

about 2% for placebo. In longer-term studies, 54% of the patients taking olanzapine gained weight, compared with 28% of the patients taking haloperidol (Eli Lilly trial 980). Weight increased with olanzapine treatment in a dose-dependent manner in at least one study (Eli Lilly trial 982, p. 15).

These and other studies are arguably flawed in they did not take in other factors, such as diet, family history, ethnicity, use of cannabis (8) and other substances, properly into account, but the tantalizing clues pointing to a causal link between olanzapine and weight gain await larger-scale studies.

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#### Drs. Graham and Perkins Reply

TO THE EDITOR: We thank the Drs. Isaac for their focus on the importance of the dietetic composition of our subjects. We share their concern that important information was missing in our investigation of the effect of olanzapine on energy balance if we did not know how it influenced the nutrient composition of diet and argue that equally important is its effect on voluntary energy expenditure. Please remember that our published results are preliminary data from the first nine subjects studied and that multiple analyses are not appropriate at this stage of the study.

Accurately measuring food consumption and voluntary energy expenditure is extremely difficult—if not impossible—in free-living outpatients with schizophrenia, yet we attempted to do this in our study. Our subjects completed 24-hour diet recalls and dietician-assisted food-frequency questionnaires at baseline and after 12 weeks of olanzapine therapy. The dietetic results and changes in voluntary activity, as measured by activity monitors worn for 3 days, will be available when the larger study is complete.

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