ROSSINI-PLATFORM TRIAL

Pillar-Specific Protocol

CARDIAC

A 'Basket Factorial MAMS' Platform Trial in Surgical Site Infection

This protocol has regard for the HRA guidance and is compliant with the SPIRIT guidelines (2025)

Version Number: 1.0

Version Date: 05-Jan-2026

CARDIAC PILLAR SPECIFIC PROTOCOL DEVELOPMENT

Protocol amendments

The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version.

Amendment number	Date of amendment	Protocol version number	Type of amendment	Summary of amendment

Funding and support in kind	
Funder(s)/Supporting Organisations	**Financial and non-financial support given:**
National Institute of Health and Care Research (NIHR)	Financial, Investigator led grant
Funding scheme	NIHR Health Technology Assessment (HTA) Programme
Funder's reference number	NIHR163832
The funder of the trial will have no role in the trial design, data collection, data analysis or data interpretation, or in the writing of the final report; and the decision to submit the report for publication. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.	

SUPPLIERS
Provision of intervention

PROTOCOL SIGN OFF

Pillar Lead for CARDIAC - Signature Page

I, the Pillar Lead, confirm that I have read and agree with the following protocol, and that I will conduct the trial in compliance with the version of this protocol approved by the REC and any other responsible organisations.

I agree to ensure that the information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical 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 study will be given; and that any discrepancies from the study as stated in this and any subsequent approved protocol will be explained.

Trial name:	ROSSINI-Platform (CARDIAC Pillar)
Protocol version number:	Version: __ __
Protocol version date:	__ __/__ __ __/__ __ __ __
Pillar Lead name:	
Signature and date:	_____ __ __/__ __ __/__ __ __ __

Sponsor statement

By signing the IRAS form for this trial, the University of Birmingham, acting as sponsor, confirm approval of this protocol.

Compliance statement

This protocol describes the CARDIAC Pillar within the ROSSINI-Platform trial only. The protocol should not be used as a guide for the treatment of patients not taking part in the Cardiac Pillar of the ROSSINI-Platform trial.

The trial will be conducted in compliance with the approved protocol, the UK Policy Framework for Health and Social Care Research, the Medicines for Human Use (Clinical Trials) Regulations 2004, Data Protection Act 2018 and the Principles of Good Clinical Practice (GCP) as set out in the UK Statutory Instrument (2004/1031), Mental Capacity Act 2005 and subsequent amendments thereof. Every care has been taken in the drafting of this protocol, but future amendments may be necessary, which will receive the required approvals prior to implementation.

Principal Investigator (PI) signature page

As Principal Investigator, I confirm that the following protocol has been agreed and accepted, and that I will conduct the trial in compliance with the approved protocol where this does not compromise participant safety.

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

Trial name:	ROSSINI-Plarform (CARDIAC Pillar)
Protocol version number:	Version: __ __
Protocol version date:	__ __ /__ __ __ /__ __ __ __
PI name:	
Name of Site:	
Signature and date:	_____ __ __ /__ __ __ /__ __ __ __

ADMINISTRATIVE INFORMATION

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Trial website	< tbc >
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ABBREVIATIONS

