MRC/CSO Social and Public Health Sciences Unit

Project: **Evaluating the impact of minimum unit pricing of alcohol on Emergency Department attendances**

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Purpose

The purpose of the Protocol is to describe the study/project and provide information about the procedures for entering participants into the study/project. Every care has been taken in drafting this protocol; however, corrections or amendments may be necessary.

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1. Summary

This study aims to investigate the impact of the introduction of minimum unit pricing (MUP) of alcohol in Scotland on alcohol-related attendances to Emergency Departments. The main study will compare attendances at two hospitals in Scotland with two hospitals in North England at three different time points. Each wave of data collection for the main study is planned to last three weeks. The first wave is planned to occur prior to the introduction of MUP in Scotland with two follow-up waves of data collection at approximately six months after and 12 months after. The main study will be preceded by an initial short pilot phase within Glasgow, to ensure the data collection instruments are appropriate. A further pilot during the month before the main baseline wave of data collection is planned across all four hospital sites.

Patients aged 16 years and over attending EDs will be asked by research staff to complete a short face-to-face interview. An ED attendance database will be maintained during data collection periods to monitor patient recruitment. The interview will include: basic demographic information; amount of alcohol consumed in the past 24 hours; whether the patient has been a victim of violence; and problematic alcohol use in the past year (assessed using a validated tool). A note will be made of the hospital unique identifier for the attendance. Research staff will retrieve additional demographic characteristics, other attendance details, and diagnoses at discharge from patient records.

The study will therefore provide valuable information on the impact of MUP and will form an important component of the planned evaluation portfolio (coordinated by NHS Health Scotland). Effects of the intervention on important population subgroups (including by deprivation, age and sex) will also be reported.

2. Introduction

2.1 Background

It has been suggested that alcohol is the most harmful substance to society once all the health, social and economic costs are accounted for [1]. The level of alcohol-related harm in the UK in general, and Scotland in particular, is high and is a major contributor to socio-economic Inequalities [2, 3]. It is also increasingly acknowledged to be a global problem, with alcohol ranked as the ninth most common cause of death worldwide [4]. The over-consumption of alcohol is associated with a multitude of health problems including an increased risk of liver disease, heart disease, unintended pregnancy, sexually transmitted infections, some cancers and accidental injuries [5-7]. Its impact extends beyond the individual, with adverse effects on families, communities and the wider economy.

A comprehensive evidence review found evidence that consistently confirms a link between alcohol price, consumption and harm, although the strength of the association varies between studies [8]. From a UK perspective, the cost of alcohol has not risen in line with the rise in disposable income and alcohol was 44% more affordable in 2010 than it was in 1980 [9]. The evidence suggests that price mechanisms, such as taxation or MUP, to restrict affordability offer some of the most effective strategies to reduce alcohol-related harm but there is limited published research to date evaluating the particular strategy of minimum unit pricing [6, 8]. Although some forms of minimum pricing have been in place in some provinces in Canada for a number of years, MUP represents a somewhat distinct policy since it sets a minimum price based purely on the alcohol content of a beverage, thereby reducing the likelihood of substitution effects. Econometric modelling suggests that introducing a MUP would have a considerable impact in Scotland and England [10-12].

Minimum unit pricing has widespread support within the Public Health community [5, 13, 14]. The National Institute for Health and Clinical Excellence has published guidelines presenting a clear case for pursuing minimum unit pricing for alcohol, with evidence underpinning the recommendation from a comprehensive systematic review and modelling exercise [15].
NHS Health Scotland has led the Scottish Government's evaluation of Scotland's alcohol strategy through the Monitoring and Evaluating Scotland's Alcohol Strategy (MESAS) programme [16]. MESAS focused on evaluating licensing reforms, delivery of alcohol brief interventions and specialist treatment services. NHS Health Scotland plans to build on MESAS by using routinely collected data to assess changes in price, consumption and alcohol-related harms at a population level that occur as a result of MUP.

The work planned by NHS Health Scotland relies on routinely collected data and hence there are a number of areas of the MUP intervention that they cannot assess, in particular individual level changes in drinking and acute health harms not captured by routine data; and the possible unintended consequences of MUP and the likely differential impact of such consequences on the young and/or disadvantaged populations. Unintended consequences may occur through: increases in the use of illicit or industrial alcohol, use of other substances, and/or reducing the buying of food rather than alcohol to offset increased prices.

This study therefore, aims to build on the planned NHS Health Scotland research programme to assess changes in drinking behaviours and selected acute health harms not captured by routine data. Different mechanisms may cause varied impacts on population sub-groups. As with any pricing policy, MUP is likely to affect drinkers on lower incomes, and those who consume greater quantities, disproportionately. This research will therefore look at potential disproportionate effects by comparing the impact across different socioeconomic groups.

Alcohol-related harm in the UK in general, and Scotland in particular, is high and is a major contributor to health inequalities. MUP has been identified as an important potential public health policy intervention to address the burden of alcohol-related health harms and to reduce health inequalities. The Alcohol (Minimum Pricing) (Scotland) Bill was introduced to the Scottish Parliament on 31st October 2011 and passed in May 2012. Following the passage of the legislation into law, MUP has been subject to substantial delays as a consequence of a series of legal challenges. However, in October 2016 the Scottish Court of Session ruled in favour of the legality of MUP [17], raising expectations that the policy may finally be implemented. However, the Scotch Whisky Association has exhausted the legal options, with a final appeal to the UK Supreme Court having failed in November 2017 [18]. The Scottish Government now plans to implement MUP on 1st May 2018. As a consequence of the implementation of MUP relatively soon, it is important that baseline data be collected as soon as practicably possible.

