The epidemiology of alcohol use disorder and public health policies to tackle alcohol-related harm: a case study of Scotland and the minimum unit pricing for alcohol.

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Abstract

Alcohol use disorder (AUD) in Scotland is a public health concern. In 2021, it was estimated that 23% of the Scottish population drank at hazardous or harmful levels, and 17% of children lived with at least one parent with AUD. In 2015, AUD contributed to 6.5% of all deaths. Alarmingly, Scotland also has high figures on alcohol-related harms compared to neighbouring UK nations like England and Wales. For instance, in 2018, Scottish alcohol-specific death rates were nearly twice as high for men and 87% higher for women compared to England & Wales; consumption was also higher in Scotland, with 9% more alcohol sold per adult in 2019 than in England. Moreover, alcohol-related harms affect some population groups more severely than others, with important implications for health inequalities. In the last two decades, the Scottish Government has introduced a series of public health strategies to tackle alcohol-related harms and the associated inequalities. The last being minimum unit pricing (MUP) for alcohol, a novel pricing policy whose promising results made the country a pioneer in introducing and evaluating population-level interventions to help reduce alcohol-related harms.

Recent studies found societal inequalities among the potential causes of the incidence of substance-related harm (including alcohol) in a population. A possible explanation is that the disadvantaged socio-economic position, jointly with the constant comparison with those in more privileged positions and a general lack of opportunity may push individuals into mental health struggles and/or in a need to escape from reality and, consequently, more vulnerable to substance use disorders when exposed.

The legal nature of alcohol and its social acceptability made the number of individuals in Scotland misusing alcohol considerably higher compared to illegal drugs, with consequent greater associated mortality in the population. Summarising, both the lawful nature of alcohol consumption and the high incidence of AUD results in a need for policy specific approaches to tackle the phenomenon.

To design policies aimed at tackling alcohol-related harm and the inequality associated with its burden, a deep understanding of the epidemiology of alcohol-related harm is needed. In particular, acknowledging that the disadvantage and health inequality caused by excessive alcohol consumption is only a reflection of a deeper cause of inequality is crucial. The process which epidemiology informs the design of a policy could be simplified in three sequential and recurrent steps. Firstly, the epidemiology identifies trigger points as well as

potential clinical and societal consequences in a theory of change which can inform policy makers on relationships to focus on to build an effective policy. Secondly, after the implementation of the policy, epidemiology (through both qualitative and quantitative investigations) can suggest the policy evaluation process highlighting the most appropriate outcomes and subpopulations to inquire. Lastly, based on the outcome of the evaluation, epidemiology can update the theory of change as well as recommend amendments to the policy to improve its efficacy. The succession of the first epidemiology assessment, policy implementation and policy evaluation is supposed to be a cyclical and iterative process, tending to the most efficient policy design.

The main body of this thesis are eight published articles on alcohol epidemiology. As articles were originally designed for different purposes, they are accompanied by an essay aimed to show the cohesion among them. In particular, the essay uses evidence from the published papers to describe the iterative process between epidemiology, policy implementation and evaluation using MUP, the most extensively analysed alcohol policy in Scotland, as a case study (three studies presented here regard MUP). The thesis also comments and discusses how MUP has been evaluated and the potential bias and sub-optimal communication between researchers and policy makers. The discussion on MUP evaluation refers mainly to the Public Health Scotland (PHS) report published in 2023, which was the main source for collecting the available evidence to inform the Scottish Government on whether to continue, suspend or reshape the policy.

Overall, the evidence shows that MUP is an effective policy in reducing alcohol consumption, but it affected the population differently and with divergences compared to what was originally theorised. While population groups with a higher incidence of alcohol-related harm are generally more affected by the policy (with a consequent reduction of health inequality), within such groups, evidence suggests that individuals with alcohol dependence were less affected. Moreover, there is evidence that most of the acute outcomes reflecting alcohol harm in societies theorised to be impacted (such as road traffic accidents and crime) were not affected. This underlines how specific societal outcomes or vulnerable subgroups need more targeted strategies and that one policy can benefit some but not everyone. Expected and unexpected results should be similarly communicated to put such complementary strategies into action. A potentially unbalanced communication of positive (expected) results to policy makers and the public opinions risk to create a sense of accomplishment and slow down a more comprehensive and structural policy action.

The publications of this thesis can be divided in two sections, each of them containing four studies. The first section named *Clinical epidemiology of AUD,* highlights some patterns in AUD patients (e.g., specificities of relapses and treatment). The second one, named *Evaluation of public health policies on AUD* is an assessment of certain policies (MUP and Covid lockdown) on specific outcomes. The explicatory essay, after a general introduction collocating studies under the same general context, uses evidence from the first section, together with other literature, to leverage the mechanisms of risk factors as a suggestion to complement MUP-like blanket policies that do not impact equally all those in need.

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In this regard, I would like to explicitly mention all the friends I had shared an office with in Lilybank Gardens. You have been the ears listening my rants, consoling (and sometimes counselling) me, a source of conversation, laughs, energy and the sunbeam making a warm smile in the gloomy Glaswegian weather (chronological mention to: Dikshyanta, Giorgio, Nicola, Heather).

A thank to my 2023, a though year that allowed me to stop, settle and see things from a different perspective. And thank you to all the friends, many of them mentioned in the previous paragraph, that made me think and realise this.

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Last year was 'fun', thank you to be there sharing the burden with me :)

A mia zia, alla mia famiglia, ai miei amici.

[…]
Suppose I thought that by this moment I would have it figured out
But instead I tend to spend my days consumed by seeds of doubt
I know, I can, I won't

Oh darling it goes on and on and on
Always forever 'til I'm barely holding on
End of my tether and I know it won't be long, it won't be long 'til it's gone

So here's to my beautiful life
That seems to leave me so unsatisfied
No sense of self but self-obsessed
I'm always trapped inside my fucking head
On and on and on, on and on and on
On and on and on, on and on and on said
Thought I'd be happier somehow
If you were wondering how I'm feeling now

I try to tell myself my best days are the ones that lie ahead
But I'm always looking back on things I wish I'd never said
I know, I can, I won't
…
…
I won't lie
I'm a mess yeah
But I'll get there
Now I won't lie
I'm a mess yeah
But I'll get there

Lewis Capaldi, How I'm feeling now

I wanted to put this lyric by Lewis Capaldi, a Glaswegian artist, not uniquely to thank Glasgow, which welcomed me for more than 6 years, but for what it has represented to me in the recent past. I listened quite compulsively to this song during the writing process of this thesis which coincided with when I was forced at home due to 'force majeure'. It reflected some of the mental health struggles I lived due but not only limited to my recent health 'adventures'. At the end of the day, this thesis talks about alcohol use disorders and as they are mental health conditions, I did not find this citation completely out of context.

"The majority of scientific progress is measured by improvements in the questions
we ask rather than the finality of our answers".

Judith Grisel on addiction research in her didactic book on Addiction

Author's declaration

I declare that, except where explicit reference is made to the contribution of others, that this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Francesco Manca

Introduction

Drinking alcohol is widely legally and socially acceptable, however, more than 1% of the global population has an alcohol use disorder (AUD)[1], defined as conditions identified by compulsive alcohol seeking and use, despite harmful consequences.

In 2018, the World Health Organization (WHO) reported that 5.3% of overall deaths and 7.3% of premature deaths worldwide were attributable to the harmful use of alcohol.[2] The mortality resulting from alcohol consumption is higher than that caused by several communicable and non-communicable diseases (e.g. tuberculosis, HIV/AIDS and diabetes)[2] commonly considered more severe health and social threats.

In 2016, in the UK, the average alcohol consumption per capita (i.e., quantity of alcohol per person per year in the 15+ years population) was 11.4 litres, exceeding the world average by 5 litres[2]. However, consumption is heterogeneous across the country. In Scotland, consumption levels have been consistently higher than in England, with most of the difference being accounted for by alcohol sold off-trade (with an average cheaper price)[3]. Consumption also led to higher figures related to alcohol-related harm and deaths: in 2018, Scottish alcohol-specific death rates were nearly twice as high for men and 87% higher for women compared to England & Wales[3]. After the covid-pandemic, consumption patterns changed, and while overall consumption decreased, there was evidence of an increase within specific high-risk groups, generating a rise in alcohol-related harm and deaths[4].

Introduction to alcohol-related harm and the Scottish context

While analysing alcohol-specific deaths can provide valuable insights into the extent of mortality directly linked to alcohol consumption in a population, it is essential to recognize that they represent only a subset of all alcohol-related deaths. Indeed, alcohol-related deaths include also all deaths where alcohol is a contributing factor, but not necessarily the sole cause. Furthermore, the harm associated with alcohol consumption extends beyond mortality and the health sphere, as it can also significantly impact the social realm. Similar to its role in mortality, alcohol's causal role in both social and health issues is predominantly contributory rather than the only cause for most problems[5].

Babor et al. [5] built a logic model linking alcohol consumption, mediating variables (toxicity, intoxication and dependence) and harm (long and short-term) to the consumer as well as to others (Figure 1).

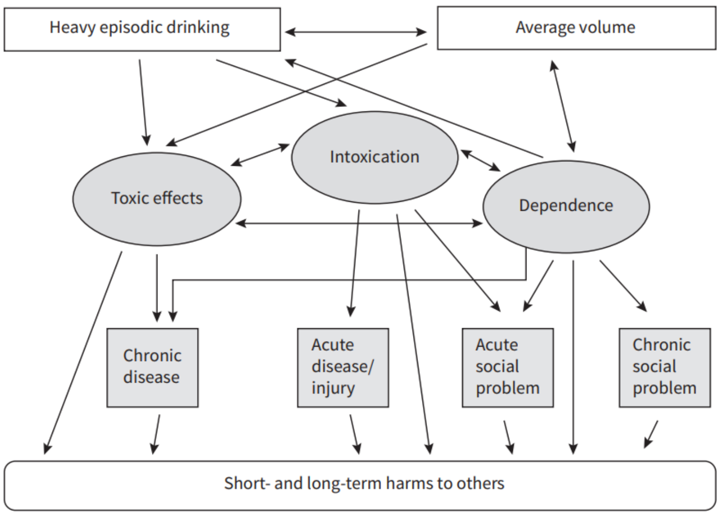

Figure 1. Relationship between alcohol consumption patterns, mediating variables and consequent harm [5].
Source: https://onlinelibrary.wiley.com/doi/epdf/10.1111/add.16003

Alcohol consumption patterns are usually characterised by heavy drinking occasions and average volume consumption. A wide range of factors can shape patterns and levels of alcohol consumption and then the consequent harm. For instance, patterns can be shaped by drinking setting (private or public) and social macro- (e.g., the overall socio-economic status[6, 7], social, but also social norms[8] etc.) and micro- contexts (e.g., peer pressure[9], family history[10], etc.), but also by the personal sphere (genetics[11], gender[12], marital status[13]). While specific drinking patterns can lead to AUD, not all alcohol-related problems are caused by AUD.

Most of the harm (direct and indirect) comes from episodic intoxication or binge drinking consumers and only a small number is related to high-risk AUD[5] (prevention paradox[14]). Therefore, a comprehensive epidemiological analysis of alcohol-related harm goes beyond the AUD population only and should identify the various consumption patterns leading to various harm. Identifying the main risk factors influencing patterns and more vulnerable populations should help to design effective prevention strategies. A comprehensive policy strategy should include a combination of primary, secondary and tertiary prevention. An effective bundle of approaches should be evidence-based, with the weight of each approach reflecting specific consumption patterns and the population groups contributing to the alcohol-related harm in society.

Reversing the order of the logic model in Figure 1, the uneven distribution of the harm in society is linked to different consumption patterns which in turn can be attributed to the varying degrees of risk factors present across subpopulations. The reason behind the alcohol-harm paradox (the fact that more socio-economic deprived groups consume less alcohol but experience more alcohol-related harms) may indeed lie in consumption patterns specific to certain subpopulations[15]. These patterns can be induced by local contexts (e.g., higher availability of cheap alcohol in more deprived areas[16]) as well as a lower capability of more vulnerable populations to cope with the harm[7], which may be due to limited access to resources and potential greater mental health fragility.

The distribution of the consumption and harm in Scotland reflects the trends just described. Non-drinkers are more frequent in more socio-economic deprived areas compared to the least deprived areas, which also have a greater prevalence of hazardous or harmful drinkers (28% vs 19%)[17]. However, among those drinking at harmful levels people in more deprived areas drink, on average, more units per week, indicating potentially more risky consumption patterns[17]. The greater direct harm of these populations is reflected also in deaths and hospital stays, which are 4.3 and 7 times higher in more deprived areas compared to least deprived[18, 19]. Latest figures for Scotland (2022) show 1,276 alcohol-specific deaths, a constant growth since 2019[5]. Overall, in 2024, alcohol harm in Scotland was estimated to cost between £5 and 10 billion per year, including health but also social costs such as labour, productivity loss and crime[20].

The extent of the problem, jointly with higher value of harms compared to other neighbouring countries raised public health concerns within the Scottish Government related to alcohol. In the last two decades the Scotland has introduced a series of policies (mostly built on primary prevention approaches) to tackle alcohol consumption and the related harm. The most recent is the minimum unit pricing (MUP) for alcohol, making the country a pioneer in implementing new policies worldwide.

Thesis aim and structure

The format of this thesis is retrospective by published work. The current essay is meant to accompanying the eight study publications constituting the main part of this thesis and having a common research theme summarised in the title *The epidemiology of alcohol use* *disorder and public health policies to tackle alcohol-related harm: a case study of Scotland and the minimum unit pricing for alcohol.*

All papers focus on Scotland and can be classified into two main categories: (i.) *Clinical epidemiology of AUD* and (ii.) *Evaluation of public health policies on alcohol-related harm*. Each category consists of four papers. While the first group emphasizes tertiary care and prevention, the second analyses policies aimed at reducing alcohol exposure and consumption in the general population (primary prevention). The essay aims to bridge these two categories by highlighting how blanket policies may have varying effects across different populations, with both potential positive and adverse impacts on the distribution of the alcohol-related burden within society. The discussion section emphasizes the importance of a deep understanding of AUD epidemiology and alcohol-related harm as the foundation not only for planning but also for evaluating AUD policies, ultimately improving public health strategies through such evaluation exercises.

All the papers in this thesis used nationwide routine Scottish datasets, allowing my research questions to focus on the entire Scottish population. Therefore, the results and conclusions are fully representative of the Scottish population, and the generalization of findings is discussed in each manuscript.

In the papers and in the rest of the manuscript I reason on how policies can diversely affect different consumer groups. For simplicity, I define here the alcohol consumer groups I refer to (and sometime implicitly refer to) hereafter. Namely, low risk consumers (those drinking below guidelines 14 units per week for women and 21 units for men); hazardous drinkers (sometimes labelled as heavy drinkers): those consuming 14-35 and 21-50 units for female and male, respectively. Harmful drinkers are those drinking over these thresholds. This classification was based on the 1995 Chief Medical Officers guidelines[21]. Despite the update of such guidelines and the use of wider classes[22], such classification is still used in recent studies to define consumer types [23, 24].

The next section of this essay is divided into two parts according to the aforementioned papers categorisation and aims to provide a general context common to all the studies. This general context is then followed by the discussion session. The full papers are attached at the end of this opening essay. Their titles are reported at the end of this subchapter. To ease the reading and distinguish the papers part of this thesis from the rest of the literature they are referenced as Paper 1-8, see notation below.

Publications

Clinical epidemiology of AUD

Paper 1.
Manca, Francesco; Lewsey, Jim. Hospital discharge location and socioeconomic deprivation as risk factors for alcohol dependence relapses: A cohort study. *Drug and alcohol dependence*, 2021, 229: 109148.

Paper 2.
Manca, Francesco, et al. Pharmacological treatments for alcohol dependence: Evidence on uptake, inequalities and comparative effectiveness from a UK population-based cohort. *Drug and Alcohol Review*, 2024.

Paper 3.
Manca, Francesco; Lewsey, Jim. Previous psychiatric hospitalizations as risk factors for single and multiple future alcohol-related hospitalizations in patients with alcohol use disorders. *Addiction*, 2024, 119.2: 291-300.

Paper 4.
Manca, Francesco, et al. Estimating the burden of alcohol on ambulance callouts through development and validation of an algorithm using electronic patient records. *International journal of environmental research and public health*, 2021, 18.12: 6363.

Evaluation of public health policies on AUD

Paper 5.
Manca, Francesco, et al. The effect of minimum unit pricing for alcohol on prescriptions for treatment of alcohol dependence: a controlled interrupted time series analysis. *International Journal of Mental Health and Addiction*, 2023, 1-16.

Paper 6.
Manca, Francesco, et al. The effect of a minimum price per unit of alcohol in Scotland on alcohol-related ambulance call-outs: A controlled interrupted time– series analysis. *Addiction,* 2024.

Paper 7.
Manca, Francesco, et al. Evaluating the impact of minimum unit pricing for alcohol on road traffic accidents in Scotland after 20 months: An interrupted time series study. *Addiction,* 2024.

Paper 8.
Fitzgerald, Niamh, et al. Lockdown and licensed premises: COVID-19 lessons for alcohol policy. *Drug and alcohol review,* 2022.

Context of the studies

1. Clinical epidemiology of AUD

While there are still criticisms in labelling substance use disorders as mental health conditions[25], they are recognised as clinical diseases since they affect a person's brain and behaviour, leading to their inability to control their use of substances[26]. Under a biopsychological perspective, addictive psychotropic substances generate multiple homeostatic reactions with 'learning' consequences, ultimately leading to long-term adaptation of the brain to the substance and lasting changes to the actual brain mechanisms[27]. The reason of repetitive exposure can vary, but usually what triggers addiction in the brain is the release of dopamine in the mesolimbic or nigrostriatal pathway. So, a sense of pleasure (or the anticipation/memory of such pleasure) inducing to the repetitive intake behaviour. It is useful defining dependence and addiction in these initial sections under a psychological perspective to appreciate the ease of relapses after recovering, meaningful also for treatment and policy purposes. Addiction is the lack of control of using a substance despite the negative consequences. The repetitive use generates tolerance in the system, so more substance is needed to produce the initial 'pleasurable' process (reinforcing the addiction process). Individuals are dependent when they experience withdrawal symptoms in absence of the substance; such symptoms are due to the counter reaction of the brain to remain in its homeostatic state[27]. Any environmental cues reminiscent of the original exposure can anticipate the brain's countereffects with withdrawal symptoms, inducing individuals to crave the substance.

As for any other mental health condition, AUD needs to be studied through (but not limited to), the epidemiology, the risk factors and treatment management of the disease. The four publications of this thesis included in this category specifically touched on all these points. A brief background connecting all these publications is presented next.

Risk factor: Dual Diagnosis. As for most mental health conditions, it is usually a range of several risk factors interacting and influencing each other to cause a substance use disorder after exposure. Papers 1 and 3 discuss aspects of social support (SS) and psychiatric comorbidities on AUD recovery; two relevant and interconnected risk factors. AUD often coexists with other psychiatric conditions (dual diagnosis). While there are no detailed figures on Scotland, in England, 63% of individuals starting treatment for substance use had a mental health treatment need, and when restricted to non-opiate and alcohol, the percentage raised to 71%[28]. However, the nature of this widespread comorbidity is still a matter of debate. For instance, the causal relationship between AUD and other psychiatric disorders is heterogeneous. Specifically, there are studies indicating that psychiatric disorders may exacerbate the role of other risk factors for AUDs[29, 30]. In contrast, other research found that AUDs could induce psychiatric syndromes, mainly due to the effects that functioning AUD may have on the psyche[29, 31]. Moreover, self-medication, which is the use of alcohol (or other substances) to handle the symptoms caused by other conditions, may create, or strengthen the bond between the use disorder and psychiatric morbidity. Treating individuals with dual diagnosis is more complex as it needs an integrated approach considering both conditions, including drugs' interaction and effect. Certainly, when the temporal nature of the relationship is clear (e.g., AUD earlier than a second psychiatric morbidity, or vice versa), it is also easier to define the causal nature of the relationship (e.g., AUD → second psychiatric morbidity, or vice versa). However, it is not always as easy as this. Hypotheses explaining these relationships include mutual direct and reverse causal pathways, common genetic or environmental causes, and shared psychopathological characteristics of broader diagnostic spectrums[32]. The environment is a key component and most people exposed to vulnerable environments such as those experiencing or at risk of experiencing homelessness, also have a disproportionately higher risk of dual diagnosis[28].

Risk factors: Social support. Social Support (SS) also falls within the environmental causes and, therefore, has a role in both AUD and other psychiatric conditions. Particularly, high levels of SS appear to buffer or protect against the full impact of mental and physical illness[33], with an overall positive impact on life expectancy comparable to physical activity or the negative influence of smoking, and obesity[34]. One of the virtuous mechanisms of action of SS is 'motivation'[35], which, regarding AUD, was found to be influential on the management of alcohol consumption[36] and increasing the will to change alcohol use[37] during recovery. Beyond motivation, relational support can also mitigate through protective resources the effect of multiple disadvantages. Conversely, low levels of SS were associated with poor physical and mental health[33].

Alcohol and inequality. As there is evidence of associations between poor SS and socio-economically disadvantaged circumstances[38], SS can be identified as a component of the health inequality concerning AUD, which is heavily distributed towards the most socio-economically deprived groups. In Scotland, as in many Western countries, the alcohol-harm paradox is often compounded by the fact that more deprived areas frequently have reduced access to support services, including alcohol treatment provision. To be equitable, since the incidence of AUD harm is more prevalent in these areas, they should have even more access to treatment than elsewhere. Furthermore, the financial inability to provide private assistance or the lack of support networks to push patients to seek AUD treatments anchors these individuals to their health condition, perpetuating this inequality in society. In Scotland in 2020, the gap in life expectancy between the most and least deprived areas was 13 years for males and 10 years for females[39]. Regarding substance use disorders, in 2022, drug misuse death rates were almost 16 times higher in the most deprived quintile compared to the least deprived[40], and alcohol-specific death rates are 4.3 times as high in the most deprived areas[18]. Paper 2 describes the socio-demographic characteristics of patients hospitalised due to AUD and highlights treatment inequality across socio-economic groups.

Barriers to treatment. One of the major barriers to accessing treatment is the gap between identification and treatment, as many who have an 'alcohol problem' do not always seek or receive treatment for it. Recent initiatives, targeting those more socially secluded but in need, such as the 'Alcohol Change UK blue light' model (if people who need support but don't come into services, services need to go out and find them through assertive outreach and then bridging the gap between identification and treatment) are potential effective and money saving approaches. People in more deprived areas are usually more vulnerable and more affected by other psychopathological syndromes compared to those residing in other areas. Therefore, targeted policies must be comprehensive and work on multiple aspects of health deprivation status, such as social exclusion, stigma and lack of integrated services for dual diagnoses whenever present.

To summarise, AUD risk factors can be condensed in two macro components: individual (including genetics, comorbidities, and personality) and the environment (including culture, SS and exposure). Given the biopsychology background, genes that have an influence on specific neuroreceptors or neurotransmitters may create higher sensitivity to a substance (e.g., alcohol). Since alcohol, as all other psychotropic drugs, influences brain mechanisms, its presence and interaction in patients with other psychiatric conditions can establish new complementary dynamics and even more complex treatment solutions (for both conditions). While certain characteristics such as comorbidities or genetic predispositions may indicate higher vulnerability to alcohol, exposure is necessary. Earlier exposure is associated with higher risks of AUD as younger individuals are often more risk taking (personality) and in individuals who still need to develop and mature their brain (which usually happen at mid-20s[41]), neural changes may determine use disorders in later years[27]. Exposure is usually triggered by the context. All these intersected links should highlight how risk factors are all interconnected, there is not a main cause inducing to AUD and how policies aimed to reduce alcohol-related harm in the AUD and in the general population need to take a comprehensive approach.

2. Evaluation of public health policies on AUD

The harmful use of alcohol has been perceived as a global threat, needing to be addressed with recognised effective policies at individual and community levels. In 2010, the WHO released the Global strategy to reduce the harmful use of alcohol. This document provided guidelines for action at country levels and recommending ten policy options, which subsequently became one of the pillars to achieve the 3rd United Nations Sustainable Development Goal[1].

In the last two decades, and preceding such global objectives, the Scottish Government started to gradually legislate and subsequently implement comprehensive nationwide intervention packages aimed at tackling the harmful use of alcohol. Chronologically, the main national policies were: the ban of discounts and restrictions in promotions of alcoholic drinks (2005 Act[42], implemented in 2009), the age verification for the sale of alcohol (2005 Act[42], implemented in 2011), the decrease in drink driving limits (Act 2012[43], implemented in 2014) and the introduction of the minimum unit price for alcohol (Act 2012[44], implemented in 2018). Scotland was the first nation to introduce a MUP associating the quantity of alcohol (a UK unit -10ml or 8g of pure alcohol-) in an alcoholic beverage with a floor price. This placed the country among the world-leader nations on alcohol policy, with many other nations interested in the evidence around the Scottish MUP's effectiveness.

Pricing policies have been recognised among the most efficient to reduce alcohol consumption[45]. MUP is included in the pricing strategies included and recommended by

[1] The new United Nations (UN) Sustainable Development Goals are 17 goals with 169 targets that all UN Member States have agreed to try to achieve by 2030. The third goal is 'Ensure healthy lives and promote wellbeing for all at all ages'. The fifth target of such goal is to 'Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol'. Two of the indicators identified by the UN division to target such goal regard treatment coverage (3.5.1) and alcohol consumption (3.5.2).

WHO in the bundle of the most effective and cost-effective measures to tackle alcohol-related harm[46]. Before Scotland, only Canada implemented minimum pricing policies (not unit though) at subnational levels. Particularly, British Columbia and Saskatchewan have a minimum price applied only to specific alcoholic beverages and adjusted constantly over the years. In British Columbia, a 10% increase in minimum price was found to be associated with a 3.4% reduction in alcohol consumption[47]; regarding alcohol-related harm, the associations were 8.95% and 9.22% decreases in acute and chronic alcohol-attributable hospital admissions[48], a 9.39% decrease in crime[49] and a 31.7% reduction in wholly alcohol-attributable deaths[50]. Similarly, for Saskatchewan, where starting floor prices were higher, a 10% increase in minimum price was associated with an 8.43% decrease in consumption.

In Scotland, MUP was implemented on 1 May 2018, and it was set at £0.50 per UK unit of alcohol. In 2017, 47% of alcohol sold in Scotland from the off-trade market was sold below MUP levels[51]. However, the decision to introduce MUP in 2012 was supported by an adaptation of the Sheffield Alcohol Policy Model (SAPM)[52], rather than on the evidence on previous Canadian price policies[51]. SAPM is a deterministic causal model combining a micro-econometric (linking changes in alcohol price to consumption) and an epidemiologic (linking alcohol consumption to related harm) component. The model predicted how different MUP levels impact alcohol consumption as well as several harm outcomes. Different model versions were released with updated estimates to provide a reliable bundle of alternatives to let the Scottish Parliament decide the most appropriate value for MUP. In one of the last SAPM releases, a £0.50 MUP predicted an average reduction in the alcohol consumption per year in the population of 3.5% and a decrease of 6.8% and 7.4% in alcohol-attributable hospital admissions and alcohol-attributable deaths, respectively[23]. According to SAPM, most health benefits would have come from the harmful drinker population (those drinking more and having most of the harm despite representing the minority of drinkers and consumption in absolute terms)[23]. Indeed, as specified by the Scottish Government, *"The policy aim of minimum pricing is to reduce alcohol-related harm by acting in two ways: to reduce, in a targeted way, the consumption of alcohol by consumers whose consumption is hazardous or harmful, and also to reduce the overall population level of consumption of alcohol."*[53] The overall price increase was forecasted to decrease the total amount of consumption, but the dynamics of the floor price focused the effect mostly on hazardous/harmful drinkers in two combined ways. Firstly, as a consequence of the higher expenditure given by the greater consumption compared to the rest of the population and secondly, by impacting more alcohol sold at low prices relatively to its strength (which is usually purchased more by hazardous/harmful drinkers).

MUP was subjected to a ‘sunset clause’, meaning that the policy was supposed to end if the Scottish Parliament did not vote for it to continue after six years (30th of April 2024). Public Health Scotland (PHS) was asked to lead an independent evaluation of MUP on both the social health and economic industry impacts of the legislation and release a comprehensive report to the Parliament in time to decide whether or not to continue the MUP policy. A final synthesis of the evidence was released in June 2023, and the pre-print versions of papers 5,6 and 7 were part of it[54]. Overall, findings showed a reduction in consumption (-3% after three years)[55] as well as a decline in deaths (-13.3%) wholly attributable to alcohol and hospitalisations due to chronic causes wholly attributable to alcohol (-7.3%), but an increase in acute hospitalisation (+9.9%)[56]. Most of the effects were more prevalent in the most socio-economically deprived groups. There was no consistent evidence of MUP effects on other previously theorised alcohol-related health outcomes. Based on this evidence, in April 2024 the Scottish Parliament voted to continue the policy and increase the minimum unit price from £0.50 to £0.65 to offset the inflation effect in the last years. The increase will operate from the 30th of September 2024. After Scotland, many other countries or regions have implemented (i.e., The Northern Territory of Australia -October 2018-, Wales-March 2020- and Republic of Ireland-January 2022-) or are considering implementing (i.e., South Africa) MUP. However, as Scotland was the first to implement the policy, the evidence from Scotland has international interest to reference short-, mid- and long-term effects. Papers 5-7 in this thesis-category relate to the evaluation of MUP.

Paper 8 analysed the repercussion on alcohol consumption (and its acute harms) of extreme public health measures not explicitly affecting alcohol, for example the first Covid-19 lockdown (initiated in Scotland on 26th March 2020). Lockdown had strong impacts on health and health behaviours. There is general evidence that overall alcohol consumption reduced (presumably because of general discomfort and social restrictions), but that certain groups already at risk of hazardous drinking increased and shifted their consumption indoors, possibly as a way to cope with social isolation[4]. The lockdown has had long-lasting effects with the risk of affecting more those already more vulnerable and undermining the impact of pre-covid public health policies aimed at tackling health inequality.

Discussion

These publications highlight a specific interrelation of AUD risk factors as well as policy implications and their effectiveness. By emphasising different effects and the inequality of treatments across subpopulations, they also exposed the complexity of studying alcohol epidemiology and policy.

Particularly, the relevance of risk factors is different across subpopulations (e.g., sex, age, income, etc.)[57], and this is due to diverse consumption patterns and overall exposure chances. Different consumption patterns are also reflected in variations of alcohol-related harm between subpopulations. For instance, there is evidence that younger people were shown to prefer to drink the largest quantities of alcohol on a few occasions per week, in contrast, older individuals are more likely to consume alcohol with greater frequency at even amounts, this especially in high and middle income countries[58]. Consequently, young individuals are at greater risk of acute harms (e.g., alcohol-related injuries and intoxications), and older individuals may experience more chronic adverse effects associated with a continuum exposure or the interaction of alcohol with other health issues or medications. This phenomenon was also reflected in alcohol-related ambulance demand (paper 4[59]), which, mostly characterising acute neediness, was higher across lower age groups and especially in correspondence with night-time and weekends, while lower and more evenly distributed toward the day for older individuals (paper 4[59]). Similarly, the prevalence of AUD is higher in more socio-economically deprived groups. Still, the effectiveness of specific risk factors such as social support in avoiding alcohol dependence re-hospitalisations was different across socio-economic groups (paper 1[60]). However, while AUD has a higher incidence and prevalence in more deprived areas, barriers to treatment are also higher in those populations (paper 2[61]), creating more challenges to design policies targeting those more in need.

The main difference in studying alcohol compared to other substances is that alcohol is legal, therefore more common (easy availability) and socially accepted. Therefore, the social perception of disorders linked to alcohol is lower than those linked to other illicit drugs[62]. In addition, the easy availability increases the consumption within the population, making AUD more common (even if diversely) across socio-economic groups compared to other drugs. While alcohol is not as addictive as other illicit drugs (in 2022 81% of the Scottish adults drank alcohol and 22% drank it at hazardous or harmful levels[17], but only 2% of consumers drank at dependence levels[63]), its widespread use makes it the second most lethal drug in the world (after tobacco) and a social and potential individual concern for most of the population exposed (which is larger than for other drugs). Furthermore, alcohol pervasive presence in society also increases the risk of relapses in those recovered from AUD, as individuals are often triggered by cues[27].

These features determine a complex framework to design and evaluate policies to tackle alcohol-related harm. Indeed, this scenario underlines how evaluating policies at subpopulation levels, focusing on the effects on individuals with different vulnerabilities and exposure to different harm is more meaningful for social purposes and, together with other complementary analyses on other outcomes or policy spillovers, would provide a more comprehensive view of the effectiveness of the policy.

After clarifying the foundation of policy evaluation in general and in relation to MUP, this discussion aims to emphasize how a deep understanding of the epidemiology of AUD is needed not only to plan and evaluate a policy for AUD, but also to communicate results and to use the evaluations to improve the policy further or complement it with additional interventions. The reasonings on MUP evaluation refers mainly to the PHS report published in July 2023, which was the main source informing the Scottish Government on whether to continue, suspend or reshape the policy.

This discussion is divided into 4 sections: Section 1 is an introduction to policy evaluation with some concepts referring to the AUD context. Section 2 discusses MUP evaluations through the PHS report. Section 3 puts together the two original categories of this thesis, showing the inequality of the burden of alcohol in relation to the policy decisions on AUD in Scotland. Section 4 lists the main strengths and limitations of the overall thesis.

1. Public policy evaluations and potential pitfalls

Introducing a policy implies the decision to shape individuals' behaviour to address/handle or make more bearable a specific problem. In this framework, the key aspect of policy decisions is the causal theory they enclose[64]. However, causal theories are based on an approximate outline of social reality's interconnections. Therefore, novel public policies built only on theoretical causal models need to be supported by empirical evidence, or they may be sub-optimal, missing unexpected or untrivial relations.

To empirically determine the effectiveness of a specific policy, it is crucial to first establish its foundations by thoroughly understanding the nature of the phenomenon being addressed. Secondly, it needs design a theory of change as a consequence of the policy and preferably hypothesise the effect of the phenomena on specific outcomes. Finally, it needs to plan the method of inquiry for searching causal relations with real-world data.

Randomised control trials (RCTs) have been recognised as the gold standard to prove causal relationships, especially in clinical/laboratory environments. However, RCTs are not always possible in social contexts due to ethical, financial or political reasons. Therefore, natural experiments are more common study design settings where social and political scientists have tried to prove causal relationships (or, whenever not feasible, 'relevant associations') correspondingly to a policy or, more in general, 'an intervention'.

The main difference between natural experiments and RCTs is the lack of random assignment to treatment or control in natural experiments, and the search of the most appropriate counterfactual is a key for the assessment of the experiment. The counterfactual acts like the control group of an RCT and should provide the result on the population of interest assuming the intervention did not happen. For this reason, the counterfactual should have characteristics as close as possible to the population of the intervention group in the pre-intervention period. While in specific contexts it is possible to mimic randomisation by controlling for observables (e.g. through methods such as matching), whenever there are confounders, making the decision on the best potential control is crucial for a robust evaluation of the intervention. Hereafter, the importance of the nature of the phenomenon and of the counterfactual with references to AUD and MUP are described.

Nature of the phenomenon

The nature of the phenomenon is the study of the field where the intervention will be implemented. For example, regarding MUP, it is understanding the complexity of public health and AUD policies, the alcohol consumers, as well as the peculiarities of the population of interest (alcohol consumers in Scotland and the general of Scottish population). This should provide a theory of change as a consequence of the rise in alcohol prices (i.e., increase in price → decrease in consumption → decrease in alcohol-related harm, change in market equilibrium) and hypothesis on relevant outcomes to be affected. The theory of change developed by PHS, represented in Figure 1, identified and classified outcomes into seven categories: 1) Alcohol-related health outcomes; 2) Compliance; 3) Price; 4) Consumption;

5) Social outcomes; 6) Alcoholic drink industry and 7) Attitudes to MUP. The theory of change also hypothesised some population groups to be more affected than others (i.e., hazardous and harmful drinkers) and ‘contributing more’ to specific outcome changes. As for many new social regulations, the theory of change also included a change in attitudes to alcohol (and maybe to the MUP regulation itself), which can be instant or gradual. All these steps can include qualitative investigations to better define the context and strengthen (or lose) causal interpretations and relations.

Figure 2. Theory of change for minimum unit pricing for alcohol, reported from Public Health Scotland, 2023[54]. Source: https://publichealthscotland.scot/media/20366/evaluating-the-impact-of-minimum-unit-pricing-for-alcohol-in-scotland-final-report.pdf

Overall, the nature of the phenomenon, by identifying the main target of the intervention and potential dynamics of the policy (e.g., how, when implanted, etc.) should also provide the insight on how the intervention ought to be evaluated.

The lack of understanding of specific features or connections could result in some important outcomes to be omitted from evaluation, mishandling methods, or undermining the causal interpretation. For instance, missing subgroups’ effects in the policy evaluation, whenever relevant, could lead to a wrong interpretation of the relationships in the data. A relevant example of this issue is the Simpson’s Paradox (SP)[65]. The concept of SP can be summarised in a specific trend pictured in several subgroups of data, while it can disappear or reverse when groups are aggregated.

While the analysis in paper 1[60] cannot be considered as a proper SP, it shows how the trend in the overall population can be reversed in specific subgroups. Table 1 shows the odds ratio of the association of being discharged in company vs alone and relapsing for AUD presented in the paper[2]. The trend in the overall population is a 20% reduction in the odds of having relapse if discharged in company. While the trend maintains across the first four most socio-economic deprived quintiles, it reverses in the least deprived quintile with a 73% increase in odds of relapsing associated with being discharged in company. The study highlights this trend, but it did not attribute any causal connotation to the analysis. Indeed, it acknowledged that important confounding variables (e.g., the severity of AUD, different availability of non-hospital services) could have a determinant role in these associations.

Table 1. Odds ratio referred to the study 'Manca, F. and Lewsey, J. (2021) Hospital discharge location and socio-economic deprivation as risk factors for alcohol dependence relapses: a cohort study.'

		Relapse	No relapse	Total	OR
Total of the population					
	in company	272	275	547	0.797
	alone	329	265	594	
by socio-economic deprivation quintiles					
1	in company	96	77	173	0.806
	alone	116	75	191	
2	in company	64	61	125	0.713
	alone	103	70	173	
3	in company	61	80	141	0.774
	alone	69	70	139	
4	in company	32	46	78	0.885
	alone	33	42	75	
5	in company	19	11	30	1.727
	alone	8	8	16	

OR= odds ratio; Socio-economic deprivation quintiles categories: 1 equal to the most socio-economically deprived quintile, 5 least deprived.

However, SP is not a true 'paradox', and it originates only when we attribute causal inference to different explanatory levels. Economics Nobel winner and psychologist Daniel Kahneman sustained that "*our mind is strongly biased towards causal explanations and does not deal well with mere statistics*[66]", and this paradox is an example of that. Along these lines, the challenge is understanding which kind of causal inference is justified based on the data we observe. Acknowledging this does not solve the causal issue, but it underlines how a policy

[2] For clarity purposes, the table reports odds ratio rather than hazard ratio as in the original publication. While the two statistics are different, this example was aimed to expose SP and odds ratio were preferred as easier to depict in a table.

decision (e.g., whether increasing the price of alcohol) needs to analyse all potential relationships and attribute a causal connotation to the relationships based on a ‘theory of change’ drawn ex-ante. A proper SP case from the alcohol literature is reported in Appendix.

SP can be due to a confounding variable and/or a disproportionate allocation of the variable within treatment and subgroups. Therefore, the occurrence of SP depends on the shape of the data. Technically, data are ‘completely immune’ to SP only if they are ergodic[3], a very uncommon feature in social sciences datasets[67]. Simulation studies highlighted how SP can appear in almost 2% of datasets[67]. However, given its counterintuitive nature, researchers can easily miss the paradox, meaning that SP can happen more often than it is reported[67], with dangerous consequences at the policy level.

Counterfactual

Counterfactuals represent what would have happened if an action (a policy) did not occur. We can only observe the real (factual) situation where the population has been exposed to the action, and we can directly measure the outcome. In contrast, the answer to the question ‘What would the outcome have been if the exposed population had been unexposed?’ is unreal (counterfactual) and cannot be observed. In theory, the causal effect of a policy on a specific outcome is, therefore, the difference between factual and counterfactual outcomes.

Taking MUP as an example, the average causal effect of introducing MUP in Scotland on alcohol consumption is the difference between the alcohol consumption in Scotland with MUP (factual) and without MUP (counterfactual). Analytically, and focusing on Scotland, let Y_S^{MUP} be the average alcohol consumption for the individuals in Scotland with MUP, and $Y_S^{Control}$ the alcohol consumption in Scotland without MUP. To get the effect of the policy in Scotland on alcohol consumption, we are interested in the difference Y_S^{MUP} - $Y_S^{Control}$. However, Scotland with and without MUP cannot be observed simultaneously. Therefore, we look for the average effect of the policy in Scotland $E[Y_S^{MUP}$ - $Y_S^{Control}]$.

