Public Health Scotland

# An analysis plan for the evaluation of the impact of alcohol minimum unit pricing (MUP) on deaths and hospital admissions in Scotland

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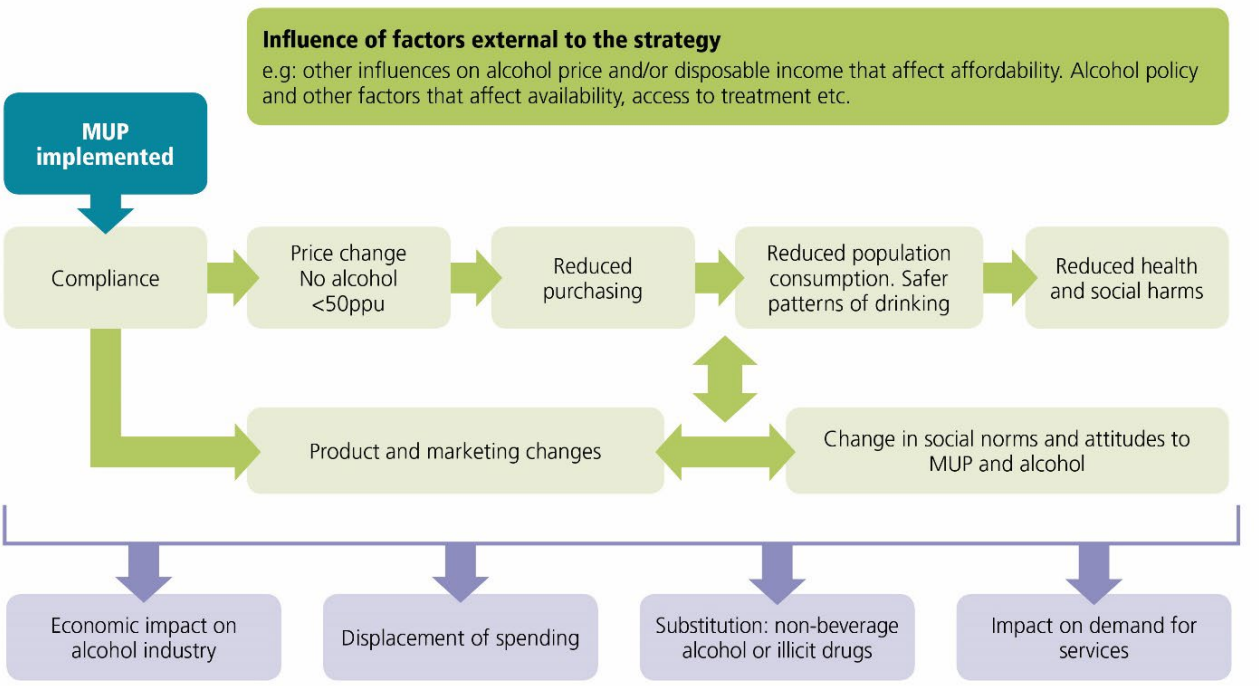
# 1. Introduction

## 1.1. Minimum unit pricing in Scotland

Scotland became the first country in the world to implement a minimum unit price (MUP) for alcoholic drinks sold in licensed premises.[1] In May 2018, 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.[2–6] The extent to which MUP has had an impact in Scotland will be determined through an overarching mixed-methods evaluation. This will provide evidence to inform Members of the Scottish Parliament ahead of the parliamentary vote on the future of MUP in Scotland in 2024.[7–9]

A theory of change was developed, setting out the intended outcomes of MUP, potential unintended impacts and how these might come about (**Figure 1**).[10,11] Among the final changes expected to be realised from the theory of change are those related to the health harms caused by alcohol consumption.

### Figure 1: Theory of change for MUP in Scotland



## 1.2. Health harms from alcohol consumption

Recent estimates from the Global Burden of Disease (GBD) study indicated that most of the health harms caused by alcohol consumption come from a range of non-communicable diseases.[12] When measured by disability-adjusted life years (DALYs) the leading alcohol-attributable disease burdens were due to cancers, alcohol use disorders and chronic liver diseases. These disease groups all exhibit high levels of health inequality.[13] The GBD study findings illustrate that health harms from alcohol consumption are wider than the direct health harms that are more widely recognised and includes conditions where the population-level harm is deemed to be partially attributable to alcohol consumption, for example liver cancer.[14] Previous research undertaken by NHS Health Scotland highlighted the substantial contribution of partially attributable alcohol health harms to total alcohol health harms in Scotland, for both males and females.[15]

