PRE-OP BIRDS

Full Title:	**Preoperative Behavioural Intervention to Reduce Drinking before elective orthopaedic Surgery (PRE-OP BIRDS) – A Pilot Randomised Controlled Trial**
Short Title/Acronym:	**PRE-OP BIRDS: Pilot RCT**
Protocol Version Number & Date:	**1.1 03 May 2017 2017**

Statement:

This protocol has regard for the HRA guidance.

RESEARCH REFERENCE NUMBERS

IRAS Number:	**222453**
NHS REC Reference:	**17/NE/0093**
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RESEARCH SPONSOR

Sponsor Name:	**The Newcastle upon Tyne Hospitals NHS Foundation Trust**
Sponsor Reference:	**8287**

RESEARCH FUNDER(S)

Funder Name:	**NIHR HTA**
Funder Reference:	**14/42/01**

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted. The Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the Research Governance Framework, Good Clinical Practice (GCP) guidelines, the relevant Standard Operating Procedures and other regulatory requirements as applicable.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

Representative of the Research Sponsor

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(print)

Position:

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(print)

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Statistician

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Trial Website	TBC

TRIAL SUMMARY

Trial Title	Preoperative Behavioural Intervention to Reduce Drinking before elective orthopaedic Surgery (PRE-OP BIRDS) – A Pilot Randomised Controlled Trial
Acronym	PRE-OP BIRDS – Pilot RCT
Summary of Trial Design	Pilot randomised controlled trial (RCT)
Summary of Participant Population	Adults (≥18 years) listed for primary elective joint (hip or knee) arthroplasty
Planned Sample Size	80 surgical patients (40 recruited to each arm), 11 Preoperative Assessment Nurses/Health Care Assistants (HCPs)
Planned Number of Sites	3
Intervention Duration	The intervention will involve 2 sessions – session 1 delivered 6-10 weeks prior to surgery lasting 20-30 minutes and session 2 an optional booster session delivered 1-2 weeks prior to surgery lasting 10-20 minutes
Follow Up Duration	Follow-up visits will take place 6 weeks' post-surgery and 6 months following initial preoperative assessment
Planned Trial Period	15 months

	Objectives	**Outcomes/Outcome Measures**
Primary	To estimate rates of patient eligibility, recruitment, willingness to be randomised and retention at 6 months' post-assessment to assess the feasibility of proceeding to a definitive RCT	Recruitment and randomisation rates defined by; - Proportion of eligible patients who agree to participate in the trial - Proportion of enrolled patients successfully followed up 6 months after baseline assessment - Rates of eligibility and reasons for ineligibility (captured through screening logs)
Secondary	- To train HCPs in the delivery of screening and brief behavioural interventions to eligible patients in the setting of a preoperative clinic and to assess fidelity of intervention delivery - To measure patient alcohol status at initial preoperative assessment, before surgery and at follow up at 6	- Fidelity of delivery assessed via transcripts of audio recordings of brief behavioural interventions delivered. - Alcohol consumption as measured by AUDIT score.

	weeks (routine clinical check) and 6 months' post-assessment - To assess completion rates for all data collection tools used in the pilot trial - To establish response variability of proposed outcome measures for a definitive trial, which will include risky drinking status and quality of life - To determine rates of secondary outcomes and perioperative complication rates including bleeding and infections - To explore the acceptability of study interventions and outcome measures with HCPs and patients. - To establish current practice nationally (and variability therein) in respect of preoperative assessment, with particular reference to management of risky drinking to inform the definition of the comparator condition for a future definitive trial	**Outcome measures:** - Minor complications - Postoperative Morbidity Score (POMS) includes wound infections - Major postoperative complications (including mortality) - Clavien-Dindo Classification - Evidence of early bleeding or thromboembolism. - Alcohol related complications - Hospital length of stay to discharge - Need for reoperation - Thromboembolism/complications including Pulmonary embolus or wound infections - Use of primary and secondary care (e.g. Number and duration of hospital encounters (perioperatively) including Hospital readmission) - Health Related Quality of Life - EQ-5D at six weeks' post-surgery and six months' post intervention. - Western Ontario and McMaster Universities osteoarthritis index (WOMAC) Functional Assessment score - Themes identified in Framework analysis of HCP and patient interview transcripts. Interviews with HCPs to be conducted after intervention delivery is complete. Interviews with patients to be conducted at 6 months after preoperative assessment. - Reported delivery of alcohol screening and intervention, other behavioural interventions as part of pre-operative assessment
Intervention	Preoperative Brief Behavioural Intervention to reduce or cease drinking in elective orthopaedic patients	

Contents

GLOSSARY OF ABREVIATIONS

{MAKE CHANGES AND ADD ROWS AS REQUIRED}

ABBREVIATION	DEFINITION
AE	Adverse Event
AR	Adverse Reaction
BCT	Behaviour Change Technique
CI	Chief Investigator
CRF	Case Report Form
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
HCP	Health Care Professional
HRA	Health Research Authority
ICF	Informed Consent Form
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials Number
NCTU	Newcastle Clinical Trials Unit
NHS	National Health Service
NJR	National Joint Registry
PAC	Pre-Assessment Clinic
PI	Principal Investigator
PIS	Participant Information Sheet
POMS	Post-Operative Morbidity Score
QA	Quality Assurance
QC	Quality Control
R&D	Research & Development
RCT	Randomised Control Trial
REC	Research Ethics Committee

SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SOP	Standard Operating Procedure
TAU	Treatment as Usual
TMG	Trial Management Group
TSC	Trial Steering Committee
TMF	Trial Master File
USAR	Unexpected Serious Adverse Reaction
WOMAC	Western Ontario and McMaster Universities Osteoarthritis index

1. BACKGROUND

Risk Factors for Postoperative Complications

Advanced age, co-morbid disease and major surgery are key factors associated with an increased risk of postoperative complications reported in recent National Confidential Enquiry into Patient Outcome and Death reports (1, 2). Early postoperative complications may lead to increased mortality, interfere with patient well-being, delay recovery and increase length of hospital stay. Importantly, surviving patients who develop even minor complications, continue to suffer a reduction in functional independence (3) and a substantial decrease in medium and long-term survival (4). It follows that the avoidance of postoperative complications through the detection of, and intervention against, known preoperative risk factors, especially in older surgical groups, should be a financial and ethical goal for all NHS institutions.

Preoperative Risk in Orthopaedic Surgery and Postoperative Outcome

Elective orthopaedic surgery (hip and knee replacements), represents a high volume component of elective major surgery, being performed in an increasingly older patient group, with a challenging timescale for preoperative optimisation (approximately 6-10 weeks from listing to surgery). Primary outcomes of improvements in mobility and daytime pain reduction are significant expectations following joint arthroplasty, and their fulfilment are important in determining patient-reported outcomes (5). Early postoperative complications such as wound infection, bleeding and thrombosis and prolonged hospital stay will have detrimental effects on these outcomes. However, preoperative risk factors including age, sex, comorbidity, socioeconomic status, lifestyle behaviour and psychological factors play an important role in functional recovery and quality of life after arthroplasty. Additionally, patients' pre-operative expectations and their fulfilment influence post-operative reports of outcome. Specifically, patients of younger age and with higher preoperative mental health report greater pre-operative expectations of recovery which in turn relates to greater improvements after surgery. (5, 6). Unfortunately, this younger group represents a minority of patients undergoing elective orthopaedic surgery. As UK life expectancy continues to increase (7) the shift in ageing demographics and the natural history of arthritic disease will lead to a higher proportion of older patients undergoing elective orthopaedic surgery, thereby increasing overall rates of short and long term mortality and morbidity.