The difference of interest can be rewritten as:

$E[Y_S^{MUP}|MUP]$ - $E\left[Y_S^{Control}\middle|no\ MUP\right]$,

[3] The individual characteristics (e.g., mean and variance) are asymptotically identical to those at the level group. Kievit et al. 2013[59].

by subtracting and adding the same term $E\left[Y_S^{Control}\middle|MUP\right]$ we obtain:

$$E[Y_S^{MUP}|MUP] - E\left[Y_S^{Control}\middle|no\ MUP\right] + E\left[Y_S^{Control}\middle|MUP\right] - E\left[Y_S^{Control}\middle|MUP\right] =$$

$$= E\left[Y_S^{MUP} - Y_S^{Control}\middle|MUP\right] + (E\left[Y_S^{Control}\middle|MUP\right] - E\left[Y_S^{Control}\middle|no\ MUP\right]) .$$

While the first term is the average treatment effect in Scotland (the aim of our evaluation), the two terms in the rounded bracket represent the selection bias, representing systematic differences between Scotland (which implemented MUP) and other countries not implementing the policy.

In RCTs, counterfactuals are represented by the control arm, which is randomly selected within the population of interest. The randomisation of the population of interest into the two arms, should guarantee that the control group has no selection bias. As natural experiments are not randomised, different strategies to minimise selection bias and confounders, and guarantee a robust estimate of the policy are needed. Controls can come from the natural world (already existent comparators similar to the treatment group) or can be artificially built to be as similar as possible to the treatment group (e.g., synthetic controls).

To minimise the presence of selection bias, controls need to be: 1) similar to the treatment group across time other than through the treatment (parallel trend); 2) exposed to the same history and threats (unobservable confounders) as the treatment; 3) data are measured consistently for both treatment and control groups.

If these conditions are not met or only partially met, it is likely that confounders/selection bias will be present, with consequent bias in the final estimates. Researchers must limit the presence of selection bias and or confounding, either through control by design or adjustment during data analysis, if they want to draw causal associations[68].

In the MUP evaluations regarding a wide range of outcomes (and in many evaluations of public health interventions in general), the most used methods are difference in differences (DiD) and interrupted time series (ITS). Like any research method, there are limitations. DiD and ITS main limitations depend on the before-after comparison with the control. Firstly, the main requirement for the validity of DiD and ITS is that the policy is not implemented based on pre-existing differences in outcomes[69](e.g., given the difference in alcohol-related harm between England and Scotland, it was decided to implement MUP in Scotland). Then, the reliability of the estimates is also dependent on the initial difference in the outcome of interest between the control and intervention group in the pre-treatment period (if the difference is relevant, the magnitude and even the sign of the estimation are very sensitive to the functional form adopted in the model[69]). Another relevant constraint is the fact that the trustworthiness of the estimates is higher just after the policy implementation, as the parallel trend assumption is more likely to hold in the short time[69]. However, for policy purposes, mid- and long-term estimates may be more relevant. Therefore, the choice of more uncertain long-term inferences over short-term estimates should be accompanied by several relevant robustness checks.

Bernal et al[70] referring to ITS, explained and categorised a wide range of controls, including 'location-based controls' (e.g., same outcome but in England) and 'Control outcome' (e.g., methadone prescriptions compared with alcohol dependent prescriptions both within the same Scottish population -paper 5[71]-) which have been the most frequently used in evaluations of MUP. Among the common limitations with other controls, location-based controls cannot exclude events that are unique to the intervention location. Similarly, control outcomes can only account for factors that have the same potential confounders of the primary outcome.

To assess the quality of the control, usually relevant background information on the pre-treatment period is used. In DiD and ITS designs, it is also useful to plot the series of treatment and control groups and view and statistically test whether there is a parallel trend pre-intervention[69]. In addition, it is also suggested to repeat the analysis with alternative controls with a parallel trend and similar background information whenever present[69]. If the final estimate with the alternative suitable control is different from the one with the original control, then the original estimate is likely to be biased[72].

Publications in this thesis evaluating MUP assessed the quality of the control showing descriptive statistics of the two comparators, they then assessed parallel trends of already decided comparators. When such parallel trends or any other condition was unmet, alternative controls were considered (e.g., methadone). Whenever there were no alternative controls, other strategies (e.g., comparators built on pre-MUP trend projections) associated with several sensitivity analyses were used.

Alternatively, whenever multiple potential controls of the same category (e.g., all 'location based' or all 'control outcome') are available, synthetic controls are also a common option. Synthetic controls are 'artificial' controls created by weighting pre-intervention characteristics of multiple candidate controls to create a new control group as similar as possible to the original treated group. While no method different from a RCT can account for unknown confounding, synthetic controls can potentially alleviate the impact of confounders if changes over time happen only for a few of the controls in the synthetic bundle.

Once controls are assessed and then selected, the unconscious attitude to increase the chances of selecting findings/methods confirming the original beliefs (confirmation bias) (e.g., selecting the control group confirming the theory of change despite better alternative comparators) should decrease**.**

Only recently, relaxations of the parallel trend assumption have started to be considered for causal inference literature[73]. These methods rely on model adjustments (e.g., use of pre-intervention differences to explain potential parallel deviations) and then to alternative estimators for causal inference. However, while the econometric methodological literature on this field is rapidly growing, its application is not frequent in public health, and they are usually used paired with conventional methods.

To summarise, a causal evaluation of a public health policy needs to have an ex-ante clear idea of the nature of the phenomenon (a comprehensive epidemiological understanding of the theme). This allows to anticipate potential patterns in the data and support their findings that can even be apparently incompatible with each other (e.g., SP paradox) by theoretical explanations and, therefore, strengthening the causal connotation of the results. Another crucial component of the policy evaluation is the method and then the choice of the right control. Different control categories can have different weaknesses and different sources of bias. Controls need to be carefully chosen and then assessed, especially when the analysis relies on one control only. Unless there are theoretical concerns, the best performing control in the pre-intervention period should be used. The final estimations should have multiple sensitivity analyses regarding both methods and controls to increase the reliability of the findings. The knowledge of the nature of the phenomenon can aid in the choice of the most appropriate counterfactual and the overall method, as well as suitable sensitivity analyses.

2. MUP evaluation

PHS released in June 2023 the report[54] on the evaluation of the impact of MUP aimed to inform the Scottish Parliament on the decision to extend, modulate or withdraw the policy. The report is a synthesis of the evidence in the academic and grey literature processed through a systematic review. The final result included studies originally funded by PHS on key outcomes identified by the theory of change, unfunded studies known to PHS in advance aimed to complement the original MUP evaluation and other studies and grey literature found through the search of the literature that subsequently contributed to the evaluation.

The report included 53 analyses on single outcomes comprised of 40 studies (a few publications analysed multiple outcomes). Of which, 39 were quantitative and 14 qualitative. The analyses of the outcomes included in this thesis belonged to the categories ‘alcohol-related health outcomes’ (papers 5-6[71, 74]) and ‘social outcomes’ (paper 7[75]). A few outcomes were analysed multiple times by different research teams, using different approaches or time frame, with consequent production of several publications on the same component. Among quantitative methods, most of them were natural experiments measuring pre and post intervention differences. Regarding the design, the analyses were: 13 ITS, 4 DiD, the remaining were mostly pre- and post-differences or broader mixed methods design comparing different approaches - e.g., ITS, DiD, synthetic controls, pre and post differences, as well as qualitative components-.

Only a minority of the studies used nationwide datasets (4 health-related studies on 4 different components: alcohol-related deaths, alcohol-related hospitalisations, ambulance callouts and alcohol dependence prescribing; and 4 studies on social outcomes on 2 components: road traffic accidents (RTA) and crime). Nationwide datasets usually remove potential selection bias on the treated group. The remaining studies used routine health data on specific subregion of Scotland[76] or, more frequently, self-reported surveys of different sizes[24, 77], or again, on sales/consumption, large market research datasets from private companies (Kantar[78, 79] and Nielsen[80]).

Results

Evidence around MUP. Alcohol consumption was estimated to be reduced by 3.5% after one year[80] and 3% after three years[55] of MUP implementation, with most of the reduction involving households that bought the most alcohol[78, 81]. The main results on alcohol-related health and social harms of this report were ‘strong evidence’ that MUP reduced deaths (-13.4%) directly caused by alcohol consumption and a likely reduction (non-statistically significant) of wholly attributable hospital admissions (-4.1%). Both results came from the same study[56]. These findings were driven by chronic conditions as deaths and hospitalisations due to alcohol-related acute causes had (non-statistically significant) increased. There was no consistent evidence across all other studies that MUP impacted other alcohol-related health or social outcomes.

The decrease in consumption interested mainly those spending more on alcoholic beverages in the pre-MUP period[82]. The negative consequences of MUP were recorded mainly through qualitative evidence. For instance, the increase in price under a general budget constraint among dependent and financially vulnerable individuals could have led to reductions on food expenditure to maintain a stable alcohol consumption[83]. Another study showed that for a minority of drinkers, especially those with probable alcohol dependence and homeless circumstances, there could have been an increase in criminal activities (e.g., stealing) to acquire alcohol, but this was not a generalised trend[84]. Both studies found a potential switch from cider or beer to spirits in response to price increases, which led to increases in acute intoxications.

This evidence synthesis exercise summarised all up-to-date results in one of the most evaluated public health policy interventions in the UK ever. The report also underlined the potential weaknesses of some studies related to specific controls, the extension to the covid period, as other minor factors were mostly accounted and controlled through sensitivity analyses and then not a major source of concern. The PHS report was the main source of evidence informing the Scottish Parliament on MUP effectiveness, inducing an extension of the policy and an increase of the floor price to £0.65 from September 2024.

Papers in this thesis in the context of the evidence surrounding MUP. Papers [5-7] in this thesis were included in the collection of evidence on MUP by PHS. Each paper focused on a different aspect of the policy's impact: Paper 5 examined the effect of the policy on alcohol dependence prescriptions; the outcome framed within the context of the high-risk/AUD population, and likely to outline chronic or long-term effects. Paper 6 focused on alcohol-related ambulance callouts, which is a health outcome potentially more sensitive than other traditional acute health outcomes such as A&E admission. Lastly, paper 7 analysed the associations between RTAs and MUP, providing evidence on an acute social outcome. All these studies found no significant associations between the policy and the outcomes of interest. Generalising the evidence generated from these three studies only, MUP had no effects on acute health outcomes, chronic health outcomes on a specific high-risk population and on social outcomes. While these findings should be considered within the broader context of the available evidence, they align with general trends observed in other evaluations, which also report a lack of evidence on acute health and social outcomes. In contrast, despite the low representativeness of alcohol-dependent prescriptions, which typically cover only 12% of the alcohol-dependent population[85], the null association in Paper 5 emphasizes the inconclusive results of the policy on harmful and high-risk consumers, including those with alcohol dependence. Indeed, while the main evidence supporting positive effects of MUP [56] found a significant 23% decrease in alcohol-dependent deaths (the highest relative decrease across all alcohol-specific conditions), Paper 5, using a nationwide dataset, along with other studies employing large repeat cross-sectional data, found no changes in consumption patterns of harmful drinkers [24]or even an increase in consumption among specific subpopulations (e.g., men drinking at harmful levels) [86]. This highlights the need to produce more consistent evidence and understand the policy's intended and unintended consequences also on high-risk individuals rather than focusing only on results on the overall population. Specific considerations around methods and strengths of each of the papers are considered in the following sections.

MUP Narrative

The overall narrative was that MUP is a policy that improved health by reducing consumption and alcohol-related harm, identified as deaths and hospitalisation. PHS concluded in the report that "*the evidence supports that MUP has had a positive impact on health outcomes, namely a reduction in alcohol-attributable deaths and hospital admissions, particularly in men and those living in the most deprived areas, and therefore contributes to addressing alcohol-related health inequalities. There was no clear evidence of substantial negative impacts on the alcoholic drinks industry, or of social harms at the population level.*" As many institutions and foreign nations have had their "eyes" on the Scottish MUP results due to their interest in the policy and potential replicability, this report and the overall results of MUP evaluations had national and international relevance. Many headlines echoed or elevated reports' conclusions; for instance, "*Minimum unit pricing achieves 'main goal' of reducing alcohol harm, report says*" (The National)[87] or "*No place for cheap alcohol: Scotland's minimum unit pricing policy is protecting lives*"(WHO)[88].

While these findings regarded the most relevant outcomes, it is also worth saying that they come only from one out of forty studies in the report. The emphasis in communicating results is greater on the significant-expected and positive results and lower on inconclusive or negative unintended consequences of the policy. Indeed, there has been a lack of reference from the press to most of the other studies that, despite a decrease in consumption, did not find consistent results on other outcomes after MUP implementation (a sort of publication bias from the press also called 'media bias'). In addition, there was no explicit reference in the narrative post-report to misalignment between modelling expectations (e.g., reductions in crime[89] and 'transport injuries'[23]) which drove the policy implementation, and real results.

As all this positive narrative which has framed the MUP came only from one study, a few extra considerations related to this fact and on the study itself are needed to draw a comprehensive picture of the policy effect based on the PHS report.

Extra considerations: bias, risks, and remedies

Overall considerations. The study providing the most direct and relevant outcomes (death and hospitalisation), was the only one finding undoubtedly positive impacts of the policy. The fact that this was the only research on such important outcomes is a weakness for the overall comprehensive evaluation of the policy. For example, regarding the outcome RTA, the first published study[90] (November 2021), reported a 0.28–0.35 (9-11%) decrease in RTAs per 1 million people after MUP implementation, concluding that the policy reduced harmful RTAs. The second published study[91] (October 2022) found no evidence of MUP having effects on fatal and drink driving RTAs (authors found a 8% increase in fatal and a 2% decrease in drink-driving RTAs, both non-statistically significant estimates at 95% level of confidence). The third study, paper 7 of this thesis (October 2023), found no evidence of MUP on night-time RTAs, but evidence of a statistically significant increase in fatal and overall RTAs whose extent differ across sensitivity analysis, but authors explained that could not be ascribed causally to the policy. Therefore, as all studies were valued of equal strength and comparable by PHS, to date, there is inconsistent evidence on this outcome produced by multitude of studies analysing the same or similar object, using different methods, and ran by different research teams. If the analysis had stopped only on the first outcome the overall narrative would have been different: MUP reduced RTAs. The evidence synthesised by a plurality of studies is usually more robust and reliable. The lack of competing studies on a specific outcome could be mentioned and presented as a weakness in a report summarising the evidence.

The study on deaths and hospitalisations. The main conclusions of the paper[56] are summarised in tables 1 and 3 of the original outcome reported below, stressing how all alcohol-related deaths and hospitalisations reduced after MUP introduction. The most evident weakness in the publication is the high difference across sensitivity analysis made with alternative control groups regarding hospitalisation (two of them finding a non-statistically significant increase in hospitalisation and one a decrease in the effect -Table 3 of the article-). This shows how the uncertainty in the analysis for hospitalisations is related to the choice of the control, and therefore the relevance of the choice of the control. The alternative controls used in a sensitivity analysis should have some meaningful reliability or they render the sensitivity analysis pointless. As earlier mentioned, when the final estimates with alternative controls are meaningfully different from the main analysis, the main estimate is likely to be biased[69].

	Effect estimate, % (95% CI)	Effect estimate, N per year (95% CI)	p value
Deaths			
All deaths	−13·4% (−18·4 to −8·3)	−156 (−243 to −69)	0·0004
Deaths from chronic causes	−14·9% (−20·8 to −8·5)	−186 (−253 to −119)	<0·0001
Alcoholic liver disease	−11·7% (−16·7 to −6·4)	Not estimated	<0·0001
Alcohol dependence syndrome	−23·0% (−36·9 to −6·0)	Not estimated	0·0093
Deaths from acute causes	6·6% (−13·7 to 31·8)	10 (−3 to 23)	0·55
Hospitalisations			
All hospitalisations	−4·1% (−8·3 to 0·3)	−411 (−908 to 86)	0·064
Hospitalisations for chronic causes	−7·3% (−9·5 to −4·9)	−622 (−880 to −364)	<0·0001
Alcoholic liver disease	−9·8% (−17·5 to −1·3)	Not estimated	0·023
Alcohol dependence syndrome	7·2% (0·3 to 14·7)	Not estimated	0·039
Alcohol psychoses	−7·2% (−12·9 to −1·1)	Not estimated	0·019
Alcohol misuse	−2·1% (−13·2 to 10·5)	Not estimated	0·73
Hospitalisations for acute causes	9·9% (−1·1 to 22·0)	146 (−65 to 357)	0·076
Acute intoxication	3·9% (−11·0 to 21·2)	Not estimated	0·63

Table 1: **Change in primary outcomes from controlled models associated with the implementation of alcohol minimum unit pricing legislation**

	Deaths wholly attributable to alcohol consumption	Hospitalisations wholly attributable to alcohol consumption
Changes to model		
Modelled using unobserved components model	−13·0% (−20·7 to −4·5)	−4·4% (−9·8 to 1·4)
Modelled difference between Scottish and English time series	−11·6% (−17·1 to −5·8)	−6·0% (−10·6 to −1·2)
Modelled pre-pandemic time series	−13·1% (−18·9 to −6·8)	−3·2% (−7·3 to 0·9)
Changes to control group		
North East England control group	−13·8% (−19·4 to −7·8)	−2·8% (−7·7 to 2·4)
North West England control group	−13·8% (−19·4 to −7·7)	0·5% (−5·2 to 6·5)
Non-geographical control group	−13·3% (−17·8 to −8·5)	2·9% (−0·4 to 6·3)
Falsification test		
Modelled implementation date 6 months earlier	−2·1% (−11·7 to 8·5)	−0·2% (−4·1 to 3·9)

Data are effect estimates, % (95% CI).

***Table 3:* Change in outcomes from controlled models associated with the implementation of alcohol minimum unit pricing legislation, by sensitivity analyses**

Figure 3 *Table 1 and Table 3 of Wyper et al. 2023[56]*

The study does not provide an ex-ante assessment of the different controls to rank their quality and the higher trustworthiness of the main analysis over the sensitivity results for either of the outcomes. It did not test for pre-intervention parallel trends either. It provided only a visual inspection of the Scotland vs England & Wales trends in the unobserved component model representation (figure 1 and 2 in the article), deciding to use England & Wales as comparator. However, regarding alcohol-specific deaths, official statistics showed an overall difference in incidence and trend between Scotland and England in the decade before MUP implementation (20.5 vs 11.7 alcohol-specific deaths per 100,000 people in Scotland and England, respectively based on 2017 ONS[4] figures which also highlight differences in historic trends between constituencies[92]). Recent statistics found a closer similarity in death rates between northern regions of England and Scotland compared to England & Wales[93]. Important differences were also found for alcohol-specific hospitalisation figures. In addition, a study included in the PHS report but on other outcomes, finding statistical significant differences in the pre-intervention indexes representing 'bad health' between constituencies judged a synthetic control (built on subset of English local authorities with the same pretreatment dynamics of the average of Scottish districts) more reliable[91]. Further, another studies evaluating associations between MUP and the prevalence of harmful drinking used Northern England as a comparator[24].

In line with these observations, controls based on northern regions of England were mentioned in the article as *potentially more similar to Scotland*. However, authors preferred

[4] Office for National Statistics. The Statistical bulletin referring to alcohol-specific deaths in 2017 – one year before MUP introduction- highlighted also that Scotland had a decreasing relative trend in alcohol-specific deaths compared to 2001, while England an increasing.

to use the aggregation of England and Wales as a comparator group. They justified their choice as in the post-pandemic time series *differences in timing of regional COVID-19 waves, and subsequent pressures on services, might not have always aligned well with country-level restrictions*. While the study controlled for country level restrictions during the pandemic, higher uncertainty, and less quality in both classifications of causes of death[94] and hospitalisations not involving Covid was recognised by statistical authorities that could have been even higher source of bias.

Therefore, to decrease overall uncertainty and increasing the likelihood of a parallel trend (higher in short term evaluations) a main analysis on the pre-pandemic series using the best control assessed in the pre-intervention period would have been ideal. This would have compared 'equally' results on more reliable controls, providing a triangulation of results and a better estimate especially on hospitalisations. Overall, consistent results across different controls makes the outcome on death more plausible, however the same considerations are functional (e.g., assessment of the controls, parallel trend etc.) to establishing the robustness of the findings also for this outcome. In particular, as deaths trends between control and treatment group were previously found to differ, the reliability of the point estimate for deaths could be challenged as well without a proper assessment of the comparator.

Other minor challenges could be represented by the predominant effect of chronic conditions such as alcohol-related cancers after just 31 months over short term alcohol-related outcomes. According to the SAPM model (one of the pillars of theory of change) chronic results would be more evident in the long-term, mentioning 20 years as the period to observe a full effect on these outcomes[23]. Similarly, a recent real-world evidence from Australia and Canada showed acute hospitalisation more sensitive to MUP in short-term despite chronic hospitalisations having a more lagged reduction[95]. Further, the massive difference in alcohol dependence syndrome between deaths (-23%) and hospitalisations (+7.2%) after MUP implementation, while all other diseases categories followed the same direction was not discussed. This difference could seem in contrast with other studies finding no clear evidence of changes in the severity of dependence[83] or no effect on prescribing for alcohol dependence found in paper 5[71]. Another recent study contemporary to[56] based on a large repeated cross-sectional data collected via 1-week drinking diaries and using Northern England as a comparator, found no association between MUP and reductions in the proportion of drinkers consuming at harmful levels (where alcohol dependent people are usually classified)[24]. This evidence increases further the inconsistency around the effects of MUP on alcohol dependence. The lack of explanations supported by further sensitivity analyses, or the theory of change, or the lack of justifications of differences with other studies, may challenge the causal relationship between MUP and these results.

Mismatching between controls and asymmetries with the theory of change, especially regarding hospitalisations, may not attribute a causal connotation to this study, which roughly claims, "*the methods used suggest plausibility that these effects can be causally attributed to MUP".* Additionally, stronger evidence in findings regarding damages from acute causes could contribute to drawing a wider picture of the policy regarding this outcome. This would assist policy makers in understanding whether complementary adjustments to address the acute harm associated with MUP may be beneficial.

Common academic bias. To all these considerations, the risks of overall academic biases such as publication bias common to all studies finding strong and positive results in a hot field is real and should be acknowledged[96]. While this specific concept could cover all publications, the study on deaths and hospitalisations should not be affected. Indeed, Wyper et al. finding only one of the two outcomes to have statistically significant effect, underlined how there was not a propensity towards publication bias. However, policy makers should be aware of another potential bias frequent whenever public health actions have been socially accepted as positive: the what-so-called `white hat bias'[97]. This is a bias leading to distortion of information or of the narrative in the service of what may be perceived to be righteous ends. As this is a bias more for the audience and the 'receiver', the task to minimise the white hat bias should be more on journal editors, peer-reviewers, and lately to all studies synthesising the evidence. Particularly, these actors should verify that results are presented correctly, avoiding reporting bias and making the non-scientific audience/policy makers aware of the potential of biases inviting them to view the evidence in hot topics more critically, especially related to rare or first-time seeing findings. Indeed, publications are generally more likely if results are novel or unexpected[96].

Trying to limit the bias while reporting. Suggesting uniform analysis protocols across different outcomes (at least for funded studies, e.g., those commissioned by the same institution like PHS) would allow an easier comparison between studies across research teams and outcomes and increase the overall trustworthiness and usefulness of the evidence synthesis. For instance,[83] and[56], both PHS funded and planned studies used different controls (England & Wales and Northern England, respectively) for time series. Similarly, using the same method to include comparator in the time series models (at least across main and sensitivity analyses) would increase the comparability of results. Again, highlighting the different post-intervention time of the studies on the same outcomes could have improved the understanding of the policy on specific outcomes.

For instance, regarding RTAs publications referred to different time frames, but they were interpreted in the same way. Specifically, the first publication was an evaluation after 8 months of the policy (finding a decrease in RTAs) and the other two (both finding consistent increase in RTAs but without causal associations to MUP) were mid-term evaluations after 20 months. All studies were assessed as equally strong by PHS (while in publication 5 I presented a different idea). Thus, according to PHS, the inclusion of the time frame could have contextualised the narrative of the policy on the RTA outcome revealing an initial decrease RTAs in immediate correspondence of MUP, followed by a null effect.

To strengthen the reliability of the evidence synthesis, PHS conducted a critical appraisal of the publications and commissioned a further critical appraisal externally to compare results, and then reach consensus on differences in ratings. However, a particular attention towards delivering the right messages to policy makers, making them aware of risk of biases, inconsistencies between studies in methods, or differentiation on long-short term effects as well as underlining differences with the original policy's expectations is central for studies with direct policy impacts.

In summary, MUP was a policy aimed at decreasing alcohol-related harm, and by affecting the most socio-economically deprived individuals more (which are those with the highest incidence of alcohol-related harm), it was intended to decrease the health inequality due to alcohol. Despite a decrease in consumption, results showed a statistical-null effect in most of the social and clinical outcomes potentially affected by the policy, except a decrease in alcohol-specific deaths (-13.4%) and hospitalisations (-4.1%). Results were well perceived by the public opinion. However, higher attention from media and technical institutions delivering the narrative is needed to make policy makers aware of potential weaknesses in the evaluations. Positive results came only from one publication. Inconsistencies in deciding the control as well as the lack of support of the theory of change in certain explanations made the causal association between MUP and decrease in hospitalisations unfitting. While the decrease in deaths is likely to be suitable, its extent may be unclear due to poor assessment of the quality of the controls. Rather than framing the narrative predominantly on successful and expected outcomes, specialists should also underline mismatching between original expectations and findings (e.g., lack of effects on social outcomes as well as increase in acute deaths and hospitalisations). To do this, a deep investigation on key publications is needed to assess methods and causal claims. This would help policy makers and modellers to appreciate the evidence more objectively, reviewing the current MUP and/or shape and better design future complementary policies.

3. General reflections on AUD in relation to public health policies to tackle alcohol-related harms

Overall, the inequality of the burden of AUD is related to exposure to alcohol in contexts with more risk factors and to more impediments in receiving care. Studies in this thesis showed how specific settings are associated with a higher risk of AUD relapses, or how alcohol consumption can be more addictive for individuals with specific comorbidities who can use it for self-medication. While the incidence of these circumstances is greater in more socio-economic deprived areas (e.g., higher psychological distress and a general concurrence of multiple social and health threats[98]), in Scotland, the access to alcohol dependence medications is more difficult in these areas (paper 2[61]). This highlights how poor access to health as well as the concentration of severe multiple disadvantages may make health inequality related to AUD structural in Scotland and only moderately influenceable by untargeted policies.

Specifically, low income, unemployment and poor physical and social environments are all components of socio-economic deprivation, as defined in Scotland[99]. These factors can trigger mental health issues (including substance use disorders) as well as they are constraints impeding to health access. The barriers to accessing healthcare include the extent to which the timing and flexibility of appointments align with people's lives (e.g., less flexibility due to unstable jobs or lack of assistance to family care duties), mistrust of services and whether people realise that an ongoing health problem requires treatment[98]. Accordingly, all these barriers are more common in individuals experiencing multiple disadvantages.

Recently, barriers to healthcare from the most vulnerable have become higher. Indeed, the recent high pressure on the NHS and the consequent provision of less healthcare after the pandemic had a twofold negative effect on health inequality. Firstly, the inability to access treatments risks deepening existing poor health, which is more common in the most deprived areas. Secondly, long waiting lists pushed individuals to take out private health insurance for a more effective healthcare service[100]. This increased the divide between those who can afford health assistance and those who cannot, and especially for mental health, worsening their social marginalisation. Specifically, regarding alcohol, the lower access to healthcare from the most vulnerable individuals increases the risk of identifying alcohol with an easy answer to more complex health and social problems, triggering AUD mechanisms.

From this reasoning it arises that AUD is not only caused by the offer of (selling) alcohol but also the cause of deeper social and individual malaise generating harmful alcohol demand. In the last decades, the Scottish Government put into action several policies aimed at making the alcohol offer less appealing, and MUP is only the last of them. To date, MUP is considered a successful policy that reduced consumption and with some evidence in reducing alcohol-related harm, long-term effects are supposed to be even more remarkable as full evidence on chronic conditions is supposed to come out after 20 years[23]. Moreover, the fact that consumption decreased more in those purchasing more alcohol before the policy implementation and the fact that the reduction in alcohol-specific deaths was greater in more deprived areas seems promising. Indeed, policies like MUP are likely to have benefits outweighing negative aspects[101]. However, their effect can be limited as acting on reducing the demand only through pricing policies (such as MUP) or previous supply policies is only one side of the problem.

Indeed, by working only on the price, it is likely that the policy will reach a saturation point, affecting fewer individuals than the total of the population with AUD. Specifically, it is questionable that MUP will affect those with an inelastic demand for alcohol; the inconsistent results of MUP on alcohol dependent individuals and its potential negative effect on this population confirm this reasoning. MUP-like policies can be only part of the solution and not the only answer to slow down the AUD epidemic in Scotland. The excitement around MUP success, which put Scotland as a world pioneer in policies to tackle alcohol-related harm, cannot allow the country to rest on its laurels as alcohol-specific deaths and other risk indicators are increasing. However, the lack of other complementary alcohol policies in Scotland after 2018 highlights this risk.

Structural interventions towards the ‘harmful demand for alcohol’ would complement the current policies to tackle AUD in Scotland. From this thesis, there can be a few policy insights focusing on treatment equality and working on the causes of AUD recurrence to reduce imbalances of the alcohol burden within the population. Firstly, referring AUD patients after hospitalisations to specific services (as many of them risk being lost after discharge and not linked with any specialist treatment services)[61]. This is particularly true for patients with specific vulnerabilities and a higher risk of relapses (e.g., poor social support environments -paper 1[60]- or high-risk comorbidities[102]). Secondly, promoting assertive outreach initiatives for individuals with potential substance or alcohol use disorders but with individual barriers to treatment and access to services (e.g., stigma or lack of acknowledging their disorders). Thirdly, working on why the distribution of the most effective treatments differs across deprivation groups (paper 2[61]), as well as increasing general levels of prescriptions for alcohol dependence in the population that looks too low[85]. Fourth, closer interaction of social and health care to increase access to treatment and avoid self-medication spirals. This thesis mainly assessed dynamics related to the AUD treatment and recovery. However, these aspects focus mostly on acute and chronic care which are essential to even the burden of AUD but cannot be the solution to the AUD epidemic if they stand alone. In general, laws, medical practice and even the imaginary availability of antidotes (alike naloxone for opiate overdoses) are insufficient. The answer must be found in the drivers to the demand side. For instance, socio-economic deprivation in Scotland is a major risk factor of poor mental health and specifically substance use disorders. More investments to reduce marginalisation and the multiple disadvantages of subpopulations at higher risk would work on the problem from its foundation.

Scotland had implemented strategies in this direction. For example, in 2017 alcohol and drug partnerships with local institutions such as health boards, local authorities, police and charities were funded to develop strategies to tackle alcohol and other substance related harm fitting local contexts. While these partnerships still work trying to understand and overcome local barriers to recovery, recent increases in alcohol-specific deaths show that they may be not enough. Indeed, the global circumstances after the pandemic changed, reshaping alcohol consumption patterns, as well as increasing need for mental health support in the populations. This highlighted the need of even more comprehensive approaches to reduce the ‘demand’ of alcohol-inducing harm.

Evaluating policies is useful to establish their effectiveness on specific outcomes. Also, analysing unexpected trends or the lack of effects in specific subpopulations can be even more beneficial as it may help to plan for complementary policies with greater effectiveness of a more comprehensive strategy. Additionally, the evaluation of a policy may also help to contextualise the policy, which, interacting with external factors (e.g., inflation and pandemic), decreases its expected effectiveness on specific outcomes or diminishes its impact in the long run. Current plans to reform MUP by increasing the floor price to £0.65

from September 2024 go in this direction. Certainly, indexing MUP to inflation as already in place in Canada[47] would decrease the chances of further amendments.

Extending the MUP policy without plans for future evaluations or price revisions suggests that policymakers believed they had sufficient and conclusive evidence to support the policy's effectiveness. However, the Scottish Government based its decision on national mid and short-term evidence and relying only on one single studying finding positive results on direct health outcomes. The lack of complementary strategies aiding those potentially negatively affected by the policy raises concerns. Specifically, there is a risk that MUP, initially targeting the general population (and indirectly focusing on the consumption of those in more deprived areas), was originally conceived as a comprehensive policy without adverse repercussions for health inequality. This conception has not changed after the evaluations. However, assessments of adverse impacts on specific subpopulations should have prompted adjustments to the original theory of change, placing the policy within a broader public health and economic context. An example of such amendments is the inclusion of mechanisms that might underlie potential harms[103]. For instance, a new theory of change could allow for different behavioural changes within subcategories of consumers (even within the classes of moderate, hazardous and harmful drinkers), as consumption patterns are not only defined by consumption but also by the context[5]. Studies on the homeless population finding MUP as a “lower” priority[104] or an insufficient measure for these populations with more complex needs[84] are an example of this. Extending evaluations and considerations on populations not greatly affected by the policy may allow greater reflections on the inequality and then equity of the policy itself. Furthermore, differentiating between short-term and long-term impacts, considering their interplay with external factors, and incorporating a mechanism for ongoing evaluation are essential to improve current theories of change, create new evidence through new evaluations and consequent policy refinement. The absence of "sunset clauses" and the fixed nature of the new MUP risks to hinder this fine-tuning approach in the near future.

4. Strengths, limitations and critical reflection of this thesis

The discussion section of each paper underlined its specific strengths and limitations. However, common features of all studies can be identified. Similarly, this discussion attempting to connect all articles under alternative points of view can have its own strengths and limitations.

Strengths. Firstly, all papers used a nationwide sample size, this increased the external validity of the studies, excluded selection bias of the treated groups, and allowed inference at national levels, with consequent higher policy relevance. Secondly, all publications had extensive sensitivity or subgroup analyses. This often-strengthened evidence of associations through multiple methods having similar findings (i.e., triangulation and integration of results) and/or shed light on different dynamics within specific population subgroups. Thirdly, the policy implications of some of these studies go beyond the mere sample size: the policy papers provided insights on evidence around hot policies for Scotland such as MUP or lockdown's effect on drinking patterns at national level. In this regard, three of the studies of this thesis were included in the PHS report, all were allocated a 'strong' score in their critical appraisal. These studies have contributed to the evidence presented to the Scottish Government to decide on MUP after five years, therefore, they have had an immediate policy influence. Lastly, this discussion briefly retracing the rationale of policy evaluation and highlighting potential pitfalls, could provide tools to make policy makers aware of communication and academic bias and limit their persuading effect.

Limitations. The limitations of this thesis are mostly related to its retrospective nature: publications coming from different ideas, grants and reasons may appear disjointed. However, this discussion connecting the dots hopefully provides the reader a more comprehensive framework of AUD, and a better understanding on why there was a need of specific policies to tackle AUD in Scotland, as well as potential explanations of their expected and unexpected effects.

Regarding the three publications in this thesis on MUP and other studies around this policy, the pandemic impeding homogeneous data collections for specific outcomes and changing consumption patterns of the population limited long-term evaluations of the policy, causing a strong limitation. Specifically, the pandemic could be seen as an external factor that introduced 'noise' in most of the time series analysing MUP's effects. As both consumption patterns and the attitude of the population toward alcohol changed, the 'noise' was likely to be stronger than the actual effect of MUP. Another effect was the lower reliability of controls during and in the short term after the pandemic. This is because different countries had different restrictions, and restrictions together with populations' characteristics had a role on how consumption patterns changed. However, while the pandemic changed consumption patterns (which are unlikely to disappear quickly), the extent of such changes could gradually decline in the long term. Future studies considering these trends may have more long-term validity, with more conclusive results. The discussion refers mainly to the analysis and implications of the PHS report published in 2023, as it was the main source of evidence informing the Scottish Government on decisions on the future of MUP. Therefore, studies published after this report were not considered.

Critical reflections. Beyond the policy impact of the second set of papers in this thesis already discussed, the thesis also extended evidence around some AUD risk factors. For instance, it quantified the association of living alone with further alcohol-related hospitalisations (paper 1[60]). Moreover, the comparison of various psychiatric comorbidities using a nationwide routine dataset (not restricted to specific subpopulations) and a consistent definition of the 'relapse outcome' across comorbidities was a novel approach facilitating the comparability of different comorbidities as risk factors (paper 3[102]).

From both the papers and this essay, a few key recommendations can emerge. Firstly, investing in research to study the barriers to treatment for AUD across specific subpopulations. For instance, paper 2[61] showed lower odds in receiving pharmacological treatments (as well as the most effective medications) for those residing in more socio-economic deprived areas but without establishing causal links. Research analysing these barriers can suggest mechanisms to reduce the gap between hard-to-reach populations and therapies, with implications for the distribution of alcohol-related burdens in society (and health inequality). Secondly, increasing the availability of data (e.g., open access or delivering restricted datasets to investigate same/similar outcomes to several research groups) may increase the quality of evidence. Thirdly, both policy makers and researchers summarising and delivering the evidence should be aware of potential communication biases. In the case of MUP, focusing also on unmet expectations of the policy as well as potential negative effects is essential. Lastly, evaluating environmental policies like MUP should be seen not only as a means to determine the policy's success but also as an opportunity to identify areas for policy improvement. Relying solely on short- and mid-term evaluations may provide misleading results, as long-term effects may involve different mechanisms. Therefore, the last recommendation is to include in an initial evaluation plan also long-term evaluations of the policy, however, this was not part of the original MUP strategy which was defined only until the sunset clause (5 years after policy implementation).

Conclusions

This thesis highlighted the crucial interaction between epidemiology analyses and the evaluation of public health policies, using the AUD field and AUD policies in Scotland as a case study.

The epidemiology, learning from existing policy interventions and designing/implementing new interventions fitting the societal context, should tackle potential health threats. Then the policy evaluation should recognise what does and does not work from the implemented policies, suggesting further interventions to adjust for unexpected negative consequences or results lower than expectations. This is supposed to be an iterative process, tending to the most efficient policy design ensuring that policy development is based on the epidemiological evidence. Clear communication of policy results and the criticalness of some evidence to policy makers are crucial for successful implementation and evaluation.

The uneven distribution of the social burden of alcohol (e.g., higher AUD incidence in more socio-economic deprived groups, different distribution between acute and chronic burden by age and deprivation) risk to make across-the-board policies like MUP in Scotland effective but insufficient. Indeed, while MUP has shown decrease in consumption and positive clinical effects, it did not consistently affect the alcohol dependent population due to a more inelastic demand. MUP cannot be enough to handle the alcohol epidemic given that, even in contexts where it is already implemented, the AUD burden is increasing (e.g., increases in Scottish alcohol-specific death). To reach the unreached by MUP, this thesis suggests complementary policies looking at the reasons driving the 'harmful demand for alcohol' and work to guarantee 'equal treatment to AUD' rather than focusing only on making the 'alcohol supply' less appealing.

Moreover, recent unplanned events such as atypical large inflation and the pandemic that has reshaped consumption alcohol patterns and increased overall mental health care needs may have reduced the effect of promising policies such as MUP. Therefore, adjustments to the original policy are needed even more to tackle AUD and the associated health inequality.

Appendix

Table A1 Representing Simpson’s Paradox from *[105]*

Table 2. Odds Ratios of driving accidents for BAC intervals, re-analyzing data of Borkenstein et al. (1964)

	Model 1	Model 2	Model 3: within usual frequency groups				
			≤yearly	monthly	weekly	3x per week	daily
BAC (ref .00)							
.01-.04%	.94	1.17*	1.20	1.04	1.08	1.13	1.46*
.05-.07%	1.14	1.71***			1.84**	1.64	1.61
.08-.10%	3.11***	3.93***			4.30***	2.52**	3.16***
.11%+	6.79***	10.68***			11.59***	7.25***	13.22***
Usual frequency (ref ≤yearly)							
Monthly		1.03					
Weekly		.78***					
3 times per week		.59***					
Daily		.37***					

* p<.05, ** p<.01, *** p<.001,

Borkenstein et al. [106] strangely found a lower risk of car accidents for low levels of blood alcohol concentration (BAC) compared to a 0 level (Model 1, Table A2). However, Hurst et al.[107] using the same data after controlling for drinking frequency pattern (potential confounder) found a greater risk of injury across all BAC levels, including low (Model 2, Table A2). This was because risk of car accidents was higher among less frequent drinkers. However, while this association could have been mistakenly interpreted as a higher tolerance among frequent drinkers, frequency drinkers had fewer accidents also when BAC was zero (individuals did not drink in that occasion -data not in table-)[105]. Furthermore, when frequency was examined separately by BAC level, the odds ratio at a given BAC was not always smaller for more frequent drinkers (Model 3, Table A2). Therefore, drinking frequency was hiding a further risk factor not observed, which did not allow to provide a full/comprehensive causal interpretation of the pattern.

Overall, the alcohol-traffic accident relationship is not linear and can be confounded and modified by consumption patterns; additionally, it should be careful to causally explain associations through hypotheses (e.g., tolerance) when there are not deep foundations of a nature of the phenomenon and/or there are not investigations on the potential causal variables.

