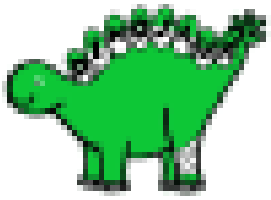
Service evaluation statistical analysis plan



DINOSAUR: Service Evaluation Study

Duration of Intravenous antibiotic therapy for Septic Arthritis or acUte osteomyelitis in a paediatRic population

Statistical Analysis Plan

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Change Control

Updated SAP version no.	Section number changed	Description of change	Date changed	Initials
1.4	8.2	Fundamental change to definition of case types	20/10/14	BA
1.5	Appendix	Changes made to several tables arising from web meeting with CI going through each table in detail.	26/11/14	BA

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Introduction

This Statistical Analysis Plan (SAP) provides a detailed and comprehensive description of the pre-planned analyses for the service evaluation study DINOSAUR.

These planned analyses will be performed by the study statistician. The analysis results will be described in a statistical analysis report, to be used as the basis of the primary research publications according to the study publication plan.

All analyses are performed with standard statistical software (SAS v9). The finalised analysis datasets, programs and outputs will be archived following Good Clinical Practice guidelines and SOP TM021 Archiving procedure in CTRC. The testing and validation of the statistical analysis programs will be performed following SOP ST001.

Definitions

OM	Acute Osteomyelitis
SA	Septic Arthritis
IV	Intra-venous
CRP	C-Reactive Protein
ESR	Erythrocyte Sedimentation Rate
Hb	Haemoglobin
Plt	Platelets
WCC	White blood-cell count
N	Neutrophils [or if a statistic then Number]
PICC	Peripherally inserted central catheter

Study Aim

Currently there is little international or UK consensus regarding the route or duration of antibiotic treatment for acute osteomyelitis (OM)/septic arthritis (SA) in children. Data regarding paediatric bone and joint infections in the UK are scarce and outdated. This service evaluation will be used to:

1. Assess current case load, disease spectrum & clinical practice in the diagnosis & treatment of OM/SA in secondary & tertiary UK care

2. Determine whether a randomised controlled trial to investigate shorter duration of intravenous antibiotic therapy for bone and joint infections in children is feasible in the future.

This will be achieved in conjunction with a future component of the study (analysis plan of which not included in this document) obtaining qualitative & quantitative data on:

a) willingness of clinicians to randomise to proposed protocol
b) willingness of patients & parents to be randomized
c) number of patients seen;
d) clinical stakeholder & consumer perception of relevant outcomes

Study Design

This service evaluation is a descriptive study, examining routinely collected clinical data for all eligible paediatric cases of OM and SA presenting at participating tertiary and secondary healthcare centres over a minimum of a 6 months period.

Participating centres

All Tertiary and Secondary centres routintely treating cases of OM or SA from across England will be invited to participate in this national service evaluation. They will record data on all cases accrued over at least a 6 month period.

Participant selection criteria

All eligible patients presenting to participating centres with a diagnosis of bone and joint infection will be enrolled with no maximum, and data will be entered into a web based database.

Inclusion Criteria

All children from birth to 16 years with a clinical diagnosis of osteomyelitis or septic arthritis admitted to participating hospitals from home, or referred from another centre.

Exclusion Criteria

Patients whose parents have specifically requested for their child not to be included in the study.

Participant identification and recruitment

Posters displayed on admitting wards notify parents and patients that the centre is participating in a national service evaluation of children's bone and joint infections. Parents will have the opportunity to inform a member of their child's care team if they do not want their child's information entered into the database.

Sample size calculations

The study is funded to enable a maximum of 1,000 cases of OM or SA to be entered into the database. In order to get an accurate national evaluation, all participating centres will be asked to record cases for at least six months. It is estimated that at least 500 cases will be accrued by around 50 centres over a 6-12 month period. All eligible cases at participating centres will be recorded.

Data Collection

We will record demographic details and details of hospitalisation(s) including transfers between hospitals; type and site of disease; routine haematology, biochemistry and microbiology; radiological procedures; surgical procedures; length of IV therapy; antimicrobials used, route and duration; reason/criteria; used for oral switch (if any); and clinical outcomes at 3 months.

