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Evaluating the impact of alcohol minimum unit pricing (MUP) on alcohol-attributable deaths and hospital admissions in Scotland

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Contents

Key points

Study methods

- Our study design allowed us to **estimate the impact of minimum unit pricing (MUP) based on the difference between outcomes following the implementation of MUP compared to a best estimate of what would have been observed had MUP not been implemented**. This best estimate of what would have occurred in the absence of MUP was developed by controlling for differences in the trend and level of health harms in England, where MUP has not been implemented, and in Scotland, by observing trends in health harms prior to MUP. Adjustments were also made to incorporate differences in COVID-19- associated restrictions over time in each country. This approach allowed us to estimate the impact of MUP by isolating it from other factors which might impact health harms, such as the COVID-19 pandemic.

- When we refer to a reduction, an increase, or no change in a health outcome following MUP implementation, this is our best estimate of the impact of MUP in comparison to what could have been expected in the absence of MUP.

Deaths

- After more than two and a half years of implementation, our best estimate is that **MUP significantly reduced deaths wholly attributable to alcohol consumption by 13.4% (95% confidence interval (CI): -18.4% to -8.3%) in Scotland**, when using a method that accounts for deaths in a geographical control area (England), where the policy was not implemented, and underlying seasonal and secular trends. **We estimate that an average of 156 (95% CI: -243 to -69) deaths wholly attributable to alcohol consumption were averted each year over the study period following MUP implementation**.

- The **overall reduction was driven by a 14.9% (95% CI: -20.8% to -8.5%) significant reduction in deaths from chronic causes wholly attributable to**

alcohol consumption, with significant reductions observed for both alcoholic liver disease (-11.7%; 95% CI: -16.7% to -6.4%) and alcohol dependence syndrome (-23.0%; 95% CI: -36.9% to -6.0%). There was some evidence to suggest an increase in deaths from acute causes wholly attributable to alcohol consumption (6.6%; 95% CI: -13.7% to 31.8%), although this effect was more uncertain. This is in part due to acute causes contributing a relatively small proportion of all deaths wholly attributable to alcohol consumption.

- Significant reductions in deaths wholly attributable to alcohol consumption were estimated for: males (-14.8%; 95% CI: -18.7% to -10.7%), females (-12.0%; 95% CI: -20.5% to -2.6%), 35- to 64-year-olds (-10.0%; 95% CI: -14.7% to -5.0%) and those aged 65 years and over (-26.7%; 95% CI: -35.6% to -16.5%). All changes were driven by deaths from chronic causes, such as alcoholic liver disease. Our results suggest that any increase in deaths from acute causes wholly attributable to alcohol consumption was likely driven by males (4.4%; 95% CI: -1.5% to 10.6%), with little evidence of any change for females (0.2%; 95% CI: -3.5% to 4.2%).

- Significant reductions in deaths wholly attributable to alcohol consumption were greatest among the four most socio-economically deprived area-based deciles, suggesting that **MUP acted to reduce inequalities in alcohol-attributable deaths in Scotland**.

- Our main estimate, a significant reduction of 13.4% (95% CI: -18.4% to -8.3%) in deaths wholly attributable to alcohol consumption, was robust to a range of different conditions as tested through our sensitivity analyses, providing greater certainty in our main finding.

- Deaths partially attributable to alcohol consumption were estimated to reduce by 8.4% (95% CI: -16.2% to 0.2%) in the study period following the implementation of MUP, although this effect was less certain than the estimated effect for deaths wholly attributable to alcohol consumption. Significant reductions in deaths from chronic causes partially attributable to alcohol consumption (-12.7%; 95% CI: -21.4% to -3.0%) offset a 7.8% increase (95% CI: -1.1% to 17.5%) in deaths from acute causes partially

attributable to alcohol consumption, although this effect on acute deaths was more uncertain.

Hospital admissions

- After more than two and a half years of implementation, our best estimate is that **MUP reduced hospital admissions wholly attributable alcohol to alcohol consumption by 4.1% (95% CI: -8.3% to 0.3%) in Scotland**, when using a method that accounts for admissions in a geographical control area (England), where the policy was not implemented, and underlying seasonal and secular trends. **We estimate that an average of 411 (95% CI: -908 to 86) hospital admissions wholly attributable to alcohol consumption have been averted each year over the study period following MUP implementation**. There was slightly more uncertainty surrounding this result than for the estimates of reduced deaths.

- The estimated **overall reduction was driven by a significant 7.3% (95% CI: -9.5% to -4.9%) reduction in hospital admissions for chronic conditions wholly attributable to alcohol consumption**, achieved through significant reductions in hospital admissions for alcoholic liver disease (-9.8%; 95% CI: -17.5% to -1.3%) and alcohol psychoses (-7.2%; 95% CI: -12.9% to -1.1%). Hospital admissions for acute conditions wholly attributable to alcohol consumption were estimated to have increased by 9.9% (95% CI: -1.1% to 22.0%), although this effect was more uncertain than for chronic conditions. This was most likely driven by a significant increase among females (15.6%; 95% CI: 2.1% to 30.9%). There was also some evidence of an increase among males (8.5%; 95% CI: -3.3% to 22.1%), although the effect for males was less certain than that for females. As admissions for acute conditions were less common, there was an overall reduction in hospital admissions wholly attributable to alcohol consumption.

- Significant reductions in hospital admissions wholly attributable to alcohol consumption were estimated for males (-6.2%; 95% CI: -10.0% to -2.3%), and while there was some evidence of an increase among females (3.1%; 95%

CI: -2.8% to 9.3%), this effect was more uncertain. A reduction in hospital admissions wholly attributable to alcohol consumption was estimated for those aged 35 to 64 years (-4.8%; 95% CI: -9.4% to 0.2%); while there was some uncertainty around this effect, evidence for changes in other age groups was weaker.

- Reductions in hospital admissions wholly attributable to alcohol consumption were greatest among the four most deprived area-based deciles, suggesting that **MUP acted to reduce inequalities in alcohol-attributable hospital admissions in Scotland**.

- Results from the sensitivity analyses were varied, suggesting less certainty around the impact of MUP on alcohol-attributable hospital admissions, than on alcohol-attributable deaths.

- Hospital admissions partially attributable to alcohol consumption were estimated to have reduced by 3.4% (95% CI: -7.3% to 0.6%), although this effect was more uncertain. Any reductions were driven by significant reductions among males (-6.9%; 95% CI: -10.2% to -3.2%), particularly for chronic conditions. We estimated that the implementation of MUP was associated with a significant increase in female hospital admissions for acute conditions partially attributable to alcohol consumption (6.1%; 95% CI: 0.7% to 11.7%).

Conclusion

- We conclude that the implementation **of MUP has reduced alcohol-attributable health harms**. The strongest evidence was that MUP reduced deaths wholly attributable to alcohol consumption, with reductions across all alcohol-attributable harm being primarily driven by reductions in chronic outcomes. Furthermore, our study has evidenced that **MUP has acted to reduce deprivation-based inequalities in alcohol-attributable health harms**.

1. Introduction

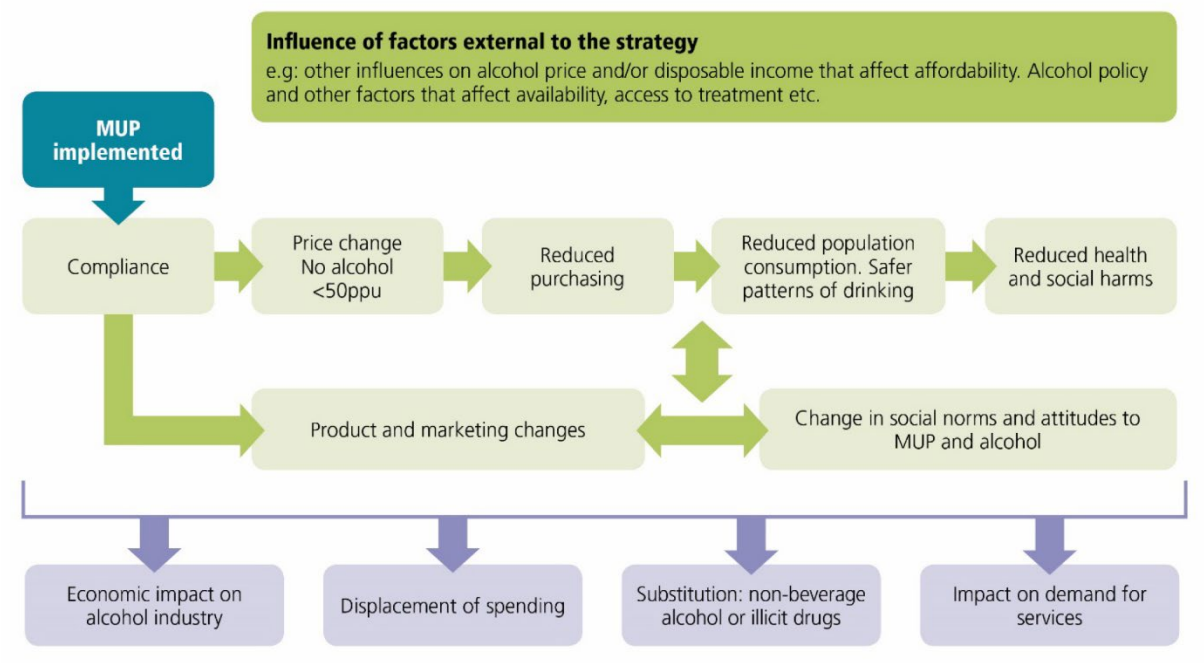
This report builds on study findings published by The Lancet, by reporting the impact on both wholly and partially attributable alcohol health harms.[1]

1.1. Minimum unit pricing in Scotland

In May 2018, Scotland became one of very few countries in the world to implement a minimum unit price (MUP) for alcoholic drinks sold in licensed premises.[2] MUP was implemented as part of a comprehensive strategy to reduce levels of alcohol consumption in Scotland, with the aim of reducing health and social-related alcohol harms, given their disproportionate scale in Scotland compared to the rest of the United Kingdom and other western European countries.[3,4,5,6,7]

The extent to which MUP has had an impact in Scotland will be determined through an overarching mixed-methods evaluation. The evaluation will provide evidence to inform Members of the Scottish Parliament (MSPs) ahead of the parliamentary vote on the future of MUP in Scotland in 2024.[8,9,10]

Figure 1. Theory of change for MUP in Scotland



A theory of change was developed for MUP in Scotland, setting out the intended outcomes, potential unintended impacts and how these might come about (**Figure 1**).[11,12] Among changes expected to be realised from the theory of change are those related to the health harms caused by alcohol consumption.

This report is from the final study in a package of work focusing on health and social harm outcomes.[13] The study used routine administrative data to estimate the impact of MUP on deaths and hospital admissions attributable to alcohol consumption in Scotland during the first 32 months following the implementation of the policy.

1.2. Study aims

The aim of this study was to evaluate the impact of MUP on alcohol-attributable health harms in Scotland. In our study, health harms were defined as alcohol-attributable mortality and morbidity, estimated using deaths and hospital admissions data, respectively.

Our primary study aim was achieved through addressing the following evaluation questions:

- How has MUP impacted deaths wholly attributable to alcohol consumption?
- How has MUP impacted hospital admissions wholly attributable to alcohol consumption?

As well as estimating the overall impact of MUP, we have also estimated how this impact varies by sex, age group and level of socio-economic deprivation. An additional aim of our study was to explore the impact of MUP on deaths and hospital admissions partially attributable to alcohol consumption.

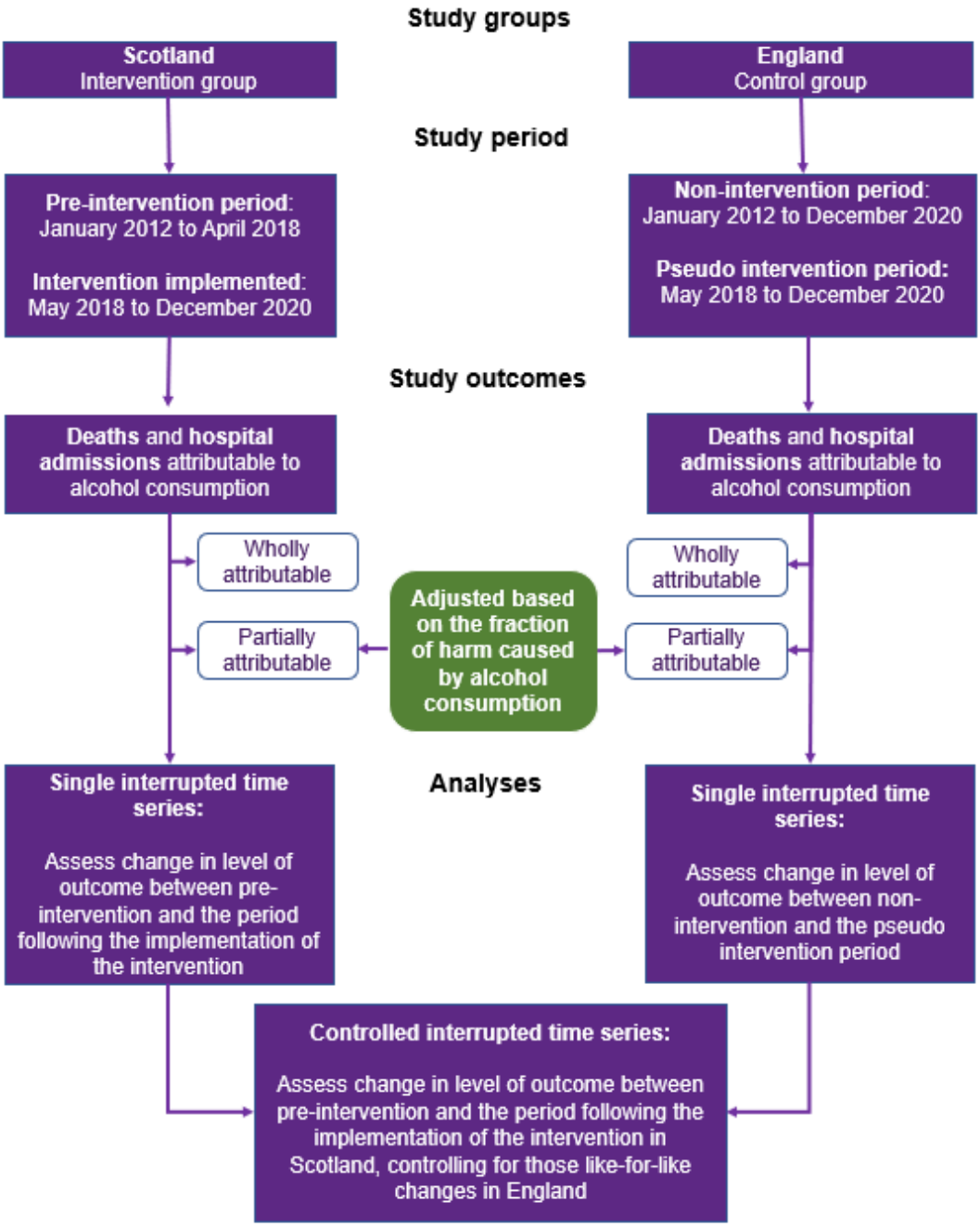
2. Methodology

Further information regarding our methodological approach can be found in our published pre-specified statistical analysis plan.[14]

2.1. Study design and period

Our study used a controlled interrupted time series study design. **Figure 2** summarises the study setting, time periods, outcomes and analyses described in detail within the methods section of this report.

Figure 2. Study flow diagram



The study setting was Scotland. The control area was England, a part of the UK where MUP has not been implemented. The main sampling frame for assessing outcomes was the period 1 January 2012 to 31 December 2020. This provided us with data for over six years before, and over two and a half years after, the implementation of MUP in Scotland. The start of the study period was selected on the basis of trends in alcohol-specific deaths in Scotland: following a period of decreasing alcohol-specific deaths from 2006 to 2012, alcohol-specific deaths steadily increased from 2012, prior to the implementation of MUP.[15] The time-specific unit of analysis used was calendar month. Outcomes were included if they occurred in the population aged 16 years and above.

We used controlled interrupted time series methods to assess whether the implementation of MUP was associated with a change in the rate of deaths, and hospital admissions, attributable to alcohol consumption. Our approach incorporated several methods to strengthen the interpretation of the impact of MUP, including:

- employing multiple approaches to incorporate data for England, our geographical control, into our analyses
- adjusting all statistical models for underlying seasonal and secular trends, and the COVID-19 pandemic and related restrictions
- performing a range of sensitivity analyses to test the robustness of our results
- shortening the study period following MUP implementation to assess the impact of MUP on deaths and hospital admissions attributable to alcohol consumption prior to the COVID-19 pandemic.

2.2. Outcome measures

All outcome measures were defined using codes from the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) applied to deaths and hospital admissions data.[16] Outcome measures were firstly defined at the level of individual health conditions and then aggregated into pre-specified wholly, or partially, attributable outcome measures.

Wholly attributable health outcomes are those where the health harm outcome was entirely attributable to alcohol consumption (for example, alcoholic liver disease). Partially attributable health outcomes are those where only a proportion of the population-level outcome was deemed to be due to alcohol consumption (for example, liver cirrhosis). A list of the ICD-10 codes used to classify health outcomes wholly and partially attributable to alcohol consumption are outlined in **Appendix 1**.

Study outcomes were assessed using a primary definition for wholly attributable outcomes, and a secondary definition for partially attributable harms, as outlined below:

- **Primary definition**: underlying cause of death (or main hospital admission diagnosis) was wholly attributable to alcohol consumption.
- **Secondary definition**: underlying cause of death (or main hospital admissions diagnosis) was partially attributable to alcohol consumption. Additionally, partially attributable injuries were further defined using external cause codes in any secondary hospital admissions diagnoses, as they cannot be defined in the main diagnosis position.

