International Journal of Pediatric Otorhinolaryngology 190 (2025) 112242

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Pneumococcal revaccination in pediatric patients with sinusitis

William G. Cohen [a], Chau Phung [b], Dominick Rich [b], Fengling Hu [b,d], Jana Bradley [c], Mark D. Rizzi [b,c], Adva Buzi [b,c,*]

[a] Department of Otolaryngology- Head & Neck Surgery, Vanderbilt University Medical Center, Nashville, TN, USA
[b] Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
[c] Division of Otolaryngology, Children's Hospital of Philadelphia, Philadelphia, PA, USA
[d] Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, PA, USA

ARTICLE INFO

Keywords:
Pneumococcal
Booster
Sinusitis
Titer
Healthcare utilization

ABSTRACT

Objectives: In pediatric patients with sinusitis and suspected low pneumococcal antibody titers, we aimed to determine the association between a pneumococcal polysaccharide vaccine booster dose (PPSV23) and healthcare utilization.

Methods: Pediatric patients with a diagnosis of sinusitis, a PPSV23 booster dose, and pre-vaccine anti-pneumococcal antibody titers (age 2–16) were abstracted from the medical records system. Sinusitis-related healthcare encounters and antibiotic prescriptions were measured for 2 years before and after PPSV23 vaccination. A mixed effects negative binomial regression was utilized to compare pre and post-vaccine healthcare utilization while accounting for age and sex.

Results: A total of 233 patients were included in the study analysis. Mean age at pre-vaccination titer was 7.99 years (±3.83), 47 (20.2 %) were immunocompromised, and nearly all patients received the complete childhood pneumococcal vaccine series. When comparing pre and post-vaccination periods, encounters decreased from an average of 2.70 (95 % CI: [2.29, 3.10]) to 1.23 (95 % CI: [1.00, 1.46]). Antibiotic prescriptions decreased from 2.58 (95 % CI: [2.17, 2.98]) to 1.18 (95 % CI: [0.93, 1.42]). Mixed effects modeling demonstrated the number of encounters after vaccination decreased 51.1 % as compared to before vaccination (95 % CI: [42.9, 58.2], $p < 0.001$) and the number of antibiotic prescriptions decreased 51.3 % (95 % CI: [42.9 %, 58.6 %], $p < 0.001$). Among immunocompromised patients, encounters were decreased by 46.9 % (95 % CI: [26.2 %, 62.1 %], $p < 0.001$) and antibiotic prescriptions by 49.2 % (95 % CI: [28.5 %, 64.2 %], $p < 0.001$).

Conclusion: PPSV23 booster vaccination was associated with a significant decrease in sinusitis-related healthcare encounters and antibiotic use among pediatric patients, including those who are immunocompromised.

1. Introduction

Acute rhinosinusitis is one of the most common pediatric bacterial infections and a significant driver of healthcare utilization [1]. As of 1996, treatment for acute sinusitis in children under 12 resulted in $1.8 billion in healthcare spending [2]. Upper respiratory tract infections (URI) are common in young children, with subsequent acute sinusitis developing in 5–10 % of cases [3]. Antibiotic prescriptions frequently follow, occurring in 82 % of associated office visits [4]. Children with acute sinusitis not only suffer from common symptoms including rhinorrhea, nasal obstruction, fever, cough, headache and facial discomfort, but they are also at risk of severe sequelae including orbital or intracranial complications [5]. Quality of life impairments are significant and well documented, in both patients and parents, including missed school/work, impaired socialization, and increased stress [6–9].

The most common organisms implicated in acute bacterial rhinosinusitis are *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* [1,10–12]. In the conjugated-pneumococcal vaccine era, *S. pneumoniae* is implicated in ~30 % of cases of acute bacterial rhinosinusitis [10]. However, both before and after the introduction of conjugated-pneumococcal vaccines,

Abbreviations: CRS, Chronic Rhinosinusitis; CVID, Combined Variable Immunodeficiency; PPSV23, Pneumococcal Polysaccharide Vaccine 23; RARS, Recurrent Acute Rhinosinusitis; URI, Upper respiratory infection.

This article is part of a special issue entitled: ASPO Featured Manuscripts published in International Journal of Pediatric Otorhinolaryngology.

