UK ADAPTIS™ STUDY PROTOCOL

Full title:	INFINITY™ with ADAPTIS™ and EVERLAST™ technology total ankle replacement follow-up
Short title:	UK ADAPTIS™ Study
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CONTENTS

1. STUDY SUMMARY

Full Title:	INFINITY™ with ADAPTIS™ and EVERLAST™ technology total ankle replacement follow-up
Short Title:	UK ADAPTIS™ Study
Phase:	Phase 4, Post-Market
Design:	A prospective multi-centre cohort series of INFINITY™ with ADAPTIS™ and EVERLAST™ Technology with Poly Insert for patients requiring primary total ankle replacement (TAR) i.e. Total Ankle Arthroplasty (TAA). Patients meeting the criteria for the study will be asked to enrol by providing written informed consent. The patients will be monitored clinically by post-operative follow-up examinations and Patient reported outcome measures (PROMs) (Manchester Oxford Foot & Ankle Questionnaire (MOXFQ), Ankle Osteoarthritis Scale (AOS), EQ5D-5L).
Duration:	The study will have a minimum 12-month recruitment period and up to 5 years post-operative follow-up.
Setting:	It is anticipated around 10 UK NHS Hospital Trusts regularly performing TAA/TAR will participate.
Sample Size:	Minimum of 200 patients.
Inclusion Criteria:	1. Male or non-pregnant female over the age of 21 years with a diagnosis of end stage ankle arthritis and requiring primary TAA/TAR and is suitable for the use of the ADAPTIS TAA/TAR. 2. Patients who are physically and mentally willing and able to comply with the post-operative follow-ups and an appropriate rehabilitation schedule. 3. Patient can understand and provide written consent.
Exclusion Criteria:	1. Patients with previous ankle arthrodesis or Patients who require revision of previously implanted TAA/TAR. 2. Any patients presenting with clinically relevant conditions prior to implantation, that would contraindicate implantation of a TAA/TAR.

Indication:	**Intended use:** It is intended to give a patient limited mobility by reducing pain, restoring alignment, and replacing flexion and extension movement in the ankle joint. **Indications for use:** • Patients with ankle joints damaged by severe rheumatoid, post-traumatic, or degenerative arthritis. • Patients with a failed previous ankle surgery.
Intervention:	INFINITY™ with ADAPTIS™ and EVERLAST™ technology with Poly Insert for patients requiring primary TAA/TAR.
Objectives:	The primary objectives of the study are to assess device survivorship and performance using rates of re-operation or revision and PROMs over a 5-year post-operative period.
Outcomes:	**Primary outcomes** are functional status (MOXFQ) at 2-year post-operative and device survivorship at 2 years. **Secondary outcomes** are: • Survivorship of the components at 2 years and 5 years post-operative. o Revision of any components (excluding incidental polyethelene exchange for infection). o Re-operation without component exchange. o Type and frequency of adverse events (AEs), specifically operative and device related AEs and serious AEs (SAEs). • Functional status, pain and disability (MOXFQ & AOS), and health-related quality of life (EQ5D-5L) at 6 months, 1 year, 2 years, and 5 years post-operative. • Clinical assessment at 6 weeks, 6 months, 1 year, 2 years, and 5 years. • Radiographic assessments at 6 months,1 year, 2 years, and 5 years.
Analysis of Results:	The analyses will be mainly descriptive. Continuous data will be summarised using means and standard deviations (or median, interquartile range, minimum and maximum as appropriate). Categorical data will be summarised using counts and percentages. Linear or logistic regression models (as appropriate depending on the outcome) will be used to

	evaluate the influence of patient, clinical and surgical factors on outcomes. AEs and SAEs will be summarised descriptively, whether they are operative or device related.