These data are to be collected from the patients' clinical notes. Training will be provided for teams at participating centres. The study will use a password protected web based data collection form that can be accessed at all participating hospitals.

Study Objectives

The study has three major objectives:

1. What are the clinical, biochemical and radiological criteria used by UK paediatricians / orthopaedic surgeons / radiologists to diagnose osteomyelitis?

2. What is the range of durations of intravenous and oral antibiotics used to treat osteomyelitis? What factors affect durations (e.g. surgery / blood tests / microbiology results).

3. What are the rates of treatment failures / complications for different:

    (a) Antibiotic regimes used at participating centres?

    (b) Surgery types used at participating centres?

and what actions were taken following a complication at participating centres?

These objectives are broken down into further sub-objectives:

1A: Describe the study sample: demographics; past medical history; presenting limbs/joints affected; and diagnosis types aiming toidentify factors predisposing children to bone and joint infections. Describe pre-presentation variables that affect drug choice, dosage and duration, in particular age, allergies and co-morbidities.

1B: Describe the clinical time-line for diagnosis: summarising the number of days from presentation when key clinical actions (1st imaging, surgery and initiation of IV antibiotics) occur.

1C: Describe the surgical procedures carried out prior to diagnosis.

1D: Summarise the types of microbiological tests carried out and the types of samples taken. Specifically, find the proportion of centres that are performing PCR tests, and testing for Panton-Valentine Leukocidin producing *Staphylococcus aureus*.

Calculate the proportion of children testing positive for: at least one micro-organism; and each specific micro-organism (using conventional techniques, ie not PCR).

1E: Describe the combinations of blood-tests carried out at presentation and summarise the test results. Find the proportion of children with elevated results for each blood-test type at presentation (results above centre-specific normal ranges), and the proportion of children with CRP_{max} occurring at presentation. Describe the types of samples.

1F: Summarise CRP_{max} by age-group and micro-organisms detected.

1G: Describe the imaging methods routinely used to aid diagnosis. What proportions of each method gave an abnormal result..

2A: Describe the clinical time-line for antibiotic treatment (specifically when antibiotics are started) Describe the types of antibiotic regimes prescribed. Summarise the number of different antibiotics given as initial treatment, and the total number of different antibiotics patients receive over the durations of treatment by each route. Summarise the numbers of children being given different types of regime: early vs

normal length of time to oral switch; dosage – how many were given normal doses throughout; shortened vs standard length of time on antibiotics.

2B: Describe the IV and oral antibiotics prescribed during hospital stay. For each antibiotic: which were prescribed at least once; which were part of the initial treatment; what was the average daily dose; with what frequency were doses given; and was the duration greater than 1 week. Were there differences in initial IV antibiotic prescriptions between secondary and tertiary site types; between children with and without penicillin allergy; and with and without sickle cell disease?

2C: Describe the combinations of blood-tests carried out immediately prior to oral switch and summarise the test results. Calculate the average CRP at oral switch as a proportion CRP_{max}. Summarise blood test results over time: from presentation through to last test.

2D: Describe the surgical procedures carried out post diagnosis but prior to discharge, i.e. therapeutic procedures. How many children had only one procedure, two procedures or more than two?

2E: Summarise the length of time spent in hospital: from hospitalisation to discharge.

[2F]: Summarise imaging carried out after initiation of IV, split by site type and image type. For each imaging type, identify cases that had at least one image carried out.

2G: Describe the antibiotic regimes prescribed at discharge (drug, dose, frequency and duration). As part of this – what percentage went home on IV as opposed to oral?

2H: Were discharge antibiotic regimes adhered to? Percentages of treatments shortened or changed post discharge, split by who made the decision: parent, hospital or GP. Describe the main reasons for non-adherence or change of regime post discharge.

3A: Describe rates of different types of complication, and cross-tabulate with types of action taken.

3B: Describe rates of Treatment Failure (Yes/No) and Any Complications (Yes/No) for different antibiotic regimes types. Measure associations between regime types and the two outcomes: Treatment Failure; and Any Complications.