All study outcomes are outlined in **Table 1** and are reported separately for wholly and partially attributable outcomes. Outcomes were assessed separately for deaths and hospital admissions.

Each outcome was defined on a month-by-month basis over the full study period. If a patient had more than one alcohol-attributable hospital admission in a monthly period, the attributes of the earliest admission were selected.

Table 1: List of study outcomes

Attributability and onset	Health outcome
Wholly attributable: both acute and chronic	**All health harms**
Wholly attributable: chronic	**All health harms**
Wholly attributable: chronic	Alcoholic liver disease
Wholly attributable: chronic	Alcohol dependence syndrome
Wholly attributable: chronic	Alcohol psychoses
Wholly attributable: chronic	Alcohol abuse
Wholly attributable: acute	**All health harms**
Wholly attributable: acute	Acute intoxication
Partially attributable: both acute and chronic	**All health harms**
Partially attributable: chronic	**All health harms**
Partially attributable: chronic	Liver cirrhosis
Partially attributable: acute	**All health harms**

2.3. Data

2.3.1. Deaths

Scottish and English death records were sourced from the National Records of Scotland (NRS) and Office of National Statistics (ONS), respectively, to define alcohol-attributable mortality.[17,18] We analysed deaths based on their date of occurrence, rather than date of registration, and included all alcohol-attributable deaths that occurred during the study period. All mortality records were sourced from finalised annual registers of death for each country over the full study period.

2.3.2. Hospital admissions

Our study defined alcohol-attributable morbidity using hospital admissions data. Scottish data were sourced based on individuals admitted to hospital as a general inpatient or day case from the Scottish Morbidity Record 01 (SMR01) dataset.[19] The data also included mental health inpatient and day cases from the SMR04 dataset. We sourced English hospital admissions data from the Hospital Episodes Statistics (HES) dataset, via NHS Digital.[20] The English hospital admissions data did not include an equivalent component of mental health inpatient and day cases.

For both Scotland and England, the analysis date was based on hospital admission date, rather than date of discharge, and health outcomes were defined by the diagnosis upon discharge. The first admission stay details were selected, meaning that an individual with multiple admissions in a single month could only be counted once in each monthly total.

2.3.3. Socio-economic deprivation

We stratified outcomes by socio-economic deprivation decile using country-specific area-based deprivation indices as a proxy for individual-level deprivation status. For Scotland, we assigned each individual's postcode of residence to a deprivation decile based on the Scottish Index of Multiple Deprivation (SIMD).[21] The approach used for Scotland was consistent for both deaths and hospital admissions. Different SIMD versions were used depending on the time period and were defined as follows: SIMD 2012 (2012 to 2013); SIMD 2016 (2014 to 2016); and SIMD 2020 (2017 to 2020).

English deprivation decile was assigned based on mapping each individual's postcode of residence to the Index of Multiple Deprivation (IMD).[22] The approach for England differed to the approach for Scotland, due to time-varying differences in English administrative geography classification and data availability. For English deaths, different IMD versions were used dependent on the time period and were defined as follows: IMD 2015 (2012 to 2015); and IMD 2019 (2016 to 2020). The definition of IMD decile for hospital admissions over the entire study period was based on IMD 2010 as that is what was routinely available from the HES dataset.

2.3.4. Populations

Relevant mid-year population estimates by sex, age group, deprivation decile and year were sourced from NRS for Scotland and ONS for England.[23,24] Populations were estimated for each month by linear (straight-line) interpolation between individual mid-year population estimates for each combination of sex, age group and deprivation decile.[25]

2.3.5. COVID-19-related government restrictions

We sourced data on the extent of government restrictions during the COVID-19 pandemic, separately for Scotland and England. This was defined using the Oxford COVID-19 Government Response Tracker (OxCGRT).[26] The stringency index of the OxCGRT reflects the differences in lockdown and restrictions over time, and between the UK Government and that of the Scottish Government. Incorporating this allowed us to reflect that the level of government response influenced on-trade restrictions for sales of alcohol. In addition, restrictions matched the challenges faced from COVID-19 infection, so high levels of restrictions were generally imposed when the impact of COVID-19 was largest on hospital admissions and deaths. The OxCGRT data used in this study were downloaded on 5 April 2022.

2.4. Alcohol-attributable fractions

Outcomes wholly attributable to alcohol consumption did not require any further adjustments: by definition, they are all caused by alcohol consumption. However, outcomes partially attributable to alcohol consumption required scaling based on the extent of their attributability to alcohol consumption. Partially attributable health outcomes are a hypothetical estimate of the impact of alcohol consumption on health harms based on the scenario of risk minimisation on the relationship between alcohol consumption and health harms. This relationship is based on systematic reviews and meta-analyses of an extensive literature that has examined the association between different levels of alcohol consumption and a range of health outcomes.

We modelled alcohol-attributable fractions (AAFs) for each health outcome partially attributable to alcohol consumption using the online interface of the International Model of Alcohol Harms and Policies (InterMAHP, version 3.0).[27] AAF analyses were undertaken at the level of each calendar year and population sub-group (country, sex, age group) to estimate AAFs and subsequently, deaths and hospital admissions partially attributable to alcohol consumption.

InterMAHP model parameters were defined in line with national guidance, with binge drinking definitions set at 8 units per day for males and 6 units per day for females.[28] The theoretical upper limit of average daily consumption was defined as the InterMAHP default value of 18.75 units. Our study used relative risks for alcohol-attributable health harms from the WHO 2018 Global Status Report on Alcohol and Health.[29] Due to our choice of relative risk set, our study assumed more conservative cardioprotective effects than have been recently published.[30,31] Regardless of recent estimates, there remain differing views on the extent of protective effects of alcohol.[32,33]

We did not consider COVID-19 health harms to be partially attributable to alcohol consumption, although we acknowledge a case could be made that COVID-19 outcomes could be causally linked to alcohol consumption through direct and indirect routes.[34] Our rationale for exclusion was that, due to the novel nature of COVID-19, we found no meta-analyses of relative risks available to enable us to develop specific AAFs.

The number of deaths and hospital admissions partially attributable to alcohol consumption were estimated by multiplying the number of each outcome (deaths and hospital admissions) by the relevant AAF. Not all health outcomes partially attributable to alcohol consumption had separate AAFs for morbidity. Where fractions were available for both mortality and morbidity, the relevant fraction was used. In the case that only the mortality fraction was available, it was applied to the count of hospital admissions.

Further information on the data inputs, and approach to estimating AAFs, can be found in **Appendix 2** and in our pre-published pre-specific statistical analysis plan.[14]

2.5. Descriptive analysis

Overall monthly rates per 100,000 residential population were estimated for each outcome measure by dividing the number of people that experienced the outcome by the total population aged 16 years and above. Monthly rates were adjusted to a common month length. Subgroup-specific rates were estimated by: sex (males and females); age group (16 to 34 years; 35 to 64 years; and 65 years and above); and socio-economic deprivation decile, using the relevant population denominators. Rates were produced for each calendar month, for each country (Scotland and England). These were required to undertake interrupted time series analyses. Time series data were decomposed into trend and seasonal components using the Seasonal-Trend decomposition LOESS (STL) methodology of Cleveland et al.[35] Seasonal diagnostics graphs were used to assess the appropriateness of the decomposition. Where there was evidence of residual seasonality, the seasonal window parameter was adjusted until no patterning in the residuals remained. To get a comparative insight into trends, we estimated the ratio of monthly decomposed trend rates between Scotland and England for overall outcomes. This was achieved by dividing the Scottish, by the English, monthly trend rate. This allows us to visualise how Scottish outcomes are changing relative to those in England.

In this report we focus on describing monthly trends, and decomposed seasonal and trend components for each country for the following outcomes attributable to alcohol consumption, using deaths and hospital admissions data:

- Wholly attributable: all health harms, chronic health harms, acute health harms.
- Partially attributable: all health harms, chronic health harms, acute health harms.

2.6. Statistical analysis

To assess the impact of MUP on our alcohol health harms outcomes in Scotland, we used controlled interrupted time series methods with seasonal autoregressive integrated moving average (SARIMA) errors.[36] Interrupted time series methods

provide a robust quasi-experimental study design, which enables underlying temporal and seasonal trends to be accounted for.[37] We have previously used this approach when evaluating the impact of the Alcohol Act, MUP and the COVID-19 pandemic on alcohol sales in Scotland.[38,39,40]

When using controlled interrupted time series methods, the counterfactual assumption is that the level and trend for the group exposed to the intervention would be expected to change in the same way as the control group. This makes controlled interrupted time series a stronger quasi-experimental design, provided the control group is appropriate, and likely subject to the same time-varying confounding factors as the intervention group. Uncontrolled interrupted time series methods assume that the level and trend in the group exposed to the intervention would have remained the same had the intervention not occurred. This increases the likelihood of missing important non-MUP-related factors impacting the frequency of study outcomes in Scotland and England during the period when MUP had been implemented. On the other hand, if external factors led to a worsening in the rate of alcohol health harms in Scotland and England, controlled interrupted time series can estimate whether MUP had a positive or negative impact over and above the underlying trends in alcohol health harms. Controlled interrupted time series takes into account all the aforementioned factors to give a counterfactual situation of the expected level of study outcomes had MUP not been implemented in Scotland. England, a neighbouring country with the same UK Government, similar economy and culture, provides an appropriate control group for a controlled interrupted time series that gives us a plausible estimate of the causal impact of MUP.

To estimate the direction, magnitude and uncertainty of the effect of MUP on deaths and hospital admissions in Scotland, we included a binary variable that took the value of 0 for the pre-MUP time period (January 2012 to April 2018) and a value of 1 after the introduction of MUP (May 2018 to December 2020).

All models were adjusted for underlying temporal and seasonal trends. In addition, we adjusted for government restrictions during the COVID-19 pandemic using the OxCGRT.[41] The stringency index of the OxCGRT was used to reflect the differences in lockdown and restrictions over time, and between the UK Government and the Scottish Government. Weighted averages were calculated using daily values so that

the index value represented full monthly periods. The default stringency index ranges from 0 to 100, but values were transformed between 0 and 1, with those closer to 1 representing the highest levels of restrictions. The OxCGRT took a value of 0 for all months prior to the start of the pandemic.

Rates were log-transformed for each study outcome to address the potential for rates to be skewed. Separate models were derived, where appropriate, for each sex, age group and deprivation decile. Separate models were derived for each sub-group stratification, rather than estimating models that include an interaction term. As a result, sub-group specific estimates may not appear to lie on either side of an overall estimate. If a time series contained observations for any period with a value of 0, the series was transformed using the inverse hyperbolic sine transformation.[42]

Time series data often exhibit evidence of outliers, which need to be modelled appropriately for efficient estimation of intervention effects. To investigate this, we extracted the residuals from each model and then applied the 'isoutlier' function in MATLAB version 9.1 update 2 to obtain a list of identified outliers using Grubbs' method,[43] the generalised extreme Studentized method,[44] a sliding window mean and scaled median. Identified outliers were incorporated into the model and the residuals were tested for white noise to ensure the model is an appropriate fit.

The uncontrolled Scottish and English models give insights into how each outcome has changed between the pre-MUP and post-MUP implementation periods but cannot be used to robustly attribute change to MUP. Therefore, we estimated controlled models that compare trends in harms in Scotland to the control area, England, where MUP was not implemented. We used a two-step approach to incorporate our control group data. Firstly, separate models were fitted to the log-transformed rate of each study outcome in Scotland and in England. Secondly, the English control-group time-series data were added as a covariate into the SARIMA models for Scotland to produce a controlled model. This approach is in line with guidance from Lopez-Bernal et al.[45] Controlled models were defined and assessed on a like-for-like basis, for example the log-transformed rate of health harm outcomes in Scottish males controlled for the log-transformed rate of health harms outcome in English males.

For both uncontrolled and controlled models, coefficients were converted into percentages using the following transformation: $100 \times e^{\beta} - 1$. For any series requiring transformation using the inverse hyperbolic sine, the coefficients from the model were converted into percentages using the formula: $100 \times e^{\beta - 0.5 \times Var(\beta)} - 1$. A p-value of less than 0.05 was used to denote statistically significant results for our overall wholly and partially attributable outcomes. For all other outcomes, significant results are reported when the 95% confidence interval does not include zero. When other important effects have been observed that are not statistically significant, we report on the direction of the effect and indicate that there was a higher degree of uncertainty around the effect.

In this report the findings from the controlled models were interpreted to evaluate the impact of MUP on deaths and hospital admissions attributable to alcohol consumption.

2.7. Sensitivity analysis

We undertook several sensitivity analyses in addition to our main analysis, as pre-specified in our published statistical analysis plan.[14] These sensitivity analyses were designed to test the robustness of our study findings on our primary study outcomes by varying the parameters used in the research that might have influenced the results.

Firstly, we truncated the sampling period to remove the impact of the COVID-19 pandemic by removing outcomes observed in 2020. We did not include January and February 2020 as there is evidence that alcohol sales had started to drop during the latter part of this period, and also there is a potential that hospital admissions and deaths outcomes were influenced by the period directly preceding the COVID-19 pandemic.[46] This provided us with 20 months of post-MUP data (May 2018 to December 2019), prior to the national lockdown and associated protection measures being introduced in the UK in March 2020.

Secondly, we adjusted the geographical level of the control group to obtain alternative geographical control groups for north-west and north-east England, that is

sub-national areas of England that are more similar to Scotland. These areas were chosen as their self-reported estimates of alcohol consumption have been shown to be comparable with similarly deprived Scottish urban areas.[47,48]

Thirdly, we adopted the use of a non-geographical control group (genitourinary conditions) for evaluating the impact of MUP in Scotland. Non-geographical controls are groups of people who have experienced a similar outcome (hospital admission or deaths) but the outcome would not have been affected by the intervention of interest, i.e. MUP. They can be used as a control group in interrupted time series designs as they would not be expected to change due to the intervention nor any other treatment that is designed to give the same effect as the intervention. [49] If they did, it would suggest the observed changes in the outcome of interest were not necessarily due to MUP.

We carried out a falsification test, by modelling the introduction of MUP as if it had happened six months earlier than it was implemented. Other sensitivity analyses related to changes in the modelling approach were also carried out. We assessed the impact of MUP using an analytical method that differs to the SARIMA approach. This was achieved using an Unobserved Components Model 15 (UCM) across the entire outcome series. UCM does not assume the data are 'stationary' (i.e. that statistical properties of the data series, such as the mean and variance, are constant over time).[50] Lastly, rather than adding the English time series data as a model covariate, we modelled the difference between the Scottish and English time series using the SARIMA approach.

2.8. Changes from pre-specified analysis plan

We published our pre-planned methodological approach in our study protocol and statistical analysis plan. Pre-specifying an approach helps eliminate the risk of selecting methods producing favourable results when undertaking multiple analyses.

We made three changes to our pre-specified published analysis plan. Firstly, we did not undertake any analyses using a further definition of partially attributable outcomes specified in our analysis plan. This definition was based on identifying deaths/hospital admissions attributable to alcohol consumption through identification

of alcohol-attributable ICD-10 codes in any cause of death/hospital diagnosis position. This definition was proposed as alcohol harms might contribute to deaths and hospital admissions but not necessarily be coded as the underlying cause/main diagnosis. In our analysis plan, we acknowledged that there were fewer opportunities to pick these codes up in Scotland compared to England, for both deaths and hospital admissions, as these are coded using more fields in England. However, upon retrieval of the data we found that levels of alcohol health harms were greater in England than in Scotland. This was an artefact due to the increased opportunity to identify and record health harms outcomes in England, relative to Scotland. This definition was not carried forward, because it would base the analysis on a position which is false, i.e. alcohol harms are greater in England than in Scotland.

Secondly, upon retrieval of outcomes data, we could not estimate the impact of MUP for a number of outcomes which we pre-specified. Where this is the case, we will have no estimate displayed. Finally, we undertook one additional sensitivity analysis for our main deaths and hospital admissions outcome only. This involved modelling the difference between the Scottish and English time series to estimate the impact of MUP, as an alternative approach to adding the English time series data as a model covariate.

2.9. Ethics and permissions

The data used in this study were sourced from Public Health Scotland (PHS) and multiple external agencies. All PHS staff undertook information governance training covering the study period. PHS staff procedures for accessing and requesting the information required to undertake this study were adhered to.

Control group data for deaths and hospital admissions in England were applied for through applications to ONS and NHS Digital, respectively.[18,51] For ONS, an application to the Secure Research Service (SRS) to access mortality data was approved (study reference number 1011523).[18] Members of the PHS team working on this study then undertook, and passed, a training assessment to become accredited researchers allowing them to access the data remotely on the ONS SRS. All members complied with the ONS SRS policies regarding accessing, handling and

requesting the release of anonymised data for use in this study. Following approval of the application for data to NHS Digital, a data sharing agreement was drafted and co-signed by members from NHS Digital and PHS.

Members of the University of Glasgow team that undertook the statistical analyses did so under the Service Level Agreement for the provision of specialist statistical support that is in place between PHS and the University of Glasgow.

2.10. Software

All data transformations were carried out using Microsoft Excel, SPSS and R software. Additionally, English deaths data were accessed remotely using Citrix Workspace to access the ONS SRS virtual environment.[18] Time series decompositions were carried out using EViews 13 software.[52] All interrupted time series modelling was undertaken using the econometrics toolbox from MATLAB 9.1 Update 2.

