TRIAL PROTOCOL

SUNRRISE

Single Use Negative pRessure dressing for Reduction In Surgical site infection following Emergency laparotomy

Version 3.0

5th August 2020

This protocol has regard for the HRA guidance

PROTOCOL DEVELOPMENT AND SIGN OFF

PROTOCOL CONTRIBUTORS

The protocol was written by the SUNRRISE Trial Management Group.

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
1	29-Oct-18	2.0	Substantial	• Update to oversight committee members. • Re-characterisation of eligibility criteria. • Clarification of consent process for participants lacking capacity in Scotland and participants losing capacity. • Update to consent/declaration forms and GP letter. • Clarification of the randomisation service. • Clarification excluded control interventions. • Inclusion of pain as a secondary outcome and addition of details of how/when this is assessed. • Inclusion of further patient diary for participants with SSI beyond 30 day and clarification on when its completion ends. • Clarification of aspects in the adverse events section, including i) inclusion of death as a reportable SAE and ii) addition of ileus as an SAE that does not require expedited reporting. • Clarification to the statistical considerations and health economics analysis sections. • Clarification that CRFs do not constitute source data • Substitution of date of birth for initials as identifier used to identify participants in correspondence alongside trial number. • Clarification of publication policy. • Minor charges relating to typographical errors, corrections to gramma and consistent/correct use of terminology.
2	05-Aug-20	3.0	Substantial	• Update oversight committee members. • Update to sponsor contact and details. • Expansion of trial setting to include Australia.so inclusion of Australian context and country-specific information. • Reference to COVID-19 added. • Minor alteration to eligibility criteria to reflect changes to follow-up due to COVID-19. • Clarification of inclusion of patients with a reasonable chance of laparotomy. • Clarification of training requirements and requirements of local team members undertaking wound reviews. • Clarification of secondary outcome to more accurately define parameters of length of stay. • Clarification to SAE reporting requirements. • Relaxation of 7-day review requirements by expansion of the window by 5 days. • Relaxation of 30-day review requirements to include remote completion of wound assessments (ideally by video call, and telephone where not possible), and expansion of the completion window by 7 days. • Minor clarifications and suggestion relating to the pathways and processes. • Clarification of the statistical analysis. • Minor administrative changes. • Minor changes relating to typographical errors, corrections to gramma and consistent/correct use of terminology.

FUNDING AND SUPPORT IN KIND	
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This is an investigator-initiated and investigator-led trial. The funders of the trial have no role in trial design, data collection, data analysis or data interpretation.	

REFERENCE NUMBERS	
Sponsor number	RG_17-239
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REC reference number	18/YH/0322 (England and Wales) 19/SS/0065 (Scotland)

CI SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol.

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 clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publically 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 planned in this protocol will be explained.

This protocol has been approved by:

Trial Name:	The SUNRRISE Trial
Protocol Version Number:	Version: 3.0
Protocol Version Date:	05 - Aug - 2020

CI Name:	Richard Wilkin
Trial Role:	Chief Investigator
Signature and date:	_____ __ __ / __ __ / __ __ __ __

Sponsor statement:

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

Compliance statement

This protocol describes the SUNRRISE Trial only. The protocol should not be used as a guide for the treatment of patients not taking part in the SUNRRISE Trial.

The study will be conducted in compliance with the approved protocol, UK Policy Framework for Health and Social Care Research 2017, the Data Protection Act 2018 and subsequent updates, and the principles of Good Clinical Practice as defined by the European Good Clinical Practice (GCP) Directive. 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.

PI SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Principal Investigator agrees to conduct the trial in compliance with the approved protocol.

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 clinical investigation without the prior written consent of the Sponsor.

This protocol has been approved by:

Trial Name:	The SUNRRISE Trial
Protocol Version Number:	Version: 3.0
Protocol Version Date:	05 - Aug - 2020
PI Name:	
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TRIAL SUMMARY

Title

Single Use Negative pRessure dressing for Reduction In Surgical site infection following Emergency laparotomy - The SUNRRISE Trial

Primary Objective

Does the use of a single-use negative pressure dressing (SUNPD) in adult patients undergoing emergency laparotomy reduce surgical site infection at 30 days post-operatively compared to cases not using the device?

Trial Design

- International, multicentre, prospective, phase III, 2 arm, randomised controlled trial with internal feasibility study; conducted in the UK and Australia under an overarching protocol with requisite country-specific adaptions, sponsored by the Universities of Birmingham (UK) and Newcastle (Australia) respectively.
- 840 participants will be randomised in a 1:1 ratio between SUNPD or surgeon's preference of dressings (which may be conventional occlusive dressings, skin glue or no dressing but not another SUNPD).

Key Eligibility Criteria

Inclusion Criteria

- Patients undergoing emergency (non-elective) laparotomy
- Procedures with a planned incision of at least 5cm
- Operations where the skin is closed primarily
- Patients aged at least 16 years in the UK, and at least 18 years in Australia
- Patient able to provide informed consent or, in the UK only, consultee/representative provides assent/consent if a patient temporarily lacks capacity
- Patients willing and able to undergo follow-up at 30 days post-op

Exclusion Criteria

- Abdominal surgery within the preceding three months from the date of randomisation
- Expected return to theatre for reopening of the laparotomy wound within 30 days

Intervention

Patients are randomised between the intervention group (SUNPD) and control group (surgeon's preference of dressing - excluding another type of negative pressure dressing). The randomisation will take place in theatre using an online or telephone-based randomisation system following commencement of closure of skin. The SUNPD will remain *in situ* for 7 days or until discharge, whichever is earlier.

Outcome Measures

Primary outcome:

- Surgical site infection within 30 days post-operation – as defined by the internationally accredited Centers for Disease Control (CDC) criteria.

Secondary outcomes:

- Length of hospital stay after surgery
- Wound complications as graded by the Clavien-Dindo scale
- Hospital re-admission rate for wound related complication within 30 days
- Health-related Quality of Life using Short Form-12 Health Survey (SF-12) and EuroQol-5 Dimension-5 Level (EQ-5D-5L)
- Serious adverse events
- Cost effectiveness
- Patient acceptability
- Health professional's acceptability of use of SUNPD (via a survey of users; UK only)

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1. BACKGROUND AND RATIONALE

1.1. Background

Surgical site infection (SSI) is a preventable post-operative complication that causes significant pain, suffering and even death. SSIs affect at least 200,000 patients in the UK each year[1-3]. At an average cost of £3500 per infection, SSIs currently cost the NHS approximately £700 million per year[4]. The rates and costs per patient are likely to be very similar in Australia, although there are no nationally collected statistics to reference. In addition to the financial burden of SSI, caused by prolonged post-operative inpatient stay and additional inpatient and outpatient treatment costs[5 6], there is significant association between the development of an SSI and morbidity and mortality rates[7]. Patients who develop an SSI are twice as likely to die as those without SSI, and around one third of post-operative deaths are attributable, at least in part, to SSI[8]. With antibiotic resistance becoming an increasingly serious global issue, there is significant health need for high quality research in this area, to try to address this potentially avoidable complication and thereby benefit both patients and healthcare providers.

Negative pressure wound therapy (NPWT) has been used since the mid-1990s to manage and promote healing in chronic open wounds. The closed negative-pressure environment serves to prevent bacterial ingress and removes blood and serous fluid exuding from the wound. Single-use Negative Pressure Dressings (SUNPD) have been developed for use on primarily closed incisions. These devices are small, highly portable and simple to apply. Their use in studies of non-abdominal wall incisions has resulted in a 50-80% reduction in SSI[9 10]. However, no multicentre, randomised controlled trials exploring the clinical effectiveness of SUNPD in reducing SSIs in patients undergoing emergency abdominal surgery have been reported.

1.2. Trial Rationale

1.2.1. Justification for participant population

Patients undergoing emergency laparotomy are at high risk of SSI

Rates of SSI vary significantly between different types of surgery. Abdominal operations carry one of the highest rates of SSI, particularly if the operation involves breach of the colon[1 11] and/or is performed in an emergency setting[12]. In the UK at present, over 30,000 emergency laparotomy operations are performed each year for a variety of life-threatening indications including intestinal obstruction, trauma, visceral perforation, ischaemia, or abdominal sepsis[13 14]. The comparable figure for Australia is approximately 12,000 procedures per year. These operations are associated with high rates of post-operative complications including SSI. High-quality studies in emergency laparotomy populations have shown consistently elevated SSI rates of 25-40% rendering this one the highest risk wounds for SSI of any surgical procedure[15 16].

Reduction of SSI rates following emergency laparotomy will clinically benefit patients

The extensive nature of emergency abdominal surgery, the inherent high levels of wound contamination and the physiological and immunological impairment produced by the underlying pathology mean that this group stands to gain significant clinical benefit from any reduction of further physiological insults such as the development of an SSI.

There are no planned or ongoing trials assessing SUNPD in the context of emergency laparotomy

There is a high level of interest in this type of intervention as indicated by several trials investigating these dressings in other types of incisions. The WHIST trial[17] is investigating the use of SUNPDs after traumatic lower limb fracture, while the DRESSING trial[18] investigates their use after Caesarean section. This shows that there is belief in the potential benefit of the dressings with utility across many different patient settings. However, there are no trials either in progress or under development that will identify results applicable to our patient group. The baseline characteristics of patients undergoing emergency laparotomy, including median

American Society of Anesthesiologists (ASA) grade, age range and level of field contamination are significantly different to the populations included in the WHIST and DRESSING trials, hence the results from these trials cannot be extrapolated to the high-risk population undergoing emergency laparotomy. A trial of SUNPD applied after emergency laparotomy is therefore essential to assess whether the device can reduce the incidence of SSI in this context.

1.2.2. Justification for design

The SUNRRISE Trial is an international, multicentre, pragmatic, phase III randomised controlled trial with internal feasibility study comparing the use of SUNPD with the surgeon's preferred dressing. The feasibility phase completed in the UK assessed the ability to recruit patients to the trial and whether or not participants tolerated the application of the SUNPD. Within SUNRRISE, surgeon's preference may be a simple self-adhesive wound dressing, glue as a dressing, or no dressing at all (but not another type of negative pressure dressing). Skin can be closed by suture (interrupted or continuous) or staples. Glue may not be used as a skin closure method in either arm of the trial. Glue can, however, be used as a dressing if the participant is randomised to the surgeon's preference of dressing arm.

Participants will be randomised to receive either SUNPD or surgeon's preference of dressing in a 1:1 ratio. Randomisation will take place after commencement of closure of skin to minimise any potential for bias due to technique changes due to knowledge of treatment allocation. Randomisation after commencement of skin closure also permits operation findings and procedures performed, i.e. the degree of contamination and whether or not a stoma was created, to be included as variables in the randomisation minimisation process. Randomisation will be done either online or via telephone, collecting only essential data, meaning this process will not delay application of the dressing or skin closure.

SUNRRISE is a pragmatic trial. The dressing allocation will not alter any other aspect of patient management. Participants entering the 'surgeon's preference of dressing' arm of the study will receive the dressing that the operating surgeon usually chooses. This pragmatic approach ensures that the trial reflects routine clinical practice as much as possible, making the results both more generalisable and a more accurate representation of the real-world effectiveness of the SUNPD devices.