Estimating the full extent of attributable health harms due to risk factors such as alcohol consumption is highly resource intensive.[16] Undertaking such assessments requires many assumptions and a wide range of data sources. This includes assumptions about causal relationships between alcohol consumption and individual health outcomes, and the extent to which levels of alcohol consumption affect the population-level frequency of harms.[17] However, understanding the wider extent of alcohol harms on health is important for policy making when developing evidence-informed priorities around tackling alcohol harms. This understanding is also required to robustly evaluate whether existing policies are tackling the range of health harms caused wholly or partly by alcohol consumption.[16]

To address these issues the International Model of Alcohol Harms and Policies (InterMAHP) was developed as an open-access portal to help researchers estimate the extent of alcohol-attributable mortality and morbidity in their country.[18] Although there are existing studies, such as the GBD study, that can provide estimates of alcohol-attributable health harms, the data inputs are not always country-specific, which means they cannot be relied upon to robustly evaluate the impact of MUP in Scotland. InterMAHP allows for dynamic customisation using specific, transparent and representative country-based inputs on mortality and morbidity outcome

occurrence, drinking prevalence and population-level alcohol consumption to estimate alcohol-related health harms more accurately.

Wholly and partially attributable health harms are routinely presented in combination when used in relation to population health surveillance. However, they are not often used as outcome measures when trying to estimate the impact of a public health intervention using controlled interrupted time series methodology. While it's important to understand the comprehensive impact of alcohol consumption on health harms, it's also important to be clear about the uncertainty in attributing changes in (wholly or partially) alcohol-related health harms to MUP.

Wholly attributable health harms can be interpreted with a high degree of certainty, attributed to alcohol consumption and to specific time periods. On the other hand, partially attributable health harms represent a hypothetical estimate based on several population-level factors: drinking prevalence; alcohol consumption levels/patterns; the risk of a specific health harm associated with alcohol consumption; and the occurrence of those health harms. The hypothetical situation is such 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. Furthermore, partially attributable alcohol health harms are 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. However, as reductions in alcohol consumption levels would be assumed to impact the health harm outcome in the year in which it occurs, change may be assumed to be happening much sooner than we are actually observing for partially attributable alcohol harms. Therefore, while partly attributable harms are an important part of the potential benefit of MUP, there remains a large degree of uncertainty 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. As these sets of health harms outcomes are, by definition, only partially attributable to alcohol consumption, their occurrence could 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 could confidently assert changes in partially attributable health harms to MUP.

## 1.3. Aims and research questions

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

Our primary study aim will be achieved through addressing the following research questions:

- What is the impact of MUP on deaths wholly attributable to alcohol consumption?
- What is the impact of MUP on hospital admissions wholly attributable to alcohol consumption?

As well as estimating the overall impact of MUP, we will also estimate how this impact varies by sex, age group and level of socioeconomic deprivation.

