BMJ Open

Cellulitis: Home Or Inpatient in Children from the Emergency Department (CHOICE): protocol for a randomised controlled trial

Laila F Ibrahim,[1,2,3] Franz E Babl,[2,3,4] Francesca Orsini,[5] Sandy M Hopper,[2,4] Penelope A Bryant[6,1,2,3]

ABSTRACT

Introduction: Children needing intravenous antibiotics for cellulitis are usually admitted to hospital, whereas adults commonly receive intravenous treatment at home. This is a randomised controlled trial (RCT) of intravenous antibiotic treatment of cellulitis in children comparing administration of ceftriaxone at home with standard care of flucloxacillin in hospital. The study aims to compare (1) the rate of treatment failure at home versus hospital (2) the safety of treatment at home versus hospital; and (3) the effect of exposure to short course ceftriaxone versus flucloxacillin on nasal and gut micro-organism resistance patterns and the clinical implications.

Methods and analysis: Inclusion criteria: children aged 6 months to <18 years with uncomplicated moderate/severe cellulitis, requiring intravenous antibiotics. Exclusions: complicated cellulitis (eg, orbital, foreign body) and immunosuppressed or toxic patients. The study is a single-centre, open-label, non-inferiority RCT. It is set in the emergency department (ED) at the Royal Children's Hospital (RCH) in Melbourne, Australia and the Hospital-in-the-Home (HITH) programme; a home-care programme, which provides outreach from RCH. Recruitment will occur in ED from January 2015 to December 2016. Participants will be randomised to either treatment in hospital, or transfer home under the HITH programme. The calculated sample size is 188 patients (94 per group) and data will be analysed by intention-to-treat. *Primary outcome:* treatment failure defined as a change in treatment due to lack of clinical improvement according to the treating physician or adverse events, within 48 h *Secondary outcomes:* readmission to hospital, representation, adverse events, length of stay, microbiological results, development of resistance, cost-effectiveness, patient/parent satisfaction. This study has started recruitment.

Ethics and dissemination: This study has been approved by the Human Research Ethics Committee of the RCH Melbourne (34254C) and registered with the ClinicalTrials.gov registry (NCT02334124). We aim to disseminate the findings through international peer-reviewed journals and conferences.

Clinical trial: Pre-results.

Strengths and limitations of this study

- Randomisation of a novel home-care intervention versus standard hospital care.
- Primary outcome relevant to clinical practice.
- First investigation of differential impact of short course antibiotics on the acquisition of resistant organisms.
- Key assessment of parental preference of treatment location.
- The antibiotics in the two arms are unavoidably different.
- Decisions to start or stop intravenous antibiotics are based on a subjective clinical opinion reflecting real clinical practice.

INTRODUCTION

Children with cellulitis receiving intravenous antibiotics are usually admitted to hospital, whereas adults commonly receive intravenous treatment at home. Various reasons have been cited including parental anxiety and the acute nature of the infection in children. However, in comparison to hospital admission, children treated at home do better psychologically and physically, have fewer investigations, are at decreased risk of hospital-acquired infections, and have subsequent decreased use of healthcare resources.[1 2] It is also less expensive (time off work and transport costs) and disruptive for families.[1 3] Some children with moderate/severe cellulitis may be safely treated at home, but criteria for this are unclear.[4] There are no randomised trials comparing home versus hospital treatment in children for cellulitis. In a recent study at our institution of children presenting with cellulitis to the emergency department (ED), 57% were discharged on oral antibiotics and 43% were treated with intravenous antibiotics due to extensive, rapidly spreading or complicated

cellulitis or worsening features despite oral antibiotics. Forty-five per cent of those with uncomplicated moderate/severe cellulitis had been started on oral therapy and cellulitis had progressed despite this.[5] Of those discharged on oral antibiotics, 10% re-presented with worsening cellulitis, suggesting there is a culture of trying oral antibiotics first and not starting intravenous antibiotics unnecessarily (unpublished data).