3. Results

3.1. Trends in alcohol health harms

Trends in the rate of alcohol health harms are presented in this sub-section. The monthly crude rate per 100,000 population, and decomposed seasonal and trend components, are presented for each country for death and hospital admissions outcomes. Additional data on average annual monthly rates by population sub-group and outcome are presented in the supplementary appendix. Results for wholly attributable and partially attributable health harms are presented separately.

3.1.1. Trends in wholly attributable alcohol deaths

Monthly rates of deaths wholly attributable to alcohol consumption were relatively stable in both Scotland and England throughout the study period (**Figure 3a; all deaths**). Seasonality was apparent in both Scotland and England and was stable throughout the entire time series, with rates peaking in January each calendar year (**Figure 3b; all deaths**). Prior to the implementation of MUP, the decomposed monthly trend rate was approximately two times higher in Scotland than England. In that time period the monthly trend rate rose a little over time in Scotland, compared to England where it stayed relatively flat (**Figure 3c; all deaths**). From late 2019 until the end of the study period, the monthly trend rate increased steadily to the highest rates across the full study period in both countries.

When disaggregated into chronic and acute causes of death, the patterns described for all deaths wholly attributable to alcohol consumption were very similar for chronic deaths. This is because most deaths wholly attributable to alcohol are caused by chronic, rather than acute, causes (**Table 2**). Therefore, monthly rates of acute deaths were much lower compared to chronic deaths (**Figure 3a; acute deaths**). Seasonality in acute deaths was apparent but was different to that previously described for all deaths wholly attributable to alcohol consumption (**Figure 3b; acute deaths**). The most notable difference was the peak in acute deaths in Scotland which appeared in February of each calendar year, unlike in England where the peak

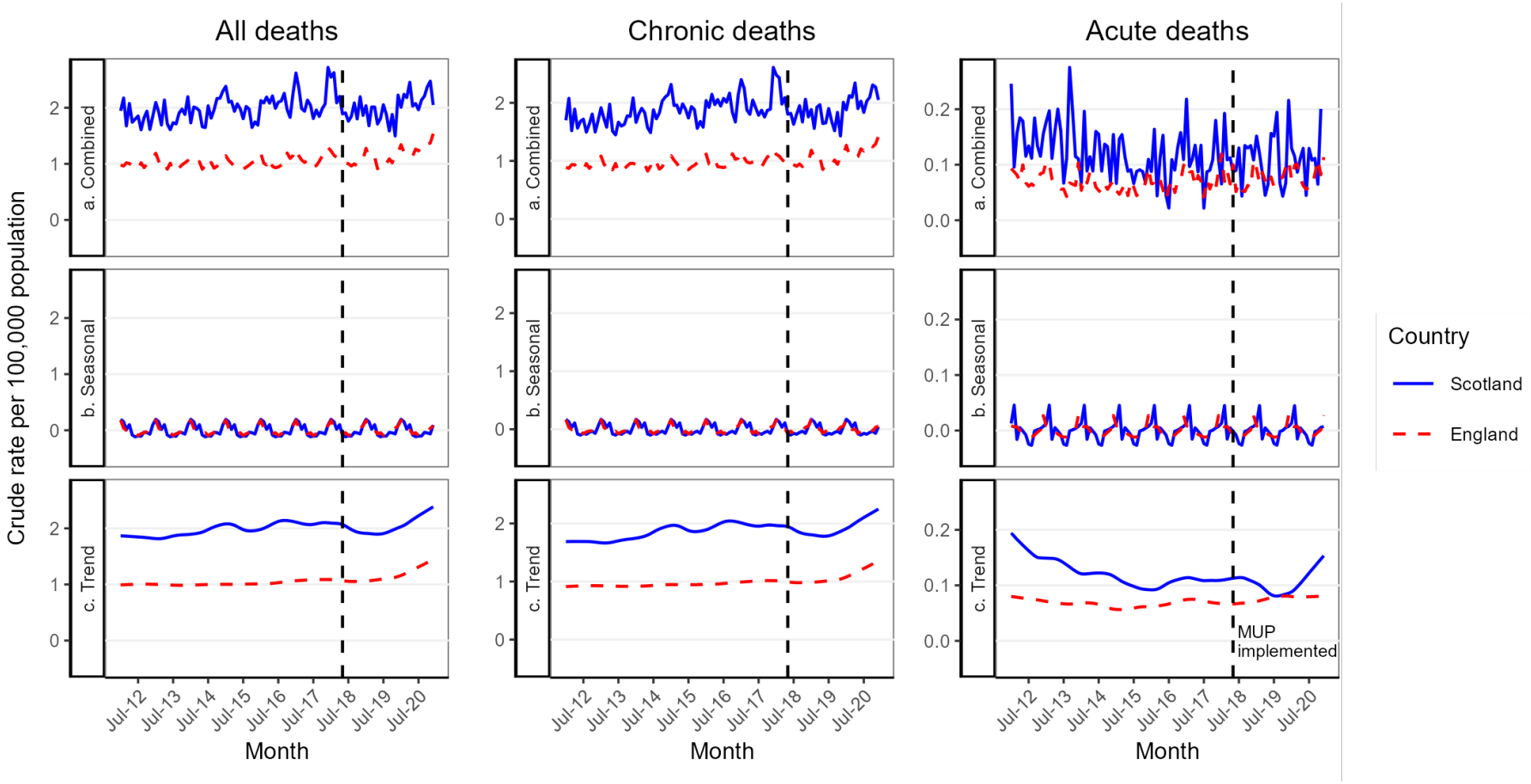
remained in January. The decomposed monthly trend rate in acute deaths in Scotland decreased from the start of the study period, until August 2019 (**Figure 3c; acute deaths**). From this point, the monthly trend rate of acute deaths in Scotland began rising until the end of the study period. In England, the monthly trend rate of acute deaths was more stable throughout the entire time series.

3.1.2. Trends in wholly attributable alcohol hospital admissions

Monthly rates of hospital admissions wholly attributable to alcohol consumption were relatively stable in both Scotland and England throughout the study period, with some exceptions (**Figure 4a; all admissions**). The monthly rate dropped to the lowest rate in April 2020, which was the first full month in which a national lockdown had been implemented in both Scotland and England, due to the COVID-19 pandemic. This reduction is therefore likely to be due to the impact of COVID-19 protection measures. Seasonality was apparent in both Scotland and England and was stable throughout the entire time series, with rates peaking in July each calendar year (**Figure 4b; all admissions**). The decomposed monthly trend rate was approximately two times higher in Scotland compared to England (**Figure 4c; all admissions**).

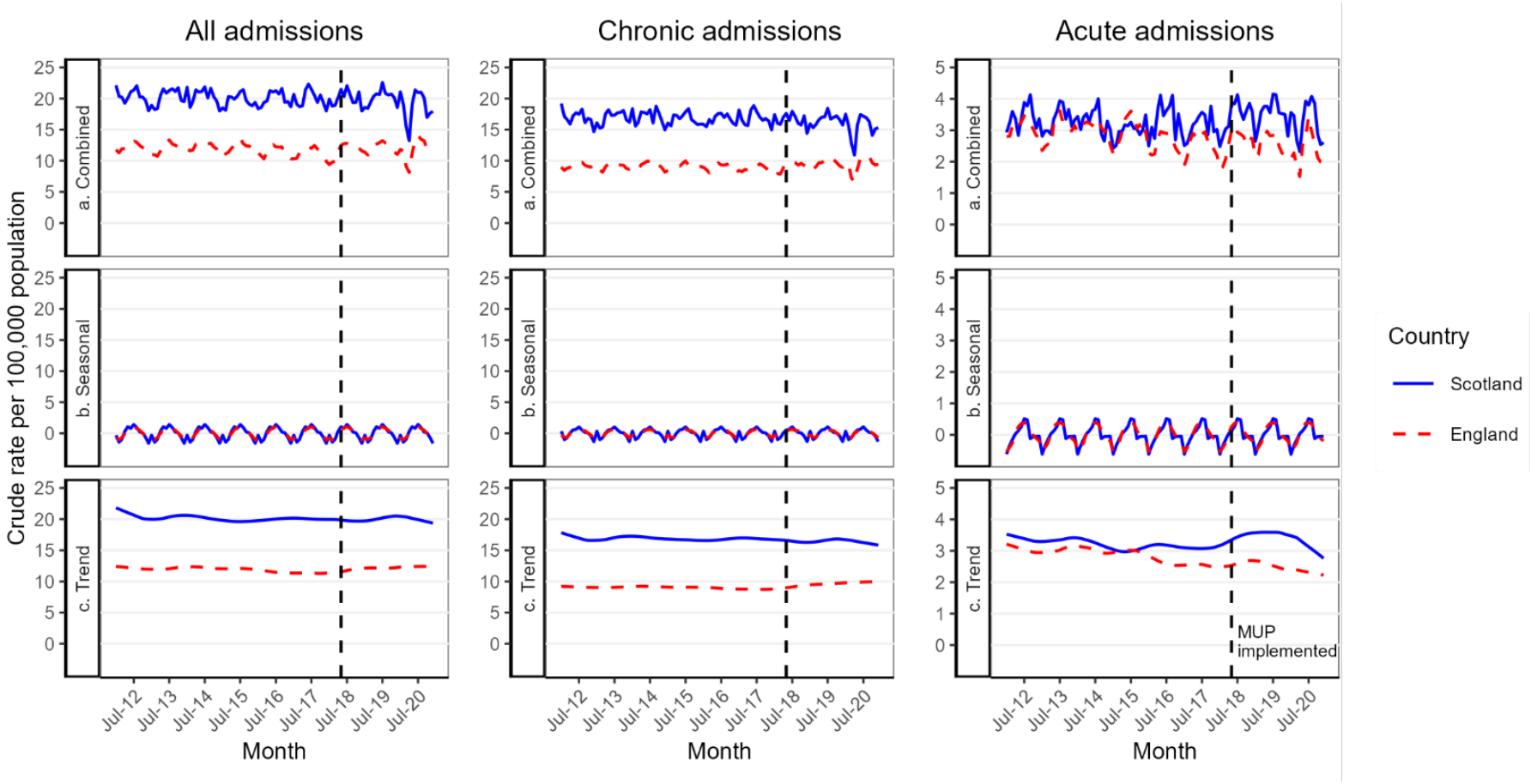
In the disaggregated data, patterns for chronic conditions were very similar to those for all conditions. This is because most hospital admissions wholly attributable to alcohol are for chronic, rather than acute, conditions (**Table 2**). Monthly rates of hospital admissions for acute conditions wholly attributable to alcohol consumption were much lower compared to chronic conditions (**Figure 4a; acute admissions**). Seasonality was apparent and similar to that previously described, with rates peaking in July and falling to their lowest in January each calendar year (**Figure 4b; acute admissions**). The decomposed monthly trend rate for acute conditions was similar in both countries until 2016 when it started to decrease in England but remained stable in Scotland (**Figure 4c; acute admissions**). Just prior to the implementation of MUP, the monthly trend rate for acute conditions began to increase in Scotland, with a smaller increase observed for England. Towards the end of the study period, monthly rates for acute conditions began decreasing in both countries, with larger reductions in Scotland.

Figure 3. Wholly attributable deaths (total, chronic and acute), crude rate per 100,000 population, Scotland and England, January 2012 to December 2020, (a) monthly rate, and decomposed (b) seasonal and (c) trend components



Note: the y-axis scale is different for acute deaths compared to all and chronic deaths.

Figure 4. Wholly attributable hospital admissions (total, chronic and acute), crude rate per 100,000 population, Scotland and England, January 2012 to December 2020, (a) monthly rate, and decomposed (b) seasonal and (c) trend components



Note: the y-axis scale is different for acute admissions compared to all and chronic admissions.

Table 2: Mean annual count of outcomes wholly attributable to alcohol, 2012–2020, by country, sex, and age group

Wholly attributable outcome per country	Total	Sex: Males	Sex: Females	Age group: 16 to 34 years	Age group: 35 to 64 years	Age group: 65+ years
Scotland: All deaths	**1,074**	**736**	**337**	**32**	**726**	**316**
Scotland: Chronic deaths	1,010	694	315	26	676	308
Scotland: Acute deaths	64	42	22	6	49	8
Scotland: All hospital admissions	**10,881**	**7,762**	**3,119**	**1,727**	**7,743**	**1,410**
Scotland: Chronic hospital admissions	9,066	6,504	2,563	1,186	6,708	1,173
Scotland: Acute hospital admissions	1,814	1,258	556	541	1,035	238
England: All deaths	**5,680**	**3,777**	**1,903**	**192**	**4,106**	**1,383**
England: Chronic deaths	5,296	3,514	1,781	148	3,805	1,342
England: Acute deaths	385	263	121	44	301	40
England: All hospital admissions	**63,555**	**43,974**	**19,568**	**10,678**	**45,084**	**7,793**
England: Chronic hospital admissions	48,839	34,214	14,620	6,008	36,735	6,096
England: Acute hospital admissions	14,717	9,760	4,948	4,670	8,349	1,698

3.1.3. Trends in partially attributable alcohol deaths

Monthly rates of deaths partially attributable to alcohol consumption increased in both Scotland and England throughout the study period (**Figure 5a; all deaths**). Seasonality was apparent in both Scotland and England and was stable throughout the entire time series (**Figure 5b; all deaths**), although it had a greater contribution to the monthly rate in Scotland. Monthly rates in both countries peaked in January each calendar year, with the lowest rates being observed in August in Scotland and in December in England. The decomposed trend rate was almost three times higher in Scotland compared to England (**Figure 5c; all deaths**). Towards the end of the study period, the trend rate started to decrease in both Scotland and England. This is likely indicative of the introduction of COVID-19 as a novel mortality risk competing with causes of death partially attributable to alcohol consumption.

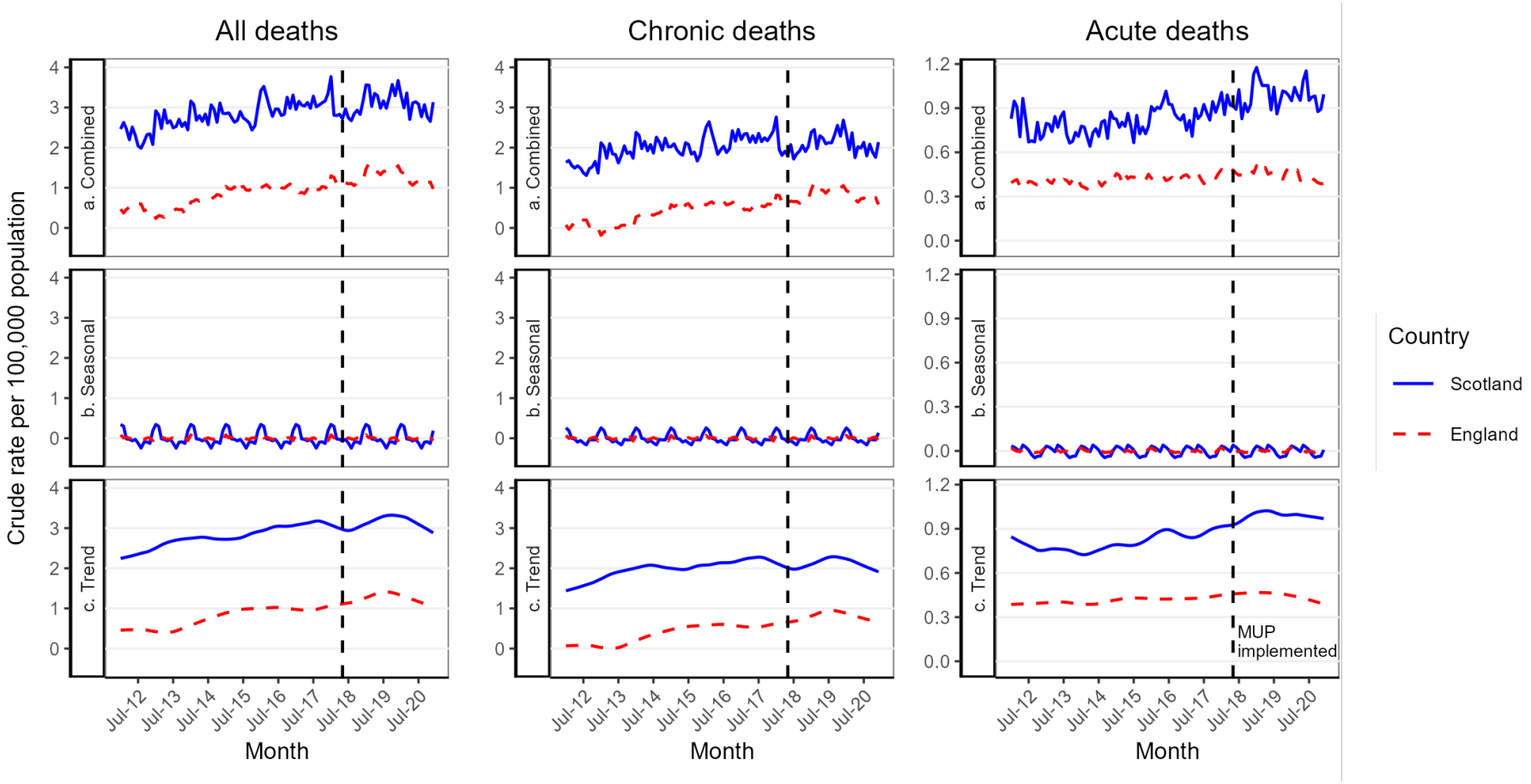
The trends already described for all deaths partially attributable to alcohol consumption largely apply to chronic causes of death also (**Figure 5; chronic deaths**). The trends observed for acute causes of death are somewhat different (**Figure 5a; acute deaths**). In Scotland the monthly rate of acute deaths was relatively stable, between the start of the time series (January 2012) and late 2015. From this point there was an upward shift in the typical monthly rate. In England the monthly rate of acute deaths was generally more stable throughout the time series. However, a rise was discernible from late 2017 onwards. Seasonality was also apparent but is somewhat different to that observed for all (or chronic) deaths partially attributable to alcohol consumption (**Figure 5b; acute deaths**). A peak in acute deaths can be seen in January in both countries, as observed with chronic deaths, but in Scotland a second peak was observed in May of each year. The lowest contribution of seasonality was in September of each year in both countries. The difference in the decomposed monthly trend rate, between countries, for chronic deaths slightly decreases following the introduction of MUP, to the end of the study period (**Figure 5c; chronic deaths**). However, for acute deaths, the monthly trend rate starts to increase at a greater rate in Scotland, compared to England, which continues into the period following MUP implementation (**Figure 5c; acute deaths**).