Glossary

Alcohol consumer category. Common categorisation of alcohol consumers into low/moderate, hazardous and harmful drinker (see below). The categorisation can change across countries. In the UK this categorisation was defined based on the number of units consumed per week in the 1995 Chief Medical Officer guidelines[21]. While such guidelines have been replaced with a broader recommendations (*drink no more than 14 units of alcohol a week to keep health risk at low levels[22]*), the categorisation is still used to define categories of alcohol consumers in recent researches (e.g., [23, 24]).

Alcohol consumption guidelines. Generally, it is the country definition of what is defined 'sensible limits of drinking' for the population and/or certain subpopulations. In the UK, the Chief Medical Officers provides the guidelines and in the 2016 update it split guidelines based on three categories of episodes: regular drinking, single drinking episodes and drinking in pregnancy.

Alcohol harm paradox. Higher socio-economic status groups are more likely to report exceeding recommended drinking limits, but those in lower socio-economic status groups experience more alcohol-related harm.

Alcohol use disorder (AUD). A medical condition characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences[108]. AUD is usually defined in ICD-10 codes in the F10.1 and F10.2 sessions. The updated version ICD-11 codes AUD can be classified in 6C40.1 and 6C40.2

Alcohol-related harm. Any harm associated with alcohol consumption, including physical, psychological and social harm. The term 'related' does not imply causality[5]. While all alcohol-specific harms are also alcohol-related, not all alcohol-related harms are alcohol-specific. For instance, deaths involving drink driving episodes, are usually recorded as alcohol-related but not alcohol-specific.

Alcohol-specific harm. Any harm causally linked with alcohol consumption. Examples are alcoholic liver disease, alcohol use disorder (addiction), alcohol poisoning.

Bias (psychology). A systematic deviation from objectivity or accuracy in judgment or perception potentially due to many factors such as personal beliefs, experiences, social factors or other.

Bias (statistics). Systematic difference between the expected and true value of an estimator.

Counterfactual. What would have happened if an action (i.e., an intervention) did not occur.

Difference in differences (DiD). A statistical method to estimate the causal impact of a treatment by comparing changes in outcomes between a treated group and a control group over time. It assumes similar trends in outcomes for both groups in the absence of treatment (parallel trend assumption).

Harmful drinker. A harmful drinker is someone whose alcohol consumption is causing damage to their health in terms of physical, psychological, or social consequences. Definition of harmful drinker can vary across countries. The WHO defines harmful drinking as "drinking that causes detrimental health and social consequences for the drinker, the people around the drinker and society at large"[109]. According to the UK 1995 categorisation it includes whose usual consumption of alcohol is more than 50/35 units per week for men/women[21].

Hazardous drinkers. Those whose usual alcohol intake is between 21 and 50 units per week for men or between 14 and 35 units per week for women[21].

Interrupted time series (ITS). Statistical analysis examining a series of data collected before and after an intervention to assess its impact. The impact is usually determined by the inference of a shift in the level of a change in trend in the series (or by the combination of the two).

Minimum unit pricing. Policy setting a minimum (floor) price per unit of a commodity below which it is illegal to sell that specific commodity.

Moderate drinker. Those whose usual alcohol intake is no more than 21/14 units per week for men/women (UK 1995 recommendations[21]).

Pattern (of drinking). Profile of drinking defined by volume drunk per episode as well as frequency and context of drinking occasion.

Prevention (primary, secondary, tertiary). Prevention is generally termed as the bundle of activities to stop people from getting diseases or to stop a disease from getting worse. Primary prevention refers to intervention measures to prevent the occurrence of a condition[110]. It usually targets the general population. Secondary prevention is the set of measures that increase the probability that a person with a condition will have it diagnosed at a stage that treatment is likely to result in cure or reduction in the severity of a condition[110]. It usually target high risk populations and in the context of alcohol it was defined as helping hazardous and harmful drinkers revert to low-risk drinking or abstain from alcohol[111]. Tertiary prevention focuses on the reduction of further complications of an existing disease, disability, or injury, through treatment and rehabilitation[110]. In the context of alcohol, it focuses on individual with already an AUD.

Prevention paradox. The fact that focusing on prevention on high-risk individuals might seem the most effective strategy to decrease the burden of disease, but it can have limited impact on reducing the overall number of cases of a disease[14].

Simpson paradox. A statistical relationship observed in a population that is reversed within all of the subgroups that form that population[67].

Theory of change. A method explaining how an intervention, or set of interventions, is expected to lead to specific development change and outcomes, based on causal pathways supported by the available evidence.

Unit of alcohol. A unit of alcohol is a measure of the amount of pure alcohol in a drink. While the concept of unit of alcohol as a way to compare different alcoholic beverages and understand their strengths is the same worldwide, the definition of unit changes across countries, making it difficult to compare consumption and or guidelines internationally. In the UK, 1 unit equals to 8 grammes of pure alcohol, which is also equivalent to 10 millilitres of pure ethanol (alcohol)[112]. In other countries 'unit of alcohol' is often defined as a 'standard drink'. Examples from other countries: in Australia a standard drink is 10 gr or 12.5ml of pure alcohol; in Canada a standard drink is 13.45 gr or 17.05 ml of pure alcohol.

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ORIGINAL PAPER

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Pharmacological treatments for alcohol dependence: Evidence on uptake, inequalities and comparative effectiveness from a UK population-based cohort

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Abstract

Introduction: We assessed the prevalence of prescribing of certain medications for alcohol dependence and the extent of any inequalities in receiving prescriptions for individuals with such a diagnosis. Further, we compared the effectiveness of two of the most prescribed medications (acamprosate and disulfiram) for alcohol dependence and assessed whether there is inequality in prescribing either of them.

Methods: We used a nationwide dataset on prescriptions and hospitalisations in Scotland, UK ($N = 19{,}748$). We calculated the percentage of patients receiving alcohol dependence prescriptions after discharge, both overall and by socio-economic groups. Binary logistic regressions were used to assess the odds of receiving any alcohol-dependence prescription and the comparative odds of receiving acamprosate or disulfiram. Comparative effectiveness in avoiding future alcohol-related hospitalisations ($N = 11{,}239$) was assessed using Cox modelling with statistical adjustment for potential confounding.

Results: Upto 7% of hospitalised individuals for alcohol use disorder received prescriptions for alcohol dependence after being discharged. Least deprived socio-economic groups had relatively more individuals receiving prescriptions. Inequalities in prescribing for alcohol dependence existed, especially across sex and comorbidities: males had 12% (odds ratio [OR] 0.88, 95% confidence interval [CI] 0.81–0.96) and those with a history of mental health hospitalisations had 10% (OR 0.90, 95% CI 0.82–0.98) lower odds of receiving prescriptions after an alcohol-related hospitalisation. Prescribing disulfiram was superior to prescribing acamprosate in preventing alcohol-related hospitalisations (hazard ratio ranged between 0.60 and 0.81 across analyses). Disulfiram was relatively less likely prescribed to those from more deprived areas.

Francesco Manca and Lisong Zhang are joint first authors.

Discussion and Conclusions: Inequalities in prescribing for alcohol dependence exists in Scotland with lower prescribing to men and disulfiram prescribed more to those from least deprived areas.

KEYWORDS
acamprosate, alcohol dependence, comparative effectiveness, disulfiram, inequality

1 | INTRODUCTION

Excessive alcohol use is related to a range of adverse health outcomes and causes societal as well as individual harm. Alcohol dependence, as defined by the National Institute for Health and Care Excellence, is 'characterised by craving, tolerance, a preoccupation with alcohol and continued drinking in spite of harmful consequences' [1]. Globally, in 2016, the estimated age-standardised prevalence of alcohol dependence was 1320.8 cases per 100,000 people [2]. In the United Kingdom, between 1990 and 2013, the estimated rate of presentation to general practice with alcohol dependence was 171 and 76 per 100,000 male and female patients, respectively [3].

International guidelines recommend pharmacological treatments for patients with alcohol dependence subsequent to detox and alongside psychosocial support, with specific medications suggested based on patients' goals (reduction in consumption or abstinence), comorbidities and capabilities to cope with potential side effects [4-6]. Concerning the United Kingdom, the National Institute for Health and Care Excellence clinical guidelines recommend that for people with mild alcohol dependence a psychological intervention is offered, and for those with moderate/severe alcohol dependence these psychological interventions can be used in combination with pharmacological treatments [1]. In the United Kingdom, nalmefene, naltrexone, acamprosate and disulfiram are the medications for treating alcohol dependence, with the last two by far the most frequently prescribed. Acamprosate helps to maintain abstinence by restoring neurotransmitters affected by excessive alcohol use and contributing to managing alcohol cravings, but it is generally effective only in someone already sober [7,8]. Disulfiram causes unpleasant symptoms if alcohol is consumed, functioning as a deterrent to alcohol drinking [9]. Due to its strong effects, manufacturers suggest that patients and their carers are counselled on the disulfiram-alcohol reaction and the National Institute for Health and Care Excellence advises monitoring patients in the initial phases of treatment [10]. The evidence directly comparing disufiram and acamprosate is based on two open-label randomised trials [11,12] and one observational study. The trials had different outcomes. One showed disulfiram to be more effective in reducing alcohol intake, increasing the number of abstinence days and reducing risks of relapse [12]. The second found that disulfiram increased the percentage of abstinent patients and reduced risk of relapse [11]. In a small observational study ($N = 353$) that directly compares the two medications, it was found that disulfiram led to a longer duration of time to alcohol relapse and higher cumulative abstinence [13]. To enhance this evidence base, as well as further randomised trials with longer-term clinical outcomes, high-quality comparative effectiveness research is needed from large, unselected cohorts identified in routine care databases.

Despite evidence on effectiveness and their inclusion in clinical guidelines, pharmacological intervention for treating alcohol dependence is underutilised in clinical practice [14,15]. When there is evidence of underutilisation, it is important to understand whether this is caused, at least in part, by some groups being less likely to receive prescriptions than others. If this happens, inequalities in health outcomes can be exacerbated if those less likely to receive prescriptions are those who are most in need (i.e., more likely to experience severe alcohol dependence). Previous studies showed potential disparities in receiving pharmacotherapy for alcohol use disorder (AUD) across ethnic [16] and socio-economic [17] groups. Studies on the United Kingdom found similar patterns [15], with males and more deprived groups less likely to receive medication. However, specific variables such as comorbidities were not considered. Further, no study analysed the inequality of prescribing across medications with the same indication of alcohol dependence but different effectiveness on alcohol abstinence. Indeed, the health inequalities associated with the burden of alcohol could be also related to imbalances in prescribing medications with different levels of effectiveness across different groups beyond the prescribing action itself.

Using a nationwide routine health-care dataset of hospitalisations in Scotland (United Kingdom), we aimed to identify the rate of people hospitalised with a diagnosis of alcohol dependence and assess the percentage of patients receiving alcohol dependence prescriptions and the extent of any difference in the odds of receiving prescriptions (by age, sex and socio-economic deprivation). Further, we compare the real-world effectiveness of acamprosate and disulfiram in avoiding the first alcohol-related hospitalisation. Lastly, we assess whether there are differences in prescribing between these two medications. Our intention is to add evidence on the inequality of the burden of alcohol associated with access to pharmacological treatment, as well as the relative effectiveness of the two most used medications for alcohol dependence in a nationwide study.

2 | METHODS

This study is composed of four different analyses included in three sections. Section 1 describes an analysis of rates of alcohol-related hospitalisations and prescriptions for alcohol dependence in this population. Section 2 analyses prescription inequality in two ways: first, the differences in odds of receiving any prescription for alcohol dependence across subpopulation groups; and second considering differences between those who receive prescriptions for acamprosate or disulfiram. Section 3 compares the effectiveness of disulfiram and acamprosate. The data sources were the same across analyses. Differences in cohort definition, size and methods of investigation are described in each section below, detailed cohort identification diagrams are in Data S1, Supporting Information.

2.1 | Data sources

We utilised a Scottish dataset linking three nationwide administrative health-care databases containing data from 2010 to 2019, dispensed prescriptions in the community (Scottish National Prescribing Information System [18]), general and acute hospitalisations (Scottish hospital records [SMR01] [19]) and deaths (National Records of Scotland) [20]. SMR01 uses International Classification of Diseases 10th Revision (ICD-10) codes to categorise patients' diagnoses.

2.2 | Analyses and pharmacological treatments

We evaluated rates and variations in the odds of receiving prescriptions for all medications in the UK guidelines with an exclusive indication for the treatment of moderate or severe alcohol dependence [1]: acamprosate, disulfiram and nalmefene. However, nalmefene was rarely prescribed and we focused on the two most common prescriptions: acamprosate and disulfiram and compared their effectiveness separately. We then ran a further analysis assessing imbalance in prescriptions between these two medications across different groups. Naltrexone is another medication that can be used for the treatment of alcohol dependence. However, in the United Kingdom, naltrexone was initially licensed only for the treatment of opioid dependence, and while it was used off-label for alcohol dependence, it became licensed for this purpose only in October 2022 [21] (out of our study period). Given that naltrexone is not exclusively indicated for alcohol dependence, and its extremely low prescription levels compared to acamprosate and disulfiram in the United Kingdom [15], we excluded it from our analyses.

2.3 | Statistical analyses

Table 1 summarises the outcome of each analysis, which are explained in detail in the sections below.

2.3.1 | Rates

We assessed the incidence rates of alcohol dependence over time. Specifically, we checked the rate of patients with a first hospitalisation of 'mental and behavioural disorders due to alcohol' (ICD F10.x, main diagnostic position). We used data from national Scottish population records as denominators to compute the percentage of individuals with alcohol dependence medications dispensed within 60 days after discharge. We determined 60 days after discharge as the maximum window to link the alcohol dependence prescription with the hospitalisation event. We assessed differences in prescriptions across age, sex and socio-economic group.

2.3.2 | Inequality

We identified a cohort between January 2010 and March 2019 with a first hospitalisation of AUD diagnoses in the main diagnostic position (see above for inclusion criteria) screening back for 10 years to avoid previous alcohol-related hospitalisation. We determined whether patients received prescriptions within 60 days from their diagnosis. We repeated the same analysis on prescriptions received any time after the diagnosis. Logistic regression was used to assess whether age, sex and socio-economic deprivation area of the patient (measured through the Scottish index of multiple deprivation [22]) were associated with the odds of receipt of prescriptions for alcohol dependence. We also adjusted for comorbidities

TABLE 1 Summary sections and outcomes.

Summary section	Outcome
Rate	a. Incidence of first AUD hospitalisation in the Scottish population b. Percentage of AUD hospitalised individuals receiving prescriptions for alcohol dependence after discharge
Inequality	
Inequality in prescription	Odds of receiving prescription ever before, 60 days before, 60 days after or ever after the first AUD hospitalisation
Inequality between acamprosate and disulfiram	Odds of receiving acamprosate vs disulfiram prescriptions 60 days after or ever after the first AUD hospitalisation
Comparative-effectiveness	Time to first AUD hospitalisation

Abbreviation: AUD, alcohol use disorder.

(measured through Charlson comorbidity score [23]), previous hospitalisation related to mental health (any ICD-10F code) and for receipt of alcohol dependence prescriptions before hospitalisation. Whenever the relationship between covariates and the dependent variable was not linear (e.g., for age), restricted cubic splines [24] were used to allow for curvi-linear associations. After excluding missing data on sex, level of deprivation or age ($n = 278$), the final sample in this inequality analysis was 19,748 individuals. We also ran an additional analysis using as the dependent variable obtaining a prescription before the hospitalisation (yes/no). This was to assess imbalances of prescriptions that aim to prevent patients being hospitalised.

2.3.3 | Comparative effectiveness

We identified patients with a first prescription of acamprosate or disulfiram without any previous hospitalisation for F10.x in the previous 10 years. The outcome under study was time to first hospitalisation for F10.x after prescription, the independent variable of interest was whether the patient was prescribed acamprosate or disulfiram. We assessed time to first hospitalisation using four approaches—Cox regression: unadjusted, adjusted for covariates (age, sex, socio-economic deprivation), covariates used in propensity scores (inverse probability weight) and an instrumental variable approach using physician prescribing preferences (IV PPP) [25]. For IV PPP, we implemented two-stage residual inclusion (2SRI) models which provide consistent estimators in non-linear models [26]. The instrument we used in our 2SRI-Cox model is the proportion of acamprosate prescribed by a particular physician in the last 10 prescriptions. While the first two approaches controlled for measured confounding by indication, the third one, providing assumptions are met, accounted for potential unmeasured confounding. Instrumental variables are useful whenever there is likely to be unmeasured confounding that would create bias in comparative effectiveness estimates that only account for measured covariates. After excluding for missing data across the covariates ($n = 67$), the sample size for the comparative effectiveness analysis was ($N = 11,238$).

The goodness of fit of every model and test for survival analyses assumptions are reported in Data S1. The analysis was performed with Stata 17 [27] and the instrumental variable models for the comparative effectiveness analyses was performed in R, using packages 'AER' and 'survival'.

3 | RESULTS

The socio-demographics regarding the imbalance in receiving prescriptions and comparative effectiveness cohorts are summarised in Table 2. Individuals in the inequality cohort had an average of 44.8 (±18) years of age, and 68% were male. Individuals receiving prescriptions were on average more than 1 year older. In the comparative effectiveness analysis cohort acamprosate was prescribed more than twice as frequently as disulfiram and it was prescribed relatively to less males and to more deprived areas.

3.1 | Rates

The rate of AUD hospitalisation slightly increased over the years (see Figure 1); it was between 3 and 4 per 10,000 inhabitants in our study period, with 6–7% individuals receiving a prescription for alcohol dependence medications within 60 days after their first hospitalisation. This percentage varied across socio-economic groups, with the least deprived groups receiving more, in percentage terms, prescriptions after hospital discharge compared to the most deprived groups (apart from in 2016). There were also differences between age categories with groups between 36 and 65 years of age receiving more prescriptions in percentage terms. In contrast, there were no relevant differences in receiving prescriptions between sexes (for figures by age groups and sex see Data S1).

TABLE 2 Summary of socio-demographic variables for cohorts with a diagnosis of alcohol dependence.

			Sex		Charlson comorbidity index			Socio-economic deprivation in quintiles				
	N.	Age, years mean (±SD)	Male	Female	0	≥1	Previous hospitalisations for mental health	First (most deprived)	Second	Third	Fourth	Fifth (least deprived)
Inequality												
Total (%)	19,748	44.8 (±18)	13,463 (68%)	6285 (32%)	14,049 (71%)	5699 (29%)	6086 (31%)	5853 (30%)	4896 25%)	3925 (20%)	2964 (15%)	2110 (11%)
Individuals receiving prescriptions	1240	46.1 (±11)	841 (68%)	399 (32%)	888 (72%)	352 (28%)	408 (33%)	275 (22%)	340 (27%)	278 (22%)	205 (17%)	142 (11%)
Acamprosate[a]	840	46.5 (±11)	541 (64%)	299 (36%)	584 (70%)	256 (30%)	267 (32%)	197 (23%)	236 (28%)	183 (22%)	136 (16%)	88 (10%)
Disulfiram[a]	349	45.3 (±11)	222 (64%)	127 (36%)	262 (75%)	87 (25%)	120 (34%)	67 (19%)	92 (26%)	80 (23%)	61 (17%)	49 (14%)
Not receiving prescriptions	18,508	44.2 (±18)	12,662 (68%)	5846 (32%)	13,161 (71%)	5347 (29%)	5678 (31%)	5578 (30%)	4556 (25%)	3647 (20%)	2759 (15%)	1968 (11%)
Comparative effectiveness												
Acamprosate	8016	44.9 (±12)	4911 (61%)	3105 (39%)	-	-	-	2874 (36%)	1969 (25%)	1451 (18%)	1030 (13%)	692 (9%)
Disulfiram	3223	43.2 (±11)	2088 (65%)	1135 (35%)	-	-	-	964 (30%)	814 (25%)	626 (19%)	473 (15%)	346 (11%)

[a]The number of patients receiving acamprosate and disulfiram prescriptions does not equate to total number of patients as nalmefene was also prescribed.

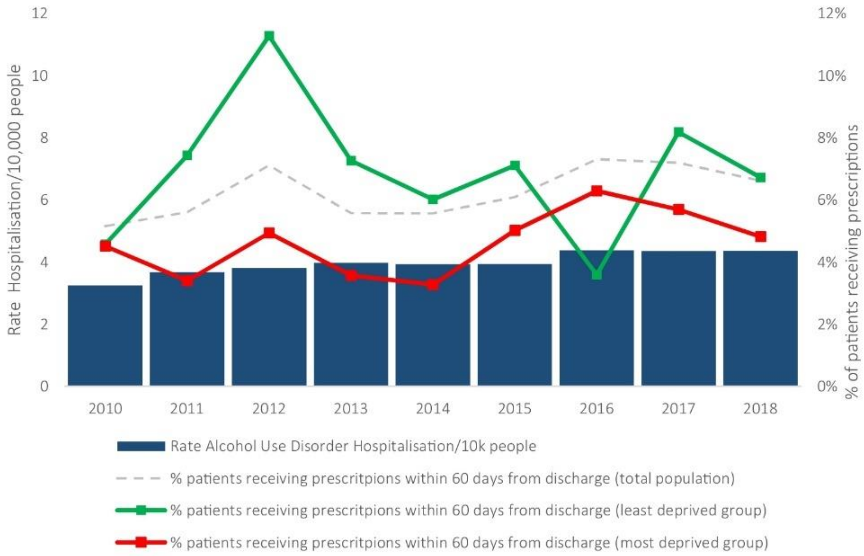

FIGURE 1 Trends and rates of alcohol use disorders hospitalisation and percentage of such individuals receiving alcohol dependence prescriptions within 60 days of the discharge date. In the figure, 2019 was removed as data were only until March.

3.2 | Inequality

The odds of receiving prescriptions with indications for alcohol dependence after 60 days from an AUD hospitalisation was associated with sex (males had 12% lower odds of receiving a prescription than females, odds ratio [OR] 0.88, 95% confidence interval [CI] 0.77–1.00—see Table 3, column 1) and age (odds increasing until 43 years of age and then decreasing in older individuals—see Data S1 for graphs showing curvi-linear association with age). Socio-economic deprivation was also associated with odds of receiving prescriptions after a secondary health-care episode: living in least deprived areas was significantly associated with an increase in odds of receiving prescriptions of at least 41% (OR 1.41, 95% CI 1.18–1.68—for the second most deprived quintile compared to the most deprived) (Table 3, column 1). Lastly, receiving prescriptions prior to hospitalisation was associated with a 23-fold increase (OR 23.42, 95% CI 19.63–27.94) in the odds of receiving prescriptions later. Being previously hospitalised for other mental health diagnoses did not have a strong association with prescriptions just after being discharged but became more precise and statistically significant (OR 0.90, 95% CI 0.82–0.98) when we did not include the 60 days constraint after hospitalisation (Table 3, column 2). In contrast, socio-economic deprivation reduced its impact in odds of receiving prescriptions after removing the 60 days constraint.

When we analysed odds of receiving prescriptions before hospitalisation (Table 3, columns 3 and 4), comorbidities (and in particular mental health comorbidities) were associated with increased odds of receiving prescriptions (OR 1.32, 95% CI 1.20–1.44). In contrast, they were associated with reduction in the odds of getting prescriptions after hospitalisation in the long term (OR 0.90, 95% CI 0.82–0.98—Table 3, column 2). We found that the odds of receiving disulfiram instead of acamprosate were associated with deprivation and with the kind of medication received before hospitalisation (Table 3, columns 5 and 6). Receiving disulfiram prior to hospitalisation was associated with an increase in odds of receiving disulfiram after (OR 6.01, 95% CI 4.08–9.08). Conversely, receiving acamprosate before hospitalisation was associated with a decrease in the odds of getting disulfiram after.

3.3 | Comparative effectiveness

The comparative effectiveness modelling shows that prescribing disulfiram, compared to acamprosate, was associated with a reduced risk of first alcohol-related hospitalisation. All three methods were consistent in their findings (Figure 2). Instrumental variable modelling produced point estimates showing larger associations but with wider confidence intervals. Point estimates across the four methods varied from hazard

TABLE 3 Inequality models of prescriptions after alcohol dependence diagnosis in primary care and AUD hospitalisations in secondary care (odds ratios and confidence intervals shown).

	Any alcohol dependence prescription after 60 days from hospitalisation (1)	Any alcohol dependence prescription ever from hospitalisation (2)	Any alcohol dependence prescriptions 60 days prior first hospitalisation (3)	Any alcohol dependence prescription ever before first hospitalisation (4)	Acamprosate versus disulfiram prescriptions within 60 days of hospitalisation—acamprosate reference (5)	Acamprosate versus disulfiram prescriptions ever after hospitalisation—acamprosate reference (6)
Sex (female reference)	0.88 (0.77–1.00)	0.88 (0.80–0.96)	0.79 (0.67–0.94)	0.72 (0.65–0.78)	1.00 (0.76–1.32)	1.10 (0.93–1.29)
Charlson Comorbidity Index (0 reference)						
≥1	0.92 (0.80–1.07)	0.91 (0.834–1.00)	1.04 (0.87–1.24)	1.09 (0.99–1.20)	0.84 (0.67–1.15)	0.77 (0.64–0.93)
Mental health comorbidity	0.92 (0.80–1.05)	0.90 (0.82–0.98)	1.28 (1.09–1.51)	1.32 (1.20–1.44)	1.11 (0.83–1.48)	1.14 (0.96–1.35)
Socio-economic deprivation (1 = most deprived, reference)						
2	1.41 (1.18–1.68)	1.05 (0.94–1.17)	1.57 (1.25–1.95)	1.28 (1.13–1.44)	1.20 (0.81–1.78)	1.42 (1.14–1.77)
3	1.62 (1.35–1.96)	1.11 (0.99–1.25)	1.33 (1.04–1.70)	1.32 (1.16–1.50)	1.41 (0.94–2.13)	1.29 (1.02–1.63)
4	1.54 (1.25–1.89)	1.07 (0.94–1.22)	1.52 (1.17–1.96)	1.37 (1.19–1.58)	1.41 (0.91–2.19)	1.47 (1.14–1.90)
5	1.45 (1.16–1.83)	1.12 (0.97–1.29)	1.63 (1.23–2.16)	1.50 (1.29–1.75)	1.92 (1.187–3.10)	1.78 (1.35–2.35)
Previous prescription in the previous 60 days[a]						
Any	23.42 (19.63–27.94)					
Acamprosate						0.51 (0.37–0.70)
Disulfiram						6.48 (4.82–8.71)
Previous prescription ever[a]						
Any		5.12 (4.66–5.63)				
Acamprosate					0.45 (0.30–0.69)	
Disulfiram					6.08 (4.08–9.07)	

Note: As the relationship with age was not linear, we applied spline, see graph for interpretation of spline in Data S1.
Abbreviation: AUD, alcohol use disorder.
[a]Any stands for 'any kind of prescription for alcohol dependence' and it is used in models referring to the overall inequality after hospitalisation (1) and (2), the variable is a dichotomous (0 = no prescriptions and 1 = prescriptions). Models (5) and (6), comparing acamprosate and disulfiram, specify the kind of prescription received before hospitalisation in a trichotomous variable (0 = no previous prescriptions, 1 = previous acamprosate prescriptions, 2 = previous disulfiram prescriptions) where the reference is 'no previous prescription'.

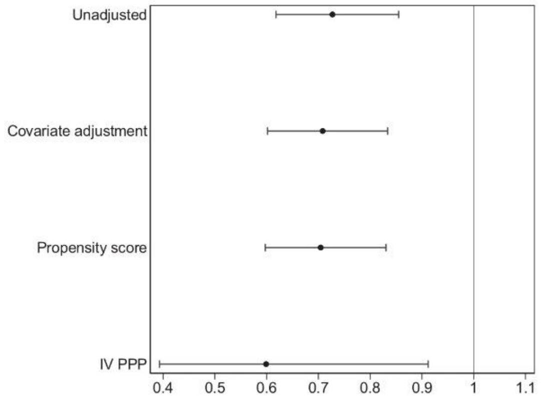

FIGURE 2 Representation of hazard ratio point estimate and 95% confidence intervals of models measuring comparative effectiveness of disulfiram and acamprosate. Acamprosate is the reference category. Circles are for point estimate related to models. IV PPP stands for instrumental variable based on Physician Prescribing Preferences.

ratio 0.60 (95% CI 0.39–0.91) for IV PPP to 0.73 (0.62–0.86) for unadjusted regression, indicating that disulfiram was associated with a reduction in the risk of alcohol-related hopitalistation between 40% and 27% compared to acamprosate. For detailed results of comparative-effectiveness analysis, see Data S1.

4 | DISCUSSION

4.1 | Prescription rates and inequality in prescription

We found the rate of alcohol-related hospitalisation to be between 3 and 4 per 10,000 population between 2010 and 2018 with 6–7% receiving a prescription for alcohol dependence medication after discharge. Our analyses highlighted that several socio-demographic factors were associated with the prescribing for alcohol dependence. Some factors such as sex, age and socio-economic areas were associated with differences in receiving prescriptions for alcohol dependence. Specifically, living in the most socio-economically deprived areas was associated with lower odds of receiving prescriptions within 60 days after the first AUD hospitalisation. The comparative effectiveness modelling suggests that patients in receipt of disulfiram had a lower risk of a first alcohol-related hospitalisation compared with those in receipt of acamprosate. Furthermore, we showed that those living in the least socio-economic deprived areas were associated with an increase in odds of being prescribed the most effective medication (disulfiram) after hospitalisation. We believe that these findings have important implications for socio-economic health inequalities for the alcohol dependent population.

Our findings are in line with other UK studies, showing a low percentage of pharmacotherapy treatment for patients with alcohol dependence. A study of patients diagnosed with alcohol dependence in primary care found that 11.7% received relevant pharmacotherapy, concluding that the prescribing of drug therapy was 'low' [13]. Our study, evaluating the percentage of prescriptions for alcohol dependence after any AUD hospitalisations (including alcohol dependence) found that between 6% and 8% of patients received alcohol dependence prescriptions, confirming that prescribing remained 'low' in secondary care.

Regarding prescription inequality, Thompson et al. [15] in a similar study regarding primary care data between 1990 and 2013, found comparable inequality patterns for sex and age and socio-economic deprivation in determining differences in odds of receiving alcohol dependence prescriptions. We found that socio-economic deprivation status was associated with disparities in receiving prescriptions within 60 days from discharge. However, in contrast, the extent of such disparities decreased for prescribing if we removed the 60 days constraint. This could suggest that distinct deprived groups can have different ease and access to care in the initial phase after hospital discharge, which is the most critical period in avoiding relapses [28]. Indeed, individuals with alcohol dependence requiring hospitalisation often require specialist alcohol treatment in hospitals or in community settings. Studies describing a lower utilisation of specialist care in groups with lower levels of educational attainment [29], can explain why we found lower prescription rates in the most deprived areas. With our data, we cannot attribute the overall inequality we found in prescriptions concerning sex and age (which are consistent across primary and secondary health care), to practitioners or to services prescribing the medications. On the contrary, we believe that a combination of factors such as the lower propensity to seek help of certain patient groups (e.g., males are less likely to seek consultation [30], especially regarding psychological matters [31]) may be responsible for this. We also found that comorbidities and previous alcohol dependence medications were associated with the odds of receiving prescriptions.

Regarding comorbidities, a history of previous mental health hospitalisations was associated with an increase in the odds of being issued prescriptions before the hospitalisation and with a reduction in the odds of getting prescriptions afterwards. This could suggest that patients with certain comorbidities are also more likely to be in contact for mental health assistance and more likely to be treated with alcohol dependence pharmacotherapies aimed to prevent a future hospitalisation. On the contrary, after a hospitalisation, existing or previous mental health conditions decreased the odds of receiving alcohol dependence prescriptions. This could imply that after severe episodes such as alcohol-related hospitalisations, patients with such comorbidities may have other recovery goals rather than abstinence (e.g., consumption reduction), or alternatively, the potential interaction with other psychotropic therapies may reduce the odds of getting alcohol dependence prescriptions.

4.2 | Comparative effectiveness

Our analysis of real-world data on a nationwide cohort in Scotland, UK shows that disulfiram was superior to acamprosate in avoiding a first alcohol-related hospitalisation. Our results are in accordance with previous evidence from small randomised control trials [11,12] and a small observational study [13] that reported disulfiram to be more effective in maintaining abstinence, craving, days until relapse and consumption and abstinence, respectively. Our instrumental variable analysis showing similar results to methods that adjust for measured confounders by indication only, strengthens the internal validity of our study. The wider confidence intervals of the IV PPP models can be ascribed to the fact that such intervals from two stage least square models have a 'tendency' to be 'large' [32]. The point estimates of the propensity score and covariate adjustment models being closer to the null may be due to a positive correlation between unmeasured confounders (captured by IV PPP) and probability of being prescribed disulfiram. Potential unmeasured confounding factors are initial alcohol dependence severity [13], as well as motivation and supervision of the patient. As disulfiram's mechanism of action is to cause unpleasant symptoms if alcohol is consumed, patients deemed more motivated to abstinence or with greater supervisory support could be more likely to be prescribed disulfiram than acamprosate. It is worth noting that we do not link the results of our comparative effectiveness analysis to the medication's pharmacological substances only, but it could be generated by a mixture of other factors such as the close monitoring suggested for disulfiram administration.

4.3 | Inequality between disulfiram and acamprosate

In our inequality analysis (Table 3, models 5 and 6), we showed how living in the most deprived areas decreased the odds of being prescribed the most effective medication to avoid alcohol-related hospitalisation compared to living in the least deprived areas. This remained the only driver of prescription imbalances between the two medications. We believe this has important implications for health inequality. However, it is not possible from this study to understand the reasons for this inequality. We attribute this to potential unmeasured factors such as likely less available assistance, supervision or close clinical monitoring (recommended for disulfiram [10]) in individuals living in more deprived areas. Other factors may be patient preference, severity of dependence or also prescriber factors. The general inequality of prescriptions for alcohol dependence combined with the inequality of the most effective in favour of the least deprived groups can partially explain the social imbalance of the burden of alcohol. In considering implications for services, we believe that improving patient access to specialist services after being hospitalised for alcohol-related reasons and developing new integrated care pathways is essential.

4.4 | Strengths and limitations

Our findings regarding prescription inequality are novel, especially on differences in prescribing of acamprosate and disulfiram, and they have relevance for current practice in care and treatment of patients with alcohol dependence after alcohol-related hospitalisations. We also believe we provided the most robust real-world comparative effectiveness evidence to date by using several different methods to account for measured and unmeasured confounders. Further, we utilised nationwide dataset for Scotland, while previous real-world studies had lower statistical power [13].

A potential limitation was that we looked at all the ICD-10 codes identifying all AUD hospitalisations rather than alcohol dependence only. We included all AUD diagnoses mainly to correct for possible errors in recording data across different alcohol-related diagnostic codes which are possible in general/acute hospital records. Indeed, in the datasets, some of the people not hospitalised for alcohol dependence but for other AUD conditions (e.g., withdrawal or intoxication) received alcohol dependence prescriptions. We are also aware that some potentially key variables were not always considered across our analyses. Specifically, both disulfiram and acamprosate (which are the most prescribed in the United Kingdom with an indication of alcohol dependence) are aimed at abstinence. However, some individuals may have moderation rather than abstinence as a goal, and this may be one of the reason for the low percentage of prescribing we found. Similarly, we used 'first alcohol-related hospitalisation' as the only outcome variable in our analysis which does not reflect other important recovery outcomes which may be important to patients but for which robust data is lacking. Some other variables describing risk factors for AUD as well as potential choice of one pharmacological therapy over another were not available to us (e.g., marital status as a risk factor for AUD [33]—but also potential proxy for support when an individual is prescribed disulfiram and/or other opportunities of direct patient supervision). While the instrumental variable analysis should have attenuated this potential source of bias, to be conservative, we discuss diverse explanations for our findings that go beyond the pharmacology of the medication to other factors such as close monitoring or patient motivation.

5 | CONCLUSIONS

Alcohol dependence medications are not extensively prescribed in Scotland, UK. Differences in prescribing exist, especially across categories of sex, age and socioeconomic status. People living in the most deprived areas have lower odds of receiving a prescription following an alcohol-related hospitalisation, which is the most critical period to avoid further hospital episodes. Living in the most deprived areas also has lower odds of receiving disulfiram. Yet, receipt of disulfiram is strongly associated with a lower chance of a further alcohol-related hospitalisation. Further consideration is needed to understand these inequalities in prescribing and to develop new strategies to reduce the societal imbalance in the burden of alcohol.

AUTHOR CONTRIBUTIONS

Francesco Manca and Lisong Zhang contributed equally to the study. Jim Lewsey, Niamh Fitzgerald, Hamish Innes and Andrew McAuley initial conception/design and funding acquisition for the study. Jim Lewsey, Francesco Manca and Lisong Zhang extension of initial project ideas/design and adaptation of the original design to the data. Francesco Manca and Lisong Zhang data analysis, visualisation. Jim Lewsey, Francesco Manca and Lisong Zhang data interpretation. Francesco Manca original draft of the study. Jim Lewsey supervision and management of Francesco Manca and Lisong Zhang. Jim Lewsey and Francesco Manca data acquisition. Jim Lewsey, Niamh Fitzgerald, Hamish Innes, Andrew McAuley, Clare Sharp, Frederick Ho, Bhautesh Jani, Srinivasa Vittal Katikireddi and Lisong Zhang editing of manuscript.

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CONFLICT OF INTEREST STATEMENT

He declares no other conflicts of interest. All other authors have no conflict of interests to disclose.

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SUPPORTING INFORMATION

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

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RESEARCH REPORT

ADDICTION SSA

Previous psychiatric hospitalizations as risk factors for single and multiple future alcohol-related hospitalizations in patients with alcohol use disorders

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Abstract

Background and aims: People with alcohol use disorder (AUD) often have co-occurring psychiatric conditions. The association between psychiatric conditions and AUD relapse has not yet been fully explored. This study aimed to quantify different psychiatric comorbidities as risk factors for first and multiple AUD rehospitalizations in patients already hospitalized once for AUD.

Methods: We used a nation-wide routine health-care database in Scotland, UK, between 2010 and 2019. Individuals with a first hospitalization for AUD (codes F10.0-9 in the ICD-10 codes) were checked for previous hospitalizations where the main or co-occurring cause was a psychiatric condition (any other F0-F99 code in ICD-10). The final cohort included 23 529 patients, 18 620 of whom did not have a history of any other psychiatric comorbidity. First, individuals with a history of any previous psychiatric hospitalization were grouped and compared with those without on the basis of time to AUD rehospitalization. Then, individuals with different histories of psychiatric hospitalization were compared with each other. Cox and Prentice, Williams and Peterson gap-time models were used for single and multiple AUD rehospitalizations, respectively.

Results: The AUD rehospitalization rate in individuals with a previous psychiatric hospitalization was 8% higher compared with those without [hazard ratio (HR) = 1.08, 95% confidence interval (CI) = 1.01–1.14]. The difference in rehospitalization rate reduced following the first rehospitalization (HR at second rehospitalization from first: 0.95, 95% CI = 0.87–1.04 and HR at third rehospitalization from second: 0.94, 95% CI = 0.84–1.07). Mood disorders and neurotic, stress-related and somatoform disorders were associated with a 54% (HR = 1.54, 95% CI = 1.38–1.72) and 39% (HR = 1.39, 95% CI = 1.17–1.66) increase in the risk of a first AUD rehospitalization. Other conditions, such as disorders due to psychoactive substance use or schizophrenia, were associated with decreases in future AUD rehospitalization (HR = 0.89, 95% CI = 0.82–0.97 and HR = 0.82, 95% CI = 0.58–1.16, respectively).

Conclusions: Patients with AUD appear to have different rates of AUD rehospitalization based on different co-occurring psychiatric conditions. Addiction-related characteristics may be more relevant risk indicators for multiple AUD readmission than psychiatric comorbidities.

KEYWORDS
Alcohol dependence, alcohol use disorder, comorbidities, mental health, multiple failure survival analysis, observational study, Prentice Williams and Peterson model, psychiatric disorders, relapse, routine health-care data

INTRODUCTION

The vulnerability of an individual to a specific substance use disorder, such as alcohol use disorder (AUD), is due to a combination of biological, physiological and developmental risk factors [1]. Specifically, for AUD, it has been shown how genetics (e.g. variations in a large number of genes [1, 2]) and the environmental and social context (e.g. social support and peer pressure [3, 4]) can be associated with addiction. Other relevant factors for AUD are personality [5] and comorbidities (i.e. the presence of additional conditions co-occurring with AUD) [6].

People with AUD often present with co-occurring psychiatric conditions [7]. The NESARC-III survey, a nationally representative study on the adult population in the United States, found that mental disorders were more prevalent in those with severe AUD. Furthermore, those mental disorders were themselves more severe [8]. This effect was more pronounced in borderline, antisocial and avoidant disorders. Other studies have shown associations between anxiety and mood disorders with the presence of any AUD [7, 9].