3C: Describe rates of Treatment Failure (Yes/No) and Any Complications (Yes/No) for different surgery types carried out post presentation. Measure associations between surgery types undertaken and the two outcomes: Treatment Failure; and Any Complications.

Description of the study population

Representativeness of cases accrued

The participating centres will be summarised and checked that they broadly represent all areas of the country. The numbers of cases withdrawn will be recorded.

Sample characteristics and initial categorisation of types of cases

The demographics of the sample (age, gender, medical history) will be described using summary statistics. Based on past medical history, cases will be categorised into four groups:

1. Simple cases
2. Complex cases
3. Current presentation due to infected implant or infected surgery from past orthopaedic surgery. (Subset of complex cases)
4. Misdiagnosed

Any children not falling into any of these categories will be excluded from the analysis.

Definitions

1. Simple cases

Children presenting with SA or OM for the first time, and with no chronic comorbidities. Specifically:

- No orthopaedic surgery 6 months prior to presentation on same limb/joint
- No chronic co-morbidities (sickle cell disease, known immunocompromise, indwelling central venous catheter or PICC, cystic fibrosis, or cerebral palsy).

2. Complex cases

Children presenting with SA or OM who already have a diagnosis of SA or OM and/or have chronic comorbidities, but who are not presenting because of an infected implant from previous orthopaedic surgery. Specifically:

- Not presenting because of an infected implant
- Any orthopaedic surgery in 6 months prior to presentation on same limb/joint
- Any chronic co-morbidities (sickle cell disease, known immunocompromise, indwelling central venous catheter or PICC, cystic fibrosis, or cerebral palsy).

3. Infected implants

Children presenting with SA or OM who already have a diagnosis of SA or OM and who are presenting because of an infected implant from previous orthopaedic surgery.

4. Incorrect diagnosis of SA/OM

Some children captured by the database were treated for SA/OM but were later found to have a different diagnosis.

Completeness of follow-up

Follow-up data are collected at a follow-up visit at around 3 months post discharge. The number lost to follow up will be reported and the reasons where known will be documented. Any deaths and their causes will be reported separately.

Study Outcomes

This study examines many measurements routinely made in the diagnosis, treatment, and aftercare of children with SA or OM. There are three areas of key interest: Diagnosis (Objective 1); Treatment (Objective 2); and Complications Arising and/or Treatment Failures (Objective 3). The key endpoints are:

Diagnosis:

- Bones and joints affected
- Time taken from first presentation to:
    1. Referral to hospital
    2. Having surgery
    3. Initiation of IV antibiotics [this time-point used also as a proxy for a diagnosis being made]
- Surgical procedures carried out prior to diagnosis
- Imaging types used (X-ray, CT scan, ultrasound, bone scan, MRI), and results obtained
- Diagnostic blood tests carried out (Hb, WBC, N, Plt, CRP, ESR) and their outcomes
- Microbiological tests carried out (presence of any of 8 named micro-organisms)

Antibiotic Treatment in and post hospital stay:

- Length of time on IV antibiotics
- Length of time on oral antibiotics
- Total length of time on antibiotics
- Length of time from presentation to discharge
- Blood tests carried out and their results
- Antibiotics prescribed (during hospital stay and at discharge)
- Dosage (Normal / High as defined in Children's British National Formulary)
- Adherence to discharge prescription
- Reasons for non-adherence or changes to prescribed regimes.

Complications / Failure of treatment

- Complication types
- Actions arising from complications
- Treatment failure (Y/N)

Analysis

The primary interest are the sub-group of children with acute SA / OM and no chronic comorbidities (simple cases). All analyses described below will therefore be carried out for this sub-group in the first instance. The other two sub-groups (chronic SA/OM and infections arising from previous orthopaedic surgery) with be analysed separately as a secondary analysis. See *Appendix A: Template Results Tables* for tables referred to in the following analysis plan.

