Dispensing of medication for alcohol use disorder; an examination of large databases in a New Zealand context

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ABSTRACT

AIM: To report dispensing of disulfiram, naltrexone, antidepressants and quetiapine for New Zealanders diagnosed with alcohol use disorder.

METHOD: The Pharmaceutical Collection is the national dispensing database for medications in New Zealand. PRIMHD is the national mental health and addiction service database. Dispensing data was extracted from the Pharmaceutical Collection and merged with diagnostic data from PRIMHD to report pharmacological treatment of alcohol use disorders in New Zealand.

RESULTS: In 2014, there were 5,004 individuals diagnosed with an alcohol use disorder by mental health and addiction services. Four hundred and eighty-nine individuals also received a major depressive disorder diagnosis. 2.1% of the group with alcohol use disorder were dispensed disulfiram and 0.7% were dispensed naltrexone. Treatment with antidepressants (12.7%) and quetiapine (5.6%) was more common. In the group with comorbid alcohol use disorder and depression, 2% were dispensed disulfiram, 0.2% were dispensed naltrexone, 27.4% were dispensed antidepressants and 11.2% were dispensed quetiapine.

CONCLUSION: Overall rates of dispensing were relatively low. Antidepressants followed by quetiapine were the most common treatments. In contrast, disulfiram and naltrexone were only used for a minority of clients. This suggests inadequate and poorly targeted pharmacological treatments are used for the treatment of alcohol use disorders in New Zealand.

The established pharmacological treatments for alcohol use disorder are disulfiram, naltrexone and acamprosate.[1–3] In New Zealand, only disulfiram and naltrexone are in receipt of a medsafe indication for alcohol use disorder. Disulfiram is fully subsidised without restriction whereas the initial use of naltrexone requires approval by a clinician in a specialist addiction service. While other medications (topiramate,[4] baclofen[5] and gabapentin[6]) show promise for alcohol use disorder, their current use in New Zealand appears minimal.[7]

The role of antidepressants for alcohol use disorder is limited. Torrens et al[8] completed a meta-analysis evaluating the efficacy of antidepressants for the treatment of alcohol use disorder in the absence of comorbid depression and did not report a significant effect of treatment on alcohol use. For patients with comorbid alcohol dependence and depression, the evidence for antidepressants reducing alcohol use is mixed. Torrens et al[8] did not report significant effects on alcohol use outcomes whereas a recent Cochrane review evaluating antidepressants for people with co-occurring depression and alcohol dependence reported low-quality evidence supporting the use of antidepressants for some alcohol

use outcomes.[9] It is important to note that the effectiveness of antidepressants for improving mood in patients with comorbid alcohol dependence and depression is also limited. Foulds et al[10] reported that large improvements in depressive symptoms occur with the commencement of treatment but additional effects of antidepressants over placebo are small even if depression is thought to be independent from alcohol use.[10] The literature on comorbid anxiety disorders and alcohol use draws similar conclusions. A Cochrane review evaluating pharmacotherapy for anxiety and comorbid alcohol use disorders concluded that there was a small amount of evidence for the efficacy of medications (primarily SSRIs) in reducing anxiety but this was limited and of very low quality.[11] In the same review, there was no evidence that alcohol use was responsive to medication.[11]

Antipsychotics have also been evaluated for the treatment of alcohol use disorder. A systematic review and meta-analysis by Kishi et al reported that antipsychotics, including quetiapine did not improve abstinence or reduce drinking or craving in patients with primary alcohol dependence.[12] Despite this, surveys that evaluate prescribing of antipsychotic medication report that off-label prescribing of antipsychotic medication (often quetiapine) is relatively common for alcohol use disorders.[13] This is despite concerns that quetiapine is misused and associated with rising community level harm through abuse and overdose[14] as well as the metabolic syndrome.[15]

Large databases have burgeoning uses in healthcare and research. One such application is the use of dispensing databases to evaluate the extent and appropriateness of treatment for health conditions. In the US, prescriptions for acamprosate grew heavily following its introduction to the market in 2005 but the absence of diagnostic data meant that other prescribing for alcohol dependence could not be characterised.[16] In Australasia, high rates of antidepressant and antipsychotic (predominantly quetiapine) prescribing have been reported in clinical file reviews and surveys of patients attending treatment settings for addiction.[7,17] In one setting,[7] diagnostic data was also available suggesting that 77.5% of patients attending residential treatment also had a comorbid psychiatric disorder (predominately unipolar depression or anxiety disorders). These studies used self-report to provide a snapshot of medication use for patients undergoing addiction treatment. The advantage of dispensing databases over self-report to estimate medication use is that they provide an accurate measure of medications dispensed to consumers and are likely to provide a more reliable record of medication consumption over time. In this study our goal is to report dispensing of disulfiram, naltrexone, antidepressants and quetiapine for patients diagnosed with alcohol use disorder through the use of dispensing data. We also wish to compare any findings with the evidence base of pharmacological treatment for alcohol use disorder to highlight key issues and make recommendations.