The primary outcome measure is SSI within 30 days of surgery, as defined by the internationally accredited Centers for Disease Control (CDC) criteria. Wound assessment will be conducted by trained assessors at either day 7 (Days 5-10) post-operatively or discharge, whichever occurs first, and again at day 30 (Days 30-44) post-operatively. The assessors will be qualified medics or nurses and further trained in the diagnosis of SSI by undertaking an online module. The successful completion of this module is a requirement for a person to be included on the delegation log as a wound assessor for the trial. Participants will maintain a structured patient diary to identify the diagnosis of an SSI within the intervening time between the two assessments.

It is not feasible to blind either the participants or the wound assessors at day 7 to the randomised treatment allocation because the presence of the negative pressure dressing is clearly identifiable. The Day 30 wound review will be undertaken by another trained wound assessor blind to treatment allocation and not previously involved in the care of the participant.

1.2.3. Choice of intervention

Recognition of the detrimental impact of SSI has resulted in prioritisation of evidence based measures to reduce the incidence as described in the National Institute of Health and Care Excellence (NICE) guideline CG74 and Quality Standard QS49 in the United Kingdom[19 20] and in the World Health Organisation guidelines[21]. These measures include timely administration of prophylactic antibiotics, choice of anti-septic skin preparation agent and maintenance of pre-operative oxygenation levels.

One under-explored area is the role of dressings applied to the closed incision at the end of the operation[22]. Traditionally, the surgical incision is covered with a simple adhesive dressing to protect the wound from contamination from the outside environment. These 'standard dressings' have been used throughout the NHS and the Australian healthcare system for many years, but a recent Cochrane systematic review identified a lack of evidence confirming any positive role in the reduction of SSI from their use[23].

Negative pressure wound therapy has been used since the mid-1990s to manage and promote healing in chronic open wounds. In this treatment, a foam pad lies over the wound, covered with a semipermeable adhesive plastic membrane. A sealed tube connects the foam to an external pump, which creates a partial vacuum over the wound. This closed negative-pressure environment serves to prevent bacterial ingress and removes blood and serous fluid exuding from the wound. Traditional NPWT devices are large, cumbersome and required specialist training for application associated with extra cost. Newer SUNPDs are smaller, highly portable and simple to apply. Whilst well established in the open and traumatic/military wound settings, more recent evidence suggests that NPWT may be clinically effective in reducing complications when applied to primarily closed incisions[9, 10]. The therapy has been included in the recent World Health Organisation guidelines on preventing SSI[21]. These guidelines recommend the use of SUNPDs in high risk wounds while taking resources into account. However, authors recognise that their recommendation is based on low quality of evidence, the majority of which comes from retrospective observational studies at high risk of selection and publication bias. The central review article that the guideline is based upon calls for further randomised studies and recognises the shortcomings of the current research[24].

The SUNPD to be used in SUNRRISE is the Smith and Nephew® SUNPD PICO® dressing. This will be used in the intervention arm of the SUNRRISE Trial. The PICO dressing is a portable, topical negative pressure dressing that provides a negative pressure of 80mmHg across the area of application. Within the SUNRRISE Trial, the dressing will stay on for a maximum of 7 days or until discharge, whichever is sooner.

1.3. COVID-19

On 11th March 2020 the World Health Organization declared the international spread of COVID-19 to represent a global pandemic. The unprecedented impact on the NHS and wider UK society led to the vast majority of clinical research being paused whilst all efforts and attentions were redirected to dealing with the pandemic. Recruitment to SUNRRISE at all sites in the UK was centrally paused on Friday 20th March 2020. Australia experienced a reduction in the rate of patients being recruited during the initial impact of COVID-19 but the trial has remained open and recruitment has continued.

There will be long-reaching or even permanent changes to the NHS and Australian healthcare system structures for delivering both patient care and clinical research as a result of COVID-19. As a result of these, we have amended some trial processes and pathways in SUNRRISE to ensure safe and practicable reopening/continuation whilst protecting the scientific and methodological integrity of the trial. These changes have been necessary in the trial entry criteria (section 5.1) and follow-up (section 9.3).

There is no additional COVID-19 risk from participation in SUNRRISE. All participants entering the trial will have already had a decision made to undertake surgery and undergone appropriate local clinical pathways such as swabbing to mitigate risks from COVID-19; there are no additional direct risks from the trial pathways, interventions or wound assessments if a patient also participates in SUNRRISE.

All patients are eligible to enter the trial regardless of SARS-COV-2 virus/antibody status; positive, negative or not tested status. However, this this information will be collected to allow us to potentially assess the impact of these factors in the analysis.

2. FEASIBILITY STUDY

2.1. Aim of internal feasibility study

The success of the feasibility study was based on three factors:

- Patient recruitment
- Adherence to the intervention
- Study dropout

The number of participants to be recruited in the six-month internal feasibility period was 70 patients from at least 5 recruiting sites.

The decision for the trial to continue was decided by pre-defined stop-go criteria. A traffic light system was used to determine continuation to the full trial.

- Green: recruitment rate >70%, adherence rate >80%, and drop-out rate <20%
  - If all three criteria are met; continue the trial with protocol unchanged
- Amber: recruitment rate 50-70%, adherence rate 50-80%, or drop-out rate 20-35%
  - If one or more of our amber criteria are met, then the study will need review to see what changes (if any) could be made to improve whichever criteria are not at the "green" level
- Red: recruitment rate <50%, adherence rate <50%, or drop-out rate >35%
  - If one or more of these criteria are met, we will discuss with the Trial Steering Committee (TSC) and the funder regarding feasibility of the study continuing

The definitions of the factors used in the stop-go criteria were:

- Recruitment rates: proportion of recruitment target achieved (aim is to recruit 70 patients)
- Successful adherence to the trial arm allocated: successful application of the appropriate dressing for at least 24 hours
- Study drop-out: complete withdrawal from the study, with no further data to be collected from the participant

In addition to these stop-go criteria, there was an assessment of safety by the Data Monitoring Committee (DMC) at the end of the feasibility phase. The decision regarding continuing the randomised controlled study was made by the TSC based on the traffic light criteria above, and confirmation from the DMC that there were no safety issues to prevent the trial from continuing.

2.2. Outcome of internal feasibility study

The feasibility study showed that patient recruitment and the randomisation process were feasible. The adherence rate was high and drop-out rate was low with all stop-go criteria, achieving the GREEN categorisation, and the trial continued with no change to the protocol.

3. AIMS AND OBJECTIVES

3.1. Aims of phase III study

Primary Objective:

To determine if the use of a SUNPD in adult patients undergoing emergency laparotomy reduces SSI at 30 days compared to surgeon's preference of dressing (which may be conventional occlusive dressings, skin glue or no dressing but not another SUNPD).

Secondary Objectives:

To determine if:

- The use of SUNPD reduces length of hospital stay after surgery
- The use of SUNPD reduces the rate of wound complications
- The use of SUNPD reduces wound complication related hospital re-admission rates
- The use of SUNPD improves health-related quality of life
- The use of SUNPD is safe in this population
- The use of SUNPD is acceptable to patients and healthcare professionals
- The use of a SUNPD is cost-effective compared to the use of the surgeon's preference of dressing

3.2. Comparison of a new method of diagnosing surgical site infection

The current established method of diagnosing SSIs is using the CDC criteria. These criteria are used for the diagnosis of wound infections in this study. The use of the CDC criteria for diagnosing wound infections involves assessment of the wound by a health professional. A new tool for diagnosing wound infections (Bluebelle) has been developed that does not require a clinical assessment[25]. This trial will allow the comparison of this tool with the clinical wound review assessment as per the CDC criteria.

4. TRIAL DESIGN AND SETTING

4.1. Trial Design

The SUNRRISE Trial is an international, multicentre, pragmatic, phase III randomised controlled trial with internal feasibility study comparing the use of SUNPD with the surgeon's preference of dressing (which may be conventional occlusive dressings, skin glue or no dressing, but not another SUNPD) after emergency laparotomy surgery. The study will take place in sites in both the UK and Australia.

4.2. Trial Setting

Any hospital undertaking emergency abdominal surgery in the UK or Australia will be eligible to participate in the trial. Prior to opening, all sites must undergo study-specific training, both on the logistical and operational aspects of the trial, and in the correct use of the SUNPD.

SUNPD training will include a standardised, optimal method of their use and will be delivered either face-to-face or via teleconference/video conference. Study-specific and SUNPD application training can be disseminated to the other members of the research team by the Principal Investigator (PI) or nominated delegates, such as the associate PI/lead trainee and/or lead research nurse. This will be captured on the SUNRRISE Site Signature and Delegation Log and SUNRRISE Training Log.

Patients who may be eligible for inclusion in the study will be identified by either the consultant or trainee surgeon once the decision to take the patient to theatre has been made.

Inpatient wound assessments (at day 7 or at discharge, whichever is first) will occur on the surgical ward. The wound assessments at day 30 will be performed in an outpatient review (or on the surgical ward in the event of the participant having not been discharged yet). The outpatient assessment may be conducted in-person or remotely.

5. ELIGIBILITY

5.1. Inclusion Criteria

- Patients undergoing emergency (non-elective) laparotomy
- Procedures with an incision of at least 5cm
- Operations where the skin is closed primarily
- Patients aged at least 16 years in UK, or at least 18 years in Australia
- Patients able to provide informed consent or, in the UK only, consultee/representative provides assent/consent if a patient temporarily lacks capacity
- Patients willing and able to undergo follow-up at 30 days post-op

5.2. Exclusion Criteria

- Abdominal surgery within the preceding three months of randomisation
- Expected return to theatre for reopening of the laparotomy wound within 30 days.

5.3. Laparoscopic surgery

Some emergency patients will undergo a laparoscopic operation. If the operation is completed laparoscopically the patient will not be eligible for SUNRRISE because the incision will be less than 5cm. Some patients undergoing laparoscopic surgery will be converted to an open operation with an incision of greater than 5cm and thus become eligible for SUNRRISE.

If there is a reasonable chance of conversion to an open operation, a patient can be approached and consented for potential entry into the trial. Given that all patients must provide written informed consent prior to surgery, it will be the responsibility of the consenting member of the research team to inform the patient at the time of consenting, that depending on the nature of their surgery, they may become ineligible to participate in the study.

If the operation is completed laparoscopically in its entirety with only incisions less than 5cm, they should not be randomised. If the operation is converted to open and an incision over 5cm is made, the patient should be randomised in the usual manner when skin closure has been commenced.

6. CONSENT

The majority of patients undergoing emergency laparotomy will be able to provide fully informed consent. There are, however, a proportion of patients who meet the inclusion criteria for the study who are either unable to provide full consent or are not able to consent at all due to a temporary impairment resulting from the indication for their emergency laparotomy. Patients may be unconscious, critically unwell, distracted by pain or anxiety, or have received large doses of opiates for pain relief, potentially affecting their ability to process information. The methods of gaining consent for inclusion in the study are different for patients who are able to provide consent and those who are not. The law around recruitment of patients that lack capacity is governed under the Mental Capacity Act in England and Wales and by Adults with Incapacity (Scotland) Act in Scotland. The terminology within each Act is different and as a result Section 6.2 of this protocol will

explain the process for including patients without capacity in England and Wales and Section 6.3 will cover patients in Scotland. Patients that temporarily lack capacity to consent will not be enrolled in Australia.

Due to the nature of emergency laparotomy, the time from the patient being approached for participation in the study and recruitment may be limited. There is therefore no minimum time between the patient (or consultee/representative) being given the information sheet for the trial and consent being obtained. This has been subject to consultation with patient representatives and approved by UK NHS and Australian research ethics committees.