Objective 1

[1A] See Section 8.2 above for demography and definition of diagnosis groups. Numbers and percentages will be calculated and results tabulated separarately for: demographics; diagnosis groups; presentation; history of orthopaedic surgery; medical history; and antibiotics prescribed prior to presentation. See Tables 1A-1,2,3,4,5,6 below

[1B] The clinical time-line from first presentation through to diagnosis will be explored. Time to hospital referral, first imaging, surgery, radiological diagnois, and initiation of IV antibiotics will all be summarised using appropriate descriptive statistics [see Table 1B-1].

[1C] The number and percentage of cases undergoing different types of surgery prior to diagnosis will be reported [see Table 1C-1].

[1D] The number and percentage of cases testing positive for at least one micro-organism, and each of 8 unique micro-organisms will be reported, split by centre type (Tertiary / Secondary). Any other micro-organisms detected will be categorised and reported as "Other". Of cultures testing positive for *Staphylococcus aureus*, the number and percentage where PVL is tested for will be reported. The number and percentage of cases where a PCR test is also carried out will be calculate by centre type. [See Table 1D-1].

The number and percentage of types of sample for micro-biological testing (e.g. blood, pus, etc.) that are typically taken from children will be reported [see Table 1D-2].

[1E] The number and percentage of cases with test results at presentation for: each of 6 blood tests; and the combinations 'CRP & ESR' and 'CRP & no ESR' will be reported, split by centre type (Tertiary / Secondary) [see Table 1E-1]. A boxplot for each of the six blood test measures at presentation will be created to show the distribution of results. Proportions with elevated results (above centre-specific normal ranges) will be calculated for each blood test type [see Table 1E-2].

The blood test result 'CRP_{max} will be summarised for culture-positive and culture negative cases and a box plot created to compare these. This analysis will be split by age-group.This is to explore whether a higher CRP_{max} is associated with particular organisms. Differences that are clinically significant will be tested for statistical significance using appropriate hypothesis tests [see Table 1E-3].

[1F] There are five imaging methods that could be requested by clinicians to aid diagnosis. The number and percentage of cases for each imaging type used prior to diagnosis will be reported, split by centre type (Tertiary / Secondary) and of these the number and percentage abnormal [see Table 1F-1].

Objective 2

Treatment of children with SA or OM takes the form of antibiotic treatment and additionally for some cases, surgical intervention. Initially antibiotics are given intravenously. At a later date, antibiotics are given orally – the timing of the switch is based on clinical judgement that the child has recovered sufficiently and is capable of taking drugs orally.

[2A] The lengths of time on IV antibiotics, oral antibiotics, and total antibiotic duration will be summarised using appropriate descriptive statistics. (Note that these times are based on what happened during hospital stay and what was **planned** at discharge. It is not possible to obtain data for the actual date when antibiotics were stopped post discharge.) Results will also be split by centre type, whether there was at least one surgical procedure after initiation of IV antibiotics, if CRP_{max} occurred at presentation, and by microbes detected. [See Table 2A-1].

Antibiotic regimes will be further summarised for the sample: Number of antibiotics given in the initial treatment; timing of oral switch (<1 wk, 1-2 wks and >2 wks)); total course of antibiotics (shortened vs standard); dose (augmented at least once vs standard dose throughout where 'augmented at least once' is defined as having at least one high dose of IV antibiotics); and total number of different antibiotics prescribed over the full treatment period [see Table 2A-2].

[2B] Antibiotics prescribed during hospital stay will be summarised using frequencies and percentages. There are a large number of antibiotics that could be prescribed by either route. Of these, 4 named IV antibiotics and 5 named oral antibiotics are of particular interest. A category labelled 'other' will be used to define all other antibiotics given by each route. For each antibiotic and route, summary statistics will be reported for whether it was part of the initial prescription; given at least once; frequency of administration of doses during a day; daily dose per kg weight of child; and duration of course (> 1 week Y/N). This will give an overview of the most commonly prescribed antibiotics during hospital stay [see Table 2B-1].

Initial IV antibiotic prescriptions will be compared between secondary and tertiary site types; between children with and without penicillin allergy; and with and without sickle cell disease [see Table 2B-2].