Preoperative Alcohol Consumption and Postoperative Complications

Increased preoperative alcohol consumption has detrimental effects on postoperative complications (8, 9). It follows that a reduction or cessation in alcohol intake before surgery may reduce perioperative risk (10, 11). However, reduction of alcohol intake in any setting represents a complex medical and psychosocial challenge. Screening for risky alcohol consumption using validated screening tools has been shown to have good patient acceptance (10, 11-14). Where a dedicated screening tool (AUDIT) has been used in the European preoperative setting (15), there was an increased detection rate of risky preoperative alcohol use when compared with clinician assessment. However, in general, these methods have not been introduced into the UK elective surgical pathways.

Preoperative Assessment before Major Orthopaedic Surgery

The development of clinics dedicated to preoperative assessment has aimed to assess patients at a much earlier stage of the surgical pathway so that they can take steps to be well prepared and in optimal condition prior to their surgery. These clinics have already demonstrated significant benefit to the NHS through the cost-effective prevention of on the day cancellations and to the improvement in day case and day of surgery arrival rates (16). However, the potential

role of preoperative assessment clinics in providing a timely opportunity to incorporate lifestyle intervention strategies to reduce preoperative risk has not been fully exploited.

Brief Behavioural Interventions before Surgery

Strong evidence exists for the effective delivery of brief behavioural interventions in the reduction of alcohol intake in primary care (17, 18), with a rapidly growing evidence-base in emergency departments (19, 20) and hospital wards (21). Less evidence exists regarding behavioural interventions to reduce alcohol consumption before surgery (8). Tonnesen et al (20) reported reduced drinking and fewer postoperative complications after disulfiram therapy. In further unpublished data, (cited in a Cochrane database Review (8)), the same group also reported that intensive motivational counselling, with an aim of achieving three months of alcohol cessation in the preoperative period reduced alcohol consumption in all patients in the intervention group. In contrast, Shourie et al (22) showed no effect on drinking outcomes of a brief behavioural intervention, although preoperative review was restricted to < 7 days before operation, a factor subsequently quoted as the major reason for intervention failure (22).

2. RATIONALE

HCP-delivered Screening and Brief Behavioural Intervention to Reduce or Cease Alcohol Consumption before Elective Orthopaedic Surgery

Since many preoperative patients may not be aware that their drinking increases their health risk, intensive or aversive approaches (e.g. disulfiram) are likely to have low acceptability in UK patients (especially in joint arthroplasty where most patients are > 65 years). Positively focused brief behavioural intervention delivered by generalist nurses may be more acceptable, although the precise content needs to be customised to this clinical context and target population.

We propose that upcoming major surgery provides an important 'teachable moment' and thus an opportunity for effective brief behavioural intervention delivery. The timely development of preoperative assessment clinics, provide an unexploited setting for dedicated, nurse-led screening and delivery of brief behavioural interventions. In terms of this proposal, the potential effect of reducing risky drinking perioperatively may have immediate benefits on the short-term clinical outcomes after surgery. Furthermore, sustained reductions in alcohol consumption are likely to support longer-term recovery (clinical and functional outcomes) as alcohol has immunosuppressant effects, as well as being a risk to future well-being in a predominantly older, orthopaedic population.

Feasibility Study

This Pilot RCT study is funded via a grant awarded by the NIHR HTA. The grant was split into two phases – a Feasibility Phase and a Pilot RCT. During the Feasibility Phase of the HTA award an alcohol screening and brief behavioural intervention was developed and a study was conducted to assess the feasibility and acceptability of screening and intervention to both staff and patients. As part of the feasibility study HCPs at the primary site were trained to deliver screening and brief behavioural intervention. Patients were recruited to the study (the recruitment target was 16 patients) and all those recruited and eligible received the behavioural intervention. Qualitative interviews were also conducted with both staff and patients. Feedback obtained in the qualitative interviews identified that the screening and intervention techniques were acceptable to both staff and patients, and were conducted without impacting on patient care.

During the Feasibility Study, focus group discussions were also held with staff members from the three sites who have elected to take part in this pilot RCT. The aim of the focus groups was to establish usual care, including how each site currently assesses a patient's alcohol intake prior to elective knee or hip arthroplasty and what, if any, treatment or support is available for alcohol reduction or cessation. From this the study team have been able to define treatment as usual within this protocol to ensure it fits with sites' current standard practice and ensure consistency throughout the study sites.

A Trial Steering Committee and Data Monitoring Committee were set up as part of the feasibility trial and multiple meetings held. Updates to the study processes as we progressed through the feasibility study were discussed with and agreed by the committees prior to implementation. These committees will continue as part of the pilot RCT.

We are now conducting this larger pilot RCT to assess the feasibility of a definitive RCT.

3. OBJECTIVES AND OUTCOME MEASURES

3.1. Primary Objective

To estimate rates of patient eligibility, recruitment, willingness to be randomised and retention at 6 months' post-assessment to assess the feasibility of proceeding to a definitive RCT.

3.2. Secondary Objective(s)

To train HCPs in the delivery of screening and brief behavioural interventions to eligible patients in the setting of a preoperative clinic service and to assess fidelity of intervention delivery.

To measure patient alcohol status at initial preoperative assessment, before surgery and at follow up at 6 weeks (routine clinical check) and 6 months' post-assessment.

To assess completion rates for all data collection tools used in the pilot trial.

To establish response variability of proposed outcome measures for a definitive trial, which will include risky drinking status and quality of life.

To determine rates of secondary outcome variables and perioperative complication rates including bleeding and infections.

To explore the acceptability of study interventions and outcome measures with HCPs (after intervention delivery is completed) and patients (at 6 months after preoperative assessment).

To establish current practice nationally (and variability therein) in respect of preoperative assessment, with particular reference to management of risky drinking to inform the definition of the comparator condition for a future definitive trial.

To establish if the intervention booster session is useful to patients and gauge their interest in attending a second intervention session closer to their surgery date.

3.3. Outcome Measures

Screening, recruitment and retention frequencies.

Alcohol consumption measured by AUDIT score.

Minor complications - Postoperative Morbidity Score (POMS) (23) includes wound infections

Major postoperative complications (including mortality) - Clavien-Dindo Classification (24)

Evidence of early bleeding or thromboembolism

Alcohol related complications

Hospital length of stay to discharge

Need for reoperation

Thromboembolism/complications including pulmonary embolus or wound infections

Use of primary and secondary care (e.g. Number and duration of hospital encounters (perioperatively) including Hospital readmission).

Life Quality - EQ-5D

Western Ontario and McMaster Universities osteoarthritis index (WOMAC) (25) Functional Assessment score

3.4. Primary Endpoint/Outcome

Recruitment and randomisation rates defined by;

- Proportion of eligible patients who agree to participate in the trial and;
- Proportion of enrolled patients successfully followed up 6 months after baseline assessment [Primary endpoint and associated outcome]
- Rates of eligibility and reasons for ineligibility (captured through screening logs)

3.5. Secondary Endpoints/Outcomes

Acceptability of the study design including attendance rates at the second session, completion of outcome measures, retention and reasons for drop-outs; as well as via qualitative work

