Wound **I**maging **S**oftware and **D**igital platf**O**r**M** to detect and prioritise surgical wounds for routine and priority review (**WISDOM**)	
WISDOM	
Version and Date of Clinical Investigation Plan:	V2.2 19/03/2025
Sponsor:	Guys and St Thomas' NHS Foundation Trust
Chief Investigator:	Melissa Rochon
Local Study Reference:	UHDB/2022/024
IRAS Number:	338141
ISRCTN/ ClinicalTrials.gov number:	We will apply to International Standard Randomised Controlled Trials Number (ISRCTN) Register.
Funder(s):	NIHR i4i reference: 204508
This protocol has regard for the HRA guidance	

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust, regulatory authorities, and members of the Research Ethics Committee.

SIGNATURE PAGE

The undersigned confirm that the following clinical investigation plan has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved clinical investigation plan and will adhere to the principles outlined in the Declaration of Helsinki, Medical Devices Regulations 2002, ISO 14155:2020, the Sponsor's SOPs, and other regulatory requirement.
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.
I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies from the trial as planned in this clinical investigation plan will be explained.

Clinical Investigation Plan v2.2 19.03.2025 authorisation signatures:

Chief Investigator:

Signature:	……..	Date: …….../……./……
Name (please print):	……Melissa Rochon……	

For and on behalf of the Trial Sponsor (if required):

Signature:	……..	Date: …….../……./……
Name (please print):	……..	
Position:	……..	

KEY TRIAL CONTACTS

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TRIAL SUMMARY

Trial Title:	**W**ound **I**maging **S**oftware and **D**igital platf**O**r**M** to assess surgical wounds for routine and priority review (**WISDOM**)
Local Study Reference:	UHDB/2022/024
Trial Design:	**Randomisation:** Mixed-block 1:1 randomisation stratified by site and sex managed by Derby CTSU. **Intervention:** (See flow chart) The intervention group will use the AI enabled platform with the new AI module for 30 days after surgery in addition to standard post-operative wound follow-up care for 60 days after surgery. Participants will be asked to submit images and information every 7 days post operatively, up until 30 days. Participants can also submit an image during the 30 days whenever they have a concern. **Control:** The control group will receive standard post-operative wound follow-up care for 60 days after surgery. Standard care, mapped during the economic scoping exercise in WP6 may include; out-patient appointments, advised to contact GP, or no follow-up. Neither of the two participating sites use Isla as their standard care. **Data collection:** We will develop online surveys for patients and staff focusing on safety, acceptability, quality of life, and barriers to underserved groups. Interviews with staff/patients exploring issues raised in surveys. Purposive sampling to include a range of ages, sex, ethnicities, physical abilities/carer dependence and socioeconomic status. Other tools include platform review, medical notes review and patient telephone calls at 30 and 60 days.
Trial Participants:	Patients ≥18 years old having coronary artery bypass graft (CABG) surgery.
Planner Number of Sites:	2
Planned Sample Size:	120 - National data shows a wound problem rate of 21% with a cardiac wound infection rate of 8%. A sample size of 120 patients should provide around 12 patients in each group with a wound problem of which 4-5 patients should have a wound infection. This is sufficient to inform feasibility, safety and acceptability data. Wound problems identified by the Isla platform include Discolouration, unexpected fluids/tissue, sutures/clips observed, incision after 14 days.
Treatment Duration:	Participants in the intervention group will be enrolled on Isla at hospital discharge or at 5 days after surgery for patients not discharged by day 5 post op. Patients will receive text requests via Isla up to 30 days after surgery.
Follow Up Duration:	**Duration of follow up:** Wound monitoring follow up is for 30 days after surgery (as per national guidelines) and we will follow up all patients for 60 days after surgery to capture readmissions and further surgery data.
Planned Start Date:	As per IRAS form start date 1st March 2024
Planned Recruitment End Date:	Estimated Last Participant First Visit (LPFV) 31st December 2024

Planned Study End Date:	Estimated Last Participant Last Visit (LPLV) – as per IRAS form study end date 28th February 2025	
	Objectives	**Outcome Measures**
Primary:	To obtain safety outcomes data To obtain feasibility outcomes data To obtain acceptability outcomes data To obtain data for economic modelling	Safety outcomes Feasibility outcomes Acceptability outcomes Economic modelling outcomes
Investigational Device:	A new AI component (a wound prioritisation module) to an existing digital surgical wound monitoring platform. The new wound prioritisation module highlights images of surgical wounds which display signs of healing complication or infection. These images are then identified as requiring urgent priority review by a clinician for assessment rather than standard review.	
Eligibility Criteria:	**Inclusion criteria:** Patients having first/redo CABG surgeries with or without additional cardiac procedures such as valve replacement, patients with chest reopening during same admission as index surgery, patients with an existing non-infected wound complication, or any other infection except surgical site. Patients without a smartphone/with physical disability/with visual impairment will be eligible if their carer is able-bodied or has a smartphone. **Exclusion criteria**: CABG requiring ventricular assist device (VAD) or extracorporeal membrane oxygenation (ECMO), ventilated or unconscious patients, or with a pre-existing surgical site infection.	

FUNDING AND SUPPORT IN KIND

Funder(s)	**Financial and Non-Financial Support Given** **NIHR i4i C**all 24
NIHR i4i	**Ref 204508**

ROLES & RESPONSIBILITIES

Sponsor

The Sponsor, Guys and St Thomas' NHS Foundation Trust, take on overall responsibility for appropriate arrangements being in place for the set-up, management, conduct and reporting of the research project. The responsibility for management of this project has been delegated to Derby CTU, as outlined in the Collaboration Agreement, and in accordance with the Delegation of Responsibilities. The sponsor is not providing funds for this study but has taken on responsibility for ensuring finances are in place to support the research.

Funder

The study is funded by NIHR i4i

Study Management Committees

Trial Management Group

The trial management group will meet regularly to oversee the day-to-day management of the trial, including all aspects of the conduct of the trial. Any problems with study conduct and participating centres will be raised and addressed during TMG meetings.

Trial Steering Committee

The trial steering committee (TSC) will oversee and supervise the progress of the trial and ensure that it is being conducted according to the clinical investigation plan and the applicable regulations. The TSC will also review safety and data monitoring and quality. The TSC is an independent body that includes majority members who are not involved with the running of the trial.

Clinical Investigation Plan Contributors

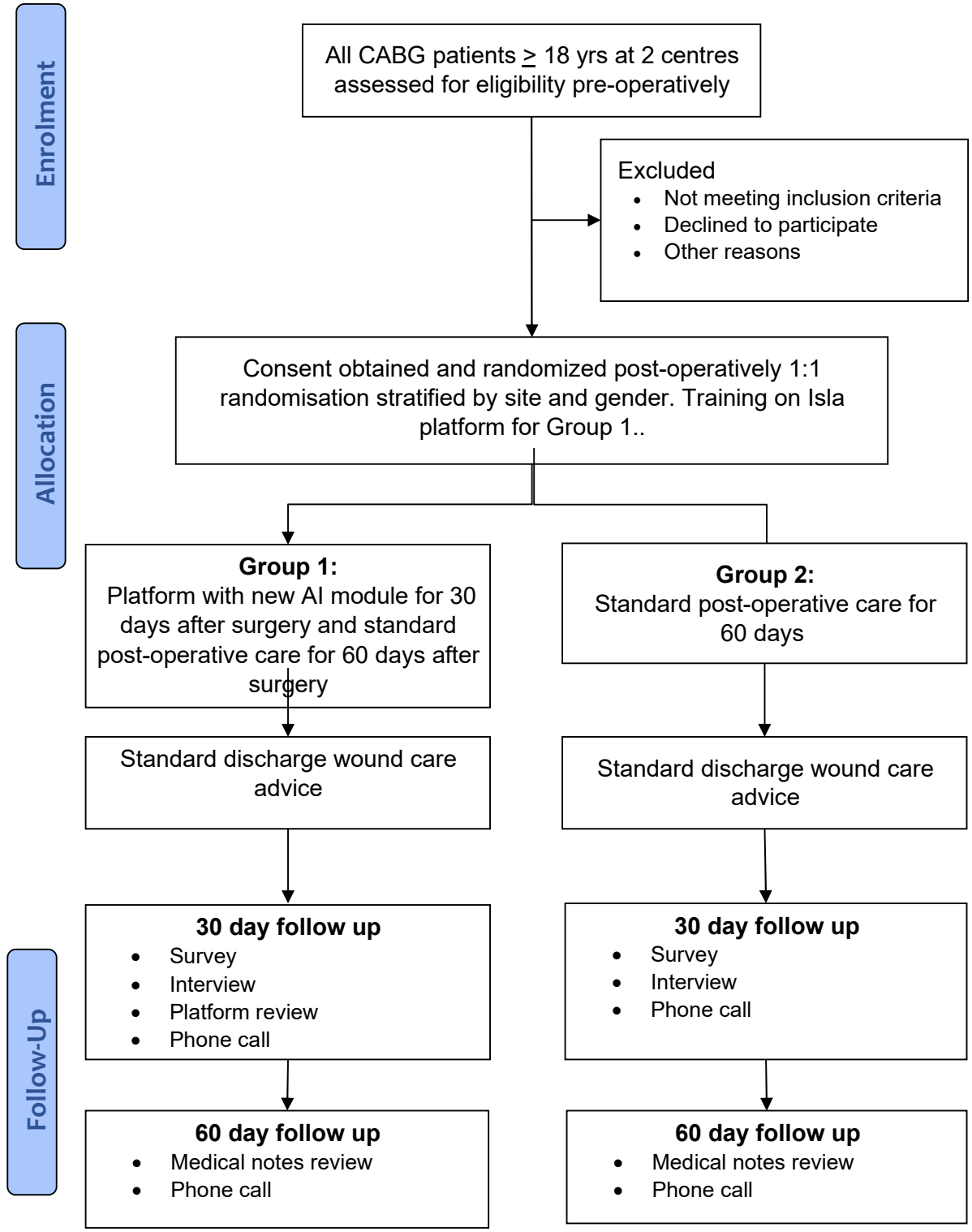
A number of contributors have been involved in the development of the CIP, these include; the Chief Investigator, Joint-Lead, Statistician, Data Manager and Trial Manager, health economist, Industry partner (Islacare), and Sponsor's representative. Contributors are responsible for inputting into the design of the study, ensuring that it is designed transparently and efficiently.

