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Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients.

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Keywords:	Surgical Site Infection, SURGERY, smartphone technology

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients.

Trial Registration: *ClinicalTrials.gov.* Reference No: NCT02704897

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Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Roles and responsibilities:

McLean KA[1], Mountain KE [1], Shaw CA[1], Drake TM[1], Ots R[1], Knight SR[1], Fairfield CJ[1], Sgrò A[1], Skipworth RJE[1], Wigmore SJ[1], Potter M[2], Harrison EM[1]

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Keywords: *Surgical Site Infection, smartphone technology, surgery*

MeSH Terms: *Surgical Wound Infection*, Diagnosis, Smartphone, General Surgery*

Abstract

Introduction

National data suggest that surgical site infection (SSI) complicates 2-10% of general surgery cases, although the patient-reported incidence is much higher. SSIs cause significant patient morbidity and represent a significant burden on acute healthcare services, in a cohort predominantly suitable for outpatient management. Over three-quarters of UK adults now own smartphones, which could be harnessed to improve access to care. We aim to investigate if a smartphone-delivered wound assessment tool results in earlier treatment.

Methods and Analysis

This is a randomised-controlled trial aiming to recruit 500 patients across NHS hospitals. All emergency abdominal surgery patients over the age of 16 who own smartphones will be considered eligible, with the exclusion of those with significant visual impairment. Participants will be randomised in a 1:1 ratio between standard post-operative care and the intervention – use of the smartphone tool in addition to standard post-operative care. The main outcome measure will be time-to-diagnosis of SSI with secondary outcome measures considering use of A&E and GP services and patient experience. Follow-up will be conducted by clinicians blinded to group allocation. Analysis of time-to-diagnosis will be by comparison of means using a Mann-Whitney U-test.

Ethics and Dissemination

This is the first randomised-controlled trial to evaluate the use of a smartphone-delivered wound assessment tool. The intervention is being used in addition to standard post-operative care. The study design and protocol were reviewed and approved by Southeast Scotland Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016). Study findings will be presented at academic conferences, published in peer-reviewed journals,

and are expected in 2020. A written lay summary will be available to study participants on request.

Trial Registration

ClinicalTrials.gov. Reference No: NCT02704897

Strengths and Limitations of this Study:

- This is the first randomised controlled trial on the use of a smartphone-delivered tool facilitate the assessment of surgical site infection and the impact on time-to-diagnosis.
- There are broad eligibility criteria, and so it is expected the results will be generalisable to a wide population of patients undergoing abdominal surgery.
- Due to the nature of the intervention, only clinicians undertaking follow-up can be blinded to randomisation status.
- All patients will receive 30-day telephone or face-to-face follow-up to determine the occurrence of surgical site infections, however the gold-standard for diagnosis remains direct clinical assessment.
- Data on patient experience and acceptability of smartphone-delivered follow-up will be collected concurrently to guide future implementation of future telehealth interventions.

Introduction

Surgical site infection (SSI) complicates 2-10% of general surgical cases, with the highest rates of infection seen after colorectal surgery[1]. Infection and re-admission rates have not significantly changed in the last 10 years. The most common causative group is *Enterobactericae* (25% of cases), with *Staph. Aureus* (10%) and MRSA (3%) accounting for a small proportion of overall cases[1]. National surveillance data from Scotland indicate that peak incidence of infection is between day 6-12 post-operatively[2].

A recent study indicated that national reports may underestimate the true incidence of SSI, and suggested that patient reported SSI is a more sensitive measure [3]. Unpublished data from our own hospital indicates that up to 25% of patients report post-operative wound infections; approximately half of these require assessment by the surgical team, but less than 1% require admission. Many of these patients had already consulted their General Practitioner (GP) or attended the Accident and Emergency department (A&E). In addition, many patients have concerns about their wounds (in the absence of infection) and may experience delays in accessing appropriate medical assessment. Thus, SSI represents a significant burden on healthcare services, in a patient group who are predominantly appropriate for outpatient management.

There is currently an increased research focus on digital health: the use of communications technology to enhance healthcare, public health and delivery of health education[4]. There are several advantages to this approach, in particular the potential to improve access to care, and help streamline usage of emergency services. Indeed, there is evidence that these technologies have been used to improve outcome[5], as well as to reduce specialist workload [6] and A&E attendances[7]. In addition, the increasing use of healthcare technology is likely to help improve automatic data collection and recording, which may be used to identify areas for future research and drive quality improvement[4].

Over three-quarters (78%) of UK adults now own smartphones [8], with at least a third using a smartphone as their primary device to access the internet [4]. Therefore, there is vast potential for the use of smartphones in digital health. Given the frequency with which patients report post-operative wound complications and the high incidence of SSI, we feel that SSI represents a good candidate for a primary measure of outcome for research in digital health. We aim to investigate if an online wound assessment tool can be used to help diagnose SSI and improve patient access to care and clinical assessment. In addition, we aim to investigate if this results in earlier intervention to treat SSI and a decreased attendance at A&E and GPs. The widespread use of smartphones, the integrated nature of their technology, and their portability means smartphones represent the best platform to deliver this tool, with the aim of facilitating rapid access to clinical care.

Objectives

This randomised-controlled trial will investigate whether a smartphone-delivered wound assessment tool can be used to diagnose wound infection and result in earlier treatment. It will also assess for a reduction in A&E and GP attendances as a result of using the intervention. Data on patient experience will be used to evaluate perceived utility of the tool.

Methods and Analysis

Overview

This is a superiority randomised-controlled trial, using a parallel two-arm design (Figure 1). Once consent is obtained, participants will be randomised in a 1:1 ratio to either the intervention arm (receiving standard post-operative care plus access to the smartphone-delivered wound assessment tool), or the control arm (standard post-operative care). Patients will be recruited from the emergency surgery inpatient service across NHS Lothian. The trial period will be 30 days. An internal pilot study in the first 80 patients recruited will be conducted to ensure the trial design is practical and deliverable. Following assessment of pilot data, there will an opportunity to adapt the trial design in response to the pilot study findings. Participants will be followed-up by a researcher blinded to the intervention status. The primary outcome measure will be the number of days from surgery to commencing treatment for SSI (time-to-diagnosis), with A&E and GP service use as a secondary outcome measure. Additional data regarding patient experience will also be collected from patients in both arms of the trial via a smartphone-delivered questionnaire at 30 days.

Research Setting

This research is being carried out in a large health board, serving a mixed urban and rural population of over 800,000. The emergency surgery service admits 300 patients per week between participating sites and performs 2500 procedures annually.

Participants

Emergency surgery in-patients who are adults (over age 16) and have undergone abdominal surgery (on the same admission as diagnosis) will be screened for eligibility. Potentially eligible patients will be screened and documented as (a) eligible and included, (b) eligible and missed, (c) eligible and declined (iv) ineligible (visual impairment) (v) ineligible (no smartphone). Written consent will be obtained by the research team in line

with Good Clinical Practice Guidance. Participation is voluntary and a patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Inclusion Criteria

Patients admitted to the emergency surgery inpatient service who meet the following criteria will be included in the study:

- Emergency surgery in-patients who have undergone abdominal surgery;
- Owners of a smartphone, with access to internet;
- Adults over the age over 16;
- Able to give informed consent.

Exclusion Criteria

Any patients with significant visual impairment preventing use of the online questionnaire will be excluded from the study (defined by self-reporting of the patient)

Study Procedures

Recruitment

The clinical team will inform potentially eligible patients about the on-going trial, and offer them further information (written and verbal from the research team). Eligible patients will be recruited as in-patients, with formal written consent taken by a member of the research team. Baseline information gathered will include: reason for admission, index procedure and date, significant co-morbidities – including history of diabetes or immunosuppression, as well as age and BMI. Participant contact details (mobile telephone number) will be entered into a secure, online data collection tool (Research Electronic Data Capture (REDCap) database) [9].

Randomisation and Blinding

Participants will be assigned in a 1:1 ratio to the intervention or control arms and provided with the appropriate information packs prior to discharge. Randomization en-bloc will be carried out using REDCap[9], utilising a computer-generated random number sequence. The emergency surgery nurses (who will provide care to patients as required during the trial), and those taking consent (which may include medical students and qualified clinicians) will not be blinded. The clinicians undertaking follow-up will be blinded to status. A trial entry will be made in the clinical notes, including contact details for the trial team should a member of the clinical team require more information or wish to discover their trial status.

Intervention

Smartphone-Delivered Wound Assessment Tool

A wound-based instrument to detect potential wound infection was developed. Our smartphone-delivered wound assessment model was based on the Centre for Disease Control and Prevention (CDC) classification criteria, and the ASEPSIS model (Additional treatment, Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria, and the duration of Inpatient Stay).[10 11] It detects symptoms of SSI and symptoms of systemic illness as a result of this, whilst being quick and simple to use (Table 1).

Participants will have access to the smartphone-delivered wound assessment tool on discharge via a link sent by short-messaging system (SMS) to their smartphones. If at any time they have concerns about their wound, they can access the tool, and will be advised based on their responses. When a patient response is submitted, the research team will be automatically notified, and prompted to reply (Figure 2).

In addition, a link to the smartphone-delivered wound assessment tool will be sent on days 3, 7, and 15 post-operatively. These time-points have been selected to include peak incidence of infection and cover the time-course of wound healing. This will ensure the collection of negative data in those without symptoms and will therefore assist in determining the specificity of the tool. If participants do not respond they will be sent a single reminder at these time-points.

Wound Photographs

Participants will be asked to upload at least one photograph of their wound each time they use the smartphone-delivered wound assessment tool. These will be reviewed by a clinical researcher and assigned into one of 3 categories: no concerns, medium-risk, high-risk. Further machine learning-based assessment of wound photographs will be investigated.

Responses

An experienced clinician will review all participant responses and photographs in real-time. Based on the response and the wound photographs, they will contact the patient by SMS with advice regarding the need for further assessment. The clinician will classify participants into 3 groups: no concern, medium-risk, high-risk. These three groups were agreed collectively by the researchers in collaboration with the emergency surgical team. Three potential outcomes were identified: (i) the patient does not require further assessment (no concern), (ii) the patient requires further assessment, but the symptoms identified suggest a mild infection (medium-risk), (iii) the symptoms suggest a potentially severe infection requiring urgent assessment (high-risk). The wound photographs will also be reviewed by the clinical researcher where available and classified into the same 3 groups. This may be used by the researcher to refine their response to the tool, if they consider this necessary.

Algorithm

An algorithm has been designed to classify participant responses into the same 3 categories listed above. This will be run on all participant responses (but will not impact on care), and will be compared with clinician rating, as a secondary sub-study. The correlation between clinician response, algorithm response and photo response will be used to determine if the algorithm can be used to assess for SSI independent of the responsible doctor.

Action from Response

Participants whose responses raise no concerns will be advised of this. Participants who report symptoms consistent with wound infection will be directed for further assessment. Those in the medium-risk group will be directed to community care whilst those in the high-risk group will be advised to return for assessment at the centre where they had their procedure. This advice aligns to the degree of concern identified above.

Wound Reviews

For those in the intervention group who are identified as high-risk, the emergency surgery nurses will collect a wound swab from the patient to test for causative organisms (and aid in confirming infection). If a wound infection is diagnosed clinically, the patient will be started with antibiotics in line with local guidelines. This will be logged in the patient's trial record. If any patients in the control group attend the emergency surgery service for a review the same procedures will apply.

GPs will be informed about their patient's participation in the trial. We will request that if a participant enrolled in the trial visits their GP a wound swab is taken, and that they are treated in line with the GP's normal practice. This will also apply to those in the medium-risk group who will be directed to their GP.

All participants will be given a log to take to any wound reviews. If an infection is diagnosed the date treatment commenced will be noted, alongside any intervention performed. This will then be returned to the trial team, and used in follow-up.

30 Day Follow-up

Both arms will receive a follow-up face-to-face or telephone consultation 30 days post-operatively (alternatively, written follow-up is also available for those with significant hearing impairment). This consultation will follow a standardized format and will be conducted with the clinical researcher blinded to the intervention status. The clinical researcher will gather data on post-operative course, any symptoms related to the wound, and any treatment offered. They will have access to the results system and any wound logs returned. On the basis of all this information, two independent, blinded researchers will determine if an infection has been present (trained using the CDC Criteria to diagnose infection).[10] Data on patient experience and service usage – A&E and GP attendances, as well as contact with emergency surgery nurses – will also be collected via a separate questionnaire delivered alongside the 30 day follow-up.

Data Analysis Plan

All analysis will be carried out on an intention-to-treat basis. We do not anticipate missing data in patient demographics. However, any missing data values will be handled using multiple imputation. The volume of missing outcome data will be recorded for the control and intervention arms, and any differences in drop-out rate noted. Thereafter patients with missing outcome data will be excluded from analysis.

Outcome Measures

This is a superiority RCT, and the primary outcome will be time from operation to diagnosis (time-to-diagnosis) of SSI. This point has been chosen (rather than time from symptom onset), as it can be more accurately recorded and is a measure of improved access to care. We assume an equal incidence of SSI in both groups and will ensure this using odds ratios. Time-to-diagnosis will be compared using Cox proportional hazard regression analysis, a *P* value of <0.05 will be considered statistically significant.

For the intervention, we will calculate the sensitivity and specificity of the researcher response, the algorithm response, and photograph response in the diagnosis of SSI. We will compare the correlation of the algorithm, which is based on questionnaire responses, with clinician advice and eventual diagnosis. Correlation analysis will be performed using Kendall tau rank test. This will assess the accuracy of the algorithm in stratifying risk, as compared to a clinician, and will indicate what additional benefit may be gained from photographic analysis.

The secondary outcome measure will be use of services: GP and A&E attendances, as well as contact with emergency surgery nurses. This data will be gathered at 30 days. Differences in number of attendees to GP and A&E will be compared using a χ^2 test. Differences in the number of attendances will be assessed using the Mann-Whitney U-test.

Data on patient experience will also be gathered via a follow-up questionnaire and analysed separately. This will help determine if an online questionnaire delivered via a smartphone has a positive impact on patient experience of care, and if it helped facilitate their access to care.

Sample Size and Power Analysis

Our primary outcome measure is time-to-diagnosis and we aim to detect a one-day difference with a power of 90% (alpha 0.05). Assuming a standard deviation of 1 day in time-to-diagnosis, 22 wound infections per group will be required. Estimating a 10% rate of wound infection (in line with National Data)[2] and a drop-out rate of 10%, a sample size of 490 will be required (recruitment target 500 patients). Analyses will be intention-to-treat.

Assuming that 50 operations are performed per week and two thirds of these patients are likely to own smartphones, we estimate there will be 30 potentially eligible patients per week. Aiming for recruitment of 25% of eligible patients, we estimate a continuous recruitment time of 16 months. This rate of recruitment will also enable the researcher to respond to all patient concerns in a timely manner.

Ethics and dissemination:

Safety

All participants will receive the normal standard of care. The smartphone-based intervention is in addition to the normal standard of care. If at any point participants have any concerns. they will be advised to contact the emergency surgery nurses regarding their care (in line with normal standard of care). Out-of-hours they will be advised to contact NHS out-of-hours services. Participants will be advised to contact the emergency surgery nurses if they have any concerns whilst they are awaiting a response to the tool. The research team will be notified automatically that a participant is awaiting a response, ensuring that in normal working hours patients receive a rapid reply. They will also be advised that if they access the tool at night, that it will not be reviewed until the following day. They will be advised to contact out-of-hours services if they require an overnight assessment. These actions will prevent any harm to patients resulting from a delayed response to the wound assessment

tool. Due to the low-risk nature of the trial, a formal data-monitoring committee has not been nominated.

Data Protection and Management

All participant data will be stored securely in a REDCap [9] database that has controlled access and is password protected. This data will be anonymised, and only available to researchers listed on the protocol. Participant responses to the questionnaire will be reported directly to the REDCap database and will not be stored on patient phones. However, patients will be advised to review the security setting on their phone if they intend to store their wound photographs. Patient details will be recorded in a trial log should any safety concerns arise necessitating they be contacted.

Ethical Approval and Dissemination Plan

The study design and protocol were reviewed and approved by Southeast Scotland Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016), and any protocol amendments will be resubmitted for review. The study is sponsored by ACCORD, a collaboration between the University of Edinburgh and NHS Lothian Research and Development. In line with Good Clinical Practice Guidance, written consent will be obtained by appropriately trained medical students or clinicians. Participation is voluntary and a patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Authorship on any papers derived from the study will be all authors involved in study design and protocol development, and any additional researchers involved in the writing group. Furthermore, patient recruiters who have recruited more than the prespecified 15 patients

to the study will be listed as a “collaborator”. All other persons involved in the study will be listed in the acknowledgements.

There are no financial and other competing interests for principal investigators for the overall trial or either study site. Study findings will be reported in line with CONSORT guidelines, and disseminated in the printed media, and learned forums, and are expected in 2020. A written lay summary will be available to study participants on request.

Patient and Public Involvement

Patients were not directly involved in the design or delivery of this trial, however data on patient experience in using the smartphone tool will be evaluated via a follow-up questionnaire. This will inform future development and dissemination of this intervention. A summary of results will be provided to all patients involved once the trial has been completed and analysed.

Authors' Contributions

The study methods and protocol were developed jointly by the all authors. All authors assisted in review of the final write-up.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

The authors do not have any conflicts of interest to declare.

Word Count: 3,064

Tables

Table 1: Questions included in smartphone-delivered questionnaire

Smartphone-delivered wound assessment
Is the pain worse than immediately after the operation?
Is there liquid coming from the wound site?
Please select which option best describes the liquid: clear, yellowish, thick and yellow, bloody, green or brown
Is there new redness around your wound site excluding the wound itself?
Is there more swelling around your wound site than at the time of surgery?
Are you experiencing a new burning sensation or heat at the wound site?
Is you wound opening or gaping?
Have you experienced fevers in the last 24 hours?
Please upload a photograph of your wound.

Figures

Figure 1: Schema of trial events for intervention and control arms

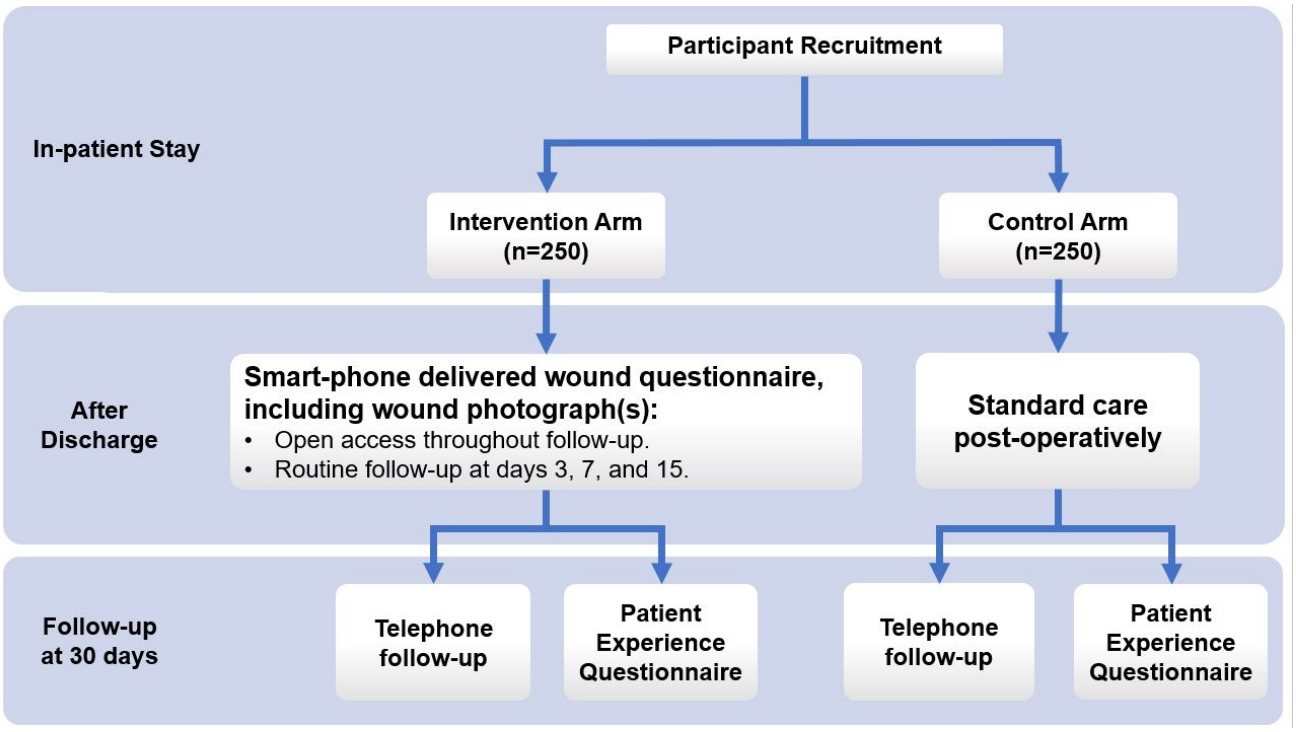
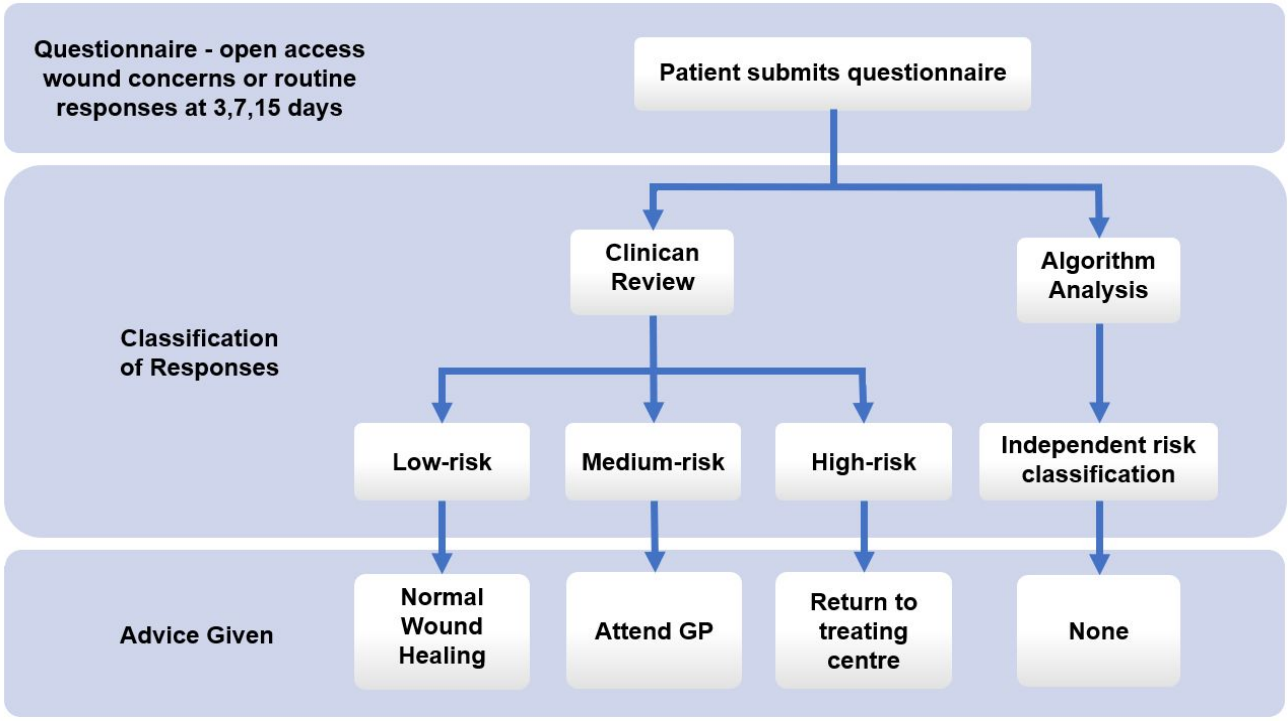


Figure 2: Handling of wound questionnaire submissions



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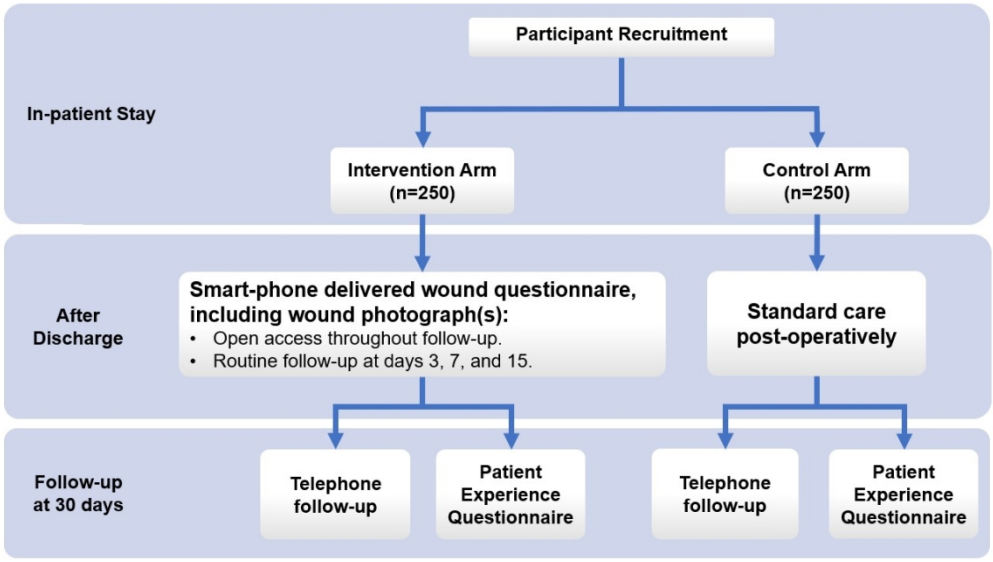

Figure 1: Schema of trial events for intervention and control arms

812x453mm (120 x 120 DPI)

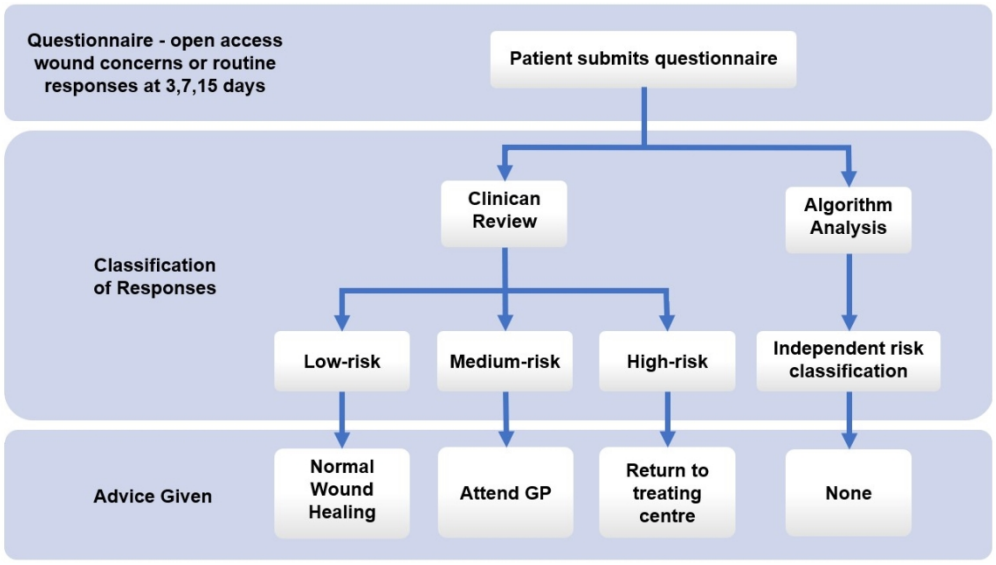

Figure 2: Handling of wound questionnaire submissions

811x454mm (120 x 120 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients**.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
	2b	All items from the World Health Organization Trial Registration Data Set ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
Protocol version	3	Date and version identifier **Page 1**
Funding	4	Sources and types of financial, material, and other support **Page 1**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **Page 1**
	5b	Name and contact information for the trial sponsor **Page 1**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **Page 1**

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **Page 1**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **Page 5-6**
	6b	Explanation for choice of comparators **Page 5-6**
Objectives	7	Specific objectives or hypotheses **Page 7**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **Page 8 (overview)**
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **Page 8 (research setting)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **Page 8-9 (Patients, inclusion criteria, exclusion criteria)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. **Page 10-13**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). **Page 17**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). **N/A**

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **N/A**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **Page 14 (outcome measures)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **Figure 1**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **Page 15 (Sample Size and Power Analysis).**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. **Page 9 (Recruitment)**
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **Page 10 (Randomisation and Blinding).**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **Page 10 (Randomisation and Blinding).**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **Page 10 (Randomisation and Blinding).**

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. **Page 10 (Randomisation and Blinding).**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **N/A**

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **Page 9 (Recruitment); Page 10 (Smartphone-Delivered Wound Assessment Tool); Table 1**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **Page 10 (Smartphone-Delivered Wound Assessment Tool); Page 13 (Data analysis plan)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. **Page 16 (Data Protection and Management).**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. **Page 13 (Data Analysis Plan / Outcome Measures)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **Page 13 (Data Analysis Plan / Outcome Measures)**
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **Page 13 (Data Analysis Plan / Outcome Measures)**

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **Page 16 (safety)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **N/A**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **Page 16 (safety)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **N/A**

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **Page 17 (Ethical Approval and Dissemination Plan)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **Page 17 (Ethical Approval and Dissemination Plan)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **Page 17 (Ethical Approval and Dissemination Plan)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **N/A**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **Page 16 (Data Protection and Management)**

Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **Page 18**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **Page 16 (Data Protection and Management)**
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **N/A**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **Page 17 (Ethical Approval and Dissemination Plan)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **Page 17 (Ethical Approval and Dissemination Plan)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **N/A**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **Supplementary File**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **N/A**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Health informatics, Patient-centred medicine
Keywords:	Surgical Site Infection, SURGERY, smartphone technology

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

Trial Registration: *ClinicalTrials.gov.* Reference No: NCT02704897

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Roles and responsibilities:

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Keywords: *Surgical Site Infection, smartphone technology, surgery*

MeSH Terms: *Surgical Wound Infection*, Diagnosis, Smartphone, General Surgery*

Abstract

Introduction

National data suggest that surgical site infection (SSI) complicates 2-10% of general surgery cases, although the patient-reported incidence is much higher. SSIs cause significant patient morbidity and represent a significant burden on acute healthcare services, in a cohort predominantly suitable for outpatient management. Over three-quarters of UK adults now own smartphones, which could be harnessed to improve access to care. We aim to investigate if a smartphone-delivered wound assessment tool results in earlier treatment.

Methods and Analysis

This is a randomised-controlled trial aiming to recruit 500 patients across NHS hospitals. All emergency abdominal surgery patients over the age of 16 who own smartphones will be considered eligible, with the exclusion of those with significant visual impairment. Participants will be randomised in a 1:1 ratio between standard post-operative care and the intervention – use of the smartphone tool in addition to standard post-operative care. The main outcome measure will be time-to-diagnosis of SSI with secondary outcome measures considering use of Emergency Department (ED) and General Practitioner (GP) services and patient experience. Follow-up will be conducted by clinicians blinded to group allocation. Analysis of time-to-diagnosis will be by comparison of means using an independent 2 sample t-test.

Ethics and Dissemination

This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis. The intervention is being used in addition to standard post-operative care. The study design and protocol were reviewed and approved by Southeast Scotland

Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016). Study findings will be presented at academic conferences, published in peer-reviewed journals, and are expected in 2020. A written lay summary will be available to study participants on request.

Trial Registration

ClinicalTrials.gov. Reference No: NCT02704897

Strengths and Limitations of this Study:

- This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis.
- There are broad eligibility criteria, and so it is expected the results will be generalisable to a wide population of patients undergoing abdominal surgery.
- Due to the nature of the intervention, only clinicians undertaking follow-up can be blinded to randomisation status.
- All patients will receive 30-day telephone or face-to-face follow-up to determine the occurrence of surgical site infections, however the gold-standard for diagnosis remains direct clinical assessment.
- Data on patient experience and acceptability of smartphone-delivered follow-up will be collected concurrently to guide future implementation of future telehealth interventions.

Introduction

Surgical site infection (SSI) complicates 2-10% of general surgical cases, with the highest rates of infection seen after colorectal surgery[1]. Infection and re-admission rates have not significantly changed in the last 10 years. The most common causative group is *Enterobactericae* (25% of cases), with *Staph. Aureus* (10%) and MRSA (3%) accounting for a small proportion of overall cases[1]. National surveillance data from Scotland indicate that peak incidence of infection is between day 6-12 post-operatively[2].

A recent study indicated that national reports may underestimate the true incidence of SSI, and suggested that patient reported SSI is a more sensitive measure [3]. Unpublished data from our own hospital indicates that up to 25% of patients report post-operative wound infections; approximately half of these require assessment by the surgical team, but less than 1% require admission. Many of these patients had already consulted their General Practitioner (GP) or attended the Emergency Department (ED). In addition, many patients have concerns about their wounds (in the absence of infection) and may experience delays in accessing appropriate medical assessment. Thus, SSI represents a significant burden on healthcare services, in a patient group who are predominantly appropriate for outpatient management.

There is currently an increased research focus on digital health: the use of communications technology to enhance healthcare, public health and delivery of health education[4]. There are several advantages to this approach, in particular the potential to improve access to care, and help streamline usage of emergency services. Indeed, there is evidence that these technologies have been used to improve outcome[5], as well as to reduce specialist workload [6] and ED attendances[7]. In addition, the increasing use of healthcare technology is

likely to help improve automatic data collection and recording, which may be used to identify areas for future research and drive quality improvement[4].

Over three-quarters (78%) of UK adults now own smartphones [8], with at least a third using a smartphone as their primary device to access the internet [4]. Therefore, there is vast potential for the use of smartphones in digital health, with a growing literature on the use in the context of postoperative community follow-up [9 10]. Given the frequency with which patients report post-operative wound complications and the high incidence of SSI, this has become a research focus in telemedicine for postoperative care [11 12]. We aim to investigate if an online wound assessment tool can be used to help diagnose SSI and improve patient access to care and clinical assessment. In addition, we aim to investigate if this results in earlier intervention to treat SSI and a decreased attendance at ED and GPs. The widespread use of smartphones, the integrated nature of their technology, and their portability means smartphones represent the best platform to deliver this tool, with the aim of facilitating rapid access to clinical care.

Objectives

This randomised-controlled trial will investigate whether a smartphone-delivered wound assessment tool can be used in the diagnosis of SSI and result in earlier treatment. It will also assess for a reduction in ED and GP attendances as a result of using the intervention. Data on patient experience will be used to evaluate perceived utility of the tool.

Methods and Analysis

Overview

This is a superiority randomised-controlled trial, using a parallel two-arm design (Figure 1). Once consent is obtained, participants will be randomised in a 1:1 ratio to either the intervention arm (receiving standard post-operative care plus access to the smartphone-delivered wound assessment tool), or the control arm (standard post-operative care). Patients will be recruited from the emergency surgery inpatient service across NHS Lothian. The trial period will be 30 days. An internal pilot study in the first 80 patients recruited will be conducted to ensure the trial design is practical and deliverable. Following assessment of pilot data, there will an opportunity to adapt the trial design in response to the pilot study findings. Participants will be followed-up by a researcher blinded to the intervention status. The primary outcome measure will be the number of days from surgery to diagnosis of SSI (time-to-diagnosis), with ED and GP service use as a secondary outcome measure. Additional data regarding patient experience will also be collected from patients in both arms of the trial via a smartphone-delivered questionnaire at 30 days.

Research Setting

This research is being carried out in a large health board, serving a mixed urban and rural population of over 800,000. The emergency surgery service admits 300 patients per week between participating sites and performs 2500 procedures annually.

Participants

Emergency surgery inpatients who are adults (over age 16) and have undergone abdominal surgery (on the same admission as diagnosis) will be screened for eligibility. Potentially eligible patients will be screened and documented as (a) eligible and included, (b) eligible and missed, (c) eligible and declined (iv) ineligible (visual impairment) (v) ineligible (no smartphone). Written consent will be obtained by the research team in line with Good

Clinical Practice Guidance. Participation is voluntary and a patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Inclusion Criteria

Patients admitted to the emergency surgery inpatient service who meet the following criteria will be included in the study:

- Emergency surgery inpatients who have undergone abdominal surgery;
- Owners of a smartphone, with access to internet;
- Adults over the age over 16;
- Able to give informed consent.

Exclusion Criteria

Any patients with significant visual impairment preventing use of the online questionnaire will be excluded from the study (defined by self-reporting of the patient)

Study Procedures

Recruitment

The clinical team will inform potentially eligible patients about the on-going trial, and offer them further information (written and verbal from the research team). Eligible patients will be recruited postoperatively as inpatients, with formal written consent taken by a member of the research team. Baseline information gathered will include: reason for admission, index procedure and date, significant co-morbidities – including history of diabetes or immunosuppression, as well as age and BMI. Participant contact details (mobile telephone number) will be entered into a secure, online data collection tool (Research Electronic Data Capture (REDCap) database) [13].

Randomisation and Blinding

Participants will be assigned in a 1:1 ratio to the intervention or control arms and provided with the appropriate information packs prior to discharge. Simple randomization will be carried out using REDCap[13], utilising a computer-generated random number sequence. The emergency surgery nurses (who will provide care to patients as required during the trial), and those taking consent (which may include medical students and qualified clinicians) will not be blinded. The clinicians undertaking follow-up will be blinded to status. A trial entry will be made in the clinical notes, including contact details for the trial team should a member of the clinical team require more information or wish to discover their trial status.

Intervention

Smartphone-Delivered Wound Assessment Tool

A wound-based instrument to detect potential wound infection was developed. Our smartphone-delivered wound assessment model was based on the Centre for Disease Control and Prevention (CDC) classification criteria, and the ASEPSIS model (Additional treatment, Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria, and the duration of Inpatient Stay).[14 15] It detects symptoms of SSI and symptoms of systemic illness as a result of this, whilst being quick and simple to use (Table 1).

Participants will have access to the smartphone-delivered wound assessment tool on discharge via a link sent by short-messaging system (SMS) to their smartphones. If at any time they have concerns about their wound, they can access the tool, and will be advised based on their responses. When a patient response is submitted, the research team will be automatically notified, and prompted to reply (Figure 2).

In addition, a link to the smartphone-delivered wound assessment tool will be sent on days 3, 7, and 15 post-operatively. These time-points have been selected to include peak incidence of infection and cover the time-course of wound healing. This will ensure the collection of negative data in those without symptoms and will therefore assist in determining the specificity of the tool. If participants do not respond they will be sent a single reminder at these time-points.

Wound Photographs

Participants will be asked to upload at least one photograph of their wound each time they use the smartphone-delivered wound assessment tool. These will be reviewed by a clinical researcher and assigned into one of 3 categories: no concerns, medium-risk, high-risk. Further machine learning-based assessment of wound photographs will be investigated.

Responses

An experienced clinician (surgical registrar or consultant) will review all participant responses and photographs in real-time. Based on the response and the wound photographs, they will contact the patient by SMS with advice regarding the need for further assessment. The clinician will classify participants into 3 groups: no concern, medium-risk, high-risk. These three groups were agreed collectively by the researchers in collaboration with the emergency surgical team. Three potential outcomes were identified: (i) the patient does not require further assessment (no concern), (ii) the patient requires further assessment, but the symptoms identified suggest a mild infection (medium-risk), (iii) the symptoms suggest a potentially severe infection requiring urgent assessment (high-risk). The wound photographs will also be reviewed by the experienced clinician where available and classified into the same 3 groups. This may be used by the researcher to refine their response to the tool, if they consider this necessary.

Algorithm

An algorithm has been designed to classify participant responses into the same 3 categories listed above (Table 1). This will be run on all participant responses (but will not impact on care), and will be compared with clinician rating, as a secondary sub-study. The correlation between clinician response, algorithm response and photo response will be used to determine if the algorithm can be used to assess for SSI independent of the responsible doctor.

Action from Response

Participants whose responses raise no concerns will be advised of this. Participants who report symptoms consistent with wound infection will be directed for further assessment. Those in the medium-risk group will be directed to community care whilst those in the high-risk group will be advised to return for assessment at the centre where they had their procedure. This advice aligns to the degree of concern identified above.

Wound Reviews

For those in the intervention group who are identified as high-risk, the emergency surgery nurses will collect a wound swab from the patient to test for causative organisms (and aid in confirming infection). If a wound infection is diagnosed clinically, the patient will be started with antibiotics in line with local guidelines. This will be logged in the patient's trial record. If any patients in the control group attend the emergency surgery service for a review the same procedures will apply.

GPs will be informed about their patient's participation in the trial. We will request that if a participant enrolled in the trial visits their GP a wound swab is taken, and that they are

treated in line with the GP's normal practice. This will also apply to those in the medium-risk group who will be directed to their GP.

All participants will be given a log to take to any wound reviews, and wound swabs may be taken of wound discharge or the wound bed as appropriate. If an infection is diagnosed the date treatment is commenced will be noted, alongside any intervention performed. This will then be returned to the trial team, and used in follow-up.

30 Day Follow-up

Both arms will receive a follow-up face-to-face or telephone consultation 30 days post-operatively (alternatively, written follow-up is also available for those with significant hearing impairment). This consultation will follow a standardized format and will be conducted with an independent clinical researcher blinded to the intervention status. The clinical researcher will gather data on post-operative course, any symptoms related to the wound, and any treatment offered. They will also have access to electronic patient record (including all microbiology results from swabs taken in the community or hospital) and any wound logs returned. On the basis of these three sources of information, two independent, blinded clinical researchers will determine if an infection has been present (trained using the CDC Criteria to diagnose infection).[14] Data on patient experience and service usage – ED and GP attendances, as well as contact with emergency surgery nurses – will also be collected via a separate questionnaire delivered alongside the 30 day follow-up (Table 2).

Data Analysis Plan

All analysis will be carried out on an intention-to-treat basis. We do not anticipate missing data in patient demographics. However, any missing data values will be handled using multiple imputation. The volume of missing outcome data will be recorded for the control

and intervention arms, and any differences in drop-out rate noted. Thereafter patients with missing outcome data will be excluded from analysis.

Outcome Measures

This is a superiority RCT, and the primary outcome will be mean time from operation to diagnosis (time-to-diagnosis) of SSI. This outcome has been chosen (rather than time from symptom onset), as it can be more accurately recorded and is a measure of improved access to care. We assume an equal incidence of SSI in both groups and will ensure this using odds ratios. Time-to-diagnosis will also be compared using Cox proportional hazard regression analysis, a *P* value of <0.05 will be considered statistically significant.

For the intervention, we will calculate the sensitivity and specificity of the researcher response, the algorithm response, and photograph response in the diagnosis of SSI. We will compare the correlation of the algorithm, which is based on questionnaire responses, with clinician advice and eventual diagnosis. Correlation analysis will be performed using Kendall tau rank test. This will assess the accuracy of the algorithm in stratifying risk, as compared to a clinician, and will indicate what additional benefit may be gained from photographic analysis.

The secondary outcome measure will be use of services: GP and ED attendances, as well as contact with emergency surgery nurses. This data will be gathered at 30 days. Differences in number of attendees to GP and ED will be compared using a χ^2 test. Differences in the number of attendances will be assessed using the Mann-Whitney U-test.

Data on patient experience will also be gathered via a follow-up questionnaire and analysed separately (Table 2). This will help determine if an online questionnaire delivered via a

smartphone has a positive impact on patient experience of care, and if it helped facilitate their access to care.

Sample Size and Power Analysis

Our primary outcome measure is time-to-diagnosis and we aim to detect a one-day difference with a power of 90% (alpha 0.05). Assuming a standard deviation of 1 day in time-to-diagnosis, 22 wound infections per group will be required. Estimating a 10% rate of wound infection (in line with National Data)[2] and a drop-out rate of 10%, a sample size of 490 will be required (recruitment target 500 patients). Analyses will be intention-to-treat.

Assuming that 50 operations are performed per week and two thirds of these patients are likely to own smartphones, we estimate there will be 30 potentially eligible patients per week. Aiming for recruitment of 25% of eligible patients, we estimate a continuous recruitment time of 16 months. This rate of recruitment will also enable the researcher to respond to all patient concerns in a timely manner.

Ethics and dissemination:

Safety

All participants will receive the normal standard of care. The smartphone-based intervention is in addition to the normal standard of care. If at any point participants have any concerns. they will be advised to contact the emergency surgery nurses regarding their care (in line with normal standard of care). Out-of-hours they will be advised to contact NHS out-of-hours services. Participants will be advised to contact the emergency surgery nurses if they have any concerns whilst they are awaiting a response to the tool. The research team will be notified automatically that a participant is awaiting a response, ensuring that in normal working hours patients receive a rapid reply. They will also be advised that if they access

the tool at night, that it will not be reviewed until the following day. They will be advised to contact out-of-hours services if they require an overnight assessment. These actions will prevent any harm to patients resulting from a delayed response to the wound assessment tool. A potential consequence of closer follow-up of these postoperative patients could be increased identification of superficial SSI which would likely otherwise self-resolve, however this would closer surveillance or treatment if appropriate (this decision is made by an independent clinician at the time of review). Due to the low-risk nature of the trial, a formal data-monitoring committee has not been nominated.

Data Protection and Management

All participant data will be stored securely in a REDCap [13] database that has controlled access and is password protected. This data will be anonymised, and only available to researchers listed on the protocol. Participant responses to the questionnaire will be reported directly to the REDCap database and will not be stored on patient phones. However, patients will be advised to review the security setting on their phone if they intend to store their wound photographs. Patient details will be recorded in a trial log should any safety concerns arise necessitating they be contacted.

Ethical Approval and Dissemination Plan

The study design and protocol were reviewed and approved by Southeast Scotland Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016), and any protocol amendments will be resubmitted for review. The study is sponsored by ACCORD, a collaboration between the University of Edinburgh and NHS Lothian Research and Development. In line with Good Clinical Practice Guidance, written consent will be obtained by appropriately trained medical students or clinicians. Participation is voluntary and a

patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Authorship on any papers derived from the study will be all authors involved in study design and protocol development, and any additional researchers involved in the writing group. Furthermore, patient recruiters who have recruited more than the prespecified 15 patients to the study will be listed as a "collaborator". All other persons involved in the study will be listed in the acknowledgements.

There are no financial and other competing interests for principal investigators for the overall trial or either study site. Study findings will be reported in line with CONSORT guidelines, and disseminated in the printed media, and learned forums, and are expected in 2020. A written lay summary will be available to study participants on request.

Patient and Public Involvement

Patients were not directly involved in the design or delivery of this trial, however data on patient experience in using the smartphone tool will be evaluated via a follow-up questionnaire. This will inform future development and dissemination of this intervention. A summary of results will be provided to all patients involved once the trial has been completed and analysed.

Authors' Contributions

(1) Conception and design: KEM, CAS, TMD, KAM, RO, AS, RS, MP, SJW, EH. (2) Drafting the manuscript: KAM, KEM, CAS, TMD, RO, SRK, CJF, AS. (4) Critical revision of the manuscript for scientific and factual content: KAM, KEM, CAS, TMD, RO, SRK, CJF, AS, RS, MP, SJW, EH. Supervision: RS, MP, SJW, EH. All authors read and approved the final manuscript.

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Competing interests

The authors do not have any conflicts of interest to declare.

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Figure 1: Schema of trial events for intervention and control arms.

Figure 2: Handling of wound questionnaire submissions.

Tables:

Table 1: Questions included in smartphone-delivered questionnaire and independent algorithm scoring system.

Smartphone-delivered wound assessment		**Algorithm scoring system**		
Question	**Response (score)**	**Low-risk**	**Medium-Risk**	**High-risk**
Is the pain worse than immediately after the operation?	No (0), Yes (1)	Inflammation Score 0	Inflammation Score ≤2	Inflammation Score ≥3
Is there new redness around your wound site excluding the wound itself?	No (0), Yes (1)			
Is there more swelling around your wound site than at the time of surgery?	No (0), Yes (1)			
Are you experiencing a new burning sensation or heat at the wound site?	No (0), Yes (1)			
		AND	**AND**	**OR**
Is there liquid coming from the wound site? If so, please select which option best describes the liquid.	No (0), Yes – clear (1), Yes – bloody (1), Yes – yellowish (1), Yes – thick/yellow (2), Yes – green/brown (2)	Discharge Score 0	Discharge Score ≤1	Discharge Score 2
Is your wound opening or gaping?	No, Yes	Not scored in algorithm		
Have you experienced fevers in the last 24 hours?	No, Yes			
Please upload a photograph of your wound.	Photograph	Not scored in algorithm		

Table 2: Questions included in smartphone-delivered 30-day patient experience questionnaire.

Smartphone-delivered 30-day patient experience questionnaire	
Question	**Available responses**
1. Did you have access to the smartphone tool?	Yes, No
2. If you had access to the tool, how many times did you use the tool (not including the reminder questions sent)?	[integer]
3. If you had access to the tool, please rate the extent to which you agree/disagree with the statements below:	
a. The tool was easy to use b. I understood the questions in the tool c. It was easy to upload my wound photo d. The response from the tool was helpful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.
4. Please rate the extent to which you agree/disagree with the statements below:	
a. It was easy to get hold of advice about my wound when needed b. I had to wait more than 1 day for advice about my wound c. The advice I received about my wound was useful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.

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15. Wilson APR, Sturridge MF, Treasure T, et al. A scoring method (ASEPSIS) for postoperative wound infections for use in clinical trials of antibiotic prophylaxis. *The Lancet* 1986;327(8476):311-12.

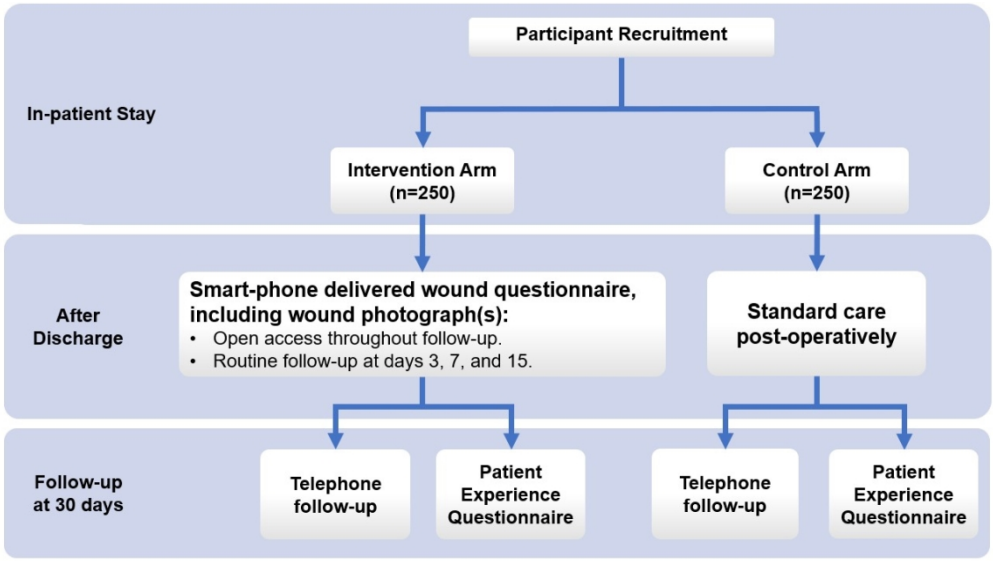

Figure 1: Schema of trial events for intervention and control arms

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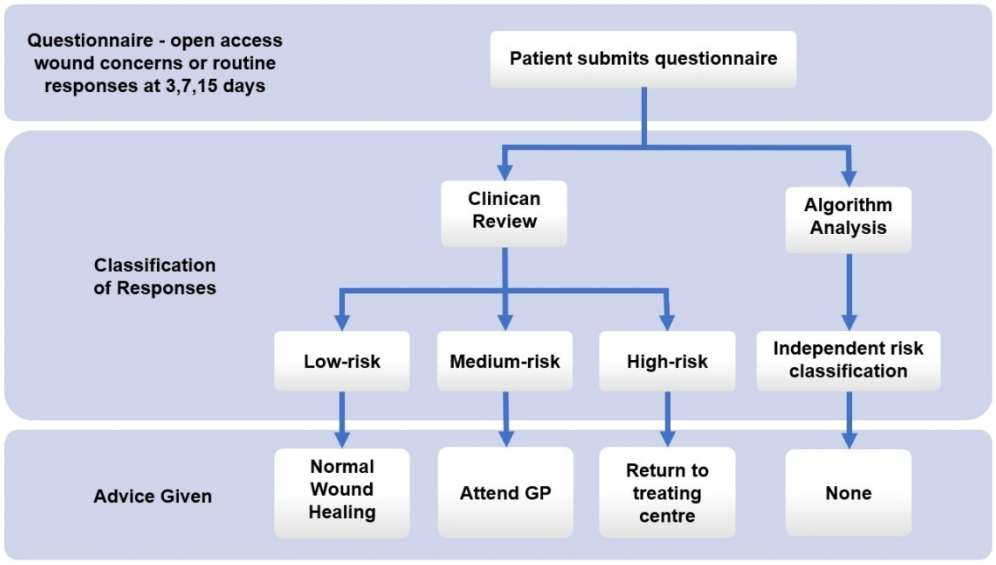

Figure 2: Handling of wound questionnaire submissions

811x454mm (120 x 120 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients**.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
	2b	All items from the World Health Organization Trial Registration Data Set ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
Protocol version	3	Date and version identifier **Page 1**
Funding	4	Sources and types of financial, material, and other support **Page 1**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **Page 1**
	5b	Name and contact information for the trial sponsor **Page 1**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **Page 1**

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **Page 1**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **Page 5-6**
	6b	Explanation for choice of comparators **Page 5-6**
Objectives	7	Specific objectives or hypotheses **Page 7**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **Page 8 (overview)**
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **Page 8 (research setting)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **Page 8-9 (Patients, inclusion criteria, exclusion criteria)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. **Page 10-13**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). **Page 17**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). **N/A**

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **N/A**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **Page 14 (outcome measures)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **Figure 1**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **Page 15 (Sample Size and Power Analysis).**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. **Page 9 (Recruitment)**
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **Page 10 (Randomisation and Blinding).**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **Page 10 (Randomisation and Blinding).**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **Page 10 (Randomisation and Blinding).**

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. **Page 10 (Randomisation and Blinding).**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **N/A**

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **Page 9 (Recruitment); Page 10 (Smartphone-Delivered Wound Assessment Tool); Table 1**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **Page 10 (Smartphone-Delivered Wound Assessment Tool); Page 13 (Data analysis plan)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. **Page 16 (Data Protection and Management).**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. **Page 13 (Data Analysis Plan / Outcome Measures)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **Page 13 (Data Analysis Plan / Outcome Measures)**
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **Page 13 (Data Analysis Plan / Outcome Measures)**

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **Page 16 (safety)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **N/A**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **Page 16 (safety)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **N/A**

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **Page 17 (Ethical Approval and Dissemination Plan)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **Page 17 (Ethical Approval and Dissemination Plan)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **Page 17 (Ethical Approval and Dissemination Plan)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **N/A**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **Page 16 (Data Protection and Management)**

Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **Page 18**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **Page 16 (Data Protection and Management)**
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **N/A**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **Page 17 (Ethical Approval and Dissemination Plan)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **Page 17 (Ethical Approval and Dissemination Plan)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **N/A**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **Supplementary File**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **N/A**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-029620.R2
Article Type:	Protocol
Date Submitted by the Author:	01-Aug-2019
Complete List of Authors:	McLean, Kenneth; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Mountain, Katie; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Shaw, Catherine; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Drake, Thomas ; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Ots, Riinu; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Knight, Stephen; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Fairfield, Cameron; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Sgrò, Alessandro; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Skipworth, Richard; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Wigmore, Stephen; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Potter, Mark; Western General Hospital, Crewe Rd S, Edinburgh, EH4 2XU, UK, Colorectal Unit Harrison, Ewen ; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery,
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Health informatics, Patient-centred medicine
Keywords:	Surgical Site Infection, SURGERY, smartphone technology

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

Trial Registration: *ClinicalTrials.gov.* Reference No: NCT02704897

Protocol version: 2.0.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Roles and responsibilities:

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Keywords: *Surgical Site Infection, smartphone technology, surgery*

MeSH Terms: *Surgical Wound Infection*, Diagnosis, Smartphone, General Surgery*

Abstract

Introduction

National data suggest that surgical site infection (SSI) complicates 2-10% of general surgery cases, although the patient-reported incidence is much higher. SSIs cause significant patient morbidity and represent a significant burden on acute healthcare services, in a cohort predominantly suitable for outpatient management. Over three-quarters of UK adults now own smartphones, which could be harnessed to improve access to care. We aim to investigate if a smartphone-delivered wound assessment tool results in earlier treatment.

Methods and Analysis

This is a randomised-controlled trial aiming to recruit 500 patients across NHS hospitals. All emergency abdominal surgery patients over the age of 16 who own smartphones will be considered eligible, with the exclusion of those with significant visual impairment. Participants will be randomised in a 1:1 ratio between standard post-operative care and the intervention – use of the smartphone tool in addition to standard post-operative care. The main outcome measure will be time-to-diagnosis of SSI with secondary outcome measures considering use of Emergency Department (ED) and General Practitioner (GP) services and patient experience. Follow-up will be conducted by clinicians blinded to group allocation. Analysis of time-to-diagnosis will be by comparison of means using an independent 2 sample t-test.

Ethics and Dissemination

This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis. The intervention is being used in addition to standard post-operative care. The study design and protocol were reviewed and approved by Southeast Scotland

Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016). Study findings will be presented at academic conferences, published in peer-reviewed journals, and are expected in 2020. A written lay summary will be available to study participants on request.

Trial Registration

ClinicalTrials.gov. Reference No: NCT02704897

Strengths and Limitations of this Study:

- This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis.
- There are broad eligibility criteria, and so it is expected the results will be generalisable to a wide population of patients undergoing abdominal surgery.
- Due to the nature of the intervention, only clinicians undertaking follow-up can be blinded to randomisation status.
- All patients will receive 30-day telephone or face-to-face follow-up to determine the occurrence of surgical site infections, however the gold-standard for diagnosis remains direct clinical assessment.
- Data on patient experience and acceptability of smartphone-delivered follow-up will be collected concurrently to guide future implementation of future telehealth interventions.

Introduction

Surgical site infection (SSI) complicates 2-10% of general surgical cases, with the highest rates of infection seen after colorectal surgery[1]. Infection and re-admission rates have not significantly changed in the last 10 years. The most common causative group is *Enterobactericae* (25% of cases), with *Staph. Aureus* (10%) and MRSA (3%) accounting for a small proportion of overall cases[1]. National surveillance data from Scotland indicate that peak incidence of infection is between day 6-12 post-operatively[2].

A recent study indicated that national reports may underestimate the true incidence of SSI, and suggested that patient reported SSI is a more sensitive measure [3]. Unpublished data from our own hospital indicates that up to 25% of patients report post-operative wound infections; approximately half of these require assessment by the surgical team, but less than 1% require admission. Many of these patients had already consulted their General Practitioner (GP) or attended the Emergency Department (ED). In addition, many patients have concerns about their wounds (in the absence of infection) and may experience delays in accessing appropriate medical assessment. Thus, SSI represents a significant burden on healthcare services, in a patient group who are predominantly appropriate for outpatient management.

There is currently an increased research focus on digital health: the use of communications technology to enhance healthcare, public health and delivery of health education[4]. There are several advantages to this approach, in particular the potential to improve access to care, and help streamline usage of emergency services. Indeed, there is evidence that these technologies have been used to improve outcome[5], as well as to reduce specialist workload [6] and ED attendances[7]. In addition, the increasing use of healthcare technology is

likely to help improve automatic data collection and recording, which may be used to identify areas for future research and drive quality improvement[4].

Over three-quarters (78%) of UK adults now own smartphones [8], with at least a third using a smartphone as their primary device to access the internet [4]. Therefore, there is vast potential for the use of smartphones in digital health, with a growing literature on the use in the context of postoperative community follow-up [9 10]. Given the frequency with which patients report post-operative wound complications and the high incidence of SSI, this has become a research focus in telemedicine for postoperative care [11 12]. We aim to investigate if an online wound assessment tool can be used to help diagnose SSI and improve patient access to care and clinical assessment. In addition, we aim to investigate if this results in earlier intervention to treat SSI and a decreased attendance at ED and GPs. The widespread use of smartphones, the integrated nature of their technology, and their portability means smartphones represent the best platform to deliver this tool, with the aim of facilitating rapid access to clinical care.

Objectives

This randomised-controlled trial will investigate whether a smartphone-delivered wound assessment tool can be used in the diagnosis of SSI and result in earlier treatment. It will also assess for a reduction in ED and GP attendances as a result of using the intervention. Data on patient experience will be used to evaluate perceived utility of the tool.

Methods and Analysis

Overview

This is a superiority randomised-controlled trial, using a parallel two-arm design (Figure 1). Once consent is obtained, participants will be randomised in a 1:1 ratio to either the intervention arm (receiving standard post-operative care plus access to the smartphone-delivered wound assessment tool), or the control arm (standard post-operative care). Patients will be recruited from the emergency surgery inpatient service across NHS Lothian. The trial period will be 30 days. An internal pilot study in the first 80 patients recruited will be conducted to ensure the trial design is practical and deliverable. Following assessment of pilot data, there will an opportunity to adapt the trial design in response to the pilot study findings. Participants will be followed-up by a researcher blinded to the intervention status. The primary outcome measure will be the number of days from surgery to diagnosis of SSI (time-to-diagnosis), with ED and GP service use as a secondary outcome measure. Additional data regarding patient experience will also be collected from patients in both arms of the trial via a smartphone-delivered questionnaire at 30 days.

Research Setting

This research is being carried out in a large health board, serving a mixed urban and rural population of over 800,000. The emergency surgery service admits 300 patients per week between participating sites and performs 2500 procedures annually.

Participants

Emergency surgery inpatients who are adults (over age 16) and have undergone abdominal surgery (on the same admission as diagnosis) will be screened for eligibility. Potentially eligible patients will be screened and documented as (a) eligible and included, (b) eligible and missed, (c) eligible and declined (iv) ineligible (visual impairment) (v) ineligible (no smartphone). Written consent will be obtained by the research team in line with Good

Clinical Practice Guidance. Participation is voluntary and a patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Inclusion Criteria

Patients admitted to the emergency surgery inpatient service who meet the following criteria will be included in the study:

- Emergency surgery inpatients who have undergone abdominal surgery;
- Owners of a smartphone, with access to internet;
- Adults over the age over 16;
- Able to give informed consent.

Exclusion Criteria

Any patients with significant visual impairment preventing use of the online questionnaire will be excluded from the study (defined by self-reporting of the patient)

Study Procedures

Recruitment

The clinical team will inform potentially eligible patients about the on-going trial, and offer them further information (written and verbal from the research team). Eligible patients will be recruited postoperatively as inpatients, with formal written consent taken by a member of the research team. Baseline information gathered will include: reason for admission, index procedure and date, significant co-morbidities – including history of diabetes or immunosuppression, as well as age and BMI. Participant contact details (mobile telephone number) will be entered into a secure, online data collection tool (Research Electronic Data Capture (REDCap) database) [13].

Randomisation and Blinding

Participants will be assigned in a 1:1 ratio to the intervention or control arms and provided with the appropriate information packs prior to discharge. Simple randomization will be carried out using REDCap[13], utilising a computer-generated random number sequence. The emergency surgery nurses (who will provide care to patients as required during the trial), and those taking consent (which may include medical students and qualified clinicians) will not be blinded. The clinicians undertaking follow-up will be blinded to status. A trial entry will be made in the clinical notes, including contact details for the trial team should a member of the clinical team require more information or wish to discover their trial status.

Intervention

Smartphone-Delivered Wound Assessment Tool

A wound-based instrument to detect potential wound infection was developed. Our smartphone-delivered wound assessment model was based on the Centre for Disease Control and Prevention (CDC) classification criteria, and the ASEPSIS model (Additional treatment, Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria, and the duration of Inpatient Stay).[14 15] It detects symptoms of SSI and symptoms of systemic illness as a result of this, whilst being quick and simple to use (Table 1).

Participants will have access to the smartphone-delivered wound assessment tool on discharge via a link sent by short-messaging system (SMS) to their smartphones. If at any time they have concerns about their wound, they can access the tool, and will be advised based on their responses. When a patient response is submitted, the research team will be automatically notified, and prompted to reply (Figure 2).

In addition, a link to the smartphone-delivered wound assessment tool will be sent on days 3, 7, and 15 post-operatively. These time-points have been selected to include peak incidence of infection and cover the time-course of wound healing. This will ensure the collection of negative data in those without symptoms and will therefore assist in determining the specificity of the tool. If participants do not respond they will be sent a single reminder at these time-points.

Wound Photographs

Participants will be asked to upload at least one photograph of their wound each time they use the smartphone-delivered wound assessment tool. These will be reviewed by a clinical researcher and assigned into one of 3 categories: no concerns, medium-risk, high-risk. Further machine learning-based assessment of wound photographs will be investigated.

Responses

An experienced clinician (surgical registrar or consultant) will review all participant responses and photographs in real-time. Based on the response and the wound photographs, they will contact the patient by SMS with advice regarding the need for further assessment. The clinician will classify participants into 3 groups: no concern, medium-risk, high-risk. These three groups were agreed collectively by the researchers in collaboration with the emergency surgical team. Three potential outcomes were identified: (i) the patient does not require further assessment (no concern), (ii) the patient requires further assessment, but the symptoms identified suggest a mild infection (medium-risk), (iii) the symptoms suggest a potentially severe infection requiring urgent assessment (high-risk). The wound photographs will also be reviewed by the experienced clinician where available and classified into the same 3 groups. This may be used by the researcher to refine their response to the tool, if they consider this necessary.

Algorithm

An algorithm has been designed to classify participant responses into the same 3 categories listed above (Table 1). This will be run on all participant responses (but will not impact on care), and will be compared with clinician rating, as a secondary sub-study. The correlation between clinician response, algorithm response and photo response will be used to determine if the algorithm can be used to assess for SSI independent of the responsible doctor.

Action from Response

Participants whose responses raise no concerns will be advised of this. Participants who report symptoms consistent with wound infection will be directed for further assessment. Those in the medium-risk group will be directed to community care whilst those in the high-risk group will be advised to return for assessment at the centre where they had their procedure. This advice aligns to the degree of concern identified above.

Wound Reviews

For those in the intervention group who are identified as high-risk, the emergency surgery nurses will collect a wound swab from the patient to test for causative organisms (and aid in confirming infection). If a wound infection is diagnosed clinically, the patient will be started with antibiotics in line with local guidelines. This will be logged in the patient's trial record. If any patients in the control group attend the emergency surgery service for a review the same procedures will apply.

GPs will be informed about their patient's participation in the trial. We will request that if a participant enrolled in the trial visits their GP a wound swab is taken, and that they are

treated in line with the GP's normal practice. This will also apply to those in the medium-risk group who will be directed to their GP.

All participants will be given a log to take to any wound reviews, and wound swabs may be taken of wound discharge or the wound bed as appropriate. If an infection is diagnosed the date treatment is commenced will be noted, alongside any intervention performed. This will then be returned to the trial team, and used in follow-up.

30 Day Follow-up

Both arms will receive a follow-up face-to-face or telephone consultation 30 days post-operatively (alternatively, written follow-up is also available for those with significant hearing impairment). This consultation will follow a standardized format and will be conducted with an independent clinical researcher blinded to the intervention status. The clinical researcher will gather data on post-operative course, any symptoms related to the wound, and any treatment offered. They will also have access to electronic patient record (including all microbiology results from swabs taken in the community or hospital) and any wound logs returned. On the basis of these three sources of information, two independent, blinded clinical researchers will determine if an infection has been present (trained using the CDC Criteria to diagnose infection).[14] Data on patient experience and service usage – ED and GP attendances, as well as contact with emergency surgery nurses – will also be collected via a separate questionnaire delivered alongside the 30 day follow-up (Table 2).

Data Analysis Plan

All analysis will be carried out on an intention-to-treat basis. We do not anticipate missing data in patient demographics. However, any missing data values will be handled using multiple imputation. The volume of missing outcome data will be recorded for the control

and intervention arms, and any differences in drop-out rate noted. Thereafter patients with missing outcome data will be excluded from analysis.

Outcome Measures

This is a superiority RCT, and the primary outcome will be mean time from operation to diagnosis (time-to-diagnosis) of SSI. This outcome has been chosen (rather than time from symptom onset), as it can be more accurately recorded and is a measure of improved access to care. We assume an equal incidence of SSI in both groups and will ensure this using odds ratios. Time-to-diagnosis will also be compared using Cox proportional hazard regression analysis, a *P* value of <0.05 will be considered statistically significant.

For the intervention, we will calculate the sensitivity and specificity of the researcher response, the algorithm response, and photograph response in the diagnosis of SSI. We will compare the correlation of the algorithm, which is based on questionnaire responses, with clinician advice and eventual diagnosis. Correlation analysis will be performed using Kendall tau rank test. This will assess the accuracy of the algorithm in stratifying risk, as compared to a clinician, and will indicate what additional benefit may be gained from photographic analysis.

The secondary outcome measure will be use of services: GP and ED attendances, as well as contact with emergency surgery nurses. This data will be gathered at 30 days. Differences in number of attendees to GP and ED will be compared using a χ^2 test. Differences in the number of attendances will be assessed using the Mann-Whitney U-test.

Data on patient experience will also be gathered via a follow-up questionnaire and analysed separately (Table 2). This will help determine if an online questionnaire delivered via a

smartphone has a positive impact on patient experience of care, and if it helped facilitate their access to care.

Sample Size and Power Analysis

Our primary outcome measure is time-to-diagnosis and we aim to detect a one-day difference with a power of 90% (alpha 0.05). Assuming a standard deviation of 1 day in time-to-diagnosis, 22 wound infections per group will be required. Estimating a 10% rate of wound infection (in line with National Data)[2] and a drop-out rate of 10%, a sample size of 490 will be required (recruitment target 500 patients). Analyses will be intention-to-treat.

Assuming that 50 operations are performed per week and two thirds of these patients are likely to own smartphones, we estimate there will be 30 potentially eligible patients per week. Aiming for recruitment of 25% of eligible patients, we estimate a continuous recruitment time of 16 months. This rate of recruitment will also enable the researcher to respond to all patient concerns in a timely manner.

Ethics and dissemination:

Safety

All participants will receive the normal standard of care. The smartphone-based intervention is in addition to the normal standard of care. If at any point participants have any concerns. they will be advised to contact the emergency surgery nurses regarding their care (in line with normal standard of care). Out-of-hours they will be advised to contact NHS out-of-hours services. Participants will be advised to contact the emergency surgery nurses if they have any concerns whilst they are awaiting a response to the tool. The research team will be notified automatically that a participant is awaiting a response, ensuring that in normal working hours patients receive a rapid reply. They will also be advised that if they access

the tool at night, that it will not be reviewed until the following day. They will be advised to contact out-of-hours services if they require an overnight assessment. These actions will prevent any harm to patients resulting from a delayed response to the wound assessment tool. A potential consequence of closer follow-up of these postoperative patients could be increased identification of superficial SSI which would likely otherwise self-resolve, however this would closer surveillance or treatment if appropriate (this decision is made by an independent clinician at the time of review). Due to the low-risk nature of the trial, a formal data-monitoring committee has not been nominated.

Data Protection and Management

All participant data will be stored securely in a REDCap [13] database that has controlled access and is password protected. This data will be anonymised, and only available to researchers listed on the protocol. Participant responses to the questionnaire will be reported directly to the REDCap database and will not be stored on patient phones. However, patients will be advised to review the security setting on their phone if they intend to store their wound photographs. Patient details will be recorded in a trial log should any safety concerns arise necessitating they be contacted.

Ethical Approval and Dissemination Plan

The study design and protocol were reviewed and approved by Southeast Scotland Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016), and any protocol amendments will be resubmitted for review. The study is sponsored by ACCORD, a collaboration between the University of Edinburgh and NHS Lothian Research and Development. In line with Good Clinical Practice Guidance, written consent will be obtained by appropriately trained medical students or clinicians. Participation is voluntary and a

patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Authorship on any papers derived from the study will be all authors involved in study design and protocol development, and any additional researchers involved in the writing group. Furthermore, patient recruiters who have recruited more than the prespecified 15 patients to the study will be listed as a "collaborator". All other persons involved in the study will be listed in the acknowledgements.

There are no financial and other competing interests for principal investigators for the overall trial or either study site. Study findings will be reported in line with CONSORT guidelines, and disseminated in the printed media, and learned forums, and are expected in 2020. A written lay summary will be available to study participants on request.

Patient and Public Involvement

Patients were not directly involved in the design or delivery of this trial, however data on patient experience in using the smartphone tool will be evaluated via a follow-up questionnaire. This will inform future development and dissemination of this intervention. A summary of results will be provided to all patients involved once the trial has been completed and analysed.

Authors' Contributions

(1) Conception and design: KEM, CAS, TMD, KAM, RO, AS, RS, MP, SJW, EH. (2) Drafting the manuscript: KAM, KEM, CAS, TMD, RO, SRK, CJF, AS. (4) Critical revision of the manuscript for scientific and factual content: KAM, KEM, CAS, TMD, RO, SRK, CJF, AS, RS, MP, SJW, EH. Supervision: RS, MP, SJW, EH. All authors read and approved the final manuscript.

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Competing interests

The authors do not have any conflicts of interest to declare.

Word Count: 3,158

Figure 1: Schema of trial events for intervention and control arms.

Figure 2: Handling of wound questionnaire submissions.

Tables:

Table 1: Questions included in smartphone-delivered questionnaire and independent algorithm scoring system.

Smartphone-delivered wound assessment		**Algorithm scoring system**		
Question	**Response (score)**	**Low-risk**	**Medium-Risk**	**High-risk**
Is the pain worse than immediately after the operation?	No (0), Yes (1)	Inflammation Score 0	Inflammation Score ≤2	Inflammation Score ≥3
Is there new redness around your wound site excluding the wound itself?	No (0), Yes (1)			
Is there more swelling around your wound site than at the time of surgery?	No (0), Yes (1)			
Are you experiencing a new burning sensation or heat at the wound site?	No (0), Yes (1)			
		AND	**AND**	**OR**
Is there liquid coming from the wound site? If so, please select which option best describes the liquid.	No (0), Yes – clear (1), Yes – bloody (1), Yes – yellowish (1), Yes – thick/yellow (2), Yes – green/brown (2)	Discharge Score 0	Discharge Score ≤1	Discharge Score 2
Is your wound opening or gaping?	No, Yes	Not scored in algorithm		
Have you experienced fevers in the last 24 hours?	No, Yes			
Please upload a photograph of your wound.	Photograph	Not scored in algorithm		

Table 2: Questions included in smartphone-delivered 30-day patient experience questionnaire.

Smartphone-delivered 30-day patient experience questionnaire	
Question	**Available responses**
1. Did you have access to the smartphone tool?	Yes, No
2. If you had access to the tool, how many times did you use the tool (not including the reminder questions sent)?	[integer]
3. If you had access to the tool, please rate the extent to which you agree/disagree with the statements below:	
a. The tool was easy to use b. I understood the questions in the tool c. It was easy to upload my wound photo d. The response from the tool was helpful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.
4. Please rate the extent to which you agree/disagree with the statements below:	
a. It was easy to get hold of advice about my wound when needed b. I had to wait more than 1 day for advice about my wound c. The advice I received about my wound was useful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.

References:

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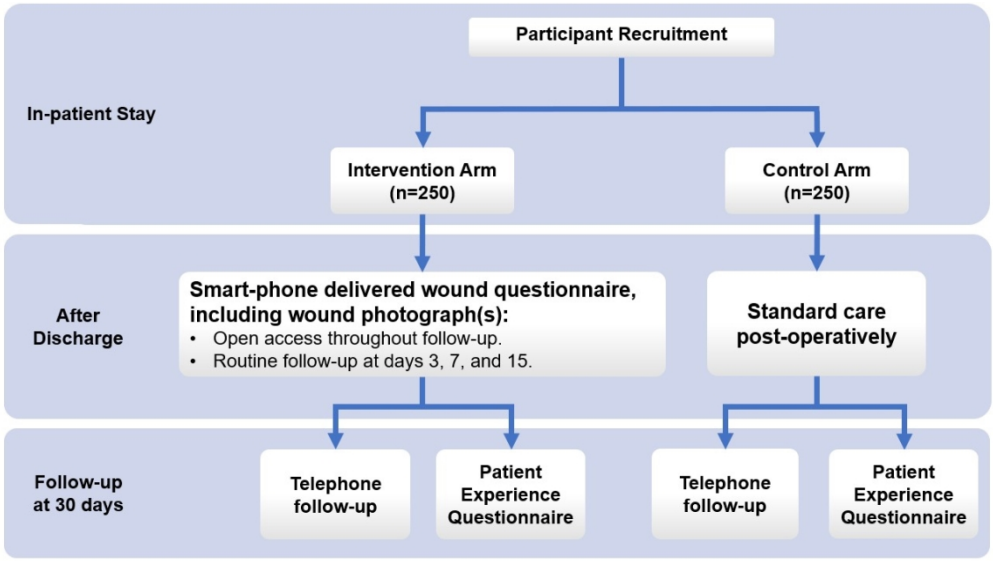

Figure 1: Schema of trial events for intervention and control arms

812x453mm (120 x 120 DPI)

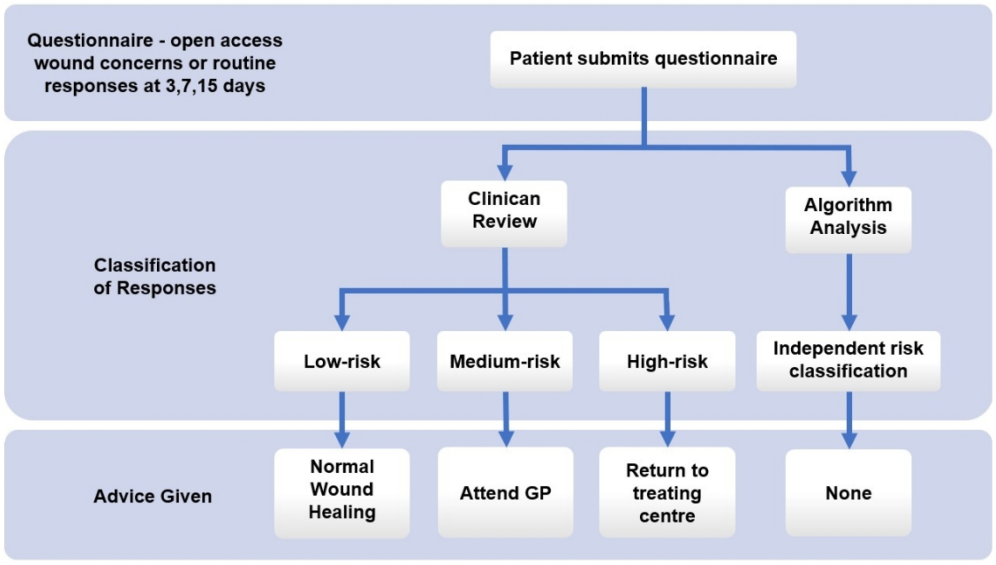

Figure 2: Handling of wound questionnaire submissions

811x454mm (120 x 120 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients**.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
	2b	All items from the World Health Organization Trial Registration Data Set ***ClinicalTrials.gov.*** **Reference No: NCT02704897**
Protocol version	3	Date and version identifier **Page 1**
Funding	4	Sources and types of financial, material, and other support **Page 1**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **Page 1**
	5b	Name and contact information for the trial sponsor **Page 1**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **Page 1**

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **Page 1**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **Page 5-6**
	6b	Explanation for choice of comparators **Page 5-6**
Objectives	7	Specific objectives or hypotheses **Page 7**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **Page 8 (overview)**
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **Page 8 (research setting)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **Page 8-9 (Patients, inclusion criteria, exclusion criteria)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. **Page 10-13**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). **Page 17**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). **N/A**

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **N/A**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **Page 14 (outcome measures)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **Figure 1**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **Page 15 (Sample Size and Power Analysis).**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. **Page 9 (Recruitment)**
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **Page 10 (Randomisation and Blinding).**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **Page 10 (Randomisation and Blinding).**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **Page 10 (Randomisation and Blinding).**

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. **Page 10 (Randomisation and Blinding).**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **N/A**

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **Page 9 (Recruitment); Page 10 (Smartphone-Delivered Wound Assessment Tool); Table 1**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **Page 10 (Smartphone-Delivered Wound Assessment Tool); Page 13 (Data analysis plan)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. **Page 16 (Data Protection and Management).**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. **Page 13 (Data Analysis Plan / Outcome Measures)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **Page 13 (Data Analysis Plan / Outcome Measures)**
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **Page 13 (Data Analysis Plan / Outcome Measures)**

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **Page 16 (safety)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **N/A**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **Page 16 (safety)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **N/A**

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **Page 17 (Ethical Approval and Dissemination Plan)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **Page 17 (Ethical Approval and Dissemination Plan)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **Page 17 (Ethical Approval and Dissemination Plan)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **N/A**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **Page 16 (Data Protection and Management)**

Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **Page 18**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **Page 16 (Data Protection and Management)**
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **N/A**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **Page 17 (Ethical Approval and Dissemination Plan)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **Page 17 (Ethical Approval and Dissemination Plan)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **N/A**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **Supplementary File**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **N/A**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-029620.R3
Article Type:	Protocol
Date Submitted by the Author:	26-Aug-2019
Complete List of Authors:	McLean, Kenneth; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Mountain, Katie; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Shaw, Catherine; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Drake, Thomas ; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Ots, Riinu; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Knight, Stephen; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Fairfield, Cameron; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Sgrò, Alessandro; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Skipworth, Richard; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Wigmore, Stephen; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery, Potter, Mark; Western General Hospital, Crewe Rd S, Edinburgh, EH4 2XU, UK, Colorectal Unit Harrison, Ewen ; University of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, United Kingdom, Department of Clinical Surgery,
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Health informatics, Patient-centred medicine
Keywords:	Surgical Site Infection, SURGERY, smartphone technology

Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): protocol for a randomized-controlled trial in emergency surgery patients.

Trial Registration: *ClinicalTrials.gov.* Reference No: NCT02704897

Protocol version: 2.0.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Roles and responsibilities:

McLean KA[1], Mountain KE [1], Shaw CA[1], Drake TM[1], Ots R[1], Knight S[1], Fairfield CJ[1], Sgrò A[1], Skipworth R[1], Wigmore SJ[1], Potter M[2], Harrison E[1]

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Keywords: *Surgical Site Infection, smartphone technology, surgery*

MeSH Terms: *Surgical Wound Infection*, Diagnosis, Smartphone, General Surgery*

Abstract

Introduction

National data suggest that surgical site infection (SSI) complicates 2-10% of general surgery cases, although the patient-reported incidence is much higher. SSIs cause significant patient morbidity and represent a significant burden on acute healthcare services, in a cohort predominantly suitable for outpatient management. Over three-quarters of UK adults now own smartphones, which could be harnessed to improve access to care. We aim to investigate if a smartphone-delivered wound assessment tool results in earlier treatment.

Methods and Analysis

This is a randomised-controlled trial aiming to recruit 500 patients across NHS hospitals. All emergency abdominal surgery patients over the age of 16 who own smartphones will be considered eligible, with the exclusion of those with significant visual impairment. Participants will be randomised in a 1:1 ratio between standard post-operative care and the intervention – use of the smartphone tool in addition to standard post-operative care. The main outcome measure will be time-to-diagnosis of SSI with secondary outcome measures considering use of Emergency Department (ED) and General Practitioner (GP) services and patient experience. Follow-up will be conducted by clinicians blinded to group allocation. Analysis of time-to-diagnosis will be by comparison of means using an independent 2 sample t-test.

Ethics and Dissemination

This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis. The intervention is being used in addition to standard post-operative care. The study design and protocol were reviewed and approved by Southeast Scotland

Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016). Study findings will be presented at academic conferences, published in peer-reviewed journals, and are expected in 2020. A written lay summary will be available to study participants on request.

Trial Registration

ClinicalTrials.gov. Reference No: NCT02704897

Strengths and Limitations of this Study:

- This is the first randomised controlled trial on the use of a smartphone-delivered wound assessment tool to facilitate the assessment of surgical site infection and the impact on time-to-diagnosis.
- There are broad eligibility criteria, and so it is expected the results will be generalisable to a wide population of patients undergoing abdominal surgery.
- Due to the nature of the intervention, only clinicians undertaking follow-up can be blinded to randomisation status.
- All patients will receive 30-day telephone or face-to-face follow-up to determine the occurrence of surgical site infections, however the gold-standard for diagnosis remains direct clinical assessment.
- Data on patient experience and acceptability of smartphone-delivered follow-up will be collected concurrently to guide future implementation of future telehealth interventions.

Introduction

Surgical site infection (SSI) complicates 2-10% of general surgical cases, with the highest rates of infection seen after colorectal surgery[1]. Infection and re-admission rates have not significantly changed in the last 10 years. The most common causative group is *Enterobactericae* (25% of cases), with *Staph. Aureus* (10%) and MRSA (3%) accounting for a small proportion of overall cases[1]. National surveillance data from Scotland indicate that peak incidence of infection is between day 6-12 post-operatively[2].

A recent study indicated that national reports may underestimate the true incidence of SSI, and suggested that patient reported SSI is a more sensitive measure [3]. Many patients will have already consulted their General Practitioner (GP) or attended the Emergency Department (ED) prior to surgical assessment. In addition, many patients have concerns about their wounds (in the absence of infection) and may experience delays in accessing appropriate medical assessment. Thus, SSI represents a significant burden on healthcare services, in a patient group who are predominantly appropriate for outpatient management.

There is currently an increased research focus on digital health: the use of communications technology to enhance healthcare, public health and delivery of health education[4]. There are several advantages to this approach, in particular the potential to improve access to care, and help streamline usage of emergency services. Indeed, there is evidence that these technologies have been used to improve outcome[5], as well as to reduce specialist workload [6] and ED attendances[7]. In addition, the increasing use of healthcare technology is likely to help improve automatic data collection and recording, which may be used to identify areas for future research and drive quality improvement[4].

Over three-quarters (78%) of UK adults now own smartphones [8], with at least a third using a smartphone as their primary device to access the internet [4]. Therefore, there is vast potential for the use of smartphones in digital health, with a growing literature on the use in the context of postoperative community follow-up [9 10]. Given the frequency with which patients report post-operative wound complications and the high incidence of SSI, this has become a research focus in telemedicine for postoperative care [11 12]. We aim to investigate if an online wound assessment tool can be used to help diagnose SSI and improve patient access to care and clinical assessment. In addition, we aim to investigate if this results in earlier intervention to treat SSI and a decreased attendance at ED and GPs. The widespread use of smartphones, the integrated nature of their technology, and their portability means smartphones represent the best platform to deliver this tool, with the aim of facilitating rapid access to clinical care.

Objectives

This randomised-controlled trial will investigate whether a smartphone-delivered wound assessment tool can be used in the diagnosis of SSI and result in earlier treatment. It will also assess for a reduction in ED and GP attendances as a result of using the intervention. Data on patient experience will be used to evaluate perceived utility of the tool.

Methods and Analysis

Overview

This is a superiority randomised-controlled trial, using a parallel two-arm design (Figure 1). Once consent is obtained, participants will be randomised in a 1:1 ratio to either the intervention arm (receiving standard post-operative care plus access to the smartphone-delivered wound assessment tool), or the control arm (standard post-operative care). Patients will be recruited from the emergency surgery inpatient service across NHS Lothian. The trial period will be 30 days. An internal pilot study in the first 80 patients recruited will be conducted to ensure the trial design is practical and deliverable. Following assessment of pilot data, there will an opportunity to adapt the trial design in response to the pilot study findings. Participants will be followed-up by a researcher blinded to the intervention status. The primary outcome measure will be the number of days from surgery to diagnosis of SSI (time-to-diagnosis), with ED and GP service use as a secondary outcome measure. Additional data regarding patient experience will also be collected from patients in both arms of the trial via a smartphone-delivered questionnaire at 30 days.

Research Setting

This research is being carried out in a large health board, serving a mixed urban and rural population of over 800,000. The emergency surgery service admits 300 patients per week between participating sites and performs 2500 procedures annually.

Participants

Emergency surgery inpatients who are adults (over age 16) and have undergone abdominal surgery (on the same admission as diagnosis) will be screened for eligibility. Potentially eligible patients will be screened and documented as (a) eligible and included, (b) eligible and missed, (c) eligible and declined (iv) ineligible (visual impairment) (v) ineligible (no smartphone). Written consent will be obtained by the research team in line with Good

Clinical Practice Guidance. Participation is voluntary and a patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Inclusion Criteria

Patients admitted to the emergency surgery inpatient service who meet the following criteria will be included in the study:

- Emergency surgery inpatients who have undergone abdominal surgery;
- Owners of a smartphone, with access to internet;
- Adults over the age over 16;
- Able to give informed consent.

Exclusion Criteria

Any patients with significant visual impairment preventing use of the online questionnaire will be excluded from the study (defined by self-reporting of the patient)

Study Procedures

Recruitment

The clinical team will inform potentially eligible patients about the on-going trial, and offer them further information (written and verbal from the research team). Eligible patients will be recruited postoperatively as inpatients, with formal written consent taken by a member of the research team. Baseline information gathered will include: reason for admission, index procedure and date, significant co-morbidities – including history of diabetes or immunosuppression, as well as age and BMI. Participant contact details (mobile telephone number) will be entered into a secure, online data collection tool (Research Electronic Data Capture (REDCap) database) [13].

Randomisation and Blinding

Participants will be assigned in a 1:1 ratio to the intervention or control arms and provided with the appropriate information packs prior to discharge. Simple randomization will be carried out using REDCap[13], utilising a computer-generated random number sequence. The emergency surgery nurses (who will provide care to patients as required during the trial), and those taking consent (which may include medical students and qualified clinicians) will not be blinded. The clinicians undertaking follow-up will be blinded to status. A trial entry will be made in the clinical notes, including contact details for the trial team should a member of the clinical team require more information or wish to discover their trial status.

Intervention

Smartphone-Delivered Wound Assessment Tool

A wound-based instrument to detect potential wound infection was developed. Our smartphone-delivered wound assessment model was based on the Centre for Disease Control and Prevention (CDC) classification criteria, and the ASEPSIS model (Additional treatment, Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria, and the duration of Inpatient Stay).[14 15] It detects symptoms of SSI and symptoms of systemic illness as a result of this, whilst being quick and simple to use (Table 1).

Participants will have access to the smartphone-delivered wound assessment tool on discharge via a link sent by short-messaging system (SMS) to their smartphones. If at any time they have concerns about their wound, they can access the tool, and will be advised based on their responses. When a patient response is submitted, the research team will be automatically notified, and prompted to reply (Figure 2).

In addition, a link to the smartphone-delivered wound assessment tool will be sent on days 3, 7, and 15 post-operatively. These time-points have been selected to include peak incidence of infection and cover the time-course of wound healing. This will ensure the collection of negative data in those without symptoms and will therefore assist in determining the specificity of the tool. If participants do not respond they will be sent a single reminder at these time-points.

Wound Photographs

Participants will be asked to upload at least one photograph of their wound each time they use the smartphone-delivered wound assessment tool. These will be reviewed by a clinical researcher and assigned into one of 3 categories: no concerns, medium-risk, high-risk. Further machine learning-based assessment of wound photographs will be investigated.

Responses

An experienced clinician (surgical registrar or consultant) will review all participant responses and photographs in real-time. Based on the response and the wound photographs, they will contact the patient by SMS with advice regarding the need for further assessment. The clinician will classify participants into 3 groups: no concern, medium-risk, high-risk. These three groups were agreed collectively by the researchers in collaboration with the emergency surgical team. Three potential outcomes were identified: (i) the patient does not require further assessment (no concern), (ii) the patient requires further assessment, but the symptoms identified suggest a mild infection (medium-risk), (iii) the symptoms suggest a potentially severe infection requiring urgent assessment (high-risk). The wound photographs will also be reviewed by the experienced clinician where available and classified into the same 3 groups. This may be used by the researcher to refine their response to the tool, if they consider this necessary.

Algorithm

An algorithm has been designed to classify participant responses into the same 3 categories listed above (Table 1). This will be run on all participant responses (but will not impact on care), and will be compared with clinician rating, as a secondary sub-study. The correlation between clinician response, algorithm response and photo response will be used to determine if the algorithm can be used to assess for SSI independent of the responsible doctor.

Action from Response

Participants whose responses raise no concerns will be advised of this. Participants who report symptoms consistent with wound infection will be directed for further assessment. Those in the medium-risk group will be directed to community care whilst those in the high-risk group will be advised to return for assessment at the centre where they had their procedure. This advice aligns to the degree of concern identified above.

Wound Reviews

For those in the intervention group who are identified as high-risk, the emergency surgery nurses will collect a wound swab from the patient to test for causative organisms (and aid in confirming infection). If a wound infection is diagnosed clinically, the patient will be started with antibiotics in line with local guidelines. This will be logged in the patient's trial record. If any patients in the control group attend the emergency surgery service for a review the same procedures will apply.

GPs will be informed about their patient's participation in the trial. We will request that if a participant enrolled in the trial visits their GP a wound swab is taken, and that they are

treated in line with the GP's normal practice. This will also apply to those in the medium-risk group who will be directed to their GP.

All participants will be given a log to take to any wound reviews, and wound swabs may be taken of wound discharge or the wound bed as appropriate. If an infection is diagnosed the date treatment is commenced will be noted, alongside any intervention performed. This will then be returned to the trial team, and used in follow-up.

30 Day Follow-up

Both arms will receive a follow-up face-to-face or telephone consultation 30 days post-operatively (alternatively, written follow-up is also available for those with significant hearing impairment). This consultation will follow a standardized format and will be conducted with an independent clinical researcher blinded to the intervention status. The clinical researcher will gather data on post-operative course, any symptoms related to the wound, and any treatment offered. They will also have access to electronic patient record (including all microbiology results from swabs taken in the community or hospital) and any wound logs returned. On the basis of these three sources of information, two independent, blinded clinical researchers will determine if an infection has been present (trained using the CDC Criteria to diagnose infection).[14] Data on patient experience and service usage – ED and GP attendances, as well as contact with emergency surgery nurses – will also be collected via a separate questionnaire delivered alongside the 30 day follow-up (Table 2).

Data Analysis Plan

All analysis will be carried out on an intention-to-treat basis. We do not anticipate missing data in patient demographics. However, any missing data values will be handled using multiple imputation. The volume of missing outcome data will be recorded for the control

and intervention arms, and any differences in drop-out rate noted. Thereafter patients with missing outcome data will be excluded from analysis.

Outcome Measures

This is a superiority RCT, and the primary outcome will be mean time from operation to diagnosis (time-to-diagnosis) of SSI. This outcome has been chosen (rather than time from symptom onset), as it can be more accurately recorded and is a measure of improved access to care. We assume an equal incidence of SSI in both groups and will ensure this using odds ratios. Time-to-diagnosis will also be compared using Cox proportional hazard regression analysis, a *P* value of <0.05 will be considered statistically significant.

For the intervention, we will calculate the sensitivity and specificity of the researcher response, the algorithm response, and photograph response in the diagnosis of SSI. We will compare the correlation of the algorithm, which is based on questionnaire responses, with clinician advice and eventual diagnosis. Correlation analysis will be performed using Kendall tau rank test. This will assess the accuracy of the algorithm in stratifying risk, as compared to a clinician, and will indicate what additional benefit may be gained from photographic analysis.

The secondary outcome measure will be use of services: GP and ED attendances, as well as contact with emergency surgery nurses. This data will be gathered at 30 days. Differences in number of attendees to GP and ED will be compared using a χ^2 test. Differences in the number of attendances will be assessed using the Mann-Whitney U-test.

Data on patient experience will also be gathered via a follow-up questionnaire and analysed separately (Table 2). This will help determine if an online questionnaire delivered via a

smartphone has a positive impact on patient experience of care, and if it helped facilitate their access to care.

Sample Size and Power Analysis

Our primary outcome measure is time-to-diagnosis and we aim to detect a one-day difference with a power of 90% (alpha 0.05). Assuming a standard deviation of 1 day in time-to-diagnosis, 22 wound infections per group will be required. Estimating a 10% rate of wound infection (in line with National Data)[2] and a drop-out rate of 10%, a sample size of 490 will be required (recruitment target 500 patients). Analyses will be intention-to-treat.

Assuming that 50 operations are performed per week and two thirds of these patients are likely to own smartphones, we estimate there will be 30 potentially eligible patients per week. Aiming for recruitment of 25% of eligible patients, we estimate a continuous recruitment time of 16 months. This rate of recruitment will also enable the researcher to respond to all patient concerns in a timely manner.

Ethics and dissemination:

Safety

All participants will receive the normal standard of care. The smartphone-based intervention is in addition to the normal standard of care. If at any point participants have any concerns. they will be advised to contact the emergency surgery nurses regarding their care (in line with normal standard of care). Out-of-hours they will be advised to contact NHS out-of-hours services. Participants will be advised to contact the emergency surgery nurses if they have any concerns whilst they are awaiting a response to the tool. The research team will be notified automatically that a participant is awaiting a response, ensuring that in normal working hours patients receive a rapid reply. They will also be advised that if they access

the tool at night, that it will not be reviewed until the following day. They will be advised to contact out-of-hours services if they require an overnight assessment. These actions will prevent any harm to patients resulting from a delayed response to the wound assessment tool. A potential consequence of closer follow-up of these postoperative patients could be increased identification of superficial SSI which would likely otherwise self-resolve, however this would closer surveillance or treatment if appropriate (this decision is made by an independent clinician at the time of review). Due to the low-risk nature of the trial, a formal data-monitoring committee has not been nominated.

Data Protection and Management

All participant data will be stored securely in a REDCap [13] database that has controlled access and designed as compliant with HIPAA-Security guidelines. This data will be anonymised, and only available to researchers listed on the protocol. Participant responses to the questionnaire will be reported directly to the REDCap database and will not be stored on patient phones. However, patients will be advised to review the security setting on their phone if they intend to store their wound photographs. Patient details will be recorded in a trial log should any safety concerns arise necessitating they be contacted.

Ethical Approval and Dissemination Plan

The study design and protocol were reviewed and approved by Southeast Scotland Research and Ethics Committee (REC Ref: 16/SS/0072 24/05/2016), and any protocol amendments will be resubmitted for review. The study is sponsored by ACCORD, a collaboration between the University of Edinburgh and NHS Lothian Research and Development. In line with Good Clinical Practice Guidance, written consent will be obtained by appropriately trained medical students or clinicians. Participation is voluntary and a

patient's decision regarding participation will not affect any aspect of their care in the case of refusal. Participants will have the right to withdraw from the study at any point.

Authorship on any papers derived from the study will be all authors involved in study design and protocol development, and any additional researchers involved in the writing group. Furthermore, patient recruiters who have recruited more than the prespecified 15 patients to the study will be listed as a "collaborator". All other persons involved in the study will be listed in the acknowledgements.

There are no financial and other competing interests for principal investigators for the overall trial or either study site. Study findings will be reported in line with CONSORT guidelines, and disseminated in the printed media, and learned forums, and are expected in 2020. A written lay summary will be available to study participants on request.

Patient and Public Involvement

Patients were not directly involved in the design or delivery of this trial, however data on patient experience in using the smartphone tool will be evaluated via a follow-up questionnaire. This will inform future development and dissemination of this intervention. A summary of results will be provided to all patients involved once the trial has been completed and analysed.

Authors' Contributions

(1) Conception and design: KEM, CAS, TMD, KAM, RO, AS, RS, MP, SJW, EH. (2) Drafting the manuscript: KAM, KEM, CAS, TMD, RO, SK, CJF, AS. (4) Critical revision of the manuscript for scientific and factual content: KAM, KEM, CAS, TMD, RO, SK, CJF, AS, RS, MP, SJW, EH. Supervision: RS, MP, SJW, EH. All authors read and approved the final manuscript.

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Competing interests

The authors do not have any conflicts of interest to declare.

Word Count: 3,154

Figure 1: Schema of trial events for intervention and control arms.

Figure 2: Handling of wound questionnaire submissions.

Tables:

Table 1: Questions included in smartphone-delivered questionnaire and independent algorithm scoring system.

Smartphone-delivered wound assessment		**Algorithm scoring system**		
Question	**Response (score)**	**Low-risk**	**Medium-Risk**	**High-risk**
Is the pain worse than immediately after the operation?	No (0), Yes (1)	Inflammation Score 0	Inflammation Score ≤2	Inflammation Score ≥3
Is there new redness around your wound site excluding the wound itself?	No (0), Yes (1)			
Is there more swelling around your wound site than at the time of surgery?	No (0), Yes (1)			
Are you experiencing a new burning sensation or heat at the wound site?	No (0), Yes (1)			
		AND	**AND**	**OR**
Is there liquid coming from the wound site? If so, please select which option best describes the liquid.	No (0), Yes – clear (1), Yes – bloody (1), Yes – yellowish (1), Yes – thick/yellow (2), Yes – green/brown (2)	Discharge Score 0	Discharge Score ≤1	Discharge Score 2
Is your wound opening or gaping?	No, Yes	Not scored in algorithm		
Have you experienced fevers in the last 24 hours?	No, Yes			
Please upload a photograph of your wound.	Photograph	Not scored in algorithm		

Table 2: Questions included in smartphone-delivered 30-day patient experience questionnaire.

Smartphone-delivered 30-day patient experience questionnaire	
Question	**Available responses**
1. Did you have access to the smartphone tool?	Yes, No
2. If you had access to the tool, how many times did you use the tool (not including the reminder questions sent)?	[integer]
3. If you had access to the tool, please rate the extent to which you agree/disagree with the statements below:	
a. The tool was easy to use b. I understood the questions in the tool c. It was easy to upload my wound photo d. The response from the tool was helpful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.
4. Please rate the extent to which you agree/disagree with the statements below:	
a. It was easy to get hold of advice about my wound when needed b. I had to wait more than 1 day for advice about my wound c. The advice I received about my wound was useful	Strongly Disagree, Disagree, Neutral / No opinion, Agree, Strongly Agree.

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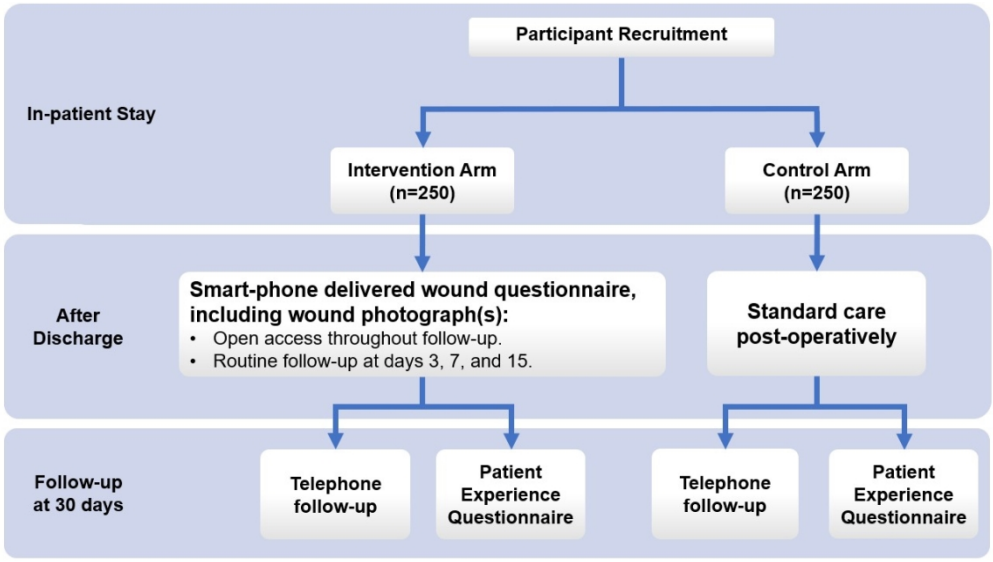

Figure 1: Schema of trial events for intervention and control arms

812x453mm (120 x 120 DPI)

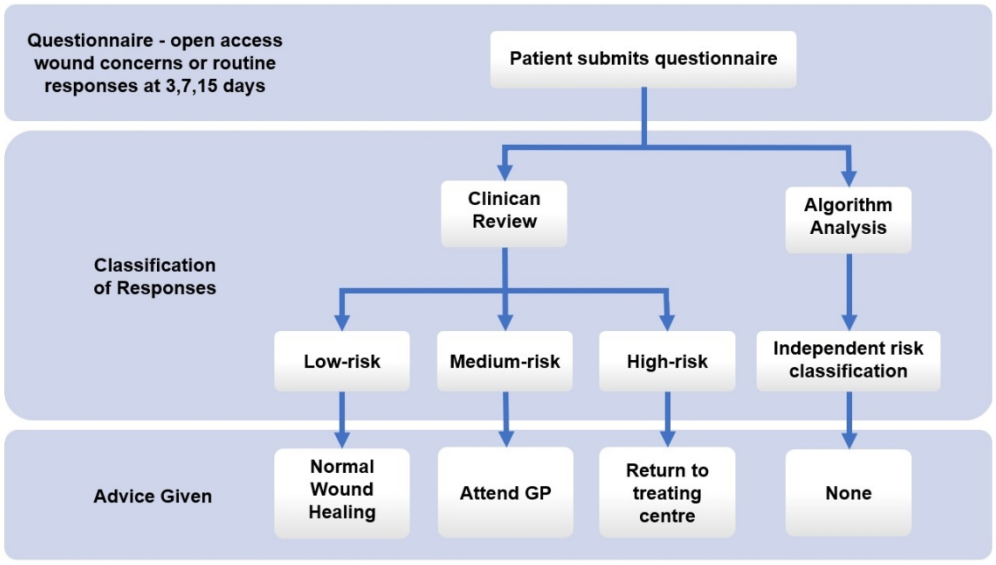

Figure 2: Handling of wound questionnaire submissions

811x454mm (120 x 120 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **Can a smartphone-delivered tool facilitate the assessment of surgical site infection and result in earlier treatment? Tracking Wound Infection with Smartphone Technology (TWIST): a randomized-controlled trial in emergency surgery patients**.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. ***ClinicalTrials.gov.* Reference No: NCT02704897**
	2b	All items from the World Health Organization Trial Registration Data Set ***ClinicalTrials.gov.* Reference No: NCT02704897**
Protocol version	3	Date and version identifier **Page 1**
Funding	4	Sources and types of financial, material, and other support **Page 1**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **Page 1**
	5b	Name and contact information for the trial sponsor **Page 1**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **Page 1**

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **Page 1**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **Page 5-6**
	6b	Explanation for choice of comparators **Page 5-6**
Objectives	7	Specific objectives or hypotheses **Page 7**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **Page 8 (overview)**
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **Page 8 (research setting)**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **Page 8-9 (Patients, inclusion criteria, exclusion criteria)**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. **Page 10-13**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). **Page 17**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). **N/A**

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **N/A**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **Page 14 (outcome measures)**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **Figure 1**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **Page 15 (Sample Size and Power Analysis).**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. **Page 9 (Recruitment)**
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **Page 10 (Randomisation and Blinding).**
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **Page 10 (Randomisation and Blinding).**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **Page 10 (Randomisation and Blinding).**

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. **Page 10 (Randomisation and Blinding).**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **N/A**

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **Page 9 (Recruitment); Page 10 (Smartphone-Delivered Wound Assessment Tool); Table 1**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **Page 10 (Smartphone-Delivered Wound Assessment Tool); Page 13 (Data analysis plan)**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. **Page 16 (Data Protection and Management).**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. **Page 13 (Data Analysis Plan / Outcome Measures)**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **Page 13 (Data Analysis Plan / Outcome Measures)**
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **Page 13 (Data Analysis Plan / Outcome Measures)**

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **Page 16 (safety)**
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **N/A**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **Page 16 (safety)**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **N/A**

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **Page 17 (Ethical Approval and Dissemination Plan)**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **Page 17 (Ethical Approval and Dissemination Plan)**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **Page 17 (Ethical Approval and Dissemination Plan)**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **N/A**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **Page 16 (Data Protection and Management)**

Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **Page 18**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **Page 16 (Data Protection and Management)**
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **N/A**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **Page 17 (Ethical Approval and Dissemination Plan)**
	31b	Authorship eligibility guidelines and any intended use of professional writers **Page 17 (Ethical Approval and Dissemination Plan)**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code **N/A**
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates **Supplementary File**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **N/A**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.