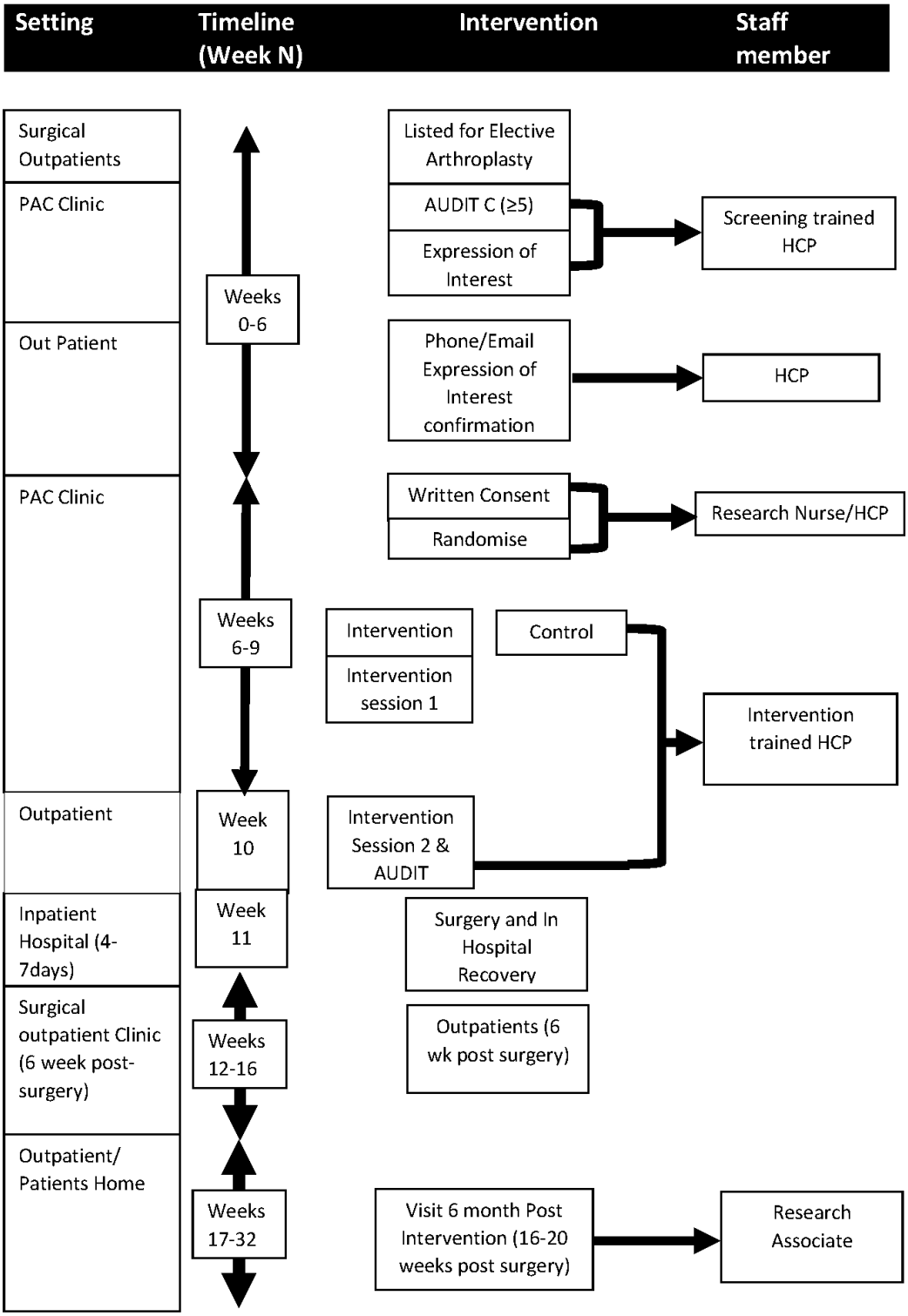
Fidelity of delivery assessment of audio recordings of brief behavioural interventions delivered.

Alcohol consumption as measured by AUDIT score.

4. TRIAL DESIGN

This is a pilot parallel group, individually randomised controlled trial (RCT) where participants (patients) will be randomised to receive either the study intervention or treatment as usual (described through the Feasibility Study conducted immediately prior to this pilot RCT). This pilot RCT will involve three centres (hospitals).

During the previous Feasibility Study an alcohol screening and brief behavioural intervention was developed and the feasibility and acceptability of the intervention to both staff and patients was assessed. We are now conducting a larger pilot RCT to assess if a future definitive trial would be feasible and if so, to inform its design and delivery.


Setting
Timeline (Week N)
Intervention
Staff member
Surgical Outpatients
PAC Clinic
Out Patient
PAC Clinic
Outpatient
Inpatient Hospital (4-7days)
Surgical outpatient Clinic (6 week post-surgery)
Outpatient/ Patients Home
Weeks 0-6
Weeks 6-9
Week 10
Week 11
Weeks 12-16
Weeks 17-32
Listed for Elective Arthroplasty
AUDIT C (≥5)
Expression of Interest
Screening trained HCP
Phone/Email Expression of Interest confirmation
HCP
Written Consent
Randomise
Research Nurse/HCP
Intervention
Intervention session 1
Control
Intervention trained HCP
Intervention Session 2 & AUDIT
Surgery and In Hospital Recovery
Outpatients (6 wk post surgery)
Visit 6 month Post Intervention (16-20 weeks post surgery)
Research Associate

5. STUDY SETTING

This is a multicentre pilot RCT which will take place in three secondary care hospital clinics dedicated to preoperative optimisation of patients before elective major surgery. All three sites have an orthopaedic preoperative surgical care pathway of six-ten weeks from preoperative assessment to surgery. Patient screening will take place in outpatient clinics or by telephone following listing for elective orthopaedic surgery. Consent, randomisation and the study intervention will be carried out in the preoperative assessment clinic and the optional intervention booster session will be delivered in the period between preoperative assessment and surgery, approximately 1 week before surgery. The booster session can be delivered by telephone or in clinic, whichever is more convenient to the patient.

The primary site (Newcastle Freeman Hospital) preoperatively reviews 17,000 elective surgical patients per year including 1200 patients per year having hip or knee arthroplasty. The Preoperative assessment clinic is staffed by approximately 14 nurses.

The second site (North Tyneside General Hospital) is part of a Trust which undertakes approximately 2000-2200 primary arthroplasty cases per year across three hospital sites and pre-operative assessment here is staffed by 12 senior nurses.

The third site (Sunderland Royal Hospital) undertake approximately 800 major joint (hip and knee) arthroplasties each year with approximately 14 nurses undertaking in pre-operative assessment

The recruitment target for the Pilot RCT is 80 patients.

6. ELIGIBILITY CRITERIA

6.1. Inclusion Criteria

Screening and Intervention Health Care Professionals:

- Currently employed as part of the pre-operative assessment team at one of the three sites as part of the pre-operative assessment team
- Willing and able to attend study specific training
- Willing and able to have intervention sessions audio recorded for fidelity assessment

Patient Participants:

- Adults aged ≥ 18 years listed for elective primary hip or knee arthroplasty
- Capacity to provide informed written consent
- Ability to write and converse in English (able to understand English sufficiently to complete the study questionnaires without the need for an interpreter)
- Those who screen positively for risky drinking (AUDIT C score ≥5 or report consuming 6 units or more in one session at least weekly)

6.2. Exclusion Criteria

Patient Participants:

- Patients scoring <5 on AUDIT C and reporting consumption of 6 units or more in a single session less than weekly.
- Patients who are not able to write and converse in English as they will not be able to effectively engage in the behavioural intervention
- Patients likely to undergo sequential (on different dates) joint replacements (for bilateral disease) within the scope of the proposal (due to reduced availability for 6 month follow up)
- Patients displaying current (active) withdrawal from alcohol; these individuals will be referred for review by an addiction psychiatrist
- Severe psychiatric disorder requiring medical therapy or severe cognitive impairment/dementia impacting on ability to interact with intervention and increasing likelihood of postoperative delirium.

7. TRIAL PROCEDURES

HCP Training and Fidelity of Delivery Assessment:
Health Care Professionals delivering the comparator condition will receive training on study procedures, screening patients using the AUDIT and completion of the EQ-5D. In addition to this, a sub group of staff at each site will be trained to deliver the screening and behavioural intervention.

The content of the intervention materials have been defined in terms of specific behaviour change techniques (BCTs) that are the 'active ingredients' of the brief behavioural intervention. Training on delivery of the intervention took place during the feasibility study and was optimised based on feedback from qualitative interviews and fidelity of delivery assessment. Each HCP also received a training manual. This training approach will continue in to the pilot RCT to equip HCPs with the knowledge and skills to support patients to either reduce their drinking to low risk levels or abstain from drinking prior to undergoing surgery. This will happen via receipt of the initial intervention (session 1) and the booster intervention session (session 2).