Contents

LIST OF ABBREVIATIONS

AE	Adverse Event
CI	Chief Investigator
CIP	Clinical Investigation Plan
CRF	Case Report Form
DMEC	Data Monitoring and Ethics Committee
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
TMG	Trial Management Group
TSC	Trial Steering Committee
TMF	Trial Master File

STUDY FLOW CHART



CLINICAL INVESTIGATION PLAN

1. BACKGROUND

Over 10 million surgical operations are performed in England annually with approximately 2.1 million having problems with wound healing, of which 500,000 lead to infection.[1] Most of these wound problems happen after patients have been discharged from hospital and they need to be identified and treated early.[2] Any delay in treating a wound can allow the problem to worsen making it harder to treat.

Digital remote surgical wound monitoring is beginning to be used to monitor patients' surgical wounds at home after they have been discharged from hospital.[3] With digital monitoring, patients upload images of their wound and some information using their smartphone in response to pre-programmed text messages.[4] This offers regular assessment during the time when wound problems are most likely to develop. Following clinician review of images submitted, patients will receive a text to say their wound does not appear to have any problems or they may be contacted for further assessment or treatment. The digital monitoring platform we developed is called Isla and is used in eight cardiac surgery centres in England. To date, over 7,000 patients have submitted 50,000 images. Early evaluations of digital wound monitoring suggest it improves clinical outcomes and has high patient satisfaction; however, it creates a new additional workload for clinicians.[4]

The study will assess a new component for a digital wound monitoring platform. The new component uses artificial intelligence to identify 'red flags' on the images patients submit to the wound monitoring platform. Criteria for priority review (red flags) are:

- Unexpected tissue (deeper than the skin) and/or fluid in the surgical wound
- Abnormal redness/discolouration of the skin spreading from the wound
- Removable stitches or surgical clips detected more than 14 days after surgery
- Incisional Separation

Images that are identified as having a possible red flag are then identified for urgent priority review. This helps clinicians manage this new workload by allowing the most urgent cases to be reviewed first.

The new wound prioritisation module has been developed and has been validated for predictivity, sensitivity and specificity, and inter-rater reliability.

We will conduct a feasibility study of our new AI module with 120 heart surgery patients at two hospitals. Each patient will be randomly allocated to receive the platform with the new detection and prioritising module (for up to 30 days after surgery) plus standard post operative wound care or standard post operative wound care only. Assessment through survey, interviews and platform review is at 30 days and through medical notes review, patient log and patient phone calls at 60 days. Outcomes will assess safety, acceptability, feasibility and health economic assessment.

2. RATIONALE

Remote wound monitoring enables clinicians to review patients' surgical wounds regularly and quickly, however the volume of images creates a new workload problem.

With a remote wound platform patients upload images of their wounds to clinicians for review. These new platforms are good for patients as wound problems can be detected and treated early. However, the success of continuous wound monitoring creates a new and increasing workload for staff as it is scaled for (potentially) millions of surgeries annually with multiple images per patient.

This feasibility study assesses a surgical wound monitoring platform that uses artificial intelligence (AI) to assist clinicians to review patients' wounds by prioritising concerning images for urgent action. This will manage staff time more effectively and expedite treatment.

The validated AI module will be assessed in a feasibility study looking at patient safety and patient and staff acceptability outcomes.

2.0. Assessment and Management of Risk

Anticipated clinical benefits

- Staff workload efficiency (images of wound with complications are prioritised for urgent review by clinical staff)
- Reduction in the number and severity of wound healing complications
- Reduction in the use of NHS resources to treat wound healing problems (including re-admission, further surgery, GP visits, wound clinic visits)
- More convenient for patients (reduced traveling and reduced time)

Anticipated adverse device events

- If the AI module fails to identify images of wounds with complications – this means the wounds will still be reviewed by the clinician within 1-2 days, but not reviewed urgently within a few hours. This is still better than standard wound follow up.
- If the AI module overidentifies wound images for urgent review – this means more images will be urgently reviewed than necessary – increasing staff workload.

Potential risks from taking part

- We are not aware of any risks to the patient from taking part. Patient data security is not a concern as the data is transferred securely using state-of-the art SHA256 encryption in transit and at rest.
- All patients will receive standard wound follow-up so we do not expect any adverse effects for patients.

3. OBJECTIVES AND OUTCOME MEASURES/ ENDPOINTS

The objectives of this randomised trial are;

- To obtain safety outcomes data
- To obtain feasibility outcomes data
- To obtain acceptability outcomes data
- To obtain data for economic modelling

3.0. Primary Outcomes

Safety outcomes**:** quality of images received, assessed by clinicians at 30 days. A quality image is one that can be used to make a clinical decision.

Acceptability outcomes: clinician and patient satisfaction using surveys and interviews at day 30. Acceptability of the intervention including attitude, burden, perceived effectiveness, ethicality, intervention coherence, opportunity costs and self-efficacy. Will also collect acceptability of being involved as a study participant.

Feasibility outcomes: recruitment rate, adherence with the module, I.e. submission of 1 photo during the 30 day period (intervention group only), loss to follow-up

Economic modelling outcomes: These will be identified through a scoping exercise and will include number and severity of wound problems/infections, wound-related hospital readmission, time to review images, further surgery to treat wounds, prescribed wound treatments, prescribed antibiotics, clinic visits, GP visits, patient travel time and quality of life data.

3.1 Secondary outcomes

Safety outcomes. More detailed discussion about reasons for compliance/non-compliance with the ISLA platform will be explored in the staff surveys and interviews and the patient intervention group surveys and interviews.

Feasibility outcomes: access/barriers to participation and willingness of participants to be randomised, and attrition rates, time and resources required to conduct assessments, number and severity of wound problems/infections, date of diagnosis.

Other secondary outcomes: number of photos received per patient, number of wound images/non wound images, number of quality images, number of requests (for images) complied with - intervention group only, number photos initiated by patients (intervention group only), number of follow-up requests.

4. TRIAL DESIGN

Two-centre, unblinded parallel-group randomised feasibility study with safety and acceptability outcomes comparing the AI module with standard care.

A total of 120 patients from will be recruited to the trial over a ten-month period. Patients will be enrolled onto the study and randomised after surgery but prior to discharge or up until day five after surgery – whichever comes first. Mixed-block 1:1 randomisation stratified by site and sex managed by Derby CTSU. Patients and staff will be aware of group allocation status.

Patients in the control group will have standard post-operative wound care follow-up. Patients in the intervention group will receive digital surgical wound monitoring with the AI module for 30 days after surgery and also standard post-operative wound care follow-up.

Standard wound follow up and the Isla digital wound monitoring platform will last for 30 days after surgery. Patients in the intervention group will be contacted via SMS text message seven days, fourteen days and twenty-one days after surgery with the link request remining open for 6 days until the next request is sent out. The exception being the last request link which will remain open until 30 days after surgery. For each request, patients are asked to submit a photo of their wound and complete the modified UKHSA wound surveillance questionnaire.[5]

At consent will collect baseline quality of life data (SF-6Dv2)

After 30 days we will collect the following data:

- online satisfaction and quality of life survey with participants in both groups
- online satisfaction survey with staff
- interviews (focusing on satisfaction and experience) with a subsection of 10 patients from both groups – 20 in total
- interviews (focusing on satisfaction and experience) with a subsection of 10 staff
-
- Phone call to all patients to discuss their wound and any treatments or healthcare interventions / engagement they may have had. (

After 60 days we will collect the following data:

- Medical case note review for all patients to identify re-admissions or further surgery
- Patient phone call to discuss their wound and any treatments or healthcare interventions / engagement they may have had and quality of life.