6.1. Patients able to provide informed consent

It will be the responsibility of the Investigator to obtain written informed consent for each participant prior to performing any trial related procedures. Members of the extended research team including consultants, registrars, core-trainees and foundation doctors as well as research nurses will be able to take consent as delegated by the PI (delegates).

The delegates who are permitted to take consent will be captured on the SUNRRISE Site Signature and Delegation Log. All those delegated to take consent must have undertaken Good Clinical Practice (GCP) training.

Investigators and delegates will ensure that they adequately explain:

- That consent is being sought for inclusion in a randomised controlled trial
- The trial is comparing different dressings aiming to reduce SSI rates
- That the intervention they receive will be allocated at random
- That participation is voluntary and the participant is free to refuse to take part and may withdraw from the trial at any time, without impact on their clinical care
- That one additional follow-up review at 30 days post-surgery is required
- That on discharge from hospital, they will be provided with a diary to fill out detailing interactions with healthcare professionals and an assessment of their health status
- That the participant will be contacted at weekly intervals via telephone or text to remind them to fill out the Patient Diary

Following discussion of the trial, the participant will be given the opportunity to ask questions. A Patient Information Sheet (PIS) will be provided to facilitate the consent process.

If the participant agrees to participate in the trial, they will be asked to initial, sign and date the latest version of the Informed Consent Form (ICF). The Investigator or delegate will then sign and date the form. A copy of the ICF will be given to the participant, a copy will be filed in the medical notes, a copy sent to the relevant SUNRRISE Trial Office; Birmingham Clinical Trials Unit (BCTU) for participants in the UK and the University of Newcastle, Australia for participants in Australia. The original ICF is to be placed in the Investigator Site File (ISF).

Details of the informed consent discussions will be recorded in the participant's medical notes. This will include the date of discussion, name of the trial, summary of discussion, version number of the PIS given to participant, version number of ICF signed and date consent received.

At each trial review, the participant's willingness to continue in the trial will be ascertained and documented in the medical notes. Throughout the trial the participant will have the opportunity to ask questions about the trial. Any new information that may be relevant to the participant's continued participation will be provided. Where new information becomes available which may affect the participants' decision to continue,

participants will be given time to consider and if happy to continue will be re-consented. Re-consent will be documented in the medical notes. The participant's right to withdraw from the trial will remain.

In the UK, if a participant loses capacity during the 30-day study period the advice/consent of a Personal Consultee/legal representative on whether the participant should remain in the study will be sought and a declaration/consent obtained as described in sections 6.2 and 6.3.

Electronic copies of the PIS and ICF will be available from the relevant SUNRRISE Trial Office; Birmingham Clinical Trials Unit (BCTU) for participants in the UK and the University of Newcastle, Australia for participants in Australia. They are to be printed or photocopied onto the headed paper of the local institution. Details of all participants approached about the trial will be recorded on the SUNRRISE Participant Screening Log.

With the participant's prior consent, their General Practitioner (GP) will also be informed that they are taking part in the trial.

6.2. Patients unable to provide informed consent (England and Wales)

Some patients who are eligible for the trial will have a temporary impairment to their ability to provide consent. This impairment will result from the condition for which they require surgical intervention. Patients who have a long-term cognitive impairment that prevents fully informed consent will be excluded from the trial.

If the patient does not have capacity for fully informed consent due to temporary impairment, where possible the trial will be briefly discussed with them, and they will be given the Summary Patient Information Sheet. In accordance with guidelines from the Health Research Authority (HRA), the trial will also be discussed with the patient's relative or carer (Personal Consultee). The Personal Consultee will be asked if the patient has expressed any prior wishes with regard to participating in research and if the patient has expressed a preference then this will be adhered to. The relative is not asked to provide consent on behalf of the patient, but rather provide an opinion on the views and feelings of the potential participant.

The patient's relative/carer must be:

- Told that they are being asked to advise on the views and feelings they believe the adult would have towards participation in the study
- Told that they are free to decide whether they wish to provide this advice or not
- Given sufficient information, in an understandable form, about the study to ensure that they provide informed advice

A Consultee Information Sheet will be provided to facilitate the assent process. If the consultee agrees that the patient should be included in the trial, the consultee will initial, sign and date the latest version of the Consultee Declaration Form.

If no Personal Consultee is available, the patient will not be included in the trial.

It is imperative that when a Personal Consultee has been consulted, as soon as the participant is able to provide informed consent, the trial is explained to them and their written informed consent is sought. The participant will be given the Patient Information Sheet for delayed consent and their consent will be documented through the initialling, signing and dating of the latest version of the Informed Consent Form for delayed consent.

If, at any stage, the participant refuses consent for involvement in the trial or asks to be withdrawn from the trial, their wishes must be adhered to.

For a small number of patients (<2%) it is anticipated that they will not regain consciousness/capacity within 30 days, as these patients will have already received the intervention and reached the primary outcome, their data will be retained for use in the final analysis. If these patients regain capacity after 30 days, where practical, the local research team will consent them for their involvement in the study.

6.3. Patients unable to provide informed consent (Scotland)

Some patients who are eligible for the trial will have a temporary impairment to their ability to provide consent. This impairment will result from the condition for which they require surgical intervention. Patients who have a long-term cognitive impairment that prevents fully informed consent will be excluded from the trial.

If the patient does not have capacity for fully informed consent due to temporary impairment, where possible the trial will be briefly discussed with them, and they will be given the Summary Patient Information Sheet. In accordance with guidelines from the HRA, the trial will also be discussed with the patient's legal representative. For the purposes of SUNRRISE, a patient's legal representative will be their nearest relative (See Appendix 1 for a hierarchical list of nearest relatives). Patients with long-term incapacity are not included in this trial so patients that have appointed a Welfare Attorney or Guardian will not be eligible.

The legal representative must be:

- Told that they are being ask to give consent on behalf of the incapacitated adult
- Told that they are free to decide whether they wish to make this decision or not
- Told that they are being asked to consider what the adult would want, and to set aside their own personal views when making this decision
- Given sufficient information, in an understandable form, about the trial to ensure that they can make an informed decision

A Legal Representative (Nearest Relative) Information Sheet will be provided to facilitate the consent process. If the legal representative consents for the patient to be included in the trial, the legal representative will initial, sign and date the latest version of the Legal Representative (Nearest Relative) Consent Form. If no legal representative is available, the patient will not be included in the trial.

It is imperative that when a legal representative has been consulted, as soon as the participant is able to provide informed consent, the trial is explained to them and their written informed consent is sought. The participant will be given the Patient Information Sheet for delayed consent and their consent will be documented through the initialling, signing and dating of the latest version of the Informed Consent Form for delayed consent.

If, at any stage, the participant refuses consent for involvement in the trial or asks to be withdrawn from the trial, their wishes must be adhered to.

For a small number of patients (<2%) it is anticipated that they will not regain consciousness /capacity within 30 days, as these patients will have already received the intervention and reached the primary outcome, their data will be retained for use in the final analysis. If these patients regain capacity after 30 days, where practical, the local research team will consent them for their involvement in the study.

6.4. Patients unable to provide informed consent (Australia)

Patients that are unable to provide informed consent in Australia will not be eligible to be enrolled in the trial.

7. RECRUITMENT AND RANDOMISATION

7.1. Participant identification and recruitment

Patients who may be eligible for inclusion in the study will be identified by either the consultant or trainee surgeon once the decision to take them to theatre has been made. Patients will be approached by a GCP trained member of the research team. This member of the research team may be either a member of the clinical team or a research nurse. The consent process will be undertaken as detailed in Section 6.

7.2. Screening logs

Screening logs will be kept in accordance with the CONSORT guidance and GCP, and filled in the ISF.

To aid completion of the SUNRRISE Participant Screening Log, on a weekly or monthly basis a member of the research team will check the theatre logbook (paper or computer based depending on local arrangements) to identify patients who have undergone an emergency laparotomy but were not randomised into the trial. The reasons for non-randomisation will be recorded on the screening log. This information may be found by reviewing the patient record or liaising with the clinical team.

7.3. Randomisation

Following consent, the participant must undergo an emergency (non-elective) laparotomy as described in the inclusion criteria to be randomised into the study. If a participant becomes ineligible, due to either pre-operative events that occur post-consent or intra-operative findings, they will not be randomised. This will be recorded in the SUNRRISE Participant Screening Log as well as the patient notes.

To minimise any potential for bias due to changes in closure technique caused by knowledge of the treatment allocation, randomisation will take place in theatre following commencement of skin closure. This timing of randomisation will also allow minimisation according to the actual operation findings and procedure performed.

Randomisation will be provided by an automated telephone randomisation system (available on **UK: 0800 2802 307** and **AUS: 001144800 2802 307**) and a secure online randomisation system (available at https://w3.abdn.ac.uk/hsru/SUNRRISE), both managed by a third party. Unique log-in usernames and passwords will be provided to those who wish to use the online system and who have been delegated the role of randomising participants into the study as detailed on the SUNRRISE Site Signature and Delegation Log. Recruiting sites will be issued a unique trial centre ID number/code to allow use of the telephone system. Both the online and telephone systems will be available 24 hours a day, 7 days a week apart from short periods of scheduled maintenance.

After participant eligibility has been confirmed and informed consent has been received, and following emergency (non-elective) laparotomy, the participant can be randomised into the trial. Paper Randomisation Forms will be provided to investigators and may be used to collate the necessary information prior to randomisation. All questions and data items on the Randomisation Form must be answered as instructed on the Case Report Form (CRF) before a trial number and treatment allocation can be given by the randomisation service. If required data items are missing, the randomisation will not be completed. Only when all the required data items are provided can randomisation be performed and a trial number and treatment allocation be provided.

Participants will be randomised in theatre by the operative team following commencement of closure of skin. Participants will be randomised at the level of the individual in a 1:1 ratio. A minimisation algorithm will be

used within the randomisation system to ensure balance in the treatment allocation over the following variables:

- Degree of contamination (clean, clean contaminated, contaminated, dirty)
- Whether or not a stoma is present (yes, no)
  - *If a stoma is present, whether it was pre-existing or formed during the operation will also be ascertained. However, this distinction will not be factored in to the minimisation process.*
- Recruiting site

So that the randomisation process is not completely deterministic, a 'random element' will be included in the minimisation algorithm. Following randomisation, a confirmatory email will be sent to the P I and nominated key members of the research team for the site.

The Investigator must keep and maintain the SUNRRISE Patient Identification Log, which links participants with their allocated trial number, and is not for submission to the Trials Office. The Investigator will also keep and maintain the SUNRRISE Screening Log which will be kept in the ISF, and should be available to be sent to the Trials Office upon request. The SUNRRISE Patient Identification Log and SUNRRISE Screening Log should be held in strict confidence.

7.4. Informing the participant's GP

If the participant (or their Personal Consultee or legal representative) has agreed, the participant's GP should be notified that they are in the SUNRRISE Trial, using the SUNRRISE GP Letter.

7.5. Blinding

It is not feasible to blind either the participants or the inpatient wound assessors at day 7 to treatment allocation because the presence of the negative pressure dressing is clearly identifiable. The Day 30 wound review will be undertaken by a trained wound assessor who will be blind to treatment allocation and who has not previously been involved in the care of the participant. The importance of blinding will be explained to participants and they will be asked to not inform the wound assessor of their treatment arm.