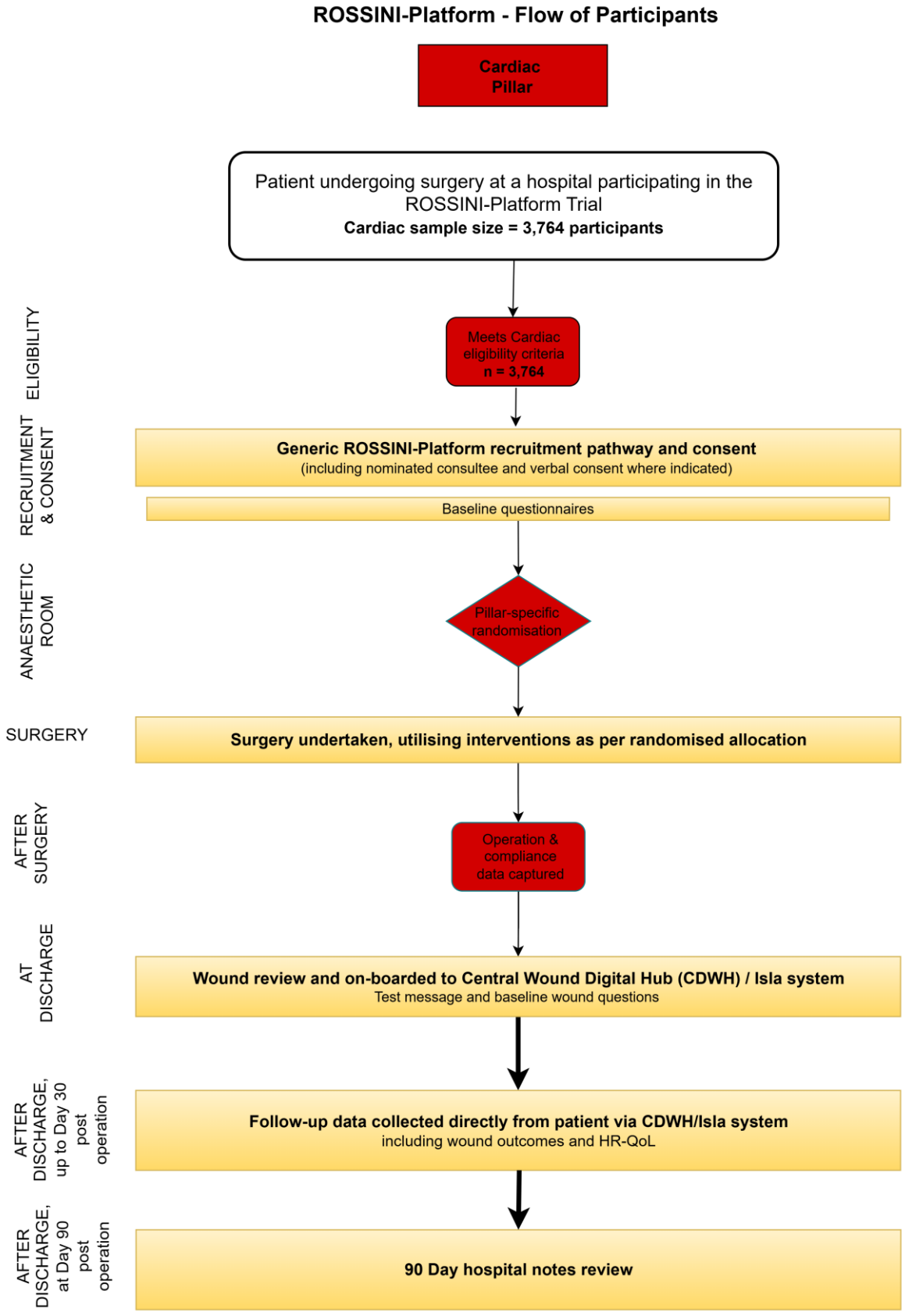
ARR	Absolute Risk Reduction
BCTU	Birmingham Clinical Trials Unit
BMI	Body Mass Index
CABG	Coronary Artery Bypass Grafting
CDWH	Centralised Digital Wound Hub
CI	Chief Investigator
ciNPWT	Closed Incision Negative Pressure Wound Therapy
CIRN	Cardiothoracic Interdisciplinary Research Network
eCRF	Electronic Case Report Form
ETMG	Executive Trial Management Group
GCP	Good Clinical Practice
HRA	Health Research Authority
ISF	Investigator Site File
MAMS	Multi Arm Multi Stage
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PHE	Public Health England
PI	Principal Investigator
PSP	Pillar Specific Protocol
RAG	Red Amber Green progression criteria
RCT	Randomised Control Trial
REC	Research Ethics Committee
RR	Risk Ratio

RSI	Reference Safety Information
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCP	Surgical Care Practitioner
SOP	Standard Operating Procedure
SSI	Surgical Site Infection
TSC	Trial Steering Committee
UK	United Kingdom
WHO	World Health Organization

ROSSINI PLATFORM: CARDIAC PILLAR TRIAL SUMMARY

INTERVENTIONS	**1.** Instrument and glove change prior to wound closure (versus standard practice) **2.** Topical gentamicin-impregnated collagen matrix between sternal edges prior to wound closure (versus none) **3.** Closed incision negative pressure wound therapy (ciNPWT) (versus standard practice)
PARTICIPANT POPULATION AND SAMPLE SIZE	**Participant Population** = approx. 20,000 operations each year in the UK. • If 80% patients are eligible across 80% of sites = 12,800/year. • Recruitment rate of 30% = 16,000 recruitable patients over 50 months. **Sample size calculation;** • 4.5% baseline SSI rate, with 2% ARR = sample size 3,764
PILLAR-SPECIFIC ELIGIBILITY CRITERIA **INCLUSIONS**	• Patients aged 18 years or older • Patients undergoing coronary artery bypass grafting (CABG) with or without a concomitant procedure via median sternotomy. Including elective, urgent and emergency operations.
PILLAR-SPECIFIC ELIGIBILITY CRITERIA **EXCLUSIONS**	Minimally invasive surgery with no sternotomy or partial sternotomy
RECRUITMENT TARGETS	• Maximum sample size required: 3764 • 20 cardiac centres • Average 5 patients per centre per month • Initial 3 month pilot phase aim to open ≥ 6 sites and ≥ 40 patients recruited.
TIMELINES	Up to 50 months of recruitment

