

The correlates and extent of prescribing of medications for alcohol relapse prevention in England

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ABSTRACT

Aims To determine the pattern and extent of prescribing of medications for alcohol relapse prevention (ARP) in England. **Design** Cross-sectional. **Setting** Specialist drug and alcohol treatment providers in England reporting to the National Drug Treatment Monitoring System. **Participants** Service users aged 18+, with alcohol the primary substance of dependence, completing a treatment journey between April 2013 and March 2016 ($n = 188\,152$). **Measurements** Prescription of medications for ARP during a treatment journey. Data on service users' demographics, treatment and clinical characteristics were extracted. **Findings** The rate of prescribing medications for ARP was 2.1% in 2013/14, 6.8% in 2014/15 and 7.8% in 2015/16. A greater likelihood of prescription was associated with treatment journey year [2014/15; adjusted odds ratio (aOR) = 3.269, 95% confidence intervals (CI) = 3.044–3.510, 2015/16; aOR = 3.823, CI = 3.560–4.106], age (25–34; aOR = 1.622, CI = 1.380–1.907, 35–54; aOR = 1.901, CI = 1.628–2.220 or 55+; aOR = 1.700, CI = 1.446–1.999), female gender (aOR = 1.129, CI = 1.077–1.184), white ethnicity (aOR = 1.219, CI = 1.077–1.380), regional prevalence of alcohol dependence (middle rate; aOR = 1.121, CI = 1.024–1.228), severity of alcohol dependence (moderate dependence without complex needs; aOR = 1.329, CI = 1.244–1.419, severe dependence without complex needs; aOR = 1.308, CI = 1.188–1.441, moderate/severe dependence with complex needs; aOR = 1.131, CI = 1.020–1.255), treatment setting (inpatient; aOR = 10.512, CI = 9.950–11.104, primary care; aOR = 2.264, CI = 2.050–2.500, residential; aOR = 3.216, CI = 2.807–3.685), prior treatment for alcohol dependence (aOR = 1.242, CI = 1.183–1.304), longer treatment journey (aOR = 1.002, CI = 1.002–1.002), more drinking days in the prior 28 days (aOR = 1.021, CI = 1.018–1.024) and drinking a higher number of alcohol units in the prior 28 days (aOR = 1.002, CI = 1.001–1.004). Living in a region of England with the lowest alcohol prevalence was associated with a lower likelihood of prescription of medication for ARP (AOR = 0.491, CI = 0.436–0.552). **Conclusions** In England, medications for alcohol relapse prevention are rarely prescribed (e.g. 7.8% in 2015/16) and those prescriptions appear to be associated with specific service user demographics, treatment and clinical characteristics.

Keywords Acamprosate, alcohol dependence, alcohol relapse prevention, disulfiram, logistic regression, naltrexone, prescribing.

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INTRODUCTION

As many as 70% of those who receive treatment for alcohol dependence relapse to drinking during the first 12 months post-treatment, with the highest rates found in the first 3 months [1,2]. Frequent episodes of withdrawal and resumption of drinking results in kindling, with withdrawal symptoms becoming more severe and a greater risk of

cognitive impairment that may make recovery even more challenging [3]. This 'revolving door' syndrome is putting increased pressure on addiction services which, in England, are facing constant retendering and cuts to funding [4]. Other areas of the health and social care system are also suffering, with alcohol-related National Health Service (NHS) hospital admissions having more than doubled since 2002/03, with an estimated

1.3 million admissions related to alcohol in 2018/19 [5] and the costs of alcohol to the UK economy estimated at £21 billion annually [6]. It can take more than 17 years for new research innovations to reach clinical practice [7]. It is therefore prudent to look to maximizing the treatment options that are already available to reduce alcohol relapse rates and the associated harms and economic burden.