Consent will be sought from HCPs who are trained to deliver the intervention to audio record consultations to assess skill acquisition, fidelity of delivery and skill drift. Each preoperative assessment HCP trained, will aim to conduct a minimum of four patient consultations where the intervention is delivered. Audio recordings will be made of all intervention sessions where the patient provides consent. All recordings will be transcribed verbatim before being deleted from the recording device. All anonymised transcripts will be assessed for fidelity of delivery. Feedback regarding skill acquisition and fidelity of delivery will be provided to HCPs for intervention sessions 2 and 4 before any subsequent consultations where the intervention is delivered take place. Where patients in sessions 2 and/or 4 do not consent to recording, fidelity of delivery assessments will be conducted and feedback provided for the next recorded session (where a patient does provide consent). If required (i.e. where fidelity of delivery falls below the 80% threshold in the 2nd consultation), the researcher will provide an additional, one to one, face to face training session, lasting up to one hour in duration to focus on components of the intervention that were omitted when it may have been appropriate to deliver them.

Following intervention delivery, HCPs involved in screening and intervention delivery will be asked if they are willing to participate in a qualitative interview. These interviews will explore their experiences of being involved in the trial, the acceptability of the trial procedures and the intervention materials. HCPs willing to be interviewed will be provided with an interview specific information sheet and the Interview session will be arranged to take place at a time and place convenient to the HCP. At the beginning of the interview session the research associate will complete the informed consent process with the HCP.

7.1. Recruitment

7.1.1. Participant Identification

Patients - who have been listed for elective knee or hip arthroplasty and provided with an appointment at the pre-assessment clinic will be screened for eligibility – those who screen positively for risky drinking (AUDIT C score ≥5 or at least weekly drinking of 6 units or more in one session) will be invited to participate. All patients who fit the eligibility criteria will be verbally informed about the study, however only those demonstrating an expression of interest will go on to receive a copy of the patient information sheet and asked to complete an expression of interest form.

7.1.2. Patient Screening (and alcohol outcome assessment)

Initial screening for alcohol consumption using the AUDIT C will occur in the outpatient clinic or by telephone following assessment and listing for elective orthopaedic surgery. Screening in the clinic will be performed by a health care professional (HCP) who will have been trained in AUDIT C use and scoring. The allocated HCP will complete the AUDIT C with each patient listed for major joint arthroplasty. The AUDIT C score will be assessed immediately for eligibility to the study. Patients who screen potentially eligible (AUDIT C ≥5) will be approached and the study discussed with them. Those that express an interest in participating will be provided with a copy of the participant information sheet. They will also be asked for permission to contact them to discuss the study further and their preferred method of contact. Expressions of interest, contact information and preferred method of contact will be recorded in writing by the HCP on the expression of interest form. The patient will then be allowed time to consider their involvement in the study (minimum 24 hours).

After this time the site will contact the patient to confirm positive expression of ongoing interest. If the patient confirms they are still interested, the pre-assessment clinic will be informed of the patients' likely participation to facilitate waiting list and preoperative assessment clinic coordination for the patients visit.

Screening may also take place over the telephone, performed by a health care professional (HCP) who will have been trained in AUDIT C use and scoring. In this instance, patients listed for elective orthopaedic surgery will be identified and a copy of the Patient Information Sheet will be posted to them with an Invitation Letter. The patient will be provided with adequate time to receive the letter and read the information sheet (minimum 3 days), after this time an appropriately trained HCP will contact the patient by telephone to gain verbal expression of interest in the study, patients who express interest will then complete the AUDIT C screen with the HCP to assess eligibility. For those patients who express interest in the study and screen eligible (AUDIT C ≥5) expressions of interest, contact information and preferred method of contact will be recorded in writing by the HCP on the expression of interest form The

patient will then be allowed time to consider their involvement in the study (minimum 24 hours).

After this time the site will contact the patient to confirm positive expression of ongoing interest. If the patient confirms they are still interested, the pre-assessment clinic will be informed of the patients' likely participation to facilitate waiting list and preoperative assessment clinic coordination for the patients visit.

Eligibility for the study will be confirmed if the elective surgical patient screens positively for risky drinking (AUDIT C score ≥5) or at least weekly drinking of 6 or more units in one session (as judged by question 3 on AUDIT C). An AUDIT C score of ≥5 indicates increased risk, risky or the likelihood of dependent drinking. There will be no upper limit of alcohol consumption that will lead to a patient being excluded from the study; only patients displaying current (active) withdrawal from alcohol will be excluded and referred for review by an addiction psychiatrist. The likely number of such patients will be very low, as GPs tend not to refer these patients for elective surgery, due to the fact that alcohol withdrawal can have life threatening complications. The number of exclusions will be recorded. Patients scoring AUDIT C <5 will receive positive feedback on their low risk drinking status.

Patients scoring AUDIT C ≥5 and who consent to take part in the study will be asked to complete the full AUDIT questionnaire at baseline, booster session (intervention only), pre-surgery, 6 week post operatively and 6 month post intervention. An appropriately trained HCP will go through the AUDIT with the patient. The full AUDIT questionnaire is more sensitive than the AUDIT C with a sensitivity and specificity of 92% and 94% respectively [23] and will therefore be used to establish any change in alcohol consumption over the study period.

7.2. Consent

Informed consent will be obtained from all participants (health care professionals and patients) taking part in the study. All participants will be free to withdraw their consent at any time.

The informed consent discussion will be undertaken by appropriately trained staff at each site, as detailed in the site delegation log.

Health care professionals involved in screening and intervention delivery will be asked to sign the informed consent form, and indicate whether or not they are willing to have their intervention sessions audio recorded, at the beginning of the training session. They will be provided with a copy of the information sheets in advance of the training session to allow them time to consider participation (minimum 24 hours). For those who agree to be interviewed separate information sheets will be provided (minimum 24 hours prior to interview) with HCPs being

given time to reflect on this before completing the consent form at the beginning of the interview session.

Health care professionals contacted about the electronic survey will be emailed and provided with a link to the survey. Participants will first be provided with an information screen explaining the purpose of the survey, once they have read this they will click through to a consent screen where they can tick to confirm they consent to take part in the survey.

Patients listed for elective orthopaedic surgery and eligible for the study (guided by response to routine questioning concerning alcohol intake in the primary centre - AUDIT C), will be approached or contacted by telephone and the study discussed with them. Those that express an interest in participating will be provided with a copy of the participant information sheet either in person or by post. They will also be asked for permission to contact them to discuss the study further and their preferred method of contact. Expressions of interest, contact information and preferred method of contact will be recorded in writing by the HCP on the expression of interest form. The patient will then be allowed time to consider their involvement in the study (minimum 24 hours).

After this time the site will contact the patient to confirm positive expression of ongoing interest. If the patient confirms they are still interested, the pre-assessment clinic will be informed of the patients' likely participation to facilitate waiting list and preoperative assessment clinic coordination for the patients visit.

At the preoperative assessment clinic, an appropriately trained HCP (not involved in screening or delivering the intervention) will initially see the patient. They will check whether the patient is still interested in participating in the study and if so, the patient will be asked to sign the informed consent form.

The patient will be given a copy of this 'fully executed' consent form to be taken home, with the original placed in the investigator site file, a copy being placed in medical notes and a copy securely faxed to NCTU for central monitoring purposes.

Patients who complete the consent process will be asked, if willing and able, to provide an alternative contact such as a relative or friend who can be contacted by the study team in the event that they are unable to reach the patient themselves via the contact information provided at expression of interest.

Patients who indicated at initial consent that they would be happy to participate in a qualitative interview will be asked again if they are willing to take part in the interview as part of Visit 6. Patients still willing to participate in an interview will be provided with an interview specific information sheet by email or post (dependent on patient preference) at least 24 hours before the interview takes place.

7.3. Randomisation

Randomisation will be administered centrally by the Newcastle Clinical Trials Unit (CTU) secure web-based system. Patients will be randomised on a 1:1 basis to receive either the Behavioural Intervention or treatment as usual.

Local research staff will be provided with a login and password for the randomisation system.