TRIAL SCHEMA



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1. PILLAR SPECIFIC PROTOCOL STRUCTURE

The structure of this protocol is different to that used for conventional trials because this trial is highly adaptive and the description of these adaptations is better understood and specified using a 'modular' protocol design. While, all adaptations are pre-specified (e.g. the dropping or addition of interventions/pillars), the structure of the protocol is designed to allow the trial to evolve over time, for example by the introduction of new interventions or pillars or both.

The protocol has multiple modules comprising the ROSSINI-Platform Master Protocol (overview and design features of the study), and multiple Pillar-Specific Protocols (PSP) (detailing all interventions currently being studied in each pillar).

The Master Protocol contains all information that is generic to the trial, irrespective of the pillars or interventions that are being tested. The Master Protocol may be amended but it is anticipated that such amendments will be infrequent. The Master Protocol does not contain information about the intervention(s), within each pillar as one of the trial adaptations is the change of interventions over time.

Information about interventions, within each pillar, is covered in a PSP. These PSPs are anticipated to change over time, with removal and addition of options within an existing pillar.

Each substantial modification to a PSP will require regulatory approval.

The Master Protocol does not contain detailed information about the statistical analysis, but this information is contained within the Statistical Analysis Plan (SAP).

1. BACKGROUND AND RATIONALE

2.1 Pillar definition

This is a pillar within the ROSSINI-Platform Trial to test the effectiveness of specific peri-operative interventions to prevent Surgical Site Infection (SSI) in patients undergoing coronary artery bypass grafting (CABG) via median sternotomy.

2.2 Pillar-specific background

Reducing healthcare-associated infections and preventing the emergence of antimicrobial resistance are national research priorities(1,2). Our research aims to develop and evaluate evidence-based systems and processes for effective antimicrobial stewardship in cardiac surgery.

SSIs are the most common healthcare-associated infections in people undergoing cardiac surgery in the UK (3). Public Health England (PHE) reports an SSI incidence of 8.6% for CABG and 2.2% for non-CABG operations at 30 days. SSI following cardiac surgery is associated with a ten-fold increase in mortality,(4) prolonged hospitalisation, (5) a six-fold increase in hospital readmissions, the need for further surgery and/or extended outpatient care.(6) The annual direct costs of treating SSIs are estimated to be over £15 million(7). A Priority Setting Partnership undertaken by the James Lind Alliance in 2019 included feedback from over 200 patients and identified reducing SSI following cardiac surgery as a national research priority(1). Antimicrobial resistance is a leading risk to global health and was the subject of a five-year (2019–2024) action plan in the UK(8). Key objectives of this plan include steps to reduce the need to avoid unintentional exposure, and optimise the use, of antimicrobials. NICE guidelines for SSI prevention published in 2019 (9) made a research recommendation that future research should focus not just on SSI prevention, but also on strategies to prevent the emergence of multi-drug resistant organisms. In addition, there is variation in the causative organisms between men and women highlighting possible health inequality (10).

SSIs are often preventable. It has been estimated that a reduction of between 39-55% in SSI rates could be made through multifaceted interventions(11). A Cochrane Review by this group (Cardiothoracic Interdisciplinary Research Network (CIRN))(12) has demonstrated that the certainty of the evidence relating to the safety and effectiveness of 22 separate SSI prevention interventions (118 randomised controlled trials (RCTs)) in cardiac surgery is low or very low. National and international treatment guidelines (9,13), including the 2019 NICE guidance for SSI prevention report similar conclusions.

Knowledge gaps contribute to clinical uncertainty and variation in care. Preliminary work now published (14) surveyed processes and procedures for SSI prevention in 139 surgical teams in 19 cardiac centres. SSI rates ranged from 1-9%. The survey demonstrated good adherence to the 2019 NICE SSI guidelines for interventions where there was greater certainty of benefit, including perioperative close glycaemic control, skin preparation with chlorhexidine in 70% alcohol, disposable drapes, and antibiotic-impregnated skin adhesive. However, this survey, along with the linked Cochrane Review, and the National Institute for Health and Care Excellence (NICE) review, identified two important components of SSI prevention where uncertainty in clinical benefit exists, and consequently wide variation in the care delivered: gentamicin-impregnated collagen matrix and closed incision negative pressure wound therapy (ciNPWT). It also identified a lack of RCTs and therefore a knowledge gap in the use of instrument and glove change prior to sternal wound closure.

