

## Letters

### Concerns regarding the recommendation against prescribing selective serotonin reuptake inhibitors in the Canadian guideline for the clinical management of high-risk drinking and alcohol use disorder

The Canadian guideline by Wood and colleagues<sup>1</sup> on the management of high-risk drinking and alcohol use disorder (AUD) highlights an under-recognized issue. Most of the recommendations are well supported, but recommendation 13's caution against the use of selective serotonin reuptake inhibitors (SSRIs) for people with AUD and non-substance-induced major depressive disorder (MDD) or anxiety warrants further consideration given potential unexplored issues.

In support of this recommendation, the guideline cites studies by Charney and colleagues<sup>2</sup> and Friedmann and colleagues,<sup>3</sup> along with a systematic review by Stokes and colleagues;<sup>4</sup> however, these studies have limitations. For example, the study by Charney and colleagues<sup>2</sup> primarily focused on AUD treatment, not depression, making it challenging to draw conclusions on use of SSRIs for AUD with comorbid depression. The study by Friedmann and colleagues<sup>3</sup> used low-dose trazodone, not an SSRI, and did not effectively distinguish between substance-induced and primary depression or anxiety disorders. In essence, these studies were not designed to assess SSRIs' efficacy for AUD with primary MDD or anxiety disorders, so using them to recommend against SSRIs in these cases is inappropriate.

Unlike studies using antidepressant monotherapy in patients with AUD, combining SSRIs with AUD treatment in those with both AUD and MDD has shown important benefits. For instance, Pettinati and colleagues<sup>5</sup> found improved outcomes with sertraline and naltrexone combination therapy. Similarly, Moak and colleagues<sup>6</sup> reported that patients took fewer daily drinks with sertraline and cognitive behavioural therapy (CBT), compared with placebo plus CBT. Integrated

care models for substance use and mental health treatment have also shown promise, improving both depressive symptoms and alcohol use outcomes.<sup>5,7</sup>

Cochrane reviews suggest that SSRIs may help treat MDD, anxiety, AUD, or co-occurring AUD and MDD or anxiety with minimal adverse effects compared with placebo.<sup>8,9</sup> Long-term studies by Cornelius and colleagues<sup>10-13</sup> show fluoxetine's persistent efficacy in reducing depressive symptoms and alcohol consumption in patients with MDD and AUD. Pragmatic trials have not found a significant difference in the antidepressant effects of SSRIs for the treatment of MDD alone compared with MDD and comorbid AUD.<sup>14-16</sup>

Untreated MDD in AUD has consequences; Samet and colleagues<sup>17</sup> found that substance-induced depression predicted post-discharge substance use, while independent MDD worsened alcohol and cocaine use disorders.

The guideline's recommendation advises against prescribing SSRIs for comorbid anxiety disorders and AUD despite limited evidence. However, some evidence suggests SSRIs may help, and strongly discouraging SSRIs is not justified, considering patients may still have debilitating symptoms after trying other treatments like psychotherapy.

In conclusion, the recommendation against use of SSRIs in patients with AUD and comorbid MDD or anxiety is not justified. Although polypharmacy should be minimized whenever possible, there is evidence that SSRIs can be effective for those with AUD and well-diagnosed comorbid MDD or anxiety disorders.

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■ Cite as: *CMAJ* 2024 March 18;196:E346-7. doi: 10.1503/cmaj.149917-1

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**Competing interests:** Anees Bahji is supported by the Canadian Institutes of Health Research (CIHR), the University of Calgary, and the Calgary Health Trust. He also reports consulting fees from the City of Calgary, honoraria from TED-Ed, and

travel grants from the Canadian Psychiatric Association (CPA), the Canadian Society of Addiction Medicine, the American Psychiatric Association, and the American Society of Addiction Medicine. He is an associate editor with the *Canadian Journal of Addiction*, board member with the International Society of Addiction Journal Editors, and co-chair of the Section of Addiction Psychiatry with the CPA. Marlon Danilewitz reports personal fees for advisory board participation, speaker fees, consulting fees, or education grants from Eisai, Otsuka, Janssen, Lundbeck, Winterlight Labs, Rapids Health, Pearls for Primary Care, the BC Psychiatric Association, and the Ontario Brain Institute. He receives a stipend from the CPA for administrative work and has received support for academic meeting attendance and presentations from Ontario Shores Centre for Mental Health Sciences, the Canadian Academy of Addiction Psychiatry, and the CPA. Matthew Sloan receives

funding from the CIHR, the Ontario Ministry of Health and Long-Term Care, Health Canada, the Centre for Addiction and Mental Health Discovery Fund, and the Department of Psychiatry, University of Toronto. He reports honoraria from McGill University Health Centre and travel awards from the Society of Biological Psychiatry and the International Society for Central Nervous System Clinical Trials and Methodology. No other competing interests were declared.

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