At the preoperative assessment clinic, an appropriately trained HCP not involved in screening or delivering the study intervention will initially see the patient and obtain full written, informed consent as described above. Once consent has been obtained the HCP will access the randomisation system, which will allocate the patient to either intervention or comparator group. This ensures that the decision to participate in the study is made without knowing the allocation.

7.4. Treatment as Usual Definition

At all three centres the usual pre-operative assessment appointment lasts approximately 45 minutes to one hour. The process involves asking patients a variety of health related questions, taking bloods and other observations such as blood pressure and electrocardiograms. As part of the pre-assessment all patients are asked about their alcohol consumption. Questions cover whether the patient consumes alcohol and if so, will establish the number of units consumed each week. Patients considered by the PAC HCP to be 'heavy drinkers' or those identified through blood and/or liver function tests are routinely referred to the consultant anaesthetist for anaesthetic review. The decision to refer for further treatment and/or detoxification before surgery then becomes a clinical decision to ensure patient safety for anaesthesia and surgery.

Additionally, at all three centres, there is specialist support available for patients to reduce or cease alcohol consumption. However, these are hospital wide services, not specific to the pre-assessment department and information or advice is not delivered by pre-operative assessment clinic staff. There is currently no standard process for identifying and referring patients to these services with identification being left to the judgement of the individual nurse.

7.5. Study Assessments

The randomly allocated intervention will be delivered at the scheduled preoperative assessment visit, approximately six weeks before elective surgery, by dedicated preoperative assessment HCPs.

Screening

This visit will take place in the outpatient clinic or by telephone. Patients will be asked to complete the AUDIT C questionnaire.

For those screened in the outpatient clinic, if the patient screens as eligible on the AUDIT C tool, the study will be discussed with them, an Expression of Interest form will be completed, and they will be provided with a copy of the participant information sheet.

For those completed by telephone, a copy of the PIS will already have been posted to the patient - an Expression of Interest form will be completed.

Expression of Interest Follow-up

This will be done by telephone. The site will contact the patient after they have had time to consider the Participant Information Sheet (minimum 24 hours). The patient will be given the opportunity to ask any further questions they have and asked if they are interested in taking part in the study.

For those screened over the telephone a follow-up call will still take place a minimum of 24 hours after the Expression of Interest has been completed with the HCP..

Visit 1 - Intervention Session 1
This visit will take place in preoperative assessment clinic. If the patient still wishes to take part in the study, written informed consent will be obtained along with details for an alternative contact (to be used if the patient cannot be reached via the primary contact provided at expression of interest). The HCP will then access the web-based randomisation service and ascertain the patient's allocation. The patient will be informed of his/her allocation and will be directed to the appropriately trained preoperative assessment HCP to receive their intervention.

If the patient is randomised to receive the study Intervention session they will first complete the standard pre-operative assessment, including being asked if they drink alcohol and how many units a week they consume along with completion of the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) as part of the joint registry. This will be followed by completion of the AUDIT and EQ-5D. Patients will go on to receive a face-to-face, 20-30 minute HCP-led consultation. This session will initially focus on behavioural intention by exploring motivation for change using brief motivational counselling techniques and BCTs (e.g., feedback on current behaviour, information about health consequences of behaviour) supported by visual aids within the intervention materials; and use of specific BCTs (e.g. goal setting; problem solving; restructuring of physical environments) to support volition (i.e. enactment and maintenance of behaviour change).

Patients will be provided with the intervention tools and a copy of the patient information leaflet 'How much is too much?' to take away with them.

Patients allocated to the treatment as usual arm will complete the standard pre-operative assessment including being asked if they drink alcohol and how many units per week they consume. They will also be asked to complete the WOMAC as part of the joint registry. This will be followed by completion of the AUDIT and EQ-5D. These patients will not receive an intervention or any further feedback on their alcohol use.

Visit 2 - Intervention Session 2
This visit is only applicable to patients allocated to receive the Brief Behavioural Intervention.

Patients in the intervention group will be offered a second intervention session lasting between 10-20 minutes in duration.

This intervention will be delivered approximately five weeks following the preoperative assessment appointment and initial behavioural intervention and

one to two weeks before surgery. Wherever possible this session will be delivered by the same HCP who delivered intervention session 1 in order to maintain continuity of care. However, this is not essential if staff availability does not allow within the timeframes specified i.e. due to annual leave. This session can be delivered either face to face in clinic or by telephone at the patient's discretion

The aim of this session is to provide feedback on performance, boost self-efficacy, prevent relapse and support maintenance of behaviour change.

Patients will also be asked to complete the AUDIT questionnaire.

Visit 3 – Before Surgery
AUDIT outcome data will be collected pre-op for all patients. If the patient is admitted to hospital the day(s) before their surgery AUDIT can be completed with them then. If however the patient is admitted as Day of Surgical Arrival (DOSA) the HCP will contact the patient by telephone between 1 and 3 days before they are due to attend hospital for surgery.

Visit 4 – Early Post-op (up to 5 days post-surgery)
The following data will be collected for all patients:

- WOMAC
- POMS (collected on day 3 and day 5 post-op)
- Clavien-Dindo Score (during hospital stay)

Visit 5 - Follow-Up Visit 1 (6 weeks post-surgery)
This visit can be conducted at the patient's outpatient visit or by telephone approximately 6 weeks after surgery. They will also be asked to confirm their contact details and to complete the following:

- AUDIT
- EQ-5D

Visit 6 - Follow-Up Visit 2 (6 months after Visit 1)
This visit will be carried out at the patient's home or over the phone depending on patient preference. Patients will be asked to complete the following:

- AUDIT
- EQ-5D

Patients who indicated at initial consent that they would be happy to participate in a qualitative interview will be asked again if they are willing to take part in the interview as part of this visit. Patients still willing to participate in an interview will be provided with an interview specific information sheet and will complete the informed consent process with the research associate, signing the informed consent form. The fully executed informed consent form will be placed in the site file and a copy posted to the patient. Interviews will build on the findings of the feasibility phase by exploring patient's experiences of being involved in the trial and assessing the acceptability of the randomisation and follow up procedures as well as the intervention (where relevant) and screening procedures. Interviews

will be carried out with approximately 30 purposively sampled trial patients. Sampling and interviews will be conducted with both intervention and control group patients and will continue until data saturation is achieved.

In order to confirm the identity of the person on the telephone (if this visit is conducted by telephone) and to establish ongoing competence (i.e. the ability to give informed consent to take part in an interview if applicable) the patient will be asked to state their address or email address along with their date of birth which the Researcher will check against their notes. In addition to this, identity and competence will be established by asking patients to report what their participation in the study has involved.

When patients attend hospital for hip, knee, ankle, elbow or shoulder replacement they are asked if they would like to take part in the National Joint Registry. The WOMAC questionnaire referred to above is collected as part of the National Joint Registry. For PRE-OP BIRDS patients who have also consented to take part in the National Joint Registry, we will be able to use the WOMAC questionnaires completed as part of that (with the patients consent) and those patients will therefore not have to complete those questionnaires again as part of this study. For those patients that have decided not to take part in the registry we will collect these questionnaires as part of the PRE-OP BIRDS study.

Staff Interviews

Following patient recruitment and intervention delivery, HCPs involved in screening and/or intervention delivery will be invited to take part in a qualitative interview conducted by the research associate. These interviews will build on the feasibility study further exploring staff experiences of being involved in the trial, the acceptability of screening and intervention materials and the feasibility of delivering screening and intervention in the pre-operative assessment clinic.

