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Reduction Of Surgical Site Infection using several Novel Interventions

Submission date 11/02/2019	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 04/03/2019	**Overall study status** Ongoing	
Last Edited 03/03/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Around a quarter of patients undergoing abdominal operations will develop an infection of the wound. If this occurs, they will need to stay in hospital for up to double the normal length to treat the infection, and they are likely to have increased levels of pain and subsequent hernia formation as well as cosmetically inferior scars. In rare cases an SSI can be very severe and cause or contribute towards a patient's death after surgery. SSI is also a significant problem for the NHS due to increased treatment costs and resource usage both in hospital and in the community. It is therefore a priority and a current NHS quality target to try and reduce SSI rates. There are many measures that surgeons can undertake during an operation to try to prevent SSI but very few of them have been subject to high-quality testing. This is often because trials undertaken to investigate them are too small or are not generalisable to the wider population. This trial has been carefully designed to investigate several interventions at once which makes it both cheaper and quicker than running several smaller separate trials. The aim of this study is to test whether a group of simple interventions, used alone or in combination during surgery, can reduce the chance of a patient developing a wound infection also known as a surgical site infection (SSI) after surgery on the abdomen (tummy).

Who can participate?
Patients 16 years or older, undergoing abdominal surgery of any type, both planned and unplanned, with an anticipated wound of at least 5 cm

What does the study involve?
Three in-theatre interventions are being assessed. Patients are randomly allocated to receive all, none or some of these in any combination. They are:
1. Chlorhexidine 2% alcohol skin preparation - a strong cleaning solution to cleanse and sterilise the skin before surgery. This will be compared against any other standard skin preparation that a surgeon may normally use.
2. An Iodophor-impregnated incise drape - a very thin plastic sheet stuck onto the skin before surgery and thought to prevent infection by trapping any bacteria left on the skin after preparation, as well as preventing new bacteria ingress. This will be compared against no drape.
3. Gentamicin-impregnated collagen implant/sponge - small absorbable sponges placed in the wound at the end of the operation that slowly disintegrate and deliver antibiotics locally to try

and kill any bacteria present that may go on to cause an SSI. This will be compared against no implant.
It is possible that these interventions might have a cumulative effect. This trial will both test each intervention and look in a rational fashion at how they might work together.

What are the possible benefits and risks of participating?
All interventions have the potential benefit of reducing the chances of developing an infection in the wound. The alternative possibility is that the interventions will not be of any benefit at all. To the best of the researchers' knowledge, none of the included interventions will increase the risk of getting a SSI and do not add any further risk to the operation itself. The skin preparation takes about 2-3 minutes to apply at the start of the operation as does the drape. The sponges are left in the wound at the end of the operation and take about 1-2 minutes to insert. As with any intervention, there is a rare risk of allergy. If patients have a documented or suspected allergy to any of the interventions (or its parts) we will not offer the patient that intervention but they can still participate in the trial.

Where is the study run from?
The study is coordinated from the University of Birmingham, Birmingham Clinical Trials Unit (BCTU).

When is the study starting and how long is it expected to run for?
March 2018 to October 2026

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
247285

ClinicalTrials.gov (NCT)
NCT03838575

Protocol serial number
CPMS 39722, IRAS 247285

Study information

Scientific Title
ROSSINI 2: A phase III, multi-arm, multi-stage (MAMS), pragmatic, blinded (patient and outcome assessor), multicentre, randomised controlled trial (RCT) with an internal pilot, to evaluate the use of several in-theatre interventions used alone or in combination, to reduce SSI rates in patients undergoing abdominal surgery

Acronym
ROSSINI 2

Study objectives
Current study hypothesis as of 24/03/2023:
Surgical site infection (SSI) is a significant problem for patients and the health service, but is potentially preventable. Up to 25% of patients undergoing abdominal operations will develop an SSI. At an average cost of £3500 per SSI, it has been estimated that SSIs currently cost the NHS around £700 million per year, largely through prolonged postoperative inpatient stay and additional inpatient and outpatient treatment costs.