Following initial treatment for alcohol dependence, usually consisting of a medically assisted detoxification, there are three safe, effective and cost-effective medications licensed for use in the United Kingdom for alcohol relapse prevention (ARP): acamprosate, naltrexone and disulfiram [8]. Medications for ARP have significant therapeutic potential with the efficacy and cost-effectiveness of acamprosate, naltrexone and disulfiram consistently demonstrated [8,9]. In a systematic review and meta-analysis conducted by Jonas *et al.* [8] the number needed to treat (NNT) to prevent return to any drinking was 12 for acamprosate and 20 for naltrexone and the NNT to prevent a return to heavy drinking was 12 for naltrexone. The National Institute of Health and Care Excellence (NICE) produced evidence-based guidelines, published in 2009, that recommend the use of acamprosate and naltrexone as first-line treatments and disulfiram as a second-line treatment for alcohol dependence [10]. These medications are not recommended as stand-alone treatments, but in combination with psychosocial intervention to support relapse prevention.

Despite their therapeutic potential, medications for ARP are being underutilized in clinical practice. Using an open cohort design of primary care health record data collected between 1990 and 2013, Thompson *et al.* [11] found just 11.7% of people were prescribed medications for ARP in the first 12 months following a diagnosis of alcohol dependence. Prescription analysis and cost data have found a consistent rise in prescribing of medications for ARP between 2006 and 2015, although this seems to have plateaued more recently [5]. The available research has either been in primary care or is limited in terms of explaining the pattern of prescribing of these medications. Better estimates of prescribing are required to understand the extent of the problem of underutilization of safe and effective medications for alcohol relapse prevention. This research aims to: (1) determine the extent of prescribing of medications for ARP in England; and (2) test for associations between prescribing and service users' demographic and clinical characteristics.

METHOD

This research was approved by the Health Research Authority London Fulham Research Ethics Committee (reference number: 18/LO/0644) on 18 April 2018.

Data source

The National Drug Treatment Monitoring System (NDTMS) is a reporting system of all service users receiving treatment by specialist community and residential publicly funded drug and alcohol treatment providers in England [12]. The NDTMS is designed and maintained by the National Drug Evidence Centre at the University of Manchester on behalf of Public Health England. Episodes of care are recorded that can be linked to form individual treatment journeys. A treatment journey is defined as:

'One or more episodes of structured treatment, at one or more providers, where there has been less than 21 days break between treatment episodes. A treatment journey ends once a client has been exited entirely from structured drug/alcohol treatment once all structured interventions and the episode have been closed. A client may be discharged from one provider but if they continue structured treatment (within 21 days of discharge) at another provider, their NDTMS treatment journey is continued' ([12], p. 68).

The type of treatment received for each treatment episode that makes up a treatment journey is recorded in the NDTMS as psychosocial or pharmacological. In November 2012, differentiation of pharmacotherapy for withdrawal or ARP was made.

Inclusion/exclusion criteria

For the current research, data were extracted for service users completing a treatment journey between April 2013 and March 2014, April 2014 and March 2015 and April 2015 and March 2016. If a treatment journey extended over the year boundary, a treatment journey is counted within the year it ended. Data were extracted for service users who: (1) reported alcohol as their primary substance of dependence; (2) were aged 18+ at the start of their treatment journey; (3) had consented to their data contributing to the NDTMS; (4) were not pregnant; and (5) treatment type was recorded (differentiation of withdrawal and relapse prevention medications).

Predictor variables

Data on participant characteristics at the start of their treatment journey was extracted including: age group (18–24, 25–34, 35–54, 55+), gender (male, female), ethnicity (white, mixed, Asian/Asian British, black/black British, other ethnic), local authority of residence, treatment for a mental health condition (yes/no), acute housing problem (yes/no) and adjunctive use of benzodiazepines, cocaine or opiates during the treatment journey (yes/no). The variable for ethnicity was collapsed into two categories, white and other ethnicity, due to small numbers of

participants in non-white ethnic groups. The local authority of residence was categorized according to the estimated rate of alcohol dependence [13]. Local authorities were grouped into the highest, middle and lowest rates of alcohol dependence per 100 of the adult population (see Supporting information, Table S1).

Treatment episode details that were extracted included: intervention setting at the start of the treatment journey (community, inpatient unit, primary care, residential) and prescription of ARP medication during the treatment journey (yes/no). The treatment journey details extracted were: treatment journey length (days), number of drinking days in the previous 28 days at the initial triage and typical units (equivalent to 10 ml (8 g) of pure alcohol) of alcohol consumed on a drinking day at initial triage and whether previous treatment for alcohol dependence has been received (yes/no).