8. TRIAL INTERVENTION

8.1. Trial Intervention

The trial intervention is the application of a SUNPD. The Smith and Nephew SUNPD is a CE-marked device, Therapeutic Goods Administration (TGA) approved, and available for routine clinical use throughout the UK and Australia. It will be used within its licensed indication in the SUNRRISE Trial. The SUNPD will be left *in situ* until discharge from hospital or until day 7 post-operatively (whichever is sooner). The dressing should not be routinely changed but if, for a clinical reason, the dressing needs to be changed, it should be replaced with another SUNPD (there are two dressings supplied in each dressing box which will allow one change at no extra cost). This change of dressing should be recorded on the Wound Assessment Day 7 or on Discharge (if sooner) CRF.

The control is the surgeon's preference of dressing (which may be conventional occlusive dressings, skin glue or no dressing, but cannot be another SUNPD). These will be left *in situ* according to local practice. When conventional occlusive dressings are used, it is expected that most participants will have this changed in hospital and discharged with a dressing in place.

8.1.1. Standardisation of dressing placement

As part of site set up, training will be provided for the PI and all research team members delivering the intervention involved in the trial in the optimum method of placement of dressings (see section 4.2). This will be provided prior to site opening to recruitment. It will then be the responsibility of the local PI to ensure that new members of the local research team are trained on placing the dressing. A summary of the method of placement will be displayed on the wall in theatre and also available in the box in theatres where the dressings are kept.

SUNPD application training can be disseminated to the other members of the research team by the PI or nominated delegates, such as the associate PI/lead trainee and/or lead research nurse. This will be captured on the SUNRRISE Site Signature and Delegation Log and SUNRRISE Training Log.

8.2. Intervention Supply and Storage

8.2.1. SUNPD Supply

Supply of the SUNPD will be maintained at the participating hospital. An initial supply of the SUNPD will be delivered to each site prior to site opening. It will then be the responsibility of the relevant SUNRRISE Trial Office to arrange for appropriate resupply and delivery arrangements to be in place at each participating hospital. The process for this will be explained during the Site Initiation Visit.

8.2.2. Dressing Storage

Appropriate arrangements must be made to ensure availability of the dressings when needed, while also ensuring that dressings supplied for the trial are not used for non-trial indications. It is recommended that the intervention dressings are stored in a marked ‘SUNPD for SUNRRISE Trial use only’ box in the emergency theatre complex. Instead of the whole stock of dressings being stored in theatres, it is advised that the research nurse/PI/Lead trainee at each site keeps the majority of the dressing stock in a secure office and regularly re-supplies the theatre box.

8.3. Dressing application

Dressings shall be applied according to manufacturer’s instructions and as shown during the site training sessions. A guideline for placement of the dressings will be provided for site use. A laminated copy of this will be provided for display in theatres used for emergency laparotomies and also for storage in the ‘SUNPD for SUNRRISE Trial use only’ box.

Once the dressings have been placed and the negative pressure commenced, any leaks should be patched with the provided reinforcement strips. The second dressing that comes in each PICO pack should be kept with the participant and if the original dressing becomes saturated during the seven days of negative pressure, the old dressing should be removed and a new dressing applied. The patching of the dressing and replacement of the dressing can be undertaken by a suitably qualified and experienced member of the participant’s clinical team. The dressings should otherwise be left in place until the pre-discharge / Day 7 wound inspection by a member of the research team. On the day of the wound assessment, the dressing will be removed by a member of the nursing staff or the research team. If the dressing has to be removed for any other reason, this should be recorded in the participant’s medical notes. The timing and reason for removal will be recorded in the Wound Assessment Day 7 or on Discharge (if sooner) CRF.

It is important to note that this is a pragmatic trial with minimal interference with the usual practice of the operating surgeon. One step that is controlled within the protocol is the closure of skin. The skin should be closed by either sutures (can be interrupted or continuous) or skin closure staples. **Glue cannot be used as a primary skin closure method in either group.** If the participant is randomised to the control arm (i.e. standard dressing), glue can be used as a wound dressing (if this is the surgeon’s normal practice).

Alternative methods of dressing are a conventional simple (not silver, honey or iodine) occlusive dressing or no dressing at all. Another type of negative pressure dressing cannot be used in the control arm.

8.4. Treatment Modification

Treatment modification is not expected to be relevant to this trial.

If the dressing is removed during a theatre visit within 7 days of the index laparotomy, the same type of dressing will be reapplied to the wound at the end of the procedure, i.e. if allocated to the SUNPD dressing, a SUNPD will be reapplied at the end of the operation. The treatment period remains 7 days from the index laparotomy. If the participant has been allocated to the control arm a dressing of the surgeon's choice will be applied as long as this is not a SUNPD. If the procedure takes place longer than 7 days after the original operation, regardless of the randomised allocation, at the end of the operation a dressing of the surgeon's choice will be applied (as long as this is not a SUNPD).

If the participant returns to theatre within 30 days, a Return to Theatre form should be completed by the research team in conjunction with the surgeon undertaking the surgery.

9. OUTCOME MEASURES AND STUDY PROCEDURES

9.1. Primary Outcome

The primary outcome is SSI within 30 days of surgery, as defined by the internationally accredited CDC criteria. Wound assessment will be conducted at day 7 post-operation or on discharge (whichever is sooner). It will also be performed at day 30 post-operation, by a blinded and trained wound assessor. The intervening period will be covered by a structured patient diary.

The following CDC definition will be used to identify an SSI:

- The infection must occur within 30-days of the index operation

AND

- The patient must have at least one of the following:
  - Purulent drainage from the wound
  - Organisms are detected from a wound swab
  - Wound opened spontaneously or by a clinician AND, at the surgical wound, the patient has at least one of: pain or tenderness; localised swelling; redness; heat; systemic fever (>38°C).
  - Diagnosis of SSI by a clinician or on imaging

9.1.1. Training in diagnosis of surgical site infections

All research team members who are undertaking wound assessments will be required to undertake the online module for the diagnosis of surgical site infections. This will ensure standardisation of diagnosis and can be accessed via the trial websites (UK: www.birmingham.ac.uk/SUNRRISE, AUS: https://hmri.org.au/sunrrise-trial) or directly using this following link: https://bctu-redcap.bham.ac.uk/surveys/?s=DFPM7YMKRJ. The assessors will hold medical or nursing qualifications; for example, doctors, nurses, advanced care practitioners or physician associates.

9.2. Secondary Outcomes

- Length of hospital stay after surgery as measured from the date of index surgery to the date of discharge

- Wound complications within 30 days post-surgery as graded by Clavien-Dindo scale (see Appendix 2)
- Hospital re-admission for wound related complications within 30 days. These will include SSIs, wound breakdown/dehiscence, seromas and wound related pain
- Health-related Quality of Life assessed using the validated Short Form-12 (SF-12) questionnaire at baseline, and day 7 and day 30, and the EuroQuol-5 Dimension-5 Level (EQ-5D-5L) at baseline, day 7, day 14, day 21 and day 30. Pain at the site of the primary laparotomy will also be assessed, using a Likert scale of 1-10 at day 7 and day 30
- Serious adverse events up to 30 days
- Cost-effectiveness assessed using a patient diary for patient reported healthcare resource usage. Healthcare usage will be taken directly from the patient diaries and the costs attributable to this will be identified
- Patient acceptability of use of their dressing via an acceptability score using a Likert scale of 1-10 at day 7, reflecting participant's assessment of the acceptability of having the dressing
- In the UK only, Health professional's acceptability of use of SUNPD (via a survey of users). This will focus on the ease of application of the dressing, the care needed to maintain/monitor the dressing while it is in place and an overall assessment of health professional's experience of the dressing

9.3. Trial Assessments

9.3.1. Screening, consent and randomisation

Screening will be undertaken by the clinical team. The clinical team will ensure that the patient meets the eligibility criteria. Once the patient has been identified they will be entered onto the screening log.

The identifying doctors/nurse/research team member should provide the PIS to the patient. If they are included on the Site Signature and Delegation Log, consent can also be taken at this stage. If they are not on the delegation log, consent should be taken by a member of the site research team.

Once written informed consent has been obtained, the Randomisation Form can be populated with demographic data by the member of the research team, a baseline EQ-5D-5L and SF-12 questionnaires will be given to the participant to complete. The participant is to be guided to complete the questions based on their health and wellbeing prior to the start of the episode that requires surgery.

9.3.2. Intervention

Once the pertinent operative details are known they should be added to the Randomisation Form. Following commencement of closure of the surgical skin wound, the operative details can be added to the Randomisation Form and randomisation process can take place. The participant will be randomised to receive either SUNPD or the surgeon's preference of dressing. The relevant dressing will then be applied in the operating theatre.

The In-Theatre form will be completed at the end of the operation. If allocated to the intervention arm, the LOT number of the dressing used will be documented on the CRF. Where possible, the operation note should not document the dressing that is used to aid blinding at the Day 30 wound review. The operation note should document that the wound was dressed "according to SUNRRISE Trial allocation" or equivalent.

9.3.3. Day 7 (or on discharge if sooner) assessment

At day 7 (assessment window: Days 5 to 10) or on discharge (whichever is first), the wound will be inspected to determine if there is any evidence of wound infection and whatever dressing is in situ removed to facilitate this. If the patient has a SUNPD in place this must be removed on day 7 at the latest. This means that if the

wound review is being performed on day 5, the dressing is removed on day 5 and the wound assessment is performed. If the wound assessment is being performed on day 9, the SUNPD is removed on day 7 and replaced with a standard dressing until day 9 when the wound is reviewed.

The wound inspection will be undertaken by a member of the research team who has been trained in the diagnosis of wound infections by undertaking the online module (can be accessed via the trial websites (UK: http://www.birmingham.ac.uk/SUNRRISE, AUS: https://hmri.org.au/sunrrise-trial), or directly using this following link: https://bctu-redcap.bham.ac.uk/surveys/?s=DFPM7YMKRJ).

As part of this wound inspection, the Wound Assessment Day 7 or on Discharge (if sooner) CRF will be completed, which includes asking the participant to rate their wound pain using a 10-point Likert scale. The participant will also be asked to complete EQ-5D-5L and SF-12 Quality of Life questionnaires and they will be given their outpatient diary. If the assessment at day 7 is undertaken when the participant is still an inpatient, the questionnaires will be completed using either the forms in the diary or separate Quality of Life questionnaires (as used at baseline). If the participant is being discharged before day 7 (and hence the wound assessment is being performed before day 7), the participant will be instructed to complete the EQ-5D-5L and SF-12 at day 7 post-operatively. These forms will be found in their Patient Diary.

9.3.4. Inpatient data capture

While the participant is in hospital, they will not be asked to complete the daily questions in the Patient Diary. If the participant is in hospital at days 7, 14, 21 or 30 post-operatively, they will be asked to complete the EQ-5D-5L assessment (days 7, 14, 21 and 30) and the SF-12 questionnaire (days 7 and 30). It is recommended that separate Quality of Life questionnaires (as used at baseline) be used whilst a participant is an inpatient but these forms in the Patient Diary can be used. If the participant is an inpatient at the time of the Day 30 assessment, the Bluebelle wound healing questionnaire does not need to be completed.