5 STUDY SETTING

The study setting will be within tertiary hospitals.

6 ELIGIBILITY CRITERIA

Participants: Patients ≥18 years old having coronary artery bypass graft (CABG) surgery.

6.1 Inclusion Criteria

- Patients having first/redo CABG surgeries with or without adjunct cardiac procedures such as valve replacement, or chest reopening during same admission as index surgery, and either no infection, or an existing non-infected wound complication, or any other infection except surgical site.
- Patients without a smartphone/with physical disability/with visual impairment will be eligible if they are willing to use a smartphone or internet provided by the study, or their next of kin or carer is able-bodied or has a smartphone.

6.2 Exclusion Criteria

- Patients having CABG requiring ventricular assist device (VAD) or
- extracorporeal membrane oxygenation (ECMO), or
- ventilated or unconscious patients, or
- pre-existing surgical site infection.

7 TRIAL PROCEDURES

7.1 Recruitment

7.1.1 Patient Identification

Potential participants will be identified by delegated hospital research site staff through surgical admissions lists. Several weeks before surgery. This timeframe is reduced for patients who are transferred from other hospitals.

7.1.2 Screening

Initial screening by a member of the usual care team will take place before surgery with final eligibility for study enrolment assessed after surgery.

7.2 Consent

Potential participants will be identified by the usual care team through screening surgical admissions lists and given brief information about the study at admission and when they are on the postoperative ward after surgery. If they express an interest in taking part, we will provide a leaflet, discuss the study with them, and answer any questions. This will be done by an appropriately delegated member of the team. The information will make it clear that the decision for whether they are allocated the AI module, or not, will be random, and to ensure that they are happy with that, to encourage retention. For patients admitted pre-operatively, information will be provided pre-operatively giving a minimum of 24 hours between receiving information about the study and seeking consent. For patents transferred in on the day of surgery, information will be given post-operatively with a minimum of 24

hours before consent is sought. We will obtain written consent after surgery before collection of any study data and randomisation. Participants will be asked at enrolment how they wish to receive dissemination information about the study (text/email/post). Participants who complete data collection will be offered £40 for their time. We will contact patients via email or telephone to obtain their bank details in order to process reimbursement for their participation in the study. We will not recruit patients who are unable to give consent.

Participants are free to decline involvement without giving reason, although where reasons are given, these will be collected as part of screening data.

If participants do not wish to participate, they will continue to receive standard post operative care and their standard of care will not change.

Informed consent will be obtained before any trial activities commence including data collection.

The Principal Investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent according to the REC approved CIP, principles of Good Clinical Practice (GCP) and Declaration of Helsinki and in accordance with the study Delegation of Responsibilities Log.

7.3 The Randomisation Scheme

Participants will be assigned to the intervention or control group, using stratified 1:1 randomisation with mixed block sizes to maximise the chances of equal allocation to groups. The participants will be stratified by site and sex (Male, Female, Intersex). Emergency unblinding will not be required as the study will not be blinded. Randomisation will take place at enrolment.

7.3.1 Method of Implementing the Allocation Sequence

Randomisation will be implemented in the electronic data capture system by Derby CTSU.

Participants will be allocated a treatment arm in the eCRF (via a Randomisation form), where allocation details will be stored online and an email notification sent to the study team. Access to the online randomisation system will be via personal username and password, and specific to role.

If participants are no longer eligible for randomisation, they will be considered “consented, but not randomised” and will not contribute to the required sample size.

7.4 Blinding

Participants will not be blinded as to their group allocation. This is because of obvious differences between the intervention and standard care. The hospital staff who are delivering wound care will be aware of the patient’s allocation status.

7.5 Baseline Data

The following data will be collected at Baseline:

- Surgery details: Procedure, Procedure type, Admission date, Operation date, Re-operation date (original submission), Discharge date. Status at discharge.
- Demographics: MedRec, Age, Gender, Ethnicity, English speaking, Location, Height, Weight, BMI, Skin tone, Smoking status, Disability, Residential Status, Smart phone access, Assistance required to take a photo.
- SF-6Dv2
- Medical History
- Patient details: NHS ID, Postcode, email address and/or contact number, app demo received, whether the patient was given a smartphone.
-

Patients who do not speak English and do not have a carer who can translate for them will not be able to participate in this feasibility study because of the need for free text communications between patients and Isla. We are interested to know if/how age, sex, location (eg. rural/urban), socioeconomic status, ethnicity, English speaking/non English speaking, and carer involvement influence patient engagement with digital wound monitoring, although we acknowledge that, due to the limited number of patients in this study and the restriction requiring English speakers (or patients with English speaking carers) any findings will be tentative and will require confirmation in a later definitive study.

7.6 Trial Assessments

Procedures relating to the clinical investigation that patients will undergo.

<u>Intervention group patients</u>

Weekly requests to submit image and information about their surgical wound using their phone via the Isla wound monitoring platform. If no problem is identified patients are sent text confirming this, if a problem is identified patients will be contacted by clinicians to provide more information which may lead to treatment (note this aspect is not new and is already used in 8 cardiac centres in England).

Intervention	
Post surgery day 7	Participant is sent SMS text requesting wound image plus response to modified UKHSA SSI post-discharge questionnaire
Post surgery day 14	Participant is sent SMS text requesting wound image plus response to modified UKHSA SSI post-discharge questionnaire
Post surgery day 21 (link open until day 30)	Participant is sent SMS text requesting wound image plus response to modified UKHSA SSI post-discharge questionnaire

<u>Both patient groups</u>

x1 online survey at 30 days (for all 120 patients – 15 mins each)

x1 online interview at 30 days (for a subset of 10 patients from each group only, lasting around 40 mins)
x1 phone call at 30 days and also at 60 days to discuss any wound healing problems for all 120 patients lasting 15 mins

Staff

x1 online survey at 30 days for all surgeons and nurses who have been involved in using Isla – 15 mins

x1 online interview at 30 days for a subset of 10 staff who have been involved in using Isla -lasting around 40 mins

Online surveys will be hosted on Dacima and the interviews will be conducted via Teams and recorded using digital audio recording. The phone call to discuss the patients wound will use the post-discharge questionnaire from the UKHSA SSI surveillance programme. Qualitative data will be analysed and grouped into themes.[7] Quantitative data will be analysed using simple descriptive statistics.

30 days has been chosen as the data collection point as this is the recommended follow-up time for a wound infection as stipulated by the national wound surveillance programme run by the UKHSA. Further data is collected at 60 days to identify any adverse events such as hospital re-admissions or further surgery the patients may have had.

We are interested to know if/how the following baseline characteristics influence patient engagement with digital wound monitoring- age, sex, location (*e.g.* rural/urban), socioeconomic status, English speaking.

7.7 Qualitative assessments

Ten interviews with patients from each of the two groups and ten interviews with staff. The interviews will be semi structured, and the schedules will be developed based on relevant literature.[3] The focus for the patients' interviews will be acceptability for the Isla platform, post-operative wound follow-up, and acceptability of taking part in the study. The staff interviews will focus on acceptability of the Isla platform and post-operative wound follow-up. The first two interviews will serve as a pilot and will be reviewed, and any amendments made to the interview schedule as required.

All interviews will take place via Microsoft Teams and will be digitally recorded with the permission of the participant. Interviews are expected to last around 40 minutes. Data from the interviews will be independently transcribed.

Interview data will be analysed using thematic content analysis.[7]

As the interviews will be remote, consent for the sub study will be conducted remotely. The research should take care to cover the Information leaflet and consent form with the participant on the recording, but only the researcher will sign the consent form. The recording of the participant giving consent will be audio recorded and transcribed.

7.8 Withdrawal Criteria

Participants who no longer wish to participate in the study can contact the researcher using the contact details provided in the patient information leaflet. Any data patients have submitted prior to withdrawing will still be used in the study. Patients will no longer receive any contact from the research study (no more requests for images, or to complete the survey, invited to take part in an interview, be phoned), although they will continue to receive standard wound follow up.

Patients who do not respond to requests to send images will be sent no more than two text message/email reminders and up to three by phone call. All patients will be sent a text/ email reminder after 2 weeks to complete the online survey. Three attempts will be made to phone patients at 30 days and 60 days. We will continue to collect study data, which are already recorded on patient records, on no-responding patients unless they explicitly withdraw their consent. Attempts to contact non-responding patients will be documented. Patients who withdraw post randomisation or are lost to follow up will not be replaced.

7.9 End of Trial

The end of trial will be defined as after the last patient last visit when all data has been received and queries resolved. The Clinical Trials Manager will notify the participating sites, MHRA and REC within 90 days of the end of the trial. The clinical trial report will be written within 12 months of the end of trial.

