

Metformin for the Prevention of Antipsychotic-Induced Weight Gain:

The Optimal Strategy

To the Editor: I read Mulsant and colleagues' letter¹ commenting on Daggolu and Chen's article,² which discussed improved adherence to, and potentially effectiveness of, second-generation antipsychotics (SGAs) coprescribed with metformin. They called attention to an important safety consideration: the association between metformin and vitamin B₁₂ deficiency based on the evidence that the prevalence of B₁₂ deficiency has been reported in 6%–50% of patients with diabetes receiving long-term treatment with metformin.

Indeed, the data concerning the prevalence of B₁₂ deficiency in patients coprescribed antipsychotics and metformin have not been well-studied. However, there is an article researching the influence of SGAs on one-carbon metabolism markers, including vitamin B₁₂, in

schizophrenia.³ The authors found that SGA, including olanzapine and risperidone, may decrease vitamin B₁₂ level after 12 weeks of SGA treatment of first-episode schizophrenia patients. This information may provide readers with a fuller grasp of the relevant issue.

In conclusion, I agree with Mulsant and colleagues' suggestion that clinicians who decide to coprescribe antipsychotics and metformin need to consider the associated risk of B₁₂ deficiency and its neuropsychiatric sequelae. Based on the relevant expert consensus,⁴ prophylactic oral supplementation should be considered in clinical practice to mitigate this risk. Furthermore, I encourage clinicians to use a shared decision-making approach based on individual risk factors and preferences, with the help of the latest guidelines,⁵ including explaining the benefits and drawbacks

of concurrent metformin with patients, when initiating antipsychotics.

References

1. Mulsant LS, Husain MO, Mulsant BH. Concurrent metformin and second-generation antipsychotics: the need to add vitamin B₁₂. *J Clin Psychiatry*. 2026;87(2):251r16260.
2. Daggolu J, Chen H. Effect of concurrent metformin on adherence to and persistence of treatment with second-generation antipsychotics in nondiabetic patients. *J Clin Psychiatry*. 2025;87(1):25m15808.
3. Misiak B, Frydecka D, Łaczmarański Ł, et al. Effects of second-generation antipsychotics on selected markers of one-carbon metabolism and metabolic syndrome components in first-episode schizophrenia patients. *Eur J Clin Pharmacol*. 2014;70(12):1433–1441.
4. Obeid R, Andrés E, Češka R, et al. Diagnosis, treatment and long-term management of vitamin B₁₂ deficiency in adults: a Delphi expert consensus. *J Clin Med*. 2024;13(8):2176.
5. Carolan A, Hynes-Ryan C, Agarwal SM, et al. Metformin for the prevention of antipsychotic-induced weight gain: guideline development and consensus validation. *Schizophr Bull*. 2025;51(5):1193–1205.

Charles Lung-Cheng Huang,
MD, PhD

Article Information

Published Online: April 6, 2026.
<https://doi.org/10.4088/JCP.251r16260b>
© 2026 Physicians Postgraduate Press, Inc.
J Clin Psychiatry 2026;87(2):251r16260b

To Cite: Huang CLC. Metformin for the prevention of antipsychotic-induced weight gain: the optimal strategy. *J Clin Psychiatry*. 2026;87(2):251r16260b.

Author Affiliations: Department of Psychiatry, Chi Mei Medical Center, Tainan, Taiwan; and Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, Taiwan.

Corresponding Author: Charles Lung-Cheng Huang, MD, PhD, Department of Psychiatry, Chi Mei Medical Center, 901, Chung Hwa Rd Yung Kang, Tainan, 710, Taiwan (psychidr@gmail.com).

Financial Disclosure: None.

Funding/Support: None.

ORCID: Charles Lung-Cheng Huang:
<https://orcid.org/0000-0002-7898-1641>