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Care and outcomes of Canadian children hospitalised with periorbital and orbital cellulitis: protocol for a multicentre, retrospective cohort study

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ABSTRACT

Introduction Skin and soft tissue infections of the eye can be classified based on anatomic location as either anterior to the orbital septum (ie, periorbital cellulitis) or posterior to the orbital septum (ie, orbital cellulitis). These two conditions are often considered together in hospitalised children as clinical differentiation is difficult, especially in young children. Prior studies have identified variation in management of hospitalised children with orbital cellulitis; however, they have been limited either as single centre studies or by the use of administrative data which lacks clinical details important for interpreting variation in care. We aim to describe the care and outcomes of Canadian children hospitalised with periorbital and orbital cellulitis.

Method and analysis This is a multisite retrospective cohort study including previously healthy children aged 2 months to 18 years admitted to hospital with periorbital or orbital cellulitis from 2009 to 2018. Clinical data from medical records from multiple Canadian hospitals will be collected, including community and academic centres. Demographic characteristics and study outcomes will be summarised using descriptive statistics, including diagnostic testing, antibiotic therapy, adjunctive therapy, surgical intervention and clinical outcomes. Variation will be described and evaluated using χ^2 test or Kruskal-Wallis test. Generalised linear mixed models will be used to identify predictors of surgical intervention and longer length of stay.

Ethics and dissemination Approval of the study by the Research Ethics Board at each participating site has been obtained prior to data extraction. Study results will be disseminated by presentations at national and international meetings and by publications in high impact open access journals. By identifying important differences in management and outcomes by each hospital, the results will identify areas where care can be improved, practice standardised, unnecessary diagnostic imaging reduced, pharmacotherapy rationalised and where trials are needed.

Strengths and limitations of this study

- This study will be the largest cohort study evaluating the care and outcomes of hospitalised children with periorbital and orbital cellulitis.
- The multicentre, retrospective cohort observational design will contribute a significant amount of data regarding the management and outcomes of children with this infection.
- The inclusion of children hospitalised at community hospitals will increase the generalisability of the study findings.
- A retrospective study is limited by the validity of diagnostic codes and the information documented in the medical record.
- As an observational design, this study will only be able to identify association rather than causation, and, given the 10-year time period, there may be differences in clinical practice over time.

INTRODUCTION

Background and rationale

Skin and soft tissue infections of the eye can be classified based on anatomic location. Those infections that are mainly anterior to the orbital septum are called periorbital cellulitis and are usually following an injury or due to spread of a local infection.[1] Infections that are posterior to the orbital septum are called orbital cellulitis and are usually a complication of sinusitis.[2] Given the clinical challenge differentiating these two infections, especially in young children, periorbital and orbital cellulitis are often considered together in hospitalised children.[3] Estimates of orbital cellulitis incidence range from 1.6 to 6 per 100 000 in paediatric patients and 0.6 to 2.4 per 100 000 in adults.[4–6] While orbital cellulitis can occur at any age, paediatric patients

represent a large burden of hospitalised cases.[6 7] Predisposing risk factors for orbital cellulitis include sinusitis, ocular surgery, orbital trauma and orbital foreign body. The causative pathogens have changed over time, with a reduction in vaccine-preventable pathogens (eg, *Haemophilus influenzae type B, Streptococcus pneumoniae*)[8] and an increase in *Staphylococcus aureus,* including methicillin-resistant *S. aureus* (MRSA).[8]

Given the severity of potential complications (eg, loss of vision, meningitis and death),[4 9 10] up to 51% of children that present to the emergency department (ED) with acute periorbital swelling and redness are hospitalised[11] for further investigations, antimicrobial therapy, adjunctive agents, specialty consulting services and surgical intervention. In most centres, children are admitted to the general paediatric inpatient unit, with consultation from otolaryngologists, ophthalmologists and other specialty services.[12–15] When a child presents with cellulitis and swelling of the soft tissues around the eye, periorbital cellulitis is diagnosed clinically in the absence of proptosis, ophthalmoplegia or pain with eye movements.[2] When these signs and symptoms are present, or if the soft tissue swelling is severe and the clinical examination is limited, then additional laboratory investigations are often performed, including complete blood count (CBC) and inflammatory markers (eg, C reactive protein (CRP)).[2 12 16]