8 INVESTIGATIONAL DEVICE

Isla is a platform which is used to monitor patients' surgical wounds by collecting self-reported data (wound images and questionnaire responses). The data is then reviewed by clinicians and patients are either contacted to obtain additional information, prescribed treatment or reassured of no wound healing concerns. Isla is currently in use in several NHS trusts. Isla is a browser-based application that staff usually access on a laptop or PC. It is a secure password protected system that is Data Protection Act and Information Governance compliant. Clinicians receive an alert when an image has been submitted – though this function can be switched off to prevent being overwhelmed with the number of alerts. Clinicians currently do not receive an alert when a red flag has been detected by the Isla new wound prioritisation module. The component under investigation in this study is a new module for the Isla platform which uses artificial intelligence to identify signs of non-healing on wound images which are then prioritised for urgent review by clinicians. Examples of non-healing signs are redness, wound gaping, exudate.

Name:	Isla Care Ltd
Address:	Huckletree, Alphabeta Building, 18 Finsbury Square, London EC2A 1AH

Name:	Isla
Number:	
Software version:	1

8.0 Name and Description of Investigational Device(s)

Isla is a remote surgical wound platform, which runs on all modern phones and tablets. Patients can use Isla to provide data (images and questionnaire responses) in response to pre-programmed text message requests. The new component under investigation is a module for the platform that uses artificial intelligence to identify 'red flags' on submitted wound images which are then prioritised for urgent review by clinicians. Examples of red flags are Discolouration, unexpected fluids/tissue, sutures/clips observed, incision

In this study, Isla will be offered to all adult patients (18 or over) having coronary artery bypass graft (CABG) surgery at the participating sites.. Isla is intended to capture information on surgical wounds remotely. The new AI module prioritises images with a concern for urgent review by a clinician. We plan to recruit 120 patients of which 60 will receive monitoring through Isla.

Isla is a digital platform. Isla sends patients text message requests for data about their wound. Patients can use their smart phone or ipad to take a photo of their wound which they send using their smart phone or email. They also provide responses to the modified UKHSA post discharge wound monitoring questionnaire.

Data is transferred securely using state-of-the art SHA256 encryption in transit and at rest. Standards include conformity with medical device regulations, General Data Protection Regulation (GDPR), NHS Digital Technologies Assessment Criteria (DTAC), the STARD-AI initiative and NICE Evidence Standards Framework for Digital Health.

Patients only use their own mobile or computing devices. There is no App to download. There is no physical contact with the Isla device. The Isla product is purely software.

8.1 Traceability of the Device

Participants will be added to the Isla platform and have a record created with a unique URL link. (The Isla URL link is a different format from the study participant ID which will have already been created by Dacima which means researchers will not confuse the participant ID with the Isla URL link. The Dacima created study participant ID will be added manually to each participants Isla record. The Dacima generated ID is the ID that will be used throughout the study). Users must be authenticated to be able to access any records, as well as being authorised to access that record. Isla records audit logs for all activity on this record, including accessing/ viewing, which include a timestamp and details of the authenticated user performing this action. The Isla platform supports "tagging"/"labelling" of patients, and this mechanism will be used to identify those patients in the study and add appropriate metadata at the patient level. Again, application/ updating of tags are recorded as audit logs. Finally, more granular data/ metadata can be incorporated into the Isla record either through structured forms (for recording health status/ symptoms etc) or through recording outcomes, which can be configured for the pathway and saved against that patient episode.

8.2 Investigator Brochure (IB)

Isla's commercial brochure can be reviewed here (Isla brochure.pdf - Google Drive), in its V1 form. Where this is updated, updates will be published to the working group. Isla also maintains a technical

specification ((Isla: Technical Specification - Google Docs), which is reviewed and updated in line with every release, as well as several user guides as Instructions For Use (IFU) (example isla.care/userguide Isla User Guide (2).pdf - Google Drive) these instructions are shared on dynamic redirect URLs, so that any updates can be replaced, and any user accessing the dynamic link will be served the most updated instructions as they change. Where appropriate, changes in use or instructions can be communicated through the Isla platform itself. Isla's change controls policy is documented here (Product release controls policy.pdf - Google Drive) for reference.

8.3 Device Storage, Supply and Accountability

The Isla platform is purely software and does not require installation for access (although can be installed for convenience). This significantly reduces complexity for supply, as users and patients can use any computer, smart phone or tablet to access and use the Isla platform.

- For staff: It is intended for existing tablets to be used on wards. Isla can be accessed through the browser (and installed if required). Users will be provided access as part of their onboarding and training and will set up personal accounts to ensure auditability. Once registered, new users will be added to relevant teams within the platform to be able to access the relevant patient cohorts, to be able to complete all capture & review requirements of the study
- For patients: Users will be requested to submit a wound assessment and associated images through the Isla platform. This request will be sent to them *via* SMS or email, containing a link, and they will be able to click on that link to progress through the submission flow using any modern phone, tablet or computer.

8.4 Assessment of Compliance

The Isla platform supports compliance:

- Monitoring: Patients will be sent automated requests as part of the pathway that they're on. Within the Isla platform users can view custom views for patients who have missed their requests or never responded to requests. This view will allow study teams to follow up non compliance to encourage to participate, understand non compliance and support patients through the process.
- As part of clinician and patient capture flows, a consent screen is presented to give the user or patient information about how and where data will be saved once uploaded to Isla. This gives the end user the opportunity to withhold consent at this point and not submit. Patients also have the ability to withhold consent from being contacted, and this will block further communication from the Isla platform
- Non compliance will be monitored, but won't result in patients being excluded from the study, as compliance is one of the things we are looking to measure to assess feasibility.

Compliance with assessment: The research nurse will document responses to patient phone calls at 30 days and 60 days to capture this data via Dacima for the online questionnaires/ surveys.

We want to document non-compliance as part of this feasibility study to inform a definitive study. Therefore, we will not withdraw any patients for non-compliance – with intervention, or with follow up assessment.

We are convening a participant advisory group to obtain feedback on how to improve recruitment and compliance.

8.5 Investigation Device(s) and Comparators

All patients will receive standard post-operative wound follow up. This might include being advised to contact the GP or the hospital if there are any wound problems and, or, being invited to an out-patient clinic appointment. Patients in the intervention group will have their wounds monitored remotely – they do this by taking images of their wound using their phone which they submit online along with responses to the modified UKHSA SSI post-discharge questionnaire. The new wound prioritisation module which is under investigation is incorporated within the digital monitoring platform and flags images for the clinical for urgent review.

9.0 PHARMACOVIGILANCE

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, where or not related to the investigational medical device and whether anticipated or unanticipated.
Adverse Device Effect (ADE)	An adverse event related to the use of an investigational medical device. *NOTE: this definition includes:* • *AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.* • *Any event resulting from use error or from intentional misuse of the investigational medical device.* • *'Comparator' if the comparator is a medical device.*
Serious Adverse Event (SAE)	An adverse event that led to any of the following: • death • serious deterioration in the health of the subject, users, or other persons as defined by one of more of the following o a life-threatening illness or injury, or o a permanent impairment of a body structure or a body function including chronic diseases, or o in-patient of prolonged hospitalisation, or

	○ medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure of a body function, • foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment. *NOTE: Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP without a serious deterioration in health, is not considered a SAE.*
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Serious Adverse Device Effect (USADE)	A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment. *NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.*
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. *NOTE: This definition includes:* • *Malfunctions, use errors, and inadequacy in the information supplies by the manufacturer including labelling.* • *Device deficiencies related to the investigational medical device or the comparator.*
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. *NOTE: this would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.*
Recording*	Information collected and transcribed to the participant's eCRF
Reporting*	Expedited to the MHRA and REC via the applicable forms listed in section 9.3.

***Only In the context of safety information / data**

9.2 Operational Definitions for (S)AEs

The intervention in this study is an AI module for a wound monitoring platform designed to flag wound images for priority review. As all patients will receive standard wound care follow up we do not expect there to be any adverse events caused by the device that will affect patients. If the new wound prioritisation module does not work, then the clinician may review a patient's wound image within two days rather than one day. This is still faster than standard wound care follow up.

The following events are expected adverse events following surgery and will be recorded in the eCRF but not expedited to the Sponsor .

- Patent develops a surgical site infection (around 8%)– record in medical notes and eCRF,
- Patient is readmitted to hospital because of a wound infection – record in medical notes and eCRF
- Patient requires further surgery to debride wound infection – record in medical notes and eCRF
- Patient develops sepsis as a result of a wound infection – record in medical notes and eCRF

The following event is a foreseeable expected serious adverse event following surgery which will be recorded and also reported to the sponsor (safetyreporting@rbht.nhs.uk),

- Patient dies following a wound infection – record in medical notes and eCRF and report
- Any patient death and cause – record in medical notes and eCRF and report

The following events are possible device deficiencies that may arise from using an AI module to prioritise non-healing wounds. These are unlikely to lead to an adverse event as all images will be assessed by a clinician. These will not be reported to the Sponsor but will be recorded:

- The module fails to identify a non-healing sign and does not prioritise a wound for urgent review – record in medical notes and eCRF – document for research data only, participant's image will still be reviewed routinely,
- The module identifies a healing wound that does not require prioritise review – record in medical notes and eCRF - document for research data only.