9.3.5. Outpatient data capture

Following discharge from the hospital, a Patient Diary will be used to record health care intervention, diagnosis of wound infection, dressing changes, antibiotics used and quality of life (EQ-5D-5L at day 7, 14, 21 and 30, and SF-12 at day 30). If the date of discharge is after day 7, then the relevant days that have passed whilst the participant is in hospital will be crossed off by the research team, ensuring that the participant starts to fill out the diary on the correct day. There will be no collection of health resource usage whist the participant is in hospital.

To help with completing the diary, a member of the research team will contact the participant by telephone or text message (as dictated by participant choice) every week to provide assistance and also to arrange their outpatient review. Prior to the review at day 30, the Bluebelle wound healing questionnaire in the diary should be completed by the participant. If the day 30 review is completed in person the diary should be collected from the participant at this hospital visit. If the day 30 review is conducted remotely the participant should be reminded to post it back to the SUNRRISE Trial Office.

9.3.6. Day 30 assessment

At day 30 (assessment window: Days 30-44; with day 0 being the day of randomisation), a blinded review will take place. If an in-person wound assessment is not possible as the patient is not able to return for an outpatient or research visit to the hospital, this wound assessment is to be conducted using real-time remote video consultation. Telephone follow up assessments of the patient and their wound status can be used as a last resort. The wound will be assessed for an infection according to the CDC SSI criteria. As part of the assessment the highest Clavien-Dindo grade of wound complication that occurred since surgery will be recorded[26].

As part of this wound inspection, the Wound Assessment Day 30 CRF will be completed, which includes asking the participant to rate their wound pain using a 10-point visual analogue scale. The participant will also be asked to complete the Quality of Life questionnaires, EQ-5D-5L and SF-12, if they have not already done so in the Patient Diary. If no wound infection is evident then the participant will have completed the study.

Prior to undergoing the Day 30 review, the participant will have completed the Bluebelle wound healing questionnaire in the Patient Diary. This assessment will be repeated with the wound assessor as part of the Day 30 review and will allow SUNRRISE to compare results with the Bluebelle questionnaire. However, if the participant remains an inpatient at the time of the Day 30 assessment, the questionnaire does not need to be completed by the patient or repeated with the wound assessor.

In order to encourage and facilitate patients to attend their in-person wound review at day 30 (where appropriate), their travel expenses in the form of taxi fares, public transport costs or parking charges will be supported.

9.3.7. Assessments after 30 days

A small number of participants will have an SSI that has not healed (ongoing SSI) at the Day 30 review. These participants will be given a second Patient Diary (Continuing involvement) and asked to complete it. If the patient is followed up remotely, the patient will be sent a Patient Diary (Continuing involvement) through the post. When the wound has healed, indicated by discharge from district nursing care or from the care of the treating clinician, the participant can stop using the Patient Diary and return it to the research team or SUNRRISE Trial Office. A very small proportion of these participants will have a long term, ongoing wound infection. It is important to identify and collect data on this small number of participants as they will incur a significant amount of healthcare costs and influence the health economics analysis. Data on interventions for wound infections, contact with healthcare professionals and ongoing wound care management is very important during this part of the data collection. Participants will be asked to continue with the diary until their wound heals or the trial follow-up period (participants may need several diaries). The research team looking after the participant will liaise with the participant to find the most practical way of managing the need for ongoing diaries. This may mean exchange of diaries via post, or when the participant visits the hospital for another reason.

9.3.8. Patient and healthcare professional acceptability of intervention

In order to assess the acceptability of the SUNPD, participants and healthcare professionals will be asked for their opinion on dressings that were used. All participants (including those allocated to Surgeon's preference of dressing) will be asked to assess the dressing that they had applied. Participants will be asked to rate the acceptability of their dressing at their day 7 or discharge assessment (whichever is first) using a 10-point visual analogue scale.

In the UK only, healthcare professionals will be asked for their assessment of acceptability via an online questionnaire. Surgeons, ward nurses and research nurses will be asked to provide feedback.

9.3.9. Bluebelle sub-study

The method of assessing wounds forms a crucial part of any trial investigating SSIs. The current method using CDC criteria relies on healthcare professionals evaluating the wound to diagnose an SSI. The Bluebelle study has proposed a new measure for SSI that can be undertaken by the patient to diagnose the presence of a wound infection as a research tool[27]. This tool would, if validated, allow subsequent research to be undertaken without the need for repeated clinical assessments. The SUNRRISE Trial provides an opportunity to compare the outcome of the patient delivered questionnaire with the clinical assessment using the CDC criteria. In order to assess this, participants will be asked to complete a Bluebelle questionnaire at

home prior to their Day 30 wound assessment (the questionnaire forms part of the SUNRRISE Patient Diary). This will be compared to the Bluebelle questionnaire completed with the wound assessor during the Day 30 wound assessment and the primary outcome measure of an SSI according to the CDC criteria.

As part of SUNRRISE, SSIs diagnosed at any assessment time points in the trial will be compared to the number of SSIs identified by a one-off Bluebelle questionnaire completed by the patient before their Day 30 wound assessment. The Bluebelle team at the Clinical Trials and Evaluation Unit (CTEU) Bristol will be given access to a limited selection of data points for them to be able to externally validate the questionnaire. Participants will be informed of this sub-study in the PIS and will be asked to provide consent for authorised individuals from the CTEU Bristol to have access to their anonymised data.

9.4. Schedule of Assessments

Activity/CRF		Pre-theatre	In-theatre	Day 7 post-op (-2/+3 days)	Day 14 post-op (± 2 days)	Day 21 post-op (± 2 days)	Day 30 post-op (+ 14 days)	Day 30+
Patient identification and screening		On-call surgical team						
Patient consent	• **Standard**	Patient & Member of the research team						
	• **Delayed (UK only)**	Consultee/Representative & Member of the research team	Patient & Member of the research team when capacity regained					
Randomisation form		Started pre-theatre by the research team	Surgeon or member of the research team					
In-Theatre form			Ideally an operating surgeon, or member of the research team					
Wound Assessment Day 7 or on Discharge (if sooner)[1,2]				Member of the research team				
EQ-5D-5L		Completed by the participant		Completed by the participant	Completed by the participant	Completed by the participant	Completed by the participant	
SF-12		Completed by the participant		Completed by the participant			Completed by the participant	
Patient diary				Completed daily by the participant following discharge from hospital until they undergo the Day 30 wound review				Patients to continue with a diary if they have an ongoing SSI
Bluebelle wound healing questionnaire							Completed by the participant independently, and then by the participant with a blinded member of the research team reviewing wound	
Wound Assessment Day 30[1]							Completed by a blinded member of the research team as an **in-person or remote (video) review**	
SAE reporting			All serious adverse events by member of the research team using SAE form or wound assessment CRF if excluded from expedited reporting					Related serious adverse events only
Return to theatre form			Member of the research team for any return to theatre following patient returning to theatre					
PI Declaration form for CFR data								Completed by PI at the end of each participant's involvement

[1] Assessment of pain undertaken by a member of the research team by asking the participant and recording the response on the CRF

[2] Score of patient acceptability of dressing undertaken by a member of the research team by asking the participant and recording the response on the CRF

Table 1: Table of assessments. Member of the research team is a person named on the local delegation log and given the assigned duty.

9.5. Participant Withdrawal

Informed consent is defined as the process of learning the key facts about a clinical trial before deciding whether or not to participate. It is a continuous and dynamic process; participants should be asked about their ongoing willingness to continue participation and this documented in the participant's medical notes.

Participants should be aware at the beginning of the trial that they can freely withdraw (discontinue participation) from the trial (or part of) at any time.

Types of withdrawal as defined are:

- The participant would like to withdraw from trial treatment, but is willing to be followed up in accordance with the schedule of assessments and if applicable using any central UK NHS or Australian healthcare bodies for long-term outcomes (i.e. the participant has agreed that data can be collected and used in the trial analysis)
- The participant would like to withdraw from trial treatment and does not wish to attend trial visits/assessments in accordance with the schedule of assessments but is willing to be followed up at standard clinic visits and if applicable using any central UK NHS or Australian healthcare bodies for long-term outcomes (i.e. the participant has agreed that data can be collected at standard clinic visits and used in the trial analysis, including data collected as part of long-term outcomes)
- The participant would like to withdraw from trial treatment and is not willing to be followed up in any way for the purposes of the trial and for no further data to be collected (i.e. only data collected prior to the withdrawal can be used in the trial analysis)

The details of withdrawal (date, reason and type of withdrawal) should be clearly documented in the source data and a Patient Discontinuation Form completed. Primary outcome data (SSI rate at 30 days) from participants who have withdrawn from the trial will be derived where possible from routine outpatient follow-up appointments or hospital records where necessary. The impact of this on the study findings will be explored in a sensitivity analysis.

10. ADVERSE EVENT REPORTING

The following section relates to adverse event reporting in the UK. Australian sites will report their events to the trial office at the University of Newcastle and the process is explained in the country-specific protocol for Australia.

10.1. Reporting Requirements

The collection and reporting of Adverse Events (AEs) will be in accordance with the Research Governance Framework for Health and Social Care and the requirements of the HRA. Definitions of different types of AEs are listed in the table of abbreviations and definitions. The Investigator should assess the seriousness and causality (relatedness) of all AEs experienced by the trial participant and this should be documented in the source data with reference to the protocol.

10.2. Adverse Events

AEs are commonly encountered in patients undergoing an emergency laparotomy. As the safety profile of the SUNPD used in this trial is well characterised, it is highly unlikely that this trial will reveal any new safety information relating to this intervention.

Therefore, the recording of selected AEs will not affect the safety of participants or the aims of the trial. For this reason, only AEs that may be related to the intervention (i.e. until 30-days post-surgery) will be collected on the Day 7 and Day 30 wound assessment CRFs.

AEs that may be related are:

- Skin reaction to the applied dressing
- Pain/discomfort related to the applied dressing

SSI/wound complications do not need to be reported as this data will be captured during routine CRF collection.

Participants may suffer from other complications from their surgery but if these are not related to their wound or the dressing, they do not need to be reported.

10.3. Serious Adverse Events

All events which meet the definition of serious, Serious Adverse Events (SAE), will be collected and recorded in the participant notes. They will also be reported on the SAE form unless otherwise excluded as detailed below. SAEs will be reported to the trial office immediately and within 24 hours of being made aware of the event.

As the dressings being tested in this trial are available and often used within the NHS and Australian Health care system, there are no Serious Adverse Events which would be anticipated as a unique consequence of participation in the trial. We would, however, expect the following events to always be reported as SAEs:

- Entero-cutaneous fistula
- Fascial dehiscence
- Death

The following events are **excluded from reporting** to the SUNRRISE Trial Office and should be recorded within the participant's notes only:

- SAEs that are related to a pre-existing condition
- SAEs that are related to symptoms or progression of the participant's disease
- Pre-planned hospitalisation

Within SUNRRISE, the following events are regarded as SAEs but are **not subject to expedited reporting** using the SAE form. They are expected potential complications of an emergency laparotomy and will be captured on the routine follow-up CRFs:

- Interventions (either within theatre, radiology department or on the ward) to drain wound infections
- Prolonged hospital stay or re-admission as a result of wound complications
- Anastomotic leak
- Intra-peritoneal collections (with or without intervention)
- Thrombo-embolic events
- Infections not related to the wound (e.g. pneumonia, urinary tract infections)
- Cardiac or central nervous system complications
- Paralytic ileus

These events, which meet the definition of serious but are not subject to expedited reporting using the SAE form will be collected and recorded in the participant's notes and on the Wound Assessment CRFs on Day 7 and Day 30.

