North Cumbria Integrated Care NHS Foundation Trust

ALASKA trial

Assessment of cooLing Application poSt Knee Arthroplasty

ALASKA, A single-centre, two-arm, controlled, prospective randomized trial comparing AIRCAST® KNEE CRYO/CUFF™ passive compressive cryotherapy with VPULSE® active compressive cryotherapy after knee arthroplasty surgery.

Version 2.1, dd 29 Nov 2024

Chief Investigator's Statement of Ownership and Content.

I, Mr Cristian Nita, confirm that this protocol is my work and is owned by me. The protocol conforms with standards outlined in the Declaration of Helsinki 1964.

Name (PRINT):_____

Signature:_____

Date: _____

RESEARCH PROTOCOL SUMMARY

TITLE:	A single-centre, two-arm, controlled, prospective randomized trial comparing AIRCAST® KNEE CRYO/CUFF™ passive compressive cryotherapy with VPULSE® active compressive cryotherapy after knee arthroplasty surgery
Short title:	ALASKA trial: Assessment of cooLing Application poSt Knee Arthroplasty
IRAS number	322564
Device description	VPULSE® VPULSE® is designed to improve patient outcomes after injury and / or surgery through reduction of pain and swelling, with the aim to reduce the need for medication. The VPULSE® system is used with anatomically designed pads, providing a continuous flow of cold and intermittent dynamic compression therapy. Motorised cold therapy intended to reduce operative site discomfort and inflammation.
Study type	Medical device trial, involving CE-marked devices used for intended purpose.
Study design	Single-centre, two-arm, controlled, prospective randomized trial.
Patient population	Adult participants who have unilateral knee replacement surgery (knee arthroplasty) and who meet the study inclusion criteria Participants must have the capacity to provide informed written consent and complete patient reported outcome measures. The study has the following sample parameters: standard deviation of 2 cm per cohort, power beta of 80%, alpha p-value of 0.05. Sample size takes into account 30% attrition rate, effect size of 0.75 (mean difference of 1.5cm on 10cm visual analogue scale) based on previous ROBOT trial results. Total of 88 patients: - 44 Patients to receive AIRCAST® KNEE CRYO/CUFF™ (current standard care, control arm) - 44 Patient to receive VPULSE® with knee-specific cuff (intervention arm)

Primary objective	To determine the level of operation-site related pain experienced at day 2 post-operation and to compare the average pain scores of patients in the AIRCAST® KNEE CRYO/CUFF™ and VPULSE® arm respectively, through administration of 10 cm visual descriptor scale (VDS) for 'at rest' pain.
Secondary objectives	Post-operative patient-reported outcome measures: Prior to surgery and 24hrs, 3, 5, 12 days, and 6 weeks post-surgery - Pain perception, using VDS pain (at rest and walking) and short form McGill pain questionnaire Prior to surgery as baseline, and 6 and 12 weeks post-surgery, knee function and quality of life measurements - Knee and Osteoarthritis Outcome Score (KOOS) - Range of motion of the affected limb Descriptive safety overview at 30 days and 12 weeks post-surgery: - Readmitted to theatre and/or hospital - Infection of wound site - Diagnosed with pulmonary embolism or deep vein thrombosis. Patient satisfaction survey at 5 days post-surgery
Sponsor	North Cumbria Integrated Care NHS Foundation Trust
Manufacturer & research grant provider	Joint Operations, supplier of VPULSE® active compression & cooling therapy device. Contact: Mike Wood, Business Development Manager, tel +44 (0)7825 881834 , email mike@jointoperations.co.uk , www.jointoperations.co.uk, Unit 11 Interface Business Park, Bincknoll Lane, Royal Wootton Bassett, Wiltshire, SN4 8SY, UK
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Organisation where research will take place	North Cumbria Integrated Care NHS Foundation Trust Orthopaedics Department Newtown Road, Carlisle CA2 7HY, UK
Planned timeline	Recruitment start date (first patient, first visit) 1 Feb 2023 Recruitment end date (last patient, first visit): 31 May 2026 Recruitment end date (last patient, last visit): 30 Sep 2026
Protocol version, date	Version 2.1, dd 29 Nov 2024

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1. LAY SUMMARY

Osteoarthritis can be treated with knee replacement procedures, where either part or the whole of the knee joint is replaced. For all major knee operations, post-surgery the site of operation can be painful. Increased pain may limit a patient's progress with post-operative mobilisation. Therefore, research is already ongoing in the field of knee surgery to determine if different type of bandaging and cooling of the affected leg post-surgery may improve patient and clinical outcomes. A relatively new method is now available which involves a combination of active compression and cooling, rather than passive compression and cooling. This may reduce pain. This present study aims to assess if active compression and cooling is better than standard passive compression and cooling in terms of keeping a patient comfortable by reducing pain and possibly improving other clinical outcomes too. A total of 88 patients will be recruited and allocated to either standard care AIRCAST® KNEE CRYO/CUFF™ (passive compression & cooling; 44 patients) and new intervention VPULSE® (active compression & cooling; 44 patients); follow-up of patients will be up to 12 weeks post-surgery. Apart from clinical outcomes such as the degree and type of pain experienced by patients, safety data such as incidence of infection and deep vein thrombosis/pulmonary embolism, plus readmission to hospital will be recorded too. The main objective of the study is whether VPULSE® is significantly better than standard AIRCAST® KNEE CRYO/CUFF™ 48 hours post-surgery when measured on a visual display pain scale.