9.3 Recording and Reporting Safety Information

All AEs, SAEs and device deficiencies must be recorded from the time of written informed consent until after the last visit.

All AEs and device deficiencies occurring during the duration of the study must be recorded in patients' medical notes and within the eCRF. The PI is responsible for checking for device deficiencies, A(D)Es and SA(D)Es when participants attend for treatment and follow-up.

- The following events are considered reportable to the MHRA (using the MEDDEV 2.7/3 SAE reporting table) and REC (via the Non-CTIMP safety report to REC form). Any SAE (whether initially considered device related or not)
- Any device deficiency that might have led to a SAE if:
    - Suitable action had not been taken or
    - Intervention had not been made or
    - If circumstances had been less fortunate.
- New findings/updates in relation to already reported events

All reportable events must be first recorded by the investigator using the applicable CTU's SAE/SADE/Device deficiency reporting form and submitted to the Derby CTSU within 24 hours of the research team becoming aware of the event; even if not all information is available at the time (further information should be provided on the CTU's Safety Follow Up Report Form). Any change of condition or other follow-up information should be sent to the CTU as soon as it is available, or at least within 24 hours of the information becoming available. Events will be followed up until the event has been

resolved or a final outcome has been reached. Safety information will be reviewed during trial management group meetings.

Derby CTSU contact information:
Email: uhdb.randdsae@nhs.net. **Telephone**: 01332 724639 or 01332 789339 (must be followed up with a written report).

For each reportable event the following information will be collected as a minimum:

- Full details of the event, including a diagnosis
- MedDRA coding (system organ class and preferred term)
- Duration (start and end dates)
- Seriousness criteria
- Outcome.
- Action taken.
- Causality *(i.e*. related to investigational medical device)
- Expectedness

9.3.1 Assessment of AEs and SAEs

9.3.1.1 Severity

The investigator should determine the severity of the AE;

- Mild: no interference with daily activities.
- Moderate: moderate interference with daily activities.
- Severe: considerable interference with daily activities (e.g. inability to work).

NOTE: to avoid confusion or misunderstanding the term "severe" is used to describe the intensity of the event, which may be of relatively minor medical significance, and is NOT the same as "serious" which is described in the safety definitions.

NOTE: changes in severity i.e. from mild to moderate do not constitute a new AE, but changes severity which impact seriousness criteria i.e. from assessed as 'not serious to 'serious', should be reported as a new (serious) event/effect.

9.3.1.2 Causality

Clinical judgement should be used to determine the relationship between use of the investigational medical device (including the medical-surgical procedure) and the occurrence of each AE;

- Not-related: relationship to the device or procedures can be excluded when:
    - The event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
    - The event has no temporal relationship with the use of the investigational device or the procedures;
    - The serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
    - The discontinuation of medical device application or the reduction of the level of

activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
    - The event involves a body-site or an organ not expected to be affected by the device or procedure;
    - The serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
    - The event does not depend on a false result given by the investigational device used for diagnosis, when applicable;
    - Harms to the subject are not clearly due to use error;
    - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
- Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- Possible: the relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- Probable: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably explained by another cause, but additional information may be obtained.
- Causal relationship: the serious event is associated with the investigational device or with procedures beyond reasonable doubt when:
    - The event is a known side effect of the product category the device belongs to or of similar devices and procedures;
    - The event has a temporal relationship with investigational device use/application or procedures;
    - The event involves a body-site or organ that
        - The investigational device or procedures are applied to;
        - The investigational device or procedures have an effect on;
    - The serious event follows a known response pattern to the medical device (if the response pattern is previously known);
    - The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible);
    - Other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
    - Harm to the subject is due to error in use;
    - The event depends on a false result given by the investigational device used for diagnosis, when applicable;
    - In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Assessment of causality must be made by a medically qualified doctor (usually the principal investigator). If a doctor is unavailable, initial reports should be submitted to the Derby CTSU without the causality assessment, but they must be followed up with a medical assessment as soon as possible.

9.3.1.3 Expectedness

The assessment of expectedness is only required if the event is deemed to be related to use of the investigational medical device.

- **Anticipated:** The medical device is thought to have a causal relationship with the event and the event is listed within the reference information used to assign causality
- **Unanticipated:** The medical device is thought to have a causal relationship with the event and the event is NOT listed within the reference information.
- **Unanticipated, causal relationship and seriousness = USADE**
-

The expectedness assessment is delegated to Chief Investigator.

CIP will be used for expectedness assessments.

9.3.2 Expedited safety reporting

For trials of investigational medical devices that are non CE-marked all reportable events must be reported to the MHRA using the MEDDEV 2.7/3 SAE reporting table (or MDCG 2020-10/2 SAE reporting table) via the MORE portal and the manufacturer. All events which indicate an imminent risk of death, serious injury, or serious illness that requires prompt remedial action for patients, users or other persons should be reported to the MHRA within 2 calendar days of Sponsor awareness. Any other reportable events must be reported within 7 calendar days of awareness by the Sponsor. In addition, all USADEs must be reported to the REC.

In addition to the reporting of individual serious adverse events as detailed above, quarterly summary reports of all serious adverse events will also be provided (Items I, II & III in tabular format) and should include the following:

I. number of serious adverse events
II. number of participants affected by those events
III. percentage of the total number of enrolled participants affected by those events
IV. A summary analysis of the serious events together with the manufacturer's conclusions

The first quarterly report should be submitted the first quarter after the first patient has been treated. The SAE reporting form should be submitted via https://more.mhra.gov.uk/login. All reporting to MHRA will be coordinated by Derby Clinical Trials Unit with assistance from ISLA.

9.4 Pregnancy reporting

It is unlikely, but possible, that pregnant women will be undergoing coronary artery bypass graft surgery. Due to the non-invasive nature of the study – taking a digital photo of a surgical wound and answering questions about a surgical wound, it is not deemed necessary to notify the CTU of pregnant

participants or follow them up until the outcome of the pregnancy. As per standard reporting criteria, if at any stage an event occurs that meets the criterion for an SAE then it must be reported as such.

9.5 Reporting Urgent Safety Measures

If any urgent safety measure is taken the research team should inform the Derby CTSU within 24 hours using the Derby CTSU's safety incident reporting form. The Derby CTSU will inform the MHRA, REC and participating sites of the measures taken and the circumstances giving rise to those measures within 3 days on implementation of the urgent safety measure.

10.0 DATA HANDLING

Study data will be entered at site into electronic case report forms (eCRF) directly by study personnel. The study will use an electronic data capture (EDC) system to store all data securely. The database will be a cloud-based EDC, built by Derby CTSU and hosted by a fully validated 3rd party vendor. Derby CTSU will be responsible for database design, build and data validation while the provider of the EDC will be responsible for hosting and storage of the study data. Access to the EDC will be via a unique username and password, and permissions for data entry and management assigned based on study roles.

After data entry is performed, validation checks will be applied to the data to ensure accuracy and consistency according to the data validation plan. All data queries generated as a result of these checks will be available online for resolution by the sites. Processing of study data and monitoring for consistency, validity and quality will be undertaken by study statisticians, data and trial manager on an ongoing basis during recruitment. After data entry is complete and all data queries have been resolved, the database will be locked and released for statistical analysis.

Participants will be identified by their unique Participant ID number assigned by the EDC system which will be manually added to each participant's Isla record. The link between participant ID and NHS number and Isla unique URL link – or other means of re-identification, will be stored securely locally at each hospital with restricted access.

Participant reported outcomes will be captured via a series of participant questionnaires (outlined in Section 3.2). The link for the on-line survey, hosted on Dacima, will be sent to patients via text or email. Paper copies will be available if requested and will be posted to the participants. Participants will complete their responses within the questionnaire booklet, and return the completed document to site, for entry onto the trial database.

10.1 System and Compliance

The eCRF (study database); used to collect outcomes with the exception of the study intervention, will be a data capture system compliant with ICH-GCP (21 CRF Part 11) and MHRA guidelines for computerised systems. Isla platform data is transferred securely using state-of-the art SHA256 encryption in transit and at rest. Isla platform conforms with medical device regulations, General Data Protection Regulation (GDPR), NHS Digital Technologies Assessment Criteria (DTAC), the STARD-AI initiative and NICE Evidence Standards Framework for Digital Health.

Data will be collected from source documents or from participants directly and input into the eCRF (see section 10.2).

10.2 Source Data

Source documents are where data are first recorded, and from which participants' CRF data are obtained. These include but are not limited to: Data collected on the Isla care platform, hospital records and patient notes, patient questionnaires, and correspondence.