3.1.4. Trends in partially attributable alcohol hospital admissions

Monthly rates of hospital admissions partially attributable to alcohol consumption were relatively stable in both Scotland and England throughout the study period, with some exceptions (**Figure 6a; all admissions**). The monthly rate in both countries dropped in March and April 2020, which was when a national lockdown had been implemented due to the COVID-19 pandemic. This reduction is therefore likely to be due to the impact of COVID-19 protection measures. Throughout the remainder of 2020, monthly rates rose but did not return to the level seen prior to the COVID-19 pandemic. Seasonality was present in both Scotland and England (**Figure 6b; all admissions**). Both countries experienced a peak in rates in February of each calendar year. In contrast, the lowest rates were observed in October in Scotland and in August in England. The contribution of seasonality was stable throughout the full study period. The decomposed monthly trend rate prior to the implementation of MUP was relatively stable in Scotland, with a slight increase observed in England which continued at an increased trajectory in the period following MUP implementation in Scotland (**Figure 6c; all admissions**). There was a relatively sharp rise in the monthly trend rate in Scotland between July 2018 and July 2019. From this point the monthly rate fell steadily in both countries. The difference in the decomposed monthly trend rate between Scotland and England slightly decreased following the introduction of MUP, to the end of the study period.

The trends previously described for all hospital admissions partially attributable to alcohol consumption, with the exception of seasonality, largely apply to both chronic and acute conditions (**Figure 6**). For chronic conditions, a peak in monthly rates in Scotland and England was observed in late winter (February and January, respectively) each calendar year and fell as the year progressed towards summer. For acute conditions the seasonal pattern was entirely opposite, with the peak in rates being observed in July and falling to a low in January, both in Scotland and England. The exception to this was a second smaller peak in rates which was seen in Scotland in December of each calendar year; this was not observed in England.

Figure 5. Partially attributable deaths (total, chronic and acute), crude rate per 100,000 population, Scotland and England, January 2012 to December 2020, (a) monthly rate, and decomposed (b) seasonal and (c) trend components



Note: the y-axis scale is different for acute deaths compared to all and chronic deaths.

Figure 6. Partially attributable hospital admissions (total, chronic and acute), crude rate per 100,000 population, Scotland and England, January 2012 to December 2020, (a) monthly rate, and decomposed (b) seasonal and (c) trend components

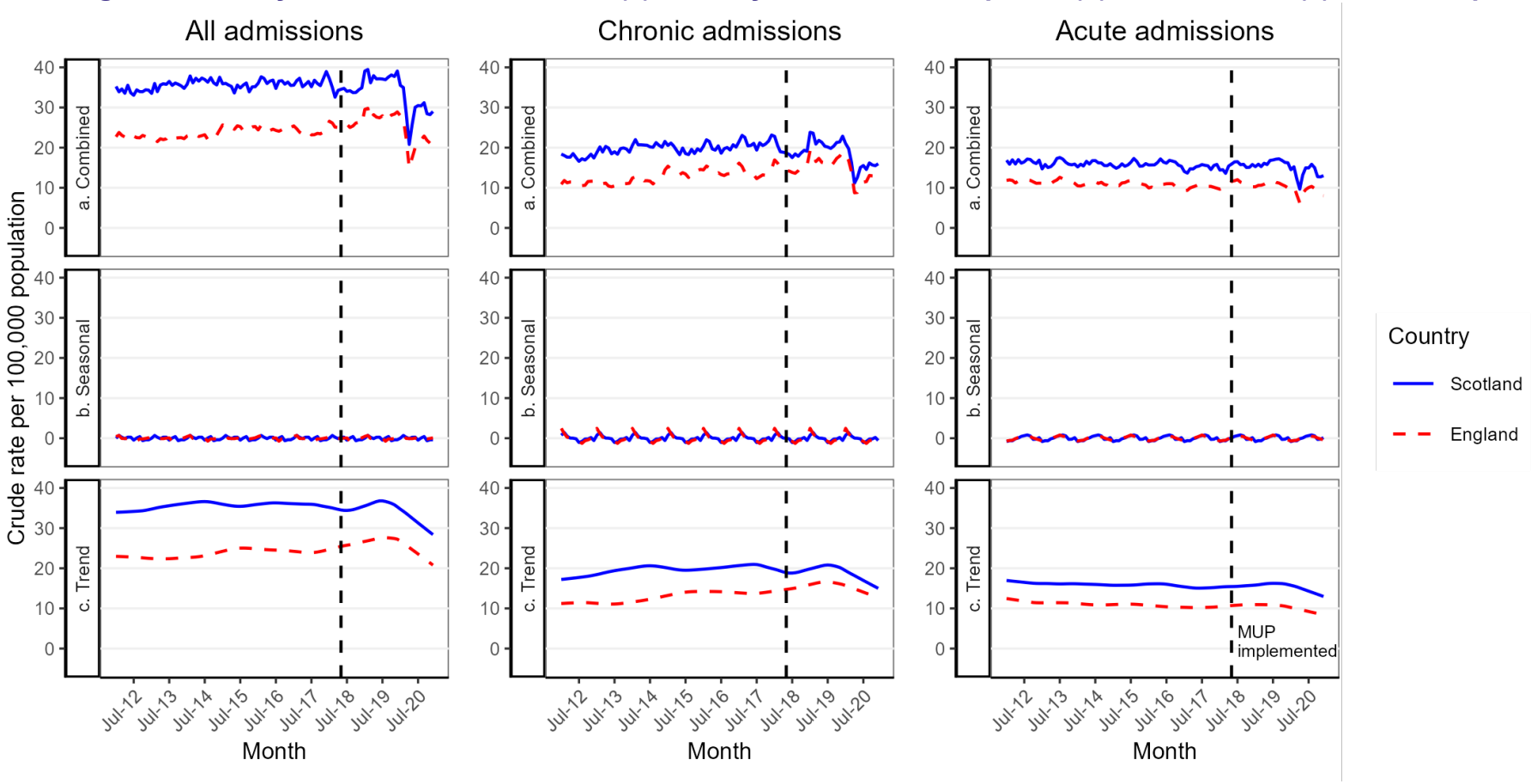


Table 3: Mean annual count of outcomes partially attributable to alcohol, 2012–2020, by country, sex, and age group

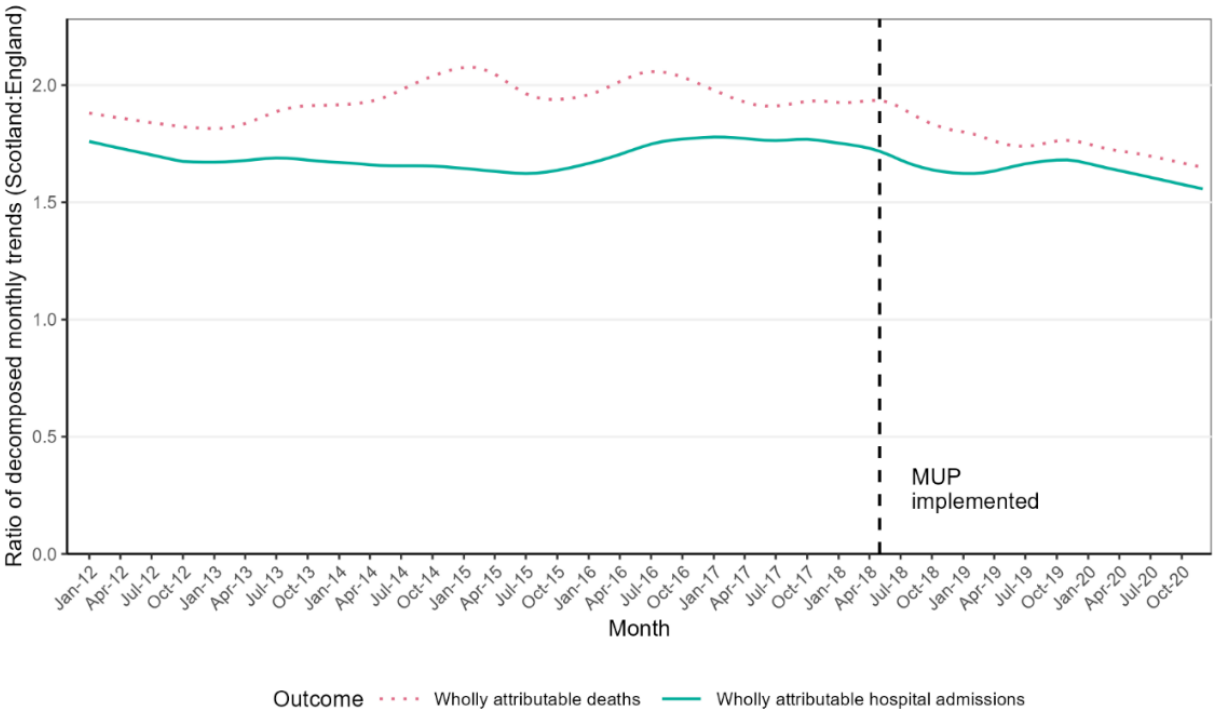
Partially attributable outcome per country	Total	Sex: Males	Sex: Females	Age group: 16 to 34 years	Age group: 35 to 64 years	Age group: 65+ years
Scotland: All deaths	**1,553**	**856**	**697**	**129**	**596**	**828**
Scotland: Chronic deaths	1,088	488	599	9	337	742
Scotland: Acute deaths	465	368	98	121	259	86
Scotland: All hospital admissions	**18,874**	**11,370**	**7,504**	**3,210**	**9,450**	**6,214**
Scotland: Chronic hospital admissions	10,453	5,688	4,765	520	5,602	4,331
Scotland: Acute hospital admissions	8,421	5,682	2,739	2,690	3,848	1,884
England: All deaths	**5,680**	**3,777**	**1,903**	**192**	**4,106**	**1,383**
England: Chronic deaths	5,296	3,514	1,781	148	3,805	1,342
England: Acute deaths	385	263	121	44	301	40
England: All hospital admissions	**12,9287**	**72,342**	**56,945**	**24,898**	**65,346**	**39,043**
England: Chronic hospital admissions	71,976	36,841	35,135	4,657	42,436	24,883
England: Acute hospital admissions	57,311	35,501	21,809	20,241	22,910	14,160

3.1.5. Comparative trends in overall health harms outcomes

Wholly attributable health harms

The ratio (Scotland:England) of monthly trend rates for wholly attributable deaths slightly increased from the start of the study period until the end of the pre-MUP period (**Figure 7**), indicating a worsening of wholly attributable deaths rates in Scotland compared to England. On the other hand, patterns for wholly attributable hospital admissions remained relatively stable during this period. Following the introduction of MUP, the ratio of monthly trend rates for wholly attributable death rates decreased until the end of the study period with some variation observed in the latter half of 2019, indicating that wholly attributable death rates improved in Scotland in this period, relative to England. The patterns following the implementation of MUP were also observed for wholly attributable hospital admissions, with consistency in variations across both deaths and hospital admissions wholly attributable to alcohol consumption.

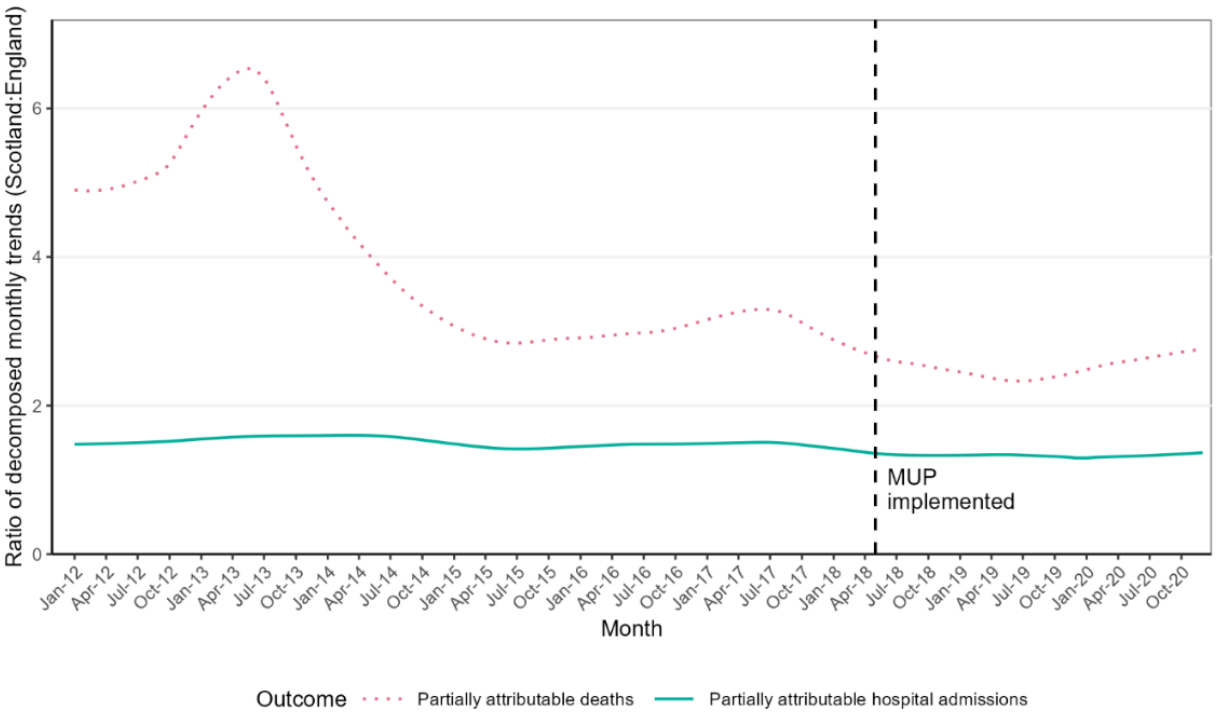
Figure 7. Ratio of decomposed monthly rates (Scotland:England) for wholly attributable deaths and hospital admissions, January 2012 to December 2020



Partially attributable health harms

The ratio (Scotland:England) of monthly trend rates for partially attributable deaths increased from the start of the study period (2012), peaking in 2013, and falling sharply until 2015 (**Figure 8**). Following this the ratio rose a little before starting to fall in 2017 and continued to do so throughout the remainder of the pre-MUP period. The pattern for partially attributable hospital admissions remained relatively stable during the same period. Following the implementation of MUP, the ratio of monthly trend rates for partially attributable death rates continued to decrease. However, from the end of 2019 to the end of the study period rates started to increase at a greater rate in Scotland relative to England. During this same period, the ratio of monthly trend rates for partially attributable hospital admissions was relatively stable until the end of the study period.

Figure 8. Ratio of decomposed monthly rates (Scotland:England) for partially attributable deaths and hospital admissions, January 2012 to December 2020



3.2. Impact of MUP on alcohol health harms

The results are presented for the Scottish controlled models only. When we refer to a reduction, an increase, or no change in a health outcome following the implementation of MUP, this is our best estimate of the impact of MUP in comparison to what could have been expected in the absence of MUP.

Results for the uncontrolled models can be found in the online Supplementary Appendix.

3.2.1. Overall impact of MUP on health harms

Wholly attributable outcomes

Deaths

Following the implementation of MUP, we estimate a significant 13.4% reduction (95% confidence interval (CI): -18.4% to -8.3%; p<0.001) in deaths wholly attributable to alcohol consumption in Scotland (**Figure 9**), when controlling for deaths in England. In the study period following the implementation of MUP, we estimate that, on average, 156 deaths (95% CI: -243 to -69) wholly attributable to alcohol consumption have been averted in Scotland each year.

The implementation of MUP was associated with an estimated 14.9% significant reduction (95% CI: -20.8% to -8.5%; p<0.001) in Scotland in deaths from chronic causes that are wholly attributable to alcohol consumption (**Figure 9**). We estimate that there were 186 fewer (95% CI: -253 to -119) deaths from chronic causes wholly attributable to alcohol consumption in Scotland each year following the implementation of MUP.

The implementation of MUP was associated with an estimated 6.6% increase (95% CI: -13.7% to 31.8%; p=0.55) in Scotland in deaths from acute causes that are wholly attributable to alcohol consumption (**Figure 9**), although there was greater uncertainty around this effect estimate, as indicated by the wide confidence interval

including zero. Our best estimate was an average annual increase of 10 (95% CI: -3 to 23) deaths due to acute causes in Scotland each year.