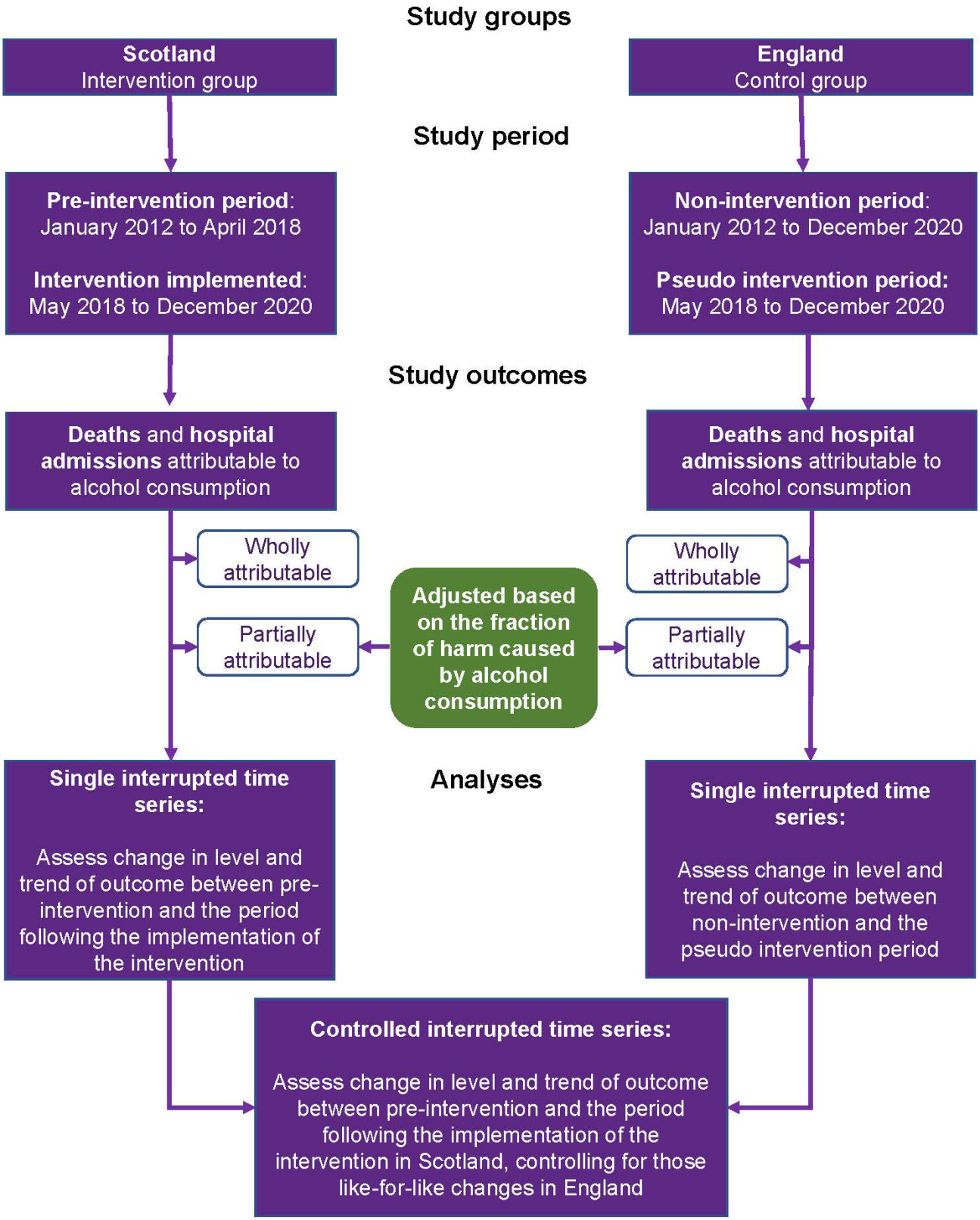
An additional aim of this study is to explore the impact of MUP on deaths and hospital admissions partially attributable to alcohol consumption. The estimates of partially attributable outcomes are more uncertain for the reasons discussed above.

# 2. Methodology and analysis

## 2.1. Study design

An observational ecological study design will be used. Figure 2 outlines the study setting, time periods, outcomes and analyses described in detail below.

## Figure 2: Study flow diagram



## 2.2. Study setting and sampling frame

The study setting will be Scotland as the geographical area exposed to MUP following its implementation on May 2018. The unexposed geographical control group will be England, a part of the UK where MUP has not been implemented. The main sampling frame for assessing outcomes is the period 1 January 2012 to 31 December 2020. The start of the study period is 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.[19] The time-specific unit of analysis is a calendar month. Outcomes included are those occurring in the population aged 16 years and above.

## 2.3. Data

### 2.3.1. Deaths

Scottish and English death records will be sourced from the National Records of Scotland (NRS) and Office of National Statistics (ONS), respectively, to define alcohol-attributable mortality.[20,21] The analysis will be based on the date of death, rather than date of death registration, and will include all alcohol-attributable deaths that occurred during the study period. All mortality records will be from finalised annual registers of deaths for each country over the full study period.

### 2.3.2. Hospital admissions

Alcohol-attributable morbidity will be defined by hospital admissions data, as is recommended by InterMAHP.[22] For Scotland, these will be based on individuals admitted to hospital as a general inpatient or day case from the Scottish Morbidity Record 01 (SMR01) dataset.[23] These will also include mental health inpatient and day cases from the SMR04 dataset. English hospital admissions will be sourced from NHS Digital from the Hospital Episodes Statistics (HES) dataset.[24]

For both Scotland and England, the analysis date will be based on hospital admission date, rather than date of discharge, and alcohol-attributable health outcomes will be defined by the diagnosis upon discharge. The first admission stay details will be selected, meaning that an individual can only be counted once in each month.

### 2.3.3. Deprivation

We will use an area-based deprivation index to classify mortality and hospital admissions outcomes by deprivation decile. In line with Public Health Scotland (PHS) analytical guidance, the Scottish deprivation decile assigned to each patient postcode of residence will be defined using the Scottish Index of Multiple Deprivation (SIMD).[25] The approach to be used for Scotland will be consistent for both deaths and hospital admissions. Different SIMD versions will be used depending on the time period and will be defined as follows: SIMD 2012 (2012 to 2013); SIMD 2016 (2014 to 2016); and SIMD 2020 (2017 to 2020).

