## Addiction

# Naltrexone lowers hospital admissions in alcohol use disorder

The risk of hospitalisation for an alcohol-related or other cause is lower when patients with alcohol use disorder are treated with naltrexone alone or in combination with disulfiram or acamprosate, a nationwide Swedish study has found. However, acamprosate monotherapy was associated with an increased risk of hospital admission for an alcohol-related cause.

Study data were gathered prospectively from national registers. Individuals with a diagnosis of alcohol use disorder were identified from four register sources, drug use data from the Prescribed Drug Register (after July 2005), dates of death from the Causes of Death Register, and demographic characteristics from the Longitudinal Integration Database for Health Insurance and Labour Market Studies Register.

All Swedish residents aged 16-64 years registered with a first-time treatment contact for alcohol use disorder between 1 July 2006 and 31 December 2016 were eligible for inclusion in the study.

The study cohort included 125,556 patients (62.5% men) with a diagnosis of alcohol use disorder, mean age 38 years. The median follow-up time was 4.6 years. During the study, 32,129 (25.6%) of the patients used medication for alcohol use disorder: 19,274 (15.4%) used disulfiram, 11,432 (9.1%) acamprosate, 10,872 (8.7%) naltrexone, 693 (0.6%) nalmefene and 6,398 (5.1%) used two or more medications concomitantly.

The primary outcome was the risk of hospitalisation for alcohol-related causes and the secondary outcomes were hospitalisation for any cause, work disability and death.

A total of 30,044 patients (23.9%) were hospitalised for an alcohol-related condition. Naltrexone alone or combined with acamprosate or disulfiram was associated with a significantly lower risk of alcohol-related hospitalisation compared with periods when the same individual did not use any of these medications.

- Naltrexone combined with acamprosate: hazard ratio (HR) 0.74 (95% CI: 0.61-0.89)
- Naltrexone combined with disulfiram: HR 0.76 (95% CI: 0.60-0.96)
- Naltrexone monotherapy: HR 0.89 (95% CI: 0.81-0.97)

Results were broadly similar for the secondary outcome of hospitalisation for any cause.

- Naltrexone combined with acamprosate: HR 0.80 (95% CI: 0.69-0.94)
- Naltrexone combined with disulfiram: HR 0.77 (95% CI: 0.64-0.94)
- Naltrexone monotherapy: HR 0.89 (95% CI: 0.83-0.96)

The use of acamprosate alone was associated with a significantly increased risk of hospitalisation for alcohol-related causes. However, acamprosate monotherapy was not associated with a higher risk of hospitalisation for any cause.

Overall, 7,832 (6.2%) patients died. The adjusted risk of all-cause mortality was not significantly lower with any of the medications studied.

However, 1,211 (2.8%) of patients who used benzodiazepines and related drugs died, and the adjusted risk of all-cause mortality was significantly higher with these drugs; HR 1.11 (95% CI: 1.04-1.19, P = 0.0034).

Overall, 4,719 (4.2%) of patients had sickness absence or received a disability pension during the study period. The use of any of the study medications did not significantly reduce the risk of work disability.

While the mainstay of treatment for alcohol use disorder is psychosocial intervention, combining psychosocial treatments with pharmacotherapy can lead to better outcomes.

Disulfiram, naltrexone and acamprosate are approved for the treatment of alcohol use disorder in the United States and Europe, and nalmefene In Europe. It has been argued that despite their potential these medications are underused, and clinicians' lack of knowledge about the medications and doubts about their effectiveness may contribute to this.

The authors conclude that naltrexone as monotherapy and in combination with disulfiram and acamprosate is associated with a lower risk of hospitalisation for alcohol-related causes and for all causes in those with alcohol use disorder; and as mortality did not increase during periods of drug use, the study results suggest the medications are safe to use.

**DR JEZ THOMPSON**

**Heikkinen M, Taipale H, Tanskanen A et al. Real-world effectiveness of pharmacological treatments of alcohol use disorders in a Swedish nation-wide cohort of 125 556 patients. *Addiction* 2021;116:1990-98**

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