2. EVALUATION SCHEDULE

Evaluation	*Pre-Op	Intra-Op	**6 weeks	6 months	1 year	2 years	5 Years
Time Window	**N/A**	**N/A**	**+/- 2weeks**	**+/- 2weeks**	**+/- 6weeks**	**+/- 3months**	**+/- 6months**
Inc./Exc. Criteria	X						
Pre-Op Clinical History	X						
Intra-Op Surgical Details		X					
Clinical Follow-Up			X	X	X	X	X
MOXFQ	X			X	X	X	X
AOS	X			X	X	X	X
EQ5D-5L	X			X	X	X	X
Radiographs	X			X	X	X	X
Adverse Events or Termination	Anytime						

***Pre-Op:** Date of or any time post the date of written informed consent up to 6 months prior to date of surgery.

****6 Weeks:** This is not an additional study-related clinical visit. Research teams will be required to review the 2- and 6-week clinical visits that occur as standard of care to report any adverse events.

If Patients exceed a 6 month wait for surgery, a radiograph will be repeated at their pre-operative assessment or on the morning of surgery as part of routine care.

Patient study consent will be valid for the 12 months from the date of consent unless withdrawn.

3. STUDY PURPOSE

An ankle replacement procedure consists of replacing the worn-out joint surfaces of the ankle with metal and plastic components that are shaped to allow continued movement of the ankle. There are several different types of ankle replacement available. Infinity ankle implants are already routinely used in NHS hospitals. The INFINITY™ with ADAPTIS™ and EVERLAST™ ankle replacement system is a development of the Infinity ankle implant, designed to attach to the bone better and to wear out more slowly.

The purpose of the UK ADAPTIS™ Study is to assess the performance and function of the newly introduced INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System for total ankle replacement (TAR) or arthroplasty (TAA) and EVERLAST™ Poly Insert that modernises and streamlines Stryker's TAA/TAR portfolio.

4. STUDY DESIGN

This is a prospective multi-centre cohort study of INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System TAA/TAR implantations.

Patients meeting the criteria for the study will be invited to enrol by providing written (electronic) informed consent.

The patients will be monitored clinically by post-operative follow-up examinations and patient reported outcome measures (PROMs).

The length of the Patient follow-up schedule in the study is based on the previously published UK INFINITY™ Study[1].

The study is set up to record data pre-operative, intra-operative, and at 6 weeks, 6 months, 1 year, 2 years, and 5 years post-operative.

5. OBJECTIVES AND OUTCOMES

5.1 PRIMARY OBJECTIVE

The primary objectives of the study are to assess device survivorship and performance using rates of re-operation/revision and functional status (MOXFQ) over a 5-year post-operative period.

5.2 PRIMARY OUTCOMES

Primary outcomes are functional status (MOXFQ) at 2-year post-operative and device survivorship at 2 years.

5.3 SECONDARY OUTCOMES

Secondary outcomes are:

1. Survivorship[2] as removal or exchange of one or more of the components (excluding incidental polyethylene exchange for infection) at 2 years, 5 years and post-operative.

    a. Revision of any components (excluding incidental polyethelene exchange for infection).

    b. Re-operation without revision

    c. Type and frequency of adverse events (AEs), specifically operative and device related AEs and Serious AEs (SAEs).

2. Functional status, pain and disability (MOXFQ & AOS) and health-related quality of life (EQ5D-5L) at 6 months, 1 year, 2 years, and 5 years post-operative.

3. Clinical assessment 6 weeks, 6 months, 1 year, 2 years, and 5 years post-operative.

4. Radiographic assessments at 6 months 1 year, 2 years, and 5 years post-operative.

6. PATIENT SELECTION

6.1 SAMPLE SIZE

This study will collect data on a minimum of 200 patients implanted with the of INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System for a TAA/TAR. A minimum of 200 patients recruited has been stipulated to accommodate any participants that withdraw from the study, ensuring a sufficient sample size is achieved.

6.2 ELIGIBILITY

The following inclusion and exclusion criteria will be used to distinguish patients eligible for enrolment into this study. Eligibility will be confirmed by the patient's treating clinician.

6.2.1 INCLUSION CRITERIA

1. Male or non-pregnant female over 21 years of age with a diagnosis of end stage ankle arthritis and requiring primary TAA/TAR and is suitable for the use for the INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System.
    a. If a female participant of child-bearing age becomes pregnant prior to surgery/after study consent, their surgery will be deferred as standard care and therefore will be withdrawn from the study.
    b. If a female participant of child-bearing age becomes pregnant during the post-operative follow-up periods, radiographic assessments are likely to still be appropriate. Local radiation protection procedure should be followed. If a pregnant participant elects not to have radiographs, other clinical assessment and PROMs data can still be recorded and they do not need to be withdrawn from the study.