2. INTRODUCTION

Major knee surgery is associated with post-surgery pain. The surgical site is subject to bleeding and inflammation-related fluid build-up in the intraarticular tissues (Holm et al, 2020). Pain may impact negatively on recovery time and active early rehabilitation due to physical impairment that it may cause ((Mizner & Snyder-Mackler, 2005). This in turn may increase hospital length of stay and poor patient reported-outcomes (Moretti et al, 2012; Williams et al, 2013). Many service improvement programmes and techniques have been introduced in knee surgery over the years, including means to reduce intra-articular bleeding, tourniquets and medication (Martin et al , 2014). Initiatives in post-surgical management of patients have had mixed outcomes. These include methods such as the use of a cold compress (Morsi 2002), cryotherapy (Adie et al, 2012), elastic bandaging (Hughes et al, 1995) and some types of compression bandaging (Anderson et al, 2008; Charalambides et al, 2005; Jonker et al, 2020).

Sole compression bandage therapy, using mainly two-layer short-stretch bandaging, is established treatment of venous ulcers and lymphoedema (Franks et al, 2004, Pike 2011). External compression is tough to aid venous return and reduces hydrostatic pressure in the leg by (i) improving the efficacy of the calf muscle pump and (ii) moving blood from the superficial to deep venous system, subsequently allowing movement of fluid from the interstitial space. The efficacy in total knee arthroplasty is still unclear due to conflicting results in the literature and heterogeneous methodology (Munk et al, 2013; Pinsornsak P & Chumchuen, 2013; Cheung et al, 2014). In a recent study involving knee osteotomy rather than arthroplasty patients, we showed a marked change in the type and temporal profile of pain experienced by patients post-surgery, see Table 1 (Jonker et al, 2020).

The above evidence regarding compression therapy involves bandaging of the most of the leg (from above knee to below ankle). VPULSE® has developed a device that combines active compression of the knee and cryotherapy. This concept is not necessarily novel; Song and colleagues summarised data from 10 randomised controlled trials, involving 522 patients in a meta-analysis of compressive cryotherapy versus cryotherapy alone in knee arthroplasty patients (Song et al, 2016). The conclusion from said study was that pain levels at up to a week post-operation were lower in the combined cryotherapy group compared to the cryotherapy only group. A 10-cm visual analogue scale for generic pain intensity was commonly deployed; the type of pain was not described in any of the studies. Similarly, cryotherapy reduces pain levels in the majority of studies conducted to date but again this is for generic pain intensity (Thacoor and Sandiford, 2019). A limitation with all treatment modalities (compression, cryotherapy or a combination of the two) is that there is a lot of variation in terms of the devices used and their application (frequency or duration).

In summary, there is a body of evidence that both compression alone, cryotherapy alone, and combined compression cryotherapy can all contribute to lower pain levels in patients after knee arthroplasty. As in the osteotomy study (ROBOT), we will here assess the levels of pain after knee replacement and also the pain profile (what type of pain experienced at what time point) when

patient are either using passive compression cryotherapy AIRCAST® KNEE CRYO/CUFF™ or active compression cryotherapy VPULSE®. The need for contemporary appraisals can be illustrated with one example publication from 2006 in which cryotherapy was compared to epidural for pain control (Kullenberg et al, 2006); the average length of stay in hospital was over 5 days in that study. Nowadays length of stay rarely exceeds 2 days, demonstrating the overall improvements made in managing post-surgery recovery of patients.

3. INVESTIGATIONAL DEVICE & INTERVENTION

3.1 Intervention

3.1.1 Control (standard care) arm - AIRCAST® KNEE CRYO/CUFF™

Once the operation is finished, a wound dressing is applied and a standard bandage is applied. It consists of one layer of soft synthetic bandage, stretching from proximal tibia to distal femur covered by a further layer of crepe bandage prior to or after tourniquet deflation, with 50% overlap of each layer. Once transferred to the ward for recovery, this standard bandage will be removed and AIRCAST® KNEE CRYO/CUFF™ cryotherapy is applied to the patient's index knee. This is a sleeve containing iced water and it will be utilised for up to 48 hours post-operation or until patient discharge, whichever of the two is sooner.

The CRYO/CUFF™ is designed to combine the therapeutic benefits of controlled cold compression to minimise hemarthrosis and swelling and reduce pain. The cuff is anatomically designed to completely fit the knee providing maximum coverage of the whole joint and allowing the whole surface area to have the continual cooling benefit of cryotherapy. The cuff is attached to the Gravity Aircast Cryo/Cuff Cooler and will hold water and ice needed for six to eight hours of cryotherapy.

3.1.2 Intervention arm - VPULSE®

Once the operation is finished, a wound dressing is applied and a standard bandage is applied. It consists of one layer of soft synthetic bandage, stretching from proximal tibia to distal femur covered by a further layer of crepe bandage prior to or after tourniquet deflation, with 50% overlap of each layer. Once transferred to the ward for recovery, this standard bandage will be removed and VPULSE compression cryotherapy is applied to the patient's index knee. As with standard treatment arm, the VPULSE cuff is applied over the routine surgical wound dressing. The cryotherapy effect is achieved by circulating cold water using a pump rather than gravity-driven cryotherapy with the current Aircast Cryo/Cuff set up that is standard care. The VPULSE also achieves compression by intermittent dynamic compression; this is an approximate pressure of 50mmHG. Further info regarding VPULSE can be obtained from the Joint Operations website: https://www.jointoperations.co.uk/buy-online/vpulse/

Apart from the difference in type of compression & cooling therapy, the protocol for both trial arms is identical. Used knee sleeves will be disposed of in line with local guidelines on disposal of clinical waste.