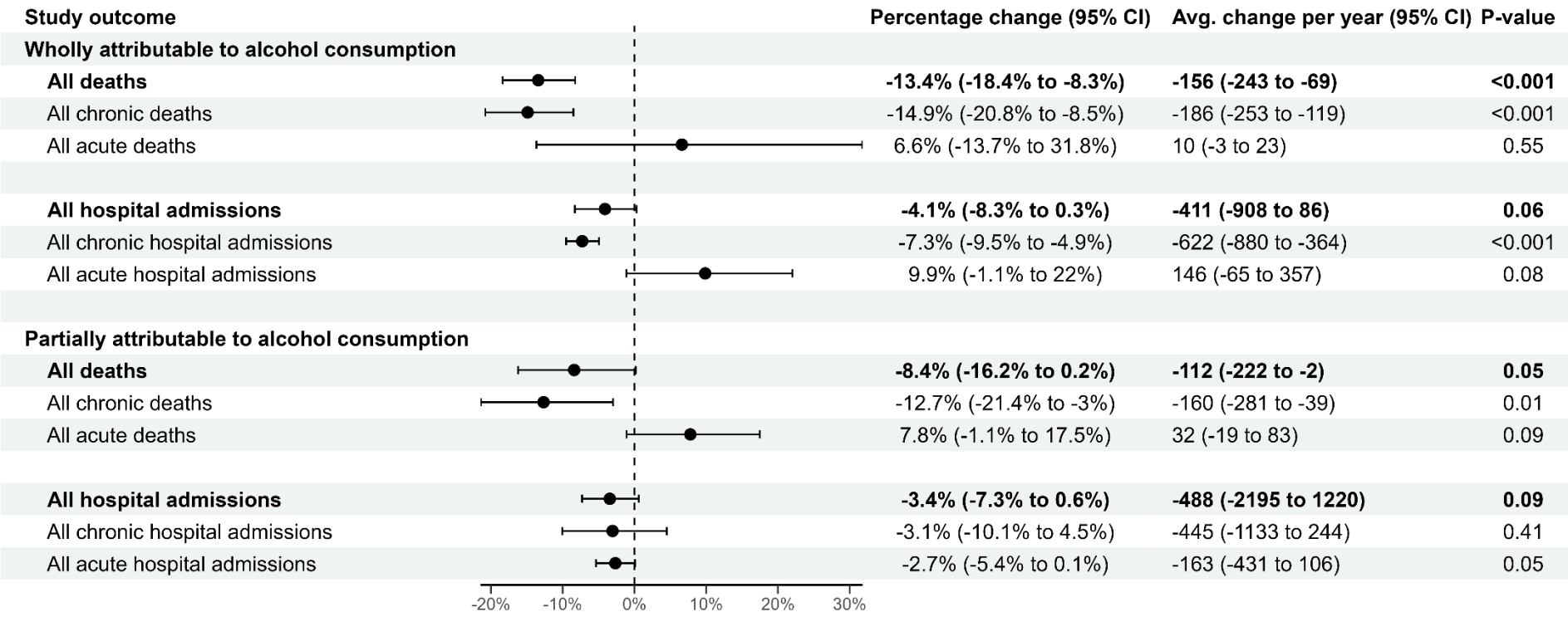
Hospital admissions

Following the implementation of MUP, we estimate an associated 4.1% reduction (95% CI: -8.3% to 0.3%; p=0.06) in hospital admissions wholly attributable to alcohol consumption in Scotland (**Figure 9**), when controlling for admissions in England, although the presence of this effect was more uncertain. In the study period following the implementation of MUP, we estimate that, on average, 411 fewer (95% CI: -908 to 86) hospital admissions wholly attributable to alcohol consumption have occurred in Scotland each year.

The implementation of MUP was associated with an estimated significant 7.3% reduction (95% CI: -9.5% to -4.9%; p<0.001) in Scotland in hospital admissions for chronic conditions wholly attributable to alcohol consumption (**Figure 9**). On average, we estimate that there were 622 fewer (95% CI: -880 to -364) hospital admissions for chronic conditions wholly attributable to alcohol consumption in Scotland each year over the study period following the implementation of MUP.

Following the implementation of MUP, we estimate a 9.9% increase (95% CI: -1.1% to 22%; p=0.08) in hospital admissions for acute conditions wholly attributable to alcohol consumption in Scotland, although there was greater uncertainty around this effect estimate than the significant decrease that was estimated for chronic conditions (**Figure 9**). The best estimate was an average annual increase of 146 (95% CI: -65 to 357) hospital admissions for acute conditions wholly attributable to alcohol consumption in Scotland each year.

Figure 9. Summary of overall changes in deaths and hospital admissions following MUP implementation



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|—|) do not cross zero.

Partially attributable outcomes

Deaths

Following the implementation of MUP, we estimate an 8.4% reduction (95% CI: -16.2% to 0.2%; p=0.05) in deaths partially attributable to alcohol consumption in Scotland (**Figure 9**), when controlling for deaths in England; this effect was less certain than that for deaths wholly attributable to alcohol consumption. Over the study period following the implementation of MUP, we estimate, on average, 112 deaths (95% CI: -222 to -2) partially attributable to alcohol consumption have been averted in Scotland each year.

The implementation of MUP was associated with an estimated significant 12.7% reduction (95% CI: -21.4% to -3.0%; p=0.01) in deaths from chronic causes that are partially attributable to alcohol consumption (**Figure 9**). We estimate that there were 160 fewer (95% CI: -281 to -39) deaths from chronic causes partially attributable to alcohol consumption each year due to the implementation of MUP in Scotland.

The implementation of MUP was associated with an estimated 7.8% increase (95% CI: -1.1% to 17.5%; p=0.09) in deaths from acute causes that are partially attributable to alcohol consumption, although there was greater uncertainty around this effect estimate than the significant decrease that was estimated for chronic causes (**Figure 9**). The best estimate was of an average annual increase of 32 (95% CI: -19 to 83) deaths from acute partially attributable causes in Scotland each year.

Hospital admissions

Following the implementation of MUP, we estimate a 3.4% reduction (95% CI: -7.3% to 0.6%; p=0.09) in hospital admissions partially attributable to alcohol consumption in Scotland (**Figure 9**), when controlling for admissions in England, although this effect was more uncertain, as indicated by the confidence interval crossing zero. Our best estimate was of 488 fewer (95% CI: -2,195 to 1,220) hospital admissions per year in Scotland, but noting the wide confidence interval indicating considerable uncertainty around this estimate.

There was limited evidence of any change in hospital admissions for chronic conditions partially attributable to alcohol consumption associated with the implementation of MUP in Scotland (-3.1%; 95% CI: -10.1% to 4.5%; p=0.41)) (**Figure 9**).

The implementation of MUP was associated with an estimated 2.7% reduction (95% CI: -5.4% to 0.1%; p=0.05) in hospital admissions for acute conditions that are partially attributable to alcohol consumption in Scotland, with some uncertainty around the presence of an effect (**Figure 9**). We estimate that over the study period following the implementation of MUP, on average 163 fewer (95% CI: -431 to 106) hospital admissions for acute conditions wholly attributable to alcohol consumption have occurred in Scotland each year.

Disease-specific outcomes

Deaths

We found that overall disease-specific outcomes for deaths wholly attributable to alcohol consumption indicated a positive impact from MUP (**Figure 10**). We estimate a significant 11.7% reduction (95% CI: -16.7% to -6.4%) in deaths from alcoholic liver disease in Scotland, when controlling for deaths in England, and a 23.0% significant reduction (95% CI: -36.9% to -6.0%) in deaths from alcohol dependence syndrome (**Figure 10**). There was little evidence of any change (0.4%; 95% CI: -3.8% to 4.9%) in deaths from liver cirrhosis (partially attributable to alcohol consumption) following MUP implementation (**Figure 10**).

Not all pre-specified outcomes could be estimated due to the small number of outcomes observed for some conditions.

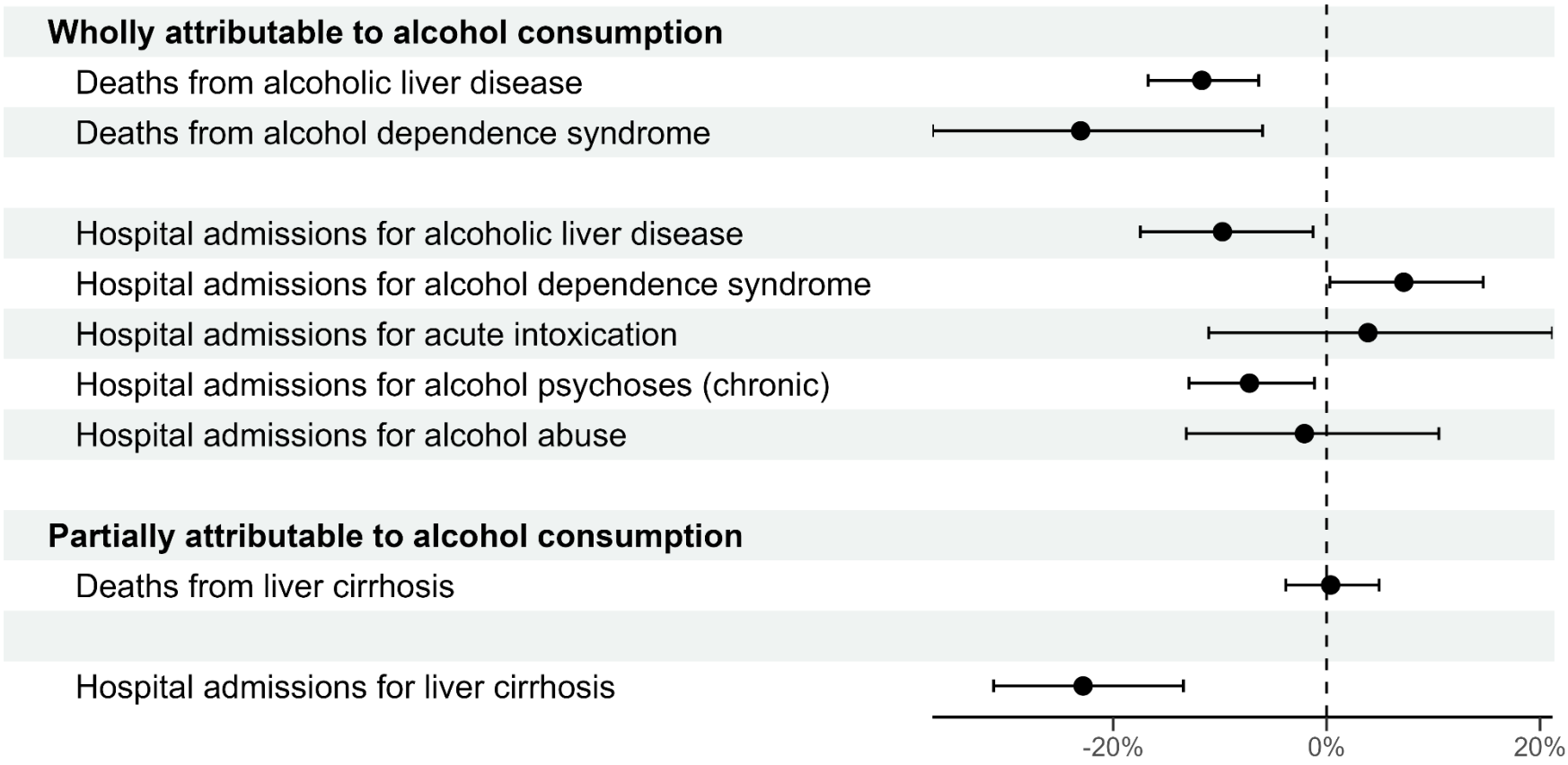
Hospital admissions

The impact of MUP on overall disease-specific outcomes wholly attributable to alcohol consumption varied (**Figure 10**). We estimated significant reductions in hospital admissions for: alcoholic liver disease (-9.8%; 95% CI: -17.5% to -1.3%) and alcohol psychoses (-7.2%; 95% CI: -12.9% to -1.1%) in Scotland, when controlling for

admissions in England (**Figure 10**). Conversely, we estimated a significant increase in hospital admissions for alcohol dependence syndrome (7.2%; 95% CI: 0.3% to 14.7%) in Scotland. We found little evidence of any change in hospital admissions for acute intoxication (3.9%; 95% CI: -11.0% to 21.2%) or alcohol abuse (-2.1%; 95% CI: -13.2% to 10.5%), following the implementation of MUP in Scotland (**Figure 10**).

We estimate a significant 22.8% reduction (95% CI: -31.2% to -13.4%) in hospital admissions for liver cirrhosis (partially attributable to alcohol consumption) following the implementation of MUP (**Figure 10**).

Figure 10. Percentage change in disease-specific outcomes following MUP implementation



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|—|) do not cross zero.

3.2.2. Impact of MUP on health harms by sex

Not all pre-specified outcomes could be estimated by sex. Where results have not been estimated, this was due to the small number of outcomes observed.

Wholly attributable outcomes by sex

Deaths

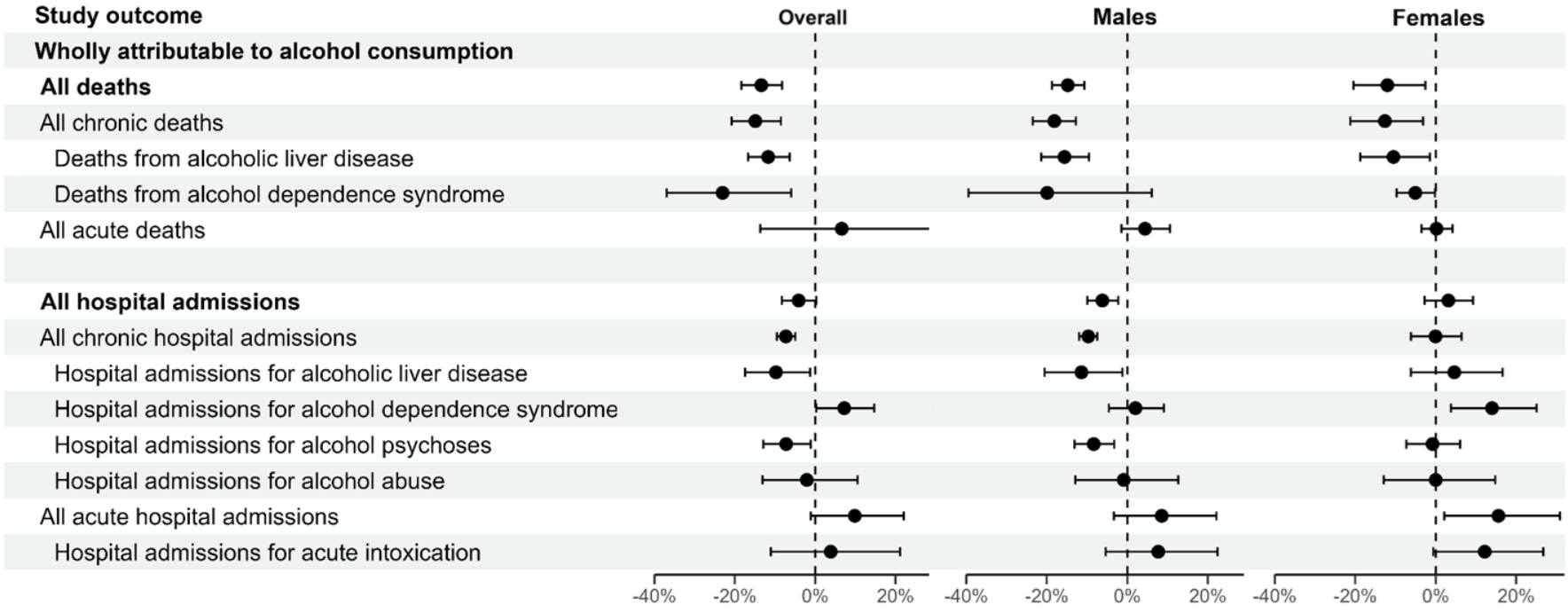
We estimate a 14.8% (95% CI: -18.7% to -10.7%) and a 12.0% significant reduction (95% CI: -20.5% to -2.6%), respectively for males and females, in deaths wholly attributable to alcohol consumption in Scotland (**Figure 11**), associated with the implementation of MUP. Significant reductions were estimated for deaths from chronic causes wholly attributable to alcohol consumption for males (-18.1%; 95% CI: -23.5% to -12.8%) and females (-12.6%; 95% CI: -21.3% to -3.1%) in Scotland. For deaths from specific diseases among males, we estimated a significant reduction in deaths from alcoholic liver disease (-15.6%; 95% CI: -21.3% to -9.5%) and a reduction in deaths from alcohol dependence syndrome (-19.9%; 95% CI: -39.5% to 6.1%), albeit there was greater uncertainty around the presence of an effect for male deaths from alcohol dependence syndrome, as indicated by the comparatively wider confidence interval. We estimated significant reductions in disease-specific deaths among females following MUP implementation (alcoholic liver disease (-10.5%; 95% CI: -18.8% to -1.5%) and alcohol dependence syndrome (-5.1%; 95% CI: -9.7% to -0.2%)). However, there was an estimated 4.4% increase (95% CI: -1.5% to 10.6%) in acute deaths wholly attributable to alcohol consumption among males, although there was greater uncertainty around the presence of an effect than that estimated significant reduction for chronic conditions. For females, there was little evidence of any change in the rate of acute deaths wholly attributable to alcohol consumption (0.2%; 95% CI: -3.5% to 4.2%) associated with the implementation of MUP.