* Corresponding author. Division of Otolaryngology, Children's Hospital of Philadelphia, 3500 Civic Center Blvd, 5th Floor, Philadelphia, PA, 19104, USA.
E-mail address: Buzia@chop.edu (A. Buzi).

https://doi.org/10.1016/j.ijporl.2025.112242
Received 10 May 2024; Received in revised form 18 January 2025; Accepted 23 January 2025
Available online 26 January 2025

a subset of pediatric patients have been shown to generate ineffective long-term pneumococcal immunity as measured by anti-*S. pneumoniae* antibody titers [13–18]. Similar findings are well documented in adults [19–23]. Consequently, physicians have often obtained anti-*S. pneumoniae* titers in the setting of recurrent sinusitis and have administered a pneumococcal polysaccharide "booster" dose to increase immunity [13–15,21,23]. Despite evidence demonstrating that pneumococcal polysaccharide vaccine booster doses are effective in adults with sinusitis and low pneumococcal titers, no such evidence exists in pediatric patients [21,23].

In this study, we investigate healthcare utilization among pediatric patients diagnosed with sinusitis and low pneumococcal titers, both before and after receiving a pneumococcal booster vaccine [23]. We hypothesize that both health system encounters and antibiotic prescriptions will decrease after vaccination. However, we do not expect to see the same degree of benefit among immunocompromised patients.

2. Methods

2.1. Patient population

All patients included in this study were treated at a single, academic, tertiary referral children's hospital. Patients were initially identified through a database search of our integrated electronic medical records system, which also includes a wide regional network of hospital associated urgent care clinics, primary care clinics, and sub-specialty providers; criteria included a chart diagnosis of sinusitis and at least one set of anti-*S. pneumoniae* titers. The cohort was further narrowed to include only those with chart documentation of a pneumococcal polysaccharide booster vaccine (PPSV23) and pre-vaccination anti-*S. pneumoniae* titers drawn between the ages of 2–16 years. This study underwent institutional review board review at the Children's Hospital of Philadelphia and was determined to meet criteria for exempt status.

2.2. Data Collection

Following assessment of eligibility, medical records were reviewed for each patient to obtain demographic characteristics and determine comorbidities. Immunocompromised patients included those with a history of solid organ transplantation, DiGeorge Syndrome, Combined Variable Immunodeficiency (CVID), autoimmune disease requiring immunosuppression, those with documented hypogammaglobulinemia, and those with diagnosed or suspected primary immunodeficiencies. Anti-*S. pneumoniae* titers were classified as normal/abnormal. In children $\leq$5 years old, abnormal titers were defined as a concentration of $<$1.3 μg/mL in $>$50 % of pneumococcal serotypes [23,24]. In children $>$5 years old, abnormal titers were defined as a concentration of $<$1.3 μg/mL in $>$30 % of pneumococcal serotypes. Post-vaccination titers were only interpreted if obtained $<$1 year post-PPSV23 vaccination-the mean interval was 145.5 ($\pm$248.8) days after vaccination.

Healthcare encounters were defined as substantive interactions (ie: clinic visits, operative procedures, interaction with medication prescription) with the healthcare system related to sinusitis. Antibiotic prescriptions met criteria if chart documentation linked the prescription to a primary complaint or diagnosis of sinusitis. Encounters and antibiotic prescriptions were tabulated for the 24 months prior to PPSV23 vaccination and the 24 months following PPSV23 vaccination. Notes stipulating a specific number of encounters or prescriptions related to sinusitis in a specified period of time were counted in a time-adjusted manner. Use of antibiotic prophylaxis was not counted in the total number of antibiotic prescriptions, but is documented in the manuscript.

2.3. Data analysis

Two primary analyses were defined in this study – the association between vaccination and encounters as well as the association between vaccination and antibiotic use. Additionally, secondary analysis of these associations in the subgroup of immunocompromised patients was performed. Associations were estimated using a mixed effects negative binomial regression model with patient-specific random intercepts. While we considered a paired *t*-test, the mixed effects model was chosen to account for the longitudinal nature of our dataset (i.e. that encounters and antibiotic use were each measured twice per patient) while adjusting for covariates of age and sex. This is an attempt to control for the possibility that patients may "age out" of sinus disease over the four-year observation period [3]. Negative binomial regression with log-link function was used to account for the count-based nature of our outcomes, including the boundary condition of zero encounters and antibiotic prescriptions. A p-value less than 0.05 was considered statistically significant. No multiple comparison correction was performed. Data was processed utilizing STATA (Version 18, College Station, TX) and R version 4.3.0.