The relationship between AUD and other psychiatric disorders is complex and bidirectional, with alcohol use as both a cause and effect of other psychiatric symptomatology. Specifically, there are studies indicating that psychiatric disorders may trigger other risk factors for AUDs [6, 9]. In contrast, other research found that AUDs could induce psychiatric syndromes, mainly due to the effects that functioning AUD may have on psychological function [6, 10]. Moreover, self-medication, which is the use of alcohol (or other substances) to manage the symptoms caused by other conditions, may create or strengthen the association between the use disorder and psychiatric morbidity.

Beyond incident AUD, another important factor for the impact of psychiatric comorbidities is relapse. Relapse can be defined as the recurrence of problematic alcohol use after a period of improvement [11]. Relapses can be triggered by numerous factors and can be partly explained by the compulsive nature of addiction itself. Previous studies have shown how long-term relapse rates can vary between 42.9 and 60.5% based on receiving treatment for AUD [12]. Therefore, relapse to AUD during or after remission and detoxication constitutes a significant public health concern. Different psychiatric conditions could lead to different experiences of withdrawal symptoms, but also different desires or cravings after remission; thus, they could have different associations with risk of relapses.

While there is evidence of an association between specific comorbidities and AUD, and the additional barriers to recovery experienced by AUD patients [13], there is limited research on how the type of psychiatric comorbidity may affect the risk of AUD relapse. Previous literature reviews [14, 15] found heterogeneous results for the role of psychiatric comorbidities on the risk of relapse. This was probably due to studies being limited to specific populations and comorbidities and inconsistencies in how relapses were defined and measured [15]. Beyond these limitations, these studies usually have either small sample size or poor follow-up—a particular challenge in this area of research, as relapses may not occur for several years.

In observational studies using routine health-care data, relapse is typically more difficult to detect. In particular, as mild AUDs are often undiagnosed and untreated, hospital records are more likely to detect severe AUD episodes (those requiring hospitalizations) or incidental AUD diagnoses. Therefore, while observational studies using routine health-care records are unlikely to capture the full chronological relapse history of all individuals, they are likely to identify the most important clinical cases. Moreover, although studies using routine health-care data may present more challenges in precisely measuring AUD relapses, they usually have longer follow-up periods and a larger sample size, suggesting stronger external validity of their findings.

By using a routine health-care database, this study aims to describe patients hospitalized due to AUD with different psychiatric comorbidities and to quantify such comorbidities as risk factors for AUD rehospitalization. Epidemiological studies typically estimate only the time to the first outcome event [16] (e.g. rehospitalization). In this study, we estimated both first and multiple AUD rehospitalizations, allowing assessment of whether the effect of comorbidities changed in further AUD episodes. We used a nation-wide database of individuals with hospitalizations due to AUD in Scotland, UK between 2010 and 2019.

METHODS

Cohort identification

This study used the General/Acute and Inpatient Day Case (SMR01) data set [17], which collects patient-level data for all episodes of hospital inpatient and day case hospitalizations from hospitals in Scotland. We identified our cohort by selecting all patients aged more than 18 years who had AUD as the main reason for their hospitalization between January 2010 and March 2019. We selected only patients with the first hospitalization for AUD in the last 10 years, by screening back 10 years in the hospital records. Diagnoses were recorded in the SMR01 data set using the International Statistical Classification of Diseases and Related Health Problems, 10th version (ICD-10 [18]); all codes under the category 'mental and behavioural disorders due to the use of alcohol' (codes F10.0-9) were identified as AUD. There were no changes to the diagnosis classification throughout the study period.

We then obtained previous hospitalizations related to psychiatric conditions from hospital records up to 10 years prior to the first AUD episode. Comorbidities were identified as previous hospitalizations with a psychiatric condition (any F0-F99 code in ICD-10, but excluding codes F10.0–9) as either the main or co-occurring cause. Events of interest were subsequent hospitalizations with AUD coded as the main cause of hospitalization.

The final cohort included 23 529 patients, 18 620 of whom did not have a history of any other psychiatric comorbidity. We first compared individuals with and without a history of previous psychiatric hospitalizations. Successively, to allow head-to-head comparisons of the impact of each psychiatric diagnosis on AUD rehospitalizations, individuals with more than one kind of previous psychiatric diagnosis were removed. We then divided patients into five subgroups based on the ICD-10 mental and behavioural disorders diagnosis received in a previous hospitalization: OMD (organic mental disorders, identified with F0 codes in the ICD-10 classification), PSU (mental and behavioural disorders due to psychoactive substance use—excluding alcohol, codes F11–19), SSDD (schizophrenia, schizotypal and delusional disorders, code F2), MD (mood disorders, code F3) and NSSD (neurotic, stress-related and somatoform disorders, code F4). Figure 1 describes the different comorbidity groups identified by this cohort.

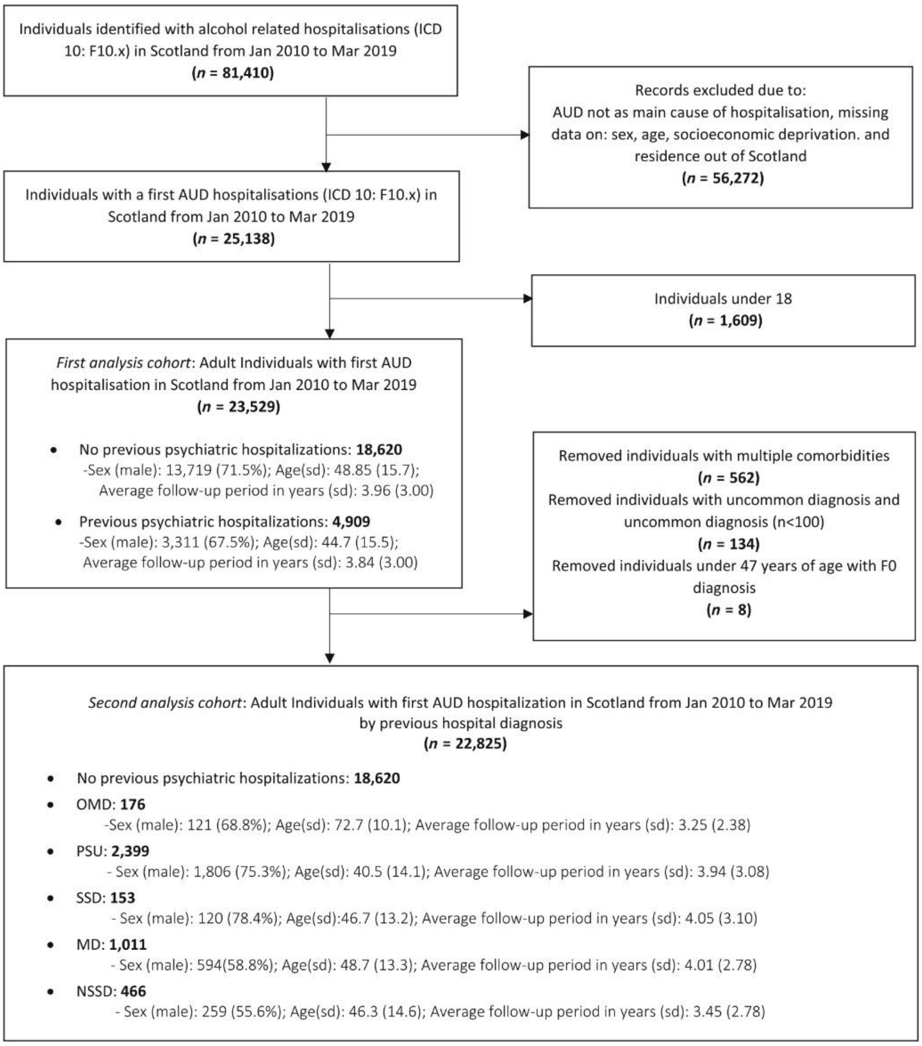

FIGURE 1 Cohort identification. MD = mood (affective) disorders; NSSD = neurotic, stress-related and somatoform disorders; OMD = organic, including symptomatic, mental disorders; PSU = mental and behavioural disorders due to psychoactive substance use—different than alcohol; SSD = schizophrenia, schizotypal and delusional disorders.

There were multiple different previous psychiatric hospitalizations in this cohort. Therefore, to ensure sufficient statistical power in this second analysis, only previous psychiatric conditions with more than 100 patients were considered.

In the OMD group, mainly composed of individuals with dementia, the distribution of age was left-skewed (see supporting information), with the few individuals aged less than 50 years having almost no rehospitalizations. Therefore, there was only a partial overlap in the distribution of age between the OMD and the reference group (those with no history of previous comorbidity). As data based-inference is only valid for the region of overlap [19], we restricted the comparison between the reference and OMD groups to an older subset, building a separate regression. This subset consisted of individuals aged more than 47 years, representing the vast majority (97%) of individuals experiencing rehospitalizations and including 95% of the original OMD group.

Analysis

Descriptive statistics on the number of rehospitalizations and prescriptions were calculated.

As therapies may influence relapse rates, we linked patients with any prescription received for alcohol withdrawal or dependence using the prescribing national data sets from Scotland [20]. We then used prescriptions for AUD as a proxy to identify if the individual was receiving therapy. By detecting whether patients received AUD prescriptions before or after their first AUD hospitalization and by identifying variations in prescribing rates among comorbidities, we aimed to provide complementary information to explain differences in rehospitalization rates. Prescriptions were those included within the National Institute for Health and Care Excellence (NICE) treatment summary for alcohol dependence [21]. For assisted alcohol withdrawal, medications were chlordiazepoxide, diazepam, carbamazepine, clomethiazole and lorazepam; for alcohol dependence, medications were acamprosate, disulfiram, naltrexone and nalmefene. Based on this, we created four variables representing prescriptions to include in our models differing by indication (withdrawal or dependence) and timing (received before or after the first AUD hospitalization). It is worth noting that while most of the medications for alcohol dependence are exclusively for AUD patients, medications for symptoms of withdrawal from alcohol are also often used for other conditions such as anxiety, mood disorders or others.

Survival models were used to estimate the association between the risk of AUD rehospitalization and previous hospitalizations related to other psychiatric reasons. We initially ran models comparing individuals without comorbidities with all those who had experienced at least one. We then compared individuals without comorbidities with all the diagnostic subgroups.

We assessed the time to first AUD rehospitalization using Cox regression. We then assessed the time to multiple AUD rehospitalizations using the Prentice, Williams and Peterson gap-time model (PWP-GT). PWP-GT models assume that recurrent events within the individual are related: individuals are not at risk for the n^{th} AUD hospitalization until they experience their $(n\text{-}1)^{\text{th}}$ [22, 23]. As PWP-GT models require a large number of study subjects for every failure time [22, 23], based on the number of subjects experiencing multiple AUD hospitalizations, we set the maximum number of rehospitalizations at three. Both Cox and PWP-GT models were then fitted with and without prescription covariates. Results and goodness of fit were compared. Separate models using death as a competing risk event were also fitted using both cause-specific hazard and Fine and Gray methodologies. Cox regressions of time to second rehospitalization (from the first) and time to third rehospitalization (from the second) were also performed to provide a more comprehensive interpretation of when multiple AUD hospitalizations occur.

As 3–15% of participants had prescriptions for alcohol dependence before their first AUD hospitalization (Table 1), a minority of our patients had already received some sort of treatment for alcohol (e.g. in primary care) prior to their first hospitalization. This confirmed that 'hospitalizations' identified only the most severe AUD episodes. To generalize our conclusions, we ran a sensitivity analysis on participants without any alcohol-dependent or withdrawal prescriptions before their first hospitalization.

There were differences in size, number of events and potential confounders between subgroup cohorts. To account for this, we used covariate adjustment, as this method is preferred to propensity score methods, especially when comparator groups have small sizes (e.g. close to 150) [24]. Model covariates were prescriptions and previous comorbidities and baseline characteristics. Patients' baseline characteristics were: sex, age, Scottish index of multiple deprivation [25] and health board location. Prescriptions between hospitalizations were presented as time-varying covariates and baseline characteristics were time-invariant covariates. There was no preregistered analysis plan for this study, so findings should be considered explorative.

RESULTS

Descriptive analysis

The percentage of patients without psychiatric comorbidities and at least one AUD rehospitalization was 28% (Table 1). This was similar to the individuals with a history of psychiatric comorbidities (27%). However, there were differences between subgroups. The OMD subgroup had the lowest percentage of individuals experiencing at least one (17%) or more (3%) rehospitalizations. MD had the highest occurrence rate throughout all subgroups, with 33% of the patients experiencing at least one rehospitalization and 16% experiencing further rehospitalizations. Death was not the main cause of censoring in any of the groups, but it was most prevalent in the OMD group (43%). This was considerably higher than all other comparators (Table 1) (Figure 1).

More than a third of the overall cohort had already received prescriptions with a potential indication for withdrawal and/or dependence prior to the first hospitalization. Individuals with a history of

TABLE 1 Number of AUD rehospitalization and prescriptions prior and after first AUD hospitalization.

	No previous hospitalization s related to psychiatric disorders (*n* = 18 620)		Previous OMD (organic, including symptomatic, mental disorders) hospitalization s (*n* = 176)		Previous PSU (mental, behavioural disorders due to psychoactive substance use—different than alcohol) hospitalizations (*n* = 2339)		Previous SSD (Schizophrenia, schizotypal and delusional disorders) hospitalizations (*n* = 153)		Previous MD (mood [affective] disorders) hospitalizations (*n* = 1011)		Previous NSSD hospitalizations (neurotic, stress-related and somatoform disorders) (*n* = 466)		All previous mental health diagnosis aggregated (including subgroup categories not included in the analysis and multiple diagnoses) (*n* = 4909)	
No. of AUD rehospitalizations														
0	13 315	72%	146	83%	1796	75%	121	79%	678	67%	341	73%	3175	73%
At least 1	5305	28%	30	17%	603	25%	32	21%	333	33%	125	27%	1136	27%
> 1	2599	14%	5	3%	268	11%	16	10%	165	16%	62	13%	609	12%
Number of deaths during follow-up period	3821 (21%)		75 (43%)		413 (17%)		32 (21%)		152 (15%)		52 (11%)		856 (17%)	
Prescriptions														
Prior to first AUD hospitalization indication for the following														
Alcohol dependence	1778	10%	<5	<3%	206	9%	16	10%	171	17%	68	15%	483	11%
Alcohol withdrawal	5252	28%	38	21%	697	29%	51	33%	397	39%	216	46%	1448	33%
Dep and/or with dep	5837	31%	39	22%	777	33%	57	37%	454	45%	235	50%	1888	37%
Cumulative prescriptions after first AUD hospitalization until third AUD relapse														
Alcohol dependence	2745	15%	11	6%	282	12%	16	10%	276	27%	94	20%	556	11%
Alcohol withdrawal	5635	30%	59	34%	732	31%	60	39%	409	40%	208	45%	1711	35%
Dep and/or with dep	6888	37%	68	38%	857	36%	66	43%	527	52%	244	52%	2098	43%

Note: Due to disclosure restrictions, in the case of fewer than five events, '< 5 was reported.

Abbreviations: AUD = alcohol use disorder; MD = mood disorders; NSSD = neurotic, stress-related and somatoform disorder; OMD = organic mental disorders; PSU = previous hospital diagnoses of other substance use; SSD = schizophrenia, schizotypal and delusional disorders; Dep = dependence.

TABLE 2 Models on first and multiple AUD rehospitalizations.

	Hazard ratio	*P*-value	95% confidence interval	
First AUD rehospitalization				
No previous psychiatric hospitalization versus any previous psychiatric hospitalization				
Any previous hospitalization	1.075	0.020	1.011	1.142
Prescriptions				
Dep prescriptions pre-first event	0.599	< 0.001	0.514	0.698
With prescriptions pre-first event	0.586	< 0.001	0.544	0.632
Dep prescriptions post-first event	0.242	< 0.001	0.202	0.299
With prescriptions post-first event	0.144	< 0.001	0.128	0.162
Analysis by hospital diagnosis				
No previous psychiatric hospitalization	–	–	–	–
OMD[a]	1.033	0.861	0.717	1.486
PSU	0.891	0.008	0.817	0.970
SSD	0.821	0.266	0.580	1.162
MD	1.541	< 0.001	1.378	1.722
NSSD	1.393	< 0.001	1.165	1.664
Prescriptions				
Dep prescriptions pre-first event	0.660	< 0.001	0.570	0.764
With prescriptions pre-first event	0.567	< 0.001	0.525	0.612
Dep prescriptions post-first event	0.255	< 0.001	0.214	0.304
With prescriptions post-first event	0.139	< 0.001	0.124	0.158
Multiple AUD rehospitalization				
No previous psychiatric hospitalization versus any previous psychiatric hospitalization				
Any previous hospitalization	1.025	0.297	0.979	1.074
Prescriptions				
Dep prescriptions pre-first event	0.514	< 0.001	0.458	0.577
With prescriptions pre-first event	0.522	< 0.001	0.493	0.553
Dep prescriptions post-first event	0.218	< 0.001	0.190	0.252
With prescriptions post-first event	0.134	< 0.001	0.122	0.148
Analysis by hospital diagnosis				
No previous psychiatric hospitalization				
OMD[a]	0.796	0.171	0.574	1.103
PSU	0.833	< 0.001	0.777	0.886
SSD	0.844	0.206	0.577	0.977
MD	1.470	< 0.001	1.084	1.281
NSSD	1.344	< 0.001	0.895	1.170
Prescriptions				
Dep prescriptions pre-first event	0.521	< 0.001	0.464	0.584
with prescriptions pre-first event	0.518	< 0.001	0.488	0.550
Dep prescriptions post-first event	0.226	< 0.001	0.197	0.260
With prescriptions post-first event	0.131	< 0.001	0.119	0.145

Note: All models adjusted for sex, age, Scottish index of multiple deprivation and Scottish health board location.

Abbreviations: MD = mood (affective) disorders; NSSD = neurotic, stress-related and somatoform disorders; OMD = organic, including symptomatic, mental disorders; PSU = mental and behavioural disorders due to psychoactive substance use—different than alcohol; SSD = schizophrenia, schizotypal and delusional disorders; Dep = dependence.

[a]Results from a separated regression, comparing only a restricted sample of control and OMD population

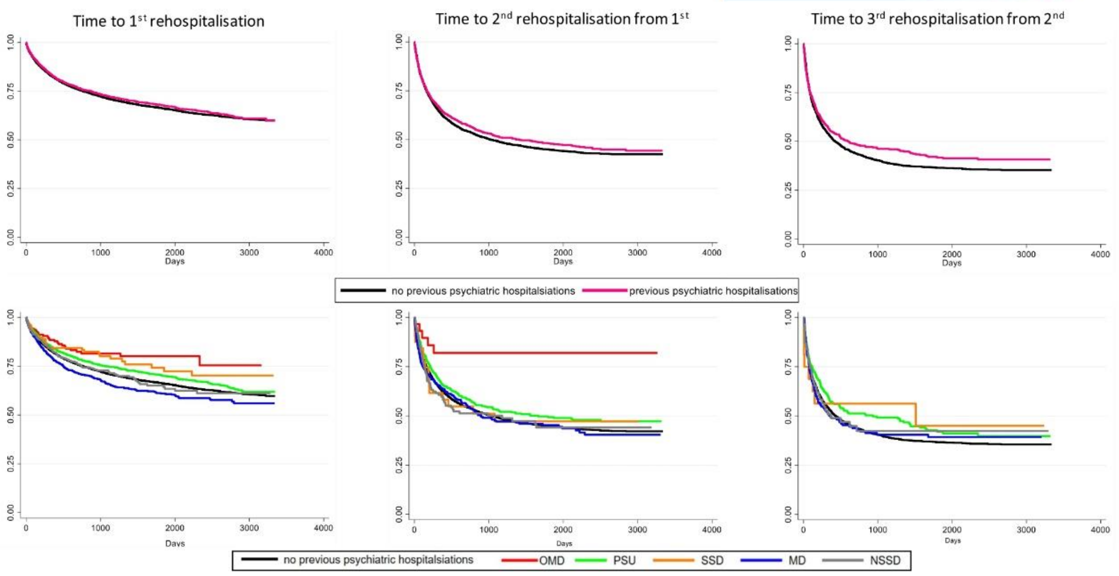

FIGURE 2 Kaplan–Meier curves of time to first, second and third rehospitalization from the previous one. Upper row: comparison between any previous psychiatric hospitalization and lack of previous psychiatric hospitalizations. Lower row: comparison across different previous psychiatric diagnosis at the hospital. Due to disclosure restrictions, the right panel of the second row does not include OMD, as at the end of the observation period there were fewer than five individuals at risk. MD = mood (affective) disorders; NSSD = neurotic, stress-related and somatoform disorders; OMD = organic, including symptomatic, mental disorders; PSU = mental and behavioural disorders due to psychoactive substance use—different than alcohol; SSD = schizophrenia, schizotypal and delusional disorders.

psychiatric hospitalizations had a higher rate of prescriptions (37 versus 31%). MD and NSSD subgroups had the highest prescription rates (45 and 50%, respectively) (Table 1). While the prescription rates increased after the first AUD hospitalization throughout all subgroups, these patterns remained. The subgroup with the lowest prescription rate after a first AUD was PSU (36%).

Inferential analysis

Time to first AUD rehospitalization

The presence of a previous psychiatric hospitalization increased the risk of future AUD rehospitalizations by 8% [hazard ratio (HR) = 1.08, 95% confidence interval (CI) = 1.01–1.14]. Within the subgroups, a history of PSU or SSD hospitalization was associated with a decreased risk of AUD relapse compared to those with no previous mental health hospitalizations. In contrast, MD and NSSD were associated with an increased risk (Table 2). Individuals with a previous MD diagnosis had the highest risk of rehospitalization among all groups: a 54% increased risk of AUD rehospitalization compared to those with no previous psychiatric hospitalizations (HR = 1.54, 95% CI = 1.38–1.72). Furthermore, those with a previous NSSD diagnosis had a 39% increased risk of readmission (HR = 1.39, 95% CI = 1.17–1.66). In contrast, individuals with a history of PSU had a 11% decreased in risk of rehospitalization (HR = 0.89, 95% CI = 0.82–0.97).

Multiple AUD rehospitalizations

When considering all subsequent AUD readmissions, all co-occurring diagnoses were associated with a relatively lower risk of recurrent AUD rehospitalization (except for SSD) (Table 2). This implies that the likelihood of relapse decelerates after the first event in all groups compared to the reference group. The median survival time reduced with the number of relapses among all categories (Figure 2).

There was an improvement in statistical goodness of fit for both single and multiple rehospitalization models after including prescriptions for alcohol dependence or withdrawal (models without prescriptions in the Supporting information). Single failure Cox models from first to second rehospitalization and from second to third rehospitalization had a lower point estimate of the hazard ratio of AUD rehospitalization for individuals with previous psychiatric diagnoses compared to time to first readmission (HR at first rehospitalization: 1.08 $P = 0.03$, HR at second rehospitalization from first: 0.95, 95% CI = 0.87–1.04, HR at third rehospitalization from second: 0.94, 95% CI = 0.84–1.07). This was also shown in the subgroup analysis: either groups initially associated with a higher (MD, NSSD and OMD) or lower (PSU and SSD) risk of AUD hospital readmission had a lower relative risk after the first AUD rehospitalization (see supporting information). Models estimating time to first rehospitalization, accounting for competing risk of death, were not substantially different to those used in the main analysis (models reported in the supporting information).

DISCUSSION

This is the first study, to our knowledge, that has used a large-scale national data set to compare the risk associated with previous psychiatric hospitalizations on future AUD hospitalizations. We found that, in patients with AUD, a previous psychiatric hospital diagnosis increased the risk of a future AUD rehospitalization by 8%. In particular, diagnoses such as mood disorders (MD) or neurotic, stress-related and somatoform disorders (NSSD) were associated with a 54 and 39% increase in the risk of individuals with an AUD hospitalization having their first AUD rehospitalization. In contrast, individuals with previous hospital diagnoses of other substance use (PSU) were associated with an 11% decrease in the risk of the first AUD readmission. Individuals with previous hospitalizations for OMD or SSD did not show a significant difference in the risk of first AUD rehospitalization with a population without history of psychiatric hospitalizations.

Overall, the time to successive multiple AUD readmission decreased after the first AUD rehospitalization. This may be because the risk set for further rehospitalizations was composed of individuals who had already severely relapsed (requiring a hospitalization), and therefore at greater risk of similar episodes. However, in our assessment of multiple AUD rehospitalizations by subgroups, the relative risk of hospitalization decreased for people with previous psychiatric admissions (with the exception of SSD). The relative risk also decreased for groups initially associated with an increase in the risk of rehospitalization (MD and NSSD), indicating that the difference between patients who already had a higher risk and those without any psychiatric comorbidity is reduced with the number of severe AUD events. This was also confirmed in single Cox regressions analysing time to further rehospitalizations (see Supporting information and Fig. 2). This may have multiple interpretations. One explanation could be that in individuals with multiple severe AUD events and a history of mental health comorbidities, other risk factors (such as family history, personality and the environment) could become more relevant in establishing the chronic pattern of AUD. This would be in accordance with previous studies illustrating that vulnerability and addiction-related characteristics are more relevant risk factors for co-occurring alcohol dependence than anxiety/depression-related traits [26]. Alternatively, the decrease in rehospitalization rates over time for people with mental health comorbidities could be due to more active follow-up. This would be consistent with the finding that most of the comorbid groups have a higher rate of prescription (Table 1). While we must acknowledge the limitations of routine hospital data in detecting all AUD relapses (see later), our findings could have implications for the patterns of the most severe AUD episodes and relapses.

Mood disorders (MD) and neurotic, stress-related disorders (NSSD) were the two conditions with the highest rate of single and multiple rehospitalization compared to the rest of the co-occurring psychopathologies analysed in this study. Depression and anxiety had already been found to be more prevalent in the AUD population [9, 26] as well as relevant risk factors for AUD [26]. Further, these two co-occurring conditions share with AUD prevalent risk factors such as stress (a common symptom in NSSD) [14, 27] and depressive symptoms (common in MD) [15] associated with the propensity of relapse to addiction in general (i.e. not necessarily related to alcohol).

We found a significant relationship between the NSSD group and AUD rehospitalization. This is in disagreement with studies using the same approach to define comorbidity (life-time diagnoses) and in line with studies identifying comorbidities if close in time with the relapse episode (28) [15]. The literature regarding anxiety and AUD relapse is heterogeneous, as the overlap between AUD and anxiety disorder symptoms can lead to misleading diagnoses when the two comorbidities are assessed close to each other [15]. Our study is based on lifetime hospital diagnoses up to 10 years before the first AUD severe event, which should ensure the distinction between the two diagnoses. We found a 40 and 34% increase in the risk of first and multiple AUD rehospitalizations for patients with NSSD (which include anxiety).

While some studies have highlighted the high rates of AUD among individuals with schizophrenia [28], to the best of our knowledge there are no studies which have examined alcohol-related hospitalizations or relapses. In our analysis, individuals in group SSD (including schizophrenia diagnoses) did not have an AUD rehospitalization rate significantly different from a population without a history of psychiatric disorders.

Individuals with a history of other substance disorders were associated with a lower risk of AUD readmission than the rest of the population. One possible interpretation could be that the reducing rate is linked to the higher psychological and physical dependence of other substances different than alcohol [29] which drive future hospitalizations, while alcohol may be only a secondary or marginal contributor.

The OMD group did not have significant differences at time to first rehospitalization, compared with a population without previous psychiatric hospitalizations. In contrast, OMD had significant differences in time to second hospitalization and with the greatest change between the two models (single versus multiple rehospitalization) throughout all subgroups. This subgroup also had the sharpest increase of any prescribed medications after a first hospitalization (Table 1). This could be associated with an increase in other complementary and specific care pathways for these patients (e.g. residential homes or care providers) after the first severe episodes characterized by close supervision that would limit alcohol consumption. Alternatively, the development of organic disorders which can reduce motivation and activity could be the leading factor in reducing alcohol consumption. However, different characteristics in this group, such as a significantly higher age at baseline, higher percentage of death and a low number of AUD rehospitalization after the first episode, may limit the comparison with this group. However, the restricted comparison we developed for this group, based on the region of overlap, should have levelled out different baseline characteristics. Competing risk analysis supported our findings.

Certainly, the most robust conclusions of this study can be drawn for groups who had the highest number of events in our study period, as well as a longer follow-up period (PSU, MD and NSSD). Conversely, studies with greater samples or more targeted studies are needed for individuals with organic mental disorders (OMD) or schizophrenia (SSD) to provide more conclusive findings on multiple severe episodes or hospitalizations.

Strengths and limitations

This study has highlighted the importance of adjusting regression models for therapies received by individuals when comparing different populations in observational studies, as different conditions may induce or require distinct levels of treatments [indeed, the rate of AUD-related prescriptions after the first AUD hospitalization varied among individuals with different psychiatric diagnoses (Table 1)]. While we recognize that psychological interventions are a key part of alcohol treatment, we were only able to obtain access to data on prescriptions. We demonstrated that prescriptions included as time-varying covariates in both single and multiple rehospitalization survival models were significant and increased the goodness of fit, generating substantial differences in terms of coefficient size and statistical significance compared with models not including them (Supporting information).

The main strength of this study was the simultaneous comparison of different psychiatric comorbidities with AUD on the risk of experiencing future AUD episodes using a single large patient cohort. Although the use of routine health-care data meant that we were not able to detect all individuals' chronological relapses we were probably able to identify the most severe AUD episodes, and we had a consistent method to recognize them among all psychiatric diagnoses. In contrast, smaller clinical studies that can identify relapses more precisely usually have smaller samples, allowing fewer comorbidity comparisons within the study. Furthermore, the definition of relapses varies among small studies [15], limiting comparison of different conditions between studies.

There were also several limitations in our study. First, prescriptions of some medications for withdrawal, such as benzodiazepines, could also be given for other psychiatric conditions. By including them separately, together with prescriptions exclusively used for alcohol dependence, we aimed to reduce this confounding effect. Secondly, some individuals with a history of mental health comorbidities may have had a greater chance of being rehospitalized for AUD in psychiatric hospitals. However, the overall low occurrence of AUD-related hospitalizations in Scottish psychiatric hospitals (6%) [30] should not be a major source of bias in our analysis. Another limitation of our study may be the potentially low accuracy of mental health diagnoses in general acute hospitalizations. This may have led to misclassification of diagnosis with some overlapping symptoms (e.g. MD and NSSD). However, we found similar findings for such groups supported by theoretical affinity in their relationship with AUD [26]. Several epidemiological studies in this area [7, 9] which have analysed subcategories of AUD (e.g. withdrawal, dependence and amnestic syndrome) argue that they have different dynamics. We aggregated all F10.x diagnoses into a single category to increase the statistical power of certain groups, as well as to overcome possible misdiagnoses at hospital admission within the AUD groups.

CONCLUSION

A history of previous psychiatric hospitalization increased the risk of a first AUD readmission in patients already hospitalized once for AUD. However, the effect differed among psychiatric conditions: PSU had a lower risk of AUD rehospitalization, while MD and NSSD had a higher risk. Overall, in patients with a history of previous psychiatric diagnoses the risk of future multiple AUD rehospitalization diminishes after the first AUD readmission compared to individuals without psychiatric comorbidities. This could suggest that addiction-related characteristics are more relevant risk indicators for recurring AUD episodes requiring hospitalizations than psychiatric comorbidities.

AUTHOR CONTRIBUTIONS

Francesco Manca: Conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); visualization (lead); writing—original draft (lead); writing—review and editing (lead). **James Lewsey:** Methodology (supporting); supervision (lead); writing—review and editing (equal).

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DECLARATION OF INTERESTS

The study was self-funded. Both authors report no financial relationships with commercial interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study were available from the Scottish National Safe Haven. Restrictions apply to the availability of these data, which were used under license for this study.

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SUPPORTING INFORMATION

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

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Estimating the Burden of Alcohol on Ambulance Callouts through Development and Validation of an Algorithm Using Electronic Patient Records

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Abstract: Background: Alcohol consumption places a significant burden on emergency services, including ambulance services, which often represent patients' first, and sometimes only, contact with health services. We aimed to (1) improve the assessment of this burden on ambulance services in Scotland using a low-cost and easy to implement algorithm to screen free-text in electronic patient record forms (ePRFs), and (2) present estimates on the burden of alcohol on ambulance callouts in Scotland. Methods: Two paramedics manually reviewed 5416 ePRFs to make a professional judgement of whether they were alcohol-related, establishing a gold standard for assessing our algorithm performance. They also extracted all words or phrases relating to alcohol. An automatic algorithm to identify alcohol-related callouts using free-text in EPRs was developed using these extracts. Results: Our algorithm had a specificity of 0.941 and a sensitivity of 0.996 in detecting alcohol-related callouts. Applying the algorithm to all callout records in Scotland in 2019, we identified 86,780 (16.2%) as alcohol-related. At weekends, this percentage was 18.5%. Conclusions: Alcohol-related callouts constitute a significant burden on the Scottish Ambulance Service. Our algorithm is significantly more sensitive than previous methods used to identify alcohol-related ambulance callouts. This approach and the resulting data have potential for the evaluation of alcohol policy interventions as well as for conducting wider epidemiological research.

Keywords: ambulance callouts; burden of alcohol; algorithm development; routine health records; paramedics; Scotland

1. Introduction

Alcohol constitutes a significant burden on emergency services in the UK [1], with the potential to undermine or delay emergency service provision to other incidents. This is particularly true for ambulance services, which often represent patients' first, and sometimes only, contact with health services. Acute alcohol episodes contribute to making ambulance clinicians' work more difficult and risky: in 2010, more than 50% of ambulance staff who responded to a UK survey reported experiencing injuries or sexual harassment whilst dealing with drunk members of the public [1]. Despite this, the burden of alcohol on ambulance services has not been extensively researched and is not routinely monitored.

In the UK, previous studies have found varying levels of burden on ambulance services arising from alcohol consumption. In 2013/14, the London Ambulance Service reported from an audit of emergency calls that 6% of calls for an emergency ambulance were associated with alcohol [2]. In the North East of England, researchers used manual examination of ambulance patient records to estimate that alcohol incidents accounted for 10% of total callouts [3], while in Scotland in 2015 respondents to a survey of ambulance clinicians estimated that 17% of incidents on weekdays and 42% on weekend nights involved alcohol [4]. It is unlikely that these differences can be fully explained by geography but are more likely to arise from the different methods used to assess whether alcohol was involved, and the different data sources used (calls, staff surveys and callouts). The specificity and sensitivity of these different methods are not frequently assessed, meaning these estimates could be biased and lead to inconsistent or misleading comparisons across regions. The North East of England study found that the reading of free-text in individual patient records allowed the identification of approximately three times the number of alcohol-related ambulance callouts, but this was labour intensive and was only performed for a sample of records [3].

Outside of the UK, the National Ambulance Surveillance System (NASS) has been established in Australia to use ambulance data for the surveillance of a wide range of presentations [5–7]. Lubman et al. (2020) describe NASS as a complex and coordinated system employing 23 researchers to monitor and map acute harms related to alcohol and other drug consumption, using ambulance callout data from services covering 82.5% of the Australian population. This system, in which researchers read and code full patient records, overcomes the challenges identified in the UK and allows for effective monitoring, description and mapping of ambulance callouts related to alcohol consumption [8] and substance misuse [9]. Such information is valuable for policymaking, including policy development and evaluation, but is resource-intensive to gather in this way.

Data from ambulance records have been used as a complementary source of information to traditional surveillance systems for other illnesses, including respiratory infections [10–12]. However, there is no general agreement on how to use this information for surveillance purposes as the type of ambulance data used and analysed (assessment from patients' initial calls [10], dispatch data, callout data, or paramedic surveys [13]) once again varies across studies.

The aim of this study was to improve the assessment of the burden of alcohol on the ambulance service. To attain this, we developed a low-cost and easy to implement automatic algorithm to screen free-text records in electronic patient record forms from ambulance callouts. In this paper, we both describe how the algorithm was developed and validated and present estimates on the burden of alcohol on ambulance callouts in Scotland between 2016 and 2019.

2. Materials and Methods

Below, Sections 2.1–2.4 focus on how the algorithm was developed and assessed. We briefly describe in Section 2.5 how the algorithm was then used to estimate alcohol-related ambulance callouts in Scotland between 2016 and 2019.

2.1. Study Setting and Dataset

The Scottish Ambulance Service (SAS) is a population-wide service and part of the National Health Service in Scotland, free at the point of delivery. SAS serves a population of 5.5 million people and attends more than half a million incidents annually. Alcohol-related callouts can currently be recorded in two main ways by ambulance clinicians when completing electronic patient record forms (ePRFs) on tablet devices at the scene of the incident. Clinicians can either select an on-screen alcohol "flag" to indicate that alcohol was a contributing factor in the callout and/or describe how alcohol was a factor in free-text fields in the ePRF. The "flag" is what currently has been used from SAS to determine whether a callout involved alcohol. Personal communication with ambulance staff explained that paramedics in practice may sometimes not use the alcohol flag on the ePRF, rather alcohol involvement would be recorded in a free-text report completed after attending to the patient. Therefore, the alcohol flag was deemed likely to underestimate the burden of alcohol on the ambulance service. Furthermore, the likelihood of clinicians selecting the alcohol flag depends in part on the prominence of that flag, which has changed in different versions of the SAS ePRF system. This makes it difficult to use the flag alone for examining trends in alcohol-related callouts or the impact of alcohol policy changes that might influence such trends.

We have automated the process of reviewing free-text fields in ePRFs by building an algorithm capable of classifying ambulance callouts as alcohol-related, using the information recorded by ambulance clinicians in free-text fields. Our development of the algorithm was based on a sample of SAS ePRFs deliberately selected to include around 1000 alcohol-related callouts, extracted between 2015 and 2019. Earlier audits suggested that around 10% of total callouts would be alcohol-related; however, in order to reduce the number of records manually scrutinised by the paramedic, we sampled more callouts coming from periods when the number of alcohol-related incidents was likely to be higher (i.e., weekend night-times—from 6 p.m. to 6 a.m.). Using a manual audit of a small sample of full ePRFs at these times, we estimated around 27% of callouts at these times were related to alcohol. We therefore sampled 3600 callouts from these weekend night-times, a further 1200 from the rest of the week, and 616 additional records sampled at random from across the entire week, in case we would have found a number lower than 1000 callouts identified as alcohol-related. This gave us a total sample of 5416 callouts.

2.2. *Assessment of Callouts as Alcohol-Related*

Every ePRF contains tick box sections describing clinical and presentation characteristics of the patient as well as several open free-text fields where paramedics enter a description of the context and circumstances of the callout using their own words. As no gold standard exists to classify alcohol-related callouts, an experienced paramedic (SK) interrogated the sample of free-text from ePRFs and used her professional judgement to classify the callout as alcohol-related or not. We defined "alcohol-related callout" as any callout where alcohol had been recorded on the ePRF as a primary cause for care (i.e., alcohol intoxication or alcohol dependence) or in those calls where the consumption of alcohol was recorded in association with the presenting condition/injury. Examples of the latter are calls relating to mental health crises, falls or assaults and consumption of alcohol was a consideration in ongoing patient assessment, treatment and care. All uncertain entries were then cross checked by a second experienced paramedic (DF) and resolved by consensus.

This classification was considered the "gold standard" for judgement of whether a callout was alcohol-related or not. Due to information governance concerns, researchers could not have access to the full free-text of every ePRF, but only paramedics or SAS staff could view and analyse them. Therefore, the paramedic also recorded verbatim, including any misspellings, any phrases in the free-text entered in each ePRF which (i) were used to classify the callout as alcohol-related, or (ii) might result in incorrect classification as alcohol-related using an automated algorithm (i.e., text containing common alcohol terms, but where the overall callout was not judged to be alcohol-related, referred to hereafter as "misleading terms"). The classification for all sampled records and extracted phrases where relevant were recorded in a spreadsheet. Researchers worked with this restricted dataset.

2.3. *Algorithm Development*

The dataset, consisting of the classified patient records and free-text extracts, was divided into a training set (80%, 4327 records) and a validation set (20%, 1089 records). Validation and training sets were not split randomly, as a non-random sample is preferable for internal validation purposes [14]. We used two different approaches to algorithm development: "manual" and "machine learning" (ML). The development and operation of the manual algorithm for identifying alcohol-related callouts can be summarised in five stages:

(a) Cleaning the extracted sections of text in the dataset for both alcohol-related and misleading terms (e.g., removing extra spaces, removing punctuation and excluding the "stop words").
(b) Identifying words common to the callouts classified by alcohol-related based on their frequency (recurrence in more than 2.5% of alcohol-related callouts) and expert opinion (e.g., extra words identifying unambiguously alcohol-related callouts such as names of specific beverages appearing in some of the remaining records classified as alcohol-related).
(c) Looking at the recurrence of words identified in (b) within the misleading terms. Focusing on the combination of one word before and one word after the words in (b) within the misleading terms. Identifying the most frequent combinations.
(d) Identifying and correcting the most common spelling errors in ePRFs of words identified in (b) and (c).
(e) Identifying every callout as "alcohol-related" whenever there was at least one of the "alcohol-related terms", except those excluded by the combinations in point (c).