[2C] Blood test results are routinely used to aid the decision to stop giving antibiotics via IV (ie. oral switch). The combinations of blood tests carried out immediately prior to (on the day before or on the day of) the oral switch will be reported as numbers and percentages. CRP as a proportion of CRP_{max} will be summarised [see Table 2C-1].

The change in blood test results over time will be explored graphically using boxplots. For each blood test type, a plot will be produced showing the distribution of results at: presentation; initial of IV; and on each day following start of IV.

[2D] The number and percentage of cases undergoing different types of surgery post diagnosis will be reported [see Table 2D-1].

[2E] Appropriate summary statistics will be used to describe length of hospital stay for cases – overall, and split by age-group and centre type [see Table 2E-1].

[2F] The number and percentage of cases with imaging after initiation of IV will be reported split by site type and image type, with results given.

[2G] Antibiotics prescribed at discharge will be summarised using frequencies and percentages. There are a large number of antibiotics that could be prescribed by either

route. Of these, 4 named IV antibiotics and 5 named oral antibiotics are of particular interest. A category labelled 'other' will be used to define all other antibiotics given by each route. For each antibiotic and route, summary statistics will be reported for whether it was given at least once; daily dose per kg weight of child; and planned duration of course. This will give an overview of the most commonly planned antibiotic regimes at discharge [see Table 2F-1].

[2H] Antibiotic regimes post discharge are not always adhered to. The number and percentage of those stopped early will be reported, split by who took the decision (Parent / Hospital / GP). In the same way the number and percentage of patients who had a change to the planned regime will be reported split by who made the change (Hospital / GP). The frequencies of 5 possible reasons for shortening or changing regime will be explored [see Table 2G-1].

Objective 3

[3A] The number and percentages of cases experiencing a complication of any kind will be reported. These will be further split by 'Complication Type', and cross-tabulated with 'Action Taken' (None / Surgery / Change of antibiotic regime / Re-admission to hospital / Other) [see Table 3A-1].

[3B] Treatment failure is determined by complications that result in certain actions. e.g. Surgery. The outcomes 'Treatment Failure' (Y/N) and 'Any Complication' (Y/N) will be cross-tabulated with three antibiotic regime variables: Timing of oral switch (Early / Standard); Total course of antibiotics (Shortened / Standard); and Overall dose (High / Normal). Associations between regime types and outcomes will be measured using odds-ratios and 95% CIs. This will give an overview of whether treatment failure and complications may be more likely for certain types of regime [see Table 3B-1].

[3C] Treatment Failure (Y/N) and Any Complication (Y/N) will be cross-tabulated with surgery undertaken (limited to surgery post presentation). Associations between surgery types and outcomes will be measured using odds-ratios and 95% CIs. This will give an overview of whether treatment failure and complications may be more likely for certain types of surgery [see Table 3C-1].

Analyses of missing data / withdrawals

As this is a service evaluation, there should be only a small number of withdrawals. Those that do occur will be documented. It may be of importance if withdrawals are clustered by centre.

Missing data will be noted and wherever possible, the reasons reported. If a large amount of data critical to the analysis are missing, some changes to the analysis plan may be needed.

Setting results in context of previous research

Once the service evaluation has been completed the results will be set in context of the existing evidence base**.**

References

1. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. Ann Int Med 2010;152. Epub 24 March.
2. ICH E3 chapter 12.

Appendix A statistical analyses plan: Template Results Tables

1A: Demographics, past medical history, and presenting limbs/joints affected.