3. Results

3.1. Cohort demographics

Inclusion criteria were met by 233 patients. Cohort demographics, comorbidities, and titer results are presented in Table 1. The mean age at pre-vaccination titer was 7.99 years ($\pm$3.83) and a majority of patients were male (n = 131, 56.2 %). Twenty percent (n = 47) of the cohort was determined to be immunocompromised based on past medical history. Nearly all patients (n = 226, 97.0 %) received the complete childhood pneumococcal vaccine series.

Table 1
Cohort characteristics.

Variable	N(%) or Mean (SD)
Total Patients	233
Age at Pneumococcal Booster (Years)	8.23 ($\pm$3.93)
Sex	
Male	131 (56.2 %)
Female	102 (43.8 %)
Comorbidities	
Trisomy 21	8 (3.4 %)
Significant Congenital Heart Disease	10 (4.3 %)
Cystic Fibrosis	3 (1.3 %)
Primary Ciliary Dyskinesia	2 (0.9 %)
IgA Deficiency	17 (7.3 %)
Autoimmune Condition on Immunosuppression	6 (2.6 %)
Combined Variable Immunodeficiency (CVID)	13 (5.6 %)
DiGeorge Syndrome	11 (4.7 %)
History of Hematologic Malignancy	6 (2.6 %)
History of Stem Cell Transplant	9 (3.9 %)
History of Solid Organ Transplant	5 (2.1 %)
Other Immunodeficiency	18 (7.7 %)
Total Immunocompromised	47 (20.2 %)
Routine Childhood Pneumococcal Vaccines	
Yes	226 (97.0 %)
No	1 (0.4 %)
Partial	1 (0.4 %)
Unknown	5 (2.2 %)
Pre-Vaccination	
Age at Titer (Years)	7.99 ($\pm$3.83)
Abnormal Titer	219 (94.0 %)
Titer to Vaccine Interval (Days)	48.91 ($\pm$59.33)
Antibiotic Prophylaxis	33 (14.2 %)
Adenoidectomy[a]	83 (35.6 %)
Sinonasal Surgery[a]	20 (8.6 %)
Post-Vaccination	
Abnormal Titer (39 unknown)	25 (13.0 %)
Vaccine to Titer Interval (n = 192)	145.46 ($\pm$248.79)
Antibiotic Prophylaxis	59 (25.3 %)
Adenoidectomy	22 (9.4 %)
Sinonasal Surgery	8 (3.4 %)

[a] No time restriction.

3.2. Titers and immunologic vaccine response

All patients had pre-vaccination titers obtained, of whom 219 (94.0 %) met criteria for abnormal pneumococcal titers. PPSV23 was administered to all patients 48.91 days (±59.33) after titers were obtained. One hundred ninety-two (82.4 %) patients had post-vaccination titers drawn, of whom 25 (13.0 %) had persistent abnormal pneumococcal titers. The average time span between booster vaccine administration and post-vaccination titer was 145.46 days (±248.79).

3.3. Healthcare encounters and antibiotic use in the Overall cohort

Outcomes from primary analyses can be found in Table 2. In the two years prior to PPSV23 vaccination, patients had an average of 2.70 (95 % CI: [2.29, 3.10]) encounters secondary to sinusitis, with a cumulative total of 628 encounters. In the two years post PPSV23 vaccination, encounters decreased to an average of 1.23 (95 % CI: [1.00, 1.46]) and cumulative total of 287. With respect to antibiotic prescriptions, patients had an average of 2.58 (95 % CI: [2.17, 2.98]) prescriptions and cumulative total of 600 prescriptions prior to PPSV23 vaccination. Following PPSV23 vaccination, the average number of prescriptions dropped to 1.18 (95 % CI: [0.93, 1.42]) and the cumulative total declined to 274. Encounter and antibiotic histograms are presented in Fig. 1.

Subsequently, a mixed effects negative binomial regression model was utilized to estimate the association between vaccination and healthcare encounters and antibiotic use while accounting for age and sex. On average, the number of encounters after vaccination decreased by 51.1 % as compared to before vaccination (95 % CI: [42.9, 58.2], $p < 0.001$). Similarly, the average number of antibiotic prescriptions after vaccination decreased 51.3 % when compared to before vaccination (95 % CI: [42.9 %, 58.6 %], $p < 0.001$).

