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**Metabolic Syndrome in  
Inpatients Treated With Clozapine**

**To the Editor:** I read with interest the important study by Dr Bai and coauthors<sup>1</sup> of metabolic factors and weight gain in schizophrenia patients treated with clozapine. They found that baseline body mass index (BMI) and BMI change over time were associated with metabolic syndrome and 4 metabolic parameters, with the notable exceptions of hyperglycemia and diabetes mellitus, which were related to duration of clozapine treatment rather than weight gain.

Metabolic syndrome in schizophrenia during antipsychotic treatment is a highly relevant and worrisome topic<sup>2</sup> in relation to at least some of the antipsychotics. Nevertheless, Bai and colleagues' valuable findings should be interpreted with caution in the context of the population studied.

It is important to note that this work studied an inpatient sample for an average period of  $57.6 \pm 27.3$  months (range, 5–96 months). In other words, the study sample would have consisted of patients who were relatively poorly responsive to clozapine (as robustly responsive patients would have been discharged sooner). It appears likely that these inpatients had limited access to foods other than those provided in the hospital compared with outpatients, who would have had much freer access to their favorite foods. While inpatients appear more reliable in terms of anthropometric and biochemical measurements, assessment of nutritional intake, and adherence to medications, these same factors limit generalizability of the results to outpatients.

In fact, it is worthy of note that (as seen in Table 1 of the article) the mean absolute change in BMI was only 1.1 over a substantial length of follow-up time, corresponding to an absolute increase of 3.5 kg (and a 4.9% relative increase) if one assumes a height of 170 cm (although another caution is an SD that is larger than the mean, implying substantial interindividual difference on this issue). These numbers are very conservative in light of previous reports that found more robust increase in BMI<sup>3</sup> or body weight<sup>4</sup> with clozapine, although confounders such as ethnicity, gender, and smoking habits should be taken into account as well.

Also pertinent is the authors' previous finding<sup>5</sup> of less weight gain in patients who experience less improvement with long-term clozapine treatment. As such, the findings of this study should be replicated, as the authors point out in their discussion, especially among outpatients, who may differ from inpatients in terms of the quality as well as the quantity of their food intake, which is a critical variable in evaluating glucose (as well as other metabolic) dysregulation. The results do not unequivocally rule out the possibility that the contribution of weight on diabetes might have been positive if the magnitude of weight gain were more prominent in the sample studied, which was found to potentially be the case in the general population.<sup>6</sup>

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