The English deprivation decile assigned to each patient postcode of residence will be defined using the Index of Multiple Deprivation (IMD).[26] The approach for England will differ to the approach for Scotland, due to time-varying differences in English administrative geography classification and data availability. For English deaths, different IMD versions will be used dependent on the time period and will be defined as follows: IMD 2015 (2012 to 2015); and IMD 2019 (2016 to 2020). The IMD decile for hospital admissions will be defined based on what is routinely available on the HES dataset, meaning that IMD 2010 will be used to define the deprivation decile for the entire study time period (2012 to 2020).

### 2.3.4. Populations

Relevant mid-year population estimates by sex, age group, deprivation decile and year will be sourced from NRS for Scotland and ONS for England.[27,28] As the time unit of analysis is defined as a calendar month, populations will be estimated for each month. Monthly populations will be estimated by linear (straight-line) interpolation

between individual mid-year population estimates for each combination of sex, age group and deprivation decile.[29]

### 2.3.5. COVID-related government restrictions

We will source data on the extent of government restrictions during the COVID-19 pandemic, separately for Scotland and England. This will be defined using the Oxford COVID-19 Government Response Tracker (OxCGRT).[30] The stringency index of the OxCGRT will be used to reflect the differences between the UK Government and that of the Scottish Government's lockdown and restrictions over time. Incorporating this will allow us to reflect on how 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 extracted for use in this study was downloaded on 5 April 2022.

## 2.4. Alcohol-attributable fractions

Estimates of drinking prevalence and patterns, population-level alcohol consumption and residential populations are required to estimate the alcohol-attributable fractions (AAFs) that are needed to estimate health harms partially attributable to alcohol consumption.[22]

In this study, we will use InterMAHP to estimate AAFs. Due to data availability, we will define all InterMAHP inputs for the population aged 16 years and above. This varies from the specification of InterMAHP, which recommends inputs for the population aged 15 years and above, although this is expected to have no noticeable impact. To enable the estimation of AAFs, InterMAHP requires the following data inputs: alcohol consumption per capita (16 years and above); prevalent drinking status (current, former and never drinkers); and binge drinking prevalence. We will define these inputs for six different demographic groups, by sex (males and females) and age group (16 to 34 years; 35 to 64 years; and 65 years and above) for each calendar year of study (2012 to 2020). We will not estimate partially attributable outcomes by deprivation decile because the level of data inputs required for

InterMAHP would be too granular to be robustly estimated. The data sources that we will use to define InterMAHP inputs match the lowest granularity specified by InterMAHP and our proposed sources align with the gold standard sources recommended by InterMAHP authors.[22]

Alcohol consumption per capita for Scotland and England (expressed as litres of pure alcohol per year) for the population aged 16 years and above will be defined using sales data from Nielsen and CGA Strategy, and cover both on and off-trade sales.[31] These estimates reflect sales across eight categories: spirits, wine, beer, cider, ready-to-drink beverages, perry, fortified wine and 'other'. The contribution of off-trade alcohol sales in these estimates has been adjusted to account for the exclusion of discount retailers in the source data. Further details regarding the methodology and conversion to per capita consumption are outlined elsewhere.[30] These sales estimates will be inflated to incorporate estimates of unrecorded alcohol consumption in the UK, as published by the World Health Organization (WHO).[32] Within InterMAHP, these will be further augmented by estimates of the mean number of units consumed by each population sub-group, derived for Scotland and England from the Scottish Health Survey (SHeS) and the Health Survey for England (HSE), respectively.[33,34] The mean number of units will be transformed into proportions within the six defined population sub-groups, where the proportions are framed relative to the males aged 16 to 34 years sub-group. Scottish drinking prevalence estimates will be sourced from the SHeS and the HSE will be used to estimate drinking prevalence for England.[35,36] A detailed breakdown of the country-specific data sources to be used as inputs into InterMAHP is outlined in **Appendix 1**.

Due to the COVID-19 pandemic, longstanding health surveys, such as SHeS and HSE, have either been paused or have had to adopt different sampling and fieldwork strategies.[37,38] This has meant that many post-2019 survey estimates are either not available or are not comparable with previous estimates. To obtain 2020 estimates for input into InterMAHP, we will linearly extrapolate estimates at the population sub-group levels based on previous trends (2012 to 2019). Although there has been evidence indicating alcohol consumption levels were impacted by the COVID-19 pandemic, estimates are not available in a form that is comparable with previous

SHeS and HSE estimates. This assumption will only impact estimates of harms that are partially attributable to alcohol consumption.