Figures 1 & 2. CRYO/CUFF™ (left) and VPULSE® device (right)

CRYO/CUFF water tank and knee sleeve

VPULSE device with knee sleeve

4. STUDY HYPOTHESIS

4.1 Primary objective

- To assess the efficacy of VPULSE® active compression & cooling device for reduction of post-operative pain after knee surgery compared with AIRCAST® KNEE CRYO/CUFF™ .

4.2 Secondary objective

- To assess the type of pain experienced by patients wearing either AIRCAST® KNEE CRYO/CUFF™ or VPULSE®.
- To assess the efficacy of VPULSE® for improvement of post-operative patient-reported outcome measures, including knee functionality, after knee surgery when compared with standard care AIRCAST® KNEE CRYO/CUFF™.

5. STUDY PROTOCOL

5.1 Study design, recruitment sites and timeline

This concerns a multi-centre, controlled prospective randomized study of CE-marked medical devices. The study will be carried out in the following NHS Trust:

- North Cumbria Integrated Care NHS Foundation Trust (both Cumberland Infirmary, Carlisle, and West Cumberland Hospital, Whitehaven. CI Mr Cristian Nita)

The study will take place in a hospital setting with support and oversight from the treating orthopaedic surgeon, nursing staff and research staff. Where appropriate, research delivery staff will be delegated to provide support with data collection and processing.

Table 2. Anticipated timeline

Month	Setup	Recruitment	Analysis	Finalise
Nov 2022	Submission for NRES/ HRA approval			
Dec 2022	NIHR portfolio adoption			
Jan 2023	NRES/HRA and Trust approval			
Feb 2023		Start recruitment		
May 2026		Finish recruitment		
Aug 2026			Follow-up complete; Analyse data.	
Sep 2026				manuscript & report writing

5.2 Participant identification and research setting

Participants will be recruited from orthopaedics clinics and all eligible patients will be invited to take part until the required numbers have been achieved. Identification will be by the orthopaedics clinical team, who are supporting the study. A screening form will be completed for potentially eligible patients to confirm that they indeed meet the trial criteria.

To summarise, the orthopaedic team will:

- Identify potentially eligible patients and ask verbal consent for them being approached about the study by a member of the R&D team
- Complete the incl/excl criteria part of the screening form (if a patient has given verbal consent to being approached by the research team then they can complete the screening form)

5.3 Consent and recruitment

Those eligible will be approached and provided with an information pack and consent form, which will be signed to indicate that informed consent has been given. Patients will be given ample time to consider taking part, more than 24 hours if they wish. The study will be first mentioned at an orthopaedics out-patient clinic visit. The direct healthcare professional will first approach a patient about the study, and after verbal consent by the patient the healthcare professional themselves or a member of the research team can go through the informed consent process.

Patients are also allowed to consent to taking part when first approached as long as the study has been discussed with the patient and they have been given time to read the patient information leaflet and opportunity to ask any questions that they may have. Participants will receive no incentives and consent will be regarded as a process and not a one-off event. Participants are free to withdraw from the study at any time without the need to give any reasons for withdrawal. Their standard of care will not be affected by either declining to participate in the study or withdrawing during participation. Data collected up to the date of withdrawal will be retained for analysis.

Participants will be randomised to either the control group (Cryo/Cuff) or the intervention group (VPULSE) any time up until the day of surgery.

5.4 Follow-up

Patients are in the study for a period of 12 weeks. Thereafter, the patient will be followed up as they would be in normal clinical practice. Study visits are aligned to hospital/clinic visits where possible. Baseline data can be collected on the day of surgery (prior the actual operation), and 12 day and 12 week post-surgery data can be collected when the patient attends for standard follow-up in the orthopaedics out-patient department. The data at 24 hrs, day 3, 5, and 12 falls outside these dates. For all outcome measures, data can be collected over the phone, via e-mail or by mail (whichever is preferred by the patient – mail is by use of freepost, to avoid patients incurring any costs). The researcher can also send reminders to the participant regarding the completion of certain outcome data at the aforementioned follow-up time points.

5.5 Outcome measures

5.5.1 Primary outcome measures

To determine the level of operation-site related pain experienced at day 2 post-operation and to compare the average pain scores of patients in the control and intervention arm respectively, through administration of 10 cm visual descriptor scale (VDS) for pain.

The study is powered to detect the established minimal clinically important difference (MCID) of 1.5 cm on a 10 cm VDS pain.

5.5.2 Secondary outcome measures

All the outcome measures are summarised in Table 3.