When intravenous treatment is required for cellulitis, flucloxacillin or cephazolin are the usual choices because they are effective against *Staphylococcus aureus* and group A streptococci, the main pathogens causing cellulitis.[6] However, they are not suitable for outpatient parenteral antibiotic therapy (OPAT) due to their frequent dosing. The majority of paediatric OPAT services are only able to deliver once daily interventions. Ceftriaxone has antistaphylococcal activity and can be administered once daily.[7] There are only a few studies in children in which ceftriaxone has been used to treat cellulitis either in hospital or OPAT, but none have compared outcomes to children treated with other recommended antibiotics.[4 7–10] There are no studies in children with cellulitis who require intravenous treatment comparing administration at home and in hospital. A study of children with moderate/severe cellulitis who were treated with ceftriaxone at a day treatment centre had an 80% success rate, but no comparison was made with children treated in hospital.[4] Other studies that have included ceftriaxone for the treatment of cellulitis in children have had cure rates of 91–96%, but have had small numbers, no comparison group and/or unclear methodology.[8 9] A small study in adults compared ceftriaxone with flucloxacillin, and while ceftriaxone resulted in a higher success rate than flucloxacillin (96% vs 70%), this was not statistically significant.[11] The differential effect of ceftriaxone and flucloxacillin on the microbiota of children has also never previously been described.

Increasingly, hospitals are developing programmes where patients who have traditionally been treated on a hospital ward are treated at home under the care of hospital doctors and nurses in Hospital-in-the-Home (HITH) programmes. While attractive in terms of resource use, it is unclear to what extent HITH care is efficacious and safe. The Royal Children's Hospital (RCH) Melbourne has the largest paediatric HITH programme in Australia. As an alternative to admission for intravenous flucloxacillin, RCH HITH developed a direct-from-the ED pathway for cellulitis, using once daily ceftriaxone and medical review at home. Since September 2012, more than 70 children at RCH with moderate/severe cellulitis have been treated successfully at home, with outcomes similar to children treated in hospital, although there may be unappreciated differences in selection criteria.[12 13]

We therefore plan to randomly assign patients with cellulitis requiring intravenous antibiotics to either be treated at home (intravenous ceftriaxone) or to the

hospital ward (intravenous flucloxacillin). The study aims to compare (1) the rate of treatment failure of home treatment with intravenous ceftriaxone versus hospital treatment with intravenous flucloxacillin; (2) the safety of treatment at home versus treatment in hospital; and (3) the effect of exposure to short course ceftriaxone versus flucloxacillin on nasal and gut microorganism resistance patterns and the clinical implications of this. The main outcome is treatment failure; defined as a change in treatment due to lack of clinical improvement or the occurrence of adverse events.

METHODS
Design
This is a single-centre, open-label, non-inferiority randomised controlled trial (RCT). This pragmatic trial aims to determine whether treatment for cellulitis administered at home is non-inferior to (ie, no worse than) treatment in hospital. It has two parallel arms with 1:1 allocation of children with moderate/severe cellulitis.

Setting
Patients will be recruited from the ED at the RCH, a tertiary paediatric hospital in Melbourne, Australia from January 2015 to December 2016.

Inclusion criteria
▶ Children aged 6 months to <18 years.
▶ Children presenting to RCH ED with moderate/severe cellulitis, that is, those assessed as needing intravenous antibiotics. Currently, there is no validated scoring system on which to base the choice between intravenous or oral antibiotics, therefore clinician judgement is the current gold standard. Although reasons may differ between clinicians, this will be accounted for by randomisation. Reasons for starting intravenous antibiotics include:
A. Failed oral antibiotics (no improvement despite 24 h oral antibiotics).
B. Rapidly spreading redness (patient/parent history).
C. Significant swelling/redness/pain.
D. Systemic symptoms/signs (eg, fever, lethargy).
E. Difficult to treat areas (eg, face, ear, toe).

Exclusion criteria
Children will be excluded if they have:
1. Complicated cellulitis defined as follows: orbital cellulitis or unable to exclude orbital cellulitis, penetrating injury/bites, suspected/confirmed foreign body, suspected fasciitis or myositis, varicella, undrained abscess including dental abscess.
2. Toxicity: tachycardia when afebrile or hypotension (both as per the limits from the 'Development of heart and respiratory rate percentile curves for hospitalised children'[14]), poor central perfusion (capillary refill >2 s).