A CT scan with contrast is frequently obtained to characterise the extent of inflammation and determine if an abscess is present. A large US-based multicentre observational study of hospitalised children with orbital cellulitis reported a median CT scan rate of 74.7% (IQR: 66.7%–81.0%).[12] Obtaining diagnostic imaging can help to describe disease severity, and the most commonly used classification system is one described by Chandler in 1970.[17] There are five classes, including periorbital (preseptal) cellulitis (Chandler criteria I), orbital cellulitis (Chandler criteria II), with the further three classes defined by the presence of a subperiosteal abscess (Chandler criteria III), orbital abscess (Chandler criteria IV) and cavernous sinus thrombosis (Chandler criteria V).

A recent systematic review suggested medical management for periorbital and orbital cellulitis, and for most patients with a subperiosteal abscess, with surgical management reserved for patients with orbital abscess and cavernous sinus thrombosis.[3] No randomised controlled trials (RCTs) have been published to guide antibiotic mode (ie, oral or intravenous), antibiotic selection or duration of therapy.[18] It is usual practice to institute intravenous for initial treatment of orbital cellulitis, subperiosteal abscess and orbital abscess.[3] Empiric antibiotics are chosen to cover both gram-positive and gram-negative pathogens and considering the local prevailing organisms. Published antimicrobial recommendations vary, but for orbital cellulitis, generally include a second or third generation cephalosporin, and cefazolin or cloxacillin, or in areas with high rates of MRSA (eg, US) vancomycin. Some authors advocate for additional anaerobic coverage with metronidazole or clindamycin if certain risk factors are present, such as dental infections or sinusitis.

Adjunctive agents, such as intranasal corticosteroids, intranasal decongestants and intranasal saline, are frequently used in hospitalised children, yet there are conflicting guidelines on whether these agents should be used[2 19] or avoided,[13] and evidence is lacking to guide practitioners.[15] A few studies have suggested that adding systemic corticosteroids to the management of patients with periorbital and orbital cellulitis may lead to superior outcomes.[14 20–22] A single centre, single masked RCT conducted in a tertiary care eye hospital in India included 21 patients with orbital cellulitis who were 10 years and older. Patients that were treated with corticosteroids reported a reduction in duration of intravenous antibiotics (control group 11.6±4.6 days; corticosteroid group 8.6±1.3 days, p=0.013), and a reduction in mean length of stay (control group 18.4±5.9 days; corticosteroid group 14.1±3.7 days, p=0.02) with similar rates of surgical intervention.[21] The use of systemic corticosteroids varies in US hospitals, with a median rate of 29.2% (IQR: 18.4%–37.5%),[12] likely due to the lack of clinical practice guidelines; little is known about corticosteroid use in other countries.

If complications develop, or if there is poor response to antimicrobial therapy, surgical management is considered. However, no standardised criteria exist to guide surgical management, and the decision is usually made at the discretion of the surgeon.[2 3] Children with orbital cellulitis who require surgery incur significantly increased costs and have a longer mean hospital length of stay.[23] The reported rate of surgery varies between 1.6% and 30%,[11 12 23–26] increasing in children with a subperiosteal abscess.[3 11]

Recent studies of hospitalised children have demonstrated variability in care and outcomes,[11 12] including use of diagnostic tests[11 24] (eg, CT scan), specific pathogens.[14 27] adjunctive corticosteroids and antibiotic exposure.[12] The variation in care highlights important unanswered clinical questions, including which pharmacological agents improve clinical outcomes, the indications for diagnostic imaging and surgical intervention and risk factors for complications. However, most prior studies are single-centred, usually in large academic tertiary care hospitals[11 24 27] or based on routinely collected administrative data,[12 23 25] which lack clinical information. Further, there are several reasons why findings from studies conducted in the US may not be applicable to the Canadian setting (eg, higher rates of diagnostic imaging, MRSA infection and corticosteroid use). Therefore, we plan to conduct multisite retrospective cohort study to describe the care and outcomes of Canadian hospitalised children with periorbital and orbital cellulitis. We plan to include children hospitalised with both periorbital and orbital cellulitis given the difficulty differentiating these infections in young children.