In line with InterMAHP guidance, we will deflate the estimate of alcohol consumption per capita by an adjustment factor of 0.8 to ensure that it corresponds with the epidemiological studies that provide the basis for relative risk estimates necessary for the calculations of AAFs.[22,39,40] This is in line with the recommendation from the technical advisory committee for the WHO.

## 2.5. Study outcome measures

All outcome measures will be defined based on 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.[41] Outcome measures will first be 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 is entirely attributable to alcohol consumption (for example alcoholic liver diseases), whereas partially attributable health outcomes are those where only a proportion of the population-level health harm outcome is 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 2**.

Study outcomes will be assessed using a primary definition and further explored using two additional secondary definitions, as outlined below:

- **Primary definition**: underlying cause of death (or main hospital admission diagnosis) is wholly attributable to alcohol consumption.
- **Secondary definition 1**: underlying cause of death (or main hospital admissions diagnosis) is wholly or partially attributable to alcohol consumption. Additionally, wholly and partially attributable injuries will be further defined

using external cause codes in any secondary hospital admissions diagnoses, as they cannot be defined in the main diagnosis position.

- **Secondary definition 2**: any cause of death (or any hospital admissions diagnoses or external cause code) is wholly or partially attributable to alcohol consumption.

The rationale for three different definitions is to balance specificity of the cause of death or hospital admission, comparability between Scottish and English data and comprehensiveness in the estimation of alcohol-attributable harms.

**The primary definition** will allow us to fully explore differences in wholly attributable alcohol harms and will be the main definition used for reporting results of primary outcomes. It ensures specificity and comparability, but at the expense of comprehensiveness.

**Secondary definitions 1 and 2** will provide more comprehensive estimates because they include both wholly and partially attributable alcohol health harms.

**Secondary definition 1** is more comprehensive, through the addition of partially attributable alcohol health harms, and also ensures comparability because it focuses on the underlying cause of death or main hospital admission diagnosis.

**Secondary definition 2** is the most comprehensive estimate, but is the least comparable because there are more opportunities to define causes of deaths and hospital diagnoses in England than in Scotland (causes of death – 16 versus 11; hospital diagnosis fields – 20 versus 6). [42] This may lead to artefactually higher estimates in England than for Scotland. Following data retrieval, all definitions will be assessed for suitability of comparisons between Scotland and England.

All pre-specified study outcomes are outlined in **Table 1** and will be reported separately based on level of attributability (wholly or partially). Primary study outcomes are denoted as those that are wholly attributable to alcohol consumption using the primary definition. All aggregated outcomes are presented in bold. When reporting study findings, interpretation of outcomes will be made in order of public health prevention importance (deaths and then hospital admissions).

Each outcome will be defined on an individual monthly basis over the full study period. For deaths where there are multiple alcohol-attributable causes of death defined, the underlying cause of death will be chosen or the cause of death that was numerically the lowest (for example the third contributing cause of death would be chosen over the fifth contributing cause of death if both were alcohol-attributable). This logic will also be applied for hospital admissions outcomes. If a patient has more than one alcohol-attributable hospital admission in a monthly period, the attributes of the earliest admission will be 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** |

## 2.6. Software

All data transformations will be undertaken using Microsoft Excel, SPSS and R software. Additionally, English deaths data are to be accessed remotely using Citrix Workspace to access the ONS Secure Research Service (SRS) virtual

environment.[21] All interrupted time series modelling will be undertaken using the econometrics toolbox from MATLAB 9.1 Update 2.

## 2.7. Analytical approach

### 2.7.1. Estimating alcohol-attributable fractions

Outcomes wholly attributable to alcohol consumption do not require any further adjustments as, by definition, the entirety of each outcome is attributable to alcohol consumption. However, outcomes partially attributable to alcohol consumption need to be scaled 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.

We will model AAFs for each health outcome partially attributable to alcohol consumption using the online interface of InterMAHP (version 3.0).[18] AAF analyses will be 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 will be 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.[43] The theoretical upper limit of average daily consumption will be defined as the InterMAHP default value of 18.75 units.

The estimation of AAFs requires the relative risk of a health outcome being attributable to alcohol consumption. Relative risks for AAFs are derived from meta-analyses and are required for alcohol-causative health outcomes. InterMAHP offer three default choices of relative risk source. Our study will use those derived from the WHO 2018 Global Status Report on Alcohol and Health.[44] This is the most recently available of the three choices, reflects a widely shared international consensus view and has close agreement with another default source (those from the Canadian Substance Use Costs and Harms Project).[45] The use of relative risks from the GBD

study were discounted due to lack of transparency over sourcing the underlying meta-analyses for alcohol-causative health conditions. Due to our choice of relative risk set, our study will assume more conservative cardioprotective effects than have been recently published.[46,47] Regardless of recent estimates, there remains differing views on the extent of the protective effects of alcohol.[48,49]

Data inputs on oesophageal cancer do not differentiate by sub-type (squamous cell 17 carcinoma (SCC) and adenocarcinoma (AC)). Alcohol consumption is only causally related to oesophageal SSC, so to avoid overestimating oesophageal cancer harms due to alcohol, InterMAHP requires an estimate of the proportion of total oesophageal cancers that are oesophageal SSC.[50] For Scotland, we sourced proportions from published data from PHS.[51] Estimates were sourced for England from NHS Digital via a request for data.[52] The proportions to be used in InterMAHP are outlined in **Table 2**.