3. Underlying comorbidities: immunosuppression, liver disease.
4. Any concurrent infection necessitating different antibiotic treatment to intravenous flucloxacillin or ceftriaxone monotherapy, for example, concurrent sinusitis or otitis media or lymphadenitis.
5. Other medical diagnoses necessitating admission to hospital for observation or treatment relating to the known medical condition.
6. Unable to obtain intravenous access.
7. Age <6 months old.
8. With mild cellulitis (ie, can be treated with oral antibiotics).

Non-English speakers will be included so long as at the time of obtaining consent, an interpreter is available. At our centre, an interpreter is available in person during normal working hours Monday to Friday and via telephone 24 h a day. An interpreter service will also be used for subsequent phone calls and clinic visits similar to routine clinical practice involving non-English speakers.

Primary outcome

The primary outcome is treatment failure defined as a change in treatment due to lack of clinical improvement according to the treating physician or adverse events, within 48 h (i,e by Day 3) from the start of the first antibiotic dose administered in the ED (Day 1). Clinical improvement is assessed by the treating physician daily and includes: reduction in fever (if fever source is cellulitis and not concurrent illness; reduction in frequency or degree of temperature), reduction in the cellulitis area (measured by the largest diameter of erythema), reduction in the severity of swelling (judged by clinician as mild, moderate or severe) and reduction in the intensity of erythema (judged by clinician on a scale of 0=no erythema to 5=severe erythema).

Secondary outcomes

1. Time to no progression of cellulitis: number of days (including fractions of days—to one decimal point) from the start of the first dose in ED to the time at which the cellulitis stops spreading past the marked area.
2. Time to discharge: number of days (including fractions of days) from the time of arrival in ED to the time the patient no longer needs hospital-based interventions/care, whether in hospital or at home.
3. Readmission rate: proportion of children readmitted to hospital within 14 days of discharge date due to the same cellulitis.
4. Representation to ED: proportion of children representing to ED within 14 days of discharge due to the same cellulitis.
5. Length of stay in ED: from triage time in ED to the time the patient leaves ED to go either home or to ward.
6. Duration of intravenous antibiotics: in days.

7. Rates of intravenous cannula needing at least one resiting.
8. Complications of cellulitis: development of abscess requiring drainage after starting intravenous antibiotics, bacteraemia.
9. Adverse events: anaphylaxis; allergic reaction (suspected or confirmed) necessitating change of empiric antibiotic; sepsis; death.
10. Microbiology:
    ▶ Rate of ceftriaxone susceptibility in bacteria isolated from a nasal or skin swab of the affected area.
    ▶ Rate of *Staphylococcus aureus* nasal carriage (methicillin-sensitive and methicillin-resistant) collected within 48 h, after 7–14 days, 3 months and 1 year after starting antibiotics.
    ▶ Rate of resistant bacteria present in stool samples collected within 48 h, after 7–14 days, 3 months and 1 year after starting antibiotics. Rates of clinical infection with resistant organisms up to 1 year after starting antibiotics.
11. Costs of hospital versus HITH treatment: including costs of beds, consumables, nursing and medical time and overheads including administrative time, information technology, use of hospital cars.
12. Patient and parent satisfaction (measured by anonymous survey) including questions from a published quality of life (QOL) tool.[15]

Patient recruitment, study procedure and data collection

ED clinicians (senior doctors, junior doctors or nurse practitioners) will identify patients with moderate/severe cellulitis presenting to RCH ED at triage or during clinical assessment (figure 1). The patient or parents of patients meeting inclusion criteria will be invited to participate in the study. Consent will be obtained for randomisation, data collection and follow-up that is not routine practice. Data collection includes: age, sex, site of cellulitis, size of area affected, prior antibiotics, underlying comorbidity not affecting inclusion, systemic symptoms and signs. In addition, consent will be requested for nasal swab samples and stool samples. Randomisation will be performed after consent is obtained by a study investigator or the ED clinician. Patients who are randomised to HITH will be prescribed intravenous ceftriaxone (50 mg/kg once daily) and those randomised to the ward will be prescribed intravenous flucloxacillin (50 mg/kg 6 hourly). A blood culture, nasal swab and where relevant a skin swab (only in the presence of discharge from the site of cellulitis) will be collected at presentation. A stool specimen will be collected within 48 h of the first dose of antibiotics.