Aim and objectives

Aim

To describe the clinical management and outcomes of Canadian children aged 2 months to 18 years hospitalised with periorbital and orbital cellulitis.

Specific objectives

1. To describe clinical outcomes, diagnostic testing, antibiotic therapy, adjunctive therapy and surgical intervention of hospitalised children with periorbital and orbital cellulitis in Canada, including trends in these outcomes over time.
2. To describe variation in clinical outcomes, diagnostic testing, antibiotic therapy, adjunctive therapy and surgical intervention by hospital and hospital type in children hospitalised with periorbital and orbital cellulitis.
3. To explore risk factors associated with surgical intervention and longer length of hospital stay among children hospitalised with periorbital and orbital cellulitis.

Significance

By identifying important differences in management and outcomes by each hospital, we will identify areas where care can be improved, practice standardised, unnecessary diagnostic imaging reduced, pharmacotherapy rationalised and where trials are needed. These principles are in keeping with the 'Choosing Wisely' campaign which serves to minimise unnecessary tests and procedures.[28] Identifying variation in healthcare is also important because it is associated with worse health outcomes and increased costs. For example, Markham *et al* found that in the US, hospitals that had greater use of diagnostic test services for children admitted with orbital cellulitis had greater costs overall and longer length of hospital stay.[12] Variation also identifies evidence gaps, which may be the result of insufficient evidence and therefore suggesting the need to resolve uncertainty with clinical trials; or if evidence exists, highlighting opportunities for implementation and knowledge dissemination activities to translate evidence to clinical practice.

METHODS AND ANALYSIS

Study design

This study is a multisite retrospective cohort study using hospital health records as the data source. This study will be conducted in the Canadian Pediatric Inpatient Research Network (PIRN), a hospital-based research network focused on improving healthcare delivery, health outcomes and health systems for hospitalised children in general paediatric inpatient units. PIRN includes both academic children's hospitals and large community hospitals in Canada. This study will include health records from a 10-year time period (1 January 2009 to 31 December 2018, inclusive).

Study population

This study will include children ages 2 months to 18 years admitted to hospital with a primary diagnosis of periorbital cellulitis or orbital cellulitis made by the attending physician at either admission to hospital or at discharge. Children with both infections will be included as clinical distinction is difficult in young children, and children whom are unwell enough to be hospitalised are treated similarly. Children will be excluded if they have the following primary diagnosis: (1) tumour of the eye or orbit; (2) orbital pseudotumour; (3) herpes simplex or herpes zoster related infection; (4) previous craniofacial or ocular surgery; (5) craniofacial anatomic abnormality (eg, craniosynostosis); (6) cellulitis related to trauma, laceration or recent surgery; (7) underlying acquired or congenital lesion (eg, dacrocystocele) or (8) immunodeficiency or immunocompromised. Children with conditions that are related to possible corticosteroid use will be included, but will be analysed as a separate group to evaluate the use of corticosteroids for periorbital and orbital cellulitis (eg, asthma).[12]

We will identify eligible patients based on *International Classification of Diseases, Ninth Revision, Canada* (ICD-9-CA) or *International Classification of Diseases, Tenth Revision, Canada* (ICD-10-CA) diagnostic codes of periorbital cellulitis or orbital cellulitis. Most Canadian provinces transitioned to ICD-10-CA in 2001, while Quebec transitioned in 2006; we have included both ICD-9-CA and ICD-10-CA codes for completion. We will use ICD-9-CA 376.0 which includes periorbital cellulitis, orbital cellulitis, orbital abscess and subperiosteal abscess and has been used in previous studies on hospitalised patients with orbital cellulitis.[12 23 25 29] We will use ICD-10-CA H05.0 for orbital cellulitis (acute inflammation of orbit) which includes numerous specific codes.