Table 3. Overview of measurements

Weeks	-12 weeks to day of surgery	0 surgery	24hrs [$]	3 days[#][#]	5 days[#][#]	12 days[#]	6 weeks*	12 weeks*
Application device post surgery		X	x					
VDS pain scale (at rest)	X		x	X	X	X	X	
VDS pain scale (walking, if capable to stand)	X		x	X	X	X	X	
McGill pain questionnaire	X		x	X	X	X	X	
Limb range of motion	X						X	
KOOS score	X						X	X
Patient satisfaction questionnaire re device use					X	X (if not returned yet at 5 days)		

** Allowed to be up to 2 weeks early or late*
 # Allowed to be up to 3 days early or late
Allowed to be up to 1 day early or late
$ Allowed up to 6 hours early or late

6. SUBJECTS

6.1 Anticipated number of research subjects

The sample size calculation does take into account a 30% patient attrition rate (withdrawal and loss to follow-up), since this involves a study with multiple time points for data collection up to 12 weeks. From other similar studies we are aware that loss to follow-up is relatively high in this group of patients. Patients will be recruited from the adult (age 18+) population routinely seen by the evaluating clinical staff members. The primary outcome measure is based on knee/leg (ie wound site) pain experienced 5-days post-surgery based on the VDS pain scale 'at rest'. The hypothetical difference in pain perception is 1.5 on a 10 cm scale which equates to a significant 'minimally clinically important difference' for pain (Kelly 2001; Lee et al 2003; Tashjian et al 2009). The values and differences observed in the ROBOT trial will be used for reference.

The non-parametric two-sided Mann-Whitney u-test is applied because the data is ordinal; 80% power and 5% significance is also applied. A priori power calculations using GPower 3.1 software, result in the following sample size summarized in Table 3.

Analysis will be performed on an intention-to-treat basis, although the number of days that a participant has worn a bandage will be recorded.

Table 4, Sample size calculation

	Mean pain score at 5 days post-op	**Standard Deviation**
Arm A (*hypothetical*)	*5.0*	*2*
Arm B (*hypothetical*)	*3.5*	*2*
	Power beta of 80%, Alpha p-value of 0.05, Effect size 0.75 Sample size required without any drop-out: 62 Sample size with 30% attrition rate included: 88 Total of 88 patients: - 44 Patients to receive AIRCAST® KNEE CRYO/CUFF™ device (current standard care, control arm) - 44 Patient to receive VPULSE® (intervention arm)	

The CONSORT guidelines require a statement on the number of patients assessed for eligibility (Schulz, Altman & Moher 2010). The number of patients screened but who did not meet the inclusion criteria or who declined to participate will be recorded, as will any patients who are lost to follow-up (Appendix 3).

6.1.1 Randomisation

Following written consent patients will be allocated at random to the one of two treatment arms, the control AIRCAST® KNEE CRYO/CUFF™ or VPULSE® intervention group, using a non-restricted randomised sequence generated for the whole sample using a free ware randomisation programme, see https://www.sealedenvelope.com/ . Each next randomisation allocation will be obtained from the sealedenvelope.com account for this ALASKA trial.

As the study involves different looking cooling devices, it is not possible to achieve blinding for the participants. However, statistical analysis is carried out blinded to group allocation, by persons who have not had contact with study participants.

6.2 Eligibility criteria

6.2.1 Inclusion criteria

- Patient who is listed for:

    - Knee arthroplasty (replacement) surgery, either partial or total knee replacement (unilateral).
- Clinical indication, in the opinion of the treating surgeon, that compression & cooling therapy may be of benefit to the patient
- Adult patients aged > 18 years
- Mental capacity to give written informed consent

6.2.2 Exclusion criteria

- Under the age of 18 years
- Unable to fully understand the consent process and provide informed consent due to either language barriers or mental capacity
- Revision of previous knee replacement or osteotomy on the index leg.
- Limited life expectancy, i.e. undergoing palliative care
- Any condition that is associated with excessive bleeding, coagulation abnormalities or any other significant haematological condition (e.g. Factor V Leiden, haemophilia).
- Cardiovascular or vascular condition that in the opinion of the treating surgeon contraindicates the use of compression bandaging, including moderate to severe peripheral arterial disease, venous leg ulcer, high dose anti-coagulant medication
- Any skin or other condition that contraindicates the use of compression and cooling therapy.
- Patients who are participating in another interventional research study involving an investigational product related to the knee procedure and its aftercare.
- The patient has concurrent (medical) conditions that in the opinion of the investigator may compromise patient safety or study objectives.
- Patient has practical or mobility issues which will prevent them from removing the device themselves

6.3 Early withdrawal of subjects

Patients have the right to withdraw from the trial at any time and without giving any reason. If a patient withdraws from the trial, any and all information gathered prior to the withdrawal will be excluded in the analysis, no further data collection will occur. If a patient does not attend a planned follow-up appointment then two more attempts will be made to contact the patient regarding the study. If still no contact can be made then the patient is deemed lost to follow-up and any collected study data will be retained.

7. SAFETY

7.1 Potential risks & benefits to study participants

There are no major anticipated personal safety risks associated with patients taking part in this study, though it is recognised that the – particularly incorrect – application of compression and cooling devices can result in skin reactions and discomfort and can potentially affect blood flow. If the research team learns of important new information that might affect the patient's desire to remain in the study, he or she will be told. Appropriate precautions are in place to ensure medical

and personal information is kept safe through adhering to appropriate governance regulations. Any adverse events will be recorded, as outlined in sections below.

For the participants in the control group there is no direct benefit in taking part in this study. They will be cared for in exactly the same manner as they normally would. For participants in the VPULSE intervention group, there may be benefits in terms of improved pain control compared to normal standard care. Although there is initial evidence that this is indeed the case, this has not yet been proven and established through a prospective randomised trial, and this study is aimed to assess this. Participants cannot claim payments, reimbursement of expenses or any other benefits or incentives for taking part in this research.

7.2 Safety reporting window and definitions

Adverse Event (AE)	Any untoward medical occurrence in a patient or other clinical investigation participant taking part in a trial of a medical device, which does not necessarily have to have a causal relationship with the device under investigation. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of the device, whether or not considered related to the device.
Serious Adverse Event	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' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at 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.