Parents will be asked to take two photos of the cellulitis area using their own camera/phone (if available) after the affected area is demarcated with indelible ink with a tape measure placed alongside the area affected. If parents do not have a camera/phone, permission will be sought from the parent to use a hospital camera to

Figure 1 Study flow chart. ED, emergency department; HITH, Hospital-in-the-Home; IV, intravenous.
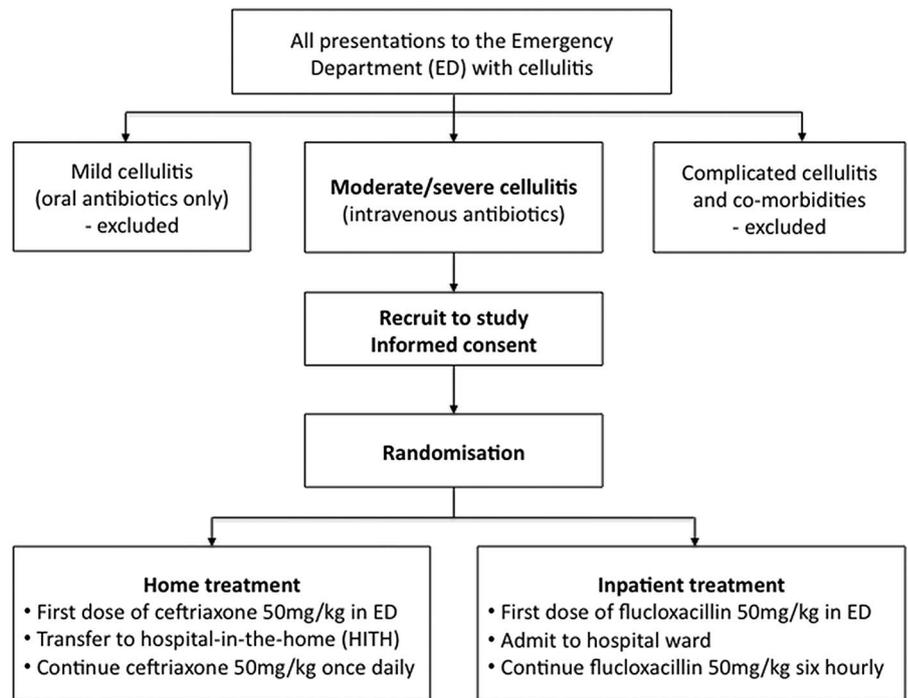
photograph the lesion. This will aid review the following day. The first dose of antibiotics will be administered in ED before the child goes either to the ward or home. After randomisation, treatment decisions for the patient will be made by the appropriate treating physician, as per usual practice: if on the ward the general

paediatrician on call, and if at home the HITH paediatrician. In hospital ward and HITH services, the management decisions for cellulitis are usually made by senior trainees/registrars in paediatrics. Sometimes a consultant will be called on to make a decision; this is more likely to occur on the ward than in HITH. Patients will

Table 1 Study schedule

Assessment/procedure	ED presentation Day 1	Day 2	Day 3 and every day until discharge	Day 7–14 after starting antibiotics	3 months after starting antibiotics	1 year after starting antibiotics
Informed consent	X					
Demographic information	X					
Clinical assessment	X	X	X			
Blood culture	X					
Skin swab	X					
Nasal swab (optional)	X			X	X	X
Stool sample (optional)	X			X	X	X
Photo on parents' phone	X	X	X			
IV antibiotics	X	X	X			
Anonymous questionnaire				X		
Final review method option 1: RCH clinic (where parents willing)				X		
Optional stool for culture and sensitivity				X		
Final review method option 2: by telephone (where parents unwilling to attend clinic)				X		
Parents to email photo of previously affected area				X		

ED, emergency department; IV, intravenous; RCH, Royal Children's Hospital.

be switched to oral therapy when there is clinical improvement of the cellulitis as judged by the treating clinician. Oral antibiotics will be cephalexin 25 mg/kg 6 hourly (as per RCH guidelines), or the most appropriate antibiotic based on microbiology results. Although patients are usually not followed up any further in hospital, in this study, all participants will be followed up as per the study schedule (table 1). If parents decline the first follow-up visit at clinic, a review will be conducted by telephone and the parents will be requested to email photos of the area previously affected with cellulitis or give a verbal report (to ensure clinical resolution). The anonymous patient/parent satisfaction survey will be posted out to the parents at Day 7–14 after starting antibiotics.