Outcome	**Source**
Demographic data	Medical case note review,
Patient satisfaction	Online survey administered via Dacima– will generate a report for storing
Patient satisfaction	Online Teams interview – will be transcribed for storing
Staff satisfaction	Online survey administered via Dacima – will generate a report for storing
Staff satisfaction	Online Teams interview – will be transcribed for storing
Wound infection data – infection status, antibiotics	Obtained through Isla or patient phone calls at 30 days or surveillance records or medical case notes. Record in medical case notes and eCRF
Intervention data – date of surgery and date of infection diagnosis, adherence with intervention (record per image with date and time), Isla submission completeness.	Obtained through Isla platform review. To be recorded in eCRF (Dacima).
Wound infection data – readmissions, further surgery, GP visits, treatment	Obtained via a Telephone call, or medical case notes. To be recorded in eCRF (Dacima) and medical case notes
Quality of life	Baseline questionnaire at consent, repeated at 30 day online survey and 60 day phone call. To be recorded in eCRF.
Consent	Consent form

eCRF entries will be considered source data for the following data - socioeconomic status (deprivation index & rural/urban location; compiled using post code), u owns smartphone, given a mobile, SSI is detected by clinicians using information available in Isla, image not sufficient quality, clinician requests another image, adverse events , adverse device effects, adherence with Isla submissions, number of images submitted, patient initiated submissions, clinician time to review images, grade of clinician reviewing images, number of attempts to phone patients, UKHSA phone call data, all health economic data obtained from patient or GP and quality of life score.

All documents will be stored safely in confidential conditions. On all trial-specific documents, other than the signed consent, the participant will be referred to by the trial participant number, not by name. Interviewees will also be referred to by their participant number on documents.

Investigators should keep records of all participating patients and all original signed informed consent forms. It is necessary for investigators to provide access to source document for monitoring and audit purposes to the Sponsor and any monitoring or regulatory authorities as deemed necessary.

10.3 Data Workflow

The DCTSU Data Management (DM) team will design the database to capture the clinical data in accordance with the best principles of clinical data management and the relevant SOP on Case Report Form and Database Selection, Development & Release developed by Derby CTSU.

When data are entered into the EDC (by site staff, the participant or DCTSU staff), validation checks will be performed on the data to ensure accuracy and consistency according to the study Data Validation Plan. All data queries generated as a result of these checks will be available for resolution by the site online. After data entry is complete, all data queries have been resolved, any required coding is complete and all forms have been signed by the PI, the database will be locked and released for statistical analysis.

All clinical data will be collected, stored, processed, and archived in accordance with the Data Management Plan for this trial and in line with the relevant SOPs on Data Entry, Data Closeout Activities and Archiving developed by the Derby CTSU and any relevant legislation.

10.4 Data Access and Security

Direct access will be granted to authorised representatives from the Sponsor, Derby CTSU, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections.

All documents will be stored safely in confidential conditions. With the exception of regulatory authorities, only authorised members of the study team will have access to source documents.

Access to the study database will be role-specific and password protected. DCTSU DM will control access, granting access to sites as recorded on the Delegation Log(s). The CI, PI, DCTSU staff and site staff will be given appropriate access & permissions dependent on their role.

Each participant will be assigned a participant ID for use on study forms, other study documents and the electronic database. The investigator and trial team will ensure that the participant's identity is protected at every stage of their participation within the trial. If any patient information needs to be sent to a third party the trial team will adhere to maintaining pseudo-anonymous participant parameters in correspondence.

Images from patients will be kept as source data and archived. Images will be made available for other research studies upon request. This will be made clear in the information given to patients and the consent form.

10.5 Archiving

At the end of the study, following completion of the end of study report, the study Sponsor will securely archive all centrally held study related documentation for a minimum of 10 years. At the end of the defined archive period arrangements for confidential destruction will be made. It is the responsibility of each PI to ensure that data and all essential documents relating to the study are retained securely for a minimum of 10 years after the end of study, and in accordance with national legislation. All archived documents must continue to be available for inspection by appropriate authorities upon request.

11.0 STATISTICS AND DATA ANALYSIS

11.1 Sample Size Calculation

This is a feasibility study and therefore, sample size calculations cannot be calculated as there are no current data which can be used as the basis of the calculations. The feasibility outcomes for this study are all binary outcomes, for which the widest confidence intervals will occur with a proportion of 0.5 (or 50%), therefore calculating a sample size for the confidence interval based on 50% give a "worst case" estimate.
Recruiting 60 patients for each treatment group into the trial (i.e. a total of 120 patients) will enable us to estimate the recruitment and drop-out rates with a 95% confidence interval of within +/- 10% even if the rates were 50% for these two feasibility outcomes (The 95% confidence interval for a sample size of 120 patients and 60 successes, i.e. 50% of patients recruited, or 50% of patients completing the study, is 41% to 59%). If the adherence to treatment rate was 50%, the adherence rate and 95% confidence interval could be estimated to within +/- 13% (the 95% confidence interval for 30 adherent patients out of 60, as this is only relevant for patients in the intervention group, is 37% to 63%). The sample size estimations were calculated using STATA V18 with command "cii proportions". In addition, national data shows a wound problem rate of 21% (our data shows 15%) with a cardiac wound infection rate of 8%.[8] A sample size of 120 patients should provide around 9 patients in each group with a wound problem of which 4-5 patients should have a wound infection. This is sufficient to inform feasibility, safety and acceptability data.

11.2 Planned Recruitment Rate

We plan to recruit 120 patients over ten months, from sites that are expected to operate on at least 1,300 eligible patients over 10 months, which equates to a maximum recruitment rate of around 11%. This should be achievable as patient-facing data collection (survey x1, phone calls x2, and interview for subset of 20 participants) is not burdensome and an RCT looking at an App to monitor surgical wounds had 69% recruitment rate.[9]

Statistical Analysis

11.2.1 Summary of Demographic/Baseline Data and Flow of Patients

Descriptive statistics will be presented to summarize the distribution of demographic and baseline variables across each of the randomisation groups. With the exception of quality of life, which will be analysed as part of the economic analysis, the continuous baseline variables (age, height, weight, BMI) will be reported with means & 95% confidence intervals (95% CI), if shown to be normally distributed,

using a normality plot, otherwise will be reported with medians & Interquartile Ranges (IQR). The categorical and ordinal variables (gender, ethnicity, English speaker, location (urban/rural), socio-economic status, disability, co-morbidities, smoking status, skin tone, residential status, surgical procedure, procedure type, Access to smartphone, assistance required to take photos?, given smartphone or ipad, comorbidities) will be reported with frequencies & percentages.

A Consolidated Standards of Reporting Trials (CONSORT) flow diagram will be produced, showing the frequency of patients/ participants;

- Assessed for eligibility,
- Frequency of each reason for not being eligible,
- Found eligible,
- Approached,
- Excluded before consent (and the frequency of each reason for exclusion),
- Consented,
- Excluded before randomisation (and the frequency of each reason for exclusion),
- Randomised,
- Allocated to each randomisation group,
- That received each allocated intervention,
- That did not receive each allocated intervention,
- Completed each follow up assessment (and the frequency of each reason for non-completion) for each analysis group,
- Analysed for each analysis group,
- Not analysed (and the frequency of each reason for not being analysed) for each analysis group.

11.2.2 Primary Outcome Analysis

Safety outcomes: quality of images received, assessed by clinicians at 30 days(a quality image is one that can be used to make a clinical decision). These will be reported using frequencies and percentages.

Acceptability outcomes: clinician and patient satisfaction using surveys and interviews at day 30. The interviews will investigate the acceptability of the intervention including attitude, burden, perceived effectiveness, ethicality, intervention coherence, opportunity costs and self-efficacy and will be analysed using qualitative methods. Will also collect acceptability of being involved as a study participant. Survey variables that are continuous will be reported with means & 95% confidence intervals (95% CI), if shown to be normally distributed, using a normality plot, otherwise will be reported with medians & Interquartile Ranges (IQR). The categorical variables will be reported with frequencies & percentages.

Feasibility outcomes: recruitment rate, adherence with the module (intervention group only), loss to follow-up. Adherence will be reported as the number and percentage of adherent patients in the intervention group. To be adherent a patient needs to submit one photo with a completed questionnaire within the 30 day period. This will be compared with the progression criteria defined below. The definitive study will proceed (or not) based on these outcomes. The number and

percentage of eligible patients recruited to the study will be reported. All feasibility outcomes will be reported with 95% confidence intervals.

Progression criteria

Criteria:	Do not proceed	Proceed with changes	Proceed
Recruitment	<10% of eligible patients consent	between 10% and <25% of eligible patients consent	at least 25% of eligible patients consent
Adherence with the module	<40% of intervention patients submit one or more images	between 40% and <80% of intervention patients submit one or more images	at least 80% of intervention patients submit one or more images
Loss to follow-up	<10% of intervention patients complete the study	between 10% and <60% of intervention patients complete the study	at least 60% of intervention patients complete the study

Economic modelling outcomes: Will include number and severity of wound problems/infections, wound-related hospital readmission, prescribed antibiotics, time to review images, further surgery to treat wounds, prescribed wound treatments, clinic visits, GP visits, patient travel time and quality of life.

11.2.3 Secondary Outcome Analysis

Safety outcomes. More detailed discussion about reasons for compliance/non-compliance will be explored in the staff surveys and interviews and the patient intervention group surveys and interviews (these will not form part of the statistical analysis). Survey data will be analysed using descriptive statistics, and qualitative data from the interviews (which will not form part of the statistical analysis) will analysed using thematic analysis.