Patient and public involvement

The patients included in this study were not involved in the development of the research question or study design and will not be involved in the conduct of the study given its retrospective nature.

Data

This study will use data from paper and electronic health records, of which the detailed parameters will vary based on each institution, which may include electronic hospital charts, health record database and diagnostic imaging database. A trained research assistant will review each individual participant for inclusion in the study. This study will be conducted at multiple hospitals across Canada including (n=8): Alberta Children's Hospital (Calgary), Stollery Children's Hospital (Edmonton), McMaster Children's Hospital (Hamilton), Hospital for Sick Children (Toronto), Lakeridge Health (Oshawa), Kingston General Hospital (Kingston), Children's Hospital of Eastern Ontario (Ottawa) and CHU Sainte-Justine (Montreal). Additional hospital sites may be added based on feasibility and resources available.

Using data provided from decision support at several hospital sites, we expect at least 300 patients per year to be enrolled in the study or 3000 patients over a 10-year period.

Each site investigator will identify eligible patients based on ICD-9-CA or ICD-10-CA codes within the specified time period. These charts will be assigned a unique number separate from the health record number. A standardised case report form (CRF) will be used for data extraction, which has been pilot tested at one centre and refined. Each site investigator will identify a research assistant (a medically trained trainee/student/nurse) and train that individual in data identification and extraction. Trained individuals will enter deidentified data directly using the electronic CRF into a secure Research Electronic Data Capture (REDCap)[30 31] online database managed at SickKids in Toronto, Canada. Data collection will begin in November 2019 with an anticipated completion date of May 2020.

Data will be collected on a number of relevant baseline characteristics that are important in the management of hospitalised children with periorbital or orbital cellulitis. Demographic information including age (in months) and sex (male/female) will be collected. Relevant medical history including history of chronic disease, vaccination status, previous history of periorbital/orbital cellulitis, history of transfer and antibiotic use from community hospital will be collected. Canadian Triage and Acuity Scale (CTAS) score[32] in ED and triage vitals, including heart rate, respiratory rate, blood pressure, temperature and weight will be extracted. Clinical characteristics at initial presentation, such as diplopia, proptosis, chemosis, painful extraocular movements, ophthalmoplegia and abnormal vision, will be collected.

Outcomes

As the primary aim of the study is descriptive, outcome data for five broad categories will be collected: (1) clinical outcomes; (2) diagnostic testing; (3) antibiotic therapy; (4) adjunctive therapy and (5) surgical intervention. Clinical outcomes include length of hospital stay, complications and revisits. Length of hospital stay (hours) will be defined based on date and time of admission and discharge. We will extract information about complications, including intensive care unit admission, vision loss, intracranial abscess, meningitis, cavernous sinus thrombosis and death. If there were any return visit within 30 days of discharge, we will collect the revisit or readmission diagnosis, including date of periorbital/orbital cellulitis related revisit or readmission.

Diagnostic tests include CBC (white blood cell count, haemoglobin and platelet count), electrolytes and inflammatory markers (ie, CRP, ESR). Blood culture location and results will be described, in addition to any culture from any other specimen collected (eg, abscess fluid). In case of a positive culture, the name of pathogens and antibiotic sensitivity results will be extracted. Date and time of CT and/or MRI scan will be collected, along with the findings. Where possible, images will be classified according to the Chandler criteria staging system[17] and if necessary, involve a radiologist.