There is a significant health need for research to address the problem of SSI, with benefit for both patients and the NHS. SSI is associated with considerable morbidity, a reduction in quality of life and increased healthcare costs, and places a significant burden on healthcare systems and individuals. Patients who develop SSIs have higher rates of pain and discomfort, with an increased risk of death following their operation.

Preventing SSI is a complex process which is affected by interventions throughout the surgical care pathway. SSI reduction measures when bundled, or poorly implemented can be ineffective or even increase SSI risk. A large proportion of SSIs are known to be caused by wound contamination by endogenous bacteria from the patient’s skin, or cross contamination from mucous membranes, hollow viscera, free pus or bowel content.

Unfortunately, clinical studies exploring the efficacy of many of these interventions are often underpowered or poorly designed, or used in low risk groups leaving uncertainty if they are clinically and cost-effective. ROSSINI 2 aims to study simple biologically plausible interventions that may decrease SSI rates after abdominal surgery, but currently lack evidence in controlled studies.

The aim of ROSSINI 2 is to determine whether several novel in-theatre interventions, used alone or in combination, result in decreased rates of SSI up to 30 days post operation in adult patient undergoing abdominal surgery.

Previous study hypothesis:
Surgical site infection (SSI) is a significant problem for patients and the health service, but is potentially preventable. Up to 25% of patients undergoing abdominal operations will develop an SSI. At an average cost of £3500 per SSI, it has been estimated that SSIs currently cost the NHS around £700 million per year, largely through prolonged postoperative inpatient stay and additional inpatient and outpatient treatment costs. Patients who develop SSIs have higher rates of pain and discomfort, with an increased risk of death following their operation.

The aim of ROSSINI 2 is to see whether three new in-theatre interventions, alone or in combination, reduce the rate of SSI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/01/2019, Wales REC 6, Fourth floor, Institute of Life Science 2, Swansea University, Singleton Park, SA2 8PP, UK; +44 (0)1792 606334; penny.beresford@wales.nhs.uk, ref: 19/WA /0019

Study design
Multi-arm, multi-stage (MAMS), pragmatic, multicentre, randomized controlled trial, with an internal pilot, exploring the use of several specific in-theatre interventions, used alone or in combination, to reduce the rates of SSIs. A non-factorial design with allocations to various combinations of the trial interventions to be used during the same operation. (Platform)

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Patients undergoing abdominal surgery for any indication

Interventions
Current interventions as of 03/03/2025:

The current interventions are:
A: None (Control)
I. Change of Gloves and Instruments immediately before fascial closure vs standard practice.
J: Dialkylcarbamoyl chloride (DACC) impregnated dressing.
K: Change of Gloves and Instruments immediately before fascial closure and Dialkylcarbamoyl chloride (DACC) impregnated dressing.

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Previous interventions as of 24/03/2023:

This multicentre, multi-arm, multi-stage, randomised clinical trial, will originally assess three separate in-theatre interventions used alone or in combination.

There will be a secure online randomisation system (available at https://w3.abdn.ac.uk/hsru/ROSSINI2) and an automated telephone randomisation system (available at +44 (0)800 2802 307) both managed by a third party (The Centre for Healthcare Randomised Trials (CHaRT) at The Institute of Applied Health Sciences at University of Aberdeen). Both systems will be available 24 hours a day, 7 days a week.

Participants will be randomised at the level of the individual in a 2:1 (control:research) ratio to either control or one of the intervention arms. There will initially be seven possible intervention arms and one control arm to which a patient can be randomised.