10.4. Reporting period

Details of all AEs that are being monitored as defined in sections 10.2 and 10.3 will be documented in source data and, where applicable, reported from the date of randomisation until 30 days post-surgery. SAEs that are judged to be at least possibly related to the use of the SUNPD (unless they are excluded in section 10.3) must still be reported in an expedited manner irrespective of how long after the SUNPD was used the event occurs.

10.5. Reporting Procedure – At UK Sites

10.5.1. Serious Adverse Events

AEs defined as serious and which require reporting as an SAE should be reported on the SUNRRISE SAE form. When completing the SAE form, the Investigator will be asked to define the causality and the severity of the AE. This will be on a five-point scale (definitely related; probably related; possibly related; unlikely to be related or unrelated).

On becoming aware that a participant has experienced an SAE, the Investigator (or delegate) must report the SAE to their own Trust in accordance with local practice and to the SUNRRISE Trial Office at BCTU.

To report an SAE to the Trial Office at BCTU, the Investigator or delegate(s) must complete, date and sign the trial specific SAE form. The completed form should be faxed or emailed to the BCTU trials team using the number or email address listed below as soon as possible and no later than 24 hours after first becoming aware of the event:

Fax SAE form to:	**00 44 121 415 8871**	**OR**	**Email SAE form to:**	**SUNRRISE@trials.bham.ac.uk**

On receipt of an SAE form, the BCTU trials team will allocate each SAE a unique reference number and return this via fax or email to the site as proof of receipt. If the site has not received confirmation of receipt of the SAE from the BCTU or if the SAE has not been assigned a unique SAE identification number, the site should contact the BCTU trials team within 1 working day. The site and the BCTU trials team should ensure that the SAE reference number is quoted on all correspondence and follow-up reports regarding the SAE and filed with the SAE form in the ISF.

Where an SAE form has been completed by someone other than the Investigator, the original SAE form will be required to be countersigned by the Investigator to confirm agreement with the causality and severity assessments.

10.5.2. Provision of follow-up information

Participants should be followed up until resolution or stabilisation of the event. Follow-up information should ideally be provided on a new SAE form, using the SAE reference number provided by the BCTU trials team. Once the SAE has been resolved, all follow-up information has been received and the paperwork is complete, the original SAE form that was completed at site must be returned to the SUNRRISE Trials Office at BCTU and a copy kept in the ISF.

10.6. Reporting Procedure – UK Trial Office

On receipt of a SAE form from the site, the BCTU trials team will allocate each SAE form with a unique reference number and enter this onto the SAE form in the section for office use only. The SAE form (containing the unique reference number completed) will be forwarded to the site as proof of receipt within 1 working day. The SAE reference number will be quoted on all correspondence and follow-up reports regarding the SAE and filed with the SAE form in the Trial Master File (TMF).

On receipt of an SAE form, the Chief Investigator (CI) or delegate(s) will independently determine the seriousness and causality of the SAE. An SAE judged by the PI or CI or delegate(s) to have a reasonable causal relationship with the intervention will be regarded as a related SAE. The causality assessment given by the PI will not be downgraded by the CI or delegate(s). If the CI or delegate(s) disagrees with the PI's causality assessment, the opinion of both parties will be documented, and where the event requires further reporting, both opinions will be provided in the report.

The CI or delegate(s) will also assess all related SAEs for expectedness. If the event is unexpected (i.e. is not defined in the protocol as an expected event) it will be classified as an unexpected and related SAE. Events which are assessed as both related and unexpected will be classified as Unexpected and Related Serious Adverse Event.

10.7. Reporting to the UK Research Ethics Committee

10.7.1. Unexpected and Related Serious Adverse Events

BCTU will report all events categorised as Unexpected and Related SAEs to the main UK Research Ethics Committees (REC) and Research Governance Team (RGT) at the University of Birmingham within 15 days.

10.7.2. Other safety issues identified during the course of the trial

The main UK RECs and RGT will be notified immediately if a significant safety issue is identified during the course of the trial.

10.7.3. Investigators

Details of all Unexpected and Related SAEs and any other safety issue which arises during the course of the trial will be reported to PIs. A copy of any such correspondence should be filed in the ISF.

10.8. Data Monitoring Committee

The independent Data Monitoring Committee (DMC) will review all SAEs.

10.9. Reporting to third parties

Smith and Nephew will be notified of any SAEs that occur in participants treated with their product. These will be forwarded periodically during the trial and sent as a list of events. No patient identifiable information will be given to the company. Any such requirements must be defined contractually and the arrangements made explicit in the PIS.

11. UK DATA HANDLING AND RECORD KEEPING

11.1. Source Data

In order to allow for the accurate reconstruction of the trial and clinical management of the subject, source data will be accessible and maintained. CRFs will be completed at the time points detailed in Section 9.

Within the SUNRRISE Trial, source data is the participant's medical notes generated and maintained at site, the completed Health-related Quality of Life questionnaires and Patient Diaries.

CRFs will be completed in hard copy at each site with originals forwarded to the BCTU when completed. A copy will be kept at the local site. The SUNRRISE Trial Office will be responsible for uploading the data from hard copy into the electronic CRF. The electronic CRF will be held on a REDCap database. REDCap is secure online database software that allows research teams to collect and store research data. The software is hosted on University of Birmingham secure servers and only accessible via controlled username and password access.

11.2. Case Report Form Completion

Data reported on each CRF will be consistent with the source data and any discrepancies will be clarified. Staff delegated to complete CRFs will be trained to adhere to GCP. CRF completion guidelines will be sent to all sites and will include guidance on:

- Dates shall be documented as: day / month / year (e.g. 23/Feb/1992) unless otherwise instructed
- Weight and height shall be provided in Kg (e.g. to 60Kg) and cm (e.g. 173cm)
- Trial-specific interpretation of data fields
- Which forms to complete and when
- What to do in certain scenarios, for example when a subject withdraws from the trial
- Missing/incomplete/unknown data
- Completing SAE forms and reporting SAEs
- Protocol and GCP non-compliances

In all cases it remains the responsibility of the site's PI to ensure that the CRF has been completed correctly and that the data are accurate. Where applicable for the trial this will be evidenced by the signature of the site's PI on the CRF or separate declaration form.

For paper CRFs, the completed originals will be submitted to the Trials Office and a copy filed in the ISF. Data collected will be transcribed onto the SUNRRISE REDCap database. Sites will return the completed paper CRFs to the SUNRRISE Trial Office for entry onto the database.

11.3. Participant completed questionnaires

Participants will complete SF-12 questionnaires at baseline, day 7 and day 30, and EQ-5D-5L questionnaires at baseline, day 7, 14, 21 and day 30.

On discharge from hospital, participants will be asked to complete a daily Patient Diary (which includes the weekly EQ-5D 5L and SF-12 questionnaires) between their discharge from hospital and their Day 30 wound review. These will be completed at home with a weekly phone call or text message from the local research team to remind the participant to complete their diary. The diary will be checked with the participant at their wound review and any missing data points will be clarified.

As part of the diary, participants will complete a Bluebelle wound healing questionnaire before seeing the research team at the Day 30 wound review. It is very important that this is completed by the participant independent from any healthcare professional. If, for any reason, participants have not completed this prior to their Day 30 wound review, they will be asked to complete it independently before the review proceeds with the research team member performing it.

11.4. Data Management

Paper CRFs must be completed, signed/dated and returned to the SUNRRISE Trial Office by the PI or an authorised member of the site research team (as delegated on the SUNRRISE Trial Site Signature and Delegation Log). Entries on the CRF should be made in ballpoint pen, ideally in black ink, and must be legible. Any errors should be crossed out with a single stroke, the correction inserted and the change initialled and dated. If it is not obvious why a change has been made, an explanation should be written next to the change.

Data reported on each CRF should be consistent with the source data or the discrepancies should be explained. If information is not known, this must be clearly indicated on the CRF. All missing and ambiguous data will be queried. All sections are to be completed. Data clarification forms (DCF) will be sent to sites requesting missing data or clarification of inconsistencies or discrepancies. In all cases, it remains the responsibility of the PI to ensure that the CRF has been completed correctly and that the data are accurate.

Processes will be employed to facilitate the accuracy of the data included in the final report. These processes will be detailed in the trial specific data management plan. Coding and validation will be agreed between the trial's manager, statistician and programmer and the trial database will be signed off once the implementation of these has been assured.

11.5. Data Security

The security of the System is governed by the policies of the University of Birmingham. The University's Data Protection Policy and the Conditions of Use of Computing and Network Facilities set out the security arrangements under which sensitive data should be processed and stored. All studies at the University of Birmingham have to be registered with the Data Protection Officer and data held in accordance with the Data Protection Act. The University will designate a Data Protection Officer upon registration of the study. The Study Centre has arrangements in place for the secure storage and processing of the study data which comply with the University of Birmingham policies.

- The System incorporates the following security countermeasures:
- Physical security measures: restricted access to the building, supervised onsite repairs and storages of back-up tapes/disks are stored in a fire-proof safe.
- Logical measures for access control and privilege management: including restricted accessibility, access-controlled servers, separate storage of non-identifiable data etc.
- Network security measures: including site firewalls, antivirus software, separate secure network protected hosting etc.
- System Management: the System shall be developed by the BCTU Programming Team and will be implemented and maintained by the BCTU Programming Team.
- System Design: the system shall comprise of a database and a data entry application with firewalls, restricted access, encryption and role-based security controls.
- Operational Processes: the data will be processed and stored within the Study Centre (University of Birmingham).
- Data processing: Statisticians will have access to anonymised data.
- System Audit: The System shall benefit from the following internal/external audit arrangements:
- Internal audit of the system
- Periodic IT risk assessments
- Data Protection Registration: The University of Birmingham has Data Protection Registration to cover the purposes of analysis and for the classes of data requested. The University's Data Protection Registration number is Z6195856.

11.6. Archiving

Archiving will be authorised by the SUNRRISE Trial office on behalf of the Sponsor following submission of the end of trial report. It is the responsibility of the PI to ensure all essential trial documentation and source documents (e.g. signed ICFs, ISF, participants' hospital notes, copies of CRFs etc.) at their site are securely retained for at least 10 years. No documents will be destroyed without prior approval from the SUNRRISE Trial Office on behalf of the sponsor.

12. UK QUALITY CONTROL AND QUALITY ASSURANCE

12.1. Site Set-up and Initiation

All participating PIs will be asked to sign the necessary agreements, including a 'Principal Investigator Declaration' and supply a current CV to the SUNRRISE Trial Office. All members of the site research team will also be required to sign the SUNRRISE Site Signature and Delegation Log, which details which tasks have been delegated to them by the PI.

Prior to commencing recruitment all sites will undergo a process of initiation and will have completed GCP training. Key members of the site research team will be required to attend a Site Initiation Visit (either as a face-to-face meeting or a teleconference/video conference) covering aspects of the trial design, protocol procedures, Adverse Event reporting, collection and reporting of data and record keeping. Sites will be provided with an ISF containing essential documentation, instructions, and other documentation required for the conduct of the trial. The SUNRRISE Trial Office must be informed immediately of any change in the site research team.

To quality assure and standardise the use of the SUNPD, all research team members delivering the intervention will undergo training on the use of SUNPD. This training will be provided prior to site opening and will be via teleconference/video conference or a face-to-face meeting. Training will be provided by a combination of members of the Trial Management Group (TMG) and representatives from Smith and Nephew.