A proxy measure of severity of alcohol dependence was constructed using the number of alcohol units consumed in the past 28 days that is reported at initial triage and an indication of complex needs through the reporting of (1) treatment for a mental health condition, (2) urgent housing need or (3) adjunctive use of benzodiazepines, crack cocaine or opiates [14]. Four severity of alcohol dependence categories were created following the methodology of Brennan *et al.* [14]: mild dependence with or without complex needs (drinking 0–15 units/day and 0–3 indicators of complex needs), moderate dependence without complex needs (drinking 16–30 units per day and 0 indicators of complex needs), severe dependence without complex needs (drinking 31+ units per day and 0 indicators of complex needs) and moderate or severe dependence with complex needs (drinking 16–30 or 31+ units per day and 1–3 indicators of complex needs).

Statistical analysis

An estimation of the proportion of service users receiving medications for ARP during a treatment period for the years 2013/14, 2014/15 and 2015/16 was calculated.

Univariable logistic regression was used to explore the independent association between demographic and clinical factors and receiving medication for alcohol relapse prevention during a treatment journey. Predictor variables included the treatment journey year, age group, gender, ethnicity, regional prevalence of alcohol dependence, journey length, drinking days, severity of dependence, treatment setting, previous treatment and treatment for a mental health condition. All potential predictors were entered into a multivariable binary logistic regression. All analyses were conducted using IBM SPSS Statistics version 26 [15]. This analysis was not pre-registered and the results should be considered exploratory.

RESULTS

Data were extracted for 188 152 people who met the study criteria. Participant demographics and characteristics are presented in Table 1 and Supporting information, Table S2. Approximately two-thirds of the sample were male (66.6%), more than half were aged 35–54 (58.6%) and the majority were of white ethnicity (96.0%). Only 2.1% of the sample had been prescribed medication for alcohol relapse prevention during a treatment journey that ended in the year 2013/14, which rose to 6.8% in 2014/15 and 7.8% in 2015/16 (Table 1).

The results of the univariable binary logistic regression are presented in Table 2. Completing a treatment journey in a later year, in an older age group, female gender, white ethnicity, greater severity of alcohol dependence, receiving treatment as an inpatient, residential or in primary care, having received treatment for alcohol dependence prior to their current journey, a higher number of drinking days prior to treatment initiation, drinking a higher number of alcohol units prior to treatment initiation and a longer treatment journey length was associated with a greater likelihood of being prescribed medication for ARP. Receiving treatment for another mental health condition and living in a region of England with the lowest or middle rates of prevalence was associated with a lower likelihood of being prescribed medication for ARP. The number of complex needs that a service user had was not associated with prescription of medication for ARP.

All variables of interest were included in a multivariable logistic regression model, the results of which are presented in Table 2. The model fitted the data well: $\chi^2 = 125.363$ [8], $P < 0.001$ (Nagelkerke $R^2 = 0.206$, Cox & Snell $R^2 = 0.073$). Characteristics that were associated with a greater likelihood of being prescribed medication for ARP during a treatment journey were: completing a treatment journey in 2014/15 or 2015/16, being in an older age group, female gender, white ethnicity, living in a region of England with a middle rate of prevalence of alcohol dependence, a greater severity of alcohol dependence, receiving treatment as an inpatient, residential or in primary care, receiving treatment for alcohol dependence prior to the current journey, a higher number of drinking days prior to treatment initiation, drinking a higher number of alcohol units prior to treatment initiation and a longer treatment journey length. Living in a region of the United Kingdom with the lowest rates of prevalence of alcohol dependence was associated with a lower likelihood of being prescribed medications for ARP. Receiving treatment for another mental health condition and the number of complex needs were not significantly associated with ARP medication prescribing when controlling for other factors.

Table 1 Participant demographic and clinical characteristics for those prescribed and not prescribed alcohol relapse prevention medication during a treatment journey.