2. Patients who are physically and mentally willing and able to comply with the post-operative follow-ups and an appropriate rehabilitation schedule.

3. Patient can understand and provide written consent.

6.2.2 EXCLUSION CRITERIA

1. Patients with previous ankle arthrodesis or patients who require revision of previously implanted TAA/TAR.

2. Any patients presenting with clinically relevant conditions prior to implantation, that would contraindicate implantation of a TAA/TAR.

6.3 PATIENT SCREENING

Patients will primarily be screened from theatre lists of patients waiting for a TAA/TAR and are eligible to receive the INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System for TAA/TAR as part of their routine

care. This will be done by a designated clinician, healthcare professional or delegated member of the research delivery team.

Patients may also be screened from orthopaedic outpatient clinics where patients have been referred through standard practice. Members of the healthcare team will screen for eligible patients and have their eligibility confirmed by their treating clinician.

All patients that have been screened will need an eligibility form completing on REDCap (Research Electronic Data Capture). For those that are eligible, a delegated member of the research delivery team will also complete a contact details form.

Potentially eligible patients will be contacted by a delegated member of the research delivery team, they will be provided a patient information sheet (PIS) in person, via their email or via post depending on patient preference. If a patient is interested, consent will be collected (a) electronically via REDCap (in person or via a link sent); (b) written consent (in person or via post) and uploaded to REDCap; (c) verbal consent which will be documented on REDCap – this will need to be followed up by either electronic or written consent. Consent will include future linkage to National Joint Registry (NJR) data and collection of radiographs for future analysis. An agreement in principle will be sought from NJR for future data access.

Each site will keep an electronic screening log, documenting the date of screening, results of screening and the primary reason for excluding a patient or reason a patient has decided not to participate as available. The screening log will be held on the secure database REDCap as hosted by the study management team at South Tees Hospitals NHS Foundation Trust.

6.4 PARTICIPANT IDENTIFIER

Each patient screened will be allocated a unique participant identifier. For those patients recruited, the unique participant identifier will be used for the duration of the study. The local research delivery team will maintain a confidential participant identification log, local patient identifiers and patient names with the corresponding unique participant identifier. This will enable records to be identified locally.

6.5 DISCONTINUATION AND WITHDRAWAL

Patients are free to withdraw from the study at any time and are under no obligation to provide a reason for doing so. Though, all attempts should be made to record the reason why the patient withdrew, this will be captured within the “Discontinuation and Withdrawal” form within REDCap.

If the patient fails to attend scheduled follow-up clinical appointments or respond to telephone calls to collect PROMs, every effort will be made to contact the patient to assess their health status. The local research delivery team should attempt to contact the patient through 3 documented attempts (phone calls, letter or email) on REDCap. The visit will be classed as “missed” if they do not respond. The local research delivery team should continue to attempt contacts for future scheduled follow-up appointments and assessments.

The patient may also be discontinued or withdrawn from the study if in the local Principal Investigator’s (PI) or CI’s opinion, continuation in the study would be detrimental to the patient’s health and wellbeing.

Withdrawing or discontinuing from the study will not affect the patient’s accessibility or quality of medical care.

Patients who withdraw or are discontinued will keep their unique participant identifier. The information that has already been collected from the patient will be included in the database and final analyses. The patient will continue to have their hospital information collected unless the patient withdraws their initial consent for this, this will be confirmed with the patient at the point they request to be withdrawn. PROMs data collection will cease at the point the patient withdraws or is discontinued from the study.

7. RISK-BENEFIT ANALYSIS

7.1 RISKS

All Patients in this study will undergo a TAA/TAR according to standard health care.