2.3 Pillar-specific rationale

2.3.1 Justification for pillar-specific participant population

The key inclusion criteria for this trial are patients aged 18 years or older undergoing CABG in isolation or with a concomitant procedure via a median sternotomy, including elective, urgent and emergency cases. A requirement for patients to be undergoing CABG was made as this population is known to be at higher risk of developing an SSI compared to non-CABG surgery. This is likely due to a combination of the associated co-morbidities in patients with ischaemic heart disease, harvesting of internal mammary arteries and the use of autografts, particularly from the lower limbs. Including CABG patients only would allow for cohort enrichment. For the same reason, patients under the age of 18 were excluded as this population primarily undergoes cardiac surgery for congenital abnormalities and therefore represents a distinctly different population.

2.3.2 Justification for choice of interventions

Intervention 1: Instrument and glove change prior to wound closure (versus standard practice)

This intervention has been conclusively shown to be effective in abdominal surgery in seven low-income and middle-income countries (absolute risk reduction (ARR): 0·87, 95% confidence interval 0·79-0·95; p=0·0032)(15). Whilst there have never been any RCTs in cardiac surgery, it is possible that it will confer a similar benefit in cardiac surgery.

Intervention 2: Gentamicin-impregnated collagen matrix left within wound prior to closure (versus none)

The Cochrane review identified a significant reduction in SSI with the use of this intervention (risk ratio (RR) 0.62, 95% confidence interval 0.46-0.84; p=0.002, I^2=48%; 5 studies, 5382 participants; certainty of evidence moderate)(12). NICE recommends that this intervention may be beneficial, but a national survey demonstrated only 13% of cardiac surgeons in the United Kingdom (UK) use it(14).

Intervention 3: Closed incision negative pressure wound therapy (ciNPWT) (versus standard adhesive absorbent dressing)

The Cochrane review showed a trend towards lower SSI with ciNPWT when compared with standard dressing (RR 0.17, 95% confidence interval 0.03-0.97; p=0.05, I^2=0%; 2 studies, 144 participants; certainty of evidence very low) (12). The 2019 NICE guidance states that the routine use of ciNPWT is cost-effective. However, a national survey found 57% of UK cardiac surgeons were not using it at all and 43% only selectively in high-risk cases(14).

2. PILLAR SPECIFIC PILOT AIMS AND OBJECTIVES

3.1 Internal pilot objectives

The trial includes a 3-month internal pilot phase at Platform, Pillar and Intervention level.

The pilot phase of the cardiac pillar will begin when the first patient is recruited to the pillar. The pilot phase will inform decisions on the continuation of the trial.

The aims of the internal pilot at pillar level are to assess:

- Number of sites opened
- Number of patients recruited
- Engagement with the Centralised Digital Wound Hub (CDWH)
- Participant-level data at Birmingham Clinical Trials Unit (BCTU)

At the end of the internal pilot phase, the Executive Trial Management Group (ETMG) and Trial Steering Committee (TSC) will review the pilot data against a set of pre-specified Red-Amber-Green (RAG) criteria:

Table 1: PILLAR Level Internal Pilot Progression Criteria

Progression Criteria	Number of sites opened	Participant recruitment	Engagement with CDWH*	Patient-level data to BCTU**
GREEN (GO)	≥ 6 sites	≥ 40 participants	≥ 95%	≥ 95%
AMBER (modify)	3 - 5 sites	11-39 participants	≥ 90 - < 95%	≥ 90 - < 95%
RED (STOP)	≤ 2 sites	≤ 10 participants	< 90%	< 90%

* Percentage of participants submitting at least one response to CDWH

**Percentage of participants submitting baseline data to BCTU

Table 2: INTERVENTION-LEVEL Internal Pilot Progression Criteria

Progression Criteria	Compliance with randomised allocation by surgeon	Relative clinician acceptance of each intervention within the pillar+

GREEN (GO)	≥ 95%	≥ 80%
AMBER (modify)	≥85 – <95%	≥ 60 - < 80%
RED (STOP)	< 85%	< 60%

[+] measured as willingness to accept it divided by its availability, considering site provision and participant eligibility prior to randomisation.

Intervention-level progression criteria relate to all interventions.