Scotland will therefore be the first country to introduce MUP nationally. If so there will be a clear difference in policy between Scotland and England. MUP is expected to have significant health impacts, but with uncertainty about size and adverse consequences. These divergent policy options coupled with uncertainty about effect size, and with the interest in MUP elsewhere in the UK and internationally, provide the opportunity to evaluate MUP as a natural experiment [19]. Evidence from Canada is confined to retrospective analysis of routine data on price, consumption and selected harms [20-23]. NHS Health Scotland plan to undertake analysis similar to that in Canada, of routine data to determine the impact of MUP on price, consumption and alcohol-related hospital admissions and deaths in Scotland. This will rely on routinely collected data and hence there are a number of areas of the MUP intervention that it cannot assess, in particular changes in drinking and acute health harms not captured by routine data; and the possible unintended consequences of MUP and the likely differential impact of such consequences on the young and/or disadvantaged populations.

Changes in acute health harms:
Alcohol-related attendances to Emergency Departments (EDs) are strongly associated with both levels of population consumption and population harms (Drummond, paper in preparation). Alcohol-related attendances to EDs that do not result in admission are not routinely collected and so will not be included in MESAS. There is a need for robust, prospective evaluation evidence to measure the effectiveness of MUP in changing this important health outcome; to determine if and how it alters alcohol use, and to monitor possible differential impacts and potential adverse consequences. Our proposed assessment of changes in alcohol-related attendances at EDs will help establish the effects of MUP on alcohol-related harms. It will also add to the evidence base on the burden alcohol places on EDs. It will make an important contribution to our understanding of the effects of MUP, which routinely collected data may miss as there is potential for secular trends to occur (for example, related to the economic downturn[24] and hospital admissions data will be subject to time lags that may make establishment of causality based purely on routine data more difficult [25]. Furthermore, primary data collection planned in this study makes use of reliable validated tools (the Fast Alcohol Screening Test (FAST) which is a shortened form of the AUDIT questionnaire designed for use in emergency departments) [26]. This tool not only quantifies levels of harmful alcohol use but allows detection of changes in drinking patterns [27]. Such information is currently not adequately collected within routine health surveys, particularly for young people and deprived populations who are most likely to be affected by the intervention [28]. Assessment of drinking patterns is crucial as different patterns of consumption (for example binge drinking compared with chronic levels of use) are associated with different patterns of health and other social harms [6, 29].

Potential unintended consequences:

A number of potential unintended consequences have been identified that might arise from the introduction of MUP:

1) Consumers may switch to alternative sources of alcohol not subject to MUP so that the price paid does not increase. Such sources include both legal (internet sales from outwith Scotland, legitimate cross-border purchase for own use [30], and home fermentation) and illegal sources (counterfeit, smuggled or stolen alcohol) [31, 32].
2) Increased alcohol-related harm could occur through substitution (e.g. to illicitly produced or industrial alcohol associated with greater toxicity) or changed drinking patterns (e.g. moving from regular drinking to binge drinking).
3) Displacement effects with reductions in alcohol-related harms being accompanied by increases in harms related to other substance use could be observed, and
4) MUP could unfairly penalise deprived populations less able to absorb the additional financial cost [33] and this may adversely affect access to other essentials such as food.

There is a need for robust, prospective evaluation evidence to measure the effectiveness of MUP in changing alcohol-related emergency department attendances; to determine if and how it alters alcohol use, whether it changes public attitudes and norms and perhaps more importantly to monitor possible differential impacts and potential adverse consequences. To the investigators' knowledge, no other studies are planned to detect these adverse impacts in a robust way. Investigation of these potential impacts is of major public health importance as it may have important impacts on the overall assessment of health benefits compared to harms, as well as the distribution of those harms.

This proposal is informed by the MRC guidance on using natural experiments to evaluate population health interventions [19] and is based on a similar framework to the portfolio of studies investigating the smoking ban in public places in Scotland [34]. Evidence on the impacts, both positive and negative, will be of interest to the public, politicians and the public health community in Scotland, the rest of the UK and internationally.

2.2 Rationale

The legislation introducing MUP includes a so-called 'sunset clause', formally a provision that the measure will expire at the end of six years, unless an order for continuation is made between the fifth and sixth year [35]. A decision on whether implementation should continue is to be based on findings from a comprehensive evaluation, which this work constitutes an important part. The need for an evaluation is also stipulated within the Alcohol (Minimum Pricing) (Scotland) Bill which states that Scottish Ministers must present to the Scottish Parliament a report on the operation and effect of the minimum pricing provisions. This report must include information about how the policy has affected relevant businesses, different population subgroups and health.

The SPHSU has considerable expertise required to carry out this evaluation. In particular, the Unit's Policy programme focuses on methodology to evaluate natural experiments and led the development of the MRC's guidance in this area. Similarly, the Inequalities programme has a long history in evaluating major public health policies (for example, the National Evaluation of Sure Start) and in particular, assessing their impact on health inequalities.

2.3 Aims/Objectives/Research questions

The overarching NIHR grant includes three related studies that together make an important contribution to the overarching evaluation of the impact of MUP in Scotland. The three research

aims and their associated studies are summarised in the Table below. The remainder of this protocol will only focus on the Emergency Department (ED) study, with a separate protocol available for the survey of alcohol-related behaviours (which involves data collection within sexual health clinics).