The potential risks for a TAA/TAR in general are:

1. Aseptic loosening of the prosthesis
2. Infection
3. Deep venous thrombosis
4. Post-operative pain
5. Heterotopic ossification
6. Fracture of the prosthesis
7. Fracture of the bone
8. Loss of muscle force
9. Nerve and vessel injury
10. Wound healing problems
11. Implant failure
12. Medical complications

13. Death

7.2 BENEFITS

The potential benefits for a TAA/TAR in general are:

1. Pain reduction
2. Increased function
3. Improved quality of life

The potential benefits for the INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System include:

1. Bony integration of the metallic components
2. Reduced pain
3. Restored alignment
4. Replacement of flexion and extension movement in the ankle

7.3 RADIATION

Radiographic assessment of the ankle will be at baseline and at 6 months, 1 year, 2 years and 5 years post-operatively.

8. DEVICE DESCRIPTION

The INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System is a two-piece semi-constrained fixed-bearing, bone-sparing total ankle prosthesis that restores mobility to a failing ankle joint. The System consists of a highly polished metal talar dome, a titanium alloy tibial tray, and Poly Insert (an ultra-high molecular weight polyethylene tibial insert). The components are available in a variety of sizes and design configurations intended for both primary and revision applications.

Through the advancement of partial and total joint replacement implants, the surgeon has been provided with a means of restoring mobility, correcting deformity, and reducing pain for man patients. While the prostheses used are largely successful in attaining these goals, it must be recognised that they are manufactured from a variety of materials and that any joint replacement system, therefore, cannot be expected to withstand activity levels and loads as would normal healthy bone. In addition, the system, including the implant/bone interface, will not be as strong, reliable, or durable as a natural human joint.

This system is manufactured according to International Conference on Harmonisation (ICH) Good Clinical Practices (GCP) in accordance with applicable Good Manufacturing Practices (GMP) and ISO 14155:2020 through relevant manufacturing and related validation processes.

The INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System Tibia Tray and Talar Dome are manufactured using an improved process known as Direct Metal Laser Sintering, also known as ADAPTIS™ 3D printing, produces a porous metal surface made from Ti6AI4V (Tibia Tray) and CoCr (Talar Dome), respectively, to interface with the bone.

The INFINITY™ with ADAPTIS™ Technology modular articular inserts are manufactured from EVERLAST™ Highly Crosslinked Polyethylene blended with Vitamin E. The propriety manufacturing process has been optimised to develop an enhanced ankle insert with retained material strength, reduced oxidation potential, and improved wear resistance. They are available in 8 sizes, with 4 thicknesses per size.

The INFINITY™ with ADAPTIS™ and EVERLAST™ technology Total Ankle System includes:

- INFINITY™ with ADAPTIS™ Technology Tibial Tray
- INFINITY™ with ADAPTIS™ Technology Chamfer-Cut Talar Component
- INFINITY™ with ADAPTIS™ Technology Flat Cut Talar Dome
- INFINITY™ EVERLAST™ Poly Insert

9. CASE REPORT FORMS

Patients will be screened for eligibility and assessed pre-operatively, intra-operatively, and post-operatively at 6 weeks, 6 months, 1 year, 2 years, and 5 years.

9.1 DATA COLLECTION

The study data/case report forms (CRF) will be collected and managed using REDCap electronic data capture tools, hosted at South Tees Hospital NHS Foundation Trust. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; (4) procedures for data integration and interoperability with external sources.

9.1.1 SCREENING AND ELIGIBILITY

1. Screening
2. Inclusion and exclusion criteria
3. Contact details

9.1.2 CONSENT

- Electronic consent (email)
- Written consent (face to face or postal)
- Verbal consent (telephone)

9.1.3 PRE-OPERATIVE CLINICAL HISTORY

1. Date of birth
2. Weight
3. Height
4. Sex

5. Indication for implantation
    a. Primary osteoarthritis
    b. Post-traumatic arthritis without previous fracture
    c. Post-traumatic arthritis with previous fracture
    d. Previous ankle surgery (non-trauma related)
    e. Inflammatory arthritis
    f. Other (please specify)