At the end of the first 3-month pilot, a second 3-month internal pilot can be triggered if deemed necessary by the TSC.

3. TRIAL DESIGN AND SETTING

4.1 Trial design

The Cardiac Pillar will be conducted as part of the ROSSINI-Platform Trial (See Master Protocol). ROSSINI-Platform is a Basket Factorial Multi Arm Multi Stage (MAMS) platform trial with multiple phase III factorial MAMS RCTs running in parallel. The Cardiac Pillar represents one of the phase III factorial MAMS RCTs.

The planned sample size for the CARDIAC Pillar is 3,764 participants.

4.2 Trial setting

There are 35 National Health Service (NHS) hospitals in the UK that perform adult cardiac surgery. This includes 29 centres in England, 3 in Scotland, 2 in Wales, and 1 in Northern Ireland. The Cardiac Pillar will aim to open in at least 20 NHS hospitals in the UK.

4. PILLAR-SPECIFIC ELIGIBILITY

5.1 Inclusion criteria

- Patients aged 18 years or older
- Patients undergoing CABG with or without a concomitant procedure, via a median sternotomy
- Able to provide informed consent

Patients undergoing elective, urgent, or emergency cases are all eligible to participate. An emergency case is defined as an unplanned immediate procedure to treat a life-threatening problem. Urgent surgery is defined as patients requiring intervention on a non-elective basis and typically within that hospital admission.

5.2 Exclusion criteria

- Minimally invasive surgery with no sternotomy or partial sternotomy.
- For intervention 2: **Gentamicin-impregnated collagen matrix**
  - Allergy to proteins contained within the sponge
  - Allergy to gentamicin or other aminoglycosides
  - Patients with myasthenia gravis
- For intervention 3: **Closed incision negative pressure wound therapy**
  - Previously confirmed or untreated osteomyelitis

5.3 Co-enrolment

Patients who have been recruited to another RCT examining an intervention that does not share a common biological pathway with impact on the primary outcome measure, are permitted to be included within this pillar.

Sites should contact the ROSSINI-Platform Trials Office to discuss co-enrolment prior to patient recruitment.

5. PILLAR SPECIFIC CONSENT CONSIDERATIONS

Most patients undergoing surgery within the Cardiac Pillar will be able to provide fully informed consent for entry into the ROSSINI-Platform trial.

The process for informed consent is detailed within the Master Protocol and the options for provision of informed consent are described and should be followed for this pillar.

It is anticipated that most patients will provide face to face consent either on paper or electronically, however, any method of consent as detailed in the Master Protocol is acceptable.

6. RANDOMISATION and BLINDING

7.1 Randomisation method

There are three interventions being tested in this pillar. Participants will be randomised in a 1:1 ratio separately for each intervention.

Intervention 1 randomisation:

- Instrument and glove change prior to wound closure (intervention)
- No instrument and glove change prior to wound closure (control)

Intervention 2 randomisation:

- Gentamicin collagen matrix (intervention)

- No Gentamicin collagen matrix (control)

Intervention 3 randomisation:

- ciNPWT (intervention)
- Standard adhesive absorbent dressing (control)

A minimisation algorithm will be used within the randomisation system to ensure balance in the intervention allocations over the following variables:

- Centre
- Sex (male, female)
- Diabetes (Yes (on medical therapy not including insulin) OR Yes (Insulin) OR Yes (Diet controlled) OR No)
- BMI (BMI < 35 kg/m^2 OR BMI ≥ 35 kg/m^2)
- Planned Bilateral Internal Mammary arteries (Yes OR No)
- Urgency (Elective OR Urgent OR Emergency)

To avoid the possibility of the intervention allocation becoming predictable, a random element will be included in the algorithm. Full details of the randomisation specification will be stored in a confidential document at BCTU.

7.2 Blinding – Additional pillar-specific measures

Within the Cardiac pillar, blinding depends on the intervention received. It is not possible to blind the surgical team in theatre but blinding of participants and those responsible for post-operative follow up will be attempted as far as is feasible.

Intervention 1: Instrument and glove change

Participants and the in-hospital research team will be blinded to the allocation.

Intervention 2: Gentamicin-impregnated collagen matrix

Participants and the in-hospital research team will be blinded to the allocation.

7. PILLAR SPECIFIC TRIAL INTERVENTIONS

As a pragmatic RCT, ROSSINI-Platform does not mandate a specific bundle of care for the prevention of SSI as part of usual care in each trial centre, as this would limit wider generalisability of the findings.