Research aims (RAs)	**Study components**
RA1: To determine the impact on alcohol-related harms and drinking patterns for the overall population and by subgroups of interest (age, sex and deprivation)	Emergency Department study; Survey of alcohol-related behaviours (C1)
RA2: To determine the impact on non-alcohol substance use for the overall population and by subgroups of interest (age, sex and deprivation).	Survey of alcohol-related behaviours(C2); Qualitative focus group study (C3)
RA3: To describe changes in experiences and norms towards MUP and alcohol use following the introduction of MUP by subgroups of interest (age, sex and deprivation).	Qualitative focus group study (C3)

The more specific research objectives (ROs) of the ED study are as follows:

1. To determine the impact of MUP on alcohol-related ED attendances amongst the general population
2. To determine whether the effect of MUP differs across the following population subgroups
    a. Age group
    b. Gender
    c. Area-based deprivation
3. To determine whether the effect of MUP varies dependent on the type of alcohol-related harm:
    a. Acute alcohol-related harms vs chronic alcohol-related harms
    b. Broad diagnostic groups (on the basis of ICD categories)
4. To investigate whether alcohol consumption (on the basis of the FAST score: sensible, hazardous, harmful, possible dependence) has changed amongst people attending EDs over time
5. To investigate whether the intervention effect size varies over time

3 Study Design/Methods

3.1 Study Design

This research is a natural experiment study of the impact of introducing MUP in Scotland. The methods involve a repeated cross-sectional audit of all alcohol-related attendances at EDs in two Scottish hospitals and two North England geographical control hospitals at three time points. On each occasion, data collection will involve a face-to-face survey administered by research nurses to ED patients over selected times during a three week time period. All study documents with the exception of the patient information sheet and consent form will be

electronic and held on an iPad. Back up paper copies will be available in case of iPad failure. The study methods and tools are based on previous studies that have been used to quantify the national prevalence of alcohol-related attendances in Emergency Departments in England [36] and by the experience of the Scottish Emergency Department Alcohol Audit, carried out across 15-20 hospitals throughout mainland Scotland between October 2005 and June 2007 [37]. Prior to formal data collection, the processes for collecting data will be piloted – initially within Glasgow only, followed by pilot data collection at all four sites.

The study has been designed to be robust to potential delays in the timing of the intervention. Since the implementation of MUP is not under the control of the investigators, it is possible that there may be delays in the timing of the intervention. Baseline data collection will occur as soon as is practically possible. The 2nd and 3rd waves of data collection will take place six and 12 months post implementation. If implementation of MUP occurs more than 12 months after baseline the 2nd wave will be conducted shortly before implementation to act as a 2nd baseline. The 3rd wave will remain as close to a 12 month follow-up as feasible. If this occurs, it will not be possible to investigate whether the intervention effect varies over time (RO5). In general, investigators will attempt to avoid conducting data collection during months that are expected to be atypical in terms of alcohol consumption (i.e. Dec-Jan and Jun-Aug). Furthermore, we will attempt to collect data for one follow-up wave at the same time of year as the baseline data, to control for seasonal variation in consumption.

Since the design of the study is by necessity non-randomised, there remains potential for confounding. Furthermore, given the need to include high-risk drinkers within the study, previous experience has demonstrated that it is not possible to conduct longitudinal research with satisfactory rates of follow-up. For this reason, repeated cross-sectional samples have been chosen. However, the validity of analysis of repeated cross-sectional samples require high response rates and for participants interviewed to be representative of the population from which they are drawn (i.e. attenders to the ED in this study). It is therefore crucial that considerable effort is made to ensure that all eligible patients attending ED during data collection periods is invited to participate. The absolute number of participants within the study is far less important.

3.2 Settings

The intervention sites and local Principle Investigator are listed in the table below.

Hospital	**Principle Investigator**	**E-mail address**
Glasgow Royal Infirmary, Glasgow	Dr Samantha Perry	Samantha.Perry@ggc.scot.nhs.uk
Royal Infirmary of Edinburgh	Dr Michele Open	michele.open@nhslothian.scot.nhs.uk
Liverpool Royal Infirmary	Dr Lynn Owens	lynno@liverpool.ac.uk
Northern General Hospital, Sheffield	Dr Christopher Yap	Christopher.Yap@sth.nhs.uk

No changes to catchment areas are expected within the four sites during the conduct of the study.

3.3 Participant Selection

The target population for the study is all patients over 16 years age who attend EDs to receive acute treatment for a health condition.

The exclusion criteria for the sample are used to decide whether to approach patients and having approached whether the patient is eligible:

Deemed clinically inappropriate to be approached.

- 'patient too unwell',
- too distressed,
- grossly intoxicated (alcohol),
- grossly intoxicated (drugs)
- Cognitive impairment
- Police in attendance,
- Clear language barrier, and no interpreter available
- Patient already participating,
- routine follow up that has been instigated by ED staff,
- Patient left dept
- Patient admitted,
- staff safety issue,
- End of shift,
- dead on arrival,
- other.

For those who are approached, the inclusion criteria are:

- >=age16,
- able to speak English and no interpreter available,
- Is a new ED presentation,
- The patient is conscious
- The patient is physically well enough
- The patient is mentally well enough
- The patient is sober enough (alcohol)
- The patient is sober enough (drugs)
- The patient is still in the department
- The patient is safe for staff to approach

During data collection periods, an ED attendance database will be maintained for all attendances to allow monitoring of patient recruitment. This will help prevent patients being approached on multiple occasions. This attendance database will be destroyed at the end of each recruitment shift. In addition, data on sex, five year age group and diagnoses for all attendees in all the three week waves, with the attendees within the study timeslots flagged, will be requested from hospital records. This is to enable the assessment of the representativeness of our sample and of our estimates of the proportion of alcohol-related attendances.