In step (a), some of the words were reduced to their stem version to also include their declension, and others were maintained in their entire original form as differences could have been meaningful for the specific disease context (e.g., drink, drinks, drunk, drank could have different connotations and the difference could be relevant when related to alcohol) (see Table A2 in Appendix A). In applying the manual algorithm to all SAS callout records, a record was deemed to be "alcohol-related" if it either was identified as alcohol-related using algorithm search of the free-text as above, or if the alcohol flag was selected on the ePRF by the ambulance staff.

The second approach used an ML algorithm based on a random decision forests [15] process and was developed using the same dataset as for the manual algorithm based on sections of free-text. Specifically, the alcohol-related words plus the alcohol flag were used as nodes of a random forest. Random forests are a series of algorithms which learn by the way an observation was classified (alcohol-related or not) and other characteristics (the free-text) to predict new observations through building a multitude of decision trees, one hundred in our case.

2.4. Assesment of Algorithm Performances

The algorithms were developed and their performance analysed in Stata version 16 [16]. The algorithms were assessed based on sensitivity, specificity and accuracy parameter estimates in the validation dataset. Sensitivity (Equation (1)) is the percentage of "true" alcohol-related callouts detected by the algorithm. It can also be interpreted as the probability that each algorithm will detect an alcohol-related callout, when the callout is judged to be alcohol-related using the gold standard of paramedic assessment.

$$\frac{\textit{True positive}}{\textit{True positive} + \textit{False negative}} \tag{1}$$

Specificity (Equation (2)) is the percentage of "true" non-alcohol-related callouts detected by the algorithm. It can also be interpreted as the probability that the algorithm detects a callout as non-alcohol-related, when the callout is judged not to be alcohol-related using the gold standard.

$$\frac{\textit{True negative}}{\textit{True negative} + \textit{False positive}} \tag{2}$$

Accuracy (Equation (3)) is a measure of statistical bias. It can also be interpreted as the proximity of measurement results to the true value [17].

$$\frac{\textit{True positive} + \textit{True negative}}{\textit{Total negative} + \textit{Total positive}} \tag{3}$$

Regarding the manual algorithm, different selections of words were tried and their performances were assessed. We selected the combination of words providing the best performance. The selected alcohol-related words (step (b) above) were the following: alcohol, drink, intoxication, vodka, bottle, drunk, buckfast, whisky, cider, beer, gin.

Table 1. Combination of words to remove from alcohol-related terms.shows the combination of words to remove (step (c)). Tables A1 and A2 describe the list of selected stop words (step (a)) and the main root words, variations and spelling mistakes we included (step (d)).

Table 1. Combination of words to remove from alcohol-related terms.

Main Word	Combination of Words to Exclude
Alcohol	"since alcohol" "any alcohol" "no alcohol" "or alcohol" "denies alcohol" "alcohol detox" "alcohol withdrawal"
Drink	"only drink" "any drink" "energy drink" "denies drink" "drink water" "not drink"
Intox	"appear intox" "not intox"
Bottle	"water bottle" "glass bottle"
Whisky	"one whisky"

2.5. Algorithm Application to Full SAS Dataset

The final selected algorithm based on the 5416 extracted records was applied by SAS analysts in SQL language to all ePRF records with complete free-text in the SAS data warehouse. Given its performance results (see below) and the ease to be implemented within the SAS warehouses, the manual algorithm was chosen for the estimation of the burden of alcohol on the Scottish Ambulance Service. The algorithm extracted monthly data for callouts deemed to be alcohol-related from 2016–2019 including the postcode (at district level) of the callout, callout characteristics (i.e., time of callout, emergency code, etc.) and patients' demographics/characteristics. Total callout data (including callouts judged to be non-alcohol-related) were also obtained. Descriptive statistics and graphs were prepared to provide estimates of the burden of alcohol on the ambulance service with particular focus on 2019, the most recent available year in the dataset.

3. Results

Below, we first describe the performance of our algorithms (Section 3.1) and then focus on the estimates of the burden of alcohol for the Scottish Ambulance System (Section 3.2).

3.1. Algorithm Performance

Results are presented on the complete free-text records applied by SAS analysts on the validation dataset. The validation dataset had a similar overall percentage of callouts determined to be alcohol-related by the paramedic (17.5%) to that detected by the algorithm when applied to the overall dataset (validation plus training) (18.5%). The manual algorithm performance was comparable with the ML algorithm, with differences only in third decimal digits in all the three indicators (see Table 2). The alcohol flag alone outperforms both the algorithms in terms of specificity but had much poorer sensitivity and overall accuracy. The current alcohol flag does not identify many false positives but the rate of true positives identified is less than half.

Table 2. Algorithm performance, including alcohol flag.

Statistic	Manual Algorithm	ML Algorithm	Alcohol Flag
Sensitivity	0.941	0.942	0.380
Specificity	0.996	0.996	1.000
Accuracy	0.986	0.987	0.890
Alcohol flag = current flag used by SAS to record alcohol-related callouts			

3.2. Alcohol-Related Callouts

The algorithm detected an increasing trend of alcohol-related callouts over the period of 2016–2019 as well as a clear difference in the volume of callouts between weekend days (Friday–Sunday) and weekdays (Monday–Thursday) (Figure 1). In 2016, the daily averages on weekdays and weekends were 161 and 243 alcohol-related callouts, respectively, whereas in 2019 they were 202 and 284. This translates into an increase between 2016 and 2019 of 25% and 14% for weekdays and weekends, respectively. The callouts show a seasonal pattern with two periods where the overall volume of callouts increased. The first period was during summer (from May to August, with the peak in July), then they rapidly decrease in September and they slightly increase every beginning of December until the 1st of January of the year after (creating a second peak) (Figure 1). It is of note that the 1st of January has on average 200 additional callouts compared to any other day of the year.

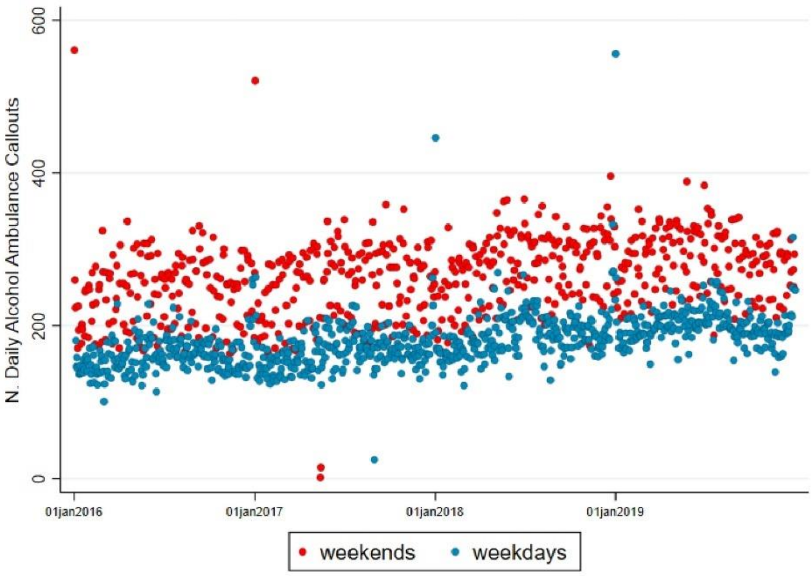

Figure 1. Daily alcohol–related ambulance callouts, 2016–2019.

In 2019, there were 536,536 ambulance callouts, of which 86,780 (16.2%) were identified as being alcohol-related (Table 3). During weekends, alcohol-related callouts represented 18.5% of the total, whereas during weekdays the corresponding figure is 14.2%. The distribution of alcohol-related callouts was slightly different between weekends and weekdays. More than 20% of alcohol-related callouts were involving individuals in the 40–54 years age group. There was also variation by sex, with males representing more than 60% of alcohol-related callouts but less than 50% of non-alcohol-related callouts. The distribution of alcohol-related callouts over hours of the day differed across age groups: overall, more callouts were to individuals residing in areas of highest socio-economic deprivation than in other areas, and this was also true for alcohol-related callouts. Almost 1 in 5 callouts to those residing in areas of highest socio-economic deprivation were alcohol-related compared to 1 in 10 to those residing in areas of lowest socio-economic deprivation. Geographical variations were also present; alcohol-related callouts are more concentrated in urban areas, and their relative weight on the total number of callouts is greater in urban areas compared to rural. Alcohol-related callouts were more likely to be rated as serious than non-alcohol-related callouts, with the distribution of alcohol-related callouts oriented towards the two most severe emergency codes (red and purple are 21.4% of the alcohol-related ambulance callouts compared to 16.7% of non-alcohol-related ambulance callouts). Additionally, the distribution of callouts over the hours of the day differed across the day of the week and age group. Specifically, during weekend nights (6 p.m.–6 a.m.) the percentage of alcohol-related callouts was 28%, while in the rest of the nights, it was 19.5%. In particular, the percentage of alcohol-related callouts on weekends peaked between the hours of 9 p.m. and 1 a.m., whereas the peak 4 h period for weekdays was between 6 p.m. and 10 p.m. (Figure 2). Younger individuals' callouts related to alcohol were more concentrated late in the night (more than 30% of callouts between 11 p.m. and 2 a.m. for 0–24 years age group) compared to older people (more than 30% of callouts between 5 p.m. and 9 p.m. for over 70 years age group) (Figure 3).

Table 3. Descriptive statistics regarding alcohol-related and non-alcohol-related ambulance callouts in 2019.

	Alcohol-Related Callouts no. (%)	**Non-Alcohol-Related Callouts no. (%)**	**Alcohol-Related Callouts as % of Total Callouts**
Total	86,780	449,756	16.2%
Day of the week			
Sunday	15,663 (18.1)	65,447 (14.6)	19.3%
Monday	10,746 (12.4)	65,509 (14.6)	14.1%
Tuesday	10,657 (12.3)	63,925 (14.2)	14.3%
Wednesday	10,250 (11.8)	62,203 (13.8)	14.1%
Thursday	10,707 (12.3)	63,349 (14.1)	14.5%
Friday	12,526 (14.4)	63,806 (14.2)	16.4%
Saturday	16,231 (18.7)	65,517 (14.6)	19.9%
Month of the year			
January	7033 (8.1)	39,054 (8.7)	15.3%
February	6586 (7.6)	34,591 (7.7)	16.0%
March	7410 (8.5)	36,851 (8.2)	16.7%
April	7297 (8.4)	36,260 (8.1)	16.8%
May	7451 (8.6)	37,463 (8.3)	16.6%
June	7622 (8.8)	36,957 (8.2)	17.1%
July	7727 (8.9)	37,258 (8.3)	17.2%
August	7527 (8.7)	37,182 (8.3)	16.8%
September	7020 (8.1)	37,329 (8.3)	15.8%
October	6889 (7.9)	38,250 (8.5)	15.3%
November	6855 (7.9)	38,129 (8.5)	15.2%
December	7363 (8.5)	40,432 (9.0)	15.4%
Emergency code [1]			
Green	147 (0.2)	965 (0.2)	13.2%
Yellow	48,250 (55.6)	242,937 (54.0)	16.6%
Amber	19,819 (22.8)	130,870 (29.1)	13.2%
Red	16,563 (19.1)	63,362 (14.1)	20.7%
Purple	1976 (2.3)	11,499 (2.6)	14.7%
Unknown	25 (0.03)	123 (0.03)	16.9%
Age group (years) [2]			
0–24	12,758 (14.7)	41,298 (10.4)	23.6%
25–39	16,863 (19.4)	48,088 (12.1)	26.0%
40–54	19,632 (22.6)	55,252 (13.9)	26.2%
55–69	16,834 (19.4)	76,461 (19.2)	18.0%
70+	12,283 (14.2)	176,228 (44.4)	6.5%

Table 3. *Cont.*

	Alcohol-Related Callouts no. (%)	Non-Alcohol-Related Callouts no. (%)	Alcohol-Related Callouts as % of Total Callouts
Sex [3]			
Female	31,612 (38.1)	218,471 (52.3)	12.6%
Male	51,378 (61.9)	199,634 (47.7)	20.4%
Scottish Index of multiple deprivation decile for patient home address [4]			
1 (most deprived)	7284 (21.8)	29,836 (15.4)	19.6%
2	5246 (15.6)	25,681 (13.3)	17.0%
3	4554 (13.6)	24,504 (12.7)	15.7%
4	3919 (11.7)	21,655 (11.2)	15.3%
5	3111 (9.3)	19,167 (9.9)	14.0%
6	2491 (7.4)	17,684 (9.1)	12.4%
7	2241 (6.7)	16,236 (8.4)	12.1%
8	1699 (5.1)	14,310 (7.4)	10.6%
9	1591 (4.8)	13,094 (6.8)	10.8%
10 (least deprived)	1306 (3.9)	11,601 (6.0)	10.1%
Scottish Index of multiple deprivation decile for callout location [5]			
1 (most deprived)	17,473 (20.1)	66,680 (15.0)	20.8%
2	12,568 (14.5)	57,671 (13.0)	17.9%
3	11,691 (13.5)	54,405 (12.2)	17.7%
4	10,102 (11.6)	49,029 (11.0)	17.1%
5	8715 (10.0)	45,223 (10.2)	16.2%
6	7355 (8.5)	44,378 (10.0)	14.2%
7	5795 (6.7)	37,472 (8.4)	13.4%
8	5286 (6.1)	34,927 (7.8)	13.2%
9	3695 (4.3)	29,427 (6.6)	11.2%
10 (least deprived)	3383 (3.9)	26,248 (5.9)	11.4%
Rural/urban areas classified by callout location [6]			
Large urban area	36,107 (41.6)	159,817 (36.0)	18.4%
Other urban area	32,514 (37.5)	164,774 (37.2)	16.5%
Accessible small town	6154 (7.1)	36,425 (8.2)	14.5%
Remote small town	3046 (3.5)	17,292 (3.9)	15.0%
Accessible rural area	5360 (6.2)	42,732 (0.1)	11.1%
Remote rural area	2555 (2.9)	22,470 (0.05)	10.2%

[1] Emergency codes are displayed in order of severity from green (least severe) to purple (most severe); [2] 8410 and 68,839 individuals did not have age recorded for alcohol-related and overall callouts, respectively; [3] 3772 and 31,601 individuals did not have sex recorded for alcohol-related and non-alcohol-related callouts, respectively; [4] 1, most deprived decile, 10 least deprived decile; 53,338 and 255,988 individuals did not have SIMD recorded for alcohol-related and non-alcohol-related callouts, respectively; [5] 717 and 4296 incidents did not have SIMD recorded for alcohol-related and overall callouts, respectively; [6] 1044 and 6246 individuals did not have rural/urban area recorded for alcohol-related and non-alcohol-related callouts, respectively.

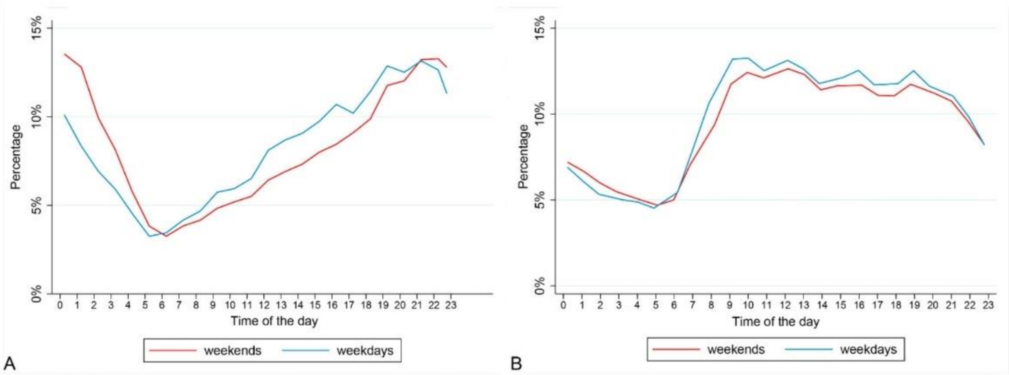

Figure 2. Distribution of alcohol-related callouts (panel **A**) and non–alcohol–related callouts (panel **B**) during hour of the day by weekend and weekdays.

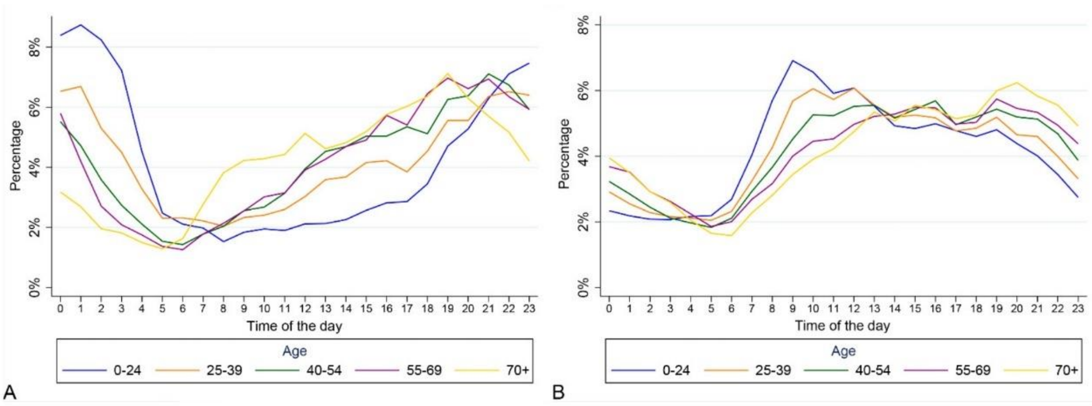

Figure 3. Distribution of alcohol-related callouts (panel **A**) and non–alcohol–related callouts (panel **B**) during hour of the day by age group.

4. Discussion

4.1. Alcohol-Related Ambulance Callouts

Using a robust methodology that we developed and validated, we have identified a high burden of alcohol on ambulance callouts in Scotland; in 2019, we estimate that approximately 16 out of every 100 callouts were alcohol-related. In addition, the proportion of alcohol-related callouts during weekends was higher than during weekdays. Beyond weekends, seasonal trends with peaks in callouts corresponded with the months of December (in particular Christmas and new year holidays) and the months with greater hours of daylight in Scotland (May–August). Thirty-five percent of callouts classed as the most severe (red and purple) were identified as alcohol-related callouts. Given the average cost of an ambulance callout in 2019 [18], the total cost of alcohol-related callouts can be estimated at approximately GBP 31.5 million, though this figure would depend on the complexity of these calls compared to non-alcohol-related callouts.

These figures provide a robust estimate of the burden of alcohol on the ambulance service in Scotland and have direct policy relevance. These data could inform wider alcohol policy decisions at both local and national government level aimed at reducing this burden, including efforts to reduce alcohol problems and dependence, as well as addressing the peak of callouts occurring at weekends. These findings raise questions about the balance of risks and benefits of current alcohol consumption and harms (and related regulations), and whether further action is needed, particularly in the light of attempts to protect health service availability in times of capacity constraints and during extraordinary events such as pandemics or disasters. It is likely that the burden of alcohol on society could be reduced by interventions focusing on its availability, affordability or attractiveness [19,20], though it remains to be seen which interventions would most directly reduce alcohol-related ambulance callouts. Further analysis would be beneficial to better understand the increase in burden at the weekends, including the extent to which this is driven by disorder nearby to or relating to consumption in licensed premises and by alcohol consumption in homes. Qualitative work with paramedics is underway to better understand their experiences of alcohol-related callouts, including the relative contribution of acute alcohol intoxication versus chronic alcohol consumption and dependence.

4.2. Strengths and Limitations of the Algorithm

The algorithms we developed outperformed an existing electronic alcohol flag in terms of overall accuracy and sensitivity, enabling the identification of a much larger burden of alcohol-related callouts than previously reported in the Scottish Parliament [21].

A feature of our methodological approach was to embed the existing alcohol flag into the algorithms. This, in our view, makes intuitive sense—the paramedic at the scene was compelled enough to press this flag as they considered alcohol to be a contributing factor and we believe that it is unlikely that this would be pressed in error. Further, embedding this into our algorithm allowed the capture of any alcohol-related callouts with no explicit mention of "alcohol" in the free-text.

The algorithm described here overcomes many of the issues around sensitivity or self-selection biases described in similar studies which used ambulance dispatch data alone [11] or in combination with paramedics' reports [13]. Furthermore, it is likely to be a very cost-effective approach compared to other systems such as the Australian system described above, in which multiple staff coded individual records. The development costs included time for a paramedic reading and screening 5416 ePRF records to classify them as alcohol-related or not, data governance management time, and researcher time to develop the approach to sampling, design and testing of the algorithm. While the limited involvement of paramedics due to disclosure reasons to screen ePRFs (one for a full assessment and another one to confirm doubtful observations) contained costs, this could have potentially reduced the quality of assessing a few records, as a higher number of reviewers to cross-examine records is usually preferred. The application of the algorithm to the SAS dataset required additional analyst and developer time. This would be the main ongoing cost of generating continuous data on the burden of alcohol on SAS, apart from costs of periodic refinement of the algorithm. Therefore, we believe that one of the main strengths of this method, beyond the high precision of the estimates, is the ease of implementation and the economical approach.

It is important to note that the results of our algorithms are based on sections of free-text filtered by a paramedic due to disclosure restrictions. Moreover, we excluded from our algorithms the sections of text coming from uncertain ePRF recording.

Whilst ML algorithms have been shown to be effective approaches for similar problems, due to their ability to identify underlying correlation structures, we did not find that our ML algorithm outperformed the manual algorithm. One explanation for this may be due to the restricted volume of free-text which was available. Indeed, the preferred way to build a random forest would have been directly on the original full free-text of the ePRF instead of on the sections of text selected through a manual interrogation of records. However, as researchers only had access to sections of free-text, with relatively low computational power, the preferred solution was not feasible.

Disclosure constraints were the main source of limitations of our algorithms. We outline the two main consequences of these limitations below. Firstly, the algorithm could under-fit the data because the word selection to build the algorithm was based on sections of free-text and not the full text contained in the ePRF. This could have generated a bias. As the algorithm is a further selection of keywords already selected and screened by a paramedic, it could not have adequately captured the underlying structure of the free-text, generating a bias due to an under-fitting of the algorithm in the training sample. Secondly, there could be a likely upward bias in the algorithm specificity. Particularly, the algorithm has been built on a population which contained more alcohol-related callouts than the average numbers in the population to gather more information on keywords related to alcohol, in an attempt to increase the proportion of true positives and therefore the sensitivity. However, the artificial increase in sensitivity could imply an indirect decrease in specificity. Specifically, artificially increasing the number of positives in our sample decreases the proportion of false negatives, i.e., decreasing the overall number of negatives, you also decrease the number of false positives, generating an upward bias in specificity (this could explain the high values in specificity in Table 1). These two causes of likely bias were driven by the limitation of access to the dataset for information governance reasons.

Furthermore, ambulance callouts to individuals with conditions where chronic alcohol consumption may have been a contributory factor, including cancers or heart attacks, are generally less likely to be classified as alcohol-related as the contribution of alcohol would normally not be observable to the paramedic at the scene in the way that acute alcohol consumption is. As a result, the figures presented here could underestimate the full burden of alcohol on the ambulance service.

It is worth noting that many of the terms used in the algorithm may be context/country-specific; indeed, a few terms such as beverage brands or slang can be common in certain countries and rare in others (e.g., "buckfast", which is one of the selected words of the algorithm, is a low-cost caffeinated alcoholic drink popular in Scotland). For this reason, when developing similar algorithms in different contexts, appropriate terms should be selected not only based on their frequency in the ePRF, but they should also be validated by experts with relevant local experience (e.g., paramedics). Potentially, experts could also add other specific unambiguous terms to increase the sensitivity of the algorithm. Therefore, although we would expect that the implementation of a manual algorithm containing the same words selected above on a system based in a different country could achieve good results, it is likely to have worse performance than one tailored to the specific context. In addition, we believe that whereas the algorithm method would still be valid in Scotland over time, the selection of words could evolve as social habits (e.g., drinking patterns and popular drinks) change or new words or products come into existence. Although the frequency of words was found to be consistent over our time frame, we suggest that the selection of words and the algorithm performance should be regularly reviewed and checked to guarantee estimates to be sensitive and consistent over time.

4.3. Further Opportunities

We describe a method to undertake epidemiologic monitoring using paramedics' notes in ePRFs, without requiring further work from paramedics or other ambulance clinicians. We describe the application of this system to alcohol-related ambulance callouts in Scotland. However, the same method could be implemented for other epidemiological investigations such as infectious disease outbreaks or chronic diseases, where free-text records may enable the identification of callouts of interest over and above any system "flag". This approach not only allows the identification of relevant callouts but also the analysis of relationships between specific callout types and other social or natural factors with spatial and temporal dimensions (e.g., socioeconomic deprivation, traffic, pollution).

In this case, tracking changes in alcohol-related callout demand could help to assess how local behaviours have changed over time, or how certain public health policies or interventions could have affected alcohol consumption and related harms. Furthermore, monitoring how the concentration can change over the week and over the hours of the day could also help to plan the allocation of ambulance resources in times of capacity constraints. These data can also have the potential to inform local alcohol premises' licensing policies and decisions, as is currently done with alcohol-related hospital admissions and death [22].

Finally, ambulance data have also been used to assist and complement the understanding of data in other fields. For instance, data from ambulance callouts linked with police data can provide additional information on security and violence in certain city districts. Specifically, previous studies found that between 66 and 90 per cent of ambulance incidents related to violence are not included in police data [23]; therefore, improved recording of alcohol in ambulance data could help to enhance our understanding of the scale of and spatio-temporal patterning of violence and alcohol-related violence and thus improve police and public health responses.

5. Conclusions

Between 2016 and 2019, the burden of alcohol for the Scottish Ambulance Service was high, with 86,780 alcohol-related callouts in 2019, representing 16.2% of total callouts. Further, the number of alcohol-related callouts increased between 2016 and 2019. Our methodological approach for identifying alcohol-related ambulance callouts is significantly more accurate than previous methods. This approach and the resulting data have the potential to evaluate alcohol policy interventions as well as for conducting wider epidemiological research.

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Appendix A

Table A1. Stop words used in the algorithm.

List of Stop Words:
a about above after again against all am an and are aren't as at be because been before being below between both but by can't cannot could couldn't did didn't do does doesn't doing don't down during each few for from further had hadn't has hasn't have haven't having he he'd he'll he's her here here's hers herself him himself his how how's i i'd i'll i'm i've if in into is isn't it it's its itself let's me more most mustn't my myself nor notof off on once only or other ought our ours out over own same shan't she she'd she'll she's should shouldn't so some such than that that's the their theirs them themselves then there there's these they they'd they'll they're they've this those through to too under until up very was wasn't we we'd we'll we're we've were weren't what what's when when's where where's which while who who's whom why why's with won't would wouldn't you you'd you'll you're you've your yours yourself yourselves

Table A2. Spelling errors and word declination to change into main word.

Main Word	Spelling Errors and Word Declination, Changed into Main Word
alcohol	alco alcoholpt alcoholic nalcohol alchol alcoh alccohol alcoholism alcohn alcohohol alcohhol
drink	drinks drinking drinkin pdrink rdrink drin drinkn drinker drinknig drinkingpt drinki drank
intox	intoxicated intoxication intoxicted intoxicat intoxicate intoxication
vodka	vodca vodkapt vodkas

Table A2. *Cont.*

Main Word	Spelling Errors and Word Declination, Changed into Main Word
bottle	bottles bottl bott
drunk	ndrunk
buckfast	backfats bukfast bakfast buckfasts
whisky	whiskey wiski whiskei whiskys whiskes whiskeys whiskies
denies	deny deniese deni denied
since	ince sinc
cider	ciders
gin	gins
beer	beers

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ORIGINAL ARTICLE

The Effect of Minimum Unit Pricing for Alcohol on Prescriptions for Treatment of Alcohol Dependence: A Controlled Interrupted Time Series Analysis

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Abstract
In 2018, Scotland introduced a minimum unit price (MUP) for alcohol to reduce alcohol-related harms. We aimed to study the association between MUP introduction and the volume of prescriptions to treat alcohol dependence, and volume of new patients receiving such prescriptions. We also examined whether effects varied across different socio-economic groups. A controlled interrupted time series was used to examine variations of our two outcomes. The same prescriptions in England and prescriptions for methadone in Scotland were used as controls. There was no evidence of an association between MUP implementation and the volume of prescriptions for alcohol dependence (immediate change: 2.74%, 95% CI: -0.068 0.014; slope change: 0% 95%CI: -0.001 0.000). A small, significant increase in slope in number of new patients receiving prescriptions was observed (0.2% 95%CI: 0.001 0.003). However, no significant results were confirmed after robustness checks. We found also no variation across different socioeconomic groups.

Keywords Minimum Unit Price for Alcohol · alcohol dependence prescriptions · Scotland · alcohol use disorder · interrupted time series · natural experiment

Introduction

Alcohol is one of the leading risk factors for premature death and disability worldwide [1]. In the United Kingdom, the incidence of alcohol-related harm is above the world average, being the fifth-ranked cause of death and serious illness [2]. Evidence shows that since the

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mid-1990s, alcohol sales per adult have been consistently higher in Scotland than in England & Wales [3], causing higher alcohol related harms as well as consumption [4]. Alcohol-related harm has also been shown to be more prevalent in certain sections of the population, widening health inequalities [5]. This is particularly evident in Scotland, where alcohol-related deaths are more than five times higher in the most socio-economically deprived areas compared to the least deprived areas [6].

The Scottish Government, recognising high levels of alcohol consumption as a major public health threat for its population, has implemented policies such as the Alcohol Act (restricting alcohol promotions within retail stores and banning quantity-based price discounts) in 2010 [7] and more restrictive drink-driving laws in 2014 [8]. Building on these earlier policies, and after a long legal battle, a minimum unit price (MUP) for alcohol came into effect in May 2018. MUP was intended to reduce alcohol consumption across the population, but to have greater effect on those who drink the most and favour cheaper products [9]. Specifically, MUP is a policy which sets a floor price of £0.50 ($0.57 or €0.58 – converted in September 2022) per UK unit of alcohol (one UK unit contains 8 g of ethanol) and applies to all alcohol sold. After 1st May 2018, alcohol products in Scotland could not legally be sold at any price equivalent to or below £0.50 per UK unit.

The introduction of MUP was supported by findings generated using a version of the Sheffield Alcohol Policy Model (SAPM) [10], an epidemiological and econometric model that estimated the potential causal impact of the policy. SAPM estimated a direct reduction in the level of alcohol consumption due to MUP, which in turn could reduce related health harms and crime [11] and reduce inequalities. SAPM focuses on overall effects and broad sub-groups of the population including hazardous and harmful drinkers, but is not well suited to estimating the impact of MUP on people with more severe alcohol dependence, who are poorly represented in the data on which the model relies. The legislation introducing MUP is subject to a 'sunset clause' meaning that the policy will lapse if the Scottish Parliament does not vote for it to continue in 2023. To inform this parliamentary process, MUP is being evaluated by a suite of studies [12], some commissioned by the national agency for public health, and some funded separately. Studies published to date have shown mixed findings. First, there is strong evidence from separate research using different data sources that there has been an overall reduction in alcohol sales associated with MUP [13, 14]. However, in the early reporting on harms, no significant variations in crime and disorder [15] or attendances to emergency departments [16] were found after the introduction of MUP. Little is known about the effect of MUP on dependent drinkers. Early studies prior to the introduction of the policy suggested that the most dependent drinkers found it hard to understand that they could not 'shop around' for a better price, but some felt that they would cut down their alcohol intake under MUP [17]. A before- and after-MUP study of people drinking at harmful levels [18] found no clear evidence that level of alcohol consumption changed, nor severity of dependence. However, a recent systematic review on MUP policies found that they could be linked to reductions in alcohol-related hospitalisations[19]. To date, only two natural experiments focused on these outcomes in Scotland finding reductions in the absolute number of patients discharged with alcohol-related liver disease after 20 months [20] and significant reductions in deaths and hospitalisations wholly attributable to alcohol consumption after 32 months of MUP introduction [21]. Finally, a qualitative study [22] found that introduction of MUP had little/no impact on people experiencing homelessness and the support services they use.

The primary aim of this study was to investigate the effect of the introduction of MUP on two relevant outcomes for the alcohol dependent population: (1) the level of prescriptions for the treatment of alcohol dependence and (2) the number of new patients receiving such prescriptions. A secondary aim was to determine whether there was variation in any effect of MUP across different socio-economic groups.

We did not have any *a priori* hypothesis of the direction of a potential effect of MUP on prescriptions for alcohol dependence. Two plausible hypotheses are that the increase in price leads to decreasing consumption, resulting over time in decreased severity (or incidence) of alcohol dependence (possibly reducing demand for medications); conversely, the increase in price makes alcohol less affordable, increasing the likelihood that people with alcohol dependence may find alcohol unaffordable and be motivated to seek alcohol services (possibly increasing demand for medications). So, wherever we would find an effect in any direction, we would explain in this way. In contrast, a lack of effect could have two potential explanations: the two effects acting in opposite direction cancelled each other out or the increase in price was not enough to affect prescriptions' demand.

Methods

Background

The National Institute for Health and Care Excellence (NICE) guideline for treatment of alcohol-use disorders [23] outlines that pharmacological intervention can be considered in combination with psychological interventions for treatment of alcohol dependence, and in particular recommends acamprosate, disulfiram, nalmefene and naltrexone.[24]. While the first three drugs have an indication exclusively for alcohol dependence, naltrexone is also used as a treatment for opiate dependence. Recent estimates reported that only around 11% of patients with a diagnosis of alcohol dependence received pharmacological treatment in the UK, however patients in Scotland were more likely to receive pharmacotherapy compared to the UK average[25]. In addition, naltrexone and nalmefene are used infrequently in the UK[25] (see volume of prescriptions in Scotland in supplementary material). For these reasons and as there was no way to distinguish naltrexone prescriptions to treat alcohol or opiate dependence in our dataset, we restricted the set of medications under study to acamprosate, disulfiram and nalmefene.

Design

We used a controlled interrupted time–series (ITS) design to evaluate whether the introduction of MUP was associated with a change in the volume of prescriptions for treatment of alcohol dependence. To account for potential substitution effects between different medications, we assessed the impact of the legislation on the total volume of prescriptions for acamprosate, disulfiram and nalmefene combined (primary outcome measure). In addition, we used the number of new patients receiving prescriptions for treatment of alcohol dependence for the first time as a secondary outcome measure. As well as modelling for the entire population, we also ran ITS models for individuals residing in the most socio-economically deprived group (based on highest decile of Scottish Index of Multiple Deprivation [26]) and the remaining population.

To produce robust and reliable findings, controlled ITS designs are usually preferred to uncontrolled designs, as long as appropriate controls can be identified. The use of a control group that is equally affected by other potential factors happening in the same time period should minimise potential confounding [27]. Theoretically, using England, a location-based control group that neighbours Scotland, has the same UK government, similar culture and also influenced by similar clinical guidelines would have been ideal. However, England had a publicly available dataset with a smaller level of granularity (only aggregated monthly volumes) and only on prescriptions (not on patients). This meant only a descriptive comparison with England was possible. Therefore, as an alternative, we ran inferential comparisons on the same outcomes (both prescriptions and patients) using prescriptions in Scotland for methadone as a control outcome [27]. This was chosen as a drug for a different form of dependence –opioid – but not affected by MUP. Data on methadone prescriptions and patients were obtained from the same source as for alcohol dependence prescriptions. As recommended elsewhere [27], controls were chosen based on *a priori* evaluation of potential confounding events. To assess the appropriateness of the controls, we first compared pre- intervention trends descriptively. For the inferential comparison we also assessed whether the intervention and control time series followed a common pre-intervention trend [28]. Nevertheless, we were aware that the population identified by the control group in the inferential analyses (opioid dependent) refers to a population with often very different characteristics to individuals with alcohol dependence, and the prescriptions may therefore be affected by different external factors. Therefore, we performed an extensive range of sensitivity analyses both on the uncontrolled interrupted time series and the control group.

Data

Data on prescriptions issued in Scotland were extracted from the Scottish national prescribing information system (PIS) for the period March 2014 to March 2020. PIS records all medicines prescribed and dispensed in the community in Scotland [29]. The PIS dataset is arranged by patient identifier and paid date (the date on which the prescription item is submitted for payment - which is always the last day of the month). Data are aggregated with daily frequency. Whereas this date of payment is always recorded, the date on which the prescription was issued ('prescribed date') or when the medication was dispensed by the pharmacy ('dispensed date') are not consistently recorded. If not recorded, the prescribed and dispensed date default to be the same as the date of payment. Therefore, the last day of the month includes not only the drugs prescribed and dispensed on that day, but also all those paid that month for which no prescribed or dispensed date was recorded. As a result, there is a peak in prescription numbers in the data on the final day of every month, which sometimes exceeds by 8–10 times the daily average for that month. Conscious that an analysis grouping observations by month would have solved these issues but would have also reduced the number of observations after MUP introduction (23 data points), we smoothed the daily data by re-distributing the peak of prescriptions at the end of the month throughout the daily levels (see supplementary material). Data on English prescriptions were from the publicly available English prescribing dataset [30] and contained aggregated monthly prescriptions issued in England (with no information on patients).

Descriptive Analysis

We calculated the monthly volume of prescriptions and new patients receiving such prescriptions before and after MUP, both overall and by socio-economic deprivation groups. As there were 23 months available after MUP introduction (May 2018 – March 2020), to identify a potential difference in prescription levels excluding possible seasonal trends, we reported and compared values for the same months over three periods: two before the intervention to remove already present trends and possible influences of a national shortage of disulfiram [31, 32] which occurred between January and October 2017, and one after.

Inferential Analysis

We used inferential models with additive seasonal autoregressive integrated moving average errors as our main statistical approach. After testing the series for stationarity, candidate models were based on autocorrelation and partial autocorrelation plots of the data and adjusted based on the correlogram of the errors. Best-fitting models were then selected using the Akaike and Bayesian information criteria and error white noise assumption was assessed by Portmanteau's test. To correct data for skewness, data were log transformed, this also allowed to interpret model covariates as percentage variation of the outcome variable. New patients receiving methadone, having three weeks over the study period with zero new patients, were not log transformed.

We estimated the size of the MUP effect by including a dummy variable in the regression assuming value 1 after MUP introduction and 0 before. A post intervention trend was also included in the regression to get an estimate of the continuing effect of MUP, that is, the slope of the change in successive time periods. Two additional dummy variables were added in the regression to account for recurrent or unusual events in the time series period. Specifically, they were, one at the end/beginning of every year to reflect the period when practitioners release a lower number of prescriptions, and one between January and October 2017 to consider the drop in prescriptions due to the national shortage of disulfiram.

Sensitivity Analyses

We performed sensitivity analyses to test the robustness of our results. Specifically, we used falsification tests simulating the intervention six months before or six months after the intervention.

As the drop in disulfiram prescriptions was relatively close to our intervention date, it may have affected our estimates whenever it could have affected physicians' future prescription attitude (a steadiness of prescriptions below 2016 volumes just after the shortage and before MUP introduction could suggest so). Therefore, whenever MUP coefficients (level or slope changes) assumed statistically significant values, an additional change in slope variable just after the shortage in disulfiram was inserted to assess this likely spread and lagged effect of disulfiram shortage avoiding potential biases. The same model using shortage of disulfiram variables and removing MUP was also performed, comparing size and significance of coefficients.

For the groups satisfying common trend assumptions [28], the analysis on the difference between intervention and control was performed, and whenever MUP had statistically significant values, falsification tests were performed on the difference.

Results

Descriptive Analysis

Prescriptions

Acamprosate and disulfiram were the most prescribed drugs for alcohol dependence, however, there was a greater relative difference between the volume of these two drugs in England compared to Scotland (see Fig. 1b). Disulfiram prescriptions dropped in 2017 (Fig. 1) due to a national shortage of supply from one of the main national wholesalers. This generated an overall decrease in prescriptions for alcohol dependence. Scotland, having a relatively higher demand for disulfiram, was more affected than England. Overall, there has been a gradual increase in the volume of prescriptions between 2014 and 2020 (Fig. 2; Table 1). During the national shortage of disulfiram (January-October 2017), prescriptions remained steady (+0.3%) compared to the same period the previous year. Ruling out the period affected by the dilsulfiram shortage, in the 21 months after the intervention there was a general increase in prescriptions (4.6%) compared to the same period from May 2014 to January 2016. On average, more than a fifth of prescriptions were for people residing in the most socio-economically deprived decile, and greater growth was registered for this group (12.7%). In England, prescriptions had an overall decreasing trend. The decrease decelerated in the last 21 months (-6.2%) compared to the previous two periods (-7.2%). The distribution in prescriptions across socio-economic deprivation deciles was similar to Scotland, however, prescriptions in the most socio-economically deprived groups decreased at a higher rate than in the rest of the population. Methadone prescriptions increased in the second time period and then decreased in the last one after MUP implementation, having an overall decline, mainly led by the most socio-economically deprived groups.