## Table 2: Oesophageal SSC cancers as a percentage of total oesophageal cancers*

| Country | Males | Females |
|---|---|---|
| Scotland | 22.7% | 47.1% |
| England | 19.4% | 47.2% |

*The estimates for Scotland were for cancers registered in 2015 to 2019, while the English estimate were for cancers registered during 2013 to 2019.

We will 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. Our rationale for exclusion is that there are no meta-analyses of relative risks available, due to the novel nature of COVID-19, to enable us to develop specific AAFs.

The number of deaths and hospital admissions partially attributable to alcohol consumption will be derived by multiplying the number of each outcome (deaths and hospital admissions) by the relevant AAF. Not all health outcomes partially attributable to alcohol consumption have separate AAFs for morbidity.[22] Where

fractions are available for both mortality and morbidity, the relevant fraction will be used. In the case that only the mortality fraction is available, that will be applied to the count of hospital admissions.

### 2.7.2. Descriptive analyses

Data will initially be analysed descriptively for our defined study outcomes. Trends and other key information will be tabulated and produced in graphical forms. Descriptive results for alcohol-attributable deaths and hospital admissions will be produced for the following stratifications: sex (males, females); age- group (16 to 34 years, 35 to 64 years and 65 years and above); deprivation (area-based deciles using relevant country-specific indices); study outcome; and country (Scotland; England). These will be presented in terms of rates per 100,000 residential population. All monthly rates per 100,000 population used in descriptive and interrupted time series analyses will be adjusted to a common month-length to account for unequal month lengths using the following formula[53]:

$$Monthly\ rate = \left(\frac{Count}{Population} \times 100{,}000\right) \times \left(\frac{365.25}{12 \times Number\ of\ days\ in\ month}\right)$$

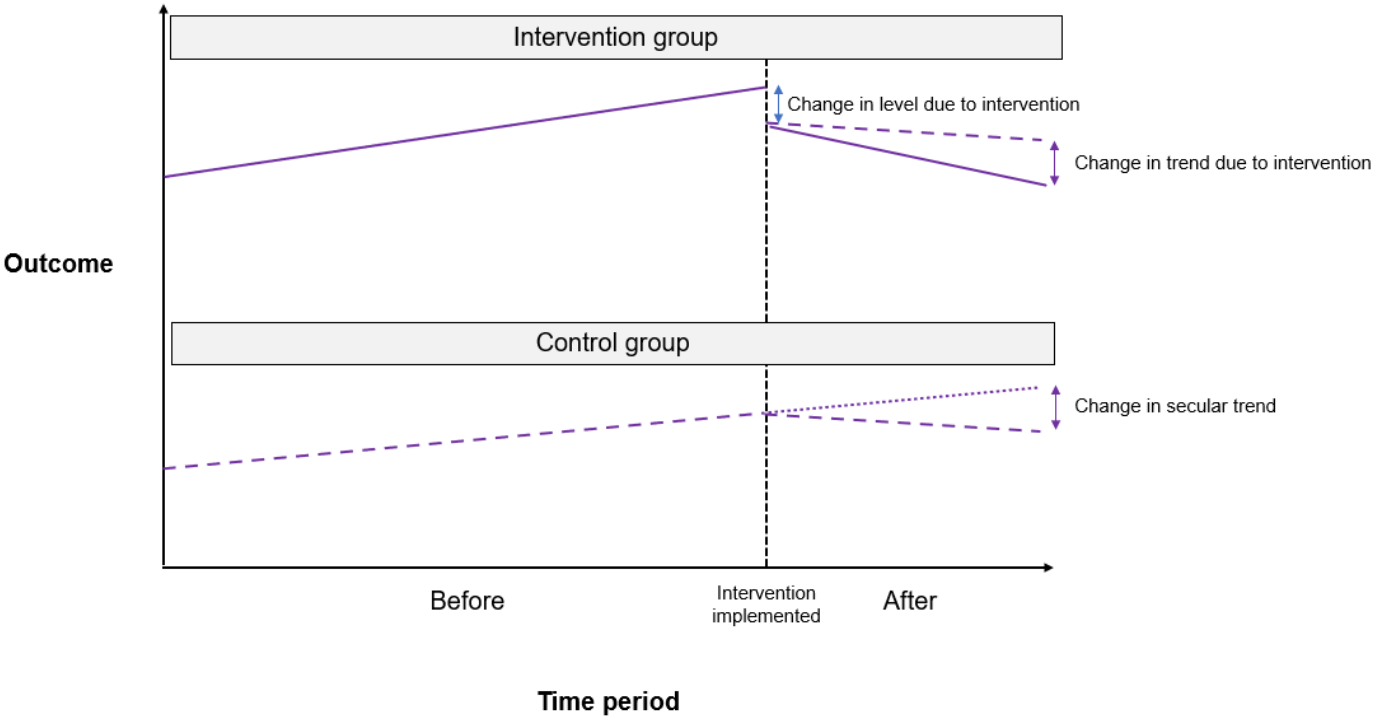
### 2.7.3. Interrupted time series analyses