6. Previous surgery to the ankle planned for operation
    a. Yes
    b. No

7. Co-existing diseases
    a. Allergies
    b. High blood pressure
    c. Previous history of VTE events (Blood Clot, Thrombosis, Embolism etc.)
    d. Ischaemic Heart Disease or previous MI
    e. Rheumatic fever, heart murmur
    f. Pacemaker
    g. Heart arrythmias

h. COPD
i. Asthma, bronchitis, emphysema
j. Arthritis, muscle disease
k. Liver disease, jaundice
l. Thyroid disease
m. Diabetes
n. Kidney disease
o. Other (please specify)

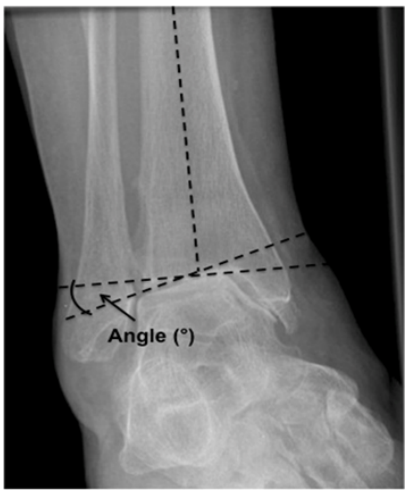
8. Radiographs
    a. Date of radiograph
    b. Date of repeat radiograph

9. Surgeon completed radiographic report
    Usual standard of care pre-operative radiographs will include a standing AP and lateral film of the ankle. Adjacent joint arthritis may be assessed by CT if usual surgeon preference but, not required for this study.

    a. Canadian Orthopaedic Foot and Ankle Society (COFAS) grade[3]
        i. Type 1 = Isolated ankle arthritis
        ii. Type 2 = Ankle arthritis with intra-articular varus or valgus deformity.
        Defined as a coronal plane deformity of more than 10 degrees
        iii. Type 3 = Ankle arthritis with hindfoot deformity, tibial malunion, midfoot ab-or adductus, supinated midfoot, plantar-flexed first ray, etc
        Hindfoot deformity defined as the angle between the lateral border of the calcaneus and the long axis of the tibia on the AP view of the ankle (varus more than 5 degrees, valgus more than 10 degrees).
        Tibial deformity defined as an angulation between the lateral border of the tibia more than 10 degrees on the AP view of the ankle.
        iv. Type 4 = Types 1-3 plus subtalar, calcaneocuboid, or talonavaciular arthritis.
        Arthritis assessed either by plain radiograph or clinical evaluation

    b. Coronal plane deformity (Midline Tibio Talar Angle – MTTA)
    Measured in degrees as the angle between a line perpendicular to the anatomical axis of the tibia and a line drawn along the top of the talar dome (see, Figure 1).
        i. Degrees
        ii. Varus or valgus

Figure 1: MTTA



9.1.4 PRE-OPERATIVE PROMS

1. Date completed
2. MOXFQ
3. AOS
4. EQ5D-5L

9.1.5 INTRA-OPERATIVE EVALUATION

1. Surgery date
2. Operative side
    a. Left
    b. Right
3. Anaesthesia Class and Type
    a. General
    b. Regional, Epidural
    c. Regional, Nerve Block
    d. Regional, Spinal
    e. Other
4. Duration of surgery
    a. Hours/Mins
5. Intra-operative AEs
    a. Yes
        i. Fracture
        ii. Nerve or Vessel Injury
        iii. other
    b. No

6. Components used and sizes
7. Patient Specific or Standard Instrumentation (PSI)

9.1.6 POST-OPERATIVE CLINICAL HISTORY

1. Follow-up timepoint
    a. 6 weeks
    b. 6 months
    c. 1 year
    d. 2 years
    e. 5 years
2. Date of assessment
3. Has the patient experienced any post-operative AE/SAEs
4. Radiograph (not required for 6 weeks)
    a. CT
    This data will be used if indicated as part of clinical care, and therefore it may not be available for all participants
    b. Plain radiograph
    c. Radiographic reporting template
    The purpose of the post-operative radiographic evaluations will be to assess, record, and report for migration, loosening, subsidence of the device, any osteolysis and cyst formation.