Instead, it is stipulated that all trial sites should adhere to a minimum set of policies as per the NICE guidance CG74 (24) on the prevention of SSI. This includes:

- The monitoring and maintenance of normothermia
- Use of a standard three-stage WHO Surgical Safety Checklist.

8.1 Standard care

This is designed to be a pragmatic trial and therefore we have a limited set of standard operating procedures.

Prophylactic antibiotics as recommended by WHO should be given as per local Trust/hospital guidelines. Skin preparation, draping and surgical technique are at the discretion of the surgical team.

8.2 Trial interventions

Intervention 1: **Instrument and glove change prior to wound closure**

The timing of the intervention should occur immediately prior to the insertion of sternal wires. The surgical team (surgeons, scrub nurse, surgical care practitioner etc.) should change gloves and use the clean instruments before handling the sternal wires or the wound edges to facilitate closure.

- Gloves: Change of sterile gloves (or outer gloves if double gloved) for all scrubbed members of the operating team including the surgeon, all assistant surgeon(s) and scrub staff.

- Instruments: A sterile set of instruments for sternal closure including a needle holder, sternal wire needle holder, sternal wire cutter, forceps, and scissors. This should be implemented in each hospital according to local practice and availability. For example, they can be separated from the main instruments at the start of the operation by the scrub nurse (e.g. wrapped in a clean swab). Alternatively, a new instrument(s) pack can be opened.

Comparator 1: No change of instruments and gloves prior to wound closure

It is assumed that instrument and glove changes prior to wound closure is not the current standard practice in most cardiac units.

The type of glove worn should be according to surgeon/scrub nurse/Surgical Care Practitioner (SCP) preference e.g. Biogel, double or single gloving.

Change of instruments or gloves will occur at other points during the case due to sterility or damage and this can continue as necessary.

Intervention 2: Gentamicin-impregnated collagen matrix left within wound prior to closure (versus none)

Collatamp G (Serb Pharmaceuticals) is a fully absorbable device composed of bovine collagen which is impregnated with gentamicin sulfate. It should be used according to the manufacturers guidance. It should be used at the end of the cardiac surgical procedure in the sternal wound, after the sternal wires have been placed but before they are crossed/tightened.

The sterile package containing Collatamp G should only be opened immediately prior to use. The field should be dried and a **dry** Collatamp G placed in between the sternal edges. One Collatamp G size 5x20x0.5cm should be used in the sternum. This contains 200mg gentamicin per implant. The total gentamicin dose for each patient should not exceed 9mg/kg body weight. The sternal should be closed as per the surgeons standard preference (e.g. single sternal wires, Myo wires, sternal plates).

Comparator 2: No gentamicin-impregnated collagen matrix, topical antibiotoics or antimicrobials

The sternum should be closed as per the surgeon's own preference.

The use of gentamicin-impregnated collagen matrix , other topical antibiotics or antimicrobials either in the sternum or within the wound is, however, not permitted.

Intervention 3: Closed incision negative pressure wound therapy (ciNPWT)

This intervention describes the application of a dressing and device combination that aims to deliver continuous negative pressure therapy to a closed wound at the end of surgery. After closing, cleaning, and drying the skin, the dressing and device combination will be applied in theatre. There are adjuncts to ciNPWT that aim to aid in the successful application and maintenance of an airtight seal that are permitted if patients are allocated to this intervention. These adjuncts include (but are not limited to) skin preparation wipes, solutions, or tapes/film (e.g. Cavalon film or Duoderm) and additional adhesive strips placed along the edges of the dressing.

This intervention aims to evaluate ciNPWT as a therapy concept rather than evaluate any individual trademarked device. Our industry partner will provide ciNPWT devices to sites throughout the duration of the trial.

Other ciNPWT devices are permitted for patients randomised to this intervention.

Sites may have a pre-existing supplier of ciNPWT devices, it is anticipated that sites will utilise the devices supplied by our industry partner but can rely on any existing stock they may hold in any scenario where stock from the trial supplier are unavailable or based on the operating surgeon's preference.

The duration of ciNPWT should be guided by the manufacturer's instruction for use. The duration of therapy delivered (in days) and the number of times the dressing was reapplied to achieve an adequate seal will be recorded for each patient randomised to this intervention.

.It should not be removed for wound review on Day of Discharge.

Intervention 3: Closed incision negative pressure wound therapy (ciNPWT) on the sternal wound

The comparator arm can include any dressing apart from those that utilise negative pressure therapy.