The nasal swab and stool sample will be requested at four different time points: (1) within 48 h of the first antibiotic dose; (2) 7–14 days after starting antibiotics; (3) 3 months after starting antibiotics; and (4) 1 year after starting antibiotics. At each time point, additional information will be collected: previous overseas travel, previous hospital admissions, household member who has been admitted to hospital overseas, other antibiotic use, other infections, medical visits or hospital admissions. These samples are optional and do not affect participation in the study.

STATISTICAL METHODS
Sample size and power calculation:
Previous data collection at RCH has shown a failure rate of standard treatment of cellulitis with flucloxacillin in hospital of approximately 5%.[16] Based on the literature and discussion with clinicians, we have determined that the intervention would be deemed acceptable if 80% of children can be successfully treated at home ,that is, a maximum difference of 15%. For a non-inferiority study design with a 15% difference, 89 patients are needed in each treatment arm (based on 80% power). Allowing for 5% dropout rate, a total of 188 are therefore required (94 in each treatment arm). Based on our previous data, we will be able to recruit this number over a 2-year period if this study remains within RCH.[12 16] However, once this study starts at RCH, depending on recruitment, we may expand this study to other centres, which would shorten the length of time to complete the study.

Randomisation
The randomisation schedule will be provided by the Clinical Epidemiology and Biostatistics Unit at the Murdoch Children's Research Institute (MCRI). The randomisation will be in randomly permuted blocks of variable length, stratified by age (6 months to less than 9 years and 9 years to 18 years) and by the presence of periorbital cellulitis. Randomisation will be enabled through the REDCap (Research electronic Data Capture, REDCap Software—V.6.6.2—copyright 2015 Vanderbilt University) web-based application housed at MCRI.

Statistical analysis
Statistical analysis will follow standard methods for randomised controlled trials and the primary analysis will be primarily by intention to treat. We will also conduct a per protocol analysis, including all randomised participants where outcome data are available. For the primary outcome Pearson's χ^2 test will be used to compare the proportion of participants who fail treatment within 48 h from the first dose. Non-inferiority will determined by calculating difference in treatment failure (risk difference and 95% two-sided CI between the failure rates in the home and hospital groups. For the home arm to be non-inferior to treatment in the hospital, the upper limit of the 95% CI must be less than 15% (as we have prespecified this as the non-inferiority margin). As a secondary analysis on the primary outcome a logistic regression model will be used to investigate whether inclusion of the stratification factor (age at randomisation) as predictor modifies the estimated effect (and 95%CI) of treatment group on the primary outcome.

Secondary continuous outcomes will be compared between the two groups using unadjusted linear regression while binary outcomes will be compared using unadjusted logistic regression. Furthermore, as explorative analyses, regression models (or logistic models according to the nature of the outcome) will also be fitted to the primary and secondary outcomes adjusting for age (as used in the randomisation), presence of fever at baseline and any other baseline and demographic variables where an imbalance is found. The appropriate survival analysis models will be used to compare time to event outcomes between the treatment groups. The statistician performing data analysis for the primary and secondary outcomes will be blinded to the treatment allocation.