	No ARP medication	ARP medication
Year journey ended		
2013/14	57 055 (97.9)	1230 (2.1)
2014/15	61 281 (93.2)	4440 (6.8)
2015/16	59 133 (92.2)	5013 (7.8)
Age, years, <i>n</i> (%)		
18–24	9036 (97.7)	217 (2.3)
25–34	34 814 (95.4)	1673 (4.6)
35–54	103 217 (93.6)	7005 (6.4)
55+	30 402 (94.4)	1788 (5.6)
Gender, <i>n</i> (%)		
Male	118 311 (94.4)	6977 (5.6)
Female	59 158 (94.1)	3706 (5.9)
Ethnicity, <i>n</i> (%) ^a		
Other	6998 (95.1)	359 (4.9)
White	167 256 (94.3)	10 173 (5.7)
Prevalence of alcohol dependence, <i>n</i> (%)		
Highest	9942 (93.4)	708 (6.6)
Middle	143 878 (94.0)	9136 (6.0)
Lowest	23 649 (96.6)	839 (3.4)
Severity of dependence, <i>n</i> (%) ^b		
Mild dependence with or without complex needs	62 872 (96.2)	2472 (3.8)
Moderate dependence without complex needs	52 945 (93.2)	3833 (6.8)
Severe dependence without complex needs	22 013 (92.1)	1882 (7.9)
Moderate or severe dependence with complex needs	26 735 (93.3)	1927 (6.7)
Treatment setting, <i>n</i> (%)		
Community	160 727 (96.4)	6038 (3.6)
Inpatient	7817 (67.8)	3711 (32.2)
Primary care	6303 (91.7)	569 (8.3)
Residential/recovery house	2622 (87.8)	365 (12.2)
Previous treatment, <i>n</i> (%) ^c		
No	70 040 (96.0)	2939 (4.0)
Yes	98 915 (93.3)	7119 (6.7)
Treatment for a mental health condition, <i>n</i> (%) ^d		
No	133 988 (94.2)	8322 (5.8)
Yes	33 149 (94.5)	1915 (5.5)
Number of complex needs, <i>n</i> (%) ^e		
0	123 490 (94.2)	7610 (5.8)
1	38 515 (94.4)	2265 (5.6)
2	3028 (92.5)	246 (7.5)
3	138 (92.6)	11 (7.4)
Number of drinking days, mean (IQR) ^f	27 (16)	28 (6)
Typical units per drinking day, median (IQR) ^g	20 (19)	24 (16)
Journey length (days), median (IQR)	120 (138)	182 (231)

Missing data: ^a3,366 (1.8%), ^b13,473 (7.2%), ^c9,139 (4.9%), ^d10,778 (5.7%), ^e12,849 (6.8%) ^f2,701 (1.4%), ^g2,701 (1.4%). ARP = alcohol relapse prevention; IQR = interquartile range.

DISCUSSION

The rate of prescribing of medications for ARP increased by 5.7% between 2013/14 and 2015/16, although it remained low at just 7.8% in 2015/16. Completing treatment for alcohol in more recent years (i.e. 2014/15 or 2015/16), older age, female gender, white ethnicity, living in a region of England with a middle-rate prevalence of

alcohol dependence, greater severity of alcohol dependence, receiving treatment in an inpatient, residential or primary care setting, having received prior treatment for alcohol dependence, longer treatment journey length, more drinking days in the 28 days prior to treatment initiation and drinking more units of alcohol in the 28 days prior to treatment initiation were associated with a greater likelihood of being prescribed medications for ARP. Living

Table 2 Univariable and multivariable binary logistic regression of participant demographic and clinical characteristics associated with the prescription of medications for alcohol relapse prevention for participants completing their treatment journey.