We intend to obtain a total sample size of at least 2820 participants across all four sites over each three week period of data collection. This equates to 235 participants per week per site of data collection. No target sample size is required for the pilot phases of the study as these phases are intended to help identify potential practical issues involved in conducting the study.

Based on the experience of the 24 hour audit of Emergency Departments in England, we have assumed that we will be able to recruit at least 50% of eligible ED attendees. We anticipate that the four sites will result in 940 recruits per week. Recruiting over three weeks pre- and post-intervention – giving a total sample size of 5640 – would mean that we would be highly powered (>80%) to detect a decrease in the proportion of alcohol-related attendances from 30% to 25% with 95% significance. We have used a base rate of 30% informed by the 24 hour audit of EDs in England and assumed a 5% decrease would be of public health importance and may be expected based on current evidence. For subgroup analyses, we would have good power (>80%) to detect an effect size of 0.23 on the FAST score among those from the most deprived quintile (estimated to be 25% of attendances) and an effect size of 0.27 among those aged 18-24 (estimated to be 15% of attendances. Two separate follow-up times are required to determine if intervention effects vary over time.

3.4 Recruitment

Promotional material to make potential participants aware of the research will be displayed in the waiting areas of the Emergency Department (ED). This material will be in place only during the weeks of data collection and emphasises that the study is not only investigating patients with a specific condition (such as alcohol dependence).

A copy of a poster is included within the Appendix (Poster v2.6). Promotional material is only being used to raise awareness of the existence of the study and informed consent will be obtained separately by the research staff.

Potential participants will first be assessed by clinical research staff to ensure they are appropriate to approach. In cases of doubt the clinical research staff will consult senior ED staff. The research team will also ask the clinical team to signpost the existence of a research study to patients if possible. Potential participants will then be approached by the research staff, given an information leaflet to explain the purpose of the study and will be given a verbal explanation of the study's aims, what participation involves and invited to ask any questions they have about the study. Patients will be asked if they would like more time to consider whether they wish to participate and if so, the research nurse will re-approach the potential participant at a later time.

Attempts will be made to brief ED staff about the study (including at continuing professional development sessions and handover periods). ED staff will be encouraged to mention the existence of the study to patients but ED staff are unlikely to have the available time to fully brief patients about the nature of the study and hence will not be responsible for obtaining informed consent.

Participants will be provided with as long as they require during their current attendance at the Emergency Department (ED) to consider whether to participate. Given that participant involvement involves completion of a short questionnaire only, it is envisaged that a proportion of patients would prefer to take part immediately following their approach. While this will be allowable, research staff will ensure that participation is fully informed prior to obtaining written consent. In particular, a low threshold will be maintained for the research staff providing time to reflect on participation and for research staff coming back at a later time. Co-enrolment, for patients also involved in other studies, will be acceptable.

Study involvement is envisaged to last 5-10 minutes of active participation for each patient involved. However, we envisage that some patients may require a greater length of time than this. To allow this, at least two research nurses will be responsible for data collection at each

shift so that adequate time is available to allow data collection from willing participants and ensure adequate time for patients to reflect on whether they wish to participate.

Research staff will emphasise that participation is entirely voluntary (with clinical care being unaffected by their decision to participate or otherwise), they are free to withdraw at any stage of data collection if they do decide to participate and that further information on their clinical outcomes will be sought from their clinical notes. Research staff will explain that all information will be kept strictly confidential and all identifiable information will be removed prior to data analysis. In addition, it will be emphasised that no information provided by patients to research staff will be recorded in ED notes or shared with ED personnel but is for research purposes only.

Informed consent will be required from all participants who take part in the face-to-face survey. This will be documented using a paper form (MUP ED Participant Consent Form v2.5). During the consent process, researchers will also seek consent for linkage to administrative health data (including Scottish Morbidity Records in Scotland and Hospital Episode Statistics in England). It will be emphasised that it is not necessary to agree to this process to take part in the study, data linkage will be carried out confidentially by NHS staff and they can withdraw from this component of the study at a future time if they wish to. The process for withdrawal will be explained (via an online form on the study website, via a telephone call or by email). This information will be included on the information leaflet and the location of this information will be indicated to participants. Again, research staff will emphasise the voluntary nature of data linkage.

Interpreter services will be used to provide information to potential participants who are not able to speak English if available at the time of approach. If it is unclear whether the participant has understood the information provided, the recruitment attempt will be excluded. Similarly, if no suitable interpreters are available, the patient will be excluded from the study. Given the nature of the questions asked, family members will not be used for interpretation purposes. Written translations of the information leaflet for a number of languages (Mandarin, Hindi, Polish) will be available for the main study but not for the pilot phases. Information included in the information leaflet will be verbally reviewed by the research staff with the patient.

3.5 Withdrawal and loss to follow up

If the participant loses capacity to consent during the process of data collection, their research data would be withdrawn from the study. As active involvement is relatively short, occurrences of this type of event are expected to be rare.

We will not be planning to re-contact participants after their involvement in the study. This is to ensure that their participation (including attendance at the Emergency Department) in the study can be kept confidential. However, we plan to make a plain language version of the study results available on the study website. A link to the study website will be included on the participant information leaflet and participants will be informed that results will be available from that source. In addition, we plan to work extensively to disseminate the results of the study to the general public through the mass media.

For participants who have provided consent for data linkage, they will have the opportunity to withdraw their consent by contacting the study team. Contact details and information on this process will be included within the Participant Information Leaflet.