Hospital admissions

For males, we estimated a 6.2% significant reduction (95% CI: -10.0% to -2.3%) in hospital admissions for conditions wholly attributable to alcohol consumption in Scotland (**Figure 11**), when controlling for hospital admissions in England, following the implementation of MUP. We estimated a significant reduction in hospital admissions for chronic conditions wholly attributable to alcohol consumption among males (-9.7%; 95% CI: -11.9% to -7.5%), but not females (0.0%; 95% CI: -6.1% to 6.4%), associated with the implementation of MUP. There were estimated significant reductions in hospital admissions for alcoholic liver disease (-11.4%; 95% CI: -20.5% to -1.2%) and alcohol psychoses (-8.4%; 95% CI: -13.2% to -3.2%) among males in Scotland. We found limited evidence of any change in hospital admissions for alcohol dependence syndrome (2.0%; 95% CI: -4.6% to 9.1%) or alcohol abuse (-0.9%; 95% CI: -12.9% to 12.6%) for males in Scotland, following the implementation of MUP. There was some evidence of an increase in hospital admissions for acute conditions wholly attributable to alcohol consumption among males (8.5%; 95% CI: -3.3% to 22.1%) and specifically for acute intoxication (7.7%; 95% CI: -5.4% to 22.4%), although there was greater uncertainty around the presence of these effects (**Figure 11**).

Among females, there was some evidence of an increase (3.1%; 95% CI: -2.8% to 9.3%) in hospital admissions for conditions wholly attributable to alcohol consumption following the implementation of MUP, although there was some uncertainty around the presence of an effect (**Figure 11**). There was no substantial evidence of any change in hospital admissions for any of the specific chronic conditions following the implementation of MUP, with the exception of alcohol dependence syndrome in which a significant increase (14.0%; 95% CI: 3.8% to 25.1%) was observed. For hospital admissions for acute conditions wholly attributable to alcohol, we estimated a significant increase (15.6%; 95% CI: 2.1% to 30.9%) for females in Scotland (**Figure 11**).

Figure 11. Percentage change in wholly attributable outcomes following MUP implementation, by sex



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|—|) do not cross zero.

Partially attributable outcomes by sex

Deaths

For all deaths that were partially attributable to alcohol consumption we estimated a significant 9.6% reduction (95% CI: -16.8% to -1.8%) for females in Scotland (**Figure 12**), when controlling for deaths in England, following the implementation of MUP. Among males we also estimated a reduction (-4.9%; 95% CI: -13.1% to 4.1%) in partially alcohol-attributable deaths, although there is more uncertainty around the presence of this effect.

We estimated significant reductions for deaths due to chronic causes that were partially attributable to alcohol consumption for both males (-14.3%; 95% CI: -24.0% to -3.3%) and females (-13.8%; 95% CI: -20.5% to -6.5%) in Scotland (**Figure 12**). There was little evidence of any change in deaths from liver cirrhosis for males (-0.8%; 95% CI: -5.7% to 4.3%), and some evidence of an increase (9.3%; 95% CI: -20.5% to 50.5%) among females, although this effect was more uncertain (**Figure 12**). There was some evidence of an increase (8.4%; 95% CI: -1.3% to 19.1%) in acute deaths partially attributable to alcohol consumption for males, following the implementation of MUP, and less convincing evidence for females (3.3%; 95% CI: -8.1% to 15.6%), but with some uncertainty around the presence of these effects.

Hospital admissions

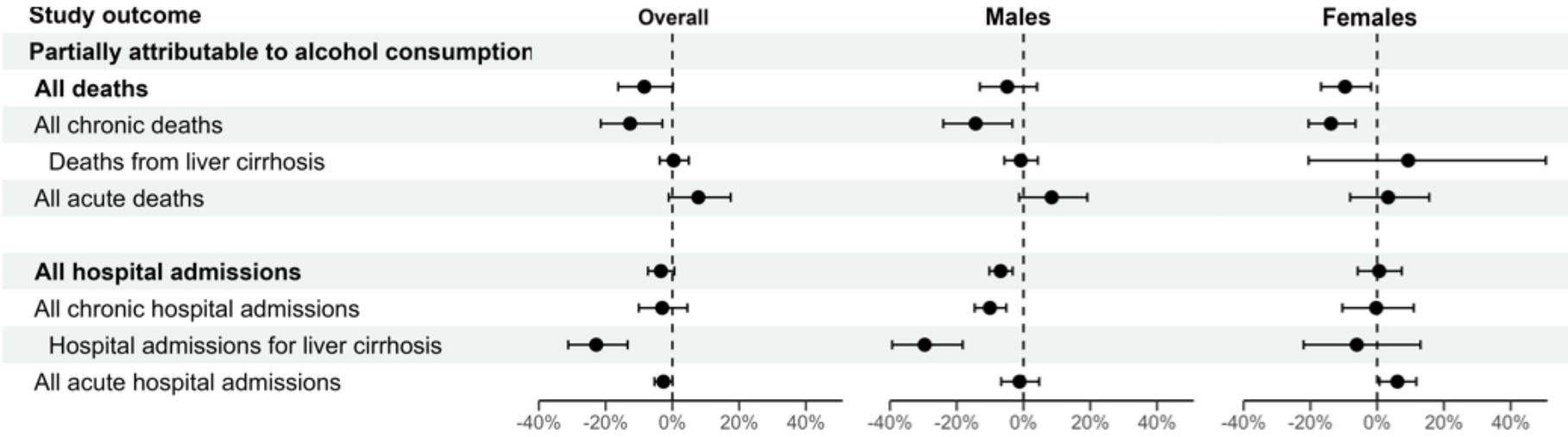
We estimated a significant 6.9% reduction (95% CI: -10.2% to -3.2%) in hospital admissions for conditions partially attributable to alcohol consumption for males in Scotland, when controlling for admissions in England, following the implementation of MUP (**Figure 12**). We found little evidence that MUP had impacted hospital admissions for conditions partially attributable to alcohol consumption for females (0.6%; 95% CI: -5.8% to 7.4%) (**Figure 12**).

Among males, we estimated a significant reduction for hospital admissions for chronic conditions partially attributable to alcohol consumption (-10.1%; 95% CI: -14.6% to -5.2%), but found little evidence of any change for acute conditions

partially attributable to alcohol consumption (-1.2%; 95% CI: -6.7% to 4.7%). In particular, MUP was associated with a significant reduction in male hospital admissions for liver cirrhosis (-29.6%; 95% CI: -39.3% to -18.2%).

There was little evidence of any change in hospital admissions for chronic conditions partially attributable to alcohol consumption among females (-0.3%; 95% CI: -10.4% to 11.0%), including for liver cirrhosis (-6.1%; 95% CI: -22.0% to 13.0%) (**Figure 12**). We estimated that the implementation of MUP was associated with a significant increase in female hospital admissions for acute conditions partially attributable to alcohol consumption (6.1%; 95% CI: 0.7% to 11.7%) (**Figure 12**).

Figure 12. Percentage change in partially attributable outcomes following MUP implementation, by sex



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|——|) do not cross zero.

3.2.3. Impact of MUP on health harms by age group

Not all pre-specified outcomes could be estimated for each age group. Where results have not been estimated, this was due to the small number of outcomes observed.

Wholly attributable outcomes by age group

Deaths

We were unable to assess any mortality outcomes for the age group 16 to 34 years due to the relatively small number of outcomes observed.

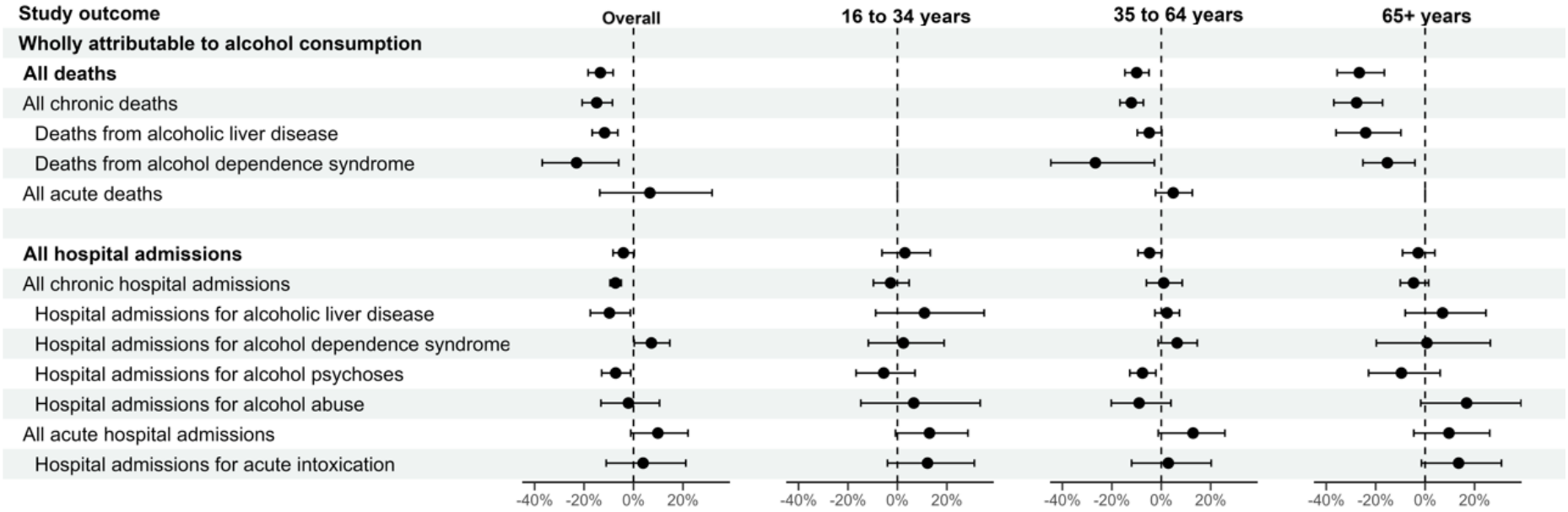
We estimated significant reductions for the 35 to 64 years (10.0%; 95% CI: -14.7% to -5.0%) and the 65 years and above (26.7%;95% CI: -35.6% to -16.5%) age groups, in deaths wholly attributable to alcohol consumption in Scotland, when separately controlling for deaths in those age groups in England, associated with the implementation of MUP (**Figure 13**). Significant reductions were observed for deaths from chronic causes wholly attributable to alcohol consumption for those aged 35 to 64 years (-12.1%; 95% CI: -16.7% to -7.2%) and for those aged 65 years and above (-27.7%; 95% CI: -36.9% to -17.2%). Estimated significant reductions in cause-specific deaths associated with MUP were observed for those aged 35 to 64 years (alcoholic liver disease (-4.9%; 95% CI: -9.7% to -0.2%) and alcohol dependence syndrome (-26.7%; 95% CI: -44.7% to -2.8%)), and for those aged 65 years and above (alcoholic liver disease (-24.0%; 95% CI: -36.0% to -9.8%); alcohol dependence syndrome (-15.3%; 95% CI: -25.2% to -4.1%); and alcohol psychoses (-14.4%; 95% CI: -21.1% to -7.1%)). However, there was some evidence of an estimated 4.8% increase (95% CI: -2.3% to 12.6%) in acute deaths wholly attributable to alcohol consumption in those aged 35 to 64 years associated with the implementation of MUP, although the presence of this effect was more uncertain than the significant reductions in deaths from wholly attributable chronic causes observed for this age group. We were unable to estimate the impact of MUP on deaths due to wholly attributable acute causes for those aged 65 years and above due to the relatively small number of outcomes observed.

Hospital admissions

We found that the impact of MUP on hospital admissions for conditions wholly attributable to alcohol consumption was not uniform across age groups (**Figure 13**). We found little evidence of any change in hospital admissions for conditions wholly attributable to alcohol consumption for those aged 16 to 35 years (3.0%; 95% CI: -6.2% to 13.3%) or for those aged 65 and over (-2.8%; 95% CI: -9.2% to 3.9%). We estimated a reduction of 4.8% (95% CI: -9.4% to 0.2%) for those aged 35 to 64 years, acknowledging a degree of uncertainty around the presence of this effect as indicated by the confidence interval including zero.

We estimated increases in hospital admissions for acute conditions wholly attributable to alcohol consumption across all age groups, with a degree of uncertainty around the presence of the effect in each case. We also found a reduction in hospital admissions for chronic conditions wholly attributable to alcohol consumption for those aged 65 years and above (-4.7%; 95% CI: -10.1% to 1.4%), again with a degree of uncertainty around the presence of an effect as indicated by the confidence interval including zero. There was some evidence that MUP was associated with reductions in hospital admissions for alcohol psychoses in each age group. The estimated effect of MUP associated with changes in other condition-specific hospital admission outcomes varied by age group.

Figure 13. Percentage change in wholly attributable outcomes following MUP implementation, by age group



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|——|) do not cross zero.

Partially attributable outcomes by age group

Deaths

We estimated that there was little evidence of change in deaths partially attributable to alcohol consumption for those aged 16 to 34 years (4.6%; 95% CI: -31.9% to 60.8%) or those aged 35 to 64 years (0.7%; 95% CI: -6.6% to 8.7%) associated with the implementation of MUP (**Figure 14**) when controlling for deaths in that age group in England. However, in those aged 65 years and above, MUP was associated with an estimated 14.4% reduction (95% CI: -27.2% to 0.6%) in deaths partially attributable to alcohol consumption, although there was a degree of uncertainty about the presence of this effect.

For those aged 35 to 64 years, estimated reductions in deaths from chronic causes partially attributable to alcohol consumption (-6.8%; 95% CI: -14.4% to 1.5%) were offset by estimated increases in deaths from acute causes partially attributable to alcohol consumption (5.1%; 95% CI: -3.7% to 14.8%) although there was a greater degree of uncertainty about the presence of these effects as indicated by the confidence interval including zero. In those aged 65 years and above, MUP was associated with a significant reduction in chronic causes of death partially attributable to alcohol consumption (-18.8%; 95% CI: -30.8% to -4.7). There was some evidence of a reduction for acute causes of deaths partially attributable to alcohol consumption (-5.7%; 95% CI: -16.4% to 6.3%), although there was considerable uncertainty around the presence of this effect.

We estimated that there was little evidence of change in deaths from liver cirrhosis for those aged 35 to 64 years (0.6%; 95% CI: -3.2% to 4.6%), and those aged 65 years and above (3.9%; 95% CI: -15.4% to 27.4%).

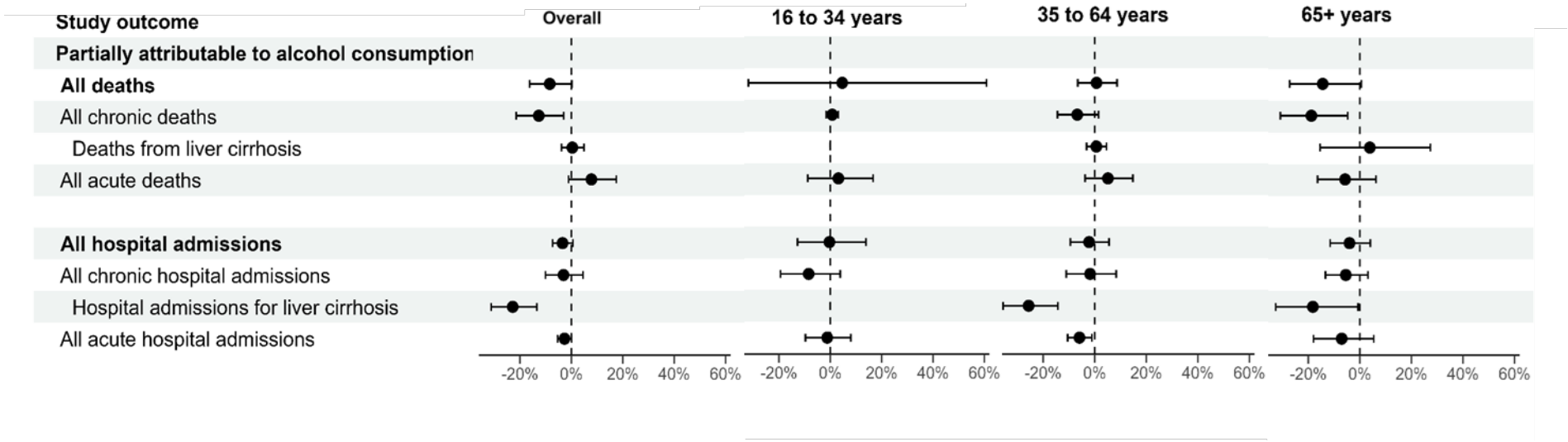
Hospital admissions

We found little evidence of any change in hospital admissions for conditions partially attributable to alcohol consumption by age group (**Figure 14**): 16 to 35 years (-0.3%;

95% CI: -12.8% to 13.9%); 35 to 64 years (-2.2%; 95% CI: -9.4% to 5.5%); and 65 years and above (-4.0%; 95% CI: -11.5% to 4.1%).

We estimated that MUP was associated with significant reductions in hospital admissions for liver cirrhosis in 35- to 64-year-olds (-25.6%; 95% CI: -35.5% to -14.3%) and in those aged 65 years and above (-18.2%; 95% CI: -32.6% to -0.7%).

Figure 14. Percentage change in partially attributable outcomes following MUP implementation, by age group



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|——|) do not cross zero.

3.2.4. Impact of MUP on health harms by deprivation

Not all pre-specified outcomes could be estimated by deprivation decile. Where results have not been estimated, this was due to the small number of outcomes observed.