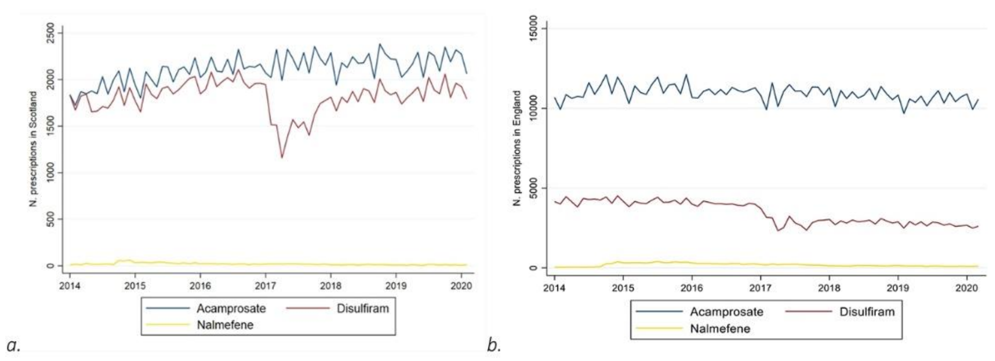

Fig. 1 Prescriptions for alcohol dependence per month between 2014 and 2020 In Scotland (a) and England (b)

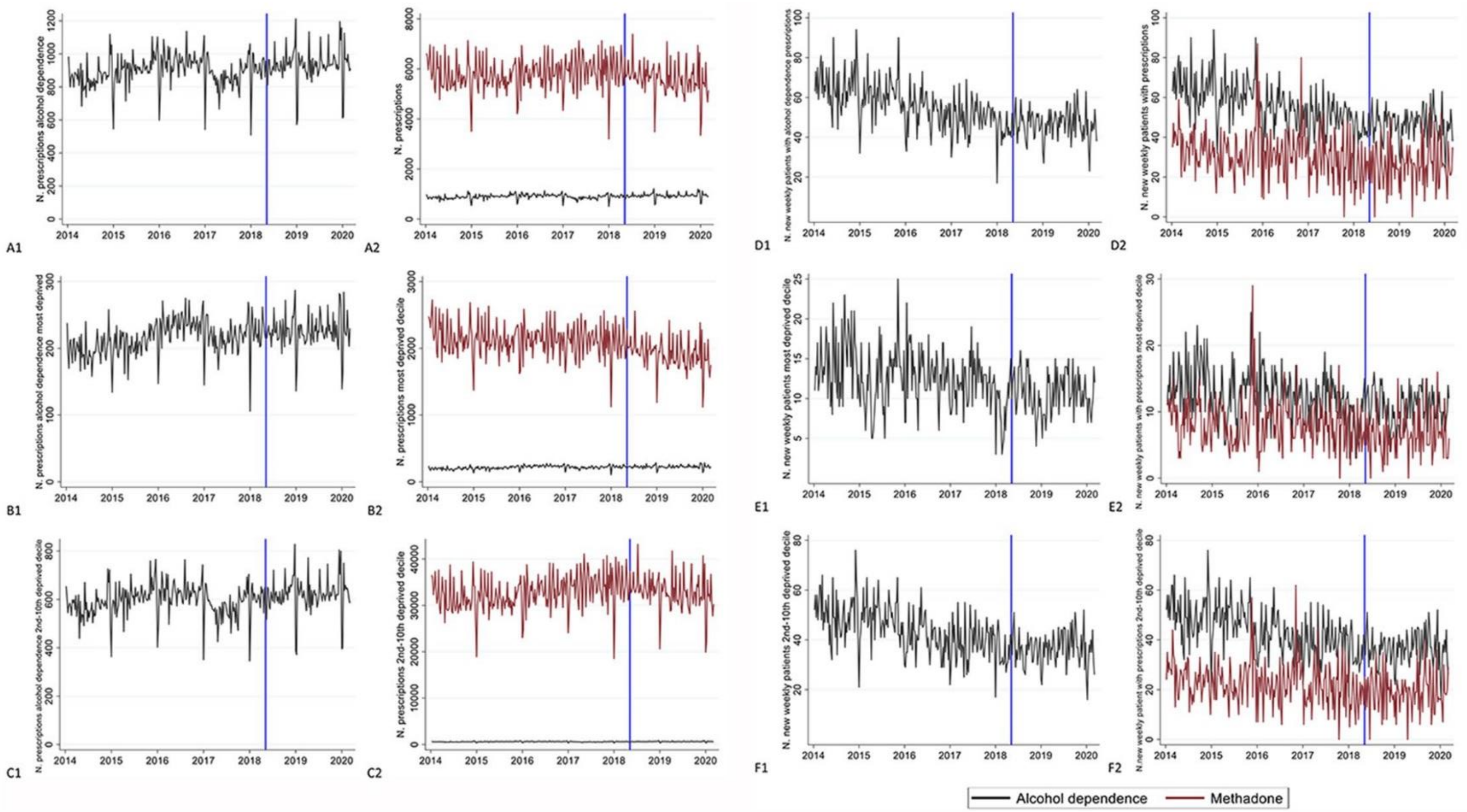

Fig. 2 Trend in weekly prescriptions for alcohol dependence in Scotland (left column) and comparison between methadone and alcohol prescription in Scotland (right column) across different outcomes. A: Total number of prescriptions. B: Prescriptions in most deprived groups. C: Prescriptions in least deprived groups. D: New weekly patients receiving prescriptions. E: New weekly patients receiving prescriptions in most deprived groups. F: New weekly patients receiving prescriptions in least deprived groups.

Number of new Weekly Patients

The number of patients receiving prescriptions for treatment of alcohol dependence for the first time declined over the years (Table 1). The trend was stable between the most socio-economically deprived group (-22.4%) and the rest of the population (-23.7%). While there were major differences in the volume of prescriptions, new methadone patients followed a similar pattern: the overall decrease in patients was −21.3% and similarly distributed between socio-economic groups (-23.1% for the most deprived decile and −20.1% in the rest of the population).

Inferential Analysis

Prescriptions

For the overall population, MUP was associated with a non-statistically significant reduction in the change of level (-2.7%; 95%CI -0.068 0.014; p=0.196) and the change in slope was estimated to be 0.0% (95%CI -0.001 0.000; p=0.707) – Table 2. There were no significant variations corresponding with MUP introduction across different socio-economic groups. Methadone prescriptions showed a statistically significant decrease in the slope of trend after MUP of 0.1% (95%CI: -0.002 -0.001; p=0.000) in the overall population and in the subpopulations.

New Weekly Patients

For weekly new patients, MUP was not associated with immediate changes. However, a significant increase in slope of the trend of 0.2% was estimated after MUP introduction for both the overall population and the least deprived deciles (Table 2). Regarding methadone, a significant gradual weekly decrease in the number of new patients was associated with MUP introduction.

Sensitivity Analysis

Whenever there were significant results in the intervention group, falsification tests bringing the analysed date of intervention forward by 6 months produced similar results (gradual change in new patients for overall population and least deprived groups). When an additional variable denoting the period post shortage of disulfiram was added to the regression in models with significant MUP terms, both this variable and the MUP variable became non-significant. When the MUP variable was removed and only the new 'post shortage' variable was left, this became significant and the model had a better fit (lower information criteria) (see supplementary material for these sensitivity analyses results).

The common trend assumption was satisfied only for the volume of prescriptions for the total population, prescriptions in least socio-economically deprived groups, and most deprived new patients. When the ITS analysis was performed on the alcohol and methadone difference for such groups, we found significant associations only for slope change in prescriptions in the least deprived groups (-0.2% 95%CI: -0.003 -0.001; p=0.007). However, these differences were not robust to falsification testing.

Table 1 *Volume of prescriptions and number of new patients with an exclusive indication for alcohol dependence †*

	Intervention Group (Scottish -alcohol dependence- prescriptions and patients)		Location based control group (England)	Control outcome (Methadone)	
	Prescriptions	New patients	Prescriptions	Prescriptions	New patients
Total population					
May 2014-Mar 2016	89738	6102	359818	568828	3284
May2016-Mar2018	90040 (+0.3%)	5031 (-23.7%)	332487 (-7.6%)	592210 (+4.1%)	2974 (-9.4%)
May2018-Mar2020	93899 (+4.3%)* (+4.6%)**	4656 (-7.5%)* (-23.7%)**	311730 (-6.2%)* (-13.4%)**	559731 (-5.5%)* (-1.6%)**	2583 (-13.1%)* (-21.3%)**
Most deprived decile*					
May2014-Mar2016	20761	1301	87924	212948	875
May2016-Mar2018	22359 (+11.1%)	1099 (-4.3%)	77166 (-12.2%)	211915 (-0.0%)	774 (-4.3%)
May2018-Mar2020	22691 (+1.5%)* (+12.7%)**	1010 (-8.1%)* (-22.4%)**	70869 (-8.2%)* (-19.4%)**	191595 (-9.6%)* (-10%)**	673 (-13%)* (-23.1%)**
Rest of population*					
May2014-Mar2016	69175	4750	221062	351039	2341
May2016-Mar2018	67439 (-2.5%)	3918 (-17.5%)	215162 (-2.7%)	377303 (7.5%)	2135(-8.8%)
May2018-Mar2020	70973 (+5.2%)* (+2.5%)**	3625 (-7.5%)* (-23.7%)**	203978 (-5.2%)* (-7.8%)**	365377(-3.2%)* (4.1%)**	1857 (-13%)* (-20.1%)**

†=The descriptive comparison was on both prescriptions and number of new patients for Scottish prescriptions in alcohol dependence and methadone and only on alcohol dependence prescriptions for English data

* Incremental percentage referring to M ay2016-March2018

** Incremental percentage referring to May2014-March2016 to avoid the inclusion of shortage in disulfiram

*** Most deprived group and rest of population do not add up to overall population figures due to missing data in patients regarding socio-economic deprivation

Table 2 *Main Output for base case analysis and falsification tests for intervention and control groups*

Model		Main analysis			Falsification tests					
					6-months pre MUP			*6-months post MUP*		
		Coefficient	95% C.I.	P-value	Coefficient	95% C.I.	P-value	Coefficient	95% C.I.	P-value
					Alcohol dependence					
Prescriptions										
Total population	MUP	-0.027	(-0.068 0.014)	0.196	-0.870	(-0.132 -0.042)	0.000	-0.013	(-0.065 0.038)	0.614
	after MUP trend	0.000	(-0.001 0.000)	0.707	0.000	(-0.001 0.000)	0.126	0.000	(-0.001 0.001)	0.863
Most deprived decile	MUP	-0.037	(-0.125 0.051)	0.408	-0.118	(-0.196 -0.040)	0.003	-0.019	(-0.101 0.062)	0.640
	after MUP trend	-0.001	(-0.002 0.001)	0.404	-0.001	(-0.002 -0.000)	0.023	-0.001	(-0.002 0.001)	0.479
2nd -10th deprived decile	MUP	-0.014	(-0.062 0.035)	0.582	-0.084	(-0.145 -0.023)	0.007	-0.005	(-0.054 0.044)	0.840
	after MUP trend	-0.000	(-0.001 0.001)	0.851	-0.000	(-0.001 0.000)	0.298	-0.000	(-0.001 0.001)	0.862
New patients										
Total population	MUP	0.054	(-0.022 0.129)	0.165	-0.008	(-0.090 0.074)	0.851	0.087	(0.006 0.169)	0.036
	after MUP trend	0.002	(0.001 0.003)	0.002	0.002	(0.001 0.003)	0.000	0.001	(-0.001 0.003)	0.216
Most deprived decile	MUP	-0.005	(-0.218 0.208)	0.964	-0.222	(0.410 -0.034)	0.021	-0.086	(-0.314 0.142)	0.462
	after MUP trend	0.002	(-0.001 0.006)	0.182	0.002	(-0.000 0.004)	0.093	0.005	(0.000 0.009)	0.047
2nd -10th deprived decile	MUP	0.041	(-0.079 0.160)	0.508	0.013	(-0.099 0.126)	0.816	0.083	(-0.043 0.210)	0.194
	after MUP trend	0.002	(0.000 0.003)	0.027	0.002	(0.001 0.003)	0.001	0.001	(-0.001 0.004)	0.280

Table 2 (continued)

Model		Main analysis			Falsification tests					
					6-months pre MUP			*6-months post MUP*		
		Coefficient	95% C.I.	P-value	Coefficient	95% C.I.	P-value	Coefficient	95% C.I.	P-value
					Methadone					
Prescriptions										
Total population	MUP	-0.011	(-0.036 0.015)	0.410	0.020	(-0.019 0.059)	0.313	-0.032	(-0.57 -0.007)	0.014
	after MUP trend	-0.001	(-0.002 -0.001)	0.000	-0.001	(-0.002 -0.001)	0.000	-0.001	(-0.002 -0.000)	0.009
Most deprived decile	MUP	-0.006	(-0.058 0.045)	0.799	-0.007	(-0.068 0.055)	0.829	-0.023	(-0.079 0.033)	0.416
	after MUP trend	-0.001	(-0.002 -0.000)	0.002	-0.001	(-0.002 -0.001)	0.001	-0.001	(-0.002 0.000)	0.052
2nd-10th deprived decile	MUP	-0.030	(-0.075 -0.015)	0.195	0.010	(-0.050 0.071)	0.740	-0.037	(-0.088 0.015)	0.163
	after MUP trend	-0.001	(-0.002 -0.001)	0.000	-0.002	(-0.002 -0.001)	0.000	-0.001	(-0.002 0.000)	0.009
*New patients**										
Total population	MUP	-2.853	(-6.198 0.492)	0.095	-3.600	(-8.356 1.164)	0.139	-0.526	(-3.300 2.248)	0.71
	after MUP trend	0.070	(0.032 0.108)	0.000	0.040	(0.003 0.077)	0.033	0.078	(0.024 0.132)	0.005
Most deprived decile	MUP	-1.487	(-3.072 0.099)	0.066	-0.653	(-2.296 0.991)	0.436	0.186	(-1.447 1.820)	0.823
	after MUP trend	0.018	(-0.010 0.045)	0.208	0.002	(-0.020 0.025)	0.853	0.011	(-0.027 0.049)	0.579
2nd-10th deprived decile	MUP	-0.634	(-4.868 3.599)	0.769	-0.602	(-5.128 3.925)	0.794	-0.745	(-4.131 2.641)	0.666
	after MUP trend	-0.033	(-0.035 0.102)	0.341	0.018	(-0.038 0.075)	0.526	0.052	(-0.027 0.131)	0.195

**number of mew weekly patients receiving methadone had three value equal to 0 in the study period, therefore there was not log transformation of the dependent variable

Discussion

This study provides evidence that MUP in Scotland was not associated with significant changes in the volume, or trend in volume, of prescriptions for treatment of alcohol dependence in the overall population after 23 months of its introduction. For new patients receiving alcohol dependence medication, statistically important results were observed but this was mirrored in falsification tests anticipating MUP introduction by 6 months, thus making the effect unlikely to be causal. This suggests that time varying (unmeasured) confounders rather than the introduction of MUP led to an increase in the number of patients receiving such prescriptions for the first time.

The null results we found could reflect that the two opposite effects of the decrease in consumption leading to a decrease in prescriptions demand and the increase in seeking alcohol services from those finding alcohol less affordable could have cancelled each other out. Alternative explanations can be that any effect was not large enough to be detected, or, that there is no causal effect of MUP intervention on level of uptake of alcohol dependence medications. Previous studies showing that people drinking alcohol at harmful levels did not change their alcohol consumption patterns due to MUP [18], as well as the similarity of trends with our control, provide support for the latter interpretation. Further, these findings may reflect limited capacity in alcohol treatment and a reluctance by some primary care doctors to prescribe treatments for dependence which may have been unchanged by MUP, even if more patients sought help[30]. Finally, another explanation for the null findings could be that the impact of MUP was limited by inflation. The current £0.50 floor price was set in 2012, in 2021 the equivalent value would be almost £0.10 greater [33] (a 20% increase). The lack of an indexing price system risks to undermine even further the MUP effects (and potential benefits) in the future. While it has been shown that MUP reduced the overall alcohol consumption in the population [13], the demand for alcohol in alcohol dependent individuals can be less price elastic, explaining our results on both patients and prescriptions. In other words, a floor price of £0.50 (which did not affect all alcohol beverages on sale) was unlikely to decrease the real income and then holding back individuals from continuing/relapsing with alcohol dependence. This was also supported by recent evidence around MUP, showing that many of the people already drinking at harmful levels were not considerably affected by MUP as they already paid more than the floor price, with no substantial difference in consumption for those with alcohol dependence [18]. Our findings are in line with this, and by showing that there was not a decrease in new patients receiving prescriptions after MUP, highlighted that the policy also was not effective to prevent people to be newly alcohol dependent (or at least did not change the number of new patients getting pharmaceutical treatment).

A more comprehensive interpretation of our results in relation to other studies, highlighting the mismatch between the reduction in alcohol consumption and outcomes on alcohol use disorders (AUD), may suggest that this £0.50 MUP can just be an 'upstream' tool at addressing aggregate level consumption and harms in the population. In contrast, other interventions such as Alcohol Care Teams may be a more effective 'downstream' approach on the management of AUD, including alcohol dependence [34].

As mentioned, the few significant associations across subgroups and outcomes with MUP introduction can be attributed to time-varying confounding. Indeed, falsification tests registered significant changes for such subgroups where the 'intervention' was placed 6 months prior to the start of the MUP. In the model on the difference in prescriptions between alcohol and methadone, given the considerable initial difference in prescription levels, results may be led by methadone trends only. This would be supported by similar significant coefficients in the difference, falsification test of the difference (supplementary materials) and coefficient and falsification tests of the methadone analysis (Table 2). In addition, regarding new patients, when we inserted additional slope variables after the national shortage in disulfiram, they generated an attenuation (and lack of statistical significance) of the MUP effect. Furthermore, when such dummy variables were maintained, and MUP variables were excluded, the overall goodness of fit of the regression increased. Therefore, these tests could explain that the significant effect found modelling the difference in prescriptions in the least deprived groups were likely caused by other factors happening earlier than MUP (including the shortage in disulfiram).

The volume of prescriptions increased from 2014 to 2020. In contrast, the number of patients receiving prescriptions for alcohol dependence for the first time decreased over the same period. This discrepancy between the two series is difficult to explain; however, therapies can have long treatment periods or individuals can relapse, causing additional prescriptions but not additional patients. Regarding patients, a recent decrease in new patients in England receiving specialist alcohol treatment was found [35] which suggests that this fall was associated with financial pressures and service reconfiguration which prompted capacity reductions. Whilst our data are from community (primary care) prescribing, pressures on general practitioners' capacity may have similarly strong effects on the number of patients in treatment and receiving prescriptions, perhaps more so than MUP.

Strengths

To the best of our knowledge, this is the first time that a study has investigated changes in the level of prescriptions for treatment of alcohol dependence after the introduction of a MUP for alcohol. This is one of the few studies examining how MUP affected clinical outcomes associated with alcohol use/dependence which can inform the Scottish Government on the decision to extend or change the current policy, or allow it to lapse after the sunset clause deadline. Further studies with similar analyses on a longer time horizon could contribute to understanding of whether/how MUP may affect the rates and severity of alcohol dependence in the Scottish population over several years or decades.

We designed a population-based study, using data from whole of Scotland (and England) and thus removing any selection bias arising from sampling. Several robustness checks assessed the strength of our results.

Limitations

England, being a neighbouring country and affected by the same shortage in disulfiram, could have been the ideal control group. However, there was a different prescription pattern between the two jurisdictions (Fig. 1): disulfiram in England made up a considerably smaller proportion of total prescriptions for alcohol dependence treatments, limiting the relevance of the overall comparison with Scotland. Regarding the comparison with methadone prescriptions, we found that the two series had common pre-intervention trends for some of the analyses. Yet, our analyses using a difference-in-difference design did not find any effect of MUP after sensitivity analyses had been conducted. We recognise, however, that even with a common trend this may not have been the most reliable comparison, especially for prescriptions, having relevantly different initial volumes. The difference was smaller regarding patients. A further limitation is that we only accounted for methadone, while data on buprenorphine (the other drug with an indication for the management of opioid dependence in the UK, which is generally less prescribed [36]), was not available to us. Acknowledging that our controls presented a few weaknesses, we performed extensive sensitivity analysis on the uncontrolled series as well as on the controls, further validating our conclusions. Finally, as already mentioned, many alcohol dependent individuals do not ever receive treatment medications [37, 38], and new patients receiving such prescriptions are just a proportion of the new alcohol dependent individuals in the population. Many patients receive instead behavioural intervention whenever medication are not considerate appropriate. Lastly, we recognise that dependence usually develops over a long period, and a longer analysis period could have helped to explain what might be happening. A challenge to modelling a longer time series is that after March 2020, the Covid-19 national lockdown considerably varied the prescription patterns. If we had extended analysis into this period it would have increased time-varying confounding.

Conclusions

MUP was not associated with a change in the number of prescriptions for pharmacological treatment of alcohol dependence in the overall population, neither with variations in the number of new patients receiving medications for alcohol dependence over a 23 months follow-up period. Further, there was no evidence of effect modification across different socio-economically deprived groups.

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Author Contributions Conceptualization, JL, FM; methodology, JL, FM; formal analysis, FM; data curation, FM, LZ; visualization, FM; supervision, JL, NF; interpretation, NF, JL, FM; writing – original draft preparation, FM; writing – reviewing and editing, NF, JL, DM, FM, AMc, CS, LZ; funding acquisition, not applicable. All authors have approved the final article.

Declarations

Conflict of interest All authors declare that they have no conflict of interest.

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RESEARCH REPORT

ADDICTION SSA

The effect of a minimum price per unit of alcohol in Scotland on alcohol-related ambulance call-outs: A controlled interrupted time−series analysis

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Abstract

Background and aims: On 1 May 2018, Scotland introduced a minimum unit price (MUP) of £0.50 for alcohol, with one UK unit of alcohol being 10 ml of pure ethanol. This study measured the association between MUP and changes in the volume of alcohol-related ambulance call-outs in the overall population and in call-outs subsets (night-time call-outs and subpopulations with higher incidence of alcohol-related harm).

Design: An interrupted time−series (ITS) was used to measure variations in the daily volume of alcohol-related call-outs. We performed uncontrolled ITS on both the intervention and control group and a controlled ITS built on the difference between the two series. Data were from electronic patient clinical records from the Scottish Ambulance Service.

Setting and cases: Alcohol-related ambulance call-outs (intervention group) and total ambulance call-outs for people aged under 13 years (control group) in Scotland, from December 2017 to March 2020.

Measurements: Call-outs were deemed alcohol-related if ambulance clinicians indicated that alcohol was a 'contributing factor' in the call-out and/or a validated Scottish Ambulance Service algorithm determined that the call-out was alcohol-related.

Findings: No statistically significant association in the volume of call-outs was found in both the uncontrolled series [step change = 0.062, 95% confidence interval (CI) = −0.012, 0.0135 $P = 0.091$; slope change = −0.001, 95% CI = −0.001, 0.1×10^{-3} $P = 0.139$] and controlled series (step change = −0.01, 95% CI = −0.317, 0.298 $P = 0.951$; slope change = −0.003, 95% CI = −0.008, 0.002 $P = 0.257$). Similarly, no significant changes were found for the night-time series or for any population subgroups.

Conclusions: There appears to be no statistically significant association between the introduction of minimum unit pricing for alcohol in Scotland and the volume of alcohol-related ambulance call-outs. This was observed overall, across subpopulations and at night-time.

Francesco Manca is the first author.

KEYWORDS
Alcohol, ambulance, interrupted time–series, minimum unit price, natural experiment, Scotland

INTRODUCTION

In 2018, it was estimated that alcohol was responsible for 5.1% of the global burden of disease and injury [1], causing both acute and long-term conditions. Alcohol-related harm, which includes injuries, violence and other accidents related to binge drinking, also places a significant strain on health-care and emergency services. Alcohol consumption in western Europe is among the highest in the world [2], and 24% of adults in the United Kingdom regularly exceed drinking the Chief Medical Officer's low-risk guidelines [3, 4]. In Scotland there are substantially higher levels of alcohol sales and alcohol-related harm than the rest of the United Kingdom [5, 6].

In 2018, to reduce consumption and alcohol-related harm in the population, Scotland implemented a minimum unit pricing policy (MUP) for alcohol of £0.50, meaning that one UK unit of alcohol (10 ml or 8 g of ethanol) cannot be sold below this threshold. As the incidence of alcohol-related harm is higher in the most socio-economically deprived areas the policy was also expected to have a greater impact upon people living in such areas, with a consequent decrease in the significant health inequalities that exist in Scotland. After 1 year of the policy, off-trade alcohol sales were observed to have fallen by 3.5% [7], an effect that was largely sustained at 3-year follow-up [8]. As overall consumption decreased, it is reasonable to expect that some alcohol-related harms would also reduce. Studies to date have found inconclusive effects of MUP on several acute measures of alcohol harm, such as no changes in alcohol-related crime [9] or in alcohol-related harms attendance within emergency departments [10]. Further, studies showing associations between MUP and decreases in deaths and hospitalizations attributable to alcohol did not find evidence of changes in hospitalizations for acute causes [11]. The legislation that introduced MUP contains a 'sunset clause', meaning that it will end after 5 years of its implementation unless the Scottish Parliament votes for it to continue. This decision will be informed by a large body of evaluation evidence, to which this study will add an additional perspective.

Many aspects of acute alcohol-related harm are typically under-reported [12,13]. Ambulance services are often the first and only health-care providers in contact with some patients who are treated in the community and who may therefore be missing from emergency departments and admissions data. This is reflected in Scottish data where, in 2019, the alcohol-related attendance to emergency departments was 8% [10], while the proportion of alcohol-related ambulance call-outs was 16% [14]. For these reasons, ambulance call-outs may be considered a 'more sensitive' thermometer of the effect of a public health policy than hospital data, especially reflecting the impact of the policy on acute alcohol-related harm. The only other international study analysing the effect of similar MUP policy on ambulance call-outs was an interrupted time–series study from Australia's Northern Territory [15]. It reported a significant negative step change but not a significant slope change in the rate of ambulance attendance post-MUP in the region. To date, no published peer-reviewed study has examined the impact of MUP or any other increase in alcohol prices on ambulance call-outs.

This study aimed to identify whether the introduction of MUP in Scotland was associated with changes in the overall volume of alcohol-related ambulance call-outs and whether there were variations across time of the day, sex, age of the patient or level of socio-economic deprivation of the call-out location.

METHODS

Study design

We used a controlled, interrupted time–series design to evaluate the impact of the introduction of MUP on alcohol-related ambulance call-outs after 20 months. We used ambulance call-outs to people aged under 13 years for any cause as a characteristic-based control, as this outcome was not expected to be impacted by the policy. However, it covered the same geographical area and was assumed to be affected by the same environmental and other unmeasured confounding factors [16].

Data set

Our data provider was the Scottish Ambulance Service (SAS), which supplied a nation-wide data set containing selected anonymized fields of all electronic patient record forms (ePRFs) of ambulance call-outs for all Scotland from 1 May 2015 to 31 October 2021, covering 3 years prior to and 2.5 years after MUP implementation. Every call-out contained information on patients' demographic characteristics, as well as deprivation deciles of the call-out location, assessed using the Scottish Index of Multiple Deprivation (SIMD) (a relative measure of deprivation ranking Scottish areas based on income, employment, access to services, health, crime, housing and education) [17]. The data set also included two markers of whether or not the call was alcohol-related: first, a marker made by ambulance clinicians at time of filling in the ePRF by selecting an on/off field to indicate whether alcohol was a 'contributing factor' in the call-out and secondly, a yes/no marker generated from an algorithm embedded in the SAS system, which analyses the free-text report in every ePRF and detecting whether the call-out was alcohol-related. Each individual record was deemed to be alcohol-related for this study if either of these markers were positive for alcohol involvement. This indicator, combining the yes/no field with the algorithm field, was developed and validated previously and found to have a sensitivity of 94%. A detailed description of the algorithm development and performance is given elsewhere [14]. Based on the algorithm, the definition of 'alcohol-related call-outs' comprises any call-out recording alcohol on the ePRF as a primary cause for care (i.e. alcohol intoxication) or in those calls where the consumption of alcohol was recorded in association with the presenting condition/injury (i.e. mental health crises, falls or assaults).

While the full data set contained records from 1 May 2015 to 31 October 2021, SAS changed their software system for recording call-outs at the end of 2017, with implementation phased in throughout different Scottish regions over several months. In this latest version of the recording system, clinicians could indicate that alcohol (or other substances) was a contributing factor in a given call-out in multiple sections of the ePRF, and as a result the implementation of the new system created a gradual increase in the volume of call-outs identified as alcohol-related, lasting over the implementation period (a couple of months), followed by a more stable level of alcohol-related call-outs from December 2017 (only 5 months before the MUP introduction). Such variation in data collection systems could generate structural breaks in the time–series, and for this reason, whenever data collection processes are inconsistent over time, it is recommended to truncate the analysis period for interrupted time–series analyses [18]. To avoid potential bias in our analysis, we chose to perform the main analysis only on the period when the new system was fully adopted (after 15 December 2017). The analytical data set was further truncated in March 2020 to avoid additional bias as a result of the COVID-19 pandemic and lockdown. The lockdown period affected not only alcohol-related ambulance call-outs but potentially also consumption patterns [19], with probably long-lasting effects. Consequently, for the main analysis, the final data set was from 15 December 2017 to 15 March 2020.

To calculate the overall effect of MUP on the burden of alcohol to the ambulance service, we would ideally analyse the number of individual patients treated by ambulance crews. However, SAS classifies its incidents in terms of call-outs, and the data do not record the actual number of patients involved in every call-out. Therefore, the unit of measurement in this analysis is 'call-out'. When we sub-grouped analysis by age, sex and deprivation (see below), whenever multiple ePRFs were recorded within the same incident the average of age and sexes was considered. A minor proportion of accidents had the same number of female and male records; when this happened, we reported it as 'male' in the main analysis. We conducted a counter-analysis changing this to 'female', and our results were insensitive to this choice.

As the characteristic-based control was determined by age (under 13-year-olds), all call-outs having missing age were removed. A small number of call-outs in this control group were identified by the algorithm as being alcohol-related (and therefore fell into both the control and intervention categories); these records were removed from the analysis. As these overlapping observations were uniformly distributed pre- and post-MUP introduction, this was unlikely to have any significant impact upon our results (Table 1).

TABLE 1 Number of alcohol-related and control (aged under 13 years) call-outs by demographics, 15 December 2017–15 March 2020.

No. of call-outs	Alcohol (%) 190 177		Under 13 (%) 58 919	
Socio-economic deprivation quintiles				
1 (most deprived)	66 399	(35.2%)	17 360	(30.0%)
2	47 436	(25.1%)	12 866	(22.3%)
3	35 108	(18.6%)	10 814	(18.7%)
4	24 337	(12.9%)	9268	(16.0%)
5 (least deprived)	15 577	(8.2%)	7504	(13.0%)
Missing	1320		1107	
Sex				
Female	69 788	(37.9%)	22 010	(42.5%)
Male	11 4318	(62.1%)	29 776	(57.5%)
Missing	6071		7133	
Age (years)				
13–25	28 966	(15.7%)	–	
26–45	52 831	(28.6%)	–	
46–65	59 010	(32.0%)	–	
> 65	43 771	(23.7%)	–	
Missing	5599	(3.0%)	–	
Sample size after removing call-outs with missing age	180 355		58 919	
Sample size after removing aged under 13 classified as alcohol	174 756		53 320	

Statistical analysis

We fitted a Seasonal Autoregressive Moving Average (SARIMA) model, able to account for autocorrelation, seasonality and underlying temporal trend. Our main model analysed the potential for a linear change in both level and slope at the point of intervention. We based this upon a potential hypothesis of a gradual effect (in case there was one), which was then tested with information criteria [Akaike information criterion (AIC) and Bayesian information criterion (BIC) statistics] of separate models. We used daily units of time. While a daily series may present challenges (e.g. double seasonality, both weekly and yearly), aggregation to weekly or monthly data points would have significantly reduced the statistical power of the analysis, due to the restricted size of the original data set following truncation for changes in reporting and the impact of the pandemic.

Daily data allowed us to control for potential time-varying confounders such as weather, which is a factor likely to have a role in alcohol consumption [20]. We had only rainfall available, and as we were assessing the overall weather for Scotland, which has sensitive differences within its territory to have a single national figure, we averaged the daily mm of rainfall in different districts with data from the Scottish Environment Protection Agency (www.sepa.org.uk). We used this as a proxy of national weather conditions. Other variables included in the model were bank holidays, months, New Year's Eve, other ambulance call-outs (any call-out different than alcohol-related or aged under 13 years) and Old Firm football matches. Old Firm matches are games between the two main football teams in Glasgow (Celtic and Rangers); such events have been associated with reports of domestic abuse potentially related to alcohol consumption and misuse [21]. We included this as a covariate, as the metro area population of Glasgow is almost a third of the Scottish population.

To reduce the skewness of our original data, we log-transformed our dependent variable. An advantage of the log transformation is that coefficients in the regression model can be interpreted as a percentage variation of the series. Our seasonal component was weekly, considering the excess in alcohol-related call-outs during weekends (almost 40% occurred on Saturday or Sunday [14]); for monthly adjustments, we inserted a categorical variable for months into our model, excess in specific days. Details of the SARIMA equation and model are reported in the Supporting information.

We performed the same analysis for our characteristic-based control outcome. We then tested for common parallel assumption by regressing the difference between series over time in the pre-intervention period [22]. After verifying the parallel trend, we ran a separate analysis on the difference between control and intervention series which, by incorporating the control into the same model as the intervention analysis, can be interpreted as a difference in difference estimator. Finally, we performed the same analysis for night-time call-outs (8 p.m. to 6 a.m.), as it was the time of the day with the highest concentration of alcohol-related call-outs [14]. All analyses were conducted using Stata version 17 [23]. This analysis was not pre-registered, and results should be considered exploratory.

Subgroup and sensitivity analyses

Subgroup analysis on different socio-economic deprivation quintiles [17], age groups (13–25, 26–45, 46–65 and > 65 years) and sex was performed on the intervention series.

Alternative modelling strategies using panel data and regressions with Newey–West standard errors based on Scottish districts were also employed, using district level covariates (e.g. rainfall levels). However, several areas with zero events over multiple dates and the consequent potential floor effects made SARIMA models on overall Scotland preferred for baseline analysis. We also ran models with weekly data; however, due to limited data points in the pre-intervention period and potential power issues, we used these as sensitivity analyses. In a further sensitivity analysis, to use all the available information prior to lockdown restrictions (May 2015–March 2020), allowing for a longer pre-intervention period, we employed a cubic spline model [24] to mitigate the fluctuation in call-outs given by changes in the recording system. Falsification tests 6 and 12 months after the intervention date were performed.

RESULTS

Alcohol-related call-outs follow a seasonal pattern with peaks at weekends and large peaks on New Year's Eve (Figure 1). In contrast, call-outs for under 13-year-olds have little variation during the week but follow more of a monthly seasonality, with an increase from September to December followed by a gradual decrease over the year (Figure 1). The overall distribution of sex and socio-economic deprivation was similar in the two groups (Table 1). Of the alcohol-related call-outs, 2.9% were also identified as aged under 13; these records were removed from the analysis (Table 1).

While the mean number of daily alcohol-related call-outs before MUP implemented was 194.3 [standard deviation (SD) = 51.0] and after implementation was 216.3 (SD = 52.4), a relative increase of 11.3%, the inferential analysis, considering seasonal and temporal trends, found that the implementation of MUP was not associated with a significant change in daily alcohol-related call-outs [step change, interpretable as an instant change in correspondence to the intervention = 0.062, 95% confidence interval (CI) = −0.012, 0.0135; slope change, the daily gradual change after intervention = −0.001, 95% CI = −0.001, 0.0001] (Table 2). For the control group, the mean number before MUP implementation was 68.4 (SD = 10.8) and 72.3 after (SD = 16.2), a 5.7% growth, with the inferential analysis also finding no significant step change.

Similarly, the difference between the intervention and control group did not show a significant result (step change = −0.010, 95% CI = −0.317, 0.298, slope change = −0.003, 95% CI = −0.008, 0.0001). There were no significant results when the analysis was restricted to alcohol-related call-outs at night-time only. In all the analyses on total and night-time alcohol-related call-outs, the slope change tended to be of the same size but in the opposite direction of the overall trend in the model, meaning that the volume of call-outs remained stable.

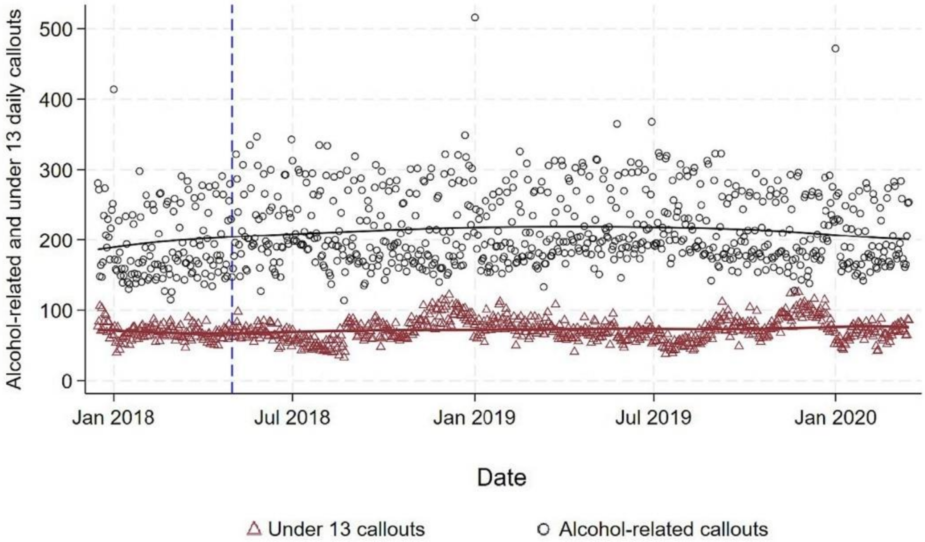

FIGURE 1 Time–series of daily alcohol-related and age under 13 years call-outs. The dashed blue line is in correspondence of the minimum unit pricing implementation date. Solid lines are local linear smooth plots of alcohol-related (black) and age under 13 years (maroon) call-outs.

Subgroup and sensitivity analyses

We found no evidence of a significant decrease in alcohol-related call-outs associated with MUP for any of the subgroups examined (different age groups, sex or call-outs to locations with different levels of deprivation). These findings are presented in the Supporting information. Where there were statistically significant changes, these happened only for measures at mid ranks of a category (e.g. variations in third and fourth socio-economic deprived quintiles, but not in the least or most deprived groups), we believe these probably arise from daily spurious variations. Similarly, significant step changes (in female patients, call-out locations in the most deprived quintile and those aged 46–65 years) on the day of the implementation of MUP are more likely to represent spurious noise in the data rather than attributable to an instant effect on the first day of MUP.

Falsification tests for total alcohol-related call-outs produced significant change in slope and trend when the intervention point was set at 6 months after the introduction of MUP and a significant change in slope, trend and overall underlying trend when set at 12 months after (Table 2). In contrast, falsification tests for the control and the difference between series were not significant. Regarding the night-time analysis, both 6- and 12-month falsification tests in the uncontrolled intervention series had significant results for overall trend and slope change. In the difference between series, only the falsification test postponing the intervention by 6 months had significant coefficients for step change (−0.143, 95% CI = −0.2635, −0.0223), slope change (−0.001, 95% CI = −0.001, 0.0001) and overall trend (0.001, 95% CI = 0.0002, 0.0012) with an expected gradual effect at the end of follow-up equal to a 35% decrease. Given the different sign on the change in slope coefficient in the 12-month falsification test, a probable explanation could be that this is a spurious effect rather than a lagged gradual effect of the policy.

Alternative models such as Newey–West with heteroskedastic and autocorrelated errors did not show significant results in both uncontrolled ITS and in the difference between the series (Supporting information). Similarly, the analysis on weekly data provided similar results to the main analysis, showing null effect of the policy across all uncontrolled and controlled series. All these analyses had non-significant coefficients of overall and post-intervention trends, but of the same extent and opposite sign, mirroring the baseline models (Supporting information). The sensitivity analysis using cubic spline on weekly data, but starting from May 2015 showed no significant results; however, it highlighted how the excessive increase in the outcome after the change in the recording system (December 2017) is greater than expected, and would have potentially added bias into our estimates (for the visual inspection of the spline and the visual effect of the change in system in the series, see Supporting information).

DISCUSSION

We did not find associations between MUP implementation and variations in the daily volume of alcohol-related call-outs. There was also no evidence of significant variations in subpopulations and, in particular, among different socio-economic groups (relevant subanalyses to assess the MUP effects on health inequality).

There could have been several reasons explaining our null findings; here, we discuss three reasons. First, many alcohol-related ambulance call-outs are generated by alcohol consumption during

TABLE 2 Regression outputs of logarithm of alcohol-related call-outs (aged under 13 years of age call-outs and difference between the two series).