Antibiotic therapy will include each individual antibiotic prescribed (eg, name, route), including whether antibiotics were prescribed before ED or in hospital (and if in hospital, if within the first 24 hours). We will extract if a peripherally inserted central catheter was inserted for therapy. Adjunctive therapy will include commonly used medications, including antihistamines, systemic corticosteroids, intranasal decongestants, intranasal corticosteroids and intranasal saline spray, including name, route, frequency and dosages. Surgical intervention will include date and time of surgery, including the type of surgery (eg, endoscopic versus open), and surgeon specialty (eg, otolaryngology, ophthalmology).

Proposed statistical methods

Baseline demographic characteristics and study outcomes will be summarised using descriptive statistics. Continuous variables (eg, age) will be summarised with means, medians and IQRs and categorical variables (eg, CTAS score) with frequencies and percentages. Where appropriate, 95% CIs will be provided. Descriptive statistics will be used for the overall cohort and to calculate hospital-level summary statistics.

Variation across hospitals in clinical outcomes, diagnostic testing, antibiotic therapy, adjunctive therapy and surgical intervention will be described. We will evaluate whether variation exceeds that expected by chance using χ^2 test or Kruskal-Wallis test. We will calculate the correlation with usage of select diagnostic tests, antibiotics and adjunctive agents with surgical intervention and outcomes using Pearson's correlation coefficient. We will also measure the intraclass correlation coefficient to understand if variation in diagnostic testing and interventions are related to hospital site.

We will conduct exploratory analysis using generalised linear mixed models (GLMMs) to identify predictors of surgical intervention. We will evaluate the following potential predictors of surgical intervention, informed by prior literature on risk factors for surgical intervention: (1) age in months; (2) sex; (3) antibiotics prior to admission; (4) CRP; (5) CT scan; (6) number of empiric antibiotics; (7) systemic corticosteroids; (8) intranasal corticosteroids; (9) intranasal decongestants and (10) presence of chronic disease. We will use univariate analysis to determine the association between surgical intervention as a binary outcome, and the independent variables. We will include all a priori selected variables from the univariate analysis in the final model, and hospital will be included as a random effect. The effect of individual predictors of surgical intervention will be reported as adjusted ORs with 95% CIs.

We will also conduct exploratory analysis using GLMMs to identify predictors of longer length of hospital stay (continuous dependent variable). We will evaluate the following potential predictors of hospital length of stay,

informed by prior literature on risk factors for longer length of stay: (1) age in months; (2) sex; (3) antibiotics prior to admission; (4) CRP; (5) CT scan; (6) number of empiric antibiotics; (7) systemic corticosteroids; (8) intranasal corticosteroids; (9) intranasal decongestants; (10) presence of chronic disease and (11) surgical intervention. We will use univariate analysis to determine the association between hospital length of stay as a continuous outcome and the independent variables. We will include all a priori selected variables in the final model, and each hospital will be included as a random effect. If necessary, non-normally distributed variables will be transformed using the Box-Cox transformation. The effect of individual predictors of surgical intervention will be reported as regression coefficients with 95% CIs. For both models, candidate predictors with data that are missing from a large number of subjects will be eliminated. If missing data are minimal, we will use multiple imputation for the missing data. We will conduct the analysis will the full dataset and with the imputed data set.

We will conduct several sensitivity analyses. We will conduct the analyses separately for patients admitted to children's hospitals versus community hospitals, and excluding children that were transferred given the possibility of double counting patients transferred from community hospitals to a tertiary care facility. We will also conduct the above analyses excluding those children discharged in less than 48 hours to focus on children that are more likely to be diagnosed with orbital cellulitis compared with periorbital cellulitis. We will also conduct the above analyses separately for only healthy children (excluding any children with a chronic condition) and excluding only those children with a higher likelihood of being prescribed corticosteroids (eg, adrenal insufficiency) to more accurately assess the use of corticosteroids for orbital cellulitis alone.