The safety reporting window for (Serious) Adverse Events is from start of the index surgery to up to and including 30 days after the index surgery. Any unscheduled medical or surgical care received by the participant outside this window is not included for safety reporting for this study. This aligns with national 30-day reporting standards for eg infection and mortality after surgery.

7.3 Procedures for recording adverse events

All SAEs need to be reported to the sponsor/host Trust R&D **within one working day** of the investigator team becoming aware of them – AEs should be reported on within two weeks of becoming aware of them. For this purpose an AE report form is completed by the researcher and/or Chief Investigator

The relationship of each adverse event to the trial must be determined by the Chief Investigator, or – only in cases where the CI is not available - another suitably qualified and delegated clinically qualified person (doctor or orthopaedics specialist nurse), according to the following definitions:

- **Related**: The adverse event follows a reasonable temporal sequence from swabbing. It cannot reasonably be attributed to any other cause.
- **Not Related**: The adverse event is probably produced by the participant's clinical state or by other modes of therapy administered to the participant.
- **Severity grading**: the Chief Investigator or – only in cases where CI is not available - suitably clinically qualified delegated person (doctor or orthopaedics specialist nurse) will also record if it concerns an AE or SAE.

This is recorded on the aforementioned AE reporting form. The forms are stored in the study site file.

Pseudo-anonymised copies of all adverse events forms will be shared with Joint Operations Ltd as soon as causality reporting has been performed and concluded.

If the CI did not perform causality of the (S)AE for a particular case, he/she will check the completed forms and countersign the case as soon as he/she is available to do so.

8. STATISTICAL CONSIDERATION AND DATA ANALYSIS PLAN

8.1 Analysis of baseline characteristics

To determine the demographics and characteristics of the patients in the two arms the following data will be collated:

- Age (yrs)
- Gender
- Height (kg), weight (cm), BMI

Data concerning the actual knee replacement procedure will also be collected, including:

- Type of surgery
    - Including type of medical device used and which leg operated on
- Length of operation (min) and blood loss (ml) during operation
- Type of anaesthetic and analgesics prescribed post-surgery
- Hospital length of stay (days)

- Moment physiotherapy and early recovery initiated
- Type of standard bandaging applied if control patient.

Any differences in distribution will be established with Chi-squared test or Mann-Whitney U-test/t-test (depending on distribution of data) as indicated.

8.2 Primary outcome statistics

To determine the level of operation-site related pain experienced at day 2 post-operation and to compare the average pain scores of patients in the control and intervention arm respectively, through administration of 10 cm visual descriptor scale (VDS) for pain.

The study is powered to detect the established minimal clinically important difference (MCID) of 1.5 cm on a 10 cm VDS pain.

The average difference between time points will be calculated per group, 2days post-surgery being the primary endpoint. 24hrs,3,5,, 12 days and 6 weeks post-surgery will also be analysed. To compare the groups, the Mann-Whitney U-test will be applied.

To avoid relying on one outcome measure related to pain, at 3, 5, 12 days, and 6 weeks post-surgery pain perception will also be measured using the short form McGill pain questionnaire. Again, to compare groups the Mann-Whitney U-test will be applied.

8.3 Secondary outcome statistics

The average baseline demographics for participants in each group will be compared to ascertain that randomisation has indeed led to comparable distribution of participants:

Sex, age, height, weight, BMI, length of stay, type of anaesthetic for surgery and type of analgesics post-surgery.

To compare outcomes between the two groups (control vs intervention), student t-test, Mann-Whitney U-test or Chi-squared test will be applied as applicable, depending on type and distribution of data.

Cox proportional hazards regression analysis will be conducted to investigate the role of bandaging and other covariates (as mentioned above) in post-surgery related pain and knee function.

The statistics apply to:

Up to 12 weeks prior to surgery, and 12 weeks post-surgery, knee function and quality of life measurements: Knee and Osteoarthritis Outcome Score (KOOS), and range of movement of the affected limb (goniometer)

Descriptive safety overview at 30 days and 12 weeks post-surgery:

- Readmitted to theatre and/or hospital
- Infection of wound site
- Diagnosed with pulmonary embolism or deep vein thrombosis
- All monitored remotely by review of patients' hospital notes.

Patient satisfaction survey at 12 days post-surgery – descriptive statistics only.

For all outcome measures and statistics, both whole cohort and surgery-specific stratification analysis will be conducted.

9. DATA HANDLING AND MONITORING

Data arising from this study is confidential. Identifiable information can only be accessed by delegated members of the study team. Anyone in the research team who does not have a substantive contract with North Cumbria Integrated Care NHS Foundation Trust or one of the recruiting NHS Trusts will need to apply for a letter of access via the NIHR research passport scheme, should they require access to identifiable study data.

Patient identifiable data will only be used within each respective Trust and by the core research team. All identifiable data is stored on password protected NHS computer systems. Anonymised data will be shared and stored using security-enabled systems such as password-protection and encryption of e-mails and files. The requirements of the Data Protection Act and NHS Code of Confidentiality will be followed at all times. All researchers will be fully trained in NHS Confidentiality and GCP. Participants' GP practices will be informed that they are taking part in the study.