Study-specific and SUNPD application training can be disseminated to the other members of the research team by the PI or nominated delegates, such as the associate PI/lead trainee and/or lead research nurse. This will be captured on the SUNRRISE Site Signature and Delegation Log and SUNRRISE Training Log.

12.2. Monitoring

Sites will be monitored via centralised monitoring from the BCTU. This will include recruitment numbers including the number of patients approached regarding the trial, randomisation numbers and completion of the follow-up period.

12.2.1. On-site Monitoring

On-site monitoring will be carried out as required following a risk assessment and as documented in the monitoring plan. Any monitoring activities will be reported to the trials team and any issues noted will be followed up to resolution. Additional on-site monitoring visits may be triggered, for example by poor CRF return, poor data quality, low SAE reporting rates, excessive number of participant withdrawals or deviations. If a monitoring visit is required, the SUNRRISE Trial Office will contact the site to arrange a date for the proposed visit and will provide the site with written confirmation. Investigators will allow the SUNRRISE Trial staff access to source documents as requested.

12.2.2. Central Monitoring

SUNRRISE will be centrally monitored, however on-site monitoring may occur if triggered. The SUNRRISE Trial Office will be in regular contact with the site research team to check on progress and address any queries that they may have. The SUNRRISE Trial Office will check incoming CRFs for compliance with the protocol, data consistency, missing data and timing. Sites will be sent DCFs requesting missing data or clarification of inconsistencies or discrepancies at a frequency and intensity determined by the Data Management plan.

12.3. Audit and Inspection

The PI will permit trial-related monitoring, quality checks, audits, ethical reviews, and regulatory inspection(s) at their site, providing direct access to source data/documents. The PI will comply with these visits and any required follow up. Sites are also requested to notify BCTU of any relevant inspections or local audits.

12.4. Notification of Serious Breaches

The sponsor is responsible for notifying the REC of any serious breach of the conditions and principles of GCP in connection with that trial or the protocol relating to that trial. Sites are therefore requested to notify the SUNRRISE Trial Office of any suspected trial-related serious breach of GCP and/or the trial protocol. Where the Trials Office is investigating whether or not a serious breach has occurred sites are also requested to cooperate with the Trials Office in providing sufficient information to report the breach to the REC where required and in undertaking any corrective and/or preventive action.

Sites may be suspended from further recruitment in the event of serious and persistent non-compliance with the protocol and/or GCP, and/or poor recruitment. The BCTU will report any major problems identified during monitoring to the Trial Management Group, TSC and the REC. This includes reporting serious breaches of GCP and/or the trial protocol to the REC. A copy of the serious breach report will also be sent to the University of Birmingham Clinical Research Compliance Team at the time of reporting to the REC.

13. END OF TRIAL DEFINITION

The end of trial will be 12 months after the final participant has completed follow-up i.e. 12 months after the date of the Day 30 wound review of the last participant. This will allow sufficient time for the completion of protocol procedures, data collection, data input and data cleaning in preparation for the database to be locked for the clinical data analysis.

13.1. Reporting in the UK

The SUNRRISE Trial Office in the UK will notify the UK REC the trial has ended and a summary of the clinical trial report will be provided within 12 months of the end of trial.

A copy of the end of trial notification as well as the summary report is also sent to the University of Birmingham RGT at the time of sending these to the REC.

13.2. Reporting in Australia

The SUNRRISE Trial Office in Australia will notify the Australian HREC the trial has ended and a summary of the clinical trial report will be provided within 12 months of the end of trial.

A copy of the end of trial notification as well as the summary report is also sent to the BCTU at the time of sending these to the HREC.

14. STATISTICAL CONSIDERATIONS

14.1. Sample Size

The justification for the sample size is based on data from the ROSSINI trial[28], which reported an SSI rate of 25% in the control group. To detect a relative reduction of 40% in SSI rates (i.e. from 25% to 15%, so 10% absolute difference) between groups using the standard method of difference between proportions (2-sided) with 90% power and a type I error rate of 5% (i.e. α=0.05), requires 336 participants per group to be randomised, so 672 in total. Assuming and adjusting for a 20% attrition/loss to follow-up rate (based on the death rate in this population being approximately 10% at 30 days; further drop out 10%), 840 participants (420 per group) will need to be recruited. Stata 15 software was used to compute the sample size calculation using the two-sample proportions test.

The 40% reduction correlates with the relative reduction being assessed in other large HTA funded SUNPD trials, such as WHIST.

14.2. Analysis of Outcome Measures

A separate Statistical Analysis Plan (SAP) will be produced and will provide a more comprehensive description of the planned statistical analyses. A brief outline of these analyses is given below.

The primary comparison groups will be composed of those who are randomised to SUNPD versus those randomised to the surgeons' preferred dressing. All analyses will be based on the intention to treat principle, i.e. all participants will be analysed in the groups to which they were randomised irrespective of compliance with the randomised allocated treatment. For all major outcomes, summary statistics and differences between groups (e.g. mean differences, relative risks) will be presented, with 95% confidence intervals and p-values from two-sided tests also given. Analyses will be adjusted for the minimisation variables listed in section 7.3 where possible, and baseline scores (where appropriate). A p-value of <0.05 will be considered statistically significant, and there will be no adjustment for multiple testing.

14.2.1. Primary Outcome Measure

The primary outcome is SSI within 30 days of surgery, as defined by the internationally accredited CDC criteria. This outcome is a binary outcome (i.e. yes/no). The number and percentage of participants reporting an SSI within 30 days of surgery will be reported by treatment group. An adjusted relative risk and 95% confidence interval will be estimated from a mixed effects log-binomial regression model. A risk difference and 95% confidence interval will also be provided. Statistical significance of the treatment group parameter will be determined from the p-value generated by the model.

14.2.2. Secondary Outcome Measures

The secondary outcomes for the trial include continuous, categorical and time to event data items.

Time to Event outcomes (Length of hospital stay after surgery):

These outcomes will be compared between treatment groups using survival analysis methods. Kaplan-Meier survival curves will be constructed for visual presentation of time-to-event comparisons. Mixed effects Cox proportional hazard models will be fitted to obtain treatment effects which will be expressed as hazard ratios with 95% confidence intervals.

Categorical outcomes (Wound complications, Hospital readmission for wound related complication(s), Serious Adverse Events):

For binary secondary outcomes, the number and percentage of participants reporting each outcome will be reported by treatment group. An adjusted relative risk and 95% confidence interval will be estimated from a mixed effects log-binomial regression model.

Continuous outcomes (QoL measures - SF-12 and EQ-5D, Likert scale for pain):

SF-12, EQ-5D-5L and the Likert scale for pain at the site of the primary laparotomy are all continuous data outcomes and therefore will be summarised using means and standard deviations. The data at both day 7 and day 30 will be compared between groups using mixed effects linear regression models to obtain an adjusted mean difference and 95% confidence interval. Data for the EQ-5D-5L is collected at baseline and days 7, 14, 21 and 30, and so as a secondary analysis this outcome will also be analysed using a mixed effects repeated measures model.

14.2.3. Planned Sub Group Analyses

Subgroup analyses will use the same variables as those in the minimisation algorithm (with the exception of centre), the operative procedure and country. Subgroup analyses will be limited to the primary outcome. The effects of these subgroups will be examined by including a treatment group by subgroup interaction parameter in the regression model. The results of subgroup analyses will be treated with caution and will be used for the purposes of hypothesis generation only.

14.2.4. Missing Data and Sensitivity Analyses

Every attempt will be made to collect full follow-up data on all study participants; it is thus anticipated that missing data will be minimal. Participants with missing primary outcome data will not be included in the primary analysis in the first instance. This presents a risk of bias, and sensitivity analyses will be undertaken to assess the possible impact of the risk. Any sensitivity analyses will not, irrespective of their differences, supplant the planned primary analyses. Full details will be included in the SAP.

14.3. Planned Interim Analysis

Interim analyses of major outcome measures and safety data will be conducted and provided in strict confidence to the independent DMC (see section 16.5). Details of the agreed plan will be written in the DMC charter and SAP.

14.4. Planned Final Analyses

The final analysis for the study will occur once all participants have completed the Day 30 assessment and corresponding outcome data has been entered onto the study database and validated as being ready for analysis.

15. UK HEALTH ECONOMICS ANALYSIS

The health economic analysis will determine the costs and benefits of SUNPD versus the surgeon's preferred dressing. The economic evaluation will be conducted from the perspective of the NHS and personal social services.

Healthcare resource utilisation will be collected for each patient alongside the trial through a patient diary included as part of the CRF. Patients with an ongoing SSI at time of discharge will continue to complete the patient diary until healing of the SSI. Items of resource use will be costed using national sources and tariffs such as the Personal Social Services Research Unit and NHS reference cost databases.

Generic health-related quality of life data will be collected using the EQ-5D-5L instrument at baseline and each follow-up assessment. Base-case analyses will be conducted using the crosswalk value sets for the

EQ-5D-5L with sensitivity analyses conducted using the EQ-5D-5L value set for England. Quality adjusted life years (QALYs) will be calculated using the area under the curve approach, with regression-based adjustment for baseline EQ-5D-5L score and minimisation variables.

A trial-based economic evaluation will take the form of a cost-utility analysis with results presented as incremental cost-utility ratios (ICURs). Data will be analysed on an intention to treat basis. Sensitivity analysis will consider the impact of missing data using appropriate techniques. Deterministic and probabilistic sensitivity analysis will be undertaken to explore the robustness of the results to plausible variations in key assumptions and variations in the analytical methods used. Cost-effectiveness acceptability curves (CEACs) will be plotted to show the probability of the intervention being cost-effective considering a range of willingness to pay thresholds per additional QALY gained.

16. TRIAL ORGANISATIONAL STRUCTURE

16.1. Sponsor

The University of Birmingham is the sponsor for this trial in the UK and the University of Newcastle, Australia is the sponsor for this trial in Australia. Each sponsor takes overall responsibility for initiation, management and financing of the trial within their respective countries.

16.2. Coordinating Centre

The UK SUNRRISE Trial Office is based at the University of Birmingham Clinical Trials Unit. The Australian SUNRRISE Trial Office is based at the University of Newcastle, Australia.

16.3. Trial Management Group

The TMG is responsible for the day to day management of the trial. The role of the TMG is to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself.

There are country-specific TMGs for the UK and Australia and the membership of these are listed at the front of the country-specific protocols. There is overlap between the TMGs to ensure consistency across sites/countries. The Australian TMG will defer to the UK TMG for all and any decisions that are made at the level of the trial as a whole.

16.4. Trial Steering Committee

The role of the TSC is to provide the overall supervision of the trial. Membership is listed at the front of this protocol. The TSC will monitor trial progress and conduct and advise on scientific credibility. The TSC will consider and act, as appropriate, upon the recommendations of the DMC or equivalent and ultimately carries the responsibility for deciding whether the trial needs to be stopped on grounds of safety or efficacy. The UK TSC will supervise the UK sites, while the Australian TSC will supervise Australian sites.

16.5. Data Monitoring Committee

There will be one DMC for the SUNRRISE trial. Data analyses will be supplied in confidence to the independent DMC, which will be asked to give advice on whether the accumulated data from the trial, together with the results from other relevant research, justifies the continuing recruitment of further participants. The DMC will operate in accordance with the SUNRRISE Trial specific charter based upon the template created by the Damocles Group. The DMC will meet on an annual basis unless there is a specific reason to amend the schedule. It convened at the end of the feasibility phase to review the safety data.