9.1.7 POST-OPERATIVE PROMS

1. Follow-up timepoint
    a. 6 months
    b. 1 year
    c. 2 years
    d. 5 years
2. Date completed
3. MOXFQ
4. AOS
5. EQ5D-5L

9.1.8 WITHDRAWAL OR DISCONTINUATION

1. Date of withdrawal or discontinuation
2. Date of last visit assessment

3. Reason for withdrawal or discontinuation
    a. Patient withdrew
    b. If in the PI/CI opinion, continuation in the study would be detrimental to the patient's well-being.
    c. Lost to follow-up
    d. Patient has died (please ensure AE/SAE form has been completed)
    e. Other (please specify)

10. ADVERSE EVENTS AND DEVICE REMOVAL EVENTS

The PI and research delivery team at each site are required to document all AEs and SAEs occurring within a 90-day post-operative period including date of occurrence, type of AE/SAE, treatment and outcome. Following this, only AE/SAEs relating to the ankle joint or related structures (i.e., ankle and surrounding structures, Achilles tendon, calf muscle, hindfoot and midfoot proximal to mid metatarsals) need to be reported.

All AEs and SAEs will need to be reported to the study management team and to host Research & Development (R&D) department according to local guidelines. Any unanticipated device of study related SAEs will need to be notified to the HRA and REC.

An SAE report form should be completed by the PI and research delivery team **within 24 hours of the site's knowledge.**

The PI will keep a copy of the AE/SAE information in their electronic Investigator Site File (eISF) at their site. If at the time of sending the report, all details are not available, then one must send it with the available data and then seek to obtain complementary information. The complementary information will be sent by the PI or research delivery team of the study site to the sponsor, Northumbria Healthcare NHS Foundation Trust, and study management team, South Tees Hospitals NHS Foundation Trust, as soon as it will be available.

In case of component revisions product related issues and/or SAEs, Stryker will be notified of the event.

Death will be both reported in the SAE report form and in the termination form part of the CRFs.

10.1 AE REPORTING

1. Date of AE/SAE

2. Glazebrook classification[4]

   a. Low grade
      i. Intra-operative bone fracture
      ii. Wound healing problems
   b. Medium grade
      i. Technical error
      ii. Subsidence
      iii. Post-operative bone fracture
   c. High grade
      i. Deep infection
      ii. Aseptic loosening
      iii. Implant failure
   d. Not related to the implant
      i. Deep vein thrombosis
      ii. Pulmonary embolism
      iii. Death
   e. Other

3. COFAS reoperation and revision coding[5]:
   a. No reoperation within or surrounding the ankle
   b. Isolated hardware removal around the ankle
   c. Repeat operation outside the ankle replacement or arthrodesis (e.g., osteotomy, fusion or ligament repair) but related to the replacement or arthrodesis
   d. Ankle gutter or heterotopic ossification debridement without exchange of metal components, with or without intact polyethylene exchange
   e. Exchange of polyethylene liner as a result of polyethylene failure
   f. Debridement of an osteolytic cyst without exchange of metal components, with or without intact polyethylene exchange
   g. Deep infection or wound complication requiring operative debridement (without exchange of metal components in ankle replacement), with or without intact polyethylene exchange
   h. Revision of arthrodesis due to malposition or non-union (no infection)
   i. Implant failure leading to revision of metal components due to aseptic loosening, component fracture, or malposition (no infection)
   j. Revision of metal component(s) secondary to infection
   k. Amputation above the level of the ankle

4. Date of re-operative/revision

10.2 REVIEW OF AE FORM

1. Date of review
2. Record action taken to resolve AE

3. Has the AE been resolved?

11. ANALYSIS OF RESULTS

Analysis of results will be organised by the CI and the study management team. A detailed Statistical Analysis Plan (SAP, see **section 11.2**) will be agreed with an expert statistician prior to conducting any analyses.

11.1 INTERIM ANALYSIS

Ongoing safety will be analysed, in particular all AEs and SAEs collected to assess the safety of the component. The decision will be made by the CI at this point as to whether the study and implantation of the component continues for more patients or is ended.