3.6 Study Procedures

Prior to the main study data collection, two pilot phases of research are planned. Data collection for the first pilot phase will occur for one day shift and one night shift with two research nurses (with honorary or substantive NHS contracts) being responsible for data collection for each shift. This pilot phase will help the research team to ensure data collection instruments are appropriate and identify any unexpected barriers to smooth conduct of the research. To achieve this, additional open-ended questions will be asked for a small subset of participants (see Interview Schedule for Pilot Phase v2.5 and Qualitative Interview for Pilot Phase Consent Form v2.5). Approximately 10-15 patients (purposively sampling for patients who have refused to take part in the main study (if possible), agreed to take part in some but not all aspects of the main study and agreed to take part in all aspects of the main study) will be interviewed in a short one-to-one qualitative interview. Diversity in age group, socioeconomic position and gender will also be sought. If following the pilot work, the research methods for further phases of the study require modification, an amendment or further application to the research ethics committee will be made as appropriate. We anticipate that further pilots would be beneficial in this phase, prior to the first wave of data collection in February. This will allow us to do more testing and refinement of the data collection processes to maximise response rate.

A second pilot phase is planned in the run-up to the first wave of the main study. This will be conducted across all four sites and will help ensure that the research staff do not interfere with the smooth operation of the ED. Identical data collection procedures for all of the above phases are planned (with modifications requiring further applications or amendments to the research ethics committee). During data collection, clinical research staff will identify patients who are not appropriate to be approached for participation in the study and should be excluded, and in cases of doubt senior clinical ED staff will be consulted. Research staff will approach all patients who are not considered inappropriate to approach.

Research staff will receive in-depth training from the research team and others, with half-day training on issues related to obtaining informed consent planned. This training will be delivered by a professional with a high level of expertise in relation to the clinical care of people with addiction (e.g. Colin Drummond, Professor of Addiction Psychiatry and Consultant Psychiatrist). It will include information on the potential for fluctuating consent and raise awareness of specific pathologies that may impede informed consent (e.g. Korsakoff's syndrome). Research staff will also be trained to provide contact details to existing facilities for assistance on issues related to alcohol use, drug use and domestic abuse, for participants who request it. Contact details for further information on alcohol issues (available from Drinkline) will be included at the end of the participant information leaflet so that all those approached can seek further information and help if they wish to do so.

3.7 Data Collection

Each wave will collect data over three weeks, ideally with one wave of data collection prior to the implementation of MUP and two post-implementation waves (after six months and 12 months). To maximise collection of both alcohol-related attendances and hazardous drinkers, data collection will occur from 2000 to 0400 on Thursday to Sunday (i.e. 32 hours per week during this time period) and 0900-1700 on Monday to Wednesday (i.e. 24 hours per week during this time period). If deemed necessary by local sites, different 8 hour timeslots will be considered, to meet local attendance patterns. As noted above, periods of the year when alcohol consumption is atypical will be avoided.

Patients will be approached by research staff to seek permission to complete a short face-to-face interview. The reasons for exclusion will be recorded electronically on the iPad along with 5 year age group and sex. Excluded patients will not be assigned a study ID and so will be completely anonymous.

All suitable patients will be approached, their eligibility confirmed, and, if eligible, informed consent will be sought and a face-to-face interview administered, based on a previously used patient questionnaire [36]. Research nurses will be responsible for obtaining written informed consent, completing the data linkage form if consent has been obtained -and then proceeding to conduct the face-to-face survey. These will all be electronic documents contained on an iPAD.

The face-to-face survey will collect information on socio-demographic details, problematic alcohol use (FAST Alcohol Screening Test), alcohol consumption in the last 24 hours, self-assessment of whether alcohol contributed to the attendance and self-report of whether the patient has been a victim of violence. Research nurses will input the information into the standardised electronic form which will include a number of options to assist with timely completion. Paper versions of the survey, and consent and linkage forms are enclosed (ED Survey v2.5). The Interview Schedule for Pilot Phase v2.5 and Qualitative Interview for Pilot Phase will be on paper only. Back up paper copies of all electronic documents will be available in case of iPad failure. An ED attendance database will be maintained for all attendances during data collection periods to allow monitoring of patient recruitment.

Research staff will retrieve additional data on participants from patient records, either during data collection sessions (if time allows), or at a later time. The following information will be sought from the clinical records:

- demographic characteristics (date of birth, sex, postcode),
- attendance details (time, triage category),
- discharge status
- diagnoses at discharge (coded by ICD10 categories) and all relevant data relating to reason for admission and diagnosis (whether ICD10 or another coding system or free text).

We will calculate the consent rate among those eligible. However we need to assess the representativeness of the interviewees and attendees in the study timeslots, and the certainty of our estimates of the proportion of attendances that are alcohol-related. To make this possible, we propose to request from hospital records anonymised information on all attendees over the three week data collection periods for each wave. We wish to ask for 5 year age groups, sex, reason for attendance, and other relevant data for diagnosis (whether ICD10 or another coding system or free text). We will request that attendees within the timeslots for the study are flagged, so that we can calculate a true recruitment rate for those interviewed and for whom we have reasons for exclusion.

Data collection will be conducted by Clinical Research Facilities (CRFs), on behalf of the study team. Each CRF will be responsible for ensuring line management of their staff, as per their usual operating procedures. The research nurses responsible for data collection will have received training, with training available for additional research nurses (to allow for rota gaps to be filled, in the event of illness etc.). It is recommended that any data collection session should include at least one more experienced research nurse, so that more junior research nurses feel adequately supported. Research nurses will be able to contact a member of the study team throughout data collection periods in the event of an emergency.