Wholly attributable outcomes by deprivation

Deaths

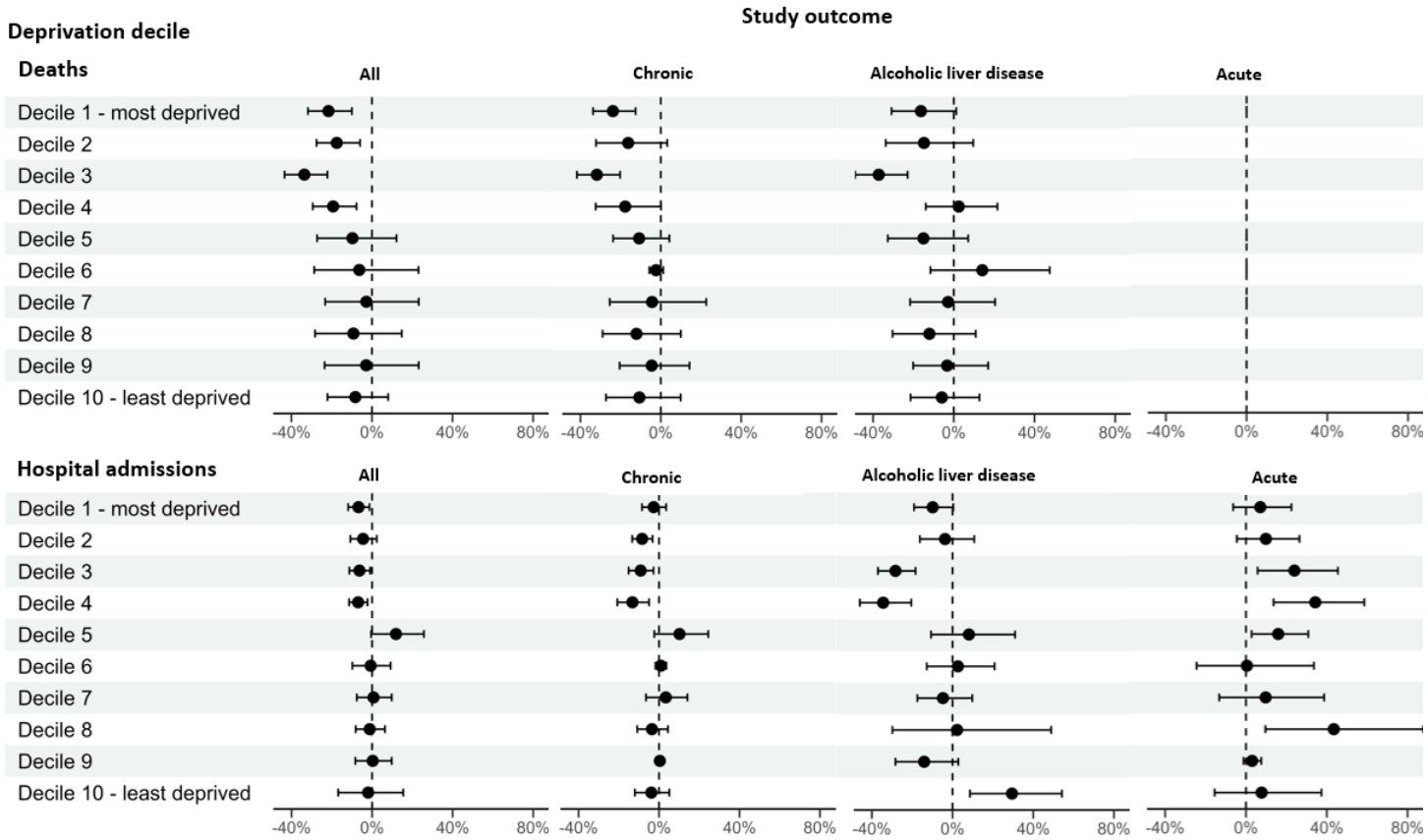
Our best estimate of effect was that MUP was associated with significantly reduced deaths wholly attributable to alcohol consumption in the four most deprived deciles (deciles 1 to 4) (**Figure 15**). There was little evidence regarding a change in deaths wholly attributable to alcohol consumption for deprivation deciles 5 to 10. In the most deprived decile, we estimated a significant 21.6% reduction (95% CI: -31.8% to -10.0%) in deaths wholly attributable to alcohol consumption associated with the implementation of MUP. The magnitude and trend of estimated reductions in deaths from chronic causes wholly attributable to alcohol consumption were similar to those described above for deaths wholly attributable to alcohol consumption. We found that MUP was associated with an estimated decrease in deaths from alcoholic liver disease in the three most deprived deciles, with the largest estimated significant reduction in decile 3 (-33.6%; 95% CI: -43.4% to -22.1%).

Hospital admissions

Hospital admissions for conditions wholly attributable to alcohol consumption reduced across the four most deprived deciles following the implementation of MUP (**Figure 15**). Significant reductions were found for deciles 1, 3 and 4, whereas the effect for decile 2 was more uncertain. In the most deprived decile, total hospital admissions for conditions wholly attributable to alcohol consumption significantly reduced by 6.8% (95% CI: -11.9% to -1.3%). For the other deprivation deciles, changes were smaller, with the exception of decile 5 where we estimated an increase in total hospital admissions for conditions wholly attributable to alcohol consumption

of 11.9% (95% CI: -0.5% to 25.7%), although there was greater uncertainty around the presence of this effect as indicated by the confidence interval including zero. The magnitude and trend of changes in hospital admissions for chronic conditions wholly attributable to alcohol consumption were similar to those described above for total hospital admissions wholly attributable to alcohol consumption. Changes in hospital admissions for alcoholic liver disease also generally followed these patterns, with the exception of the least deprived decile where we estimated a significant increase in these hospital admissions of 29.4% (95% CI: 8.6% to 54.2%). We estimated increases in hospital admissions for acute conditions wholly attributable to alcohol consumption across several deprivation deciles, with varying levels of certainty around the presence of the effect across the deciles.

Figure 15. Percentage change in wholly attributable outcomes following MUP implementation, by deprivation decile



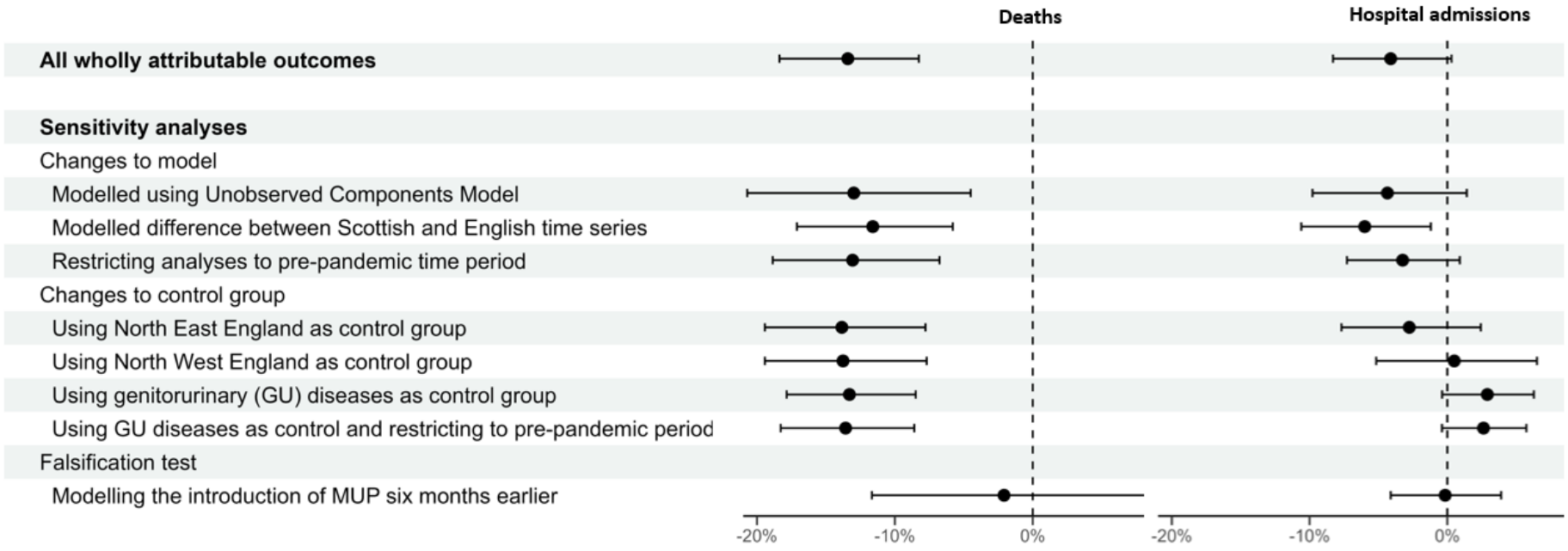
Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|—|) do not cross zero.

3.2.5. Sensitivity analyses

We performed sensitivity analyses to test the robustness of our study findings that MUP was associated with an estimated 13.4% significant reduction in deaths wholly attributable to alcohol consumption. The results of our sensitivity analyses confirm this result, with our sensitivity analyses ranging from an estimated significant reduction of 11.6% to 13.8% (**Figure 16**). In the falsification test, where we modelled the introduction of MUP six months before its actual implementation, we found little evidence of any impact being associated with the false implementation date (-2.1%; 95% CI: -11.7% to 8.5%). This increases the likelihood that our main findings are attributable to the implementation of MUP, following the true implementation date.

There was greater variation in the results of our sensitivity analyses to test the robustness of our study, finding that MUP was associated with an estimated 4.1% reduction in hospital admissions for conditions wholly attributable to alcohol consumption. The use of a different analytical method (-4.4%; 95% CI: -9.8% to 1.4%) and restricting the analysis time frame to pre-pandemic periods (-3.2%; 95% CI -7.3% to 0.9%) yielded the most similar estimates, but as with the main estimate of 4.1%, had a higher degree of uncertainty associated with the presence of the effect. In the falsification test, where we modelled the earlier introduction of MUP, we found this not to be associated with any change in hospital admissions (-0.2%; 95% CI: -4.1% to 3.9%). This increases the likelihood that our findings are attributable to the implementation of MUP, following the true implementation date. The main differences we observed, compared to our main estimate, were driven by the choice of control group. We found that using north-east England confirmed the estimated direction of the result although the estimated effect was smaller and had greater uncertainty associated (-2.8%; 95% CI: -7.7% to 2.4%), whereas when using north-west England as a control group (0.5%; 95% CI: -5.2% to 6.5%) we found little evidence that MUP was associated with a change in hospital admissions for conditions wholly attributable to alcohol consumption. Using a non-geographical control group indicated that MUP was associated with an increase in hospital admissions for conditions wholly attributable to alcohol consumption.

Figure 16. Results of sensitivity analyses undertaken on overall health harms outcomes



Note: Models include trends in deaths or admissions (as per the outcome of interest) in England (geographical control) as a covariate, adjustment for underlying seasonal and secular trends, and for the introduction of COVID-19-related restrictions. Effect estimates (●) are statistically significant to the 95% level where the confidence limits (|—|) do not cross zero.

4. Discussion

4.1. Main findings

Our study of just over two and a half years following the introduction of MUP provides evidence that the implementation of the policy reduced deaths and hospital admissions attributable to alcohol consumption relative to what might have been expected in the absence of MUP. Based on the controlled interrupted time series results, our best estimate was a significant reduction in deaths wholly attributable to alcohol consumption of 13.4%, equivalent to averting 156 deaths per year, on average. Our best estimate for the impact of MUP on hospital admissions was a reduction of 4.1% in hospital admissions for conditions wholly attributable to alcohol consumption, equivalent to averting 411 hospital admissions per year, on average. There was greater uncertainty surrounding our main findings for hospital admissions, compared to deaths, wholly attributable to alcohol consumption.

These results give us an estimate of the difference between study outcomes following the implementation of MUP, compared to a counterfactual situation in which MUP was never implemented. The counterfactual situation was developed by incorporating time series data for Scotland prior to the implementation of MUP, and for the full time period from England, where MUP was not implemented. This two-step approach allowed us to generate a robust estimate for comparison purposes, of the outcomes expected if MUP had not been implemented, as well as adjusting for underlying seasonality and secular trends. Therefore, it is reasonable to conclude that MUP caused the reductions observed, and not some other external factor.

We found that the greatest reductions in deaths and hospital admissions wholly attributable to alcohol consumption were in the four most deprived deciles, highlighting the positive impact MUP has had in contributing to tackling deprivation-based inequalities in alcohol-attributable health harms. The impact of MUP on deaths attributable to alcohol consumption was positive for males and females, and across age groups. Additionally, we found that MUP had a positive impact in reducing the impact of liver- and neuropsychiatric-related deaths (alcoholic liver disease and

alcohol dependence syndrome). The impact of MUP on hospital admissions attributable to alcohol consumption was generally positive across sub-groups.

There were potential indications that MUP led to a worsening of acute outcomes, for both deaths and hospital admissions wholly attributable to alcohol consumption. Due to acute outcomes making up a relatively small proportion of alcohol harms (6% of deaths wholly attributable to alcohol consumption; 17% of hospital admissions wholly attributable to alcohol consumption), these estimates were highly uncertain with wide confidence intervals. However, these findings were found across almost all sub-groups. Improvements in chronic outcomes drove changes in overall outcomes, offset slightly by small increases in adverse acute consequences. However, overall there is a net benefit of the policy on overall deaths and hospital admissions, findings which were confirmed in almost all sub-group analyses (sex, age group and deprivation decile).

Similar to results observed for deaths wholly attributable to alcohol consumption, the impact of MUP on deaths partially attributable to alcohol was not uniform across chronic and acute deaths. However, the scale of reduction in deaths from chronic causes partially attributable to alcohol consumption more than offset any potential increase in deaths from acute causes partially attributable to alcohol consumption to produce an overall net benefit on total deaths partially attributable to alcohol consumption associated with the implementation of MUP.

Hospital admissions for chronic and acute conditions partially attributable to alcohol consumption have been positively influenced by the implementation of MUP, which slightly differs to the non-uniform impact on chronic and acute conditions hospital admissions wholly attributable to alcohol consumption.

4.2. Strengths and limitations

A key strength of our study lies in its use of routinely collected health outcome data. Scottish and English mortality death registration systems are known to be high-quality data sources with good completion of cause of death information and associated demographic attributes, such as age and sex. This gives us a high level of certainty that the mortality data we have used to identify outcomes attributable to

alcohol consumption is of the highest possible quality. This is also true for outcomes identified using hospital admissions data, but to a lesser extent. The occurrence of hospital admissions outcomes can be artefactually impacted, for example increases in system pressures such as bed and workforce capacity could reduce admissions, giving the misleading impression that harms had gone down. Many of these system pressures have been exacerbated by the COVID-19 pandemic, although these same pressures were increasing during the pre-pandemic periods.[53,54] Hospital admission outcomes may also be impacted by variations in clinical practice. Mortality outcomes are a more direct measure of alcohol-related harms and thus there is less uncertainty associated with their interpretation, compared to hospital admissions.

We were unable to obtain hospital admissions data on a complete like-for-like basis between Scotland and England. Our Scottish data included outcomes from both general and mental health inpatient and day cases, whereas our data for England only reflected general inpatient and day cases. At an aggregate level, this is less likely to be problematic assuming that there is no divergence in trends in mental health inpatient and day cases between Scotland and England. However, there will be additional uncertainty when interpreting results for individual outcomes, given there may be an underlying element of immortal time bias from the potential exclusion of a time interval in a patient's hospital stay, which may result in a different outcome classification.[55] Generally mental health inpatient and day cases would be expected to indicate a higher level of neuropsychiatric outcomes than general inpatient and day cases. As we select the first details in a stay, there may be a degree of artefactual differences in that neuropsychiatric outcomes are over-represented in Scotland, relative to England. Conversely this could mean that alcoholic liver disease may be under-represented in Scotland, relative to England, if patients were to have initially presented for a neuropsychiatric condition and are subsequently treated for alcoholic liver disease.

We assessed a wide range of aggregate and individual outcomes, which range from those wholly and partially attributable to alcohol consumption, to specific alcohol-attributable conditions. Some represent stronger evidence than others that changes observed were due to MUP-led changes in alcohol consumption. There are important differences in the levels of certainty associated with each level of attributability, which

are independent of any uncertainty associated with interpreting outcomes that occur infrequently. Wholly attributable health harms, such as alcoholic liver disease, can be interpreted with a high degree of certainty, attributed to alcohol consumption and to specific time periods. On the other hand, estimates of partially attributable health harms represent a hypothetical situation in that the fraction of health harm attributable to alcohol is estimated based on current levels of alcohol consumption being reduced to a theoretical minimum risk exposure level. They are also varied in relation to lag-periods between exposure and incidence of alcohol-related health harms. For example, changes in the incidence of cancer outcomes would take much longer to be realised than changes in the incidence of liver cirrhosis outcomes. Therefore, while partially attributable harms are an important part of the potential benefit of MUP, there remains less certainty around when these would be expected to be realised and what proportion of the change in those harms should be attributed to any change in alcohol consumption caused by MUP. Their occurrence could also be influenced by exposure to other risk factors or by the success of other public health or medical interventions. This raises further uncertainty over the degree to which we can confidently assert changes in partially attributable health harms to MUP.

Controlled interrupted time series analysis is a well-established method used to evaluate interventions that are implemented across a whole population. It allows for the observed situation following an intervention to be modelled against a counterfactual situation of what might have happened had the intervention not been implemented. It develops this counterfactual by accounting for existing underlying trends in the pre-intervention time series, and those observed in a control area.

We incorporated outcome data for the best available geographical control, England, into our models. By comparing with and controlling for any change in alcohol health harms in England in the pre-MUP time period, and the post-implementation time period of over two and a half years, we can be more confident that any observed changes in Scotland are due to MUP rather than another external factor that might affect alcohol consumption and health harms in both Scotland and England.