Ethical issues and dissemination
Prior to starting of the study and on an on-going basis, ED clinicians have had education sessions to inform them about the study. The appropriate information sheet will be given to the parent and/or child, the study explained and written consent requested. Where parents do not give consent, the ED clinician will make the decision about treatment location. Photos will be identified only by the subject unique identifier assigned for the study and will be stored in a password-protected database. Data will be entered into a password-protected database enabled through the REDCap (Research electronic Data Capture, REDCap Software—V.6.6.2—copyright 2015 Vanderbilt University) web-based application housed at MCRI. The case report forms will be kept in a locked filing cabinet, accessible only by the researchers. Consent to collect information will be sought from participants who deviate from the protocol. All data will be retained until 7 years after last contact with patients or once all patients involved in the study have reached 25 years of age (whichever is longer) as per the ethics requirements for our institution.

We aim to disseminate the findings through international peer-reviewed journals and international conferences either as an oral or a poster presentation.

At the end of the study a summary of the results will also be posted to the participants. Results will be reported as an analysis of group data rather than individual data and will contain only de-identified information.

Risk management, adverse events and patient safety

There are no foreseeable additional risks to patients or their families by participating in this study. HITH has been shown to be a safe programme under which children can be treated at home for many conditions, and there will be daily medical review of all patients. Families on the HITH programme have direct access via telephone to an experienced nurse 24 h a day and this nurse is supported by a medical team. Potential adverse events in this study would be an allergic reaction to either of the antibiotics used, and these will be reported to the study's independent data safety monitoring board. Serious adverse events such as overwhelming sepsis or death are not expected in this study as cellulitis in children is a condition not associated with such morbidity and mortality. None of the patients in our prospective study of home treatment of cellulitis developed sepsis or any other serious adverse event.[16]

Independent safety and data monitoring committee

An Independent Safety and Data Monitoring Committee (ISDMC) have been established. The ISDMC consists of two independent clinicians and a biostatistician whom, collectively, have experience in the management of paediatric patients with cellulitis and in the conduct and monitoring of randomised controlled trials. The ISDMC will function independently of all other individuals and bodies associated with the conduct of the study. The ISDMC will review all data by treatment arm every 6 to 10 months. The first planned ISDMC review is in October 2015.

Time plan

We have thus far recruited 52 of the planned 188 patients. We plan to complete recruitment by the end of 2016.

DISCUSSION

Our study will be the first RCT to evaluate the effectiveness and safety of home intravenous antibiotics for children directly from ED. If treatment at home is found to be non-inferior, the benefits for children/families and cost-effectiveness for healthcare constitutions will lead to this pathway (direct-from-the ED to home) becoming standard care.

Our study design has some unavoidable limitations. Although the main aim is to compare standard care in hospital with the novel intervention of home treatment, the antibiotics in the two arms are also necessarily different. Intravenous flucloxacillin or cephazolin (usual standard care) require dosing 3–4 times a day in children, which is not feasible for home treatment. The alternative of administering these via a continuous infusion would require a form of central line access, which in children may require sedation or anaesthesia, with associated increased risks and time in hospital. The only intravenous antibiotic viable for home use in this acute direct-from-ED context is therefore once daily ceftriaxone, and from our previous study we do not anticipate differences in antibiotic efficacy.[16] Although longer term use of ceftriaxone has been associated with increased acquisition of resistant organisms in adults, this has not been shown in healthy children or for very short courses as anticipated in this study. To address the potential issues of resistance development this study is specifically designed to detect any changes in the nasal and gut micro-organisms and any clinically relevant consequences of such changes. Another limitation of this study is that this is a single site, single city study. Antibiotic resistance is geographically influenced, and the availability/skills of home-based care programmes for children may not be available to many centres. These factors may limit applicability to other areas.

This study will likely have a high impact on clinical practice not only in our own clinical institution but also on a wider global scale. The successful use of home antibiotics is the tip of the iceberg, as it can be expanded to include many common medical conditions ensuring children can go home directly to be treated under the HITH programme and avoid hospitalisation. We anticipate that this would ultimately impact on health policy.