A minimisation algorithm will be used within the online randomisation system to ensure balance in the treatment allocation over the following variables:
1. Centre
2. Urgency (planned, unplanned)
3. Predicted contamination (clean, clean-contaminated, contaminated, dirty)
4. Stoma (yes – existing, yes – likely to be created during procedure, no - unlikely to be created during procedure)

The interventions include:
- 2% Alcoholic Chlorhexidine SKIN PREP
- Iodophor-impregnated incise DRAPE
- A Gentamicin-impregnated SPONGE

During Stage 1 and Stage 2 of ROSSINI 2, participants are randomised into the following arms:
A – Control (none)
B – Skin prep
C – Drape
D – Sponge
E – Skin prep and drape
F – Skin prep and sponge
G – Drape and sponge
H – Skin prep and drape and sponge

UPDATE (2021) :
On 15/12/2021, the results of the first interim analysis (end of Stage 2) were presented and reviewed by the independent DMC. They made the recommendation to drop the intervention arms containing Intervention 2, Iodophor-impregnated incise DRAPE. The DMC recommendations were discussed by the ROSSINI 2 TMG, independent TSC, Sponsor and Funder at a meeting on 07/01/2022. Following this meeting, it was agreed that the following arms containing Intervention 2, Iodophor-impregnated incise DRAPE, would close to recruitment:

C - DRAPE
E - SKIN PREP & DRAPE
G - DRAPE & SPONGE
H - SKIN PREP & DRAPE & SPONGE

UPDATE (2023):
On 25/01/2023, the results of the second interim analysis (end of Stage 3) were presented and

reviewed by the independent DMC. They made the recommendation to drop the intervention arms containing Intervention 3, Gentamicin-impregnated SPONGE. The DMC recommendations were discussed by the independent TSC, the ROSSINI 2 TMG and Sponsor at a meeting on 31/01 /2023. Following the meeting, it was agreed that the following arms containing Intervention 3, Gentamicin-impregnated SPONGE, would close to recruitment:

D - SPONGE
F - SKIN PREP & SPONGE

Each participant will undergo randomisation at time of surgery (Day 0) and will be expected to participate in ROSSINI 2 until their Day 30 Wound Assessment. Any patients who have an ongoing wound infection at 30 days postoperatively will continue to have ongoing active follow-up every 30 days until resolution to capture health economic and resource use data.

Previous interventions:
This multicentre, multi-arm, multi-stage, randomised clinical trial, will assess three separate in-theatre interventions used alone or in combination.

There will be a secure online randomisation system (available at https://w3.abdn.ac.uk/hsru /ROSSINI2) and an automated telephone randomisation system (available at 0800 2802 307) both managed by a 3rd party (The Centre for Healthcare Randomised Trials (CHaRT) at The Institute of Applied Health Sciences at University of Aberdeen). Both systems will be available 24 hours a day, 7 days a week.

Participants will be randomised at the level of the individual in a 2:1 (control:research) ratio to either control or one of the treatment groups. There will initially be seven possible treatment arms and one control arm to which a patient can be randomised.

A minimisation algorithm will be used within the online randomisation system to ensure balance in the treatment allocation over the following variables:
1. Centre
2. Urgency (planned, unplanned)
3. Predicted contamination (clean, clean-contaminated, contaminated, dirty)
4. Stoma (yes – existing, yes – likely to be created during procedure, no - unlikely to be created during procedure)

The interventions include a skin preparation solution (2% alcoholic chlorhexadine skin prep) that is applied to the skin before starting surgery, a skin drape (Iodophor-impregnated incise drape) - a thin impregnated plastic sheet applied to the skin before making the incision, and a sponge (gentamicin impregnated implant), which is an implant that contains antibiotics that is placed into the wound before closure.

Participants are randomised into the following arms:
A – Control (none)
B – Skin prep
C – Drape
D – Sponge
E – Skin prep and drape
F – Skin prep and sponge
G – Drape and sponge
H – Skin prep and drape and sponge

Each participant will undergo randomisation at time of surgery (Day 0) and will be expected to participate in ROSSINI 2 until their Day 30 Wound Assessment. Any patients who have an ongoing wound infection at 30-days postoperatively will continue to have ongoing active follow-up every 30 days until resolution to capture health economic and resource use data.