11.2 STATISTICAL ANALYSIS PLAN

The analyses will be mainly descriptive. Continuous data will be summarised using means and standard deviations (or median, interquartile range, minimum and maximum as appropriate). Categorical data will be summarised using counts and percentages. Graphs will be produced to display trajectories in outcomes over time. Linear or logistic regression models (as appropriate depending on the outcome) will be used to evaluate the influence of patient, clinical and surgical factors on outcomes.

AEs and SAEs will be summarised descriptively and using graphs by whether they are operative, or device related.

12. PUBLICATION OF RESULTS

It is anticipated that a publication of the study results will be compiled and submitted to a peer-reviewed journal. The CI of the study will have the responsibility of being primary author of such publications.

The study will be registered in the ISRCTN Trial Register and/or in clinicaltrials.gov by the CI.

13. MONITORING

Patient's medical records will be available for monitoring, auditing and inspection purposes by the Sponsor, study management team, or any regulatory authorities as appropriate.

Independent study and data monitoring will be carried out by the study management team. Regular study management meetings will review study progress and seek opinion from independent members at interim data analysis or as required. A study monitoring plan will be developed prior to ethics approval.

14. ETHICAL CONSIDERATIONS

14.1 DECLARATION OF HELSINKI

The study is to be conducted according to globally accepted standards of good clinical practice, in agreement with the "Declaration of Helsinki, October 2008", in accordance with the medical research involving human subjects act (WMO) and in accordance with local regulations.

In accordance with the Declaration of Helsinki centre will gain written Independent Ethics Committee approval prior to enrolling Patients in the study according to HRA regulations within the UK via IRAS system. HRA approval and local site level R&D approvals will be sought prior to the start of the study.

14.2 INFORMED CONSENT

If a patient is interested in participating in the study, consent will be collected (a) electronically via REDCap (in person or via a link sent); (b) written consent (in person or via post) and uploaded to REDCap; (c) verbal consent which will be documented on REDCap – this will need to be followed up by either electronic or written consent.

The study team will consider the consent to be valid for up to 12 months as routine waiting lists for this procedure can be long. The study team will ensure patient is happy to continue with the study procedure or follow up at every visit. Patients lacking capacity to consent and unable to understand written English will be excluded the study due to the follow up requirements and limitations with collecting data using PROMs.

14.3 PERSONAL DATA PROTECTION

All data recorded in the CRFs if used for further evaluation are coded by a unique participant identifier. Identifications are restricted to authorised person. In all data analyses the identity of patients will remain anonymous.

Anonymised patient data may be stored and electronically processed for the purpose of scientific evaluation.

By providing informed consent, the patient accepts that the information from this study, including certain personal data and results of examinations, will be collected, and processed for the purposes of the study and for any scientific research under the supervision of the Sponsor in compliance with the Data Protection Act (2018).

Anonymised information from this study may be used for product registration, product performance monitoring and scientific research investigating new treatments, interventions, and management procedures so that patient care outcomes are continually improved. The study results may be used for regulatory, scientific or commercial purposes and may be published but it will not be possible to identify the patient.

15. REFERENCES

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16. ACRONYMS WITH DEFINITIONS

Acronym	Definition
AE	Adverse Events
AOS	Ankle Osteoarthritis Scale
CI	Chief Investigator
COFAS	Canadian Orthopaedic Foot and Ankle Society
CRF	Case Report Form
CT	Computed Tomography
eISF	Electronic Investigator Site File
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
HRA	Health Research Authority
ICH	to International Conference on Harmonisation
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomised Controlled Trial Number
MI	Myocardial Infarction
MOXFQ	Manchester Oxford Foot Ankle Questionnaire
MTTA	Midline Tibio Talar Angle
N/A	Not Applicable
NHS	National Health Service
NJR	National Joint Registry
PI	Principal Investigator
PIS	Participant Information Sheet
PROMs	Patient Reported Outcome Measures
R&D	Research & Development
REC	Research Ethics Committee
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
TAA	Total Ankle Arthroplasty
TAR	Total Ankle Replacement
UK	United Kingdom
VTE	Venous thromboembolism