Feasibility outcomes: access/barriers to participation and willingness of participants to be randomised, and attrition rates and time and resources required to conduct telephone assessments to patients and phone calls to GPs to collect antibiotic data. To contribute to sample sizes for a definitive trial - numberof wound problems/infections will be collected. Wound severity, wound-related hospital readmission, further surgery to treat wounds, prescribed wound treatments, prescribed antibiotics, clinic visits, GP visits will also be collected for the economic analysis (?).

Other secondary outcomes: number of photos received (per patient), number of requests (for images) complied with - intervention group only, number photos initiated by patients (intervention group only), number of follow-up requests.

For all secondary outcomes, continuous variables will be reported using descriptive methods such as means & 95% confidence intervals (95% CI). Categorical variables will be reported with frequencies & percentages.

11.3 Subgroup Analyses

There will be no subgroup analyses.

11.4 Adjusted analyses

There will be no adjusted analyses.

11.5 Interim analysis and criteria for the premature termination of the trial

There will be no interim analyses.

The Sponsor may suspend or prematurely terminate either the entire study, or the study at an individual site, for significant reasons that must be documented (e.g. an unacceptable risk to participants or serious repeated deviations from the clinical investigation plan/ regulations). If this occurs the Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e. participants, investigators, participating sites, REC, regulatory bodies).

11.6 Analysis Groups

Recruitment rate (including access and barriers to recruitment and willingness to be randomised) will be assessed as a percentage of all eligible patients, regardless of treatment allocation. Patients who were consented but not randomised will not be included in the recruitment rate. Adherence to the module will be assessed based on patients allocated to the intervention. Loss to follow-up will be assessed based on all randomised patients..
All other patient-based analyses will be reported based on allocated treatment, except for adverse events and adverse device events, which will be reported based on the treatment the patients received.

11.7 Procedure(s) to Account for Missing or Spurious Data

Missing and spurious data will be reported, but as the analyses will all be descriptive, missing and spurious data will not be imputed.

11.8 Other Statistical Considerations

A health economic analysis plan and early model have been prepared and have informed the design of this study particularly with respect to data collection. See next section for details of the economic evaluation.
Adverse device effects and adverse events , will be reported using frequencies and percentages.

11.9 Health Economic Evaluation

An economic investigation was included as the provision of the intervention will involve additional upfront direct costs. The intervention is unlikely to be widely adopted unless it can be shown to be cost-effective. In order for the intervention to be cost effective, the initial upfront cost will need to be offset by savings later in the clinical pathway and/or deliver positive impacts on health outcomes. The economic investigation will comprise two stages: an initial scoping exercise and an economic evaluation on completion of the clinical study. The scoping exercise has been undertaken to inform

the design of this study. This involved a search for relevant economic evaluations and existing evidence base, the development of an early model and drafting of a health economic analysis plan.
The economic evaluation will compare health outcomes and costs in the intervention and control arms using a probabilistic decision model. This will provide an estimate of the probability of cost-effectiveness of the intervention compared to standard of care and identify key parameters for cost-effectiveness for further investigation in a clinical trial. We will also explore the impact of different models of providing the intervention service.

12 MONITORING, AUDIT & INSPECTION Monitoring plan

The Investigator(s) must ensure that source documents and other documentation for this study are made available to study monitors, the REC or regulatory authority inspectors. Authorised representatives of the Sponsor and competent authority may visit the participating sites to conduct audits/ inspections.
Monitoring and source data verification will be conducted by the Derby CTSU according to the study monitoring plan. The extent and nature of monitoring will be determined by the study objectives, purpose, design, complexity, blinding, number of patients and sites, and endpoints.

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.0 Peer review

This study has been peer reviewed as part of the NIHR i4i application process.

13.1 Public and Patient Involvement

To determine patient and public needs and preferences, we commissioned a national survey through the Patient Association to find out PPI views on using images for SSI prevention, which received over 400 completed responses.[10]

Evaluation of the monitoring platform at five cardiac centres with 137 patients helped identify outcome measures, and 30 bedside pilots helped with platform development.[11] This patient engagement led to changes to the platform relating to, for example, text message content, camera function and an email option.

Additionally, we developed the study proposal in collaboration Keith Wilson, our PPI co-applicant, who we have worked with previously. We also presented our proposal to the Brompton & Harefield Cardiovascular Lay Advisory Group who suggested that we provide potential participants for our clinical with information before surgery, not just after, and that we add Healthwatch to our list of organisations through which we recruit PPI group members and disseminate.

Our WISDOM PPI group reviewed all study documentation including the quality of life tool – SF-6Dv2
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13.2 Research Ethics Committee (REC) & Regulatory Compliance

The investigation will be conducted in compliance with the approved clinical investigation plan, the Declaration of Helsinki, the principles of Good Clinical Practice (GCP) Medical Devices Regulations 2002 and ISO 14155:2020.

The clinical investigation plan and all related documentation *(e.g*. informed consent form, participant information sheet, questionnaires) have been reviewed and received approval by a Research Ethics Committee (REC). The trial has been classified as a clinical investigation for a medical device and has received a notice of no objection from the UK competent authority, the Medicines and Healthcare Regulatory Agency (MHRA).

The investigator will not begin any participant activities until approval from the HRA and REC has been obtained and documented. Any additional requirements imposed by the REC, HRA and regulatory authority shall be followed. All documentation and correspondence must be retained in the trial master file/ investigator site file. Substantial amendments that require HRA, REC and MHRA (where applicable) review will not be implemented until the HRA, REC (and MHRA) grants a favourable opinion (with the exception of those necessary to reduce immediate risk to participants.

It is the responsibility of the Chief Investigator to ensure that an annual progress report (APR) is submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, annually until the study is declared ended. The CI is also responsible for notifying the REC and MHRA of the end of trial (see Section 7.10) within 90 days, however if the study ends prematurely, the notification must be submitted within 15 days. Within one year of the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC.

Before any site can enroll a patient into the trial confirmation of capacity must be sought from the site's research and development (R&D) department. In addition, for any amendment that will potentially affect the site's permission, the research team must confirm with the site's R&D department that permission is ongoing.

13.3 Clinical Investigation Plan Compliance/ Non-Compliance Reporting

The investigator is responsible for ensuring that the study is conducted in accordance with the procedures described in this clinical investigation plan. Prospective, planned deviations and/or waivers to the clinical investigation plan are not acceptable, however accidental deviations (non-compliances) may happen and as such these must be recorded. Non-compliances should be recorded in the eCRF and/or a non-compliance log kept in the ISF.

All non-compliances should be reviewed and assessed by the PI (or appropriately delegated individual) to determine if they meet the criteria of a "serious breach" (Section 12.6). Non-compliances which are found to frequently recur are not acceptable, will require immediate action, and could potentially be classified as a serious breach. Corrective and preventative actions should be documented in line with Derby CTSU procedures.

Manufacturers must notify the MHRA of all deviations relating to UK study sites only as soon as they have been made aware of them. Details about the nature of the deviation, when it occurred, where it

occurred, and any proposed corrective and preventative actions should be provided. All deviations should be compiled in a copy of "The MHRA Protocol Deviation Tracker" and sent to the MHRA via email at info@mhra.gov.uk.

Principal investigators may be disqualified for the following:

- Fraud & misconduct
- Severe lack of PI oversight
- Lack of response to findings arising from monitoring and/or audits
- Constant non-compliance and a lack of action once identified.

A Log of non-compliances will be sent to the sponsor in line with TMG reporting.

13.4 Notification of Serious Breaches to GCP and/or the Clinical Investigation Plan

A "serious breach" is a departure from the clinical investigation plan, Sponsor procedures (*i.e.* SOPs), or regulatory requirements 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.

If the PI (or delegate) is unsure if a non-compliance meets these criteria, they should consult the Derby CTSU for further guidance. If a serious breach is identified the investigator should notify the Derby CTSU immediately (*i.e.* within 1 working day) using the MHRA 'notification of serious breaches of GCP or the trial protocol' form. The report will be reviewed by the Derby CTSU and CI, and where appropriate, the Derby CTSU will notify the MHRA and REC within 7 calendar days of being made aware of the breach.

13.5 Data Protection and Patient Confidentiality

The trial will be conducted in accordance with the Data Protection Act 2018. The investigator must ensure that participant's anonymity is maintained throughout the study and following completion of the study. Participants will be identified on all trial specific documents (except for the informed consent form and enrolment log) only by the participants study specific identifier (and initials if deemed necessary). This identifier will be recorded on documents, biological samples and the database. The Investigator Site File will hold an enrolment log detailing the study specific identifier alongside the names of all participants enrolled in the study.
All documents will be stored securely with access restricted to trial staff and authorised personnel.

Melissa Rochon will act as the custodian of the data generated in the trial.