	Main analysis				Falsification test 6 months				Falsification test 12 months			
Coefficient		*P*-value	95% CI		Coefficient	*P*-value	95% CI		Coefficient	*P*-value	95% CI	
Alcohol, overall												
Step change	0.062	0.091	−0.012	0.1354	0.011	0.694	−0.042	0.063	−0.067	0.009	−0.116	−0.017
Slope change	−0.001	0.138	−0.001	0.1×10^{-5}	−0.001	0.000	0.2×10^{-3}	0.001	-0.4×10^{-3}	0.005	−0.001	-0.1×10^{-3}
Overall trend	0.001	0.136	-0.1×10^{-5}	0.001	0.4×10^{-3}	0.000	0.2×10^{-3}	0.001	0.3×10^{-3}	<0.001	0.2×10^{-3}	0.4×10^{-3}
U13, overall												
Step change	0.006	0.949	−0.192	0.205	0.027	0.754	−0.145	0.200	−0.029	0.724	−0.192	0.133
Slope change	−0.001	0.513	−0.003	0.002	-0.3×10^{-3}	0.430	−0.001	0.001	-0.3×10^{-3}	0.533	−0.001	0.001
Overall trend	0.001	0.515	−0.001	0.003	0.2×10^{-3}	0.551	−0.001	0.001	0.2×10^{-3}	0.261	-0.1×10^{-3}	0.001
Difference, overall												
Step change	−0.01	0.951	−0.317	0.298	−0.074	0.584	−0.340	0.191	−0.084	0.208	−0.214	0.047
Slope change	−0.003	0.257	−0.008	0.002	−0.001	0.504	−0.004	0.002	−0.001	0.516	−0.004	0.002
Overall trend	0.003	0.252	−0.002	0.007	0.001	0.430	−0.001	0.003	0.001	0.421	-0.1×10^{-4}	0.002
Alcohol, night-time												
Step change	0.056	0.338	−0.059	0.171	−0.039	0.472	−0.145	0.067	0.004	0.917	0.077	0.086
Slope change	−0.001	0.054	−0.002	0.1×10^{-5}	−0.001	0.000	−0.001	-0.4×10^{-3}	−0.001	0.001	−0.001	-0.3×10^{-3}
Overall trend	0.001	0.074	-0.1×10^{-5}	0.002	0.001	0.001	0.3×10^{-3}	0.001	0.3×10^{-3}	0.006	-0.9×10^{-4}	0.001
U13 night-time												
Step change	0.022	0.846	−0.205	0.247	0.108	0.180	−0.05	0.267	−0.017	0.848	−0.187	0.154
Slope change	-0.4×10^{-3}	0.719	−0.003	0.002	-0.5×10^{-4}	0.855	−0.001	0.001	-0.4×10^{-3}	0.395	−0.001	0.4×10^{-3}
Overall trend	0.001	0.688	−0.002	0.003	-0.1×10^{-4}	0.909	−0.001	0.001	0.2×10^{-3}	0.118	-0.6×10^{-3}	0.5×10^{-3}
Difference, night-time												
Step change	0.123	0.138	−0.040	0.285	−0.143	0.020	−0.264	−0.022	−0.107	0.113	−0.240	0.025
Slope change	0.0004	0.638	−0.001	0.002	−0.001	0.009	−0.001	-0.2×10^{-3}	0.12×10^{-3}	0.422	-0.4×10^{-3}	0.001
Overall trend	−0.001	0.523	−0.002	0.001	0.001	0.010	0.2×10^{-3}	0.001	0.1×10^{-3}	0.687	-0.1×10^{-3}	0.3×10^{-3}

Abbreviation: CI = confidence interval.

weekends and night-times [14], much of which takes place in licensed premises (bars, clubs), and MUP does not affect the price of alcohol sold in such premises. We found a potential lagged effect of MUP in a decrease in alcohol-related call-outs at night-time after 6 months, but we believe that this was most probably a spurious finding, as it was not supported by any theory of change *ex-ante* (see below).

Secondly, the types of drinking or individuals that generate alcohol-related ambulance call-outs may not be as price-elastic as other alcohol consumption. This may be caused by the extent of the policy (£0.50) that could have been too low to affect acute outcomes, which constitute a relevant part of ambulance call-outs. This would be in line with other studies showing null or controversial associations between MUP and acute outcomes (e.g. road traffic accidents [25] and hospitalizations [11]). Understanding what percentage of alcohol-related ambulance call-outs are linked to off-trade versus on-trade consumption and to single-occasion versus dependent drinking would help to unpick what happened. Such data are not available in Scotland, although there have been initiatives in emergency departments to identify where people were drinking prior to an alcohol-related visit [26]. Finally, the overall reduction in consumption due to MUP may have been generated by small reductions by a large population of drinkers. This is supported by an overall reduction in consumption (3% after 3 years [8]), but with limited evidence on alcohol-addicted [27] and harmful drinkers [28]. While this would have long-term benefits in terms of reduced alcohol-related disease (e.g. alcoholic liver disease, as already shown in midterm evaluations [11]), which would be expected to reduce pressure on the health service, it would have minor effects on our outcome measure in this study, which is more focused upon acute harm.

The significant increasing trends in alcohol call-outs in a few of the subgroups may have appeared because our analysis started in December and included only a few months (not an entire year) before MUP implementation. Therefore, a short pre-intervention period could limit the analysis trend, which shows higher variability (standard deviations) after MUP implementation for both series. This could explain why the effect of the underlying trend is always offset by the slope change, which describes a flat curve after MUP. We found several step changes in our subgroup analyses as well as in some falsification tests; however, it is worth noting that we used daily data that are subjected to more noise due to the high level of granularity. To avoid misleading conclusions, we focused more upon significant changes in slope (which imply a continuous change over time from the intervention) rather than on step changes. When falsification tests provided significant results in the overall uncontrolled alcohol-related series, we found no evidence of effect in the series of the differences and similar results (but not statistically significant) in the control (aged under 13 years) series. The lack of significance may be due to power issues, as the number of under 13-year-old call-outs was lower than the number of alcohol-related ones. Therefore, we would not force the interpretation of the significance of our falsification tests as a delayed effect of the policy. In contrast, in night-time call-outs we found a significant decrease in falsification tests after 6 months, both in the uncontrolled series and in the series of the difference. While this could be interpreted as a lagged effect of the policy, the 12-month falsification test found a non-significant increase suggesting that such results were probably due to daily noise or the use of a suboptimal control group, rather than lagged effect of the policy.

We believe that our study provides a valuable contribution to evaluating the impact of MUP in Scotland by focusing on its impact on alcohol-related ambulance call-outs; that is, on an acute and critical frontline emergency service. The use of a reliable measure of alcohol-related ambulance call-outs throughout the whole of Scotland is a strength, although our study also has several limitations. Most importantly, the power of the study was limited by the short pre-intervention period due to the change in the recording system and the consequent use of daily data that we explained extensively earlier. ITS using daily data can detect quick and instant variations; however, they may have more challenges in detecting persistent long-term effects. Therefore, our results are more robust regarding short-term daily variations, and may be less definitive and affected by more uncertainty for inference of long-term repercussion of the policy. This could be ascribed as the main limitation of our study, as policymakers may be more alert to long-term implications. However, despite the lower power, our analyses on weekly series (more likely to effectively model cyclical patterns) showed similar results. Other potential limitations are related to our control group. We found different seasonal patterns between the intervention and control series [alcohol-related call-outs followed weekly fluctuations, while under 13-year-old call-outs had a yearly seasonality (Figure 1)]. In addition, certain covariates (e.g. weather) affected the two series differently, suggesting that the two populations were intrinsically different. However, we controlled for weather and we believe that this was the best control available to us, as a location-based controls such as that used in similar analyses on MUP in Scotland [7,9] would have been difficult. For instance, there are multiple ambulance trusts in the rest of the United Kingdom, and none have embedded a reliable marker for identifying that call-outs are alcohol-related [29]. In addition, while there could be theoretical concerns, our control satisfied statistical tests for parallel trend assumption in both daily and weekly models. While not ideal, our characteristic-based control accounted for local variations such as weather, specific bank holidays, features within ambulance service such as changes in ambulance service provision and the National Health Service (NHS) funding environment.

CONCLUSIONS

Minimum unit pricing for alcohol set at a rate of £0.50 per UK unit of alcohol and implemented in Scotland in May 2018 was not associated with changes in the volume of alcohol-related ambulance call-outs. Further, no reduction in such call-outs was associated with MUP for any subgroups analysed, including different sexes, ages or the level of deprivation of the call-out location. The limited impact of MUP upon dependent drinkers and on prices in bars/clubs most probably explains these findings.

AUTHOR CONTRIBUTIONS

Francesco Manca: Conceptualization (supporting); formal analysis (lead); methodology (lead); visualization (lead); writing—original draft (lead); writing—review and editing (equal). **Jim Lewsey:** Conceptualization (equal); funding acquisition (equal); methodology (equal); supervision (lead); writing—review and editing (lead). **Daniel Mackay:** Conceptualization (equal); formal analysis (supporting); funding acquisition (equal); methodology (supporting); supervision (supporting); validation (lead); writing—review and editing (equal). **Colin Robert Angus:** Conceptualization (equal); funding acquisition (equal); supervision (equal); visualization (supporting); writing—review and editing (equal). **David Fitzpatrick:** Conceptualization (equal); funding acquisition (equal); writing—review and editing (equal). **Niamh Fitzgerald:** Conceptualization (lead); funding acquisition (lead); supervision (equal); writing—review and editing (lead).

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DECLARATION OF INTERESTS

All authors have nothing to declare with respect to any current or potential interest or conflict in relation to this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study were obtained from SAS. Restrictions apply to the availability of these data, which were used under license for this study.

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SUPPORTING INFORMATION

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

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RESEARCH REPORT

ADDICTION SSA

Evaluating the impact of minimum unit pricing for alcohol on road traffic accidents in Scotland after 20 months: An interrupted time series study

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Abstract

Background and aims: On 1 May 2018, Scotland implemented Minimum Unit Pricing (MUP) of £0.50 per unit of alcohol with the aim to lower alcohol consumption and related harms, and reduce health inequalities. We measured the impact of MUP on the most likely categories of road traffic accidents (RTAs) to be affected by drink-driving episodes (fatal and nighttime) up to 20 months after the policy implementation. Further, we checked whether any association varied by level of socio-economic deprivation.

Methods: An interrupted time series design was used to evaluate the impact of MUP on fatal and nighttime RTAs in Scotland and any effect modification across socio-economic deprivation groups. RTAs in England and Wales (E&W) were used as a comparator. Covariates representing severe weather events, bank holidays, seasonal and underlying trends were adjusted for.

Results: In Scotland, MUP implementation was associated with 40.5% (95% confidence interval: 15.5%, 65.4%) and 11.4% (−1.1%, 24.0%) increases in fatal and nighttime RTAs, respectively. There was no evidence of differential impacts of MUP by level of socio-economic deprivation. While we found a substantial increase in fatal RTAs associated with MUP, null effects observed in nighttime RTAs and high uncertainty in sensitivity analyses suggest caution be applied before attributing causation to this association.

Conclusion: There is no evidence of an association between the introduction of minimum unit pricing for alcohol in Scotland and a reduction in fatal and nighttime road traffic accidents, these being outcome measure categories that are proxies of outcomes that directly relate alcohol consumption to road traffic accidents.

KEYWORDS
alcohol, interrupted time series, natural experiment, minimum unit price, road traffic accidents, Scotland

Francesco Manca and Rakshita Parab are both first authors.

INTRODUCTION

Alcohol-related harm is high in the United Kingdom (UK), with alcohol being the fifth largest risk factor for deaths and ill-health across all ages [1]. Within the UK, in 2020, Scotland had the highest alcohol-specific death rate of the constituent countries—21.5 per 100 000 persons, compared to 19.6, 13.9 and 13.0 in Northern Ireland, Wales and England, respectively [2].

Following a package of other measures aimed at reducing alcohol consumption and subsequent harm in Scotland, the Scottish Government implemented a minimum unit price for alcohol (MUP) on 1 May 2018 [3]. MUP in Scotland sets a floor price of £0.50 per unit of alcohol (one unit = 8 g or 10 mL of ethanol), below which it cannot be legally sold. As well as reducing overall harms, the aim of MUP is to reduce inequalities by targeting sales of cheap and high-strength alcohol products mainly purchased by the most socio-economically disadvantaged groups (who have the highest levels of alcohol-related harms) [4–6]. Scotland was the first country to implement nationally a homogeneous MUP for alcohol volume in beverages. Therefore, evaluations of MUP in Scotland for a range of outcomes have international relevance.

Evidence on the effectiveness of MUP in Scotland is starting to emerge. It has been shown that MUP implementation was associated with a reduction in alcohol sales per adult of 3% [7] after 3 years and with a decline in deaths wholly attributable to alcohol consumption after 32 months [8]. However, MUP was not associated with changes in alcohol-related emergency department visits [9] nor alcohol-related crimes [10] or medical prescriptions for alcohol dependence [11].

It is well established that alcohol use is associated with road traffic accidents (RTAs), with a dose–response relationship between fatal injury and blood alcohol concentration [12]. Further, alcohol consumption by pedestrians is a significant factor in a subset of RTAs that do not involve drink-driving. However, there is only a small evidence base on how minimum alcohol prices are associated with RTAs. A Canadian study [13] observed that increases in provincial minimum alcohol prices were associated with reductions in alcohol-related traffic violations (but not in non-alcohol-related traffic violations). In 2020, a regional report from the Northern Territory of Australia regarding the implementation of MUP at a different extent to that used in Scotland ($1.30 per 'standard drink', which is equal to £0.75 per UK unit -currency conversion in July 2022) reported a significant instant reduction in the level of alcohol-related RTAs resulting in injury or fatality [14]. In 2021, a study investigating the effect of MUP on RTAs in Scotland [15] found a reduction of 0.28 to 0.35 fewer daily motor vehicle collisions per million inhabitants (an important reduction considering an average of 3.23 RTAs per million across the study period). This study (as well as Coomber *et al.*) [14] has short post-intervention periods (8 months). However, it is plausible that MUP's indirect effects on alcohol-related harms have different-size lagged impacts, which take longer follow-up periods to emerge as previously shown for other outcomes and contexts [16, 17]. Further, any differential effects across levels of socio-economic deprivation (an aim of MUP policy in Scotland) were not considered. More recently, another evaluation on severe and alcohol-related RTAs with a longer post-intervention period (20 months) found a non-significant 8% increase in fatal RTAs after the policy implementation [18].

This paper aims to evaluate whether the introduction of MUP in Scotland was associated with any change in the level of RTAs most likely to be affected by drink-driving episodes (fatal and night-time) in the first 20 months after implementation. Further, we evaluated whether any association varied by level of socio-economic deprivation.

METHODS

Design

We used an interrupted time series (ITS) design to establish whether MUP implementation in Scotland was associated with a variation in the level of RTAs most likely to be alcohol-related. Where possible, ITS designs formally use a control group to reduce potential bias because of time-varying confounding. However, a suitable control group should be exposed to common events that potentially influence the intervention series and, at the same time, it should not be exposed to other events that could influence the control series only [19]. Different pre-intervention trends may underline potential different time-varying confounders between the two series, identifying an inappropriate control (i.e. violating the so-called parallel trends assumption). Therefore, we included the comparator in the model only when the parallel trends assumption was satisfied and we limited the analysis to a comparison between the series, focusing on uncontrolled ITS results when it was not. In addition, to provide a controlled result on outcomes not satisfying the parallel trend assumption, we built an 'artificial' counterfactual with the prediction of the series built on the pre-MUP period and then we estimated the policy effect with the difference between the predicted and actual values.

Outcomes

We used as primary outcomes weekly fatal and night-time (from 6 PM to 6 AM) RTAs. These are RTAs subcategories likely to be alcohol-related according to official UK Government figures [20]. For all analyses, we used the corresponding data for England and Wales (E&W) as a geographical comparator group. We assessed the impact of the legislation also on the total number of total weekly RTAs (secondary outcome) to facilitate comparison with previous studies [15]. Regarding night-time and total RTAs, analyses were repeated for two socio-economic deprivation groups: the most deprived 10th and the rest of the population, as measured by either the Scottish Index of Multiple Deprivation (SIMD) (Scotland) [21] or Index of Multiple Deprivation (IMD) (E&W) [22]. We did not run the same analysis for fatal as the number of observations was too low given the level of granularity of the subcategories.

For the two main outcomes, we also repeated the analysis of the number of RTAs per 100 000 residents. This would potentially control for differences in level of road traffic and the number of cars in the two constituencies. However, the number of residents is yearly estimates only approximating the true number of inhabitants that can vary within years, with the number of inhabitants itself only being a proxy of numbers of road users, so we presented both analyses.

Data

To assess the effect of a policy regarding alcohol pricing on RTAs, data on failed breath tests and drink-driving episodes would comprise an ideal outcome, however, such data has numerous difficulties. For instance, the accuracy of drink-driving data strictly depends on breath tests for non-fatal accidents and from coroner reports for fatal accidents. However, toxicology data coming from coroners are usually accessible only for 60% of the cases [20], producing high sampling uncertainty around official drink-driving estimates. Therefore, because drink-driving outcomes have these methodological uncertainties, we used data on certain categories of RTAs more likely to be alcohol-related. Data on RTAs and casualties in the United Kingdom were obtained from the Road Safety Statistics Division at the UK Department for Transport [23]. The routine dataset (STATS19) contains all personal injury accidents on public roads reported to the police [24]. In the dataset, every accident was recorded with the level of severity, date and time and with the number of casualties. The casualties dataset contained a variable on the IMD for RTAs recorded in England or Wales only. For Scotland RTAs, we used the postcode of the casualties to obtain SIMD for each casualty. Whenever RTAs involved more than one person, the lowest socio-economic deprivation level was used for analysis. Alternative analyses using the highest level of deprivation were also run. The data covers the period 1 January 2016 to 31 December 2019, providing 28 months (121 weeks) before the intervention and 20 months (87 weeks) after; to the best of our knowledge, there was no change in the data collection process during the study period. As most other MUP evaluations [9, 11, 25], we preferred to remove the period of the coronavirus disease 2019 lockdown as it was likely to affect the outcomes. Specifically, road traffic limitations and general movement restrictions had a major effect on RTAs. Moreover, as restrictions were different between Scotland, England and Wales, including such period would have added bias to the analysis.

Statistical analysis

We used weeks as level of data aggregation to remove daily 'noise' and multiple seasonalities (weekly and yearly) for easier detection of the trend component of the series. We first ran a descriptive analysis to assess the general trend and patterning of weekly RTAs over time and to detect any outliers. We, then, used Seasonal Autoregressive Integrated Moving Average models (SARIMA) for inferential analyses. To reduce the impact of outliers and remove exponential variance and for ease of comparison with other studies, the outcome variable was log-transformed. With log-transformed series, the coefficient of independent variables in the SARIMA models can be approximately interpreted as the percentage variation in the level of RTAs. The effect of MUP was assessed by introducing a binary variable in the SARIMA model, assuming a value of 0 before the week the policy was introduced and 1 after. An underlying pre-intervention deterministic trend variable [26] considering the time elapsed since the start of the study was used as a model covariate. Alternative models with both a change in level and trend were analysed, but based on information criteria, models including a change in level only were selected for the analysis. Different SARIMA models were assessed using a correlogram of the series and after model estimation assessment of white noise of the residuals using portmanteau test [26]. The best fitting model was then selected based on information criteria, Models were further adjusted for weeks with severe weather events (collected by the Met Office for the United Kingdom) [27] and weeks with bank holidays.

For the two main outcomes, we evaluated the intervention effect in three ways. We first assessed the MUP coefficients in the uncontrolled series and compared them in the two constituencies. Second, for the outcomes satisfying the parallel trends assumption, we considered models of the difference between the series, log (RTAs in Scotland)-log (RTAs in E&W), as the outcome (these models would produce a difference-in-differences type estimate directly accounting for the comparator [28]). Last, we used the forecast built on SARIMA models on the pre-MUP Scottish series as counterfactual and used the difference between the predicted and actual series as estimates for the policy effect [29].

Fatal RTAs had low weekly numbers in both Scotland and E&W. In particular, in Scotland, several weeks had zero records. Therefore, a commonly used $\log(x + 1)$ transformation was applied to the series. However, it has been recently shown that results based on this transformation may provide biased estimates [30], therefore, alternative sensitivity analyses were used to address this (as described below). Regarding socio-economic deprivation groups for E&W, there was a substantial difference in the average amount of weekly missing data in the period before (n = 326) and after MUP (n = 161) implementation (Table 1). This led to an artificial increase in the number of the E&W series analysing socio-economic deprivation, whereas, overall, the number of RTAs decreased overtime (Figure 1). This missingness in the socio-economic deprivation data for the E&W series would limit the meaning of the inferential analyses and results on such series are reported only in Supporting Information for completeness. In contrast, missing data on the level of deprivation in Scotland were similarly distributed between pre- and post-intervention periods, providing more reliable results.

To compare our findings with previous evidence on the effect of MUP on RTAs [15], we reproduced our analysis on total RTAs, using both the full length of our series and also a shorter post-intervention period ending in December 2018 mirroring the previous study. In this analysis, we started our time series in 2016 and 2018 using both weekly and daily time units. For all analyses Stata17 [31] software was used.

Sensitivity analysis

Two alternative analyses for RTAs concerning fatalities were considered to account for an excess of zeros and a general low number of events. Specifically, a different transformation with inverse hyperbolic sine transformation (IHS) with small-sample bias correction [30] and a generalized linear model (negative binomial) were used and compared with the main analysis. Data on RTAs in most socio-economic deprived decile during night times in Scotland contained only 3 zeros in the series, and we used the same alternative sensitivity analyses for this category for completeness. To further validate the analysis, falsification tests anticipating and delaying the intervention by 6 and 12 months were performed.

The planned analyses were not preregistered and results should be considered exploratory.

RESULTS

The average weekly number of RTAs before and after MUP implementation is shown in Table 1 in both Scotland and E&W. The weekly number of RTAs in Scotland and E&W per 100 000 inhabitants between 1 January 2016 and 31 December 2019 is shown in Figure 1. The level of weekly RTA was consistently higher in the period before MUP in both intervention and the comparator for both night-time and total RTAs, but not for fatal RTAs (Table 1). Nevertheless, a declining trend can be identified within both pre- and post-MUP periods for both intervention and the comparator (Figure 1). Again, although this tendency is common to most of the subcategories, for fatal RTAs there was an increasing trend over time in Scotland: +0.7 pre- and +0.5 post-MUP (rise of 20% and 15%, respectively). For E&W, the pattern of the differences was less distinct within the two periods.

The introduction of MUP was associated with a significant increase in fatal RTAs of 40.5% (95% CI = 18.3%–62.7%) and a statistical non-significant rise in night-time RTAs of 11% (95% CI = −1.1% to 24.0%) (Figure 2, full model outputs presented in Supporting Information). For the corresponding period, in E&W there was a statistical non-significant increase in both categories. There was also no statistically significant association between the overall level of RTAs and the introduction of MUP in Scotland for the most socio-economically deprived 10th and for the second to 10th deprived 10th groups. The underlying trend was negative in all the models indicating a decreasing pattern of all series over time, and it was always statistically significant, except for the model regarding fatal RTA in E&W (see Supporting Information). Because the difference in the log of fatal RTAs between the two intervention groups was the only series satisfying common trend requirements (see Supporting Information), we performed the analysis on the difference for this group only. This analysis detected a positive increase in fatal RTAs after MUP introduction (Table 2). The MUP estimates based on the prediction of the pre-MUP period detected a statistically significant effect in the fatal RTAs series (3.5%, CI = 2.6%–4.3%) and statistically non-significant in night-time RTAs (2.9%, CI = −2.3% to 8%). Overall, models on the RTAs per 100 000 inhabitants have the same direction of association.

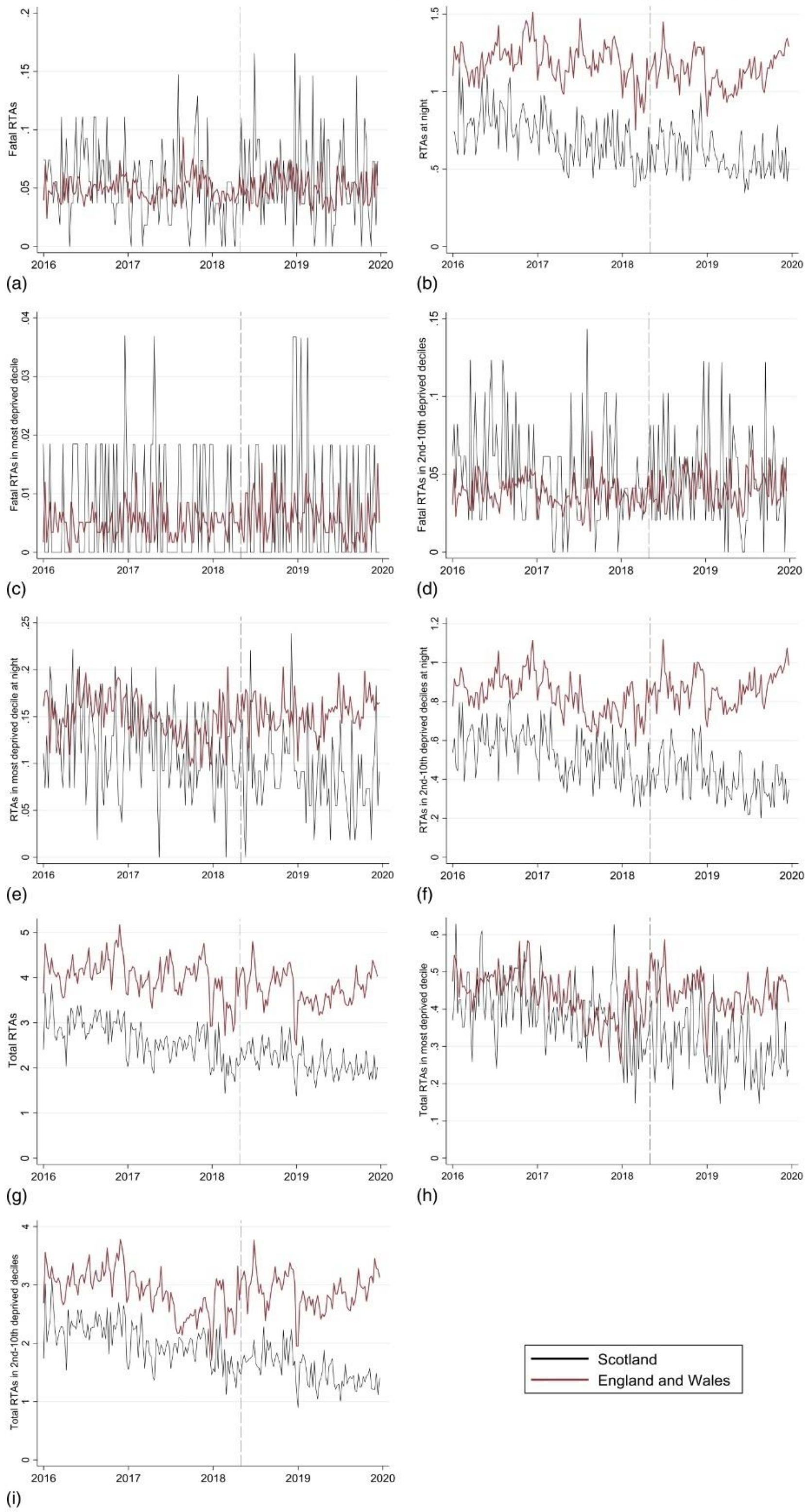
By reproducing a similar analysis to [15] on the total number of RTAs with 8 months post-intervention follow-up and using weekly time units, Scotland was associated with a significant relative increase in total RTAs of ∼10%, with a corresponding increase of 5.8% in E&W. When we used daily time units, the series had parallel trends only if we started and ended the analysis in 2018 (like in Vandoros *et al.*) [15], but

TABLE 1 Average weekly number of RTAs in Scotland and England and Wales before and after MUP implementation.

	Scotland			England and Wales		
	Pre-MUP, 1 January 2016–30 April 2018	Post MUP, 1 May 2018–31 December 2019	Year on year difference	Pre-MUP, 1 January 2016–30 April 2018	Post MUP, 1 May 2018–31 December 2019	Year on year difference
Total RTAs	143.85 (23.9)	117.28 (16.7)	−26.5 (−18%)	2365.26 (247.7)	2227.2 (223.7)	−138.07 (−6%)
Fatal	2.86 (1.7)	3.19 (2.1)	0.33 (+11%)	28.84 (6.0)	29.76 (7.1)	0.91 (3%)
Night-time	39.13 (9.0)	31.83 (6.9)	−7.30 (−19%)	400.45 (71.6)	674.12 (66.3)	−26.33 (−4%)
Most deprived 10th group[a]	21.33 (4.9)	16.36 (4.7)	−4.98 (−23%)	256.88 (36.8)	262.25 (28.4)	5.37 (+2%)
2nd–10th deprived group[a]	110.91 (19.4)	83.68 (16.3)	−27.23 (−25%)	1694.53 (221.6)	1717.72 (189.9)	23.19 (+1%)
Night-time most deprived 10th group[b]	6.34 (2.5)	4.89 (2.3)	1.45 (−23%)	87.26 (13.9)	91.66 (10.8)	4.4 (+5%)
Night-time 2nd–10th deprived group[b]	29.29 (6.8)	22.10 (6.1)	7.19 (−25%)	488.27 (59.4)	514.24 (52.8)	25.97 (+5%)

Note: Values in parentheses are standard deviations (1st–2nd and 4th–5th columns) or percentage variations (3rd–6th columns).
Abbreviations: MUP, minimum unit pricing; RTAs, road traffic accidents.
[a]Missing data for Scotland were 1634 (13 per week on average) pre-intervention and 1006 (12 per week on average) post intervention for Scotland. In England and Wales missing data were 39 388 (326 per week on average) pre-intervention and 14 064 post intervention (161 per week on average).
[b]Missing data for Scotland were 467 (4 per week on average) pre-intervention and 277 (2 per week on average) post intervention for Scotland. In England and Wales missing data were 15 122 (125 per week on average) pre-intervention and post intervention 5809 (68 per week on average).

FIGURE 1 Weekly road traffic accidents (RTAs) per 100 000 residents in Scotland (black) and England and Wales (maroon) between 1 January 2016 and 31 December 2019. Dash vertical line represents date of minimum unit pricing implementation. Comparison across different outcomes: (a) fatal RTAs, (b) night-time RTAs, (c) fatal RTAs in most socio-economically deprived group (lowest 10th of SIMD/IMD), (d) fatal RTAs in all other socio-economically deprived groups, (e) night-time RTAs in most deprived group, (f) night-time RTAs in all other deprived groups, (g) total RTAs, (h) total RTAs in most deprived group and (i) total RTAs in all other deprived groups.



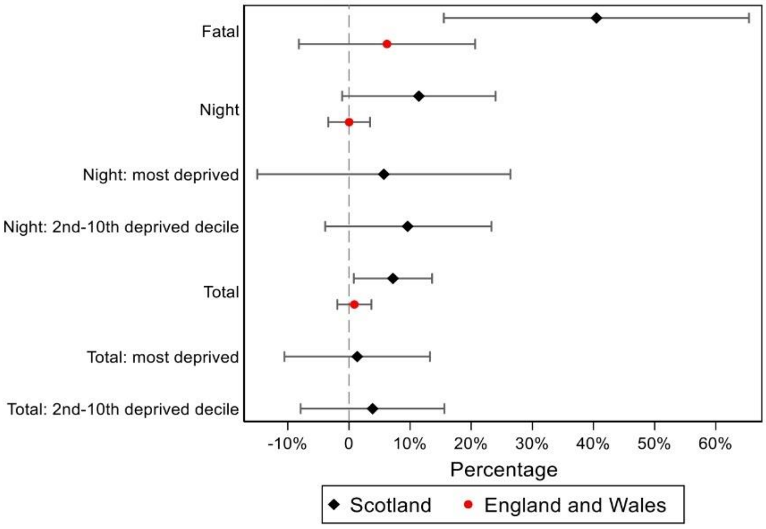


FIGURE 2 Change (%) in different categories of road traffic accidents (RTAs) associated with minimum unit pricing (MUP) implementation. Inferential results from uncontrolled series. Models regarding socio-economic deprivation groups are shown only for Scotland. England and Wales had different number of missing data per week regarding deprivation pre- and post-MUP, likely to generate biased estimates.

Bars represent 95% confidence intervals, with point estimates represented by symbols. Positive estimates represent an increase in RTAs after MUP policy implementation.

not if we started in 2016. By restricting the dataset to 2018 only and analysing the series of the difference between the groups, MUP coefficient was not statistically significant (see Supporting Information).

Sensitivity analysis

Concerning fatal RTAs, IHS transformation with small sample correction produced models with associated increases of 45% for the period after MUP implementation for Scotland and E&W, respectively. In line with these results, the negative binomial model for Scotland provided a significant increase of 53% and 9.5% in the incident rate ratio for Scotland and E&W, respectively. Although all these alternative models produced different point estimates, they did not change the positive association of fatal RTAs with MUP introduction. The only falsification test providing a statistically significant point estimate for the policy coefficient was the one delaying the intervention by 6 months for the night-time series. All others series (including fatal) had not significant estimates.

DISCUSSION

This study found that the introduction of MUP in Scotland was associated with an increase in fatal RTAs, but with no variation in the level of night-time RTAs. Additionally, we did not find differential effects of the policy on RTAs across socio-economic deprivation groups. Overall, we found no evidence that the introduction of MUP could be associated with reductions in the RTAs most likely to be alcohol-related in Scotland for the first 20 months of its implementation. This may be in contrast with the economic theory suggesting a decrease in alcohol-related RTAs as a consequence of an increase in alcohol price (that had already led to a reduction in alcohol consumption in the population) [7].

The increase in fatal RTAs could have multiple explanations, such as some qualitative evidence that MUP led people to switch from consuming strong beers and ciders to drinking spirits and getting more intoxicated [32]. Although the pattern of the Scottish series having a low number of weekly observations may have produced high uncertainty in the estimates, the alternative models taking into account potential floor effects detected a significant positive association between MUP and fatal RTAs in line with the main analysis. Last, falsification tests detecting a null effect at both 6 and 12 months after the introduction of the policy strengthen the reliability of the positive association we found between MUP and fatal RTAs. However, the relevant difference in the magnitude of the coefficients between methods (Table 2, first row, last two columns) underline the high uncertainty of our estimates regarding this series. This could be attributable to potential floor effects in the series of the difference happening only for one of the two groups (Scotland) and not for the other. As a result, we would not recommend an interpretation of the point estimates, but of the overall (positive) association consistent across all the models.

Overall, we found no difference in night-time RTAs and a transient increase in fatal RTAs. One explanation for the lack of decrease is that the floor price of £0.50 could have been too low to generate such an effect with visible repercussions on drink-driving/pedestrian road safety and then in RTAs. Moreover, the general reduction in alcohol consumption because of MUP [33] may not have sufficiently reduced consumption in those most likely to be drink-drive offenders. Further, MUP did not affect all alcohol on sale, such that prices in pubs and restaurants that typically were

TABLE 2 The effect of MUP on fatal and night-time RTAs—uncontrolled ITS, ITS on the difference between the series and difference between predicted and actual values.

		Uncontrolled ITS		ITS on the difference (Scotland–E&W)		Difference with the predicted values	
		Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
Scotland							
Fatal RTAs	Log (RTAs)	0.405	(0.183–0.627)	0.338	(0.041–0.630)	0.035	(0.027–0.043)
	Log (RTAs per 100 000 residents)	0.021	(0.008–0.034)	0.025	(0.008–0.043)	0.021	(0.012–0.030)
Night-time RTAs	Log (RTAs)	0.114	(−0.011 to 0.240)	-	-	0.029	(−0.023 to 0.080)
	Log (RTAs per 100 000 residents)	0.115	(−0.002 to 0.232)	-	-	0.036	(−0.033 to 0.106)
E&W							
Fatal RTAs	Log (RTAs)	0.074	(−0.082 to 0.206)	-	-	-	-
	Log (RTAs per 100 000 residents)	0.003	(−0.032 to 0.009)	-	-	-	-
Night-time RTAs	Log (RTAs)	0.000	(−0.034 to 0.035)	-	-	-	-
	Log (RTAs per 100 000 residents)	0.009	(−0.40 to 0.570)	-	-	-	-

Abbreviations: E&W, England and Wales; MUP, minimum unit pricing; ITS, interrupted time series; RTAs, road traffic accidents.

already above the floor price of £0.50 did not increase. Another explanation could be that even if RTAs affected by alcohol drinking were theoretically affected by MUP, the period to assess such changes in our analyses (20 months) was too short to allow certain drinking behaviours to change.

As recommended [19], we selected the comparator group based on a priori judgment to avoid potential additional bias to the study. We chose E&W based on theoretical considerations (intervention and comparator are both part of the United Kingdom and likely to have similar underlying temporal trends in RTAs) and other MUP evaluations using the same comparator [8, 15, 18, 33]. However, E&W satisfied the parallel trend assumption only for the fatal RTA outcome. Even for this group, several challenges including the differences concerning RTAs, such as casualty rates [34] between the two groups, the aforementioned concerns in the fatal RTAs data and the wide difference in point estimates between alternative controlled estimates (Table 2) suggest cautious interpretation of our results is required and we do not claim a causal effect. Indeed, when there is no suitable comparator, the interpretation of results should be cautious and limitations should be acknowledged [35] to avoid misleading causal attributions [36]. In contrast, the additional analyses we did on predictions generating a counterfactual can have causal connotations. However, the low goodness of fit (see Supporting Information) of the training pre-intervention model for the fatal series (because of low sample size and potential floor effects) suggests cautious interpretations for these analyses as well. At the same time, there are minor concerns on causal connotations for the night-time outcome.

Additionally, national statistics for Great Britain [20] show a sharper decrease in drink-driving accidents than in all other RTAs, suggesting that some environmental or behavioural factors in the population may act as confounders in both intervention and control areas by generating this RTAs reduction over time. In this scenario, our analysis already identifying an overall decreasing trend for night-time and total RTAs, but an increasing coefficient of MUP, may indicate a variation of this pattern, such as a deceleration of a decrease in RTAs.

Previous evidence

Regarding our main outcomes, Francesconi *et al.* [18] inquiring about fatal RTAs in Scotland after MUP found a statistically non-significant increase of 8% in this outcome. The study used both difference-in-difference and synthetic control methods using E&W and a selection of E&W local authorities as comparators, respectively. The authors preferred synthetic analysis as a few pre-intervention outcomes with potential explanatory power were different between the two groups; this could also explain our challenges in using E&W as a comparator.

On the total number of RTAs, our results contrast with those already published [15]. In the previous evaluation of MUP in Scotland on RTAs [15], the authors, using a difference-in-difference design, found that total RTAs increased in 2018 and by showing that Scotland had lower growth than E&W, associated this relative decrease to

MUP. Using a longer time frame (adding 2 years before intervention and one after), weekly data, a different study design and accounting for underlying trends, we found an increase in total RTAs from our inferential models after MUP. When we ran the analysis only in 2018 with daily data to emulate the previous evaluation, we found evidence of parallel trends, but not a significant MUP effect (still, our results are likely to differ because of different covariate adjustments). However, we did not find evidence of parallel trends, when we extended the pre-intervention period using daily data from 2016. This suggested that the pre-intervention period was not long enough to establish a robust parallel trend assumption and that the two constituencies had some essential differences [34]. The consequences of this are that in Stockwell *et al.* [16] the results were that the effect of MUP implementation may have generated 1.52 to 1.90 fewer daily collisions in Scotland, which, based on our weekly figures (Table 1), is a decrease of 7.4% to 9.2% (a substantial effect considering that overall MUP was associated with a 3.5% reduction in overall alcohol consumption) [33]. We believe that by analysing a longer pre- and post-intervention period and considering seasonality and autoregressive components, we have provided a more robust analysis, especially for medium-term effects. Other studies [17], focusing on emergency department visits rather than on RTAs, showed that raising minimum alcohol pricing in Saskatchewan, Canada was associated with a lagged decrease in motor vehicle-collision-related ED visits only for women over 25 years old. The authors reported that their main hypothesis of a reduction in vehicle-collision-related emergency department visits because of a raise in minimum alcohol pricing was not substantiated by their findings.

CONCLUSION

After 20 months of implementation, there is no evidence of a decrease in fatal, night-time and total volume of RTAs as a consequence of MUP implementation in Scotland. Further, there is no evidence of differential effects by level of socio-economic deprivation.

AUTHOR CONTRIBUTIONS

Francesco Manca: Conceptualization (equal); data curation (equal); formal analysis (lead); methodology (equal); writing—original draft (lead); writing—review and editing (equal). **Rakshita Parab:** Formal analysis (equal); writing—original draft (supporting). **Daniel Mackay:** Supervision (supporting); validation (equal). **Niamh Fitzgerald:** Supervision (supporting); writing—review and editing (supporting). **Jim Lewsey:** Conceptualization (equal); superivison (lead); writing—review and editing (equal).

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DECLARATION OF INTERESTS

None to declare.

