Predictors and correlates for weight changes in patients treated with olanzapine and weight mitigating agents: A post-hoc analysis

by Stauffer et al.

Weight gain along with antipsychotic treatment is a serious problem in the treatment of schizophrenia and bipolar disorder. The present study wants to explore the relationship between changes in appetite or eating behaviors and subsequent weight change for adult patients with schizophrenia or bipolar disorder treated with olanzapine and adjunctive potential weight mitigating agents. The authors emphasize that it is not an analysis that compares the efficacy or effectiveness of these agents. They included 158 patients with a BMS ≥25 kg/m² from 3 previously published RCTs and analyzed for categorical weight loss ≥2 kg and weight gain ≥1 kg. Variables that were evaluated as potential predictors of weight outcomes included baseline patient characteristics, factors of the Eating Inventory, individual items of the Eating Behavior Assessment, and the Visual Analog Scale. Predictors/correlates of weight loss ≥2 kg included: high baseline BMI, low baseline interest in food, and a decrease from baseline to endpoint in appetite, hunger, or cravings for carbohydrates. Reduced cognitive restraint, increase in hunger, and increased overeating were associated with a higher probability of weight gain ≥1 kg. They conclude that the association between weight gain and lack of cognitive restraint in the presence of increased appetite suggests potential benefit of psychoeducational counseling in conjunction with adjunctive pharmacotherapeutic agents in limiting weight gain during antipsychotic drug therapy.

The paper is clearly written, and the question is well defined. The questions are of interest for psychiatry. No such study has been published before to my knowledge which tries to find predictive factors for weight changes along with antipsychotic treatment. This is a post-hoc analysis with its methodological limitations. It may be suitable to identify potential predictors. These need to be confirmed in prospective trials.

There are, however, a variety of methodological questions that need to be answered before making clear conclusions.

Major Compulsory Revision
First, it remains unclear why the authors only included patients with a BMS ≥25
kg/m². They state in the discussion that people with a lower BMI are more likely to gain weight. Thus, there is a risk of Bias when only including patients with a higher BMI. Second, if the major question is whether a weight changes during antipsychotic treatment can be predicted it seems more appropriate to me to include patients who only received the antipsychotic and not a weight mitigating agent. These may have an influence on the time dependent variables such as decrease in appetite, craving for carbohydrates or hunger. Again, this is a potential source of bias.

I understand why the authors did not perform a subgroup analysis of patients with schizophrenia and bipolar disorder, they could, however, include “diagnosis” to the regression model. This could give an idea, whether patients with schizophrenia and bipolar disorder may differ in reasons for weight change.

In the discussion they should more clearly point out that the analysis was only done in patients who were treated with olanzapine. Maybe reasons for weight change differ when using another antipsychotic.

In the introduction they spend a whole page on describing the CATIE results. This can only be of interest in this context if drop-out rates in the olanzapine arm are mainly due to weight gain. Otherwise this passage can be omitted.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no financial competing interests in relation to this paper.

I have acted as a consultant for AstraZeneca, Eli Lilly, Janssen, Novartis and Wyeth and has acted as an expert witness for AstraZeneca, Eli Lilly and Janssen. I received research funding from AstraZeneca, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi-Synthelabo and Wyeth. In addition, I am a member of a speakers’ bureau for AstraZeneca and Janssen, and have accepted paid speaking engagements in industry-sponsored symposia from AstraZeneca, Eli Lilly, Janssen and Pfizer and travel or hospitality not related to a speaking engagement from AstraZeneca, Eli Lilly, and Janssen.