Author affiliations
[1]RCH@Home Department, The Royal Children's Hospital, Parkville, Victoria, Australia
[2]Murdoch Children's Research Institute, Parkville, Victoria, Australia
[3]Department of Paediatrics, University of Melbourne, Melbourne, Victoria, Australia
[4]Emergency Department, The Royal Children's Hospital, Parkville, Victoria, Australia
[5]Clinical Epidemiology and Biostatistics Unit, Murdoch Children's Research Institute, Parkville, Victoria, Australia
[6]Infectious Diseases Unit, Department of General Medicine, The Royal Children's Hospital, Parkville, Victoria, Australia

Contributors LFI, PAB and FEB were responsible for identifying the research question and the design of the study. SMH and FO were responsible for refining the design and developing the research protocol. All authors have contributed to the development of the protocol, the implementation of the study and enrolment of patients. LFI was responsible for the drafting of this paper. All authors provided comments on the drafts and have read and

REFERENCES

1. Svahn BM, Remberger M, Heijbel M, et al. Case-control comparison of at-home and hospital care for allogeneic hematopoietic stem-cell transplantation: the role of oral nutrition. *Transplantation* 2008;85:1000–7.
2. Small F, Alderdice F, McCusker C, et al. A prospective cohort study comparing hospital admission for gastro-enteritis with home management. *Child Care Health Dev* 2005;31:555–62.
3. Balaguer A, Gonzalez de Dios J. Home versus hospital intravenous antibiotic therapy for cystic fibrosis. *Cochrane Database Syst Rev* 2012;(3):CD001917.
4. Gouin S, Chevalier I, Gauthier M, et al. Prospective evaluation of the management of moderate to severe cellulitis with parenteral antibiotics at a paediatric day treatment centre. *J Paediatr Child Health* 2008;44:214–18.
5. Ibrahim LF, Hopper SM, Babl FE, et al. Who can safely have antibiotics at home? A prospective observational study in children with moderate/severe cellulitis. *Pediatr Infect Dis J* 13 Nov 2015. [Epub ahead of print] www.ncbi.nlm.nih.gov/pubmed/26569189
6. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. *Clin Infect Dis* 2005;41:1373–406.
7. Nelson SJ, Boies EG, Shackelford PG. Ceftriaxone in the treatment of infections caused by Staphylococcus aureus in children. *Pediatr Infect Dis* 1985;4:27–31.
8. Frenkel LD. Once-daily administration of ceftriaxone for the treatment of selected serious bacterial infections in children. *Pediatrics* 1988;82(3 Pt 2):486–91.
9. Kulhanjian J, Dunphy MG, Hamstra S, et al. Randomized comparative study of ampicillin/sulbactam vs. ceftriaxone for treatment of soft tissue and skeletal infections in children. *Pediatr Infect Dis J* 1989;8:605–10.
10. Brugha RE, Abrahamson E. Ambulatory intravenous antibiotic therapy for children with preseptal cellulitis. *Pediatr Emerg Care* 2012;28:226–8.
11. Vinen J, Hudson B, Chan B, et al. A randomised comparative study of once-daily ceftriaxone and 6-hourly flucloxacillin in the treatment of moderate to severe cellulitis—Clinical efficacy, safety and pharmacoeconomic implications. *Clin Drug Investig* 1996;12:221–5.
12. Ibrahim LF, Hopper SM, Sacks B, et al. Pilot study of the safety and acceptability of parenteral antibiotics in children referred from the Emergency Department directly to Hospital-In-The-Home. *The 8th World Congress of the World Society for Pediatric Infectious Disease (WSPID 2013)*; Cape Town, South Africa, 2013.
13. Ibrahim LF, Hopper SM, Babl FE, et al. A comparison of treatment at home or in hospital for moderate/severe cellulitis in children. *Australasian Society for Infectious Diseases Annual Scientific Meeting*; Adelaide, Australia, 2014.
14. Bonafide CP, Brady PW, Keren R, et al. Development of heart and respiratory rate percentile curves for hospitalized children. *Pediatrics* 2013;131:e1150–7.
15. Orme LM, Babl FE, Barnes C, et al. Outpatient versus inpatient IV antibiotic management for pediatric oncology patients with low risk febrile neutropenia: a randomised trial. *Pediatr Blood Cancer* 2014;61:1427–33.
16. Ibrahim LF, Hopper SM, Babl FE, et al. The CHOICE study: Cellulitis treatment at Home Or Inpatient in Children from Emergency. *Australasian College for Emergency Medicine Annual Scientific Meeting*; Melbourne, Australia, 2014.