Sample size

We expect at least 300 patients per year to be enrolled in the study or 3000 patients over a 10-year period. Based on prior studies, the rate of surgical intervention is between 1.6% and 30%.[11 12 23–26] With an estimated sample size of 3000 patients hospitalised with orbital cellulitis, we conservatively estimate that at least 250 patients will receive surgical intervention. For the exploratory analysis using GLMMs to identify predictors of surgical intervention, we will have sufficient degrees of freedom to evaluate at least 10 independent variables, with the assumption of at least 10 patients with the outcome per predictor variable.[33] Based on prior studies, the median length of stay ranges from 4 days for uncomplicated orbital cellulitis[12 23] to 7 days for patients who require surgery. For the exploratory analysis using GLMMs to identify predictors of longer length of hospital stay, based on the estimated sample size of 3000 patients, we will have sufficient degrees of freedom to evaluate at least 11 independent variables.

Data storage and management

Each site investigator will be responsible for protocols around data extraction, storage and security. Data will either be entered directly into the secure online electronic REDCap database or will be collected using paper form (hard copy) by the Site Investigator and his/her staff and then entered into REDCap. Regular data quality checks will review missing data and check for outliers and discrepancies. For data safety and security, the electronic data will be maintained under secure, password-protected conditions while hard copy records will be kept in a locked office, and access will only be given to authorised study personnel. Each subject will be given a unique identification code. The code breaking information will be kept separate from the data extraction files and totally inaccessible to individuals outside the research team and will only be available to the Site Investigator at each site. All electronic documents will be protected by password on network, and all electronic data will be stored at SickKids, Toronto. The complete data set will be analysed at SickKids.

ETHICS AND DISSEMINATION

Ethical considerations

This study has obtained approval of the Research Ethics Board (REB) at each participating site, including Clinical Trials Ontario (CTO) (CTO1858) for all Ontario sites, and the local REB for each non-Ontario participating hospital, including Stollery Children's Hospital in Edmonton (Pro00092733), Alberta Children's Hospital in Calgary (REB19-1163) and Centre Hospitalier Universitaire (CHU) Sainte-Justine in Montreal (2020–2381). This retrospective study does not involve contact with human subjects and thus will not incur major risks to the patients who provided the data. For the study objectives, the patient's age is necessary, for which only age (in months) will be used, and date of hospital admission and hospital discharge. No date of birth, medical record number or other personal identification information will be extracted. The main risk to participants is a breach of privacy/confidentiality, which will be minimised as outlined in the data storage and management section.

Dissemination and data sharing

The study will be reported according to the Strengthening the Reporting of Observational Studies in Epidemiology Statement: Guidelines for Reporting Observational Studies.[34] Data and resources will be shared among the study team. The corresponding author will be responsible for the data and analysis. Each participating site can request access to the data for ancillary studies. All coinvestigators will be acknowledged as members of the '*POC Multicenter Study Group*' on any academic output. Study results will be distributed using a broad dissemination strategy, including presentations at national and international meetings, and publications in high impact open access journals.

Strengths and limitations

Strengths

The current study will be the largest cohort study of hospitalised children with periorbital and orbital cellulitis and will contribute a significant amount of data regarding the management and outcomes of children. Prior studies on hospitalised children have been single-centred, usually in large academic tertiary care hospitals or based on routinely collected administrative data. Few studies have included children hospitalised at community hospitals, despite a large proportion of children being managed in this setting.[35] A major barrier to the inclusion of community hospitals in paediatric research is the lack of research resources and infrastructure.[36] By partnering with academic institutions, this study will achieve the dual objective of increasing the generalisability of the study findings while supporting community physicians involvement in research. The perspectives of the range of clinicians who care for these patients, including hospital paediatricians from children's and community hospitals, otolaryngologists and ophthalmologists, have been incorporated. This approach helps to facilitate knowledge translation (KT) through using an integrated KT approach, where the research is embedded into the clinical setting in which it is intended to be translated. Last, by advancing the development of a Canadian Pediatric Inpatient Research Network, this study will lay the foundation for future observational studies, clinical trials and implementation studies focused on building the evidence-base for hospitalised children on general paediatric inpatient units.