Intervention Type
Mixed

Primary outcome(s)
The SSI rate up to 30 days after surgery as defined according to the 2017 Centers for Disease Control (CDC) and Prevention criteria.
The following CDC definition will be used to identify deep incisional or superficial incisional SSIs:
1. The infection must occur within 30-days of the index operation
AND
2. The infection must involve the skin, subcutaneous, muscular or fascial layers of the incision
AND
3. The patient must have at least one of the following:
3.1. Purulent drainage from the incision
OR
3.2. Wound opened spontaneously or deliberately by a clinician
o AND the patient has at least one of: pain or tenderness; localised swelling; erythema or heat; fever (>38°C).
OR
3.3. Organisms are cultured from a culture taken from the wound using an aseptic technique
OR
3.4. Diagnosis of SSI by a clinician or on imaging

Key secondary outcome(s))
Current secondary outcome measures as of 24/03/2023:
1. 30-day postoperative mortality rate (POMR)
2. 30-day postoperative wound complication rate, assessed using Clavien-Dindo classification
3. Serious Adverse Events up to 30 days (wound or intervention-related only)
4. Length of hospital stay after surgery as measured from the date of surgery to the date of discharge
5. Hospital re-admission for wound-related complications within 30 days
6. Occurrence of unplanned wound reopening and/or re-operations within 30 days post-operation
7. Preference-based QoL measure (EQ-5D-5L) at baseline, Day 7 (or discharge) and Day 30
8. Cost-effectiveness, measured using health utility questionnaire at Day 30 and 'Ongoing SSI' (Day 60, Day 90 etc)

Previous secondary outcome measures:
1. 30-day postoperative mortality rate (POMR)
2. 30-day postoperative complication rate, assessed using Clavien-Dindo classification
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8. Cost-effectiveness, measured using health utility questionnaire at Day 30 and ‘Ongoing SSI’ (Day 60, Day 90 etc)

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/03/2023:

1. Patients undergoing an abdominal operation, these include colorectal, hepatobiliary, upper GI, urological, vascular, or gynaecological operations
2. Patients undergoing abdominal operations (open or laparoscopic extraction site) with a planned incision of at least 5 cm
3. Patients aged 16 years or older
4. Patients able and willing to undergo a wound assessment at day 30-37 after surgery
5. Patients able and willing to give written informed consent
6. All contamination strata, including clean, clean-contaminated, contaminated or dirty surgery
7. Patients undergoing planned (elective or expedited) or unplanned (emergency) surgery

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Previous inclusion criteria:

1. Patients undergoing colorectal, hepatobiliary, upper GI, urological, vascular, or gynaecological operations
2. Patients undergoing abdominal operations (open or laparoscopic extraction site) with a planned incision of at least 5 cm
3. Patients aged 16 years or older
4. Patients able and willing to give written informed consent
5. All contamination strata, including clean, clean-contaminated, contaminated or dirty surgery
6. Patients undergoing planned (elective or expedited) or unplanned (emergency) surgery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 03/03/2025:

1. Previous laparotomy within 3 months prior to randomisation
2. Operations where the wound is not anticipated to be closed primarily

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Previous exclusion criteria:

1. Previous laparotomy within 3 months prior to randomisation
2. Patients with a new or documented allergy/intolerance to any of the study interventions (chlorhexidine, iodine, collagen or gentamicin) will not be randomised to an arm containing this intervention, but will still be eligible for recruitment to other arms of the study
3. Patients with end-stage renal failure where gentamicin administration would otherwise be contra-indicated (according to local policy) will not be randomised to arms containing the gentamicin-impregnated sponge

Date of first enrolment
07/03/2019

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital Birmingham (lead site)
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2TH

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme; Grant Codes: 16/31/123

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request - exact details not yet known.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.0	03/09/2020	04/09/2020	No	Yes
Participant information sheet	version 2.0	24/01/2019	26/04/2023	No	Yes
Participant information sheet	version 3.0	18/07/2020	26/04/2023	No	Yes
Participant information sheet	version 4.0	12/07/2022	26/04/2023	No	Yes
Participant information sheet	version 5.0	24/02/2023	26/04/2023	No	Yes
Protocol file	version 1.0	02/12/2018	04/09/2020	No	No
Protocol file	version 2.0	18/07/2020	04/09/2020	No	No
Protocol file	version 3.0	12/07/2022	26/04/2023	No	No

Protocol file	version 4.0	24/02/2023	26/04/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes