DEXACELL

Statistical Analysis Plan

DEXACELL: DEXAmethasone as an adjunctive therapy for the management of CELLulitis - a randomised controlled trial in urgent secondary care

Version:

SAP V2.0, 23 Apr 2026

This statistical analysis plan is based on protocol version 5.0, 07 JAN 2025

Sponsor:	North Bristol NHS Trust
Sponsor reference number	5411
IRAS number or other identifier	1009877
Coordinating centre	Exeter Clinical Trials Unit
ISRCTN number	ISRCTN76873478
Funder reference number	NIHR153216

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DOCUMENT CONTROL SHEET

Version number	Date	Reason for update	Description of changes
1.0	22 Jan 2026		Original version
2.0	23 Apr 2026	Correction, clarification and improvement prior to the final analysis and unblinding	1) Sensitivity Analysis 1 was changed to better reflect the design of the trial 2) Supplementary Analysis 2 was updated to use a continuous time model from the new Sensitivity Analysis 1 instead of a discrete time model 3) Population for Supplementary Analysis 1 was updated 4) Time intervals for the descriptive analysis of the primary outcome were updated 5) Daylight Time Saving was addressed 6) Dates and times used for PGI-I timepoint 6 site staff scores were clarified 7) Algorithm allocating PGI-I scores to timepoints was updated 8) Length of antibiotic course algorithm and presentation were clarified

			9) Logistic mixed effects model analysis for unscheduled healthcare use by Day 14 was added 10) Adverse event presentations will not be split into “by Day 14” and “by Day 90” 11) Serious adverse events will not be presented with a split by action taken 12) Data collected outside of protocol specified Day 14 and Day 90 visit windows will be used in the analyses 13) Site metrics presentations were removed 14) Some table mock layouts were updated 15) Estimation methodology for linear mixed effects models was updated from default Stata to REML 16) Sap v1.0 and v2.0 finalisation timelines were clarified 17) Other minor updates

CONTENTS

1. INTRODUCTION

1.1 PURPOSE OF THE STATISTICAL ANALYSIS PLAN

This Statistical Analysis Plan (SAP) provides guidelines for the analysis and presentation of results for the DEXACELL trial.

Version 1.0 of this SAP was written prior to the end of follow up and final analysis. Version 2.0 was finalised prior to the final analysis.

This plan, along with all other documents relating to the analysis of this trial, will be stored in the 'Statistics' section of the electronic Trial Master File.

Health economics related outcomes will be covered in the Health Economics Analysis Plan.

1.2 TRIAL DESIGN AND METHODS

1.2.1 TRIAL DESIGN

This is a pragmatic, multi-centre, double-blind, placebo-controlled, randomised, parallel group, phase 3 superiority trial of dexamethasone in adults with a clinical diagnosis of cellulitis. Participants were randomised 1:1 via a minimisation algorithm with a random element to receive either 8 mg of dexamethasone twice with the second administration 24 hours after the first one or to a matching placebo tablet. The trial included an internal pilot phase and will include a parallel health economic evaluation.

1.2.2 PRIMARY OBJECTIVE AND ESTIMAND

The primary estimand of interest is the effect of the addition of dexamethasone to usual care compared to placebo and usual care on the total pain measured over 3 days post baseline.

The primary estimand will be analysed on the evaluable intention-to-treat population.

All intercurrent events except death will be analysed according to the treatment policy.

Target population	People with clinically diagnosed cellulitis (with exceptions specified in the inclusion and exclusion criteria, Section 1.4). More detail about the analysis set used for the primary estimand is given in Section 5.
Treatment conditions	Usual Care + Dexamethasone 8mg orally on recruitment, then dexamethasone 8mg orally ~24 hours later vs. Usual Care + Matched placebo capsules on recruitment, then matched placebo capsules ~24 hours later
Outcome variable	Total pain over the first 72 hours after baseline measured as an area under the curve (AUC) rescaled to 0-100 and generated from participant provided NRS pain scores taken at baseline and 6 subsequent 12-hourly timepoints measured on a scale of 0-10

Handling of intercurrent events* (not incorporated by the population or treatment condition)	Treatment policy will be used for the following intercurrent events: Change in clinical status post-randomisation (including change in diagnosis or surgical management) Early unblinding No treatment despite randomisation Incorrect treatment received (not as randomised) Early treatment discontinuation Dose delay (not permitted, protocol deviation) Dose modification (not permitted, protocol deviation) Seeking additional healthcare input Death cannot be analysed under the treatment policy, so (if observed in <= 1% of the participants) it will be analysed under the hypothetical policy: scores missing due to death will be imputed according to the rules specified in Section 10.1.2. The hypothetical policy is acceptable for this trial since death is not anticipated to be frequent, expected or related to the diagnosis or treatment under investigation. Alternative policies may be considered if death is observed more often. Change in treatment pathway will not be considered an intercurrent event as this is a pragmatic trial. Intermittent missing data and missing data after participant withdrawal from the trial will not be considered intercurrent events in line with ICH E9 (R1) addendum [2].
Population level summary	Between-group adjusted difference in means in the primary outcome. A Wald 95% confidence interval and a corresponding Wald test p-value will also be provided. More detail about the estimation methodology is given in Section 10.1.2.

1.2.3 SECONDARY OBJECTIVE(S) AND ESTIMANDS(S)

The effect of the addition of dexamethasone to usual care compared to placebo and usual care on:

- **Patient Global Impression of Improvement (PGI-I) on Day 1, Day 2 and Day 3 post-randomisation**
- **Analgesia usage (whether it was used, number and type of analgesia therapies used) over the first 72 hours post-randomisation**
- **Antibiotic usage (whether they were used, route, type, and post-randomisation length of course) up to Day 14 post-randomisation**
- **Whether the participant was (re)admitted to hospital by Day 14 post-randomisation**
- **Frequency of complications of dexamethasone use by Day 14 post-randomisation**

- **Whether and how much any unscheduled healthcare (not necessarily cellulitis related) was used until Day 14 post-randomisation**
- **Whether cellulitis recurred by Day 90 post-randomisation**
- **Frequency of serious and/or potentially related adverse events by Day 90 post-randomisation**
- **Pain experienced at Day 14 post-randomisation**
- **Patient Global Impression of Improvement (PGI-I) at Day 14 post-randomisation**

The approach to intercurrent events for the model-based analyses of the secondary estimands will be the same as for the primary objective/estimand except for death. Death cannot be handled under the treatment policy. Therefore, the following approaches will be used.

Death will be handled according to the hypothetical policy for the model-based analyses of the following secondary estimand:

- Patient Global Impression of Improvement (PGI-I) on Day 1, Day 2, Day 3 post-randomisation

Death will be handled according to the while-alive policy for the model-based analyses of the following secondary estimands:

- Whether the participant was (re)admitted to hospital by Day 14 post-randomisation
- Whether any unscheduled healthcare (not necessarily cellulitis related) was used until Day 14 post-randomisation
- Whether cellulitis recurred by Day 90 post-randomisation

Death will be handled according to the principal stratum of "always survivors" policy for the model-based analyses of the following secondary estimands:

- Patient Global Impression of Improvement (PGI-I) at Day 14 post-randomisation
- Pain experienced at Day 14 post-randomisation

The details are given in Section 10.2.

Death will be handled under the while-alive policy for descriptive analyses.

Populations are given in Section 5, outcome variable descriptions are given in Section 1.3.2, population level summary statistics are given in Section 10.2.

Details about health-related quality of life, measured by EQ-5D-5L, and health, social care and broader societal resource use, measured by a resource use questionnaire, (see Section 1.3.2 below) will be given in the Health Economics Analysis Plan.

1.2.4 EXPLORATORY OBJECTIVE(S) AND ESTIMAND(S)

Exploratory subgroup analyses are described in Section 10. No other exploratory analyses are planned.

1.3 OUTCOME MEASURES

1.3.1 PRIMARY OUTCOME

The primary outcome is total pain over 72 hours since baseline measured as an area under the curve (AUC) generated from participant provided NRS pain scores taken at baseline and 6 subsequent 12-hourly timepoints. Pain is measured on a scale of 0-10 at each timepoint using the NRS pain scale. Participants will be included in the primary evaluable intention-to-treat analysis if they contribute at least 2 out of a possible 7 pain scores, with the second pain score being at least 24 hours after the baseline pain score. The AUC will be calculated using the

trapezoidal rule by plotting the scores at the reported times when they were collected then joining those points linearly to calculate the AUC. The AUC will be rescaled to 0-100 to give a standardised AUC. More detail is given in Section 10.1.

1.3.2 SECONDARY OUTCOME(S)

1. **Health-related quality of life, measured by EQ-5D-5L at baseline, Day 3, Day 14 and Day 90 post-randomisation**

The details will be given in the Health Economics Analysis Plan.

2. **Patient Global Impression of Improvement (PGI-I) measured daily for first 3 days post-randomisation**

The PGI-I score is collected on Day 1, Day 2, Day 3 and Day 14 on a 7-point Likert Scale from 1 = "Very much better" to 7 = "Very much worse". 0 corresponds to "Not assessed". A higher score corresponds to less improvement.

3. **Analgesia usage (number and type of analgesia taken over first 3 days) post-randomisation**

Types of analgesia are collected as free text and will be mapped to a WHO ATC3 class by a clinician.

4. **Antibiotic usage (route, type, and post-randomisation length of course) up to Day 14 post-randomisation**

Types of antibiotics taken are collected as free text and will be mapped to a WHO ATC3 class by a clinician.

Length of the antibiotic course will be calculated as described in Section 10.2.3.

5. **(Re)admissions to hospital by Day 14 post-randomisation**

(Re)admissions to hospital by Day 14 post-randomisation are collected as a binary secondary outcome ("Yes"/"No").

6. **Complications of dexamethasone use by Day 14 post-randomisation**

Severe hyperglycaemia, gastrointestinal bleeding and psychosis are complications of special interest on this study.

Severe hyperglycaemia is defined as ketoacidosis, hyperglycaemic hyperosmolar state or hyperglycaemia requiring new use of insulin and will be determined using the reported adverse event data.

7. **Any unscheduled healthcare usage (not necessarily cellulitis related) until Day 14 post-randomisation**

Unscheduled healthcare usage is collected as the number of usages by type of healthcare.

8. **Health, social care and broader societal resource use, measured by a resource use questionnaire at baseline and Day 90 post-randomisation**

The details will be given in the Health Economics Analysis Plan.

9. **Recurrence of cellulitis by Day 90 post-randomisation**

Recurrence of cellulitis by Day 90 post-randomisation is collected as a binary secondary outcome ("Yes"/"No").

10. **Pain experienced at Day 14 post-randomisation**

Pain at Day 14 is measured on the NRS pain scale.

11. **Patient Global Impression of Improvement (PGI-I) measured at Day 14 post-randomisation**

The PGI-I score is collected on Day 1, Day 2, Day 3 and Day 14 on a 7-point Likert Scale from 1 = "Very much better" to 7 = "Very much worse". 0 corresponds to "Not assessed". A higher score corresponds to less improvement.

12. **Serious and/or potentially related adverse events by Day 90 post-randomisation**

Adverse events are collected at Day 14 and Day 90.

Only serious or related adverse events (AR/SAE/SAR/SUSAR) are recorded in the eCRF, from the time of randomisation up to the 90-day follow-up timepoint.

Psychosis, gastrointestinal bleeds and severe hyperglycaemia are adverse events of special interest and are always classified as serious in this trial.

Deaths are reported in both the 'SAE' and 'Notification of Death' eCRF forms in REDCap.

MedDRA 27.1 coding of adverse reactions and serious adverse events will be used.

1.3.3 EXPLORATORY OUTCOME(S)

Exploratory subgroup analyses are described in Section 10.3. No other exploratory analyses are planned.

1.4 ELIGIBILITY

This trial is focused on adult patients who present to emergency and urgent care with cellulitis.

Inclusion criteria

- Aged 16 years old or over
- A current clinical diagnosis of cellulitis at any body site except the orbit (periorbital/orbital cellulitis)
- Able to provide informed consent

People of child-bearing* potential must be willing to:

- Use a highly effective method of contraception** (and must agree to continue 3 months after the last dose of the IMP)
- Inform the trial team if pregnancy occurs during trial participation

** Potential participants are considered not of child-bearing potential if their sex at birth was male or they are surgically sterile (i.e. they have undergone a hysterectomy, bilateral salpingectomy, or bilateral oophorectomy) or they are postmenopausal (no menses for 12 months without an alternative medical cause).*

*** Highly effective contraception is defined as one of the following: combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal); progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, or implantable); intrauterine device(IUD); intrauterine hormone-releasing system (IUS); bilateral tubal occlusion; vasectomised partner; practising true sexual abstinence (when this is in line with the preferred and usual lifestyle of the individual).*

Exclusion criteria

Patients may not enter trial if ANY of the following apply:

- Orbital or periorbital cellulitis, surgical site infection, or planned surgical management (e.g. abscess) as managed under a different clinical pathway
- Allergy to dexamethasone
- Contraindication to dexamethasone due to concurrent medication (e.g. cobicistat)
- Has known current invasive fungal infection**
- Has known current gastric or duodenal ulceration
- Already on systemic corticosteroids
- Unable to take oral medication
- Lack of capacity
- Inability to complete follow-up procedures
- Prisoner*

People of child-bearing potential only:

- Pregnant***, breastfeeding, or planning to conceive in next 3 months

**This does not exclude patients in police custody, though consideration should be given to whether they are able complete the trial follow-up procedures.*

*** This includes only invasive infections such as pulmonary aspergillosis and does NOT include cutaneous infections such as athlete's foot, vaginal thrush etc.*

****Must have a negative pregnancy test no more than 7 days prior to initiation of treatment.*

1.5 RANDOMISATION

Randomisation was complete at the time of the signing of version 1.0 of this SAP.

Allocation to the two study groups was stratified by recruiting site and participants were allocated using a minimisation algorithm with a random element, on the following factors:

1. Prior antimicrobial therapy for the current episode of cellulitis ("Yes"/"No")
2. Diabetes status, defined by a known diagnosis of either type 1 or type 2 diabetes mellitus ("Yes"/"No")
3. Severity of Cellulitis (Eron Class 1 vs all other classes)

The minimisation algorithm was based on Pocock and Simon's Method but with enhancements that added further non-determinism to the process, with a random element (80%). Within each site, the first three allocations used simple random sampling.

This was implemented through the bespoke web-based randomisation service provided by the Centre for Healthcare Randomised Trials (CHaRT), ensuring allocation concealment and replicability. Blinded kit lists had been generated by an unblinded senior statistician and had been provided to CHaRT before the trial opened to recruitment.

Once the online randomisation process was complete, the system indicated to the user a blinded pack ID which was dispensed to the participant, it did not indicate whether the participant had been allocated to receive IMP or placebo.

The online randomisation system automatically sent an email to ExeCTU and the site team confirming the randomisation had taken place and the pack ID had been allocated. Site staff noted in the medical records that the patient was enrolled into the trial. Site staff then completed and sent the approved letter to the participant's GP (e.g. via post or secure email) informing the GP that their patient entered the trial.

Further details can be found in "DEXACELL randomisation statistical requirements v1.0" in 12. Randomisation of the eTMF.

1.5.1 PACK/KIT ID LISTS

Pack IDs for the individual bottles of IMP and placebo were produced by the unblinded senior statistician according to the Work Instruction WI-001-IMP pack ID production (8.2.1 of the eTMF).

1.6 SAMPLE SIZE

Participants were randomised on a 1:1 basis to receive dexamethasone plus usual care or placebo plus usual care. The required sample size was calculated using the Power Analysis Sample Size (PASS) software based on detecting a between-group difference in total pain, from randomisation over the first 3 days post-randomisation, of 10 points, based on a standardised area-under-the-curve approach (on a scale of 0-100), with pain NRS collected twice-daily.

The minimum clinically important difference (MCID) in pain is 10 points, based on previously reported emergency care literature [11]. The conservative standard deviation (SD) estimate (30 points) was based on previous cellulitis trials reporting pain at single timepoints, reviewed in a recent meta-analysis [12]. Based on these assumptions, the target standardised effect size was determined to be 0.33. This estimate of the pooled SD and the 95% CIs were reviewed by the unblinded senior statistician and by the closed DMC members at the end of the internal pilot phase.

191 participants in each allocated group with primary outcome data gives 90% power to detect the MCID of 10 points, assuming a SD of 30 points, at the two-sided 5% statistical significance level. The recruitment target was 450 participants (225 per allocated group), allowing for up to 15% of participants not returning any NRS pain score 24 hours after the baseline score.

1.7 BLINDING

This trial is double-blinded and therefore neither clinicians nor participants know which treatment was allocated. This was achieved by the IMP manufacturer over-encapsulating, packaging, and labelling the IMP and placebo doses to look identical. The IMP/placebo packs were labelled with blinded pack IDs and the randomisation system automatically assigned a pack ID to be dispensed to the participant after randomisation was complete.

Only the unblinded senior statistician, the IMP manufacturer, the developers of the randomisation system and the head of the ExeCTU ISDM team have access to the master list which indicates which pack IDs relate to placebo packs, and which relate to dexamethasone packs, as required for their role.

The randomised allocation is stored separately from the rest of the data within the randomisation system and the corresponding pack ID for each participant to receive was issued from a standard list that the unblinded senior statistician had created and provided only to the unblinded team members.

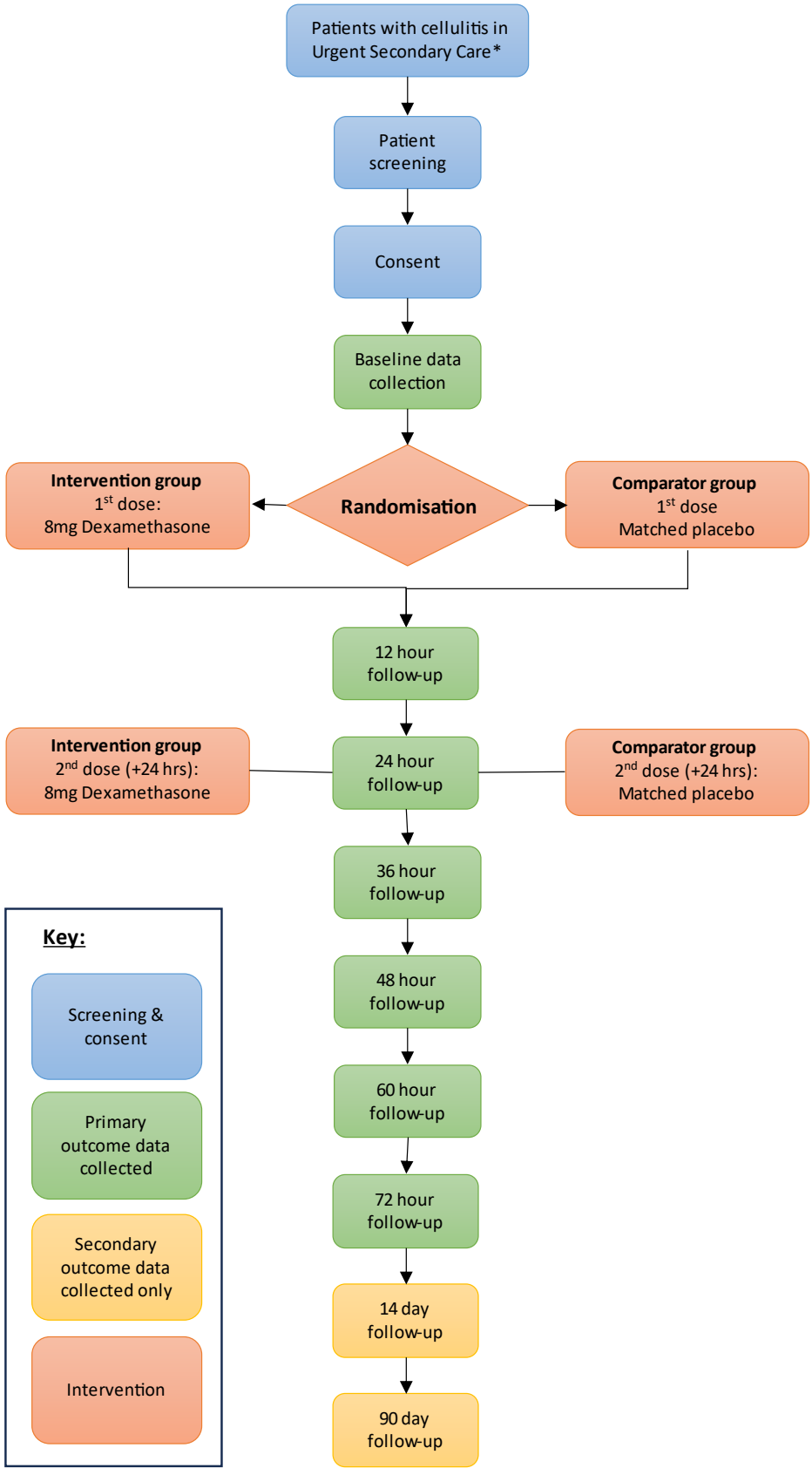
The trial statistician undertaking analyses will be blinded until the primary statistical analysis of the primary outcome is complete. Where possible, the research teams at the trials centre and sites will remain blinded.

The unblinded senior statistician is unblinded throughout the trial.

Prior to recruitment, a Blinding of Trial Statistician (BOTS) risk assessment was undertaken which outlined the blinding status and reasoning for the given blinding status of both the trial and the senior statistician. This is stored in Section 13. Statistics within the eTMF.

Participants who were unblinded early will be presented.

1.8 TRIAL SCHEMA



**Emergency Departments, Ambulatory Care Units, Same Day Emergency Care*

The participants will be followed up to 90 days after randomisation.

The end of the trial will be after the last 90 day follow up is complete, all data queries have been resolved, the database locked, and the analyses completed.

2. TRIAL REPORTING

2.1 FINAL ANALYSES

The DEXACELL trial has only a single analysis point, a final analysis, to be conducted after the final follow up has occurred and data has been cleaned in preparation of final data lock.

The final analysis will be conducted as a blinded analysis by the blinded trial statistician with the remainder of the trial team to receive the blinded results so that key interpretations of the results can be drawn prior to the unblinded senior statistician revealing the allocation.

The primary analysis will be conducted at the point of final analysis.

2.2 TRIAL OVERSIGHT COMMITTEES

The timing and scope of reporting to, the responsibilities of and the type of feedback from the Trial Steering Committee, the Data Monitoring Committee, the Trial Management Group and the PPI group are described in the protocol Section VI.

3. DATA QUALITY

3.1 DATA VALIDATION

The Data Management Plan describes the data management processes for the trial and outlines the different types of checks that are routinely carried out by the data management team, including: (a) automated and programmed system checks in REDCap; (b) manual checks listed in the Data Checks Specification; (c) Data listings. In addition to these, and checks outlined in the Randomisation Requirements document, the following checks will be conducted by the blinded trial statistician periodically on blinded data:

- Screening date, eligibility confirmation date, randomisation date, baseline NRS pain score date, dose 1 date, hospital (re)admission date, cellulitis onset date, antibiotic start date, withdrawal from treatment and/or trial dates, Day 14 and Day 90 visit dates, death dates, early unblinding dates and, where applicable, times, completeness and plausibility
- Hyperglycaemia, gastrointestinal bleeding, psychosis question answers will be compared to the reported MedDRA PTs
- Whether the question about prior antimicrobial therapy contradicts the questions about prior antibiotic treatment

Additional validation checks may be done if considered necessary. Linked fields may be checked for inconsistencies.

3.2 DATA COMPLETENESS

Completeness of the primary outcome of NRS pain scores and the following secondary outcomes – PGI-I scores, analgesia usage, antibiotic usage, (re)admission to hospital, complications, unscheduled healthcare usage and recurrence – will be presented and reported for each scheduled visit/timepoint per protocol.

Completeness of NRS pain scores in the first 3 days post-baseline will be reported by allocated treatment group, site and selected demographic and baseline characteristics (age at screening group (< 50, >= 50 and < 60 and >= 60), sex, ethnicity, baseline NRS pain score, prior (to hospital attendance) antimicrobial therapy for this episode of cellulitis ("Yes"/"No"), severity of cellulitis (stage 1 vs stage 2-4), diabetes ("Yes"/"No"), cellulitis location (lower limb vs other), NSAID usage at time of randomisation (user vs non-user).

Approaches to handling missing data for the analyses are described in Section 10.1.2 and Section 10.2.

4. PREPARATION OF DATASETS AND DOCUMENTING ANALYSES

REDCap Academic is the Clinical Data Management System for the trial data. Randomisation and pack ID information is stored in the CHaRT system which is integrated into REDCap by an Application Programming Interface (API). The only data passed from CHaRT to REDCap is randomisation date and the pack IDs specified at randomisation. REDCap does not contain any unblinded data.

The unblinded senior statistician will export the unblinded randomisation and drug status reports that have been set-up in CHaRT and save the data within the DEXACELL Restricted SharePoint site.

The unblinded senior statistician will merge the data from REDCap and CHaRT using a Stata program specifying 1:1 merging using 'participant ID' variable. Stata programs used for this purpose will be saved in the DEXACELL Restricted SharePoint site.

Blinded trial data from REDCap will be exported by a designated member of the ISDM team and stored in the DM Working Directory on SharePoint.

For reproducibility, as a minimum, the primary analysis will be double coded by an unblinded senior statistician.

5. DEFINING ANALYSIS POPULATIONS

The analysis populations for both the primary and the secondary effectiveness objectives/estimands will be kept as close as possible to the randomised population.

Baseline characteristics and exposure will be presented on the randomised population.

Disposition data will be presented on the screened population unless specified otherwise.

Outcome	**Analysis Population**
Total pain measured over 3 days post baseline	Evaluable intention-to-treat population: all randomised participants with a baseline NRS pain score and at least one other NRS pain score at least 24 hours after the baseline
Health-related quality of life, measured by EQ-5D-5L at baseline, Day 3, Day 14 and Day 90 post-randomisation	The details will be given in the Health Economics Analysis Plan.
Patient Global Impression of Improvement (PGI-I) measured daily for first 3 days post-randomisation	All randomised participants with at least one PGI-I score reported post-randomisation
Analgesia usage (number and type of analgesia taken over first 3 days) post-randomisation	All randomised participants
Antibiotic usage (route, type, and post-randomisation length of course) up to Day 14 post-randomisation	All randomised participants

(Re)admissions to hospital by Day 14 post-randomisation	All randomised participants with a (re)admission to hospital answer reported by Day 14 post-randomisation
Complications of dexamethasone use by Day 14 post-randomisation	All randomised participants
Any unscheduled healthcare usage (not necessarily cellulitis related) until Day 14 post-randomisation	All randomised participants who used eCRF version 2 or above ** Healthcare usage questionnaire was updated shortly after the start of data collection to include any unscheduled healthcare usage (not necessarily related to cellulitis). Because of that the data collected prior to the questionnaire update in version 2 of the eCRF is not directly comparable to the data collected after the update. Therefore, participants who filled in only the old version will be excluded from the analysis.*
Health, social care and broader societal resource use, measured by a resource use questionnaire at baseline and Day 90 post-randomisation	The details will be given in the Health Economics Analysis Plan.
Recurrence of cellulitis by Day 90 post-randomisation	All randomised participants with a recurrence of cellulitis answer reported by Day 90 post-randomisation
Serious and/or potentially related adverse events by Day 90 post-randomisation	All randomised participants; All treated participants
Pain experienced at Day 14 post-randomisation	All randomised participants with an NRS pain score reported at Day 14 post-randomisation
Patient Global Impression of Improvement (PGI-I) measured daily at Day 14 post-randomisation	All randomised participants with a PGI-I score reported at Day 14 post-randomisation

Sensitivity, supplementary and additional analyses may use other populations as specified in Section 10.

Imputation is described in Section 10.1.2 and Section 10.2.

A table with the number of participants in each population will be presented.

6. TRIAL POPULATION

A CONSORT flow diagram will be produced to illustrate the flow of participants through the trial. Specifically, the number of patients and percentages of patients screened, eligible, approached, consented, randomised, who received dose 1, who received dose 2 (self-reported), reached the end of the 12-hourly follow up period, reached the 14 day follow up and reached the 90 day follow up, and the number included in the primary analysis will be presented. The number and percentage of participants who withdrew from trial between each data collection timepoint will also be presented.

The denominator for the percentages will be the population in the previous step except for the following: those who received dose 2, reached the end of the 12-hourly follow up period, reached the 14 day follow up and reached the 90 day follow up, those who were included in the primary analysis. For these the percentages will be calculated out of the randomised participants.

Where applicable the CONSORT flow diagram will be split by allocated treatment group.

The reasons for ineligibility, non-approach, non-consent will also be presented overall and separately by site. Free text fields within the “Other” reason category will also be presented.

Reasons for change in participation status and reasons for exclusion from the primary analysis will be presented as described in Section 6.4.

6.1 SCREENING

The total number of patients screened, eligible, approached, and consenting to the trial will be reported in the CONSORT flow diagram.

Reasons for not being eligible, approached and patient not consenting will be presented in separate tables by site. Free text fields within the "Other" reason category will also be presented.

Screening data on age, sex assigned at birth and ethnicity for the screened patients will also be reported in a separate table.

6.2 RECRUITMENT/RANDOMISATION

The following information on randomisation will be reported by allocated treatment group:

- Number and percentage of participants whose NRS pain and PGI-I scores were collected via SMS, manually or through a mix of SMS and manual methods overall and in each collected demographic and baseline characteristics group for NRS pain scores

Number of participants who consented but dropped out prior to randomisation will be presented in the CONSORT flow diagram.

Participants who withdrew consent for trial treatment or were found to be ineligible prior to randomisation were withdrawn from the study and no further data for them was collected. These participants were not counted towards the recruitment target. This will be presented in the CONSORT flow diagram.

6.3 PARTICIPANTS RANDOMISED IN ERROR OR WHO HAD A CHANGE IN CLINICAL STATUS AFTER RANDOMISATION

The following data will be presented by allocated treatment group:

- Participants found to have been ineligible at point of recruitment/randomisation and therefore were randomised in error
- Participants who had a change in clinical status (including an alternative diagnosis / surgical management) during the trial

Both categories of participants will be included in the primary estimand analysis according to the treatment policy.

6.4 CHANGE IN PARTICIPATION STATUS POST-RANDOMISATION

The PeRSEVERE principles [13] will be followed for participants who cease to engage with the trial.

All data reported on the 'Change in participants status' form will be reported by allocated group on all randomised participants.

This data will also be presented by allocated group and sex assigned at birth ("male"/"female") on all randomised participants.

Participants will be able to flexibly change their participation in the study by selectively ceasing any or all of the following aspects:

- Their allocated treatment (intercurrent event for the primary estimand, Section 1.2.2)
- Remote follow-up

- Passive data collection from medical records where relevant (except where required for reporting of serious adverse events)

The frequency and percentage for each type of change in status will be presented, together with reasons and who requested the change.

Additionally, participants who consented but withdrew from trial prior to randomisation will be presented.

If it becomes apparent that a participant has lost capacity and is unable to complete a follow-up timepoint (e.g. delirium at Day 14), this will be recorded in the eCRF but they will not be withdrawn from any aspect of the trial unless a personal consultee requests this. Their original consent will remain legally valid and unless withdrawn by a consultee they should be contacted again at the next follow-up timepoint and a new assessment of capacity carried out.

Additionally, the following data on follow up will be reported:

- Date the data lock was taken
- Number and proportion of randomised participants at the primary analysis, number of alive participants who withdrew from trial by the primary analysis, reason for absence of the primary outcome by allocated treatment group, not included in the primary analysis due to missing primary outcome. The data will be presented by allocated group and also by sex assigned at birth (“male”/”female”) on all randomised participants
- Withdrawal from trial and reasons for it by site

6.5 NON-COMPLIANCE (DEVIATIONS, VIOLATIONS AND SERIOUS BREACHES)

Non-compliances are defined as either a deviation, violation or serious breach and reported on the Non-Compliance Form.

The frequency of each category of deviation/violation/serious breach will be reported by allocated treatment group overall and by site.

7. BASELINE CHARACTERISTICS

There will be no formal between-group testing of baseline data.

Participants’ baseline characteristics will be summarised descriptively by allocated treatment group. The mock table with the baseline characteristics collected and reported is given in Section 16.3.23, Section 16.3.25.

NEWS2 score is a sum of individual scores for respiration rate (per minute), SpO2 scale 1 (%) or SpO2 scale 2 (%), whether the participant is on room air or supplemental oxygen, systolic blood pressure (mmHg), pulse (per minute), consciousness level and temperature (°C). SpO2 scale 2 (%) is used for participants with diagnosed hypercapnic respiratory failure, SpO2 scale 1 (%) is used in all other cases. We will assume none of the participants had hypercapnic respiratory failure on this trial. Appendix 16.2 (Section 16.2) specifies score assignment for each of the components of the NEWS2 score [14]. No risk (score 0), low risk (aggregate score 1 to 4), low to medium risk (score of 3 in any single parameter), medium risk (aggregate score 5 to 6), high risk (aggregate score of 7 or over) categories will be presented [15].

Index of multiple deprivation will be determined based on the participant’s postcode [16] [17]. This will be done only for English postcodes.

Antibiotic usage before randomisation for this episode of cellulitis will be presented in a separate table, as in Section 16.3.24.

Types of antibiotics taken are collected as free text and will be mapped to a WHO ATC3 class by a clinician.

Length of antibiotic course will be calculated as the difference between the last day of use of any antibiotic (capped at randomisation) and the first day of use of any antibiotic based on all the reported antibiotic start dates and lengths of courses minus days on which no antibiotics were taken and will be measured in days.

If the antibiotic name, start date or length of the course is missing or invalid the record will be excluded from analysis. Antibiotics started more than 60 days prior to randomisation will not be used in the analysis.

Additionally, all the baseline characteristics analyses will be repeated by sex subgroup so that any differences between the male and female participants at baseline can be identified visually.

Participants who withdrew from treatment and, separately, withdrew from trial will also be presented by baseline characteristics.

Post-randomisation corrections to baseline characteristics which serve as minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) and other covariates in the primary analysis model will be used in all the analyses, however, footnotes summarising participants who had their pre-randomisation information corrected will be added.

Corrections to baseline NRS pain scores are allowed only in case of a typographical error.

8. TREATMENT/INTERVENTION RECEIVED

The following information will be presented as counts and percentages by allocated treatment group for the randomised participants:

- Participants who were randomised but did not start treatment
- Participants who received dose 1
- Participants who did not receive dose 2

This is equivalent to early treatment discontinuation.

- Participants who received dose 2

This is equivalent to completing treatment.

- Participants who did not report receiving or not receiving dose 2

Time from randomisation to dose 1 will be calculated as the difference between dose 1 datetime and randomisation datetime, will be presented in minutes, and will be summarised descriptively.

The treatment is administered as soon as possible after randomisation. If the site staff prefer to delay dose 1, randomisation should be postponed so that dose 1 is administered soon after it.

The participants self-report whether they took dose 2. Dose 2 can be taken within 6 hours of the 24-hour mark post-randomisation. All participant reported answers about whether they took dose 2 will be used in the analysis, regardless of how long after the designated timepoints of 8 am/8 pm they were collected.

Dose modifications are not permitted on this study.

Any dose modifications or delays in dose 1 administration are reported as protocol deviations.

The number of participants who received the wrong treatment (not according to their allocation) by allocated treatment group will also be presented. These participants will be presented in the allocated treatment group in all the analyses unless otherwise specified.

Analgesia and antibiotics use is collected at baseline and on Day 14. Data presentations for these are covered in Section 10.2. No other prior, concomitant and post treatment medication use is collected.

No significance testing will be carried out with regard to this data.

9. SAFETY ANALYSIS/HARMS

Safety data analysis is covered in Section 10.2.8.

10. ANALYSIS

10.1 PRIMARY OUTCOME

10.1.1 NULL HYPOTHESIS

The null hypothesis for the primary estimand on the DEXACELL trial is:
There is no difference in total pain over the first 72 hours after baseline in participants with cellulitis when receiving Dexamethasone + Usual Care or just Usual Care.

This null hypothesis is to be assessed using a two-sided test with a 5 % significance level.

No adjustments for multiplicity will be performed as only one statistical hypothesis will be tested for this trial.

10.1.2 METHODS

AUC Calculation

AUC will be calculated using the trapezoidal rule by plotting the scores at the reported times when they were collected then joining those points linearly to calculate the AUC:

$$AUC_{t_i - t_{i-1}} = (t_i - t_{i-1}) * \frac{(s_i + s_{t-i})}{2}$$

$$AUC_{(k-0)} = \sum_{t_i=1}^{Tk} AUC_{t_i - t_{i-1}}$$

t_i is timepoint i, s_i is NRS pain score at t_i, baseline corresponds to $t_i = 0$, last reported timepoint corresponds to T_k.

The AUC will be rescaled to 0-100 to give a standardised AUC.

Descriptive Analysis

The primary outcome in the DEXACELL trial will be presented descriptively and graphically by allocated treatment group both as a calculated outcome measure (AUC) and as an individual score at the following time intervals: up to 12 hours, 12 to 24 hours, 24 to 36 hours, 36 to 48 hours, 48 to 60 hours, 60 to 72 hours, more than 72 hours. If a participant has more than one score in a time interval, the average of those scores will be used.

A descriptive analysis will also be done by selected demographics and baseline characteristics subgroups, as given in Section 16.3.2916.3.29.

Primary Analysis Model

Testing of the primary outcome will be conducted by fitting a linear mixed effects model with site included as a random effect and minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) as well as age at screening, sex and a baseline NRS pain score included as fixed effects. The result of this model will produce a between-group adjusted difference in mean overall pain over 3 days with a Wald 95% confidence interval and a corresponding Wald test p-value.

0 Pain Scores, Missing Data, Daylight Saving Time, Data Issues, Varying Follow Up Intervals

Participants with no reported pain at all time points (NRS score 0) will have the AUC equal to 0 and will be included in the analysis.

Timepoints that are missing will be interpolated linearly from the nearest available previous and subsequent timepoint. If there are no further subsequent timepoints, a last observation carried forward approach will be used for all subsequent timepoints after the final non-missing timepoint. This will include cases when the score is missing due to death which is in line with the hypothetical policy.

SMS prompts are sent every 12 hours despite Daylight Saving Time changes, and all the SMS prompt and site staff score times are collected in the current correct time. Because of this, for the affected participants an hour will be added or subtracted, respectively, from the affected SMS prompt and score times. This approach will also be used in the Days 1 - 3 PGI-I score analysis described further.

In instances where two measures have been provided for the same timepoint for any reason, the original score and the original timestamp will be used and any later scores/timestamps for that timepoint will be disregarded. Furthermore, if a previous timepoint has a later timestamp than a subsequent timepoint, the instance which is furthest from the designated window will be considered missing. Retrospectively added NRS pain scores will not be used. This approach will also be used in the Days 1 - 3 PGI-I score analysis described further.

Baseline scores are collected immediately before randomisation at the same hospital visit, hence why total pain over the first 72 hours is measured from baseline score collection time rather than randomisation.

The collection window for the scores collected through SMS is up to 12 hours from the receipt of the SMS for all the timepoints after baseline except for the final timepoint which has no restriction.

Some of the scores are collected by the site staff. These scores should be collected as close as practically possible to the 8 am/8 pm mark, however, at a minimum, each follow-up should be at least 6 hours after the previous one. This means that the scores collected by site staff can be prior to the 8 am/8 pm mark.

Site staff scores collection times do not have seconds, so seconds will be imputed as ":30" for all site staff scores. If the collection time is after randomisation for a baseline score because of this imputation, seconds will be equal to those of the randomisation timestamp. This approach will also be used in the Days 1 - 3 PGI-I score analysis described further.

The first interval – between the baseline score and the score reported at the next 8 am/ 8 pm mark – may be shorter than 12 hours, as the first collection timepoint is at the next 8 am/ 8 pm mark after randomisation. Therefore, if the time between baseline and the time the last score was reported is shorter than 72 hours, the last observation will be carried forward towards the 72-hour mark. If this time is longer than 72 hours, the 72-hour NRS pain score will be interpolated from the last score before and the first score after the 72-hour designated timepoint (8 am/ 8 pm) (any scores reported more than 24 hours after the 72-hour designated timepoint (8 am/8 pm) will be disregarded). In that way, the unstandardised AUC for all the participants will reflect the overall pain over exactly 72 hours after baseline. AUC will be rescaled by multiplying it by 10/72 for all the participants.

The number and percentage of participants with the time between the baseline score and the last reported score over the first 3 days <= 72 hours, > 72 hours and <= 96 hours, and > 96 hours, as well as with a missing last observation will be presented. A figure showing the distribution of these follow up times with regard to this outcome in the first 3 days post-baseline will also be presented.

The time between the baseline score and the last reported score will be calculated as the difference between the latter and the former and will be presented in hours.

Sensitivity Analysis 1

A contrast of rescaled AUC summary statistics in the treatment group versus control group will be calculated based on a fitted mean function from a longitudinal mixed effects model [18][19]. Estimation relies on likelihood under the Missing at Random assumption.

The model will have a participant random intercept and a participant random slope for linear time with unstructured covariance between them, and a site random intercept. A continuous time covariate and linear splines will be included together with their interactions with the allocated treatment group. The spline knots will be at 12, 24, 36, 48 and 60 hours. The model will also have minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) as well as age at screening, sex, baseline NRS pain score included as fixed effects.

The model equation will be the following:

$$\begin{aligned} Y_{ijk}(t) = \ & \beta_0 + \beta_1 * trt_{jk} + \beta_2 * t_{ijk} + \beta_3 * trt_{jk} * t_{ijk} + \\ & + \beta_4 * max(t_{ijk} - 12, 0) + \beta_5 * trt_{jk} * max(t_{ijk} - 12, 0) + \\ & + \beta_6 * max(t_{ijk} - 24, 0) + \beta_7 * trt_{jk} * max(t_{ijk} - 24, 0) + \\ & + \beta_8 * max(t_{ijk} - 36, 0) + \beta_9 * trt_{jk} * max(t_{ijk} - 36, 0) + \\ & + \beta_{10} * max(t_{ijk} - 48, 0) + \beta_{11} * trt_{jk} * max(t_{ijk} - 48, 0) + \\ & + \beta_{12} * max(t_{ijk} - 60, 0) + \beta_{13} * trt_{jk} * max(t_{ijk} - 60, 0) + \\ & + \beta_B^T X_{jk} + u_k + d_{1jk} + d_{2jk} * t_{ijk} + \varepsilon_{ijk}, \end{aligned}$$

where k is the subscript for the site, j is the subscript for the participant, i is the subscript for the timepoint at which the participant's pain is measured, Y_{ijk} is the NRS pain score, t_{ijk} is the continuous time since randomisation variable measured in hours, trt_{jk} is the dummy variable for the treatment group, $\beta_B^T X_{jk}$ are the baseline participant-level covariate effects, d_{1jk} is the random intercept for the participant, d_{2jk} is the random slope for the participant, u_k is the random intercept for the site, ε_{ijk} is the random error term.

The distribution of the random effects and the random error term are as follows:

$$\begin{pmatrix} d_{1jk} \\ d_{2jk} \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_1^2 & \sigma_{12} \\ \sigma_{12} & \sigma_2^2 \end{pmatrix}\right),$$

$$u_k \sim \mathrm{N}(0, \sigma_{site}^2),$$

$$\varepsilon_{ijk} \sim \mathrm{N}(0, \sigma^2)$$

The formula for the rescaled AUC summary statistic contrast is as follows:

$$\begin{aligned} AUC_1 - AUC_0 = & \int_0^{72} \big(\beta_1 + \beta_3 * t + \beta_5 * max(t - 12, 0) + \beta_7 * max(t - 24, 0) + \beta_9 * max(t - 36, 0) + \beta_{11} \\ & * max(t - 48, 0) + \beta_{13} * max(t - 60, 0)\big) * 10/72 \, dt = \\ = & \left(\beta_1 * 72 + \beta_3 * \frac{72^2}{2} + \beta_5 * \frac{max(72 - 12, 0)^2}{2} + \beta_7 * \frac{max(72 - 24, 0)^2}{2} + \beta_9 * \frac{max(72 - 36, 0)^2}{2} + \beta_{11} \right. \\ & \left. * \frac{max(72 - 48, 0)^2}{2} + \beta_{13} * \frac{max(72 - 60, 0)^2}{2}\right) * 10/72 \end{aligned}$$

The Wald 95% confidence interval for the contrast will be provided.

The population for this analysis will be the same as for the primary analysis.

The model may be simplified in case of problems with estimation.

Sensitivity Analysis 2

If imbalances are noted between the trial groups in the baseline characteristics besides those used in the primary analysis (a difference of >10% points between arms for a categorical variable (provided there are at least 10 participants in the category) or a difference > 1 standard deviation for a continuous variable) and thought to be predictive of the outcome, a sensitivity analysis adjusting for these characteristics in addition to those already listed may be conducted. Smaller imbalances could be adjusted for if thought to be strongly predictive of the outcome. The population will be the same as in the primary analysis.

Supplementary Analysis 1

A supplementary analysis will be performed measuring total pain over the first 60 hours after baseline.

This analysis will have a different estimand – total pain over the first 60 hours after baseline – however, it will remove the necessity to impute the interval between 60 hours and 72 hours for most participants.

The 60-hour pain score will be interpolated from the neighbouring scores. If no score is reported after the 60-hour mark but before the 84-hour mark after baseline the last observation will be carried forward to the 60-hour mark. In that way, the unstandardised AUC for all the participants will reflect the overall pain over exactly 60 hours after baseline. AUC will be rescaled by multiplying it by 10/60 for all the participants.

Otherwise, the same approach to modelling will be used.

The population will be all randomised participants who had a baseline pain score and a score 24 hours after the baseline score but within 24 hours of the time the SMS was sent for timepoint 5.

Supplementary Analysis 2

The same model as described in the Sensitivity Analysis 1 will be used to estimate treatment effect at 72 hours. The Wald 95% confidence interval will be provided.

Model Diagnostics

Model diagnostics will be performed. Additional sensitivity analyses may be performed if the model shows lack of fit or any assumptions are violated. Alternative models may also be considered.

10.2 SECONDARY OUTCOMES

For all the secondary outcomes data collected outside of the protocol specified collection windows (+/- 2 days for Day 14 and +/- 7 days for Day 90) will be used in the analyses, unless specified otherwise. Data collected from the medical records will also be used in the analysis.

Day 3 data points and any data points before it will be considered missing if collected more than 24 hours after the designated Day 3 8 am or 8 pm timepoint.

10.2.1 PATIENT GLOBAL IMPRESSION OF IMPROVEMENT (PGI-I) MEASURED DAILY FOR FIRST 3 DAYS POST-RANDOMISATION

Descriptive Analysis

The non-missing and non-0 PGI-I scores will be presented descriptively and graphically by allocated treatment group at each timepoint.

Analysis Model

A linear repeated measures mixed effects model with participant and site as random effects and post-baseline PGI-I scores as the outcome will be estimated. A "timepoint" categorical fixed effect and its interaction with the allocated treatment group will be included. The model will have minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) as well as age at screening, sex, baseline NRS pain score included as fixed effects. This model will produce a between-group adjusted difference in mean scores with a Wald 95% confidence interval.

Missing Data, Timepoints

No imputation will be performed for this analysis; however, the repeated measures model will implicitly impute the partially missing outcomes under the Missing at Random underlying assumption.

Death will be handled according to the hypothetical policy under the assumption that outcomes among those who died have the same distribution as the outcomes among those who did not die.

The collection windows for the PGI-I scores are the same as for the NRS pain scores, as described in Section 10.1.2.

Times at which site staff collected PGI-I scores for timepoint 6 were not collected, therefore, times at which site staff collected NRS pain scores for timepoint 6 will be used.

For this secondary analysis and for the by timepoint descriptive analyses mentioned above the scores will be assigned to the following time intervals: 12 to 36 hours, 36 to 60 hours, more than 60 hours since baseline. These will be used as Day 1, Day 2 and Day 3 timepoints respectively. If a participant has more than one score in a time interval, the average of those scores will be used.

Model Diagnostics and Sensitivity Analyses

Model diagnostics will be performed. Additional sensitivity analyses may be performed if the model shows lack of fit or any assumptions are violated. An ordinal logistic mixed effects model or an alternative modelling approach such as dichotomising the categories and using a logistic regression may be considered.

10.2.2 ANALGESIA USAGE (NUMBER AND TYPE OF ANALGESIA TAKEN OVER FIRST 3 DAYS) POST-RANDOMISATION

This secondary outcome will be presented descriptively by allocated treatment group by reporting the count and percentage of participants who used non-opioids, adjuvants (including NSAID), weak opioids and strong opioids (WHO pain ladder [20]) and, as a next level, each ATC3 class of analgesia in the first 72 hours following randomisation.

The number of uses of each analgesia type were collected as free text and will, therefore, not be summarised.

10.2.3 ANTIBIOTIC USAGE (ROUTE, TYPE, AND POST-RANDOMISATION LENGTH OF COURSE) UP TO DAY 14 RANDOMISATION

Route of administration post-randomisation will be presented as the number and percentage of participants for whom each route of administration was used.

Type of antibiotic taken will be presented as the number and percentage of participants who took each ATC3 class of antibiotic in each allocated treatment group.

Length of antibiotic course will be calculated in the same way as described in Section 7 with the last day any antibiotic was taken as the end date and the first day any antibiotic was taken (or day of randomisation if the course started prior to randomisation) as the start date, excluding days on which no antibiotics were taken.

The collected data does not allow to distinguish the original antibiotic prescription and additional antibiotic use post-randomisation. Nearly all the participants are expected to use antibiotics post-randomisation. Therefore, the logistic mixed effect model analysis for additional antibiotics use cannot be performed. Post-randomisation antibiotic use will be summarised descriptively.

Length of the antibiotic course will be capped at Day 14.

10.2.4 UNSCHEDULED HEALTHCARE USAGE UNTIL DAY 14 POST-RANDOMISATION

Unscheduled healthcare usage until Day 14 post-randomisation will be presented descriptively as a summary of the number of occurrences of each unscheduled healthcare type use in each allocated treatment group and overall.

0 occurrences will be included when the summary statistics are calculated.

Additionally, whether the participant used any unscheduled healthcare until Day 14 post-randomisation will be analysed in the same way as described in Section 10.2.5. The population will be all randomised participants who used eCRF version 2 or above.

10.2.5 (RE)ADMISSIONS TO HOSPITAL BY DAY 14 POST-RANDOMISATION AND RECURRENCE OF CELLULITIS BY DAY 90 POST-RANDOMISATION

The number of “Yes” outcomes and their percentage out of the non-missing answers will be presented descriptively.

The secondary outcome will be analysed using a logistic mixed effects model with site as a random effect and a binary/dichotomised outcome variable. The model will have minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) as well as age at screening, sex, baseline NRS pain score included as fixed effects. The model will produce an odds ratio of the outcome “Yes” versus the outcome “No” in the outcome variable conditional on site-specific effect with a Wald 95% confidence interval.

No imputation will be performed for this analysis.

Deaths will be handled according to the while-alive policy.

Model diagnostics will be performed. Additional sensitivity analyses may be performed if the model shows lack of fit or any assumptions are violated. Alternative models may be considered.

10.2.6 COMPLICATIONS OF DEXAMETHASONE USE BY DAY 14 POST-RANDOMISATION

Number and percentage of participants with severe hyperglycaemia, gastrointestinal bleeding and psychosis by Day 14 post-randomisation will be presented.

10.2.7 PAIN EXPERIENCED AT DAY 14 POST-RANDOMISATION, PGI-I AT DAY 14 POST-RANDOMISATION

The non-missing and non-0 PGI-I and non-missing NRS pain scores will be presented descriptively and graphically by allocated treatment group.

Responses outside of the visit windows will be considered missing.

These secondary outcomes will be analysed using a linear mixed effects model with site as a random effect. The model will have minimisation factors (prior (to hospital attendance) antimicrobial therapy for the current episode of cellulitis, diabetes and severity of cellulitis (Eron Stage 1 vs all other stages)) as well as age at screening, sex, baseline

NRS pain score included as fixed effects. The model will produce a between-group adjusted difference in mean scores with a Wald 95% confidence interval.

No imputation will be performed for this analysis.

Deaths prior to Day 14 will be handled according to the principal stratum of "always survivors" policy. The estimand targets the treatment effect on Day 14 among participants who would survive Day 14 under either treatment under the assumption that the randomised treatment does not affect mortality over the 14-day follow up which is plausible for this trial.

Model diagnostics will be performed. Additional sensitivity analyses may be performed if the model shows lack of fit or any assumptions are violated. Alternative modelling approaches such as dichotomising the categories and using a logistic regression or using a Mann Whitney U test, or a Permutation test based on the Mann Whitney U test statistic (in case of many ties) may be considered.

10.2.8 SERIOUS AND/OR POTENTIALLY RELATED ADVERSE EVENTS BY DAY 90 POST-RANDOMISATION

Non-serious ARs, SARs, SUSARs, unrelated SAEs and SAEs overall will be tabulated as frequency and percentage of participants with the respective System Organ Class and Preferred Term, and frequency of each adverse event.

Participants with SARs, SUSARs, unrelated SAEs and SAEs overall will be presented with a split by categories of severity and outcome. The participant will be counted in the category corresponding to the "worst" adverse event with the given SOC and/or PT.

Participants which had SARs, SUSARs, unrelated SAEs and SAEs overall and the number of events will also be presented by reason for seriousness.

SARs, SUSARs, unrelated SAEs and SAEs overall which led to change in participation status will also be presented.

Non-serious ARs will also be summarised overall and by severity.

The total number of deaths will be reported together with the primary cause of death.

Analyses will be performed for the randomised participants by allocated treatment group, only adverse events at the time or after randomisation will be included. Analyses will be repeated on the treated participants, by actual treatment group, and only adverse events at the time or after dose 1 administration will be included.

If the adverse event start date is missing the adverse event will be assumed to have started after randomisation/dose 1. Randomisation date or dose 1 date will be used depending on the analysis population: all randomised or all treated participants, respectively.

10.3 SUBGROUP ANALYSIS

Although the trial is not powered for subgroup analysis, a small number of pre-specified exploratory analyses will be undertaken on the primary outcome for subgroups of particular interest: cellulitis location (lower limb vs other), NSAID usage at time of randomisation (user vs non-user), diabetes diagnosis ("Yes"/"No") and sex ("Male"/"Female"). These analyses will be carried out by refitting the mixed effects linear regression model described for the primary analysis (see Section 10.1.2) with a subgroup fixed effect and an interaction between the allocated treatment group and the subgroup of interest fixed effect on the same population as in the primary analysis but only for those for whom the subgroup is not missing. These subgroup analyses will be performed only if there are at least 10 participants in each subgroup. The results will be presented in table format with mean effects

conditional on site specific effect and their 95% CIs. The results may also be presented in log-scale as forest plots. No inference will be made as these analyses are hypothesis forming in nature.

10.4 ADDITIONAL ANALYSES

An additional unadjusted analysis will be performed for each fitted model. This analysis will aid future meta-analysis.

Additional analyses may be performed if considered necessary and justified.

Post-hoc analyses will be labelled as such.

10.5 DECISION CRITERIA

This trial has an internal pilot phase. Trial progress was assessed after the first 6 months of participant recruitment. In close consultation with the DMC, TSC, Sponsor and funder it was considered whether any remedial actions or trial closure were required. More details are given in Section 4 of the protocol.

This estimate of the pooled SD used to calculate the sample size, and 95% confidence intervals were reviewed by the unblinded senior statistician and by the closed DMC members at the end of the internal pilot phase.

10.6 CONVENTIONS

Continuous variables will generally be summarised by presenting means, standard deviations, minimums and maximums. If the distributions of the continuous variables appear to be skewed means and standard deviations will not be reported, instead median and IQR will be reported. Skewness of the distributions will be investigated visually and using the Pearson's measure of skewness.

Durations are calculated as the end day (minute or second, depending on the date precision) minus the start day (minute or second) plus 1 to include both the end day (minute or second) and the start day (minute or second) in the duration as a conservative approach unless specified otherwise. For example, the length of the antibiotic course includes both the start day or the course and the end day of the course, as the former can happen early in the day while the latter can happen late in the day.

The default Stata 18.0 estimation methodology will be used for all the estimated models, unless specified otherwise. REML estimation methodology will be used for linear mixed effects models.

11. ECONOMIC EVALUATION

There will be a separate Health Economics Analysis Plan which will detail the economic evaluation analyses.

12. STATISTICAL SOFTWARE

Stata version 18.0 or later, or R version 4.5 or later, will be used for the analysis.

13. STORAGE AND ARCHIVING

Snapshots/exports of the data are stored here:

DEXACELL/*restricted* Blinded - Stats

Analysis code is stored here:

DEXACELL/Stats Working Docs/Analysis/scripts

Restricted area:

DEXACELL/*Restricted*UnblindedDocuments/

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16. APPENDICES

16.1 APPENDIX 1 ABBREVIATIONS AND ACRONYMS

Abbreviation or Acronym	Meaning
API	Application Programming Interface
AR	Adverse Reaction
AUC	Area Under the Curve
BDP	Bristol Drugs Project
BMI	Body Mass Index
BOTS	Binding of Trial Statisticians
CI	Confidence Interval
DAG	Drug Allocation Group
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
eTMF	Electronic Trial Master File
GP	General Practitioner
HRA	Health Research Authority

ICH	Internation Council for Harmonisation
IMP	Investigational Medicinal Product
IQR	Interquartile Range
IRAS	Integrated Research Application System
IRSCTN	International Standard Randomised Controlled Trials Number
ISDM	Information Systems and Data Management
IUD	Intrauterine Device
IUS	Intrauterine Hormone-Releasing System
MCID	Minimum Clinically Important Difference
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare Products Regulatory Agency
MICE	Multiple Imputation by Chained Equations
NEWS 2	Nation Early Warning Score 2
NHS	National Health Service
NRS	Numeric Rating Scale
NSAID	Nonsteroidal Anti-Inflammatory Drug
PAG	Patient Advisory Group
PASS	Power Analysis Sample Size
PGI-I	Patient Global Impression of Improvement
PPI	Patient and Public Involvement
PT	Preferred Term
REC	Research Ethics Committee
REML	Restricted Maximum Likelihood
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SMS	Short Message Service
SOC	System Organ Class
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMG	Trial Management Group
TSC	Trial Steering Committee

16.2 APPENDIX 2 NEWS 2 SCORING SYSTEM [14]

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

16.3 APPENDIX 3 MOCK DATA PRESENTATIONS

16.3.1. EARLY UNBLINDING (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Unblinded Early	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.2. NRS PAIN SCORES COMPLETENESS, FIRST 3 DAYS POST-BASELINE

Allocated Treatment Group:

	Number (%) Completed	Number (%) Completed by SMS	Number (%) Collected by Staff
Baseline Pain Score	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 3	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 4	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 5	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 6	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Participants With Minimum 2/7 Pain Scores ***(must include baseline & one other at least 24 hours later)***	XXX (XXX.X%)		

Responses are summarised against the respective SMS prompt.

Notes: The table will be paged by allocated treatment group: Treatment Group A, Treatment Group B, Overall.

This table will be repeated with responses split into the following groups: “Up to 12 Hours”, “12 to 24 Hours”, “24 to 36 Hours”, “36 to 48 Hours”, “48 to 60 Hours”, “60 to 72 Hours”, “More Than 72 Hours”. If a participant has more than one score in a time interval, the average of those scores will be used. Columns “Number (%) Completed by SMS” and “Number (%) Collected by Staff” will not be presented.

16.3.3. NRS PAIN SCORES COMPLETENESS BY SITE, FIRST 3 DAYS POST-BASELINE

Allocated Treatment Group:

		Number (%) Completed	Number (%) Completed by SMS	Number (%) Collected by Staff
Baseline Pain Score	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 1	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 2	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 3	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 4	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 5	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 6	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Participants With Minimum 2/7 Pain Scores ***(must include baseline & one other at least 24 hours later)***	**Site 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Site 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Responses are summarised against the respective SMS prompts.

Notes: The table will be paged by allocated treatment group: Treatment Group A, Treatment Group B, Overall.

16.3.4. NRS PAIN SCORES COMPLETENESS BY SUBGROUP, FIRST 3 DAYS POST-BASELINE

Allocated Treatment Group:

			Number (%) Completed	Number (%) Completed by SMS	Number (%) Collected by Staff
Subgroup Name 1	**Baseline Pain Score**	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 1	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 2	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 3	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 4	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 5	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	SMS 6	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Participants With Minimum 2/7 Pain Scores *(must include baseline & one other at least 24 hours later)*	**Category 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		Category 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Subgroup Name 2	**…**	**…**	…	…	…

Responses are summarised against the respective SMS prompts.

Notes: The table will be paged by allocated treatment group: Treatment Group A, Treatment Group B, Overall.

Notes: The following demographic and baseline characteristics will be analysed: age at screening group (< 50, >= 50 and < 60 and >= 60), sex, ethnicity, baseline NRS pain score, prior (to hospital attendance) antimicrobial therapy for this episode of cellulitis (“Yes”/”No”), severity of cellulitis (stage 1 vs other stages), diabetes (“Yes”/”No”), cellulitis location (lower limb vs other), NSAID usage at time of randomisation (user vs non-user).

16.3.5. PGI-I SCORES COMPLETENESS, FIRST 3 DAYS POST-RANDOMISATION

Allocated Treatment Group:

	Number (%) Completed	**Number (%) Completed by SMS**	**Number (%) Collected by Staff**
SMS 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SMS 3	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Responses are summarised against the respective SMS prompts.

Notes: The table will be paged by allocated treatment group: Treatment Group A, Treatment Group B, Overall.

This table will be repeated with responses split into the following groups: “12 to 36 Hours”, “36 to 60 Hours”, “More Than 60 Hours”. If a participant has more than one score in a time interval, the average of those scores will be used. Columns “Number (%) Completed by SMS” and “Number (%) Collected by Staff” will not be presented.

16.3.6. OTHER SECONDARY OUTCOMES COMPLETENESS (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
NRS Pain Score (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Patient Global Impression of Improvement (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Analgesia Usage (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Antibiotic Usage (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Re-Admission to Hospital (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Recurrence of Cellulitis (Day 90)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Complications (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Unscheduled Healthcare Usage (Day 14)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Where several fields are collected, the outcome is considered completed if all the fields are non-missing.

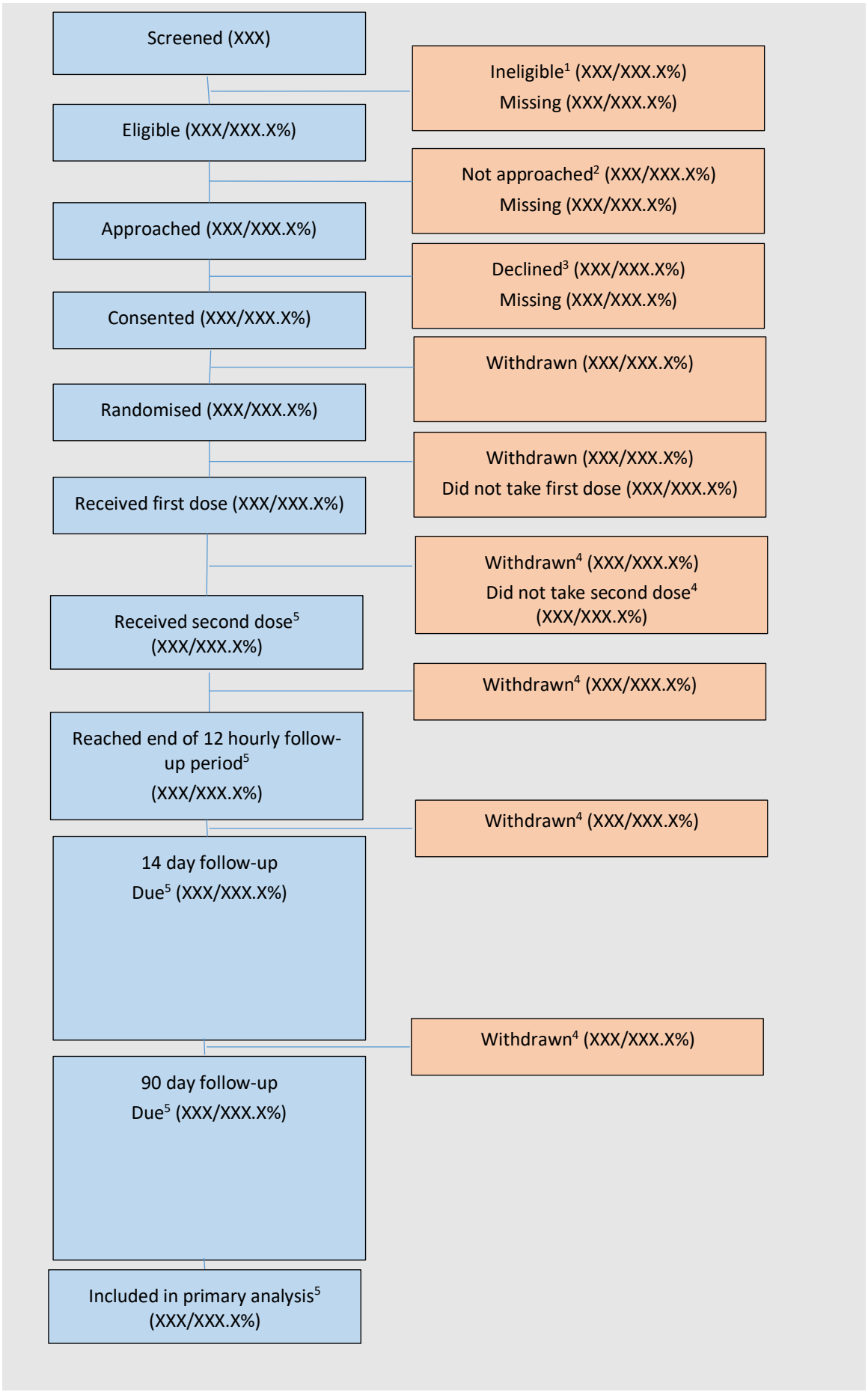
16.3.7. ANALYSIS POPULATIONS (ALL RANDOMISED PARTICIPANTS)

Outcome	Analysis Population	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Total pain measured over 3 days post baseline	**Evaluable intention-to-treat population: all randomised participants with a baseline NRS pain score and at least one other NRS pain score at least 24 hours after the baseline**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Health-related quality of life, measured by EQ-5D-5L at Day 3, Day 14 and Day 90 post-randomisation	**The details will be given in the Health Economics Analysis Plan.**			
Patient Global Impression of Improvement (PGI-I) measured daily for first 3 days post-randomisation	**All randomised participants with at least one PGI-I score reported post-randomisation**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Analgesia usage (number and type of analgesia taken over first 3 days) post-randomisation	**All randomised participants**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Antibiotic usage (route, type, and post-randomisation length of course) up to Day 14 post-randomisation	**All randomised participants**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
(Re)admissions to hospital by Day 14 post-randomisation	**All randomised participants with a (re)admission to hospital answer reported by Day 14 post-randomisation**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Complications of dexamethasone use by Day 14 post-randomisation	**All randomised participants**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Any unscheduled healthcare usage (not necessarily cellulitis	**All randomised participants who used eCRF version 2 or above**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

related) until Day 14 post-randomisation				
Health, social care and broader societal resource use, measured by a resource use questionnaire to Day 90 post-randomisation	**The details will be given in the Health Economics Analysis Plan.**			
Recurrence of cellulitis by Day 90 post-randomisation	**All randomised participants with a recurrence of cellulitis answer reported by Day 90 post-randomisation**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Pain experienced at Day 14 post-randomisation	**All randomised participants with an NRS pain score reported at Day 14 post-randomisation**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Patient Global Impression of Improvement (PGI-I) measured daily at Day 14 post-randomisation	**All randomised participants with a PGI-I score reported at Day 14 post-randomisation**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Healthcare usage questionnaire was updated shortly after the start of data collection to include any unscheduled healthcare usage (not necessarily related to cellulitis). Because of that the data collected prior to the questionnaire update in version 2 of the eCRF is not directly comparable to the data collected after the update. Therefore, participants who filled in only the old version will be excluded from the analysis.

16.3.8. CONSORT FLOW DIAGRAM



[1]Reasons for ineligibility are listed in table XXX.

[2]Reasons for non-approach are listed in table XXX.

[3]Reasons for decline will be listed in table XXX.

[4]Withdrawn from trial.

[5]Denominator for the percentage is randomised participants.

If the date of the event (ex., Received second dose) and the date of the withdrawal are the same, the withdrawal is considered to have happened after the event.

Screened patients contain re-screened patients as a double entry.

Notes: The diagram will be split by allocated treatment group starting at the "Randomised" block.

16.3.9. REASONS FOR INELIGIBILITY (ALL SCREENED PATIENTS)

	Number (%) of Screened Patients Confirmed Ineligible by Reason Given (N = XXX)																	
	St George's Hospital (11)	Addenbrookes Hospital (12)	Bristol Royal Infirmary (13)	Derriford Hospital (Plymouth) (14)	Salford Royal Care Org (15)	Southmead Hospital (16)	Royal Berkshire Hospital (17)	Hull Royal Infirmary (18)	Manchester Royal Infirmary (19)	St Marys Hospital (Imperial) (20)	Leicester Royal Infirmary (21)	Barts: Royal London (22)	Barts: Newham UH (23)	Wexham Park Hospital (25)	James Cook (South Tees) (26)	University Hospital Lewisham (27)	Watford (West Hertfordshire) (29)	Milton Keynes (30)	Overall
Not aged 16 years or over	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
No current clinical diagnosis of cellulitis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Isn't able to provide informed consent	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Not willing to use an effective method of contraception	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Not willing to inform the trial team if pregnancy occurs during trial participation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Orbital or periorbital cellulitis, surgical site infection, or planned surgical management (e.g. abscess) as managed under a different clinical pathway	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Allergy to dexamethasone	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Contraindication to dexamethasone	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)

due to concurrent medication (e.g. cobicistat)																			
Has known current invasive fungal infection	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Has known current gastric or duodenal ulceration	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Currently on systemic corticosteroids	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Unable to take oral medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Lack of capacity	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Inability to complete follow-up procedures	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Prisoner	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Pregnant, breastfeeding, or planning to conceive in next 3 months	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Other	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	XX (XXX.X%)
Total	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**XX (XXX.X%)**

Screened patients contain re-screened patients as a double entry.

16.3.10. CATEGORISED OTHER REASON GIVEN FOR INELIGIBILITY OF SCREENED PATIENTS (ALL PATIENTS WITH OTHER REASON FOR INELIGIBILITY)

Reason	Overall (N = XXX)
Medical Contraindications or Comorbidities	XX (XXX.X%)
Consent or Cognitive Barriers	XX (XXX.X%)
Operational or Logistical Barriers	XX (XXX.X%)
Diagnostic Uncertainty or Not Cellulitis	XX (XXX.X%)
Study Eligibility Issues	XX (XXX.X%)
Surgical or Alternative Management	XX (XXX.X%)

16.3.11. REASONS FOR NON-APPROACH (ALL ELIGIBLE PATIENTS)

	Reasons for Non-Approach of Eligible Patients (N = XXX)							
	Language Barrier[1]	**Clinical Condition Changed**	**Staffing Unavailability**	**IMP Unavailability**	**Technical/ Logistical Issues**	**Other**	**Missing**	**Total**
St George's Hospital (11)	X	X	X	X	X	X	X	X
Addenbrooke's Hospital (12)	X	X	X	X	X	X	X	X
Bristol Royal Infirmary (13)	X	X	X	X	X	X	X	X

UHP (Plymouth) (14)	X	X	X	X	X	X	X	X
Salford Royal (15)	X	X	X	X	X	X	X	X
Southmead Hospital (16)	X	X	X	X	X	X	X	X
Royal Berkshire Hospital (17)	X	X	X	X	X	X	X	X
Hull Royal Infirmary (18)	X	X	X	X	X	X	X	X
Manchester Royal Infirmary (19)	X	X	X	X	X	X	X	X
St Mary's Hospital (Imperial) (20)	X	X	X	X	X	X	X	X
Leicester Royal Infirmary (21)	X	X	X	X	X	X	X	X
Barts, Royal London (22)	X	X	X	X	X	X	X	X
Barts, Newham (23)	X	X	X	X	X	X	X	X
Wexham Park Hospital (25)	X	X	X	X	X	X	X	X
James Cook (South Tees) (26)	X	X	X	X	X	X	X	X
University Hospital Lewisham (27)	X	X	X	X	X	X	X	X
Watford (West Hertfordshire) (29)	X	X	X	X	X	X	X	X
Milton Keynes (30)	X	X	X	X	X	X	X	X
Overall	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**

[1]If a language barrier is given as the reason for non-approach; the first languages spoken by those patients are reported here: XXX.

16.3.12. CATEGORISED OTHER REASON GIVEN FOR NON-APPROACH OF ELIGIBLE PATIENTS (ALL PATIENTS WITH OTHER REASON FOR NON-APPROACH)

Reason	**Overall (N = XXX)**
Operational or Logistical Barriers	XX (XXX.X%)
Consent or Cognitive Barriers	XX (XXX.X%)
Medical Contraindications or Comorbidities	XX (XXX.X%)
Diagnostic Uncertainty or Not Cellulitis	XX (XXX.X%)
Study Eligibility Issues	XX (XXX.X%)
Follow-up or Monitoring Concerns	XX (XXX.X%)

16.3.13. REASONS FOR NON-CONSENT (ALL APPROACHED PATIENTS)

	Reasons (%) for Non-Consent of Approached Patients (N = XXX)									
	SMS Cost	**Unwilling/ Unable to Complete F-Up**	**Cannot Read/Write**	**Not Interested in Research**	**Concern About Time Burden**	**Doesn't Think Study Will Benefit Them**	**Language Barrier[1]**	**Discharged Before Decision**	**Other**	**Total**
St George's Hospital (11)	X	X	X	X	X	X	X	X	X	X
Addenbrooke's Hospital (12)	X	X	X	X	X	X	X	X	X	X

Bristol Royal Infirmary (13)	X	X	X	X	X	X	X	X	X	X
UHP (Plymouth) (14)	X	X	X	X	X	X	X	X	X	X
Salford Royal (15)	X	X	X	X	X	X	X	X	X	X
Southmead Hospital (16)	X	X	X	X	X	X	X	X	X	X
Royal Berkshire Hospital (17)	X	X	X	X	X	X	X	X	X	X
Hull Royal Infirmary (18)	X	X	X	X	X	X	X	X	X	X
Manchester Royal Infirmary (19)	X	X	X	X	X	X	X	X	X	X
St Mary's Hospital (Imperial) (20)	X	X	X	X	X	X	X	X	X	X
Leicester Royal Infirmary (21)	X	X	X	X	X	X	X	X	X	X
Barts, Royal London (22)	X	X	X	X	X	X	X	X	X	X
Barts, Newham (23)	X	X	X	X	X	X	X	X	X	X
Wexham Park Hospital (25)	X	X	X	X	X	X	X	X	X	X
James Cook (South Tees) (26)	X	X	X	X	X	X	X	X	X	X
University Hospital Lewisham (27)	X	X	X	X	X	X	X	X	X	X
Watford (West Hertfordshire) (29)	X	X	X	X	X	X	X	X	X	X
Milton Keynes (30)	X	X	X	X	X	X	X	X	X	X
Overall	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**	**XX (XXX.X%)**

[1]If a language barrier is given as the reason for declining consent; the first languages spoken by those patients are reported here: XXX.

16.3.14. CATEGORISED OTHER REASON GIVEN FOR NON-CONSENT OF APPROACHED PATIENTS (ALL PATIENTS WITH OTHER REASON FOR NON-CONSENT)

Reason	Overall (N = XXX)
Patient Declined Participation (General)	XX (XXX.X%)
Medication or Steroid Concerns	XX (XXX.X%)
Contraception-Related Declines	XX (XXX.X%)
Medical Contraindications or Comorbidities	XX (XXX.X%)
Capacity or Cognitive Barriers	XX (XXX.X%)
Follow-up or Monitoring Concerns	XX (XXX.X%)
Study Design Concerns	XX (XXX.X%)
Clinician or Team Decision	XX (XXX.X%)
Operational or Logistical Barriers	XX (XXX.X%)

16.3.15. DEMOGRAPHICS (ALL SCREENED PATIENTS)

		Overall (N = XXX)
Age (Years)		XXX, XXX (XX.X) [XXX – XXX]
Sex at Birth	**Male**	XXX (XXX.X%)
	Female	XXX (XXX.X%)
Ethnicity	**Asian (Bangladeshi, Chinese, Indian, Pakistani, Other)**	XXX (XXX.X%)
	Black (African, Caribbean, Other)	XXX (XXX.X%)
	Mixed or Multiple Ethnic Groups (White and Asian, White and Black African, White and Black Caribbean, Other)	XXX (XXX.X%)
	White (English, Welsh, Scottish, Northern Irish or British, Irish, Gypsy or Irish Traveller, Roma, Other)	XXX (XXX.X%)
	Other Ethnicity (Arab, Other)	XXX (XXX.X%)

Screened patients contain re-screened patients as a double entry.

Notes: Missing category will be added to each block if the information is not available for any patients.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.16. DEMOGRAPHICS AND BASELINE CHARACTERISTICS BY METHOD OF COLLECTION (ALL RANDOMISED PARTICIPANTS)

Allocated Treatment Group:

		Scores Collected Via SMS (N = XXX)	Score Collected Manually (N = XXX)	Scores Collected Both Via SMS and Manually (N = XXX)
Age (Years)		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
BMI		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Baseline Clinical Observations	**Temperature**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	Systolic Blood Pressure	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	Diastolic Blood Pressure	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	Respiratory Rate	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]

	Pulse	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	Oxygen Saturation	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
Clinical Frailty Score[1]		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Time Since Cellulitis Onset Until Randomisation		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Baseline NRS Pain Score	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	Score 0	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Sex at Birth	**Male**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Female	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Gender	**Man**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Non-Binary	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Woman	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Self-Described	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Prefer Not to Say	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Transgender	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Prefer Not to Say	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Ethnicity	**Asian (Bangladeshi, Chinese, Indian, Pakistani, Other)**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Black (African, Caribbean, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Mixed or Multiple Ethnic Groups (White and Asian, White and Black African, White and Black Caribbean, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	White (English, Welsh, Scottish, Northern Irish or British, Irish, Gypsy or Irish Traveller, Roma, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other Ethnicity (Arab, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Supplemental Oxygen	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Level of Alertness	**Alert: Fully Awake**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confusion (New): New Onset or Worsening Confusion	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	Voice: Responds to Verbal Stimulus	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Pain: Responds to Pain Stimulus (e.g. Supra-Orbital Pressure)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Unresponsive (No Response to Verbal or Pain Stimulus)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
NEWS2 Score	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	No Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Low Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Low to Medium Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Medium Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	High Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Index of Multiple Deprivation	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX (XX.X) [XXX – XXX]
	1st Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	2nd Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	3rd Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	4th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	5th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	6th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	7th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	8th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	9th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	10th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Homeless	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Postcode Outside of England	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Incorrect or Missing Postcode	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Severity of Cellulitis (Eron Classification)	**Class 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	All Other Classes	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Location of Cellulitis[2]	**Leg**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Foot	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Foot	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	Right Lower Limb (Not Foot)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Lower Limb (Not Foot)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other Than Leg	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Hand	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Hand	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Upper Limb (Not Hand)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Upper Limb (Not Hand)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Facial	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Abdomen	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Groin	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Groin	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Cellulitis Cause	**Insect Bite / Sting**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Related to Skin Breakage	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Unknown	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Prior (to Hospital Attendance) Antimicrobial Therapy for Current Episode of Cellulitis	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Analgesia Usage in the Last 3 Days Prior to Hospital Attendance[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Paracetamol	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Ibuprofen or Other NSAID	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Weak Opioids	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Strong Opioids	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Use of Injecting "Street" Drugs (Within the Last Month)	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Current	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Historic	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Diabetes	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Type 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Type 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Comorbidities[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Peripheral Vascular Disease	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Chronic Leg Oedema	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Morbid Obesity	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Risk Factors for Steroid Adverse Events[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Recent or Previous Gastric Ulcers	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Required Proton-Pump-Inhibitors in the 1 Month Prior to Hospital Admission	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Prescribed Proton Pump Inhibitors Whilst in Hospital for This Admission	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Measured only on those who are 65 years old or older at screening.

[2]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

Only the NRS pain scores used in the primary analysis are considered.

Notes: The table will be paged by allocated treatment group: Treatment Group A, Treatment Group B, Overall.

Missing category will be added to each block if the information is not available for any participants.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.17. PARTICIPANTS FOUND INELIGIBLE BUT RANDOMISED IN ERROR (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Participants Found to be Ineligible but Randomised in Error	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.18. PARTICIPANTS WHO HAD A CHANGE IN CLINICAL STATUS DURING THE TRIAL (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Participants Who Had a Change in Clinical Status During the Trial	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.19. CHANGE IN PARTICIPANT STATUS (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Withdrawn from Trial Before Randomisation[1]				XXX (XXX.X%)
Withdrawn from Receiving Allocated Treatment		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reason for Withdrawal	**Time Burden**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Dissatisfied with Taking Part	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Doesn't Feel They are Benefitting	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Personal Reasons Unrelated to Study	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confidentiality Concerns	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Participant Was Added to the Wrong DAG	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Who Requested Withdrawal	**Patient**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Clinician	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Withdrawn from Remote Follow-Up		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reason for Withdrawal	**Time Burden**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Dissatisfied with Taking Part	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Doesn't Feel They are Benefitting	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Personal Reasons Unrelated to Study	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confidentiality Concerns	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Participant Was Added to the Wrong DAG	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Who Requested Withdrawal	**Patient**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Clinician	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Withdrawn from Passive Data Collection from Routine Medical Records (Except SAE)		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reason for Withdrawal	**Time Burden**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Dissatisfied with Taking Part	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Doesn't Feel They are Benefitting	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Personal Reasons Unrelated to Study	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confidentiality Concerns	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Participant Was Added to the Wrong DAG	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Who Requested Withdrawal	**Patient**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Clinician	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]The denominator is the number of participants who consented.

Notes: This table will be repeated by sex. "Withdrawn from Trial Before Randomisation" will not be displayed.

16.3.20. PARTICIPANTS WHO REACHED PRIMARY ANALYSIS (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Reached Primary Analysis[1]		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Dead		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Alive at Primary Analysis but Withdrew from Remote Follow-Up		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reason for Withdrawal	**Time Burden**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reached Primary Analysis But Not Included in Primary Analysis Due to No Post-Baseline Score at Least 24 Hours After Baseline		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Defined as reaching the time of SMS 6 in the SMS follow up.

Notes: This table will be repeated by sex.

16.3.21. REASONS FOR WITHDRAWAL FROM TRIAL BY SITE (ALL RANDOMISED PARTICIPANTS)

Site:

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall
Withdrawn from Remote Follow-Up		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Reason for Withdrawal	**Time Burden**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Dissatisfied with Taking Part	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Doesn't Feel They are Benefitting	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Personal Reasons Unrelated to Study	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confidentiality Concerns	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Participant Was Added to the Wrong DAG	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.22. PROTOCOL DEVIATIONS, PROTOCOL VIOLATIONS AND SERIOUS BREACHES OVERALL AND BY SITE

		Treatment Group A	Treatment Group B	Overall
Overall	**Protocol Deviations**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Protocol Violations	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Serious Breaches	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Site 1	**Protocol Deviations**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Protocol Violations	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Serious Breaches	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Site 2	**Protocol Deviations**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Protocol Violations	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Serious Breaches	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
…	**Protocol Deviations**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Protocol Violations	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Serious Breaches	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Some protocol deviations, violations and serious breaches may not be attributable to a site or an allocation group.

Notes: Protocol Violations and Serious Breaches rows will be reported by site only if their number is more than 0.

16.3.23. DEMOGRAPHICS AND BASELINE CHARACTERISTICS (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Age (Years)		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
BMI		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Baseline Clinical Observations	**Temperature**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Systolic Blood Pressure	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Diastolic Blood Pressure	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Respiratory Rate	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Pulse	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Oxygen Saturation	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Clinical Frailty Score[1]		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Time Since Cellulitis Onset Until Randomisation		XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Baseline NRS Pain Score	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 0	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Sex at Birth	**Male**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Female	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Gender	**Man**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Non-Binary	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Woman	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Self-Described	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	Prefer Not to Say	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Transgender	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Prefer Not to Say	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Ethnicity	**Asian (Bangladeshi, Chinese, Indian, Pakistani, Other)**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Black (African, Caribbean, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Mixed or Multiple Ethnic Groups (White and Asian, White and Black African, White and Black Caribbean, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	White (English, Welsh, Scottish, Northern Irish or British, Irish, Gypsy or Irish Traveller, Roma, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other Ethnicity (Arab, Other)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Supplemental Oxygen	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Level of Alertness	**Alert: Fully Awake**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Confusion (New): New Onset or Worsening Confusion	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Voice: Responds to Verbal Stimulus	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Pain: Responds to Pain Stimulus (e.g. Supra-Orbital Pressure)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Unresponsive (No Response to Verbal or Pain Stimulus)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
NEWS2 Score	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Low Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Low to Medium Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Medium Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	High Risk	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Index of Multiple Deprivation	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	1st Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	2nd Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	3rd Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	4th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	5th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	6th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	7th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	8th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	9th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	10th Decile	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Homeless	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Postcode Outside of England	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Incorrect or Missing Postcode	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Severity of Cellulitis (Eron Classification)	**Class 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	All Other Classes	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Location of Cellulitis[2]	**Leg**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Foot	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Foot	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Lower Limb (Not Foot)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Lower Limb (Not Foot)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other Than Leg	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Hand	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Hand	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Upper Limb (Not Hand)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Upper Limb (Not Hand)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Facial	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Abdomen	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Right Groin	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Left Groin	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Cellulitis Cause	**Insect Bite / Sting**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	Related to Skin Breakage	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Other	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Unknown	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Prior (to Hospital Attendance) Antimicrobial Therapy for Current Episode of Cellulitis	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Analgesia Usage in the Last 3 Days Prior to Hospital Attendance[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Paracetamol	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Ibuprofen or Other NSAID	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Weak Opioids	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Strong Opioids	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Use of Injecting "Street" Drugs (Within the Last Month)	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Current	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Historic	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Diabetes	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Type 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Type 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Comorbidities[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Peripheral Vascular Disease	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Chronic Leg Oedema	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Morbid Obesity	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Risk Factors for Steroid Adverse Events[2]	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Recent or Previous Gastric Ulcers	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Required Proton-Pump-Inhibitors in the 1 Month Prior to Hospital Admission	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

	Prescribed Proton Pump Inhibitors Whilst in Hospital for This Admission	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Measured only on those who are 65 years old or older at screening.

[2]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

Notes: The table will be repeated by sex subgroup, for those who discontinued treatment and for those who discontinued trial.

Missing category will be added to each block if the information is not available for any participants.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.24. ANTIBIOTICS USAGE BEFORE RANDOMISATION FOR THIS EPISODE OF CELLULITIS (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Antibiotics Usage Before Randomisation for This Episode of Cellulitis	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Not Reported	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Length of Antibiotic Course (Days)	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Route of Administration[1]	**Oral**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Intravenous	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Topical	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
ATC3 Class of Antibiotic Used[1]	**Class 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Class 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

[2]Includes both those who did not take antibiotics and those who took them but did not report taking them.

Number of participants and percentage of participants out of the randomised participants are presented against each class.

Notes: The table will be repeated by sex subgroup, for those who discontinued treatment and for those who discontinued trial.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.25. TIME SINCE CELLULITIS ONSET TO RANDOMISATION BY PERCENTILE (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Minimum	XXX	XXX	XXX
25th Percentile	XXX	XXX	XXX
50th Percentile	XXX	XXX	XXX
75th Percentile	XXX	XXX	XXX
Maximum	XXX	XXX	XXX

If the cellulitis onset time is missing the time since cellulitis onset is considered missing.

Measured in days.

Notes: The table will be repeated by sex subgroup, for those who discontinued treatment and for those who discontinued trial.

The information will also be presented graphically.

16.3.26. EXPOSURE TO TREATMENT (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Randomised but Did Not Start Treatment	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Received Dose 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Unknown if Received Dose 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Did Not Receive Dose 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Received Dose 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Did Not Report Receiving or Not Receiving Dose 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Time from Randomisation to Dose 1 (Minutes)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Received Treatment Not As Allocated	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Notes: A footnote about presenting mean and SD or median and IQR for skewed data will be added.

16.3.27. MODEL BASED ANALYSES

	Estimate	Standard Error	95% CI Upper Boundary	95% CI Lower Boundary	P-Value
Variable 1	XXX	XXX	XXX	XXX	XXX
Variable 2	XXX	XXX	XXX	XXX	XXX
…	…	…	…	…	…
Random Effect 1	XXX	XXX	XXX	XXX	XXX
…	…	…	…	…	…
Contrast 1	XXX	XXX	XXX	XXX	XXX
…	…	…	…	…	…

Repeated for all model-based analyses in Section 10.

16.3.28. PRIMARY OUTCOME – NRS PAIN SCORES AND AUC – BY TIME INTERVAL (PARTICIPANTS INCLUDED IN PRIMARY ANALYSIS)

NRS Pain Score	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Baseline	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Up to 12 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
12 to 24 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

24 to 36 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
36 to 48 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
48 to 60 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
60 to 72 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
More Than 72 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
AUC	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

If a participant has more than one response in the time interval the average of those responses is used.

Notes: This information will also be presented graphically.

This table will be repeated for the "Pain experienced at Day 14 post-randomisation" outcome and for the "PGI-I score at day 14 post-randomisation" outcome with one row for Day 14.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.29. PRIMARY OUTCOME – NRS PAIN SCORE – BY DEMOGRAPHICS AND BASELINE CHARACTERISTICS SUBGROUPS (PARTICIPANTS INCLUDED IN PRIMARY ANALYSIS)

Time Interval:

		Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Age (Years)	**< 50**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	>= 50 to 60	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	>= 60	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
BMI	**< 20**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	>= 20 and < 25	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	>= 25 and <30	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

	>= 30	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Baseline NRS Pain Score	**Score 0**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 1	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 2	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 3	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 4	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 5	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 6	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 7	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 8	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 9	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Score 10	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Sex at Birth	**Male**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Female	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Gender	**Man**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Non-Binary	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Woman	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Self-Described	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Prefer Not to Say	XXX, XXX (XX.X)	XXX, XXX (XX.X)	XXX, XXX (XX.X)

		[XXX – XXX]	[XXX – XXX]	[XXX – XXX]
Transgender	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Prefer Not to Say	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Ethnicity	**Asian (Bangladeshi, Chinese, Indian, Pakistani, Other)**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Black (African, Caribbean, Other)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Mixed or Multiple Ethnic Groups (White and Asian, White and Black African, White and Black Caribbean, Other)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	White (English, Welsh, Scottish, Northern Irish or British, Irish, Gypsy or Irish Traveller, Roma, Other)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Other Ethnicity (Arab, Other)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
NEWS2 Score	**No Risk**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Low Risk	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Low to Medium Risk	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Medium Risk	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	High Risk	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Index of Multiple Deprivation	**1st Decile**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	2nd Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	3rd Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	4th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	5th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	6th Decile	XXX, XXX (XX.X)	XXX, XXX (XX.X)	XXX, XXX (XX.X)

		[XXX – XXX]	[XXX – XXX]	[XXX – XXX]
	7th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	8th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	9th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	10th Decile	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Homeless	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Postcode Outside of England	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Incorrect or Missing Postcode	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Severity of Cellulitis (Eron Classification)	**Class 1**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	All Other Classes	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Location of Cellulitis[1]	**Leg**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Right Foot	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Left Foot	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Right Lower Limb (Not Foot)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Left Lower Limb (Not Foot)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Other Than Leg	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Right Hand	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Left Hand	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Right Upper Limb (Not Hand)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

	Left Upper Limb (Not Hand)	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Facial	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Abdomen	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Right Groin	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Left Groin	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Other	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Cellulitis Cause	**Insect Bite / Sting**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Related to Skin Breakage	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Other	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Unknown	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Prior (to Hospital Attendance) Antimicrobial Therapy for Current Episode of Cellulitis	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Analgesia Usage in the Last 3 Days Prior to Hospital Attendance[1]	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Paracetamol	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Ibuprofen or Other NSAID	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Weak Opioids	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Strong Opioids	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Use of Injecting "Street" Drugs (Within the Last Month)	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

	Current	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Historic	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Diabetes	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Type 1	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Type 2	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Comorbidities[1]	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Peripheral Vascular Disease	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Chronic Leg Oedema	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Morbid Obesity	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Risk Factors for Steroid Adverse Events[1]	**Yes**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Recent or Previous Gastric Ulcers	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Required Proton-Pump-Inhibitors in the 1 Month Prior to Hospital Admission	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	Prescribed Proton Pump Inhibitors Whilst in Hospital for This Admission	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
	No	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

[1]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

If a participant has more than one response in the time interval the average of those responses is used.

Notes: The following time intervals will be presented: "Up to 12 Hours", "12 to 24 Hours", "24 to 36 Hours", "36 to 48 Hours", "48 to 60 Hours", "60 to 72 Hours", "More Than 72 Hours". If a participant has more than one score in a time interval, the average of those scores will be used.

The table will also be presented for AUC.

Missing category will be added to each block if the information is not available for any participants.

Footnote 2 may be modified to replace means and standard deviations with median and IQR if applicable.

16.3.30. FOLLOW UP LENGTH OVER THE FIRST 3 DAYS (PARTICIPANTS INCLUDED IN PRIMARY ANALYSIS)

	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
<= 72 hours	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
> 72 hours and <= 96 hours	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
> 96 hours	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Missing SMS 6 NRS Pain Score	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.31. SECONDARY OUTCOME – PGI-I SCORE, DAYS 1 – 3 – BY TIME INTERVAL (ALL RANDOMISED PARTICIPANTS WITH A POST-BASELINE SCORE)

PGI-I Score	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
12 to 36 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
36 to 60 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
More Than 60 Hours	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

If a participant has more than one response in the time interval the average of those responses is used.

Notes: This information will also be presented graphically.

A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.32. ANALGESIA USAGE IN THE FIRST 72 HOURS POST-RANDOMISATION, REPORTED ON DAY 14 (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Analgesia Usage in the First 72 Hours Post-Randomisation	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
ATC3 Class of Analgesia Used[1]	**Non-Opioid**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
		XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Class 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…			
	Adjuvant (Including NSAID)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

Number of participants and percentage of participants out of the randomised participants are presented against each type.

Notes: A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.33. ANTIBIOTICS USAGE POST-RANDOMISATION (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Antibiotics Usage Post-Randomisation	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Not Reported[2]	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Length of Antibiotic Course (Days)	**N, Mean (SD) [Min – Max]**	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Route of Administration[1]	**Oral**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Intravenous	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Topical	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
ATC3 Class of Antibiotic Used[1]	**Class 1**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Class 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

[1]Participants may belong in more than one category so the numbers may add up to more than the number of randomised participants.

[2]Includes both those who did not take antibiotics and those who took them but did not report taking them.

Number of participants and percentage of participants out of the randomised participants are presented against each class.

Notes: A footnote about presenting median and IQR for skewed data will be added if applicable.

16.3.34. UNSCHEDULED HEALTHCARE USAGE UNTIL DAY 14 POST-RANDOMISATION (ALL RANDOMISED PARTICIPANTS WHO USED ECRF VERSION 2 OR ABOVE)

	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Back to a Hospital, Accident and Emergency (A&E) Department or Other Urgent Care Centre	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Re-Admitted to a Hospital Ward for an Overnight Stay	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Appointment with a Doctor (GP), Nurse or Other Healthcare Professional at a GP Surgery, Health Centre, Walk-In Centre, Over the Telephone or at Home	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Received 'Hospital at Home' Care	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]
Consultation at a Pharmacy	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]	XXX, XXX (XX.X) [XXX – XXX]

16.3.35. BINARY SECONDARY OUTCOMES (ALL RANDOMISED PARTICIPANTS WITH A NON-MISSING BINARY OUTCOME)

Secondary Outcome Measure	Treatment Group A	Treatment Group B	Overall
Re-Admission to Hospital (Day 14)	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)

Unscheduled Healthcare (Day 14)[1]	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)
Recurrence of Cellulitis (Day 90)	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)	XXX/XXX (XXX.X%)

Number of "Yes" answers, number of non-missing answers and percentage of "Yes" answers are presented.

[1]Out of all the participants who used eCRF version 2 or above.

16.3.36. COMPLICATIONS (ALL RANDOMISED PARTICIPANTS)

		Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Severe Hyperglycaemia	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Not Reported	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Gastrointestinal Bleeding	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Missing	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
Psychosis	**Yes**	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	No	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
	Missing	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

16.3.37. SERIOUS ADVERSE REACTIONS (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	Treatment Group B (N = XXX)	Overall (N = XXX)
Any *Adverse Event Type*	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
SOC 1	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
PT1	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
PT2	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
…	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
SOC 2	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
…	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX

Number, percentage of participants out of the randomised participants, number of events is presented in each row.

Only the adverse events after the randomisation date are presented.

Notes: This table will be repeated for SUSARs, SAEs overall, unrelated SAEs, non-serious ARs. This table will also be repeated for SAEs on the randomised participants who changed their participation status.

This table will also be repeated on the treated participants split by actual treatment group. Only adverse events that started after the dose 1 date are presented for the analyses based on the treated participants.

16.3.38. SERIOUS ADVERSE REACTIONS BY SEVERITY (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)			Treatment Group B (N = XXX)			Overall (N = XXX)		
	Category 1	**Category 2**	**…**	**Category 1**	**Category 2**	**…**	**Category 1**	**Category 2**	**…**
Any *Adverse Event Type*	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SOC 1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
PT1	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

PT2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
SOC 2	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
…	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)

Number and percentage of participants out of the randomised participants is presented in each row.

The participants are only counted in the "worst" category.

Only adverse events after the randomisation date are presented.

Notes: This table will be repeated for SUSARs, SAEs overall, unrelated SAEs, non-serious ARs.

This table will also be repeated on the treated participants by actual treatment group. Only adverse events after the dose 1 date are presented for the analyses based on the treated participants.

SARs, SUSARs, SAEs overall and unrelated SAEs will be presented by severity and outcome. Non-serious ARs will be presented by severity.

16.3.39. SERIOUS ADVERSE REACTIONS BY REASON FOR SERIOUSNESS (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Fatal	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
Life Threatening	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
Persistent or Significant Disability/Incapacity	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
Congenital Anomaly/Birth Defect	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
Required/Prolonged Hospitalisation	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX
Is Otherwise Considered Medically Significant by Investigator	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX	XXX (XXX.X%), XXX

Number, percentage of participants out of the randomised participants, number of events is presented in each row.

Only the adverse events after the randomisation date are presented.

Notes: This table will be repeated for SUSARs, SAEs overall and unrelated SAEs.

This table will also be repeated on the treated participants by actual treatment group. Only adverse events after the dose 1 date are presented for the analyses based on the treated participants.

16.3.40. DEATHS (ALL RANDOMISED PARTICIPANTS)

	Treatment Group A (N = XXX)	**Treatment Group B (N = XXX)**	**Overall (N = XXX)**
Deaths	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)