Limitations

This study has several limitations. First, using ICD codes to identify eligible patients may miss some children that would have met eligibility criteria, including those that were given a broader diagnosis (eg, cellulitis of the face) and those with an incorrect ICD code. However, given the large number of sites and number of patients identified with decision support, we anticipate that only a small number of patients will be missed. Second, given its retrospective nature, included data will be limited by what is documented in the medical record; a prospective design would facilitate more complete documentation, particularly clinical data. We minimised the impact of incomplete documentation in our CRF by focusing on binary outcomes, acknowledging that precise information on dosing and duration of therapy, along with clinical findings, may be variable. We also pilot tested the CRF extensively prior to implementation. Third, as an observational study, we will only be able to illustrate association rather than causation, if any predictors are identified with surgical outcome or prolonged length of stay. However, the analyses outlined are exploratory in nature. Fourth, given the 10-year time period, there may be differences in clinical practice not captured in our study that may account for differences in care and outcomes, which may act as unmeasured confounders.

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Contributors PJG conceived and designed the study, drafted the first version of the manuscript and revised subsequent versions of the manuscript. PCP and SM conceived and designed the study and revised the manuscript. NB, OD, JF, CP, JQ, GV, GW, MS, NK, AB, RK, AS, EMP, AR and NW participated in the design of the study and manuscript revisions. All authors have read and given final approval of the submitted manuscript.

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REFERENCES

1 Rimon A, Hoffer V, Prais D, *et al*. Periorbital cellulitis in the era of Haemophilus influenzae type B vaccine: predisposing factors and etiologic agents in hospitalized children. *J Pediatr Ophthalmol Strabismus* 2008;45:300–4.
2 Howe L, Jones NS. Guidelines for the management of periorbital cellulitis/abscess. *Clin Otolaryngol Allied Sci* 2004;29:725–8.
3 Wong SJ, Levi J. Management of pediatric orbital cellulitis: a systematic review. *Int J Pediatr Otorhinolaryngol* 2018;110:123–9.
4 Murphy C, Livingstone I, Foot B, *et al*. Orbital cellulitis in Scotland: current incidence, aetiology, management and outcomes. *Br J Ophthalmol* 2014;98:1575–8.
5 Soroudi ACR, Pan D, Baker R. An epidemiologic survey of orbital cellulitis. *Investig Ophthalmol Vis Sci* 2003;44:786.
6 Capra G, Liming B, Boseley ME, *et al*. Trends in orbital complications of pediatric rhinosinusitis in the United States. *JAMA Otolaryngol Head Neck Surg* 2015;141:12–17.