Methods

The Pharmaceutical Collection is a data warehouse containing the vast majority of dispensing data in New Zealand. Dispensing information for all prescriptions for disulfiram, naltrexone, the class of antidepressants, and quetiapine presented in New Zealand between 1 January 2014 and 31 December 2014 was extracted from the Pharmaceutical Collection. We chose these medications for two reasons: firstly; to explore the use of medsafe-indicated medications for alcohol use disorder and secondly; to consider the extent of antidepressant and quetiapine prescribing given the concerns about limited efficacy and widespread use described in the introduction. Dispensing data were provided with a unique identifier and demographic variables (age, sex, ethnicity and deprivation index).[18]

PRIMHD is the national information collection service for the Ministry of Health, New Zealand. The PRIMHD dataset records service activity and outcomes data for all health consumers who receive treatment from public sector secondary care and non-governmental organisation mental health and addiction services.[19] PRIMHD data includes the principal diagnosis for those attending secondary care services. A principal diagnosis is required to be submitted to PRIMHD within 91 days of face-to-face activity. More than one principal diagnosis can be submitted for an episode of care although this is not typical

and for this sample, a comorbid diagnosis is likely to represent a second episode of care. Diagnostic data were extracted from the PRIMHD database for the same study period (1 January 2014 and 31 December 2014). All clients with current diagnoses of alcohol use disorder (encompassing DSM-IV and ICD-10-AM coded Alcohol Abuse and Alcohol Dependence) and DSM-IV and ICD-10-AM coded major depression disorder were identified through the use of the same unique identifier provided for the Pharmaceutical Collection extraction.

Data were provided by the Ministry of Health, New Zealand and were analysed using SAS version [9.4]. Data from the Pharmaceutical Collection and PRIMHD were merged through the use of the unique identifier. This meant that dispensing data were extracted for the group with a diagnosis of alcohol use disorder (in the absence and presence of a comorbid diagnosis of depression). Descriptive analysis was then used to characterise the demographics and dispensing data for this sample.

Ethics approval for this project was granted by the Human Research Ethics Committee of the University of Otago (approval ID HD16/003).

Results

In 2014, there were 5,004 individuals given a diagnosis of alcohol use disorder and 6,959 individuals were given a diagnosis of depression. Four hundred and eighty-nine individuals received a diagnosis of both depression and alcohol use disorder during the study period.

Demographic data were only available from the Pharmaceutical Collection. This means demographic data is reported for the 1,422 individuals who were diagnosed with alcohol use disorder and for whom dispensing data was available. The mean age of the cohort was 52.2 years. 64.9% of the sample were female. The majority were of European ethnicity (85.1%), 10.3% were of Māori ethnicity, 4.2% were of Asian ethnicity and 2.6% identified as Pacifika.

Table 1 reports dispensing data for the group with alcohol use disorder and for the sub-group who received a principal diagnosis for alcohol use disorder and depression in 2014.

For the group with alcohol use disorder, antidepressants were the most commonly dispensed medication (12.7%) followed by quetiapine (5.6%). Only a minority received treatment with disulfiram or naltrexone. The group with comorbid alcohol use disorder and depression were dispensed antidepressants and quetiapine at a higher rate (27.4% and 11.2% respectively) but disulfiram and naltrexone were again only dispensed to a minority.

Table 1: Dispensing for alcohol use disorder.

Alcohol use disorder (n)	**5,004**
Dispensed disulfiram (%)	103 (2.1%)
Dispensed naltrexone (%)	35 (0.7%)
Dispensed antidepressant (%)	636 (12.7%)
Dispensed quetiapine (%)	278 (5.6%)
Alcohol use disorder and depression (n)	**489**
Dispensed disulfiram (%)	10 (2.0%)
Dispensed naltrexone (%)	1 (0.2%)
Dispensed antidepressant (%)	134 (27.4%)
Dispensed quetiapine (%)	55 (11.2%)

Discussion

Pharmacological treatments for patients with alcohol use disorder in a public sector secondary care sample of New Zealanders consists largely of antidepressants and to a lesser degree, quetiapine. A small proportion of our sample were dispensed disulfiram and even fewer received naltrexone. For the sub-group with comorbid alcohol use disorder and depression, antidepressants and quetiapine remained the most frequent treatments, and dispensing of disulfiram and naltrexone occurred for less than 3% of the sample.