TABLE 1A-1

Demographics	Appropriate Summary Statistics
Age (years)	
Male	
Ethnicity	
European North/East/Mid	
European South (Mediterranean)	
European Roma	
African/Caribbean North African	
African/Caribbean Sub Saharan	
African/Caribbean Afro-caribbean	
Asian Indian Subcontinent	
Asian SE (Vietnam, Thailand, Indonesia, Malaysia, Phillipines)	
Asian East Asia (China, Japan, Korea)	
Asian West Asia (Afghanistan, Iranian)	
Middle Eastern Turkish	
Middle Eastern Arab peninsula	
Other/Mixed	

TABLE 1A-2

Diagnosis Group	Appropriate Summary Statistics
Simple[a]	
OM	
SA	
Complex[b]	
OM	
SA	
Presentation due to infected implant or surgery from previous orthopaedic surgery	
Misdiagnosed	
Types of diagnoses for misdiagnosed:	
Cellulitis	
Discitis	
Reactive arthritis	
Invective arthritis	
Joint effusion	
Abscess	
Other	
Unknown/Undecided	

[a]Acute SA/OM with no co-morbidities; [b] 'Chronic SA/OM' or' Acute SA/OM with co-morbidities'

TABLE 1A-3

Presentation	**All**	**Simple (n=?)**	**Complex (n=?)**
Presenting to:			
Outpatient Clinic			
Inpatient			
GP			
Emergency Department			
Walk-In Centre			
Not known			
Limbs/Joints affected*:			
Hip			
Shoulder			
Knee			
Ankle			
Wrist			
Skull			
Mandible			
Humerous			
Clavicle			
Radius			
Ulna			
Pelvis			
Rib			
Femur			
Tibia			

Fibia

Sternum

Elbow

Foot

Calcaneum

Lumbar vertebrae

Cervical vertebrae

Thoracic vertebrae

Sacrum vertebrae

*Categories not mutually exclusive, so more than one bone/joint can be recorded per patient.

TABLE 1A-4

History of Orthopaedic Surgery	Any	In 6 months prior to presentation (same bone/joint as at presentation)
Yes?		
Bone/joint affected*:		
Knee		
Clavicle		
Radius		
Ulna		
Humerus		
Tibia		
Femur		
Ankle		
Side:		
Right		
Left		
Both		

TABLE 1A-5

Medical History	Yes	No	Not tested / unknown
Co-morbidities indicating complex case:			
Sickle cell disease			
Known immunocompromise			
Indwelling central venous catheter or PICC			
Cystic Fibrosis			
Cerebral Palsy			

TABLE 1A-6

Medical History	Simple	Complex	Other
Other Medical Conditions:			
Congenital cardiac disease			
Diabetes Mellitus			
Purpura Fulminans			
Malnutrition			
Other			
Immune modulating treatment in last 6 calendar months?			
Steroid			
Radiotherapy			
Chemotherapy			
Azathioprine			
Cyclosporin			
Cyclophosphamide			
Rituximab			

Lefluvomide

Tacrolimus

Sirolimus

Other

Infection History in the last 12 calendar months?

Pneumonia

Septicaemia

Pyelonephritis

Cellulitis / soft tissue infection

Meningitis

Osteoarticular infection

Abdominal sepsis

Varicella

Other

History of Trauma in the last month?

Other Surgery in 12 months prior to presentation?

Pre-presentation variables that affect drug choice, dosage and duration. (Simple cases only)

TABLE 1A-7

Antibiotic Medical History	**N(%)**	**Route**		**Duration**
		IV	**Oral**	**> 1 week**
Penicillin allergy		-	-	-

Antibiotics (1 month pre-presentation)

- Any
- Flucloxacillin
- Clindamycin
- Cefuroxime
- Ceftriaxone
- Amoxicillin
- Co-Amoxiclav
- Rifampicin
- Vancomycin
- Fusidic Acid
- Teicoplanin
- Other

1B: The clinical time-line for diagnosis

TABLE 1B-1

Diagnostic and hospital stay Time-line (Days)	**Appropriate Summary Statistics**
From first presentation to:	
Hospital Referral	
1st Imaging	
Pre-diagnosis surgery	
Radiological diagnosis	
Initiation of IV antibiotics	
(proxy for diagnosis of OM/SA)	

1C: Surgical procedures carried out post presentation and prior to diagnosis (before or on the same day as initiation of IV antibiotics).