7 Atfeh MS, Khalil HS. Orbital infections: five-year case series, literature review and Guideline development. *J Laryngol Otol* 2015;129:670–6.
8 Peña MT, Preciado D, Orestes M, *et al*. Orbital complications of acute sinusitis: changes in the post-pneumococcal vaccine era. *JAMA Otolaryngol Head Neck Surg* 2013;139:223–7.
9 Lee S, Yen MT. Management of preseptal and orbital cellulitis. *Saudi J Ophthalmol* 2011;25:21–9.
10 Crosbie RA, Nairn J, Kubba H. Management of paediatric periorbital cellulitis: our experience of 243 children managed according to a standardised protocol 2012-2015. *Int J Pediatr Otorhinolaryngol* 2016;87:134–8.
11 Rudloe TF, Harper MB, Prabhu SP, *et al*. Acute periorbital infections: who needs emergent imaging? *Pediatrics* 2010;125:e719–26.
12 Markham JL, Hall M, Bettenhausen JL, *et al*. Variation in care and clinical outcomes in children hospitalized with orbital cellulitis. *Hosp Pediatr* 2018;8:28–35.
13 Hauser A, Fogarasi S. Periorbital and orbital cellulitis. *Pediatr Rev* 2010;31:242–9.
14 Davies BW, Smith JM, Hink EM, *et al*. C-Reactive protein as a marker for initiating steroid treatment in children with orbital cellulitis. *Ophthalmic Plast Reconstr Surg* 2015;31:364–8.
15 Okonkwo ACO, Powell S, Carrie S, *et al*. A review of periorbital cellulitis guidelines in Fifty-One acute admitting units in the United Kingdom. *Clin Otolaryngol* 2018;43:718–21.
16 Jabarin B, Eviatar E, Israel O, *et al*. Indicators for imaging in periorbital cellulitis secondary to rhinosinusitis. *Eur Arch Otorhinolaryngol* 2018;275:943–8.
17 Chandler JR, Langenbrunner DJ, Stevens ER. The pathogenesis of orbital complications in acute sinusitis. *Laryngoscope* 1970;80:1414–28.
18 Al-Nammari S, Roberton B, Ferguson C. Towards evidence based emergency medicine: best bets from the Manchester Royal Infirmary. should a child with preseptal periorbital cellulitis be treated with intravenous or oral antibiotics? *Emerg Med J* 2007;24:128–9.
19 Bedwell JR, Choi SS. Medical versus surgical management of pediatric orbital subperiosteal abscesses. *Laryngoscope* 2013;123:n/a–8.
20 Yen MT, Yen KG. Effect of corticosteroids in the acute management of pediatric orbital cellulitis with subperiosteal abscess. *Ophthalmic Plast Reconstr Surg* 2005;21:363–6. Discussion 6-7.
21 Pushker N, Tejwani LK, Bajaj MS, *et al*. Role of oral corticosteroids in orbital cellulitis. *Am J Ophthalmol* 2013;156:178–83.
22 Chen L, Silverman N, Wu A, *et al*. Intravenous steroids with antibiotics on admission for children with orbital cellulitis. *Ophthalmic Plast Reconstr Surg* 2018;34:205–8.
23 Mahalingam-Dhingra A, Lander L, Preciado DA, *et al*. Orbital and periorbital infections: a national perspective. *Arch Otolaryngol Head Neck Surg* 2011;137:769–73.
24 Le TD, Liu ES, Adatia FA, *et al*. The effect of adding orbital computed tomography findings to the Chandler criteria for classifying pediatric orbital cellulitis in predicting which patients will require surgical intervention. *J Aapos* 2014;18:271–7.
25 Marchiano E, Raikundalia MD, Carniol ET, *et al*. Characteristics of patients treated for orbital cellulitis: an analysis of inpatient data. *Laryngoscope* 2016;126:554–9.
26 Santos JC, Pinto S, Ferreira S, *et al*. Pediatric preseptal and orbital cellulitis: a 10-year experience. *Int J Pediatr Otorhinolaryngol* 2019;120:82–8.
27 Sharma A, Liu ES, Le TD, *et al*. Pediatric orbital cellulitis in the Haemophilus influenzae vaccine era. *J Aapos* 2015;19:206–10.
28 Friedman JN. Saying Yes to the less: making it easier to choose wisely. *J Pediatr* 2017;184:4–5.
29 Foster CE, Yarotsky E, Mason EO, *et al*. Molecular characterization of Staphylococcus aureus isolates from children with periorbital or orbital cellulitis. *J Pediatric Infect Dis Soc* 2018;7:205–9.
30 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
31 Harris PA, Taylor R, Minor BL, *et al*. The REDCap Consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
32 Bullard MJ, Chan T, Brayman C, *et al*. Revisions to the Canadian emergency department triage and acuity scale (CTAS) guidelines. *CJEM* 2014;16:485–9.
33 Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373–9.
34 von Elm E, Altman DG, Egger M, *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;335:806–8.
35 Leyenaar JK, Ralston SL, Shieh M-S, *et al*. Epidemiology of pediatric hospitalizations at general hospitals and freestanding children's hospitals in the United States. *J Hosp Med* 2016;11:743–9.
36 McDaniel CE, Jennings R, Schroeder AR, *et al*. Aligning inpatient pediatric research with settings of care: a call to action. *Pediatrics* 2019;143:e20182648.