These findings have two main implications. Firstly, the majority of the sample are either not receiving pharmacological treatment for alcohol use disorder or are receiving treatment for which the evidence base is limited. Although it is likely that some of the cohort have secondary diagnoses of depression and anxiety made in primary care, antidepressants and quetiapine do not appear efficacious for those with alcohol use disorders without comorbid depression and there is only limited evidence supporting their use in the presence of comorbid depression and anxiety. Secondly, only a minority of the sample with alcohol use disorder received treatment specifically targeting their alcohol use. Although these treatments only confer modest benefits, the evidence base suggests that these are better trialed than antidepressants alone.

Rates of dispensing were lower than surveys assessing medication use among patients attending addiction treatment settings.[7,17] This discrepancy may highlight the key distinction between reported medication use and medication use measured by dispensing databases, which is more likely to reflect the actual health behavior of individuals. Other factors for the apparently low dispensing rates are less clear. It is possible that this group attending secondary care services may have other barriers to receiving pharmacological care such as the relative lack of medical staff in addiction services or lack of confidence in the role of pharmacotherapy by prescribers for this group.

An unexpected finding was the demographic breakdown of those with alcohol use disorder who were also dispensed medication. The gender mix was characterised by a greater proportion of females. This is at odds with epidemiological surveys that report substance use disorder to be more common found among males.[20] However, studies that report dispensing according to gender typically find that women are substantially over-represented in dispensing databases.[21,22] These studies attributed their findings to differences in health seeking behavior between genders and prescribing practices of clinicians. If our finding is replicated, there are implications for the understanding of how people of different gender access and comply with pharmacological treatments for addiction.

Our data cannot tell us why prescribers chose antidepressants and quetiapine over addiction-focused pharmacotherapy. In part, this may relate to lack of information about relative efficacy of different treatment options for prescribers. It may also be that the qualitative experience of alcohol use disorder causes individuals to seek medications that they believe will better alleviate distress over addiction-focused alternatives even when evidence does not support this approach.

Limitations

The Pharmaceutical Collection is a comprehensive national dispensing database capturing the vast majority of prescriptions dispensed in New Zealand. Acamprosate is an exception as it does not receive a government subsidy for use in New Zealand. This means that any dispensing of acamprosate is unable to be measured by the Pharmaceutical Collection. This limits the degree to which our dispensing data can be generalised to countries in which acamprosate is available although it seems unlikely that the broad prescribing trends described in this study will be affected by this limitation.

The PRIMHD dataset was used to provide diagnostic information. The Ministry of Health, New Zealand acknowledge that the PRIMHD dataset is incomplete for two reasons: individuals who have received an episode of care but are not given a diagnosis and individuals who are given non-specific diagnoses that do not accurately reflect their clinical issues.[23] The Ministry of Health also advise that principal diagnoses are more likely to be given for longer episodes

of care. As a consequence, our sample will not include all patient with alcohol use disorder who attended specialty services in 2014 but nonetheless reflects a large scale, real world sample of patients attending secondary services for inpatient or outpatient treatment of alcohol use disorder. The PRIMHD dataset did not provide demographic data. These means we were only able to characterise the sub-sample that were also dispensed medication. We would have liked to explore whether the male:female discrepancy was also present in the overall sample but due to this limitation in the dataset we were unable to examine this possibility further. We consider that these limitations in the PRIMHD dataset mean that absolute rates of dispensing should not be presumed from our study but that the prescribing trends remain valid and deserving of consideration.

In summary, we report evidence that in New Zealand, pharmacological treatment for patients with a diagnosis of alcohol use disorder largely consists of treatment with antidepressants and quetiapine and that alcohol use disorder-focused treatment with disulfiram and naltrexone is limited. We highlight this finding because treatment with antidepressants and quetiapine for alcohol use disorder is largely ineffective despite taking precedence over specific addiction-focused pharmacotherapy. We recognise that prescribing habits are complex and arise in the context of interactions between the scientific literature, and patient and prescriber preference. However, we suggest that current treatments for alcohol use disorder are not optimal and that outcomes could be improved with better adherence to the clinical trial evidence base.

Competing interests:
Dr Beaglehole reports grants from Otago Medical School during the conduct of the study.

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