	Univariable		Multivariable	
	OR (95% CI)	P	OR (95% CI)	P
Year journey ended				
2013/14				
2014/15	3.361 (3.152–3.584)	< 0.001	3.269 (3.044–3.510)	< 0.001
2015/16	3.932 (3.691–4.190)	< 0.001	3.823 (3.560–4.106)	< 0.001
Age, years				
18–24				
25–34	2.001 (1.734–2.309)	< 0.001	1.622 (1.380–1.907)	< 0.001
35–54	2.826 (2.465–3.240)	< 0.001	1.901 (1.628–2.220)	< 0.001
55+	2.449 (2.123–2.825)	< 0.001	1.700 (1.446–1.999)	< 0.001
Gender				
Male				
Female	1.062 (1.020–1.107)	0.004	1.129 (1.077–1.184)	< 0.001
Ethnicity				
Other				
White	1.186 (1.064–1.321)	0.002	1.219 (1.077–1.380)	0.002
Prevalence of alcohol dependence				
Highest				
Middle	0.892 (0.824–0.965)	0.005	1.121 (1.024–1.228)	0.014
Lowest	0.498 (0.450–0.552)	< 0.001	0.491 (0.436–0.552)	< 0.001
Severity of dependence				
Mild dependence with or without complex needs				
Moderate dependence without complex needs	1.841 (1.748–1.939)	< 0.001	1.329 (1.244–1.419)	< 0.001
Severe dependence without complex needs	2.174 (2.044–2.313)	< 0.001	1.308 (1.188–1.441)	< 0.001
Moderate or severe dependence with complex needs	1.833 (1.724–1.949)	< 0.001	1.131 (1.020–1.255)	0.020
Treatment setting				
Community				
Inpatient	12.637 (12.060–13.242)	< 0.001	10.512 (9.950–11.104)	< 0.001
Primary care	2.403 (2.197–2.628)	< 0.001	2.264 (2.050–2.500)	< 0.001
Residential/recovery house	3.706 (3.311–4.147)	< 0.001	3.216 (2.807–3.685)	< 0.001
Previous treatment				
No				
Yes	1.715 (1.641–1.792)	< 0.001	1.242 (1.183–1.304)	< 0.001
Treatment for a mental health condition				
No				
Yes	0.930 (0.884–0.979)	0.005	0.951 (0.862–1.049)	0.316
Number of complex needs	1.013 (0.972–1.055)	0.549	0.990 (0.899–1.091)	0.846
Number of drinking days	1.047 (1.045–1.050)	< 0.001	1.021 (1.018–1.024)	< 0.001
Typical units per drinking day	1.009 (1.009–1.010)	< 0.001	1.002 (1.001–1.004)	0.007
Journey length (days)	1.003 (1.002–1.003)	< 0.001	1.002 (1.002–1.002)	< 0.001

OR = odds ratio; CI = confidence interval.

in a region of England with the lowest prevalence rate was associated with a lower likelihood of being prescribed medication for ARP.

Data recorded in the NDTMS represent all prescribing by specialist community and residential publicly funded drug and alcohol treatment providers in England. These services are usually responsible for initiation of prescribing of medications for ARP with prescriptions continued in primary care, as recommended by NICE [10]. Although additional initiation of ARP medication prescribing may occur in primary care and within privately funded drug and

alcohol treatment services, the NDTMS captures the majority of initial prescriptions of ARP medications. NICE recommends medications for ARP as a first-/second-line treatment in conjunction with psychological therapy. Although there will be a proportion of service users who are unable to take medications to support ARP due to contraindicated conditions (e.g. severe hepatic or renal impairment), the rates of prescribing found in this study can be considered low. The low rates of prescribing found in this study are in keeping with research in primary care [11] and prescription analysis and cost data in the United

Kingdom [5]. Low rates in prescribing of medications for ARP are not unique to the United Kingdom, with similarly low rates reported in Australia [16], the United States [17] and Germany [9]. The findings of the current research suggest that medications for ARP are being prescribed as a last resort, rather than as first- or second-line treatments as recommended by NICE, with older age, longer treatment journey length and having received treatment previously for alcohol dependence associated with a greater likelihood of being prescribed medications for ARP. It is estimated that up to 70% of individuals relapse during the first 12 months following treatment for alcohol dependence, with the initial 3 months being the most vulnerable time [2]. Given the established efficacy of these medications (see [8,10]), the low rates of prescribing indicate a missed opportunity to provide additional evidence-based support for those in recovery from alcohol dependence that has the potential to reduce the high rates of relapse to drinking. The current research also found that those who were more severely dependent were more likely to be prescribed medication for ARP. This was also supported by a greater likelihood of being prescribed medications for ARP for those who were drinking on more days at treatment entry and those who received treatment as an inpatient or in a residential setting. This is in keeping with NICE guidelines, that recommend medications for ARP be prescribed to those who are moderately or severely alcohol -dependent.