13.6 Financial and Other Competing Interests for the Chief Investigator, Principal Investigators at Each Site and Committee Members for the Overall Trial Management

Guy's and St Thomas' NHS FT has a commercial collaboration arrangement with Islacare Ltd for surgical site infection surveillance and related artificial intelligence. Melissa Rochon, an employee of GSTT, provides ad hoc consultancy services to Islacare Ltd as a fee-for-service arrangement, whereby GSTT receives all fees paid by Islacare Ltd.

Joint Lead Judith Tanner has no competing interests that may influence the study design, conduct or reporting to disclose. This includes no ownership interests, no commercial ties and no non-commercial conflicts.

13.7 Indemnity

It is the responsibility of the sponsor organisation to ensure adequate and appropriate insurance cover for the design, conduct and management of the research project. Given that this study is sponsored by Royal Brompton and Harefield Hospitals (RBHH) part of GSTT, NHS indemnity will apply NHS bodies are liable for clinical negligence and other negligent harm to individuals covered by their duty of care. However, NHS indemnity does not offer no-fault compensation for non-negligent harm and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm. They are able to consider an ex-gratia payment in the case of a claim.

The Sponsor will indemnify RBHH staff conducting research in an NHS environment through the NHS Litigation Authority (NHS LA).

Patients who are unable to participate due to lack of technological resources will be offered equipment to enable them to participate. This includes ipads or smart phones. (we expect this to be a very small number of participants).

13.8 Amendments

If changes to the study are requested, these must be discussed with the sponsor, who is responsible for deciding if an amendment is required and if it should be deemed substantial or non-substantial. Substantial amendments will be submitted to the relevant regulatory bodies (MHRA, REC, HRA) for review and approval. The amendments will only be implemented after approval (from the MHRA if applicable) and a favourable opinion from REC has been obtained. Non-substantial amendments will be submitted to the HRA for their approval/ acknowledgment. Amendments will not be implemented until all relevant approvals are in place.

13.9 Access to Final Trial Dataset

Access to the full dataset will initially be limited to the sponsor, joint-chief investigators, project manager and the steering group to ensure that the overall results are not disclosed by and individual trial site prior to the main publication.

Research staff at the participating sites will not have access to the full dataset unless a formal request is approved by the steering committee.

14 DISSEMINATION POLICY

The clinical investigation will be registered on a publicly accessible database and the results of the investigation will be made publicly available. The UK medical devices regulations require that a written report of a clinical investigation must be produced. This must contain a critical evaluation of all the data collected during the clinical investigation.

14.1 Dissemination Policy

Data arising from the study will be owned by the Sponsor and shared with collaborators in accordance with the Terms and Conditions of the study Collaboration Agreement. Relevant reporting guidelines *e.g.* CONSORT will be followed depending on the type of publication *e.g.* trial, qualitative paper. NIHR will be acknowledged on all forms of dissemination. Publications and conference posters will be submitted to NIHR prior to submission. A final study report will be submitted to NIHR with a shortened PPI friendly version published on the study website. Participating site investigators do not have permission to publish trial data without the approval of the Sponsor in line with the study Collaboration Agreement. Study participants will be notified of publications *via* the study newsletters and *via* email if they choose to provide contact details. It will not be possible for participants to request specific results, instead, participants will be informed at the time if they have a wound complication or not. Our PPI group will inform the dissemination strategy and will contribute towards dissemination *e.g.* webinars, publications, podcasts.

14.2 Authorship Eligibility Guidelines and any Intended Use of Professional Writers

Authors of the final report are the joint leads, all named co-applicants and Derby CTU staff. International Committee of Medical Journal Editors (ICME) criteria will be followed for authorship of manuscripts submitted for publication. Individual named authorship will be used and not group authorship. Professional medical writers will not be used.

15 REFERENCES

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16 APPENDICES

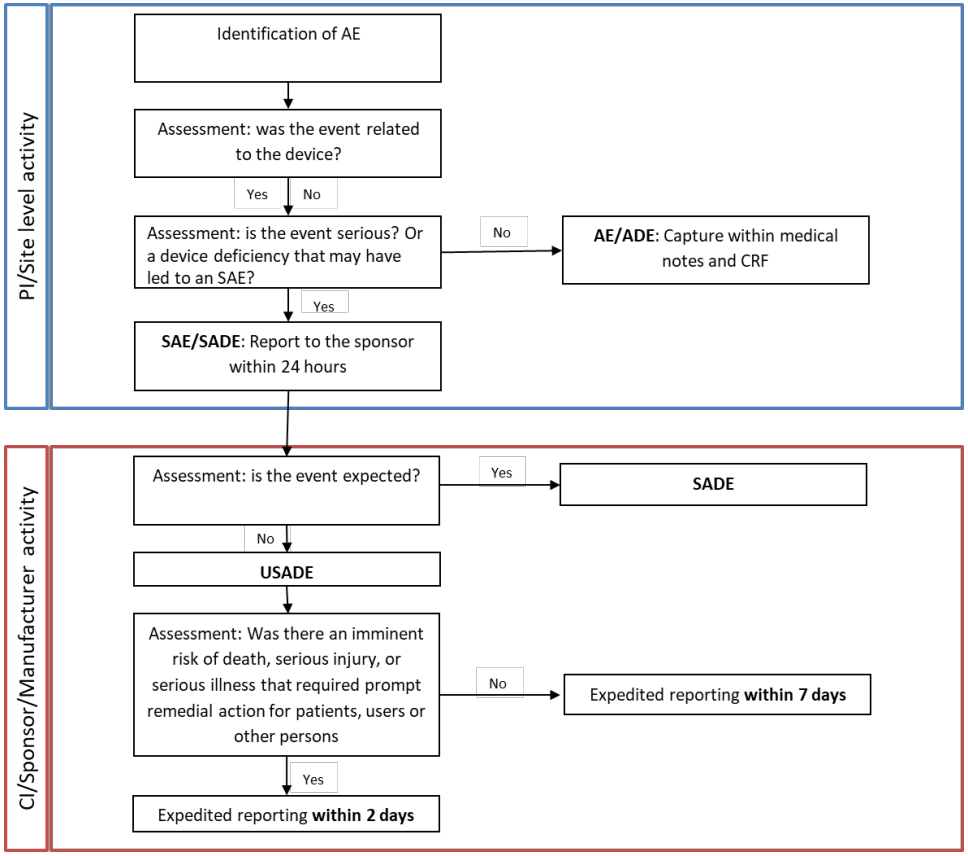
16.1 Appendix 1 – Schedule of Assessments

	VISIT							
Assessment / Data Item	**SCREENING**	**BASELINE**	**TREATMENT PERIOD**				**30 DAY FU**	**60 DAY FU**
			Day 7	**Day 14**	**Day 21**	**Day x***		
Screening	x							
Inclusion / Exclusion Criteria	x	x						
Consent		x						
Demographics		x						
Medical History		x						
Surgery Details		x						
Randomisation		x						
Intervention			x	x	x	x		
SF-6Dv2 (Participants)		x					x	x
Modified UKHSA SSI post-discharge questionnaire outcome							x	
Modified UKHSA SSI post-discharge questionnaire (via ISLA)			x	x	x	x	x**	
Satisfaction Survey (Staff)							x	
Interviews (Participants)							x	
Interviews (Staff)							x	
Healthcare Treatment Log (GP visits, 111 calls etc.)							x	x
Adverse Device Effects & Device Deficiencies			x	x	x	x	x	
Adverse Events		x	x	x	x	x	x	x
Non-compliances		x	x	x	x	x	x	x
Antibiotics							x	x

End of Study / Withdrawal								X

NOTE: *Patient may submit images outside of planned visit days, date (and study day) of submission will be recorded.
**** Redacted version asked via phonecall at day 30.**

16.2 Appendix 2 – Safety Reporting Flow Chart



16.3 Appendix 3 – Amendment History

Amendment No.	Clinical investigation plan version no.	Date issued	Author(s) of changes	Details of changes made
1	V2.0	31 January 2024	JT JB JT	We have added 'quality of life throughout the protocol'. The statistician has added more detail to the protocol on reporting of continuous variable reporting (page 20) and sample size calculations (p34) and added the study progression criteria which were missing (p35). We have added a sentence to clarify the wound healing information that will be obtained through the 30 day phone call and attached the UKHSA post-discharge questionnaire which is part of standard care.
2	V2.1	03 May 2024	VC VC VC VC DD JB	Updated the schedule of assessments to capture SF-6 at baseline and the modified UKHSA SSI post-discharge questionnaire (via the app and redacted version at Day 30) Removed reference to SF-36 Baseline data content specified in detail in section 7.5 and removed the descriptive stats elements. Note added re: changes in severity & serious criteria of adverse events Legacy mentions of pregnancy in the eligibility criteria have been removed. References to site-specific data collection have been removed from the 30-day phone assessment of wound healing and healthcare engagement. All patients will answer the same questionnaire during the 30-day phone assessment.

3	V2.2	19 March 2025	KC	Added: method of collecting information for processing participant reimbursement

Detail all clinical investigation plan amendments. Amendments must be submitted to the Sponsor for approval prior to submission to the REC committee or MHRA.