion reflects the evidence provided.

Authors' objectives
To quantify the adverse effects on body weight of drugs that are consistently reported as obesogenic, and that are used in the treatment of chronic disease.

Searching
MEDLINE (1966 to 2004), EMBASE (1980 to 2004), PsycINFO (1967 to 2004) and the Cochrane Controlled Trials Register were searched; the search terms were reported. The reference lists of all relevant papers were also checked. The searches were limited to English language papers.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of at least 3 months' duration were eligible for inclusion.

Specific interventions included in the review
Studies that compared 'obesogenic' drugs with placebo, an alternative drug or other treatment were eligible for inclusion. Studies that primarily investigated the use or effect of a combination of 'obesogenic' drugs were excluded, as were studies where the drug was used to treat a disease usually characterised by weight loss. The drugs included were valproate, lithium, clozapine, olanzapine, risperidone, ziprasidone, prednisone, insulin, glipizide, glibenclamide, chloropropamide, troglitazone, rosiglitazone, pioglitazone, nortriptyline, doxepin, amitriptyline, atenolol, metoprolol and propranolol. Doses ranged from 0.25 to 2,115 mg/day and follow-up ranged from 12 weeks to 10 years.

Participants included in the review
Participants aged over 18 years old that had been prescribed a drug considered obesogenic were eligible for inclusion. The patients included had the following conditions: bipolar disorder, epilepsy, schizoaffective disorder, schizophrenia, psychosis, borderline personality disorder, acute mania, alcohol dependence, Graves ophthalmopathy, type 2 diabetes, depression, hypertension and post-myocardial infarction.

Outcomes assessed in the review
To be eligible for inclusion outcome measures had to include measured weight change reported quantitatively. Studies in which body weight was self-reported were excluded.

How were decisions on the relevance of primary studies made?
Two reviewers independently applied the inclusion criteria.

Assessment of study quality
Two independent reviewers assessed study quality in terms of randomisation, allocation concealment, inclusion and exclusion criteria, and intention-to-treat analysis.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
The studies were grouped by drug type and tables were available to evaluate differences between the studies..

**Results of the review**
Forty-three RCTs (n=25,663) were included.

The methods of randomisation and concealment were not described in 72% of the studies. In 11 studies the method of randomisation was clearly described and considered adequate. Intention-to-treat analysis was used in 51% of studies.

Weight change differed greatly amongst the different categories of drugs; weight gain was the result of treatment in the majority of studies (up to 10 kg at 52 weeks), with some of the greatest weight gains in patients prescribed antipsychotic treatment. Weight loss was observed in 8 studies.

In 6 studies investigating whether weight gain was dose-related, three found no relationship. Some correlation was found for insulin and one study suggested that higher doses of rosiglitazone may lead to a clinically significant increase in body weight.

**Authors' conclusions**
The review provided evidence of the weight gain potential of some common drugs.

**CRD commentary**
The research question was well-defined and the inclusion criteria were clear with regard to the interventions, participants, outcomes and study design. Four relevant databases were searched. However, the authors made no attempt to identify unpublished studies and limited the search to English language studies, which might have introduced publication and language bias into the review. Some aspects of quality were assessed by two reviewers, which reduces the potential for errors and bias. Owing to the heterogeneity between studies, the authors synthesised the studies narratively, which was appropriate. The method of data extraction was not described in this review. There were several possible sources of potential error and bias but the authors' conclusion is appropriate given the evidence provided.

**Implications of the review for practice and research**
Practice: The authors stated that the potential of weight gain should be discussed with patients prior to the institution of therapy, both for medico-legal grounds and to ensure weight maintenance is promoted and adhered to.

Research: The authors stated that future clinical trials should always document weight changes.

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