To assess the impact of MUP on our alcohol health harms outcomes in Scotland, we will use controlled interrupted time series methods with seasonal autoregressive integrated moving average (SARIMA) errors.[54] Interrupted time series methods provide a robust quasi-experimental study design which enables underlying temporal and seasonal trends to be accounted for.[55] We have previously utilised this approach when evaluating the impact of the Alcohol (Minimum Pricing) (Scotland) Act 2012, MUP and the COVID-19 pandemic on alcohol sales in Scotland.[56–58]

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 3**). This makes

a controlled interrupted time series a stronger quasi-experimental design than an uncontrolled interrupted time series, since 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, a controlled interrupted time series can estimate whether MUP had a positive or negative impact over and above the underlying trends in alcohol health harms. To estimate the direction, magnitude and uncertainty of the effect of MUP on deaths and hospital admissions in Scotland, we will include a binary variable that will take 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). England will be defined as the control group not exposed to the MUP intervention.

## Figure 3: Visual representation of hypothetical outcome time series pre- and post-intervention by group




All models will be adjusted for underlying temporal and seasonal trends. In addition, we will adjust for government restrictions during the COVID-19 pandemic using the OxCGRT.[59] The stringency index of the OxCGRT will be used to reflect the differences in lockdown and restrictions over time, and between the UK Government

and the Scottish Government. Weighted averages will be calculated using daily values so that the index value represents full monthly periods. The default stringency index ranges from 0–100, but will be transformed between 0 and 1, with values closer to 1 representing the highest levels of restrictions. The OxCGRT will take a value of 0 for all months prior to the start of the pandemic.

Rates will be log-transformed for each study outcome to address the potential for rates to be skewed, and separate models will be derived, where appropriate, for each sex, age group and deprivation decile. As separate models will be derived for each sub-group stratification, rather than estimating models that include an interaction term, sub-group specific estimates may not appear to lie on either side of an overall estimate. If a time series contains observations for any period with a value of 0, the series will be transformed using the inverse hyperbolic sine transformation.[60]

Time series data often exhibit evidence of outliers, which need to be modelled appropriately for efficient estimation of intervention effects. To investigate this, we will extract the residuals from each model and then apply the 'isoutlier' function in MATLAB version 9.1 update 2 to obtain a list of identified outliers using Grubbs' method,[61] the generalised extreme Studentized method,[62] a sliding window mean and scaled median. Identified outliers will be incorporated into the model and the residuals will be tested for white noise to ensure the model is an appropriate fit.

The uncontrolled Scottish and English models will be used to 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 will also estimate controlled models that compare trends in harms in Scotland to the control area, England, where MUP was not implemented. We will use a two-step approach to incorporate our control group data. Firstly, separate models will be fitted to the log-transformed rate of each study outcome in Scotland and in England. Secondly, the English control-group time-series data will be 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.[63] Controlled models will be defined and assessed on a like-for-like basis, for example the log-transformed rate of health harms outcome in Scottish males controlled by log-transformed rate of health harms outcome in English males.

For both uncontrolled and controlled models, coefficients will be 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 will be converted into percentages using the formula: $100 \times e^{\beta-0.5\times Var(\beta)-1}$. A p-value of less than 0.05 will be used to denote statistically significant results.

We will use findings from the controlled models to evaluate the impact of MUP on deaths and hospital admissions attributable to alcohol consumption.

## 2.8. Sensitivity analyses

Several pre-specified sensitivity analyses will be undertaken to test the robustness of our study findings on our primary study outcomes.