All paper data will be held in secure locked environments in the office of the Research & Development department in the Cumberland Infirmary, Carlisle and West Cumberland Hospital, Whitehaven. Data released (e.g. by publication) will contain no information that could lead to the identification of an individual participant. Upon completion of the study the site files will be archived for a period of 15 years in line with local archiving policy and procedures. Direct access to data only will be granted to authorised representatives from the sponsor / host institution, grant funder and medical device provider (Joint Operations) and the regulatory authorities to permit trial-related monitoring, audits and inspections.

This investigator-initiated trial will be monitored in terms of conduct of the study by the in-house research team, led by the Chief Investigator, who will convene on a monthly basis in person or via phone/e-mail. A formal trial steering committee will not be convened for this trial – however, when data is available for 50% of the sample an interim analysis will take place to assess if there are any points of concern to consider. The study can be audited by the in-house R&D department as part of their rolling audit programme of sponsored and hosted research studies. As part of the research grant agreement, anonymised study data will be shared with Joint Operations for review and for

potential publication purposes. No identifiable data, including on potential exemplar case photos, will be contained in any of this data.

10. GOVERANCE OF STUDY

10.1 Approvals

This study will be conducted in compliance with the protocol approved by the Health Research Authority, National Research Ethics Service, and local Trust R&D Approval, and according to Good Clinical Practice standards including the Declaration of Helsinki (1964, Amended Oct 2013). No deviation from the protocol will be implemented without the prior review and approval of the aforementioned review bodies, except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported according to policies and procedures

10.2 Sponsor & Indemnity

North Cumbria Integrated Care NHS Foundation Trust is the sponsor of this study and therefore NHS indemnity applies for design, conduct and management of the study. The company Joint Operations has provided a grant for this study by means of provision of the VPULSE devices worth £2,660.

Patients will not be given financial incentives for taking part in the study. Travel expenses are not offered in this study since patients are not seen in clinic more frequently than they would normally attend as part of their normal care pathway.

11. PUBLICATION AND DATA-SHARING POLICY

The study will be registered on ISRCTN or Clinical Trials Gov website, in line with CONSORT guidelines on good practice in clinical research.

The results of this study are planned to be disseminated through:

- Peer-reviewed manuscript in scientific journal
- Internal report to the funder of the trial, company called Joint Operations

As stated in the PIL and ICF, anonymised study data will be shared with Joint Operations as part of the research grant agreement.

A summary of the main findings can be supplied to participants on request and this will be stated in the informed consent form.

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APPENDIX 1. TOOLS AND ASSESSMENTS

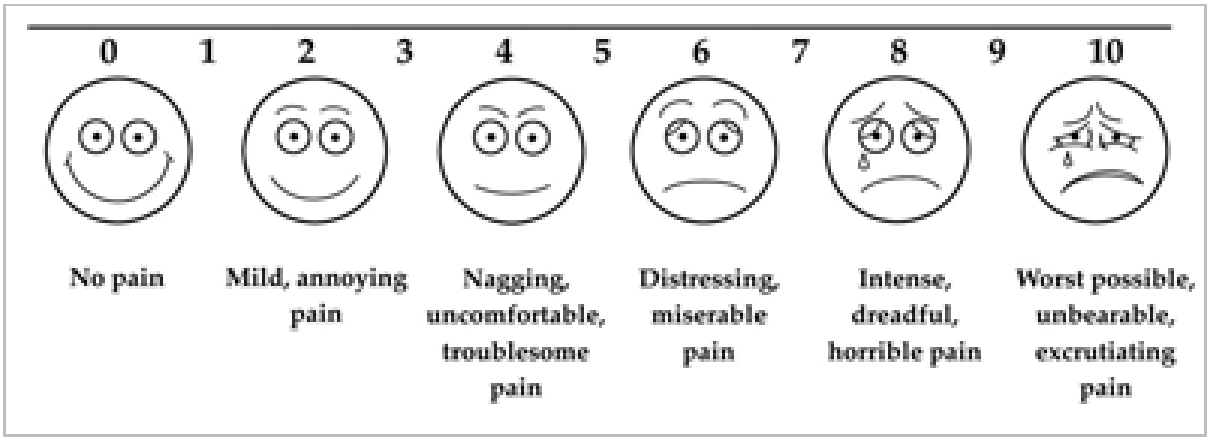
This appendix contains:

- Visual Descriptor Pain scale
- Short-form McGill pain questionnaire

The KOOS score and Bandage Patient Satisfaction Questionnaire are enclosed separately to this protocol.

Visual Descriptor Pain score

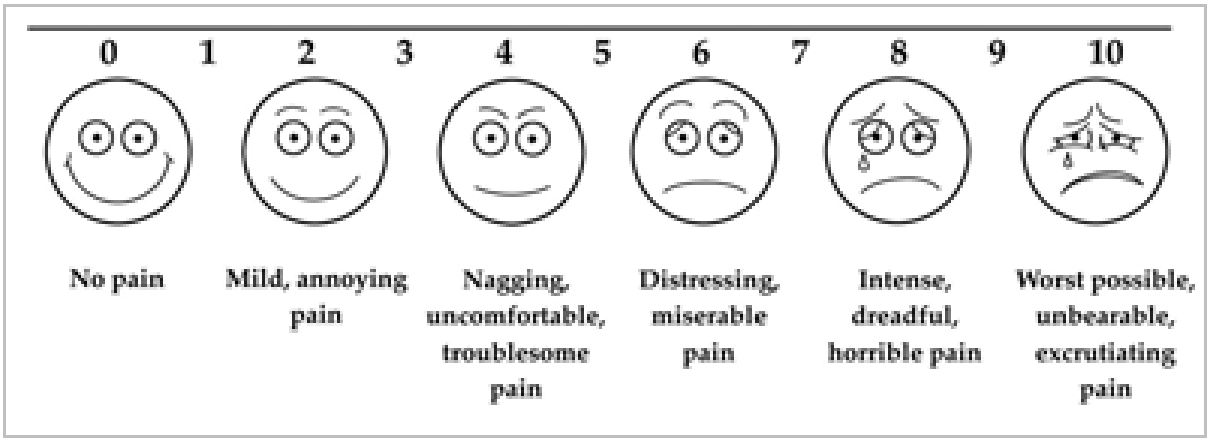
How painful has your leg, the one has been operated on, been **in the last day when resting**:



Please put a vertical line on the numbered bar above. We kindly ask you consider the affected knee when you answer this question.

Visual Descriptor Pain score

How painful has your leg, the one has been operated on, been **in the last day when walking**:



Please put a vertical line on the numbered bar above. We kindly ask you consider the affected knee when you answer this question.

Short-form McGill pain questionnaire

How painful has your leg, the one has been operated on, been **generally in the last day**

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0) _____	1) _____	2) _____	3) _____
SHOOTING	0) _____	1) _____	2) _____	3) _____
STABBING	0) _____	1) _____	2) _____	3) _____
SHARP	0) _____	1) _____	2) _____	3) _____
CRAMPING	0) _____	1) _____	2) _____	3) _____
GNAWING	0) _____	1) _____	2) _____	3) _____
HOT/BURNING	0) _____	1) _____	2) _____	3) _____
ACHING	0) _____	1) _____	2) _____	3) _____
HEAVY	0) _____	1) _____	2) _____	3) _____
TENDER	0) _____	1) _____	2) _____	3) _____
SPLITTING	0) _____	1) _____	2) _____	3) _____
TIRING/EXHAUSTING	0) _____	1) _____	2) _____	3) _____
SICKENING	0) _____	1) _____	2) _____	3) _____
FEARFUL	0) _____	1) _____	2) _____	3) _____
PUNISHING/CRUEL	0) _____	1) _____	2) _____	3) _____