The study will be coordinated by a project coordinator based at the SPHSU who in turn will be supported by a post-doctoral researcher. These individuals will be responsible for ensuring distribution of materials for data collection to the sites and liaising with CRF staff to coordinate the study and in particular, ensure that data collection processes are followed consistently across sites and over time. During each wave of data collection, all paper-based forms should be stored securely using existing CRF facilities, with any data linkage forms stored separately from

consent forms. Consent forms, should be returned to the SPHSU using secure couriers at the end of each three week data collection period. It is the responsibility of the project coordinator to monitor transfers of the data and consent forms to the SPHSU. All electronic survey and linkage data will be sent through electronic secure transfers to the SPHSU server. This approach has been previously applied by members of the study team for randomised controlled trials conducted within the ED setting.

3.8 Data Analysis

Primary outcome

The primary outcome will be changes in absolute numbers of alcohol-related attendances as defined by any one of:

- patient self-reports attendance is alcohol-related
- patient reports alcohol consumption in past 24 hours of ≥8units in men or ≥6 units in women
- patient not approached because too intoxicated with alcohol

Secondary outcomes

Secondary outcomes will be changes in:

- absolute number of alcohol-related attendances by age/sex/deprivation
- problematic alcohol use (as defined by the Fast Alcohol Screening Test (FAST))
- mean FAST score
- prevalence of binge drinking in the past week
- reason for attendance (coded by ICD10)

After the first post-intervention wave, we will test for differences in the outcomes between the intervention and comparison groups using a fixed-effects regression model, with individuals nested within EDs, before and after adjustment for relevant covariates including baseline levels of alcohol-related attendance, demography, triage category etc. We will also attempt to determine the nature of the effect more precisely in terms of whether a dose-response effect according to the time since MUP was implemented (through a test of the significance of an interaction between time and intervention). We will test for interactions of the intervention with defined important covariates (including age, gender, deprivation quintile, disease diagnostic categories) to investigate the possibility of differential intervention effects and will subsequently stratify the analyses if indicated.

4. Research Governance and Regulatory Issues

4.1 Ethical issues

This study (titled 'Evaluating the Impact of Minimum Unit Pricing of Alcohol on Patients Attending the Emergency Medicine Department Setting: A Natural Experiment') has been considered by NHS Research Ethics Committee Scotland A – reference 12/SS/0120 at a meeting held on 9 August 2012. The application received a favourable ethical opinion. One issue that was raised by the Committee was consideration of withdrawal of consent to data linkage. This has resulted in a minor alteration of the Participant Information Leaflet (PIL), to provide information for participants on how to withdraw their consent to linkage. There has been one amendment since the original submission, this was to change to the electronic questionnaire and use of iPads. We have taken this further with our current amendment.

We have developed an electronic interface which will simplify and enhance the data

collection by showing only relevant questions to the participants. To maximise completion these will be shown individually through an appealing graphic interface. Moreover, participants will be able to skip any questions and withdraw at any stage of the interview process.

Data collection will be done through the iPad and stored locally temporarily and uploaded onto a secure server through a 256-bit encrypted connection whenever an internet connection is available. This will happen at least twice a day. All iPads will be remotely monitored (through geolocation), and access blocked and data stored retrieved and wiped out remotely in case of theft or entry of incorrect password. This will considerably limit the possible loss of documents and simplify storage of study documents.

To obtain the most valid self-reported data, patients (and their parent or guardian if applicable) will be told as part of the informed consent procedure that the participant's answers will not be disclosed to their parent or guardian or the ED staff and that participation in the study is not dependent on alcohol consumption. Screening for eligibility will be conducted using the iPad overseen by a research nurse who will introduce and deliver the interview, if applicable, to each eligible and consenting patient.

4.2 Data Monitoring

The Principal Investigator will be overall responsible for monitoring the quality of data collected. The postdoctoral researcher will be responsible for day-to-day management of data collection. External monitoring of data collection will be via the Advisory Group (described below).

4.3 Data Management

The original data will be imported to new SAS files (.DAT) for data management and the original files backed up unaltered on the Unit's network drive only accessible to the project team. Data cleaning, manipulations and analysis will be performed in separate coding/syntax files. We will provide well documented (i.e. with extensive commenting) SPSS/SAS/R syntax so that all processing of data and results are reproducible. Metadata information on all variables of are already documented by the data sources. Recoded or derived variables necessary for secondary analysis will be documented and original variables retained to enable the data to be used accurately and effectively.

4.4 Data Storage and Retention

Consent forms, questionnaires and data linkage forms will be linked by a personal identifier number on each document. However, they will immediately be separated and stored separately in locked cabinets at the research site until they can be collected and transferred to the MRC/CSO Social and Public Health Sciences Unit for processing. All paper questionnaires are stored, de-identified, in locked storage areas with strictly controlled access and handled according to MRC Good Research Practice Guidelines. Consents are stored separately in a dedicated secured area. Similarly, paper data linkage forms will be stored separately in a dedicated secured area. We will ensure that the electronic questionnaire data, and data linkage forms are stored separately in three secure databases to maintain full confidentiality for these data.

Questionnaires, data linkage forms and consent forms have a 5 digit identifier which links the three documents. There are no names or other unique identifiers on the questionnaire and the questionnaire is held separately from the consent form at all times during both electronic and physical transport and storage. All personnel working with the data have signed confidentiality agreements and are trained in good research practice. Staff entering data do not see the consent forms and have no way to identify who completed the questionnaires they process.

Consent forms will be processed at the MRC/CSO Unit by logging the individual ID number as proof of receipt. No names are entered onto the database. Once logged, the consent forms are stored securely in the locked consent cabinet. Paper questionnaire data is entered onto the study database by ID number. No personal identifier is linked to the questionnaire data. Paper data linkage forms will be stored separately from both the consent forms and clinical data. As described above we will apply similar confidentiality and security standards to the electronic data.