DATA AVAILABILITY STATEMENT

Data are publicly available and were obtained on request from the Road safety statistics division at the UK Department for Transport.

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SUPPORTING INFORMATION

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

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Lockdown and licensed premises: COVID-19 lessons for alcohol policy

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Abstract

Introduction. *The COVID-19 pandemic necessitated unprecedented changes in alcohol availability, including closures, curfews and restrictions. We draw on new data from three UK studies exploring these issues to identify implications for premises licensing and wider policy.* ***Methods.*** *(i) Semi-structured interviews (*n = 17*) with licensing stakeholders in Scotland and England reporting how COVID-19 has reshaped local licensing and alcohol-related harms; (ii) semi-structured interviews (*n = 15*) with ambulance clinicians reporting experiences with alcohol during the pandemic; and (iii) descriptive and time series analyses of alcohol-related ambulance callouts in Scotland before and during the first UK lockdown (1 January 2019 to 30 June 2020).* ***Results.*** *COVID-19 restrictions (closures, curfews) affected on-trade premises only and licensing stakeholders highlighted the relaxation of some laws (e.g. on takeaway alcohol) and a rise in home drinking as having long-term risks for public health. Ambulance clinicians described a welcome break from pre-pandemic mass public intoxication and huge reductions in alcohol-related callouts at night-time. They also highlighted potential long-term risks of increased home drinking. The national lockdown was associated with an absolute fall of 2.14 percentage points [95% confidence interval (CI) −3.54, −0.74;* P = *0.003] in alcohol-related callouts as a percentage of total callouts, followed by a daily increase of +0.03% (95% CI 0.010, 0.05;* P = *0.004).* ***Discussion and Conclusions.*** *COVID-19 gave rise to both restrictions on premises and relaxations of licensing, with initial reductions in alcohol-related ambulance callouts, a rise in home drinking and diverse impacts on businesses. Policies which may protect on-trade businesses, while reshaping the night-time economy away from alcohol-related harms, could offer a 'win–win' for policymakers and health advocates.* [Fitzgerald N, Manca F, Uny I, Martin JG, O'Donnell R, Ford A, Begley A, Stead M, Lewsey J. Lockdown and licensed premises: COVID-19 lessons for alcohol policy. *Drug Alcohol Rev* 2022;41:533–545]

Key words: COVID-19, alcohol policy, alcohol availability, ambulance, licensing.

Introduction

The COVID-19 pandemic necessitated unprecedented changes in alcohol availability with closures, curfews and operating restrictions in many countries. Complete sale bans were introduced in several countries [1,2], whereas in others, including the UK and Australia, alcohol retailers were designated as essential services and permitted to trade throughout the pandemic [3]. Shops and online retailers, including supermarkets, are likely to have benefitted significantly [3,4], where they stayed open while bars were closed.

Other pandemic control measures also have implications for where, when and how much alcohol is drunk. It may be 'easier' to drink alcohol where people work more from home with less need to drive and lower visibility [5]. Greater consumption or alcohol problems may also be driven by increased caring responsibilities, stress levels, bereavement, isolation, job insecurity and poverty with reduced access to services and social supports, particularly affecting women, ethnic minority and economically disadvantaged groups [5,6]. Accurately assessing and appropriately responding to the above changes is not easy. In the UK, overall alcohol sales fell during the first national lockdown (driven by

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falls in on-trade sales, especially beer, while premises were closed), but then largely recovered [7]. UK survey data from early in the pandemic indicates that high-risk drinking may have increased, more so in women and disadvantaged groups, while affluent groups were more likely to report attempts to cut down their consumption, raising concerns about exacerbations of existing inequalities [8,9]. Internationally, findings are diverse with some studies reporting stability [10], others increases in consumption and harms [11,12] or decreases [13,14], but with unequal distribution of changes in population subgroups found in these and other studies [10,15–17]. With the exception of a survey in the Americas, which found that increases in heavy episodic drinking were more common in men [14], many studies have raised concerns about disproportionate increases in women's drinking, perhaps due to stress [18–20].

Alongside changes in alcohol consumption, a general decline in healthcare utilisation for non-COVID-19 issues was observed early in the pandemic, with decreases across wide ranging conditions [21–24]. A US study found a 31% decrease in ambulance responses for April 2020 compared to the previous year [25]. Fear of infection and a desire to avoid burdening health services may explain these falls; though health behaviours, including alcohol consumption may also be a factor. In Canada, alcohol-related visits at accident and emergency departments decreased at the beginning of the pandemic but to a lesser extent than other visits [26]. In New York City, during the initial COVID-19 peak in spring 2020, hospital visits for alcohol withdrawal increased while those for alcohol use decreased [27]. To date, to the best of our knowledge, the impact of COVID-19 on alcohol-related ambulance callouts has not been reported.

Much UK public discourse has centred on hardships for hospitality businesses arising from public health measures with surprisingly little discussion of reduced pressures on emergency services [28,29]. The burden of alcohol on health services is well documented, including recent work estimating that 16.2% of all ambulance call-outs in Scotland are alcohol-related [30]. This discourse contrasts with examples elsewhere of governments placing or maintaining restrictions on alcohol explicitly to reduce this burden on front-line services [31,32]. Shifts to home drinking may lead to increases in consumption, gender-based violence or risks for children [5,33], including neglect or modelling of parental drinking [34,35]. Much is still to be understood about the impact of COVID-19 on alcohol consumption, harms and services: the diversity in methods, local experiences and control measures and the time periods of each study, makes interpretation difficult and a nuanced approach is necessary.

Meanwhile government policy has moved on apace in many countries to considering post-pandemic recovery. While some public health experts have drawn attention to the need for stronger alcohol controls to protect health services and public health [4,36], there are signs that an emphasis on protecting business recovery may make politicians reluctant to act [37]. Consideration of the balance of regulation affecting on and off trade premises will be critical, having perhaps been neglected in the past [3] and there is an urgent need for evidence to inform policy deliberations. Existing studies which can 'pivot' towards COVID-19 can provide timely, relevant data.

In this paper, we: (i) review primary qualitative data from interviews which took place during the pandemic for two separate studies not originally focused on COVID-19; and (ii) analyse secondary data on alcohol-related ambulance call-outs during the first UK national lockdown. Using this data, we seek to inform discussions of the following three questions:

1. How might the pandemic have reshaped regulation of alcohol sales via the local premises licensing system in England and Scotland?
2. What are ambulance clinicians' experiences and views of alcohol-related ambulance callouts during the pandemic?
3. How did alcohol-related ambulance callouts in Scotland change in volume and timing during the first UK national lockdown compared to non-alcohol callouts?

Together, these sources can contribute to an understanding of the potential implications of changes in the alcohol regulatory environment and related behaviours during the pandemic, for public health and emergency service utilisation in the short and medium term.

Methods

Overview and ethics

First, we report in-depth interview data from a study on the role of public health in licensing [38] in which professional stakeholders interviewed in late 2020 discussed how COVID-19 had affected licensing issues. Second, we report ambulance clinicians' experiences of alcohol-related callouts during the pandemic, from in-depth interviews also conducted as part of a broader study [39]. Ethical approval was granted by the University of Stirling National Health Service, Invasive or Clinical Research ethics committee for both studies (NICR 16/17-064/064A and NICR 19/20056) and full informed consent obtained from participants. Finally, we present descriptive statistics for overall and alcohol-related ambulance callouts in Scotland before and after the national UK lockdown. No ethical approval was required for the secondary analysis of non-identifiable callout data, but Research and Development governance approval was obtained from the Scottish Ambulance Service.

Context

In response to the pandemic, the UK Government, in tandem with the Scottish Government, initiated a national lockdown requiring all 'on-licence' premises (where alcohol is sold for consumption on the premises), including bars, restaurants and nightclubs, to stop trading from 20 March 2020. In Scotland, such premises remained fully closed until 19 June, when they were permitted to re-open to serve alcohol in outdoor spaces (e.g. beer gardens) only, with indoor spaces opening in Scotland from 15 July. From early July in England, premises gradually re-opened with social distancing and other requirements in place, albeit implemented to varying degrees [40]. Prevailing restrictions on trading were stepped up or down throughout 2020 and the first half of 2021, varying geographically within and between Scotland and England. 'Off-licence premises' (shops licensed to sell alcohol) were permitted to open throughout the pandemic period. To summarise, the biggest changes in alcohol availability at various times were: (i) complete closures of on-licensed premises; (ii) rolling closures of on-licence premises in some areas, with imposed early closing times when open; and/or (iii) a ban on sales of alcohol indoors (in Scotland only). COVID-19 restrictions were generally imposed by the national (UK) or devolved (Scottish) Governments, but there was some local variation due to the localised system of licensing of premises that exists in the UK, see [38,41]. A detailed timeline of changes in Scotland and England is provided in Figure 1.

Study 1: In-depth interviews from the 'Evaluating the impact of alcohol licensing in England and Scotland' (ExILEnS) study

Sampling: As part of the wider ExILEnS study [38], we recruited 20 public health teams covering 14 English and six Scottish areas, varied in rurality and region, where the public health team was actively engaged in alcohol licensing. Purposive sampling of individual stakeholders for in-depth telephone interviews focused on diversity in terms of location (Scotland vs. England) and remit of interviewees (public health, licensing staff, police, local politicians and licensing lawyers). *Recruitment and consent*: Potential participants were identified via professionals who took part in initial site visits and/or interviews, with researchers following up with nominated individuals. Each was provided with an information sheet and gave written or audio-recorded informed consent. *Final sample and data collection*: Of 53 interviews conducted, 17 were conducted during the COVID-19 pandemic between August and October 2020 (see Figure 1). These 17 interviews form the dataset reported here. All were audio-recorded. Bespoke interview topic guides were developed for interviewees with different remits and included questions relevant to licensing on public health team activities, outcomes and alcohol-related harms. The same topic guides were used pre- and during COVID-19. The 17 interviews (averaging 74 min) were not specifically focused on COVID-19, but 15 participants spontaneously raised the topic. Table 1 outlines the profile of these interviewees. *Analysis*: Interviews were professionally transcribed, then anonymised and imported into NVivo 12 for reflexive thematic analysis. This approach was used given its focus on fluid coding processes and reflection on/engagement with the data. RO coded all transcripts against a set of categories created using deductive (reviewing research questions and topic guides) and inductive approaches (reading transcripts), to describe potentially important features in the data. One category was 'COVID-19'. After initial coding, all COVID-19 extracts from the 15 interviews were reviewed in detail by NF in discussion with RO, to identify the range and diversity of responses in relation to this topic, which formed the dataset for this paper. NF wrote up the findings, which were reviewed and refined in discussion with RO, with any discrepancies regarding interpretation resolved between both authors.

Study 2: In-depth interviews from 'Impact of minimum pricing for alcohol on ambulance callouts in Scotland' (IMPAACT) study

Study 2 consisted of in-depth qualitative interviews as part of a wider study which started in May 2019 and will finish at the end of 2021 and which focused on the impact of alcohol and of minimum unit pricing of alcohol, on ambulance callouts and ambulance service provision. *Sampling*: We recruited 27 ambulance clinicians working in frontline practice for the Scottish Ambulance Service (SAS), with diversity in terms of experience, seniority, gender and role (e.g. paramedics, paramedic technicians) as well as geographic variation across regions. *Recruitment and consent*: Eligible clinicians were

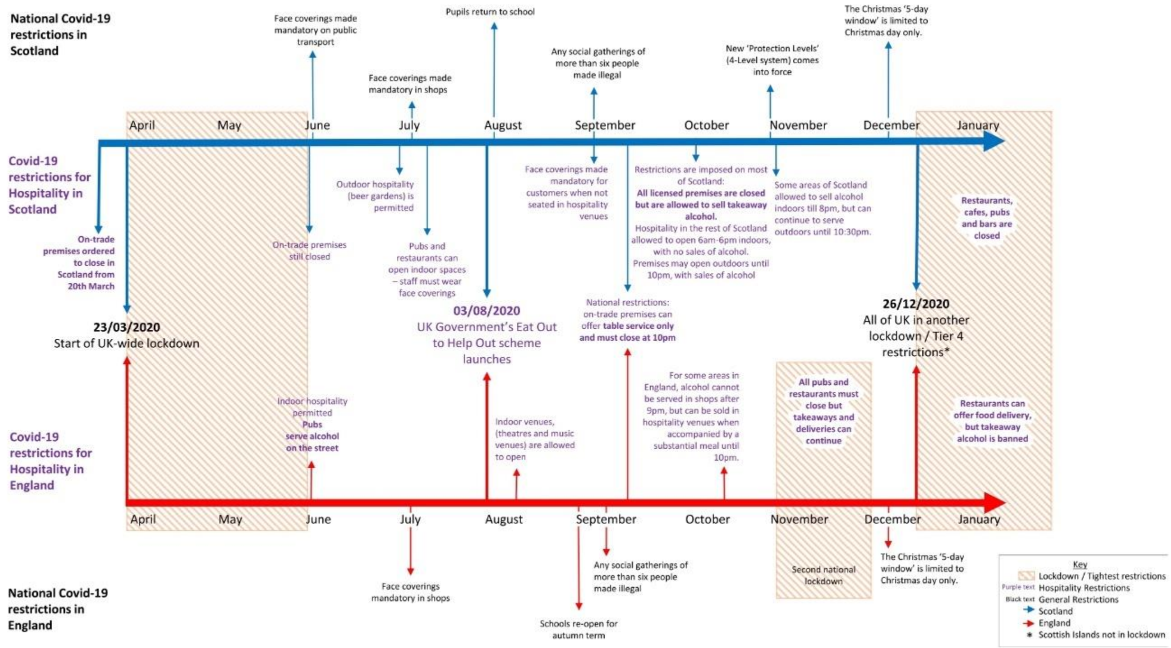

Figure 1. *Map of COVID-19 restrictions in Scotland and England.*

Table 1. *Study 1 profile of interviewees providing data for this paper*

Interview no.	Country	Stakeholder group	Gender	Experience (years)	Interview date	Duration (min)
46	England	Public Health	Female	3	4 September 2020	58
53	England	Public Health	Female	20	17 September 2020	78
43	England	Licensing Team	Male	17	21 August 2020	85
44	England	Licensing Team	Female	17	26 August 2020	59
38	Scotland	Licensing Team	Male	10	12 August 2020	72
42	England	Elected Representative	Male	3	20 August 2020	72
40	England	Elected Representative	Male	2	14 August 2020	73
45	England	Elected Representative	Female	14	03 September 2020	90
48	Scotland	Elected Representative	Male	11	09 September 2020	93
50	Scotland	Elected Representative	Female	13	15 September 2020	60
54	England	Licensing Lawyer	Female	10	28 September 2020	53
39	Scotland	Licensing Lawyer	Male	24	13 August 2020	73
49	Scotland	Licensing Lawyer	Female	7	14 September 2020	82
47	England	Licensing Police	Male	2	09 September 2020	91
41	Scotland	Licensing Police	Female	17	20 August 2020	72

invited to express interest in taking part via an email from SAS managers and then through a blanket email to all frontline clinicians in SAS. Participants were provided with an information sheet and gave written or audio-recorded informed consent. *Final sample and data collection*: From those who expressed interest ($n = 118$), 27 were selected in accordance with our sampling strategy and took part in telephone interviews, of which 15 were conducted during the COVID-19 pandemic. Although the interview questions were mainly on the impact of alcohol on SAS, 13 participants spontaneously raised the issue of changes in alcohol-related harms during the pandemic (see Table 2). They were prompted further on the topic by the researcher. These discussions form the dataset for this paper. Interviews were audio-recorded. *Analysis*: With participant permission, interview recordings were professionally transcribed, anonymised and imported into NVivo 12 for analysis. Three members of the research team (IU/JM/AF) coded the transcripts against a set of categories created using

Table 2. *Study 2 profile of interviewees providing data for this paper*

Interview no.	Region	Job title	Gender	Experience (years)	Interview date	Duration (min)	COVID-19 topic raised by?
14	East	Technician and trainee paramedic	Male	4	23 April 2020	106	Interviewee
15	North	Technician	Female	13	29 April 2020	90	Interviewee
16	West	Technician	Male	4	01 May 2020	65	Interviewee
22	North	Ambulance technician and other	Male	11	12 August 2020	35	Interviewer
23	West/North	Air crew	Male	16	12 September 2020	81	Interviewer
17	West	Paramedic	Male	11	11 December 2020	77	Interviewee
26	East	Paramedic	Male	36	22 January 2021	62	Interviewee
27	East	Advanced paramedic	Female	25	25 January 2021	81	Interviewee
24	West	Ambulance technician	Male	4	14 December 2020	85	Interviewer
18	East	Paramedic	Male	32	17 November 2020	101	Interviewee
25	West	Other	Male	28	20 January 2021	45	Interviewee
19	West	Ambulance technician	Female	3	27 November 2020	91	Interviewee

deductive (reviewing research questions and topic guides) and inductive approaches (reading transcripts). After the initial coding, NF, JM and IU discussed the emerging themes and extracts from the transcripts which related to COVID-19 in detail. This supported the writing of the first draft of findings by NF, which JM and IU reviewed before submission.

Study 3: Lockdown and licensed premises

Study 3 utilised electronic patient record data from SAS to describe trends in alcohol-related ambulance callouts in Scotland between 1 January 2018 and 30 June 2020, before and during the first UK-wide COVID-19 lockdown when all on-licence premises were closed. Alcohol-related ambulance callouts were defined as those identified using an algorithm that makes use of free text notes completed by ambulance staff in electronic patient records for each callout as well as an alcohol 'flag'—a field in the electronic patient record allowing ambulance clinicians to indicate if a callout is alcohol-related. The algorithm was validated and performed well with 98% accuracy [30]. Our analyses utilised both a descriptive and an inferential approach. First, we created graphs and tables describing ambulance callouts over time, alcohol-related or not. To facilitate comparison, we also computed alcohol-related callouts per 100 000 residents using mid-year population estimates [42]. Then, we conducted an interrupted time series analysis [43] on alcohol-related callouts as a percentage of total callouts. Specifically, a seasonal autoregressive integrated moving average analysis was performed to take into account of seasonal variations in the callout trends and a change in level and of slope associated with lockdown was tested for. We analysed the proportion rather than the count of alcohol-related callouts to isolate the effect of lockdown on alcohol alone, removing any effect of a general decline in health care (and ambulance service) demand during the first waves of the pandemic.

We discuss the findings of each of the studies in turn below.

Results

Findings across these studies provide evidence of profound changes due to COVID-19 and related public health measures that are relevant to alcohol policy, including the practices and experiences of public sector professionals, licensed businesses and members of the public.

Findings from the ExILEnS study of public health involvement in licensing

Key issues identified from this analysis included reductions in stakeholders' focus on licensing, concerns about alcohol-related harms associated with relaxation of licensing rules and observations on the impact of restrictions on different licensed businesses.

Licensing stakeholders reported that COVID-19 had '*changed the whole face of licensing*' and gave specific examples relating to changed priorities and ways of working. Some public health actors had to withdraw from their work on alcohol licensing to focus on pandemic-related work, halting partnership work with other licensing stakeholders. One public health actor raised concerns on this basis, suggesting that new licensing applications/proposed variations to existing licenses might not be given the same level of scrutiny from a public health perspective. In contrast, other partnership working, such as between the police and environmental health officers and licence holders and elected members, was strengthened because of opportunities to work more closely together on COVID-19-related matters. Second, several stakeholders expressed concern about relaxation of licensing regulations, which they feared might not fully reversed. A national decision was taken in England to permit licensed premises forced to close during the lockdown to sell takeaway alcohol, resulting in '*people wandering around the street with, you know, plastic pint pots, which is what they're allowed to do now*' (F, Elected Member England). This was reportedly done without consultation and experienced as '*pulling the rug out from under*' (undermining) local licensing stakeholders. As businesses reopened following the first UK lockdown, interviewees reported that multiple licences were granted to permit the sale of alcohol for consumption in areas outside premises. Licensing team members explained that the volume of such applications meant they were unable to visit premises prior to applications being considered as they normally would do. A public health interviewee suggested that some premises would '*sneak in an hour change*' (a request for additional hours of trading), as part of these applications. Another raised concern about expansion in availability through outdoor drinking when premises re-opened because '*especially just now…everybody's needing to turn everything in to a beer garden just to keep the business going, you know, with social distancing etc.*' (O, Police, Scotland).

Finally, interviewees reported unevenly distributed impacts of COVID-19 on businesses, noting that some were more vulnerable to collapse, including '*small corner pubs*', nightclubs and live music venues. Those able to provide online or home delivery sales were well-positioned to benefit from the pandemic, but stakeholders were concerned about whether age verification procedures would be properly implemented, with delivery drivers having to maintain social distancing. Nightclubs were required to remain closed until the second half of 2021, but many 'hybrid' late-night venues with similar characteristics to nightclubs were permitted to open.

Findings from the IMPAACT study of alcohol's impact on the ambulance service

Ambulance clinicians reported '*huge differences*' as the number of callouts relating to alcohol they attended late at night had '*plummeted*', when premises were closed completely or under curfew, although there were some increases in domestic callouts and concerns raised about home drinking.

Closures and other restrictions affecting pubs and nightclubs meant '*nowhere near the same amount of public intoxication or mass intoxication… there's been much less in the way of assaults that involve alcohol, unconscious people outside that involve alcohol, falls that involve alcohol, all these things we've noticed a massive drop in*' (Interviewee #24). Another welcomed this change, explaining:

> '*It's so nice to go to work on a Friday night knowing that you don't have to go into pubs and clubs… it's made a huge difference. And although you know you will get occasions, you will get parties, you will get illicit parties or you will get people still drinking, but you don't get that whole war, you know battlefield environment…*' (#26).

Others reported that they were no longer dealing with '*drunken idiots*' and therefore '*going to genuine calls*' (#27). This contrasted with the initial period of time when pubs/bars reopened after the first national lockdown, which was described as '*pandemonium*' (#25). One paramedic reported that the reduction in callouts experienced when premises were closed in the first lockdown (March to June 2020) was more pronounced than in the second in early 2021.

Alongside this reduction, domestic alcohol-related incident numbers appeared to have gone up, though '*not a massive increase*' (#14). Tensions or domestic violence in homes were felt to be exacerbated by couples being forced to spend more time at home together. Second, the ease of internet purchases and supermarket home deliveries of alcohol meant people did not need to leave their houses to access alcohol. Third, people with prior alcohol dependence were reported to be '*now struggling because they have nothing else to do*' (#27). Others reported that '[people with alcohol issues] *now can't go out and they sit in the house all day drinking, and they drink and drink and drink and drink and drink*' and added their view that isolation from friends affects the mental health of these patients.

While some ambulance clinicians expressed a hope that people might be less inclined to call an ambulance for minor issues post-pandemic, others described fears about longer-term consequences arising from new alcohol consumption habits formed during the pandemic that might persist.

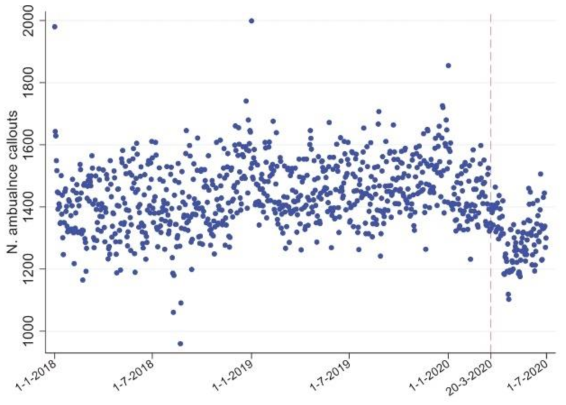

Figure 2. *Total ambulance callouts in Scotland. Each dot = daily ambulance callouts. Dashed red line indicates the date of the order to close all hospitality venues (including pubs). Outliers correspond to public holidays, including New Year's Eve.*

'… alcohol intake is definitely increased in the house. My thoughts on when this is all finished, the people that used to go socializing, might not… I still think the younger generation will go back out to the nightclubs and the public houses and that, probably forty year old people upwards…I think they might get used to being in the house drinking, why get dressed and go out, when I can just sit here and watch TV and do what I've been doing for the last seven months' (#18)

'All these people can't stay at home drinking without a consequence at some point.' (#23)

Findings from the study of alcohol-related ambulance-callouts during lockdown

Ambulance callouts of all causes from March to June 2020 decreased in number compared to the previous year, with falls of 1.1% in March, 12.3% in April, 11.5% in May and 10.9% in June (Figure 2, Table 3). Alcohol-related ambulance callouts (Figure 3) fell much more sharply, driven largely by April figures, when they fell by 23%. In April 2020, the proportion of overall ambulance callouts related to alcohol was 14.5% or 2.2% lower than what it was in the same month in 2019 (16.7%); in relative terms, this was a 13% fall compared to the previous year. Both total

Table 3. *Ambulance callout counts and distribution in January–June 2019 and January–June 2020*

	2019			2020			% Variation		
Month	Alcohol	Non-alcohol	Overall	Alcohol	Non-alcohol	Overall	Alcohol	Non-alcohol	Overall
Full week (Monday–Sunday)									
January	7034	39 053	46 087	6887	38 133	45 020	−2.1%	−2.4%	−2.3%
February	6585	34 591	41 176	6354	35 076	41 430	−3.5%	1.4%	0.6%
March	7409	36 848	44 257	6423	37 337	43 760	−13.3%	1.3%	−1.1%
April	7298	36 263	43 561	5553	32 638	38 191	−23.9%	−10.0%	−12.3%
May	7451	37 463	44 914	6659	33 085	39 744	−10.6%	−11.7%	−11.5%
June	7622	36 957	44 579	6620	33 087	39 707	−13.1%	−10.5%	−10.9%
Weekends (00.00 Friday–23.59 Sunday)									
January	3056	15 074	18 130	3290	16 210	19 500	7.7%	7.5%	7.6%
February	3457	15 082	18 539	3404	16 045	19 449	−1.5%	6.4%	4.9%
March	4319	17 812	22 131	3164	15 684	18 848	−26.7%	−11.9%	−14.8%
April	3543	14 716	18 259	2416	13 289	15 705	−31.8%	−9.7%	−14.0%
May	3792	15 774	19 566	3400	16 070	19 470	−10.3%	1.9%	−0.5%
June	4244	17 481	21 725	2926	13 490	16 416	−31.1%	−22.8%	−24.4%
Weekend nights (Friday 20.00 to Saturday 06.00 and Saturday 20.00 to Sunday 06.00)									
January	1145	3543	4688	1263	3836	5099	10.3%	8.3%	8.8%
February	1380	3471	4851	1373	3878	5251	−0.5%	11.7%	8.2%
March	1706	4033	5739	953	3340	4293	−44.1%	−17.2%	−25.2%
April	1370	3368	4738	700	2913	3613	−48.9%	−13.5%	−23.7%
May	1517	3884	5401	1078	3465	4543	−28.9%	−10.8%	−15.9%
June	1659	4019	5678	991	3090	4081	−40.3%	−23.1%	−28.1%

Table 4. *Output of regression of interrupted time series on the percentage of alcohol related callouts*

	Coefficient	$P > \|z\|$	95% confidence interval
Bank holiday	1.615	0.000	(1.172, 2.058)
Sat&Sunday	4.995	0.000	(4.508, 5.482)
Friday	1.735	0.000	(1.221, 2.249)
Trend	0.001	0.313	(−0.001, 0.004)
Lockdown	−2.142	0.003	(−3.542, −0.742)
Lockdown Trend	0.032	0.004	(0.010, 0.054)
January 1st	10.636	0.000	(0.117, 12.156)
Constant	13.274	0.000	(11.902, 14.645)

callouts and alcohol-related callouts fell by similar proportions in March, May and June 2020, considering callouts at all times of the week/day (Table 3). Prior to the pandemic, there was a consistently greater volume of alcohol-related callouts at weekends compared to weekdays (Table 3), unlike other callouts (Figure 2). This difference disappeared in April 2020 when there were large drops in weekend alcohol-related callouts and then reappeared gradually. Weekend (00:00 Friday to 23:59 Sunday) alcohol-related callouts fell by 31.8% in April, whereas other weekend callouts fell by only 9.7%. The drop in alcohol-related callouts was even more stark at weekend night-times (20:00 Friday to 06:00 Saturday and 20:00 Saturday to 06:00 Sunday), which fell by 48.9% in April 2020 compared to a fall of 13.5% in other callout types (Table 3). After April, the proportion of alcohol related callouts gradually started to follow pre lockdown levels, but at weekends and weekend night-times, alcohol-related call-outs were still substantially lower in June 2020 than in the previous year (Table 3).

The average number of alcohol related callouts per 100 000 residents in the month preceding lockdown (21 February–20 March 2020) was 4.06, but fell to 3.74 in the 3 months of lockdown (20 March–30 June 2020), reaching a low point in the first month (21 March–20 April 2020) of 3.36. Levels appeared to be returning to pre-lockdown volumes from the end of May 2020 (3.93 alcohol related callouts per 100 000 residents in the week 22–28 May 2020).

The interrupted time series analysis found an association between lockdown and the proportion of callouts that were alcohol related. This proportion (alcohol-related callouts as a percentage of total callouts) showed an absolute reduction of 2.14 percentage points (95% CI -3.54, -0.74; P=0.003). In relative terms, this corresponds to a 13% reduction in the proportion of callouts that were alcohol-related compared to the period before the lockdown (1 January 2018–20 March 2020). This association was immediate and then lessened over time with a significant daily increase

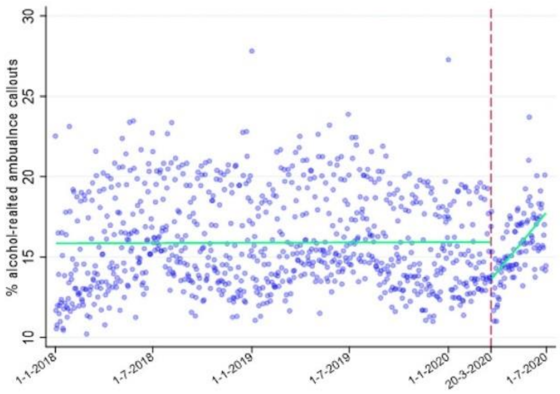

Figure 3. *Alcohol-related ambulance callouts as percentage of total callouts. Green solid lines are linear fitted trends over time before and after first day of lockdown, indicated by the dashed red line, when all hospitality venues (including pubs) were ordered to close.*

(post lockdown announcement) in the percentage of alcohol related callouts of 0.03% (95% CI 0.010, 0.05; $P = 0.004$). The analysis finds that the proportion of alcohol-related call-outs compared to total call-outs came back to pre-lockdown levels after approximately 2 months, at the end of May 2020 (Table 4 and Figure 3).

Discussion

In most countries, the COVID-19 pandemic and related public health measures profoundly changed aspects of life in ways that were largely unanticipated, including unprecedented changes to alcohol availability. Our data suggest at least four broad impacts with implications for alcohol harms and policy: relaxation of some aspects of licensing policy, significantly fewer alcohol-related ambulance callouts initially followed by a resurgence, perceived increases in home drinking and diverse impacts on businesses.

Implications for licensing policy

First, licensing stakeholders highlighted that restrictions on capacity and sales of alcohol indoors had led to an increase in applications from bars/pubs to serve alcohol in spaces outdoors and an increase in premises permitted to offer home delivery. When physical distancing remains a requirement, meaning reduced customer numbers indoors, extra outdoor space is unlikely to increase overall availability of alcohol, but it may increase risks of public disturbance via noise or other antisocial behaviour. It may be difficult to reverse outdoor licences granted during the pandemic, even when physical distancing is no longer required, suggesting a significant increase in overall capacity in those venues. A shift towards outdoor drinking renders alcohol consumption (and any related drunkenness) more visible, including to children and people in recovery from alcohol problems who may be passing by. The pandemic may have contributed to expansions in availability as licence applications received less public health scrutiny, but may have had some benefits in building relationships between stakeholders seen as important for facilitating successful public health engagement in licensing [44].

Reductions in alcohol burden on ambulance services during lockdown

Second, qualitative data from the Scottish Ambulance Service indicate that the pandemic period, during which premises were either closed completely or not open late at night, was associated with a substantial reduction in demand for ambulances arising from alcohol consumption. The quantitative data shows that total alcohol-related callouts fell even more than overall ambulance call-outs in the first months of lockdown, but rebounded after 2 months. The reduction was particularly acute at weekend night-times however, and call-outs at these times remained lower than usual through to the third month after lockdown. Considering the reports of ambulance clinicians, it seems clear that reductions in call-outs were linked to the closure of licensed premises and the night-time economy (NTE), more than 'stay at home' measures introduced at the same time, even though these probably reduced socialising in people's homes. Exceptionally good weather in May 2020 may have mitigated the latter effect, perhaps explaining a rebound in weekend callouts that month even with premises still closed; that disappeared in June 2020. They reported clearly that, in normal times, many ambulance callouts are associated with people in or around pubs/bars/clubs in the NTE and that these were greatly reduced. The views expressed by paramedics are powerful and give pause for thought about whether business recovery post-COVID has to mean a return to the '*mass intoxication*' and '*battlefield environment*' on city streets, which they described. As premises re-open and especially in Scotland where the ambulance service is under intense pressure in 2021 [45], authorities should be looking to avoid this. There is surely an opportunity for politicians and clinicians to show leadership in pushing for better alcohol policies that protect frontline services. Effective multi-faceted interventions already exist to reduce drunkenness [46] and violence [47] and could be more widely and consistently deployed, although are unlikely alone to be transformative.

Transforming the night-time economy to rely less on alcohol?

It is timely to consider whether economic prosperity in the NTE must rely on alcohol and whether there is a third way or 'sweet spot' approach via policies which transform and build the NTE to prioritise other forms of entertainment, food, music or more family-friendly environments. The nature of such policies and their feasibility and acceptability to communities [48,49] and trade stakeholders [50], plus their likely and actual effectiveness in balancing prosperity and reducing harms, requires further consideration and research. Strategic planning policies at local authority level [51], availability and promotion of no/very low alcohol products [52] and 'place-shaping' in the licensing system, through which premises perceived as lower risk (restaurants, arts venues) are prioritised in licensing policy over others with a strong alcohol focus [48] may all have a role to play. Further work is underway to collate and assess the feasibility and acceptability of innovative initiatives in this space to inform policymaking [53].

Increased home drinking during the pandemic

The third issue highlighted by both licensing stakeholders and ambulance clinicians, is that the pandemic shifted alcohol sales and drinking from the on- to off-trade, exacerbating existing trends. Reportedly driven by increases in home delivery of alcohol coupled with closures of premises and 'stay at home' orders, interviewees' perceptions of increases in home drinking are supported by sales and survey data from other sources [7,9,54]. While the proportion of alcohol-related callouts returned to that of pre-lockdown periods shortly after May 2020, callouts were spread throughout the week; while the incidence at weekends remained persistently lower, especially at night. This suggests that after the first 2 months of lockdown, ambulance services may have already been seeing an increase in demand arising from home drinking. It is difficult to know what types of call-outs would have generated these trends, however it could have arisen from a rise in outdoor get-togethers/house parties, increased consumption in groups vulnerable to liver failure or acute harms or greater incidence of alcohol withdrawal. Research in Cardiff, Wales [55]) found a significant decrease in emergency department visits by people injured by violence, driven by a large reduction in visits due to violence outside the home. No significant increase in emergency department visits resulting from violence at home was noted. For injury outside the home, significant decreases were found in emergency department visits by female individuals younger than 18 years and by male individuals in all age groups, those injured with weapons and those in which the perpetrator was a stranger, acquaintance or security officer [55]. The relationship between emergency service utilisation and alcohol during the pandemic is likely to be highly context specific. It will also hugely depend on the pattern of restrictions in place as illustrated by findings from North America [26,27] outlined earlier and evidence from South Africa finding reduced emergency attendances during total and partial alcohol sales bans [56].

Overall implications of the pandemic for alcohol policy

Overall, it seems likely that the closure of licensed premises led to net reductions in the burden of alcohol-related harm on emergency services, even with a shift to home drinking, but that this was relatively short-lived. Total closures or prohibitions are neither practical nor desirable in a liberal society however and our data support the suggestions of others that an associated shift to home drinking may result in mid- and long-term harms [5,33]. In the longer term, the cheaper price of alcohol bought from off-licence premises enables consumption of greater amounts of alcohol at home, raising the risk of conditions (cancer, hypertension, etc.) that would not arise during the follow-up period in this study, nor be easily identified as alcohol-related in ambulance/emergency department data. Interventions to raise the price of off-trade alcohol (such as increases in or the introduction of minimum unit pricing) are likely the most effective available option to reduce shop-bought alcohol consumption [57,58]. Minimum unit pricing can also reduce the price differential between on and off trade premises, which may encourage people to drink in licensed premises; it may therefore support the hospitality sector, while protecting health [59]. Drinking (or drunkenness) at home is more visible to children than drinking by adults in bars/pubs where children are not permitted. Furthermore, for vulnerable subgroups, home drinking may be associated with exacerbations of domestic violence, isolation and alcohol dependence [4,5]. As discussed by Reynolds and Wilkinson [3], the rise in home drinking illustrates a blind spot in licensing policy: systems largely designed to control 'outlet density' and maintain public order [60], have failed to adapt to address online sales or hidden harms associated with home drinking. The introduction of a 'public health' objective for alcohol licensing in Scotland perhaps signalled the intention to take a broader approach, but arguably without the requisite systems locally to fully realise hoped-for benefits [44,61]. There is now an opportunity to consider tighter controls on online sales/home delivery of alcohol, alongside pricing interventions as above, which would protect public health without impacting on (or perhaps supporting) the recovery of hospitality sectors post-COVID.

How the pandemic may be reshaping the on-trade alcohol sector

A final issue raised by our data is that the pandemic is likely to have longer term impacts on the alcohol sector [62]. Smaller premises and nightclubs, even if permitted to open, have been particularly affected, as distancing requirements were often impractical. Independently-owned businesses may be less likely to have the financial reserves to survive the hardship of lockdowns, despite government support and are reportedly being bought up by large pub companies [63]. Such chains may have greater lobbying power, which policymakers and other stakeholders in licensing will need to be equipped to handle. Furthermore, several larger pub companies also produce and supply alcohol for sale in shops and may therefore oppose measures to reduce home drinking, even if they might benefit bars. Independent bar owners and policy stakeholders should be mindful of these conflicting interests in trade associations that represent both on- and off-trade interests.

Strengths

This paper provides timely, relevant data to inform current debates around how to support businesses to recover from the COVID-19 pandemic, while still protecting public health and health services. It makes pragmatic use of new data arising spontaneously in two studies not designed to focus on COVID-19 and reports new analyses of data on ambulance call-outs during the pandemic. Drawing together data from three studies allows for triangulation across the datasets and we found broad agreement on issues raised by the different sources, allowing us to draw questions and hypotheses from the findings.

Limitations

There are however, some important limitations to bear in mind. The ExILEnS study was not focused on the pandemic and questions regarding the issues reported were not explored with all interviewees. Furthermore, relevant data were naturally only available from interviews conducted after the start of the first UK lockdown in March 2020, during which time only two public health stakeholders were interviewed. The views reported in the ExILEnS study are mostly those of others without a specific public health remit (but who work with/alongside public health)—a larger sample of public health stakeholders may broaden and strengthen findings relating to alcohol harm implications of the pandemic. In contrast, in the IMPAACT study, a strength is the varied sample of interviewees in terms of region, role and length of service and that questions about the pandemic were included in the topic guide. Both studies capture professional perspectives but there is also a need for in-depth qualitative research to understand consumer experiences, including their view of possible long-term outcomes of changes in alcohol consumption. Considering the quantitative ambulance callout data, while the algorithm used to identify alcohol-related callouts has been found to be highly accurate [30], it may have over or underestimated alcohol-related callouts. People may be less likely to call an ambulance for domestic incidents and it may be more difficult to identify alcohol as a factor in a callout to a home compared to callouts to licensed premises, which may be a source of bias. Nonetheless, the drop in callouts is unlikely to be explained solely by these factors, is triangulated by the qualitative reports of ambulance clinicians and mirrors the findings regarding emergency department visits from a fairly similar context in Cardiff, Wales [55]).

Conclusion

Drawing on new data from three studies, we report potential impacts of the COVID-19 pandemic that have implications for public health and alco hol policy. Licensing stakeholders reported the liberalisation of licensing laws that may increase availability of alcohol and the possible reshaping of the on-trade sector as different premises types and businesses are more or less negatively affected by the pandemic. There were large short-term reductions in alcohol-related ambulance callouts while public health measures closed or severely restricted on-trade premises, especially at weekend night-times and reports from both licensing and ambulance interviewees of rises in home drinking with potential long-term consequences. Paramedics gave stark reports about the volume of late night alcohol-related callouts prior to the pandemic. We argue that these reports should give pause for thought about the wisdom of a return to 'normal' in the night-time economy and tentatively draw on prior literature to suggest possible approaches to both reduce harm and support business recovery. At a time when policymakers are reluctant to be seen to hurt already suffering hospitality sectors, but also wish to protect health services, it is going to be vital for politicians, advocates and lobbyists alike to find win–win' policies that can do both.

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Conflict of Interest

The authors have no conflicts of interest.

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