TABLE 1C-1

Surgery types	**Rate n (%)**
Any	
Aspiration	
Incision and drainage	
Drill decompression	
Curettage/excision	
Arthrotomy	
Arthroscopy	
Amputation	

Debridement

Fasciotomy

Compartment decompression

Secondary closure

Skin graft

Other plastic surgery

1D: Summary of range of tests carried out and sensitivity of conventional microbiological tests. (Simple cases only)

TABLE 1D-1

	N(%)
Children with at least one conventional test carried out	
At least one micro-organism detected	
Specific mirco-organisms detected by conventional testing:	
Staphylococcus Aureus	
PVL tested for?	
Kingella Kingae	
Streptococcus pyogenes	
Pseudomonas	
Group b Streptococcus	
Salmonella	
Candida	
Tuberculosis	
Other	
PCR testing carried out	

Types of sample used for conventional microbiological testing. (Simple cases only)

TABLE 1D-2

	N(%)

Number of different sample types taken

- 0
- 1
- 2
- >2

Sample types. Children that had at least one:

- Pus (periosteal)
- Bone biopsy
- Pus/Wound swab
- Joint aspirate
- Other

1E: Blood-tests carried out at presentation. (Simple cases only)

TABLE 1E-1

Blood tests at presentation	**N(%) with at least one measurement on day of presentation**	**Summary statistic for test results**	**% with elevated* results**
Hb			
WCC			
N			
Plt			
CRP			
ESR			
CRP & ESR		-	-
CRP & *not* ESR		-	-
CRP_{max} occurring at presentation		-	-

*Above the centre specific normal range

1F: Comparing average CRP_{max} for each culture negative vs. positive, by age-group. (PCR and conventional test results combined; Simple cases only).

TABLE 1F-1

Microbe	**Summary statistics for CRP_{max}**					
	< 1 year		**1-6 years**		**6-16 years**	
	+ve	**-ve**	**+ve**	**-ve**	**+ve**	**-ve**
Staphylococcus Aureus						
Kingella Kingae						
Streptococcus pyogenes						
Pseudomonas						
Group b Streptococcus						
Salmonella						
Candida						
Tuberculosis						
Other						

1G: Imaging types routinely used to aid diagnosis (On day of or prior to initiation of IV; Simple cases only).

TABLE 1G-1

Imaging Type	N(%) with at least one image	Number (%) Abnormal
X-ray		
CT scan		
Ultrasound		
MRI		
Bonescan		

What is the range of durations of intravenous and oral antibiotics used to treat osteomyelitis?

2A: The clinical time-line for antibiotic treatment.

TABLE 2A-1

Antibiotic Treatment Time-line (Days)	**Appropriate Summary Statistics**
Length of time on:	
IV	
Oral[(a)]	
Total[(b)]	

[(a)]Use time on oral antibiotics pre-discharge plus planned duration, as proxy for actual duration.

[(b)] Length of time treated with any antibiotic (for some children oral antibiotics were given concurrently to IV. So the Total length of time is not necessarily the time on IV plus the time on Oral)

Types of antibiotic regimes experienced.

TABLE 2A-2

Antibiotic Regime	**All**	**Centre Type**	
		Tertiary	**Secondary**
Number of different antibiotics given at initiation of treatment			
1			
2 or more			
Timing of oral switch			
Very Early (< 1 week)	Also report median & IQR for each category here		
Early (1-2 wks)			
Standard / Late (> 2 wks)			

Total course of antibiotics

Shortened (< 6 weeks)

Standard (> 6 weeks)

Dose

Augmented at least once[(a)]

Standard throughout

Total number of antibiotics prescribed

IV:

1

2

>2

Oral:

1

2

>2

[(a)]At least one IV antibiotic given at a high dose

2B: IV and oral antibiotics prescribed prior to discharge.