8.3 Contraindications

Specific contraindications to each of the included interventions are:

Intervention 1: **Instrument and glove change prior to wound closure**

- None

Intervention 2: Gentamicin-impregnated collagen matrix left within wound prior to closure (versus none)

- Allergy to proteins contained within the sponge
- Allergy to gentamicin or other aminoglycosides
- Patients with myasthenia gravis

Intervention 3: Closed incision negative pressure wound therapy (ciNPWT)

- Previously confirmed or untreated osteomyelitis

8.3.1 Concomitant medication(s)/intervention(s)

Not applicable.

8.3.2 Prohibited medication(s)/intervention(s)

There are no prohibited medications within this pillar.

8.4 Intervention modification or discontinuation

Intervention 1: Instrument and glove change prior to wound closure

The intervention should not be modified and should be performed as per the guidance outlined above. The intervention is only applied intra-operatively and therefore cannot be discontinued.

Intervention 2: Gentamicin-impregnated collagen matrix left within wound prior to closure (versus none)

The intervention is single use is fully absorbable and is only applied intra-operatively. Therefore it cannot be discontinued. It should only be used as per the manufacturer's instructions detailed above.

Intervention 3: Closed incision negative pressure wound therapy (ciNPWT)

The ciNPWT dressing should only be applied as per the guidance outlined above and should not be modified.

The dressing should remain in place for the the duration as per manufacturer's instructions . The dressing should also be re-evaluated if there is frank opus or blood evident within the dressing. The dressing should be changed for another ciNPWT dressing. In the event of participant request due to discomfort, the dressing can be removed prior to day 7and an alternative dressing (as per local guidance) can be placed.

8.5 Intervention supply and storage

8.5.1 Intervention supplies

The interventions used within the ROSSINI-Platform trial are either supplied free of charge by the manufacturer of the intervention or they are obtained from standard hospital stock.

For those interventions supplied for free directly from the manufacturer an initial supply of the interventions will be delivered to each site prior to site opening. The process for appropriate resupply and delivery arrangements will be explained during the Site Initiation Visiit.

The industry partners supporting the provision of interventions for the Cardiac Pillar of the ROSSINI-Platform Trial are:

Intervention 1: Instrument and glove change prior to wound closure

- No supplier required / not applicable – Standard hospital stock used

Intervention 2: Gentamicin-impregnated collagen matrix

- Collatamp G (Serb Pharmaceuticals)

Intervention 3: Closed incision negative pressure wound therapy (CiNPWT)

- Industry partner

8.5.2 Packaging and labelling

There are no special packaging or labelling requirements for the Interventions being used in the ROSSINI-Platform Cardiac Pillar.

Appropriate arrangements must be made to ensure availability of the Intervention(s) when needed, while also ensuring that intervention(s) supplied for the trial are not used for non-trial indications. It is recommended that the trial interventions (or box in which they are held) be marked with a label "For ROSSINI- Platform Trial Use Only". The labels will be provided in the ISF and are available from the ROSSINI-Platform Trial Office should sites require additional supplies.

8.5.3 Intervention storage

All interventions will be stored in a secure, clean, dry place free from damp at room temperature and within the supplied sterile packaging. No specific special requirements are required above the standard storage conditions of theatre products and refrigeration will not be necessary. Any excess intervention material will be disposed of in the hospital's standard clinical waste bins as per local hospital protocol. Interventions supplied for free must only be used for patients within the trial, randomised to the arm in question. Any centres using the interventions supplied for free outside the trial setting may be cautioned, asked to withdraw from the trial or be asked for reimbursement.

8.5.4 Storage deviations

Not applicable. There are no special storage requirements for the interventions being provided free of charge via the ROSSINI-Platform Trial Office, and therefore we do not expect any storage deviations to occur.

For any trial interventions that are from standard hospital stock, sites should follow local policies and SOPs.

8.5.5 Intervention recalls

In the event that a trial intervention provided via the ROSSINI-Platform Trial Office directly to participating sites, is recalled by the manufacturer, the ROSSINI-Platform Trial Office will promptly notify all participating sites and hospitals of the recall. The notification will include details of the recall, including the reason, the specific intervention batches affected (if these details have been provided by the manufacturer) and any immediate actions required (i.e. cease the use of the recalled intervention immediately, quarantine any remaining stock of the recalled intervention to prevent further use.

For any interventions not supplied via the ROSSINI-Platform Trial Office i.e. where the intervention is taken from standard hospital stock, sites should follow usual Trust procedures / recall SOPS for any intervention recalls.

8.5.6 Accountability

Each individual recruiting site shall be responsible for ensuring adequate stock of Gentamicin-impregnated collagen matrix and consumables as well as ciNPWT devices and adjuncts prior to randomisation of patients into the trial.