Electronic Survey of Pre-operative Assessment Clinics

To capture further details of usual care for preoperative alcohol screening and interventions, an electronic survey of clinical leads from pre-operative assessment units throughout the UK will be conducted. The survey will contain open and closed questions and will seek respondents' views about the current practices within their respective units. An invitation to complete the online questionnaire (surveymonkey.com) will be sent to lead clinicians in anaesthetic departments with pre-assessment clinics (N= approximately 120) with a URL to access the survey. Perioperative Medicine Clinical leads will be contacted via a Royal College of Anaesthetists (RCOA) website. The RCOA Perioperative Medicine Leadership group (Chair Prof Monty Mythen – Member of the trial TSG) will be asked for permission to use this contact list. Two reminders at three and six weeks after initial contact will be used to stimulate response. Upon following the URL, an electronic version of the information sheet will be displayed with an electronic version of the consent form. Clinicians will have to complete check boxes to indicate that they have read and understood the information sheet and consent to being involved in the survey before they can proceed to the survey questions. At the end of the survey clinicians will be asked to click a button to 'Finish and submit' their responses. A thank you screen will then be displayed. The data set will be closed at 12 weeks after initial contact.

7.4.3 Schedule of Events

Procedure	**Visit**						
	Screening **In clinic or by telephone**	**Visit 1** Approx. 6-8 weeks before surgery at PAC Appointment	**Visit 2** **(Intervention Arm only)** Approx. 1-2 weeks before surgery by phone or in clinic	**Visit 3** Immediately Pre-op 1 and 3 days before attendance at hospital for surgery	**Visit 4** Up to 5 days post-surgery while patient is still in hospital	**Visit 5** Approx. 6 weeks after surgery at time of routine 6 week post-surgery appointment	**Visit 6** Approx. 6 months after Visit 1 by phone or at patient's home
AUDIT C	X						
AUDIT Baseline		X					
AUDIT Outcome			X	X		X	X
Consent		X					
Randomisation		X					
Brief Behavioural Intervention or comparator (treatment as usual)		X	X				
EQ-5D		X				X	X
WOMAC		X			X		
POMS					X		
Clavien-Dindo Score					X		

7.4 Withdrawal Criteria

All participants (HCPs and patients) have the right to withdraw from the trial at any time without having to give a reason. Investigator sites should try to ascertain the reason for withdrawal and document this reason within the Case Report Form and the medical notes of patient participants.

The Investigator may discontinue a participant from the trial at any time if the Investigator considers it necessary for any reason including:

- Symptomatic deterioration
- Participant withdrawal of consent
- Significant protocol deviation or non-compliance
- Investigator's discretion that it is in the best interest of the participant to withdraw
- An adverse event that requires discontinuation of the trial intervention or renders the participant unable to continue in the trial
- Termination of the clinical trial by the sponsor

Patient participants who withdraw from the trial will not be replaced. Where HCP participants withdraw an additional member of staff will be trained to deliver screening and intervention. All data provided by a participant up to point of withdrawal will be retained.

7.5 End of Trial

End of trial is defined as last patient last visit.

8 TRIAL INTERVENTION

8.1 Name and Description of Interventions

Brief Behavioural Intervention – the intervention will provide patients identified as increased or high risk drinkers with simple, structured advice regarding alcohol consumption, the benefits of reducing alcohol intake and some practical ways in which they can reduce their alcohol intake. The intervention documents will act as a visual guide and provide staff with prompts on how to structure and deliver this advice to patients. Patients will be provided with the intervention documents to take away with them. They will also be provided with a copy of the Department of Health's information leaflet 'How much is too much?'

The intervention will be delivered over two sessions – the first session will last approximately 30 minutes, while the second session will be an optional booster session and will last approximately 10 to 20 minutes.

Treatment as Usual - will complete the standard pre-operative assessment and complete the study specific baseline measures (AUDIT and EQ-5D). These patients will not receive an intervention or any further feedback on their alcohol use

9 SAFETY REPORTING

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant, including occurrences which are not necessarily caused by or related to the intervention under study.
Adverse Reaction (AR)	An untoward or unintended response in a participant to which is related to the intervention under study i.e. that a causal relationship between the trial intervention and an AE is at least a reasonable possibility and the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial intervention qualify as adverse reactions.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • Results in death • Is life-threatening* • Requires inpatient hospitalisation or prolongation of existing hospitalisation • Results in persistent or significant disability/incapacity • Consists of a congenital anomaly or birth defect • Other important medical events that jeopardise the participant or require intervention to prevent one of the above consequences * - life-threatening refers to an event in which the participant was at immediate risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to the trial intervention, based upon the information provided.
Unexpected Serious Adverse Reaction (USAR)	A serious adverse reaction, the nature and severity of which is not consistent with the known information about the intervention under study.

9.2 Recording and Reporting AEs/ARS

This study involves patient participants receiving either a behavioural intervention or treatment as usual. The behavioural intervention involves providing patients with advice and guidance on the benefits of reducing alcohol consumption before major surgery. There is therefore very little risk involved for the participants by taking part. We will therefore not record adverse events (AEs) during this pilot RCT.

9.3 Recording and Reporting SAEs/SARs

All adverse events that meet the definition of serious (as outlined in section 9.1 above) will be regarded as a Serious Adverse Event and will need to be reported as part of this trial (save for the exceptions listed in section 9.3.1 below). All SAEs, regardless of causality or expectedness, will be reported to the CI, NCTU and sponsor as soon as the site becomes aware of the event. SAEs will be captured from when a participant enters the study through to completion of their final study visit.

The initial SAE report will be made by the site PI (or delegate) completing the agreed SAE form which is sent via SOHO66 (secure fax to email system) to the Senior Trial Manager, Trial Manager, CI and nominated sponsor contact. The initial report can if necessary be made to the Clinical Trials Unit by telephone or e-mail and followed up formally using the SAE form. In the case of incomplete information at the time of initial reporting, or follow up information, a new SAE form must be completed and sent via the secure system as soon as possible.

Contact details for reporting SAEs:
Trial Manager, Newcastle Clinical Trials Unit
Nicola Goudie, Nicola.goudie@ncl.ac.uk 0191 208 7187

Please send the completed and signed SAE form(s) using the SOHO66 secure network

FAO PRE-OP BIRDS TRIAL MANAGER to: 0191 5804757

For each SAE the following information will be collected:

- Full details in medical terms and case description
- Event duration (start and end dates, if applicable)
- Action taken
- Outcome
- Seriousness criteria
- Causality in the opinion of the investigator
- Whether the event is considered expected or unexpected.

9.3.1 SAE reporting exclusions:

The following do not need to be reported as SAEs as part of this trial:

- Wound infections as this is captured as part of the trial outcome measures within the POMS questionnaire
- Evidence of early bleeding or thromboembolism as this is captured as part of the trial outcome measures within the Clavien Dindo score
- Neurological Alcohol related complications as this is captured as part of the trial outcome measures within the POMS questionnaire
- Need for reoperation as this is captured as part of the trial outcome measures
- Thromboembolism/complications including Pulmonary embolus or wound infections as this is captured as part of the trial outcome measures within the Clavien Dindo score and POMS questionnaire
- Hospital readmission as this is captured as part of the trial outcome measures
- Pre-planned hospitalisations should not be reported as an SAE
- Pre-existing conditions that the participant was suffering from before inclusion in the trial or worsening of pre-existing conditions do not need to be reported as SAEs
- Scheduled procedures for pre-existing conditions should not be reported as an SAE – this includes the participant coming into hospital for their Hip/Knee replacement surgery.

9.4 Recording and Reporting USARs

All USARs occurring from the intervention must be reported to the NHS REC. The Sponsor will perform this reporting.

The assessment of expectedness will be performed by the CI against the known information for the trial.

USARs must be reported no later than 15 calendar days after the Sponsor has first knowledge of the event. Any relevant follow-up information should be sought and reported as soon as possible after the initial report.

As soon as a site suspects that a SAR may be a USAR they must contact the CI, sponsor representative and the trial manager immediately. The reporting timeframe starts at day 0 when the Sponsor is in receipt of a minimum set of information:

- Sponsor trial reference and trial name (sponsor reference)
- Patient trial number and date of birth
- Name of intervention
- Date of notification of the event
- Medical description of the event
- Date and time of the onset of the event (including event end date if applicable)

- Causality assessment
- Seriousness of the event, particularly if life threatening or fatal
- An identifiable reporter (e.g., Principal Investigator)

This information must be provided on the study USAR report form. The site is expected to fully cooperate with the Sponsor, CI and NCTU in order that a full and detailed report can be submitted to the NHS REC within the required timelines.