TABLE 2B-1

Antibiotic	Given at least once	Part of initial prescription	Daily dose per kg weight of child	Frequency					Duration
				6 hourly	8 hourly	12 hourly	Once daily	Other	(> 1 week)
IV									
Flucloxacillin									
Clindamycin									
Cefuroxime									
Ceftriaxone									
Other									
Oral									
Flucloxacillin									
Clindamycin									
Amoxicillin									
Co-Amoxiclav									
Rifampicin									

Other

TABLE 2B-2

Antibiotics given as part of first treatment	Centre Type		Given had a penicillin allergy	Given had sickle cell disease
	Tertiary	Secondary		
IV				
Flucloxacillin				
Clindamycin				
Cefuroxime				
Ceftriaxone				
Other				
Oral				
Flucloxacillin				
Clindamycin				
Amoxicillin				
Co-Amoxiclav				
Rifampicin				
Other				

2C: Blood-tests carried out immediately prior to oral switch

TABLE 2C-1

Blood tests	**Number (%) of cases with test results immediately prior to switch**		**Summary statistic for test results**	**As a proportion of CRP_{max}**
	Tertiary	**Secondary**		
Hb				-
WCC				-
N				-
				-
CRP				
ESR				-
CRP & ESR			-	-
CRP & *not* ESR			-	-

2D: Surgery occurring after the initiation of IV antibiotics (post diagnosis).

TABLE 2D-1

Surgery types	Rate n (%)
All	
Aspiration	
Incision and drainage	
Drill decompression	
Curettage/excision	
Arthrotomy	
Arthroscopy	
Amputation	
Debridement	
Fasciotomy	
Compartment decompression	
Secondary closure	
Skin graft	
Other plastic surgery	

2E: Length of stay in hospital by age-group and site type.

TABLE 2E-1

Centre type	All	Age group		
		< 1 year	1-6 years	6-16 years
All				

Tertiary

Secondary

2F: Imaging types routinely used post diagnosis.

TABLE 2F-1

Imaging Type	Number (%) of cases imaged at least once post-diagnosis		Number (%) Abnormal
	Tertiary	Secondary	
X-ray			
CT scan			
Ultrasound			
MRI			
Bonescan			

2G: Antibiotic regimes prescribed at discharge. As part of this – what percentage went home on IV as opposed to oral antibiotics.

TABLE 2G-1

Antibiotic	N(%)	Daily dose per kg weight of child	Planned Duration
Went home on			
IV		-	-
Oral		-	-
IV			
Flucloxacillin			
Cefuroxime			
Ceftriaxone			
Benzyl Penicillin			
Other			
Oral			
Flucloxacillin			
Cefalexin			
Co-Amoxiclav			
Other			

2H: Were discharge antibiotic regimes adhered to? Percentages of treatments shortened or changed post discharge, split by who made the decision: parent, hospital or GP. What were the main reasons for non-adherence or change of regime post discharge?

TABLE 2H-1

Adherence to prescribed antibiotic regimes	Number (%)
Stopped early by:	

Parent

Hospital

GP

Changed by:

Hospital

GP

Reason for shortening / change of regime:

Unpalatable antibiotic

Diarrhoea

Rash

Resolution of symptoms

Recurrence of infection

3A: Complication types by action taken.

TABLE 3A-1

Complication	N (%)	Action taken				
		None	Surgery	Change of antibiotic regime	Re-admission to hospital	Other action
Any Complications						
Complication type:						
Fever						
Recurrence of Infection						
Dislocation						
Subluxation						
Pathological Fracture						
Sinus						
Other						

3B: Treatment failures and complications by type of antibiotic regime.

TABLE 3B-1

Antibiotic Regime	Treatment Failure?			Any complication?		
	Yes	No	Odds ratio	Yes	No	Odds Ratio
Timing of oral switch						
Early (< 2 weeks)						
Standard / Late (> 2 wks)						
Total course of antibiotics						

Shortened (< 6 weeks)

Standard (> 6 weeks)

Dose Repeated for IV and oral separately

High

Majority Lower range

3C: Treatment failures and complications by type of surgery.

TABLE 3C-1

Surgery	Treatment Failure?			Any complication?		
	Yes	No	Odds ratio	Yes	No	Odds Ratio
Surgery undertaken after date of 1st presentation						
Aspiration						
Incision and drainage						
Drill decompression						
Curettage/excision						
Arthrotomy						
Arthroscopy						
Amputation						
Debridement						
Fasciotomy						
Compartment decompression						
Secondary closure						
Skin graft						
Other plastic surgery						