Access to data will be restricted to members of the research team during fieldwork and processing at the MRC/CSO Unit. Where data input occurs outside the Unit, external companies (who have all signed strict confidentiality agreements) are not given access to any identifiable data.

Storage and use of data after the end of the study
Long term storage of data is at Iron Mountain, a commercial data storage facility. All data are held in secure conditions with, for paper-held data links to the contents of the sealed boxes held on a database at the MRC/CSO Unit. For electronic data secure electronic archives are used. Access to the data is controlled and permission from the data guardian for the study is required to access long-term archived data.

Strict data protection policies will be followed as outlined in the University of Glasgow's data protection policy (http://www.gla.ac.uk/services/dpfoioffice/policiesandprocedures/dpa-policy/). The data will be worked from and stored upon the unit's secure protected server (only accessible to the project team). Upon completion of the project, the data will then be archived in line with University of Glasgow University guidance on data archiving and the MRC's 'Personal Information in Medical Research' guidance document.

5 Project Management

5.1 Project Manager

The Project Manager with responsibility for the day to day management of the project is:
Ross Forsyth – Ross.Forsyth@glasgow.ac.uk

5.2 Project Management Group

The Project Team for the ED study consists of the following members:

Name	Division/Organisation
Alastair H Leyland	MRC/CSO Social & Public Health Sciences Unit
S Vittal Katikireddi (SVK)	MRC/CSO Social & Public Health Sciences Unit
Andrew Millard (AM)	MRC/CSO Social & Public Health Sciences Unit

Name	Division/Organisation
Ross Forsyth (RF)	MRC/CSO Social & Public Health Sciences Unit
Samantha Perry (SP)	Glasgow Royal Infirmary, Glasgow
Janet Johnstone (JJ)	Glasgow Clinical Research Facility
Michele Open (MO)	Royal Infirmary of Edinburgh
Miranda Odam (MOd)	Edinburgh Clinical Research Facility
Christopher Yap (CY)	Sheffield
Erica Wallis (EW)	Sheffield Clinical Research Facility
Lynn Owens (LO)	Liverpool Clinical Research Facility
Patient representative (TBA)	
Colin Drummond (CD)	Institute of Psychiatry, Kings College London
Paolo Deluca (PD)	Institute of Psychiatry, Kings College London
Lesley Graham (LG)	Information Services Division, National Services Scotland
Clare Beeston (CB)	NHS Health Scotland
Gerry McCartney (GMc)	NHS Health Scotland
Lyndal Bond (LB)	University of Melbourne

The Project Management Group will meet three times per year throughout the project. Initial meetings will focus on planning data collection, followed by monitoring data collection and planning research outputs. All meetings are to be considered strictly confidential.

Minutes of PMG meetings will be taken on the SPHSU template and a Decision Log will be created and maintained by the Project Manager.

In addition to the regular meetings of the PMG for the ED study, investigators of the NIHR-funded MUP evaluation grant will meet twice per year. SVK, AL the postdoctoral researcher and the project manager will also be involved in the conduct of the study on unintended consequences of MUP (with data collection in sexual health clinics). Lastly, SVK will also contribute to the conduct of the qualitative focus group study that is led by Stirling University. These joint members will be responsible for ensuring communication is maintained across different studies within the MUP evaluation portfolio.

5.3 Steering Group

A Steering Group will be established with membership drawn from academics not involved in the study. Members of the Steering Group will likely include Professor John Frank (Director of the Scottish Collaboration of Public Health Research and Policy), Prof Tim Stockwell (who has led an evaluation of reference pricing of alcohol in Canada), Scottish Government, third sector alcohol representatives (such as Alcohol Focus Scotland) and members of the public. Meetings will be held six monthly. To enable participation by members not based in Scotland, meetings will use video/teleconference facilities. Involvement of potential end-users of the research

(including policymakers, advocacy groups) as well as public representation is intended to ensure the research is carried out in a sensitive and policy-relevant manner.

All discussions of the Steering Group will be considered to be confidential.

5.4 Project Filing Structure

The project files will be kept on a secure drive that are accessible to the SPHSU staff directly involved in the project. Responsibility for managing version control of the project files will rest with the postdoctoral researcher (to be appointed). Sub-folders created include: Grant Application; Closure and Archiving; Correspondence and Reports; Data; Data Collection; Dissemination and Impact; Ethics and Governance; Finance and Legal; Intervention and Process Evaluation; Meetings; Protocol; Risk and SOPs.

The electronic project files will be kept on:

T:\projects\MUP ED

The paper project files will be kept by the Population Health Research Facility during the study conduct, followed by archiving using University of Glasgow preferred suppliers.

6. Dissemination

6.1 Communication method

The key communications channels are:

- NIHR research report
- Journal Publication (possible targets):
    - *The Lancet*
    - *British Medical Journal (BMJ)*
    - *PLoS Medicine*
    - *International Journal of Epidemiology (IJE)*
    - *Addiction*
- Conference presentations (possible targets):
    - Society for Social Medicine
    - Kettil-Bruun Society
    - European Public Health Association conference
    - Scottish Faculty of Public Health conference
- Face-to-face dissemination with Scottish, UK and international policymakers
- Mass media, with issuing of press releases to increase the likelihood of gaining media interest
- Talks aimed at the public with an interest in public health and/or addiction e.g. events run by the Edinburgh Science Festival, local addiction charities

6.2 Publication Policy

All individuals who fulfil the ICMJE criteria for authorship will be invited to be an author of research outputs. It is expected that this is likely to include the study investigators (AHL, SVK, LG, CD, LB, GMc), key collaborators (TP, PD), clinical leads at the four sites and the postdoctoral researcher.

All publications relating to the project will be authorised by the PMG. Furthermore, the Advisory Group will be notified of plans to publish research outputs. Presentations will be authorised by a minimum of the Principal Investigator (AHL), but attempts will be made to gain approval from the overall PMG if time allows.

6.3 Public Engagement and Knowledge Exchange

This study has direct policy relevance and has been developed in close collaboration with policymakers within NHS Health Scotland and the Scottish Government. Ongoing discussion with policymakers is planned for throughout the project, with invited presentations to NHS Health Scotland and Scottish Government expected. More formally, the findings of this study will be formally submitted to the Scottish Government to contribute to their report on the impact of MUP which is to be laid to the Scottish Parliament.

Given the political sensitivity around the project, care will be necessary to ensure interim results are not publicly disclosed. Finalised results will be communicated to the general public by actively engaging the mass media.

7. Project Milestones / Timelines

The following sets out the key project milestones points when key decisions must be taken or key milestones should be reached:

1. Approval of major amendment to NHS REC and approvals for site-specific NHS R&D
2. Recruitment of postdoctoral researcher
3. Agree membership of the Advisory Group and hold first meeting
4. Submit protocol paper for publication in an open-access journal
5. Pilot data collection processes within Glasgow
6. Agree timing of baseline data collection across all four sites and pilot data collection processes across all four ED sites and quality assure collected data
7. Collect baseline data (wave 1) over three weeks and transfer data to SPHSU
8. Conduct analysis of baseline data
9. Collect follow-up data at approximately six months post-implementation of MUP, with transfer of baseline data shortly after
10. Conduct analysis of initial follow-up data
11. Collect follow-up data at approximately twelve months post-implementation of MUP, with transfer of baseline data shortly after
12. Statistical analysis of main results
13. Communicate findings of initial results to key stakeholders
14. Draft and submit first substantive results paper
15. Conduct additional analyses (RO3 and RO4) for further results papers
16. Submit further papers
17. Hold dissemination event
18. Submit final report to NIHR

A project timeline is included in Appendix A.

8. Project Risk Assessment

The risks relevant to the project are recorded in the risk assessment form and contained in the initial Project Risk/Issue log on:

T:\projects\MUP ED\Risk and SOPs\Risk Assessment Form.xlsx

The Risk Log will be reviewed and updated at Project Management Group meetings.

9. References

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Appendix A: Project Timeline – three year view and first 6 months detail

Year	2017					2018											2019												2020		
Calendar month	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M
Project month	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Tasks																																
REC/R&D approval																																
Recruit postdoc																																
Advisory group established																																
Submit protocol paper																																
Pilot data collection (Glasgow)																																
Pilot data collection (all sites)																																
Collect baseline data																																
Analysis of baseline data																																
Collect wave 2 data																																
Initial analysis of follow-up data																																
Collect wave 3 data																																
Analysis of main findings																																
Communicate initial findings to stakeholders																																
Submit first results paper																																
Additional analyses																																
Submit further papers																																
Dissemination event																																
Submit NIHR report																																
PM Group meetings																																
Advisory Group meetings																																

Approximate Month		November			December					January				February				March					April				May			
Week		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Week start date (Monday)	**Lead***	6.11	13.11	20.11	27.11	4.12	11.12	18.12	25.12	1.01	8.01	15.01	22.01	29.01	5.02	12.02	19.02	26.02	5.03	12.03	19.03	26.03	2.04	9.04	16.04	23.04	30.04	7.05	14.05	21.05
Ethics approval (needed for prepilot and pilots)	RF																													
SSI approval (R&D finance)	RF, DM																													
Agree consistent timings for training - pilots, baseline - Share this plan with local sites and ask for detailed site plans	DM																													
Print and distribute pre/pilot/baseline information leaflets and consent forms (at site printing if possible, with local logos)	KA																													
Produce, Print and distribute pre/pilot/baseline posters (at site printing if possible, local logos)	KA																													
Programme and distribute iPADS (secure storage of these is a site responsibility)	? PD + MRC																													
Arrange and deliver training for pre-pilot (Glasgow)	PD KA DM RF																													
Pre-pilot the tools (Glasgow only, 2 days and 2 nights)	DM																													
Make any amendments required to tools and forms	DM RF VK AL																													
Apply for ethics approval for amendments	RF, DM																													
Arrange to translate information and consent form	KA																													
Hold a site co-ordinators information meeting teleconference	DM																													
Arrange travel and accomm for training and QA visits	KL																													
Deliver training to research nurses and data co-ordinators at all 4 sites	PD KA DM RF																													
Carry out pilots (all sites, confirm days, visit each site to QA)	DM…																													
Collect baseline data, and visit to QA	DM…																													
Receive and store electronic secure file transfer of data on exclusions 3 weekly for data collection period	RF																													
Arrange data collection from hospital records and survey data at site	RF DM																													
Arrange secure file transfer for hospital records and survey data	RF																													
Arrange receipt, logging, and secure separate storage for paper or electronic consent and linkage forms	RF																													
Document data collection methods at each site	DM																													
Clean baseline data (pilot and hospital records)	DM																													
Report descriptively on baseline data	DM																													
Report on documented data collection procedures at each site	DM																													
Plan further analyses	DM RF KA VK AL and others																													
Draft Protocol paper	DM RF KA VK AL and others																													
Distribute materials for second wave	?																													
Maintain contact with sites	?																													
holiday	all tbc																													
Second data collection (avoiding August if possible)	?																													
*Leads DM: Drew Millard, RF: Ross Forsyth, KA: Kim Appleton, KL: Kirsten Lindsay, PD: Paolo Deluca.																														