VAS NO PAIN ——— WORST POSSIBLE PAIN

PPI

0 NO PAIN _____
1 MILD _____
2 DISCOMFORTING _____
3 DISTRESSING _____
4 HORRIBLE _____
5 EXCRUCIATING _____

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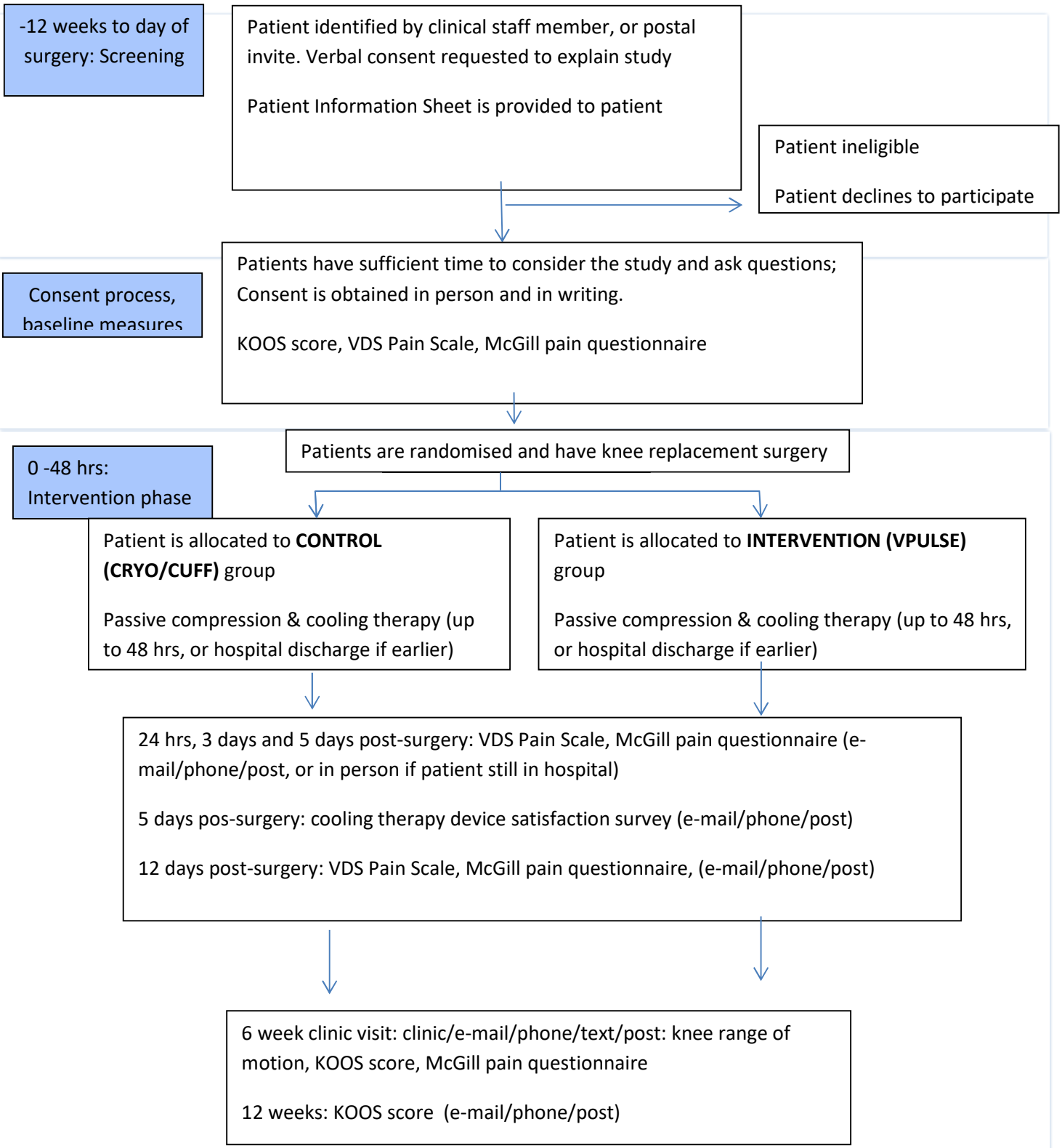
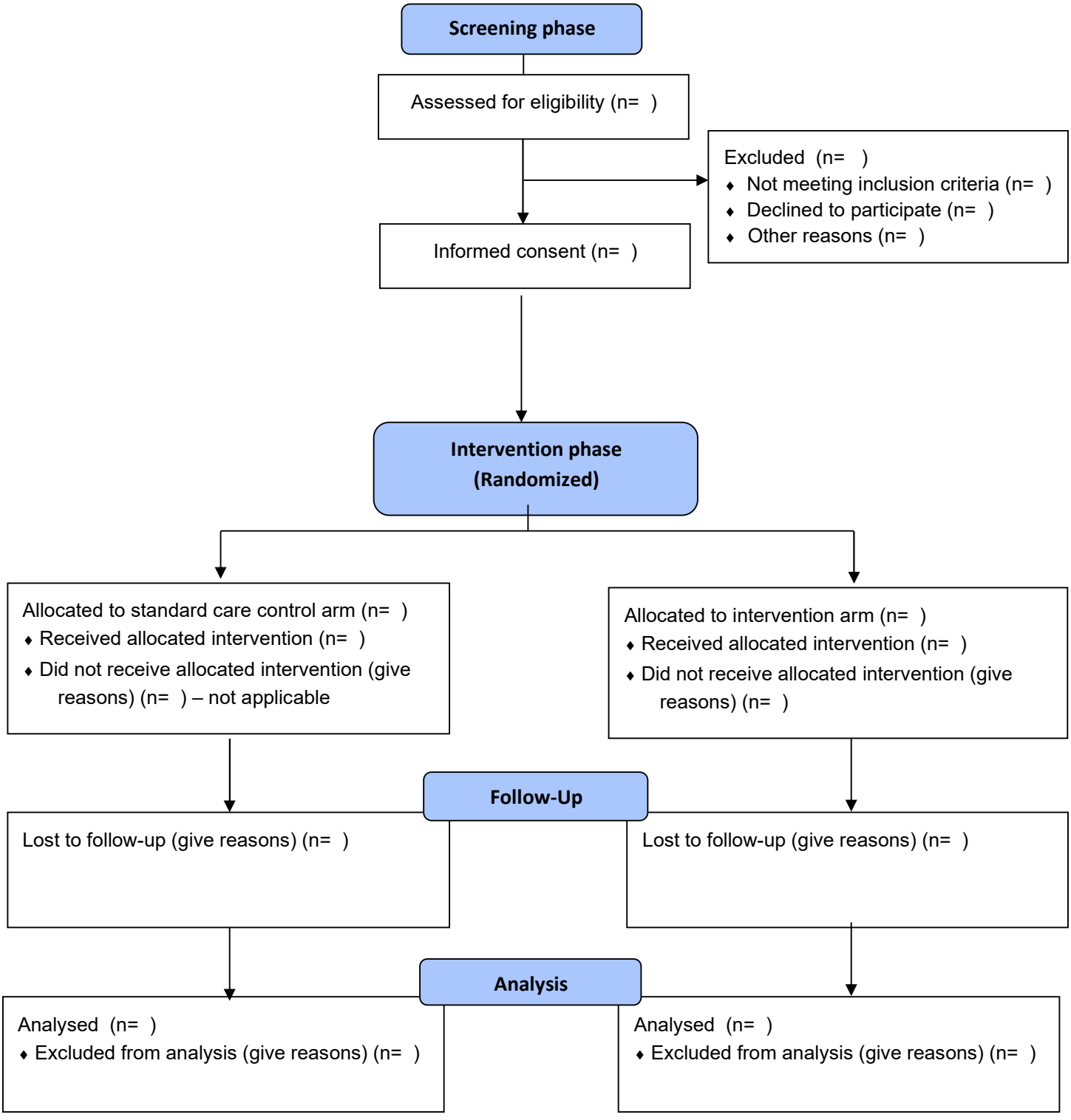
The short-form McGill Pain Questionnaire (SF-MPQ). Descriptors 1–11 represent the sensory dimension of pain experience and 12-15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe. The Present Pain Intensity (PPI) of the standard long-form McGill Pain Questionnaire (LF-MPQ) and the visual analogue scale (VAS) are also included to provide overall intensity scores.

The McGill Pain Questionnaire: Major properties and scoring methods . Melzack, 1987

APPENDIX 2. STUDY PARTICIPANT FLOWCHART



APPENDIX 3. CONSORT FLOWCHART



**Based on CONSORT Flowchart (Moher et al, 2001)*