The reasons for low rates of prescription of medications for ARP despite their proven efficacy are likely to be complex and multi-faceted. This research found that there was a lower likelihood of being prescribed medications for ARP for service users living in regions of England with the lowest prevalence rates, suggesting some geographical inequalities in treatment access in England. Morley *et al.* [18] found lower dispensing ratios of acamprosate and naltrexone for those in the most socially disadvantaged groups and those living in more remote locations. Further research is needed to investigate the potential socio-economic and geographical variations in access to medications for ARP in England. Research has consistently identified limitations in skills and knowledge of medications for ARP as a barrier to them being prescribed [19–24]. Cuts to the budget to provide specialist alcohol services in England has raised concerns about a reduction in specialist addiction psychiatrists, clinical psychologists and nurses [4]. Concerns about the safety and efficacy of medications for ARP [21,25–27], perceptions of service user need or demand [19,21,25], access to a prescriber within a health-care service [19,24,25,28,29] and the cost of medications and insurance coverage [22,23,25,30–32] have also been identified as barriers to prescribing. Another potential barrier may be comorbid physical health conditions; for example, severe hepatic impairment that may preclude prescribing [10]. Little research has focused upon

the service-user perspective. Mark *et al.* [22] conducted focus groups with service users who had received treatment for alcohol dependence in the previous 3 years. Willingness to take medications, perceptions of the addiction potential of medications and awareness of medications for ARP were identified as barriers. More recently, Haley *et al.* [33] conducted interviews with service users with an alcohol use disorder to establish attitudes to medications for ARP. Concerns regarding the medication's effectiveness and potential drug interactions and side effects were found to be potential barriers to being prescribed medications for ARP. Strategies to address these barriers to prescribing medications for ARP need to be developed and implemented in health-care systems to increase the utilization of medications for ARP.

Research to investigate methods of increasing the utilization of medications for ARP has taken place in the United States. A pilot study of a multi-faceted educational intervention for improving acceptance of naltrexone found improved knowledge of naltrexone and utilization of this knowledge in practice [34]. The introduction of a medication management group, established to address clinicians' concerns of the time burden of ongoing medication management, resulted in a threefold increase in prescribing rates [35]. A significant 3.4% increase in prescription of medications for ARP was achieved using a multi-faceted educational outreach programme within the Veterans Health Administration (VHA) in the United States [36]. This research group completed further work using a multi-faceted approach, including educational outreach, aimed at three stakeholder groups: local clinical champions, primary care prescribers and service users [37]. Although there was an increase in rates of prescription of medications for ARP following introduction of the intervention, it was not significant compared to rates of prescribing at control sites.

Limitations

This research used a large data set of all service users attending publicly funded alcohol treatment services in the United Kingdom. However, the research results must be interpreted while considering some limitations. The NDTMS does not record a formal diagnosis of alcohol dependence using ICD or DSM criteria, and it only began recording severity of alcohol dependence questionnaire (SADQ) scores in April 2017. Therefore, there is no severity of alcohol dependence measure available prior to this year. A proxy measure for severity of alcohol dependence was used that had been established through expert consultation [14]; however, it may still not be an accurate reflection of dependence severity. The NDTMS only records data from publicly funded alcohol treatment providers in England; it does not capture prescriptions initiated in privately funded

drug and alcohol services. A further limitation that must be considered is that differentiation between the medications for ARP was not possible. There may be variations in prescribing rates and correlates that could not be identified in this research.

CONCLUSION

Medications for ARP are underutilized for the treatment of alcohol dependence in England. Strategies to increase their use in clinical practice are needed to support service users' efforts to remain alcohol free and reduce the health and social harms associated with relapse to drinking.

Declaration of interests

None.

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Author contributions

Kim Donoghue: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 England Local Authority banding by estimated prevalence of alcohol dependence.

Table S2 Participant demographic and clinical characteristics for the whole sample.