

## CAPSULE COMMENTARIES

# Capsule Commentary on Anthenelli et al., Predictors of Neuropsychiatric Adverse Events with Smoking Cessation Medications in the Randomized Controlled EAGLES Trial



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Psychiatric symptoms are more common among individuals who smoke than among the general population,<sup>1</sup> and are of potential concern to clinicians when patients attempt to quit. This study by Anthenelli et al.,<sup>2</sup> a secondary analysis based on data from their large Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) trial,<sup>3</sup> examined predictors of moderate to severe neuropsychiatric significant adverse events (NPSAEs) with smoking cessation medications. Smokers with and without a history of psychiatric disorders were examined separately. Results showed that NPSAEs were higher among those with a history of psychiatric disorders, and that in both cohorts prior suicidal ideation, current anxiety symptoms, and White race increased the risk. Among those with a history of psychiatric disorders, female sex, younger age, and greater nicotine dependence severity were also predictive of a NPSAE.

This is an important area of investigation given that 4% of smokers in the original study experienced a NPSAE regardless of treatment arm. The analyses leverage the strengths of this large clinical trial, examining risk factors separately by psychiatric history, with adequate statistical power. However, the exclusion of smokers with untreated or unstable mental health conditions and substance use disorders is a limitation. Such individuals deserve inclusion in future research given their potentially heightened risk of symptom exacerbation with smoking cessation medications.

Smoking cessation is a critical public health priority,<sup>4</sup> yet clinicians know little about which smokers are at greatest risk for NPSAEs when they attempt to quit. As anticipated, patients with a history of psychiatric symptoms were more likely to experience NPSAEs, and these patients must remain a key

focus. However, for clinicians, the results also give direction on which factors to be aware of more broadly, apart from history of mental health problems. Specifically, screening smokers for current anxiety symptoms (even at the moderate level), and especially for history of suicidality, could help clinicians plan for careful monitoring of mental health symptoms during the quitting process.<sup>5</sup> Continued research is needed to understand the mechanisms underlying the association of these risk factors with NPSAEs and how to mitigate this risk.

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#### Compliance with Ethical Standards:

**Conflict of Interest:** The authors have no conflicts of interest with this article.

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