PIs will be informed of all USARs by the NCTU.

9.5 Responsibilities

Principal Investigator

- Checking for AEs and ARs when participants attend for treatment or follow-up
- Using medical judgement in assigning seriousness and causality and providing an opinion on expectedness of events.
- Ensuring that all SAEs and SARs, including USARs, are recorded and reported to the Sponsor within 24 hours of becoming aware of the event and provide further follow-up information as soon as available.
- Ensuring that AEs and ARs are recorded and reported to the Sponsor in line with the requirements of the protocol.

Chief Investigator

- Clinical oversight of the safety of trial participants, including an ongoing review of the risk/benefit.
- Using medical judgement in assigning seriousness, causality and expectedness of SAEs where it has not been possible to obtain local medical assessment.
- Using medical judgement in assigning expectedness to SARs.
- Immediate review of all USARs.
- Review of specific SAEs and SARs in accordance with the trial risk assessment and protocol.

Sponsor

- Assessment of expectedness of any USARs
- Expedited reporting of USARs to the REC within required timelines
- Notification of all investigator sites of any USAR that occurs

Trial Steering Committee and Data Monitoring Committee

- Review of safety data collected

10 STATISTICAL CONSIDERATIONS

10.1 Analysis Population

All analyses will be conducted on an intention to treat basis, with sensitivity analyses used to investigate the impact of removing individuals who did not receive the interventions as allocated.

10.2 Statistical Analyses

As this is a pilot trial the main analyses will be descriptive, in order to inform the design of a further definitive trial.

10.2.1 Analysis of the Primary Outcome Measure

The primary outcomes are pilot feasibility outcomes. We will report the numbers of eligible patients seen over the recruitment period, and the resulting rates of recruitment, compliance with randomisation, and data completion. Non completers will be characterised.

10.2.2 Analysis of Secondary Outcome Measures

The pilot feasibility trial will also assess performance of potential outcome measures for a definitive trial. We will ascertain data completeness of the instruments and any potential bias in the completion of follow-up data, to inform the choice of instruments in a future trial. The majority of the outcome data will be presented in simple descriptive tables presenting percentages, means and standard deviations or 5-number summary (as appropriate), for each arm of the study. This information will be used to inform the design, choice of primary outcome, necessary sample size and approach to the analysis, of the future definitive trial.

10.2.4 Analysis of electronic Survey Data

This data is collected to establish current practice nationally (and variability therein) in respect of preoperative assessment, with particular reference to management of risky drinking. The analysis will be descriptive.

10.3 Statistical Size Calculations

The pilot trial will aim to obtain data from 40 risky drinkers in each trial arm, to estimate the critical parameters to the necessary degree of precision with a continuous primary outcome. Allowing for a loss to follow up of 25%, this should provide data at 6-months after preoperative assessment for up for 30 patients per arm (based on current recommendations for external pilot trials (26)). Thus we estimate that 400-500 surgical patients would need to be screened across the three sites to enrol 80 risky drinkers (AUDIT≥8). The target recruitment sample size

will be kept under review and recruitment will cease when we estimate that 60 patients will provide data at 6 months post intervention.

10.4 Qualitative Analysis

Qualitative data from HCP and patient interviews will be analysed using Framework analysis. This is a recommended approach for qualitative health research with objectives linked to quantitative investigation (9). NVivo analysis software will be used to aid indexing and charting. The data will be repeatedly read and coded independently by two researchers within a framework of *a priori* issues and those identified by participants (patients or HCPs) or emerging from the data. Any divergence between coders will be discussed on an on-going basis to inform the analysis and resolve divergence in their interpretations of the data. Analysis will be discussed at regular meetings of the research team to identify areas for closer consideration (including negative case analysis) and to enhance credibility of the thematic framework and interpretation (11, 12).

Qualitative work will also explore influences on patient recruitment, implementation and receipt of the study interventions and data collection methods. Analysis of the likelihood of embedding study interventions in clinical practice (HCP data) will be informed by Normalization Process Theory (13). This model considers factors that affect implementation in four key areas; how people make sense of a new practice (coherence); the willingness of people to sign-up and commit to the new practice (cognitive participation); their ability to take on the work required of the practice (collective action); and activity undertaken to monitor and review the practice (reflexive monitoring). The approach is increasingly used in studies of the implementation of interventions in health care (www.normalizationprocess.org). Analysis will consider how well the behavioural intervention is introduced and incorporated for both patients and HCPs.

10.5 Fidelity of Delivery Analyses

Consultations with a participating patient will be audio recorded to allow an assessment of skill acquisition and fidelity of delivery post-training. Audio recordings will be transcribed verbatim. A Research Associate trained in the use of the Behaviour Change Taxonomy Version 1 (BCT v1) and an expert coder will independently code all consultation transcripts to assess skill acquisition (for feedback purposes) and fidelity of delivery of each specific BCT. A coding frame/fidelity checklist based on the BCTv1 will be used to identify whether each BCT was delivered faithfully as planned. Where discrepancies in coding exist, the RA and expert coder will meet to resolve these via discussion. Where coders agree in one instance but not another, the percentage of positive agreement will be calculated.

11 DATA HANDLING

11.1 Data Collection Tools and Source Document Identification

Data regarding the number of patients approached, screened and interested in taking part will be collected via a screening log completed by health care professionals conducting screening.

The AUDIT C will be used to screen patients. The full AUDIT will be used to collect data related to alcohol consumption at the initial study visit, booster session (where applicable), immediately pre-op, 6 week post op and 6 months post-intervention. At intervention session 1 this questionnaire will also include patient age and gender.

The EQ-5D will be used to collect data related to quality of life at the initial study visit, early post-op, 6 week post op and 6 months post-intervention.

WOMAC will be used to collect data regarding pain and physical function at the initial study visit and early post-op.

Clavien Dindo Score and POMS questionnaire will be collected early post-op to assess if any complications have been suffered by patients following surgery.

Questionnaire data collected early post-op will be collected by a Research Nurse or fellow. This data will be collected either via review of the patient's medical notes (for those questionnaires collected as part of the National Joint Registry) or by completion of the questionnaire with the participant (for those not collected as part of the NJR).

Data regarding delivery of the key aspects of the intervention will be collected using a hard copy of the data capture form (paper CRF).

Data from interviews will be audio recorded and transcribed verbatim.

Trial data for an individual patient will be collected by each PI or their delegated person and recorded in the electronic case report form (eCRF) for the trial. Patient identification on the eCRF will be through a unique trial identifier number. A record linking the patient's name to the unique trial identifier number will be held only in a locked room at the trial site, and is the responsibility of the PI. As such, patients cannot be identified from eCRFs. The CI or delegated person will monitor completeness and quality of data recording in eCRFs and will correspond regularly with site PIs (or their delegated team member) with the aim of capturing any missing data where possible, and ensuring continuous high quality of data.

Patients will complete the paper assessment tools as required. The tools will also only be identified using the unique patient identifier number. Data will be entered at sites onto a secure online system, with the paper originals remaining at site.

Audio-recordings of recruitment/consent discussions will contain patient identifiable information. The original recordings will be encrypted and password protected and sent to Newcastle University where selected recordings will be transcribed using purposeful sampling.

11.2 Data Handling and Record Keeping

All data collected by screening and intervention staff will be stored in the investigator site file.

In order to arrange the 6 month post-intervention visit the research associate will visit the site to access patient contact details.

11.3 Access to Data

Staff involved in the conduct of the study, including the PIs, research associate, trial management team and NHS staff involved in screening and intervention will have access to the site files.

The study data and patient medical records may be looked at by monitoring or auditing personnel from an Independent Ethics Committee (IEC) or other regulatory authorities, or the hospital Trust.

Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor, its designee, Regulatory Authorities, the Data Monitoring Committee (DMC) or the REC. Secure anonymised electronic data may however be released to the Study Statistician for analysis. The PI and study site staff involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

Access to the MACRO™ database will be granted to site's PIs, their delegated data entry personnel at sites and NCTU trial management team for monitoring purposes.

The CDMS (MACRO) used for this trial is fully compliant with all regulatory frameworks for research of this nature. It uses a secure web-based interface for data entry; no data are stored on computers at site. The system has an inbuilt back-up facility, through Elsevier's hosting partner Rackspace's secure premises in London, and is managed and supported by the Rackspace team.

The Research Associate and co-investigators will have access to anonymised transcripts of intervention sessions and qualitative interviews which will be stored on the University computer system. These will not include any identifiable information.

11.4 Archiving

All study data will be stored for 5 years and in accordance with GCP and the sponsor and NCTU SOPs

12 MONITORING, AUDIT & INSPECTION

A trial monitoring plan will be developed based upon the trial risk assessment, and this plan will be agreed by the Trial Management Group, the Trial Steering Committee and the Sponsor.

Monitoring of study conduct and data collected will be performed by a combination of central review and site monitoring visits and external Data Monitoring Committee to ensure the study is conducted in accordance with GCP. Study site monitoring will be undertaken by Newcastle CTU. The main areas of focus will include consent, serious adverse events, data completeness and accuracy and essential documents in study. All monitoring findings will be reported and followed up with the appropriate personnel in a timely manner. Full details regarding the monitoring to be undertaken as part of the study can be found in Monitoring Plan.

The trial may be subject to audit by representatives of the Sponsor or inspection. Each investigator site will permit trial-related monitoring, audits and regulatory inspection including access to all essential and source data relating to the trial.

Data will be analysed by the Trial Statisticians and reported to an external independent DMC at least annually, in open and closed sessions according to the DMC Charter, as agreed with the DMC members at the start of the trial.

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee Review and Reports

The NCTU will obtain a favourable ethical opinion from an NHS Research Ethics Committee (REC) prior to the start of the trial. All parties will conduct the trial in accordance with this ethical opinion.

The NCTU will notify the REC of all required substantial amendments to the trial and those non-substantial amendments that result in a change to trial documentation (e.g. protocol or patient information sheet). Substantial amendments that require a REC favourable opinion will not be implemented until this REC favourable opinion is obtained. The sponsor will notify the REC of any serious breaches of GCP or the protocol, urgent safety measures or USARs that occur during the trial.

An annual progress report will be submitted each year to the REC by NCTU until the end of the trial. This report will be submitted within 30 days of the anniversary date on which the original favourable ethical opinion was granted.

The NCTU will notify the REC of the early termination or end of trial in accordance with the required timelines.

13.2 Peer Review

The protocol has been reviewed and authorised by the Sponsor, funder, Chief Investigator, Trial Manager and Trial Statistician.

13.3 Public and Patient Involvement

Internal audit work has been conducted using the AUDIT screening tool in the primary unit. This allowed for discussions, with involved patients, around acceptable processes to address alcohol screening and estimation of consumption in the pre-surgical context. It was established that it would be possible to conduct alcohol reduction and other lifestyle interventions, using the preoperative setting as an opportune treatment window. This experience provided an initial impression that patients are receptive to screening and intervention procedures in the preoperative context.

In addition, internal audit of 714 patients undergoing knee and hip replacements demonstrated a mean age of 69 years (95% CI 67-69) and 68 years (95% CI 67-69) respectively. Two thirds (66%) of the patients were above 65 years and 15% were above 80yrs. Understanding these demographics has promulgated the involvement of members of a Newcastle University-affiliated older people's group, Voice North, who actively volunteer to assist North East researchers. We have involved Voice North during the outline and full application phases and will continue their involvement throughout the study.

Three members of Voice North are also involved in the Trial Steering Committee as lay members.

13.4 Protocol Compliance

Protocol deviations, non-compliances or breaches are departures from the approved protocol. Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and must not be used.

Unintentional protocol deviations will be documented and reported to the Sponsor in accordance with NCTU SOPs.

Deviations that are found to frequently recur at a site are not acceptable and could be classified as a serious breach

13.5 Notification of Serious Breaches to GCP and/or the Protocol

A serious breach is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the subjects of the trial; or
(b) the scientific value of the trial

The sponsor must be notified immediately of any incident that may be classified as a serious breach. The sponsor will notify the NHS REC within the required timelines in accordance with the sponsor SOP.

13.6 Data Protection and Patient Confidentiality

All investigators and trial site staff must comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. Access to data will be limited to the minimum number of individuals necessary for quality control, audit, and analysis.

Personal data will be regarded as strictly confidential. Original paper case record forms containing study data will be stored in the investigator site file at each research site. All study files will be securely stored and access restricted to staff involved in the study. Research staff at sites will enter data from paper forms onto a secure web-based electronic database. Data will be entered using participant unique study numbers only. Access to this database will be password protected and limited to staff at research sites or Newcastle University who are involved in the study.

To preserve anonymity, any data leaving the sites will identify participants by their initials and a unique study identification code only.

Essential data will be retained for a period of at least 5 years following close of study in line with sponsor policy.

The CI will be the data custodian.

13.7 Indemnity

The sponsor will provide indemnity in the event that trial participants suffer negligent harm due to the management of the trial. This indemnity will be provided under the NHS indemnity arrangements for clinical negligence claims in the NHS.

The substantial employers of the protocol authors will provide indemnity in the event that trial participants suffer negligent harm due to the design of the trial.

The study sites will provide indemnity in the event that trial participants suffer negligent harm due to the conduct of the trial at their site. For NHS Organisations this indemnity will be provided under the NHS indemnity arrangements for clinical negligence claims in the NHS. NHS Organisations must ensure that site staff without substantive NHS contracts hold honorary contracts to ensure they can access patients and are covered under the NHS indemnity arrangements. Study staff without NHS contracts e.g. General Practitioners or Dentists will provide their own professional indemnity.

13.8 Amendments

It is the responsibility of the Research Sponsor to determine if an amendment is substantial or not and study procedures must not be changed without the mutual agreement of the CI, Sponsor and the Trial Oversight Committee.

Substantial amendments will be submitted to the REC and will not be implemented until this approval is in place. It is the responsibility of the NCTU to submit substantial amendments.

Non-substantial amendments may be made at any time with a record of the amendment held in the Trial Master File. Any non-substantial amendment that requires an update to the trial documentation will be submitted to the NHS REC for acknowledgement of the revised version of the document.

Substantial amendments and those minor amendments which may impact sites will be submitted to the relevant NHS R&D Departments for notification to determine if the amendment affects the NHS permission for that site. Amendment documentation will be provided to sites by the NCTU.

13.9 Access to the Final Trial Dataset

The final trial data set will be stored electronically in secure files on the university system. Initially the final trial data set will be accessible only to the trial statisticians. Upon completion of the final analysis the final trial data set will be made available

to the CI, the trial statistician, the RA and three of the co-applicants (Prof Eileen Kaner, Dr Leah Avery and Dr Catherine Haighton). Following completion of the analysis, copies of the data will be sent to the PI at each site on a CD or DVD disc.

14 DISSEMINATION POLICY

The introduction of a brief behavioural intervention into preoperative assessment provides an important opportunity to develop multidisciplinary teams, working towards improving postoperative outcomes. This proposed research includes specialities involved with surgical care including surgeons, behavioural specialists, perioperative physicians and nurses. Team members will be committed to disseminate the findings through local and national presentations to varying clinical groups. Furthermore, team members have delivered numerous lectures and presentations at national and international meetings especially regarding the use of preoperative assessment clinics in the optimisation of patients prior to surgery, behavioural interventions and screening and behavioural interventions targeting alcohol consumption. This will be continued in light of the findings of the present proposal.

Relevant findings will be published in open access medical and scientific peer reviewed journals such as Health Technology.

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