Given that the COVID-19 pandemic hit the UK during the post-implementation period, affecting where people were able to purchase and consume alcohol, including a

geographical control area with similar purchasing and consumption habits to Scotland was of particular importance. We included adjustment for the physical distancing, and other associated measures, implemented in the UK in response to the COVID-19 pandemic. We did that separately for Scotland and England to account for differences in how and when restrictions were introduced by the different governments. We also carried out a sensitivity analysis which used a shorter follow-up period to remove any potential pandemic-related impacts, which yielded similar results.

We ran a series of sensitivity analyses to test the robustness of the results from our primary model and obtained largely similar results for death outcomes, substantiating the interpretation of these results.

4.3. Interpretation

Previous findings have indicated that alcohol sales reduced by 1.1% in Scotland, and increased by 2.4% in England & Wales, in the period following the implementation of MUP. The introduction of MUP has therefore been protective against the backdrop of recent trends in alcohol consumption in the UK, with a best estimate that MUP had reduced alcohol population-level sales by 3.0% in Scotland compared to what would have been expected in the absence of MUP.[56,57] Several prior studies have evidenced that the greatest reductions in alcohol sales were found in households that had purchased the most alcohol prior to MUP being implemented.[58,59,60] Our study found that the implementation of MUP, and subsequent reduction in alcohol sales, has reduced alcohol health harms in Scotland. Deaths wholly attributable to alcohol consumption significantly reduced by 13.4%, and hospital admissions wholly attributable to alcohol consumption reduced by 4.1%. The impact of MUP was well-aligned with health harms outcomes in terms of public health importance; that is the results were most positive in reducing deaths attributable to alcohol consumption, followed by reducing hospital admissions for chronic conditions. However, reducing morbidity remains an important goal of public health. We also found that MUP reduced deaths and admissions partially attributable to alcohol consumption. It is likely that effective strategies to reduce alcohol-related health harms will have wider impacts, mitigating the scale of challenge faced from non-communicable diseases

now, and in the future.[61] Although these estimates are more uncertain, they suggest that MUP is contributing to the reduction of wider health harms caused by alcohol-related non-communicable diseases.

We found larger reductions in health harms in the four most deprived deciles, and for males, which are sub-groups where alcohol-related health harms are disproportionately high, indicating the positive impact of MUP in tackling health inequalities. It has been illustrated previously that the sub-groups that suffer the greater health harms from alcohol tend to purchase the cheapest alcohol.[62] Additionally, the dose-response relationship between alcohol consumption and most attributable harms are exponential, which mean that risk reductions are greater for changes in heavier drinkers, compared to moderate drinkers, if both groups reduced their consumption by the same level.[63] Given that MUP has led to changes in these product types, our findings are consistent with the mechanisms outlined in the MUP theory of change. Additionally, as our estimates for the impact of MUP on deaths are generally greater than the impact on hospital admissions, this could be partly explained by the success of increasing the lifespan of individuals who would otherwise have died had MUP not been implemented. It is likely that those individuals remain vulnerable to alcohol-attributable health harms and therefore require additional preventative, routine and emergency support from the health and care system to prevent further health harms from alcohol consumption.

We found that the impact of MUP was most positive in tackling chronic outcomes. These include those related to alcoholic liver disease and neuropsychiatric disorders. We did not observe any negative impacts of MUP on alcohol psychoses (including alcoholic withdrawal) across sub-groups. We observed a worsening of acute outcomes (intoxication/poisoning) following the introduction of MUP, although these findings had the highest degree of uncertainty associated with them. The high degree of uncertainty was, in part, due to the fact that these outcomes account for a very small proportion of overall alcohol health harms. This may warrant further investigation to investigate potential mechanisms. One such mechanism based on evidence from other studies might be that some groups have reduced spending on and intake of food due to spending more on alcohol.[64] This could plausibly lead to faster intoxication. Another possible explanation is that some dependent drinkers and

their family members reported switching from cider to spirits (particularly vodka). Although this may have led to an overall reduction in their consumption, it could lead to quicker intoxication.[65]

Recent estimates of alcohol-specific mortality, during the COVID-19 pandemic, have indicated a worsening in both Scotland and England compared to pre-pandemic estimates.[66] Our study period did not include data for 2021. However, published estimates of alcohol-specific mortality illustrate that the age-standardised rate of alcohol-specific mortality increased by 7% from 2020 to 2021 in England, compared to 4% in Scotland. It is therefore unlikely that the inclusion of mortality outcomes from 2021 would have altered our findings. There have been reports that alcohol consumption and patterns have been influenced by the COVID-19 pandemic. Furthermore, there have also been suggestions that COVID-19 may interact with existing liver problems, and potentially increase vulnerability to those already at the highest risk of alcohol-related harms.[34] Our study spans the first year of the pandemic and takes into account patterns in England. These recent trends in the UK may make it difficult to see the impact of MUP in routinely published statistics. However, our study has illustrated that MUP has had a protective effect in preventing additional health harms that would have likely occurred in Scotland if MUP had not been implemented.

5. Conclusion

We conclude that MUP has been effective in reducing levels of alcohol-attributable harm in Scotland. The strongest supporting evidence was that MUP significantly reduced deaths wholly attributable to alcohol consumption. Overall reductions in alcohol-attributable harm were mostly driven by reductions in chronic outcomes. There were increases in some acute outcomes, although these results were more uncertain than results for chronic outcomes. Acute outcomes make up a relatively small proportion of alcohol-attributable harm and were largely offset with reductions in chronic outcomes, resulting in an overall net reduction. We have shown the greatest reductions to have occurred in the 40% most socio-economically deprived areas in Scotland, suggesting that MUP acted to reduce inequalities in alcohol-attributable health harms in Scotland.

Appendix 1: Alcohol-attributable ICD-10 code definitions

All ICD-10 diagnosis codes to be used to define health outcomes wholly attributable to alcohol consumption are given in Tables A1.1 and A1.2. ICD-10 diagnosis codes to be used to define health outcomes partially attributable to alcohol consumption are outlined in Table A1.3 and A1.4. External ICD-10 cause codes, which cannot be coded in the main position of hospital admission records are given in **bold**, where applicable.

Table A1.1: Chronic outcomes wholly attributable to alcohol consumption

Outcome group and individual outcome	ICD-10 code definition
Endocrine: alcohol-induced pseudo-Cushing's syndrome	E24.4
Neuropsychiatric: alcohol psychoses	F10.3–F10.9
Neuropsychiatric: alcohol abuse	F10.1
Neuropsychiatric: alcohol dependence syndrome	F10.2
Neuropsychiatric: degeneration of nervous system due to alcohol	G31.2
Neuropsychiatric: alcoholic polyneuropathy	G62.1
Neuropsychiatric: alcoholic myopathy	G72.1
Cardiovascular: alcoholic cardiomyopathy	I42.6
Digestive: alcoholic gastritis	K29.2
Digestive: alcoholic liver disease	K70
Digestive: alcohol-induced acute pancreatitis	K85.2
Digestive: alcohol-induced chronic pancreatitis	K86.0

Table A1.2: Acute outcomes wholly attributable to alcohol consumption

Outcome group and individual outcome	ICD-10 code definition
Neuropsychiatric: acute intoxication	F10.0
Injuries: poisoning by alcohol	T51.0, T51.1, T51.2, T51.3, T51.8, T51.9 Accidental poisoning: **X45, Y15** Intentional: **X65**
Injuries: excessive blood level of alcohol	R78.0
Injuries: evidence of alcohol involvement determined by blood alcohol level	**Y90**

Table A1.3. Chronic outcomes partially attributable to alcohol consumption

Outcome group and individual outcome	ICD-10 code definition
Communicable diseases: tuberculosis	A15–A19
Communicable diseases: HIV	B20–B24, Z21
Communicable diseases: lower respiratory tract infections	J09–J22
Cancer: oral cavity and pharynx cancer	C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C12, C13, C14, D00.0
Cancer: oesophageal cancer	C15, D00.1
Cancer: colorectal cancer	C18–C21, D01.0–D01.4
Cancer: liver cancer	C22, D01.5
Cancer: pancreatic cancer	C25, D01.7
Cancer: laryngeal cancer	C32, D02.0
Cancer: breast cancer	C50, D05
Endocrine: diabetes (Type 2)	E11, E13, E14
Neuropsychiatric: epilepsy	G40, G41
Cardiovascular: hypertension	I10–I13, I14, I15

Outcome group and individual outcome	ICD-10 code definition
Cardiovascular: ischaemic heart disease	I20–I25
Cardiovascular: atrial fibrillation and cardiac arrhythmia	I47–I49
Cardiovascular: haemorrhagic stroke	I60–I62, I69.0–I69.2
Cardiovascular: ischaemic stroke	I63–I67, I69.3
Cardiovascular: oesophageal varices	I85
Digestive: liver cirrhosis	K74
Digestive: acute pancreatitis	K85.0, K85.1, K85.8, K85.9
Digestive: chronic pancreatitis	K86.1–K86.9
Digestive: chronic hepatitis	K73

Table A1.4: Acute outcomes partially attributable to alcohol consumption[a,b,c]

Outcome group: injuries Individual outcome	ICD-10 code definition
Motor vehicle collisions	**V1**[1]**, Y85.0**
Falls	**W00–W19, Y30**
Drowning	**W65–W74, Y21**
Fire	**X00–X09, Y26**
Assault/homicide	**X85–Y09, Y87.1**
Self-poisoning by substances other than alcohol	T36–T50, T52–T65, T96–T97 Accidental poisoning: **X40–X44, X46–X49, Y10–Y14, Y16–Y19** Intentional: **X60–X64, X66–X69**
Other unintentional injuries	**V2**[2]**, W20–W52, W53–W60, W61, W62, W63, W64, W75–W84, W85–W99, X10–X33, Y20, Y22–Y25, Y27–Y29, Y31–Y34, Y85.9, Y86, Y87.2, Y89.9**

Outcome group: injuries Individual outcome	ICD-10 code definition
Other intentional self-harm	**X70–X84, Y87.0**
Other intentional injuries	**Y35, Y89.0**

a Transport accident external ICD-10 codes are defined as V01–V99 and for the purposes of allocation to individual outcomes are defined as V1 and V2.

b V1 will be defined by external ICD-10 codes: V02.9, V03.1, V03.9, V04.1, V04.9, V09.2, V09.3, V12.3–V12.9, V13.3–V13.9, V14.3–V14.9, V19.4, V19.5, V19.6, V19.9, V20.3–V20.9, V21.3–V21.9, V22.3–V22.9, V23.3–V23.9, V24.3–V24.9, V25.3–V25.9, V26.3–V26.9, V27.3–V27.9, V28.3–V28.9, V29.4, V29.5, V29.6, V29.9, V30.4–V30.9, V31.4–V31.9, V32.4–V32.9, V33.4–V33.9, V34.4–V34.9, V35.4–V35.9, V36.4–V36.9, V37.4–V37.9, V38.4–V38.9, V39.4, V39.5, V39.6, V39.9, V40.4–V40.9, V41.4–V41.9, V42.4–V42.9, V43.4–V43.9, V44.4–V44.9, V45.4–V45.9, V46.4–V46.9, V47.4–V47.9, V48.4–V48.9, V49.4, V49.5, V49.6, V49.9, V50.4–V50.9, V51.4–V51.9, V52.4–V52.9, V53.4–V53.9, V54.4–V54.9, V55.4–V55.9, V56.4–V56.9, V57.4–V57.9, V58.4–V58.9, V59.4, V59.5, V59.6, V59.9, V60.4–V60.9, V61.4–V61.9, V62.4–V62.9, V63.4–V63.9, V64.4–V64.9, V65.4–V65.9, V66.4–V66.9, V67.4–V67.9, V68.4–V68.9, V69.4, V69.5, V69.6, V69.9, V70.4–V70.9, V71.4–V71.9, V72.4–V72.9, V73.4–V73.9, V74.4–V74.9, V75.4–V75.9, V76.4–V76.9, V77.4–V77.9, V78.4–V78.9, V79.4, V79.5, V79.6, V79.9, V80.3, V80.4, V80.5, V81.1, V82.1, V83.4, V84.4, V85.4, V86.0, V86.1, V86.3, V87.0–V87.9, V89.2, V89.3, V89.9.

c V2 will be defined as all transport accident external ICD-10 codes not defined by V1.

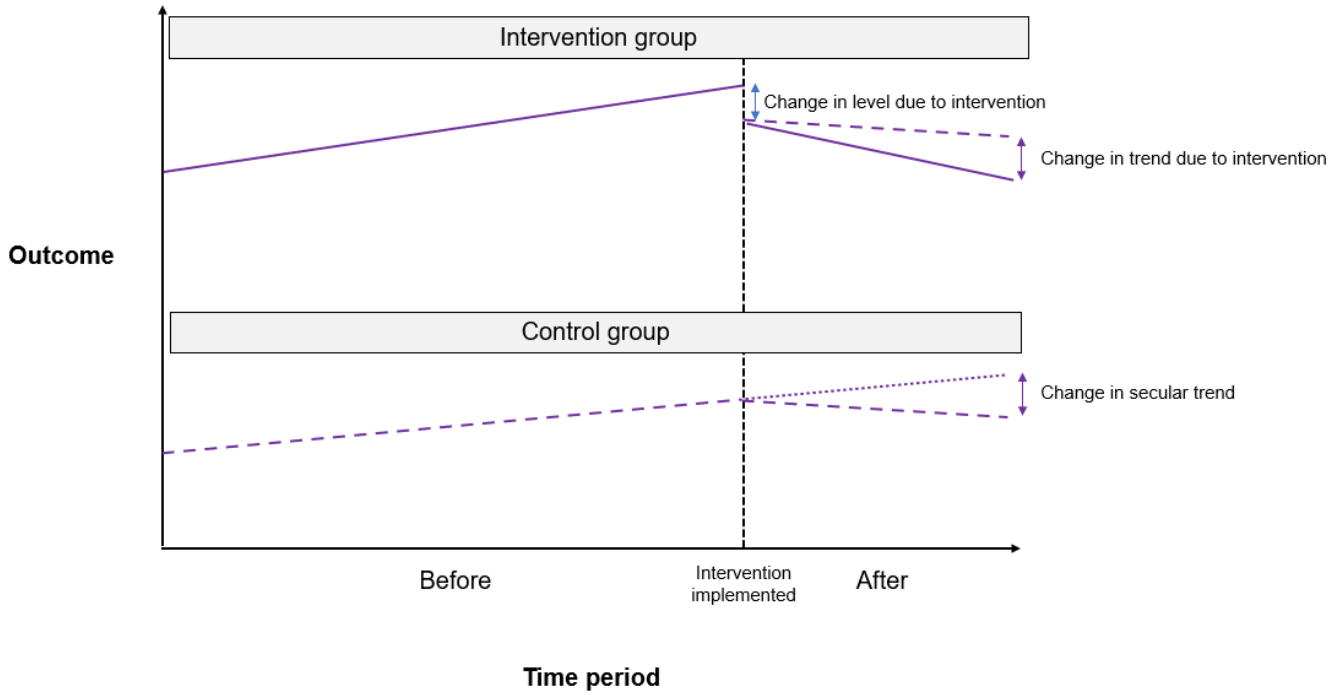
Appendix 2: Study inputs for generating alcohol-attributable fractions

Data input	Scotland	England
Alcohol consumption per capita (litres ethanol per year)	Nielsen/CGA combined on and off-trade sales (population 16 years and above)	Nielsen/CGA combined on and off-trade sales (population 16 years and above)
Relative consumption	Source: SHeS Definition: mean number of units per week. For each sub-group, estimates are expressed as a proportion compared to the males aged 16–34 years sub-group.	Source: HSE Definition: mean number of units per week. For each sub-group, estimates are expressed as a proportion compared to the males aged 16 to 34 years sub-group.
Prevalence of lifetime abstainers	Source: SHeS Definition: % always non-drinkers	Source: HSE Definition: % always non-drinkers
Prevalence of current drinkers	Source: SHeS Definition: % current drinkers	Source: HSE Definition: % current drinkers
Prevalence of former drinkers	Definition: calculated as 1 minus the prevalence of lifetime abstainers/current drinkers, as these categories are mutually exclusive	Definition: calculated as 1 minus the prevalence of lifetime abstainers/current drinkers, as these categories are mutually exclusive
Prevalence of binge drinkers	Source: SHeS Definition: % units per day defined as binge drinking (males – 8+ units; females – 6+ units)	Source: HSE Definition: % units per day defined as binge drinking (males – 8+ units; females – 6+ units)
Population estimates	NRS mid-year population estimates	ONS mid-year population estimates

Appendix 3: Description of controlled interrupted time series

When using controlled interrupted time series methods, the counterfactual assumption is that the level and trend for the group exposed to the intervention would be expected to change in the same way as the control group (**Figure A3.1**). This makes controlled interrupted time series a stronger quasi-experimental design than an uncontrolled interrupted time series, as an uncontrolled design assumes that the level and trend in the group exposed to the intervention would have remained the same had the intervention not occurred. Therefore, if external factors led to a worsening in the rate of alcohol health harms in Scotland and England, controlled interrupted time series can estimate whether MUP had a positive or negative impact over and above the underlying trends in alcohol health harms.

Figure A3.1: Visual representation of hypothetical outcome time series pre- and post-intervention by group



Appendix 4: Controlled interrupted time series – results tables

Supplementary tables outlining the results from controlled interrupted time series models are available **here on the PHS website**.

Appendix 5: Uncontrolled interrupted time series – results tables

Supplementary tables outlining the results from uncontrolled interrupted time series models are available **here on the PHS website**.

Appendix 6: Sensitivity analyses – results tables

Supplementary tables outlining the results from a range of sensitivity analyses are available **here on the PHS website**.

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