Additional meetings may be called if recruitment is much faster than anticipated and the DMC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if a safety issue is identified. The DMC will report directly to the TSC who will convey the findings of the DMC to the TMG. The DMC will oversee the data from both the UK and Australian trials.

If participants randomised to the SUNPD arm are doing overwhelmingly better or worse than those not randomised to this group (i.e. control arm) with respect to SSI rates at 30 days, then this effect may become apparent before the target recruitment has been reached. Alternatively, new evidence could emerge from other sources to suggest that SUNPD is definitely more, or less, effective than control. To protect against any unnecessary continuance of the trial in this event, interim analyses of major endpoints and safety data will be supplied during the period of recruitment to the study, in strict confidence, to the DMC along with updates on results of other related studies, and any other analyses that the DMC may request.

The DMC will advise the chair of the TSC if, in their view, any of the randomised comparisons in the trial have provided both: a) proof beyond reasonable doubt that for all, or for some, types of patient one particular intervention is definitely indicated or definitely contra-indicated in terms of a net difference of a major endpoint, and b) evidence that might reasonably be expected to influence the patient management of many clinicians who are already aware of the other main trial results. Unless this happens, however, the TSC, the collaborators and all of the central Trial staff (except the statisticians who supply the confidential analyses) will remain ignorant of the interim results.

Appropriate criteria of proof beyond reasonable doubt cannot be specified precisely, but a difference of at least $p<0.001$ (similar to a Haybittle-Peto stopping boundary) in an interim analysis of a major endpoint may be required to justify halting, or modifying, the study prematurely. If this criterion were to be adopted, it would have the practical advantage that the exact number of interim analyses would be of little importance, so no fixed schedule is proposed. Given the proposed use of the Haybittle-Peto boundary, no adjustment for multiple testing (to control the overall type I error rate) is proposed, i.e. the threshold for statistical significance at final analysis will still be $p=0.05$.

A separate DMC reporting template will be drafted and agreed by the DMC including an agreement on which outcomes will be reported at interim analyses. The statistical methods stated in this SAP will be followed for the agreed outcomes.

17. ETHICAL CONSIDERATIONS

The trial will be performed in accordance with the recommendations guiding physicians in biomedical research involving human subjects, adopted by the 18th World Medical Association General Assembly, Helsinki, Finland, June 1964, amended at the 48th World Medical Association General Assembly, Somerset West, Republic of South Africa, October 1996 (website: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/).

In the UK, the trial will be conducted in accordance with the UK Policy Framework, the applicable UK Statutory Instruments, (which include the current data protection requirements within the UK and Guidelines for Good Clinical Practice (GCP). The protocol will be submitted to and approved by the REC in the UK prior to circulation.

In Australia the trial will be conducted in concordance with the Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2) – Annotated with TGA Comments (9 November 2016) and in compliance with applicable laws and regulations. The study will be performed in accordance with the

NHMRC Statement on Ethical Conduct in Research Involving Humans (© Commonwealth of Australia 2007) and the principles laid down by the World Medical Association in 2008. The Investigators shall comply with the protocol, except when a protocol deviation is required to eliminate immediate hazard to a participant.

Before any participants are enrolled into the trial within a country, the PI at each site is required to obtain the relevant local approvals (e.g. R&D approval in the UK, site specific approval in Australia). Sites will not be permitted to enrol participants until written confirmation of local approval is received by the SUNRRISE Trial Office in the respective country. It is the responsibility of the PI to ensure that all subsequent amendments gain the necessary local approval. This does not affect the individual clinicians' responsibility to take immediate action if thought necessary to protect the health and interest of individual participants.

18. CONFIDENTIALITY AND DATA PROTECTION

Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018. This is a European Regulation, but, in principle, compliance with it is required for all organisations that share data with a European entity, hence the regulation applies to the data management in this study.

Participants will always be identified using only their unique trial identification number and initials on CRFs and correspondence between the Trials Office and the participating site. Participants will give their explicit consent for the movement of their consent form, giving permission for the trial office in their country to be sent a copy. This will be used to perform in-house monitoring of the consent process.

The Investigator must maintain documents not for submission to the Trials Office (e.g. Patient Identification Logs) in strict confidence. In the case of specific issues and/or queries from the regulatory authorities, it will be necessary to have access to the complete trial records, provided that participant confidentiality is protected.

The Trials Office will maintain the confidentiality of all participant's data and will not disclose information by which participants may be identified to any third party other than those directly involved in the treatment of the participant and organisations for which the participant has given explicit consent for data transfer. Representatives of the Sponsor and/or trial office may be required to have access to participant's notes for quality assurance purposes but participants should be reassured that their confidentiality will be respected at all times.

19. UK FINANCIAL AND OTHER COMPETING INTERESTS

This is an investigator-initiated and investigator-led trial funded by Research for Patient Benefit Programme of the NIHR along with support from Smith and Nephew. The Industry partner is providing the trial dressings free of charge. They do not have any input into the trial design, data collection, analyses or interpretation of the findings.

20. UK INSURANCE AND INDEMNITY

The University of Birmingham has in place Clinical Trials indemnity coverage for this trial which provides cover to the University for harm which comes about through the University's, or its staff's, negligence in relation to the design or management of the trial and may alternatively, and at the University's discretion provide cover for non-negligent harm to participants.

With respect to the conduct of the trial at Site and other clinical care of the participant, responsibility for the care of the participants remains with the NHS organisation responsible for the Clinical Site and is therefore indemnified through the NHS Resolution.

The University of Birmingham is independent of any pharmaceutical company, and as such it is not covered by the Association of the British Pharmaceutical Industry (ABPI) guidelines for participant compensation.

21. PUBLICATION POLICY

Results of this trial will be submitted for publication in a peer reviewed journal. The manuscript will be prepared by the TMG. Any secondary publications and presentations prepared by Investigators must be reviewed by the TMG. Manuscripts must be submitted to the TMG in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues. Authors must acknowledge that the trial was performed with the support of The University of Birmingham.

At the Day 30 wound assessment, participants will be reminded of the details of the trial website which they were given on the PIS that they received. Following completion of the trial, a lay summary of the results of the trial will be provided on the website for the participants to see the results. Results will be also be disseminated to patient groups and prepared for news organisations including local hospital newsletters.

21.1. Authorship policy

The main results manuscript of the trial and any subsequent secondary analysis manuscripts using the data collected in the trial will be published under a corporate authorship policy. An example of this is 'The SUNRRISE Trial Collaborators and the North West Research Collaborative and the West Midlands Research Collaborative'. There will be no named authors in the main authorship line but individuals will be named within the paper and roles will be defined. All collaborators will be named and will be PubMed citable.

The authorship policy will closely mirror the suggestion published by the National Research Collaborative[29]. Authors will be listed as per their involvement within each part of the study/manuscript. There will be a steering committee, writing group and list of local collaborators. To be included in the list of local collaborators, the collaborator needs to have been involved in the pathway of at least 6 participants. Local collaborators will be listed according to hospital and then alphabetically. Local trainee and consultant leads will be identified. This policy is subject to minor revisions according to journal requirements.

Presentations that result from the trial will follow a similar authorship policy. Where possible abstracts should be submitted under the corporate banner as described above. It is acknowledged that it may not be possible to submit abstracts in this form to all conferences in which case named authors can be submitted along with the study group and two research collaboratives. Any posters or oral presentations should have the corporate authorship as the main authorship line but may also include the presenting author below this.

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23. ABBREVIATIONS AND DEFINITIONS

23.1. Abbreviations

Abbreviation	Term
ABPI	Association of the British Pharmaceutical Industry
AE	Adverse Event
ASA	American Society of Anesthesiologists (ASA) Physical Status Classification System
BCTU	Birmingham Clinical Trials Unit
CDC	Centers for Disease Control criteria
CEACs	Cost-Effectiveness Acceptability Curves
CI	Chief Investigator
CRF	Case Report Form
DCF	Data Clarification Form
DMC	Data Monitoring Committee
EQ-5D-5L	EuroQol- 5 Dimension 5-Level
GCP	Good Clinical Practice
HRA	Health Research Authority
HREC	Human Research Ethics Committee
ICF	Informed Consent Form
ICURs	Incremental Cost-Utility Ratios
ISF	Investigator Site File
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPWT	Negative pressure wound therapy
PI	Principal Investigator
PIS	Patient Information Sheet
QALYs	Quality Adjusted Life Years
REC	Research Ethics Committee
RGT	Research Governance Team
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SSI	Surgical Site Infection
SUNPD	Single-use Negative Pressure Dressings
SF-12	Short Form - 12 Health Survey
TGA	Therapeutic Goods Administration
TMG	Trial Management Group
TSC	Trial Steering Committee
UoB	University of Birmingham
UoN	University of Newcastle, Australia

23.2. Definitions

Adverse Event	**AE**	Any untoward medical occurrence in a participant or clinical trial subject participating in the trial which does not necessarily have a causal relationship with the intervention received.
Birmingham Clinical Trials Unit	**BCTU**	The co-ordinating centre for the trial.
Personal Consultee		A person who cares for the adult lacking capacity or is interested in that person's welfare, but is not doing so for remuneration or acting in a professional capacity.
Related Event		An event which resulted from the administration of any of the research procedures.
Serious Adverse Event	**SAE**	An untoward occurrence that: • Results in death • Is life-threatening* • Requires hospitalisation or prolongation of existing hospitalisation • Results in persistent or significant disability or incapacity • Consists of a congenital anomaly/ birth defect • Or is otherwise considered medically significant by the Investigator**
Source data		All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial
Unexpected and Related Event		An event which meets the definition of both an Unexpected Event and a Related Event
Unexpected Event		The type of event that is not listed in the protocol as an expected occurrence.

24. APPENDIX 1 – MENTAL HEALTH (SCOTLAND) ACT 1984 RELATIONSHIP HIERARCHY

The Adults with Incapacity (Scotland) Act uses the hierarchy of relationships defined in the Mental Health (Scotland) Act 1984 as the definition of nearest relative. In decreasing order of closeness, these are:

a) Spouse
b) Child
c) Father or mother
d) Brother or sister
e) Grandparent
f) Grandchild
g) Uncle or aunt
h) Nephew or niece

25. APPENDIX 2 – CLAVIEN-DINDO CLASSIFICATION OF POST-OPERATIVE COMPLICATIONS

Grade	Description	Management of wound infections and other wound complications
I	Any deviation from the normal post-operative course not requiring surgical, endoscopic or radiological intervention. This includes the need for certain drugs (e.g. antiemetics, antipyretics, analgesics, diuretics and electrolytes), treatment with physiotherapy and wound infections that are opened at the bedside	• None / conservative management • On ward intervention
II	Complications requiring drug treatments other than those allowed for Grade I complications; this includes blood transfusion and total parenteral nutrition (TPN)	• Antibiotic drug treatment
III	Complications requiring surgical, endoscopic or radiological intervention	• Surgical intervention • Radiological intervention
IV	Life-threatening complications; this includes CNS complications (e.g. brain haemorrhage, ischaemic stroke, subarachnoid haemorrhage) which require intensive care, but excludes transient ischaemic attacks (TIAs)	• ITU admission
V	Death of the patient	n/a – death and associated details reported using SUNRRISE SAE form

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