Each site must ensure that stock levels are adequate prior to randomisation to avoid protocol deviation.

8. PILLAR SPECIFIC ADVERSE EVENT REPORTING

Within the ROSSINI-Platform trial there are adverse events which are either:

1. Common to all pillars within the platform
2. Pillar-specific

The Master Protocol describes the process for adverse event reporting within the ROSSINI-Platform. This includes a description of:

- The reporting period for ALL safety events within the ROSSINI-Platform
- The process for reporting of ALL safety events within the ROSSINI-Platform
- Serious Adverse Events (SAEs) common to all pillars requiring expedited reporting within the ROSSINI-Platform
- SAEs common to all pillars requiring non-expedited reporting within the ROSSINI-Platform

Please refer to the Master Protocol for the process for safety reporting which must be followed.

9.1 Pillar-Specific Serious Adverse Events requiring expedited reporting to the Trial Office

Within this pillar, the expected intervention-specific adverse events requiring expedited reporting are:

- Allergic reaction to proteins contained within the sponge
- Allergic reaction to gentamicin or other aminoglycosides

Events requiring expedited reporting should be reported on a SAE electronic Case Report Form (eCRF) and submitted to the ROSSINI-Platform Trial Office within 24 hours of site becoming aware of the event.

Events subject to expedited reporting and should be reported according to the process detailed in Section 11.5.3 of the Master Protocol.

9. REFERENCE LIST

1. Lai FY, Abbasciano RG, Tabberer B, Kumar T, Murphy GJ. Identifying research priorities in cardiac surgery: a report from the James Lind Alliance Priority Setting Partnership in adult heart surgery. BMJ Open. 2020;Sep;10(9):e038001.
2. Annual Report of the Chief Medical Officer Volume Two, 2011 Infections and the rise of antimicrobial resistance. 2011.
3. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR. Report. 2018;2018;163.
4. Gelijns AC, Moskowitz AJ, Acker MA, Argenziano M, Geller NL, Puskas JD. Management practices and major infections after cardiac surgery. J Am Coll Cardiol. 2014 Jul;29;64(4):372–81.
5. Joshi V, Vaja R, Richens D. Cost analysis of gentamicin-impregnated collagen sponges in preventing sternal wound infection post cardiac surgery. J Wound Care. 2016 Jan;2;25(1):22–5.
6. Rochon M, Makecha S, Morais C, Luff D, Richardson Persaud-Rai B, Tibbles S, et al. A quality improvement approach to reducing readmission for surgical site infections. Wounds UK. 2016;12((2):31.
7. Jenks PJ, Laurent M, McQuarry S, Watkins R. Clinical and economic burden of surgical site infection (SSI) and predicted financial consequences of elimination of SSI from an English hospital. J Hosp Infect. 2014;Jan;86(1):24–33.
8. Health D. UK 5-year action plan for antimicrobial resistance 2019 to 2024 [Internet]. Available from: https://www.gov.uk/government/publications/uk
9. The National Institute for Health Care Excellence (NICE. NICE SSI. 2019;
10. Boyle M, Vaja R, Rochon M, Luhana S, Gopalaswamy M, Bhudia S, et al. Sex differences in surgical site infections following coronary artery bypass grafting: a retrospective observational study. J Hosp Infect. 2024 Apr 1;146:52–8.
11. Schreiber PW, Sax H, Wolfensberger A, Clack L, Kuster SP. The preventable proportion of healthcare-associated infections 2005–2016: Systematic review and meta-analysis. Infect Control Hosp Epidemiol. 2018 Sep 20;2018;39(11):1277–95.
12. Network CIR, L R, R V, D B, JM A, M R. Interventions to prevent surgical site infection in adults undergoing cardiac surgery. Cochrane Heart Group;
13. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, Jonge S, Vries F. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;Dec;16(12):e288–303.
14. Aktuerk D, Ali JM, Badran A, Balmforth D, Bleetman D, Brown CS, et al. National survey of variations in practice in the prevention of surgical site infections in adult cardiac surgery, United Kingdom and Republic of Ireland. J Hosp Infect. 2020 Dec 1;106(4):812–9.

15. Andoh AB, Francis AA, Abdulkarim AA, Adesunkanmi AO, Salako AA, Soladoye A, et al. Routine sterile glove and instrument change at the time of abdominal wound closure to prevent surgical site infection (ChEETAh): a pragmatic, cluster-randomised trial in seven low-income and middle-income countries. The Lancet. 2022 Nov 19;400(10365):1767–76.

10. APPENDIX