Firstly, sensitivity analyses that truncate the sampling period to remove the impact of the COVID-19 pandemic will be undertaken by removing outcomes observed in 2020. We will 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 for hospital admissions and deaths outcomes to have been influenced by the period directly preceding the COVID-19 pandemic.[64] This will provide 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 will adjust 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 have been chosen as self-reported estimates of alcohol consumption have been shown to be comparable with similarly deprived Scottish urban areas.[65,66]

Thirdly, we will adopt the use of a non-geographical control group 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 who would not have been affected by the intervention of interest, that is 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 or any other treatment that is designed to give the same effect as the intervention.[67] If they did, it would suggest the observed changes in the outcome of interest were not necessarily due to MUP.

When defining a negative control, we screened all health conditions, excluding those conditions that were wholly, or partially, attributable to alcohol consumption, or if they could have plausibly been impacted by the MUP theory of change. Furthermore, the choice of the non-geographical control group needed to result in deaths and hospital admissions, so that health harm outcomes could be defined within the same sources as our alcohol-attributable outcomes. As a result of this preliminary analysis, our choice of non-geographical control will be defined as genitourinary diseases.

Further planned sensitivity analyses include modelling the introduction of MUP as if it had happened six months earlier than it was implemented and assessing the impact of MUP using an analytical method that differs to the SARIMA approach.

# 3. Ethics

The data used in this study will be sourced from PHS and multiple external agencies. All PHS staff have undertaken valid information governance training. PHS staff procedures for accessing and requesting the information required to undertake this study will be adhered to.

Control group data for deaths and hospital admissions in England were applied for through applications to ONS and NHS Digital, respectively.[21,68] For ONS, an application to the SRS to access mortality data was drafted and subsequently approved (study reference number 1011523).[21] 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 have agreed to comply 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 will undertake the statistical analyses are doing so under the Service Level Agreement for the provision of specialist statistical support that is in place between PHS and the University of Glasgow.

As this work relates to the secondary use of existing datasets, it will not result in the creation of a new dataset. On completion of the study, it will be stored within the PHS research governance system.

## 4. Reporting and dissemination

The findings from this work will align with the wider dissemination strategy of the MUP evaluation and will include tailored outputs to target policy, public and academic audiences. These will vary from institutional reports published by PHS, journal submissions, presentations to relevant stakeholders (such as the Scottish Government and third-sector organisations). Other dissemination approaches will be used to promote findings to wider audiences such as the use of social media, television, radio and newsprint. Findings will also be included in the final evaluation report, which is scheduled to be published during 2023.

Pre-publication dissemination will include sharing findings and reports with the MUP Consumption and Health Harms Evaluation Advisory Group (EAG). Any feedback that is received from this group will be assessed and may be incorporated into any revised and subsequently published works, with relevant acknowledgement. PHS, the EAG and the Scottish Government will formalise a plan and timescale for dissemination of study findings.

# Appendix 1: InterMAHP inputs to estimate alcohol-attributable fractions

## Table A1: List of country-specific data inputs for InterMAHP

| 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<br><br>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<br><br>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. |
| Prevalence of lifetime abstainers | Source: SHeS<br><br>Definition: % always non-drinkers | Source: HSE<br><br>Definition: % always non-drinkers |
| Prevalence of current drinkers | Source: SHeS<br><br>Definition: % current drinkers | Source: HSE<br><br>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<br><br>Definition: % units per day defined as binge drinking (males – 8+ units; females – 6+ units) | Source: HSE<br><br>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 2: 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 A2 and A3. ICD-10 diagnosis codes to be used to define health outcomes partially attributable to alcohol consumption are outlined in Table A4 and A5. External ICD-10 cause codes, which cannot be coded in the main position of hospital admission records are given in bold, where applicable.

## Table A2: 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 A3: 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<br><br>Accidental poisoning: **X45**, **Y15**<br>Intentional: **X65** |
| Injuries: excessive blood level of alcohol | R78.0 |
| Injuries: evidence of alcohol involvement determined by blood alcohol level | **Y90** |

## Table A4. 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 |

| Outcome group and individual outcome | ICD-10 code definition |
|---|---|
| Endocrine: diabetes (Type 2) | E11, E13, E14 |
| Neuropsychiatric: epilepsy | G40, G41 |
| Cardiovascular: hypertension | I10–I13, I14, I15 |
| 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 A5: Acute outcomes partially attributable to alcohol consumption[1,2,3]

| Outcome group: injuries<br><br>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<br><br>Accidental poisoning: **X40–X44**, **X46–X49**, **Y10–Y14**, **Y16–Y19** |

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

1 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.

2 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.

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

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