3.4. Healthcare encounters and antibiotic use among immunocompromised patients

In the two years prior to PPSV23 vaccination, immunocompromised patients had an average of 3.085 (95 % CI: [1.914, 4.256]) encounters secondary to sinusitis, with a cumulative total of 145 encounters. In the two years post PPSV23 vaccination, encounters decreased to an average of 1.681 (95 % CI: [0.936, 2.426]) and cumulative total of 79. With respect to antibiotic prescriptions, immunocompromised patients had an average of 3.021(95 % CI: [1.793, 4.250]) prescriptions and cumulative total of 142 prescriptions prior to PPSV23 vaccination. Following PPSV23 vaccination, the average number of prescriptions dropped to 1.553 (95 % CI: [0.809, 2.298]) and the cumulative total declined to 73.

Utilizing the mixed effects model, post-vaccination immunocompromised patients were found to have, on average, a 46.9 % decrease (95 % CI: [26.2 %, 62.1 %], $p < 0.001$) in encounters and a 49.2 % decrease (95 % CI: [28.5 %, 64.2 %], $p < 0.001$) in antibiotic prescriptions compared to pre-vaccination immunocompromised patients.

4. Discussion

Although low anti-pneumococcal antibody titers are a known risk factor for recurrent sinusitis, little data exists regarding the utility of pediatric pneumococcal booster vaccination [15,22,25]. In this study, we investigate the outcomes of 233 patients with sinusitis who received the PPSV23 vaccine, reporting the association between booster vaccination, healthcare encounters, and antibiotic utilization. Among patients in this cohort, PPSV23 vaccination was associated with a 51 % drop in sinusitis-related healthcare encounters and antibiotic use. Immunocompromised patients had a similar, though reduced, response, with a decrease of 47–49 %.

In 2021, Bareiss et al. published a similar study in adults, investigating the response to PPSV23 vaccination among patients with chronic rhinosinusitis (CRS) and recurrent acute rhinosinusitis (RARS) [23]. They demonstrated a high prevalence of non-protective pneumococcal antibody titers, with ~90 % responding appropriately to booster vaccination. Clinically, adult patients with CRS and RARS had a decrease in the number of healthcare encounters by 73 % and 49 % respectively [23]. Our pediatric cohort had a similar humoral response to revaccination, though underlying rates of non-protective titers cannot be compared. However, pediatric patients diverged clinically. Though they had a similar decrease in healthcare utilization to adults with RARS, adults with CRS responded more favorably. This divergence is unsurprising given the differences in age and underlying pathophysiology between adults and children [26]. Furthermore, while our cohort had a near parallel drop in healthcare encounters and antibiotic usage (~50 %), adults with both CRS and RARS only had a 19–21 % decrease [23]. A potential explanation for this discrepancy is the high rate of antibiotic use in the pediatric sinusitis population [4].

While past studies investigating PPSV23 booster vaccination in both pediatric and adult patients have demonstrated positive humoral responses, few have occurred after the addition of conjugated-pneumococcal vaccines to the routine childhood vaccination schedule [14,15,17,27]. Despite invasive pneumococcal disease being the primary target of vaccination, the pathogenesis of pediatric sinusitis and otitis media has changed as well, with decreased contributions from specific pneumococcal serotypes to acute infection [28–30]. When considering the previously described associations between pneumococcal vaccination and sinusitis and otitis media, the positive safety profile of PPSV23 vaccination, and our data demonstrating a ~50 % reduction in healthcare utilization after booster vaccination, PPSV23 booster vaccination may be a useful tool in pediatric cases of refractory or recurrent sinusitis, even among those with prior conjugated-pneumococcal vaccination [31].

This study has several important limitations to note. First, due to the retrospective, observational nature of our study and the absence of a control group to directly account for age, we are unable to conclusively state that PPSV23 vaccination was responsible for each patient's observed clinical changes. Despite this, our results closely mirror existing literature in the adult population and hopefully will promote further rigorous study of this intervention. Although we attempt to control for age in our mixed effects model, a randomized, prospective study design is necessary to fully account for age-related patterns in sinus disease and the natural disease course.

Additionally, patients both entered and left our health system over the course of four years; presumably, these patients sought care outside of our institution. Consequently, visits and antibiotic prescriptions were likely missed in our accounting, despite utilizing the history recorded in clinic notes and chart linkage with other institutions. However, this favors the null hypothesis given that patients with continued symptoms likely continued to seek tertiary level care, while those with improvement in symptoms would be more likely to return to their local health system. Furthermore, because there is no comparison group in our study and we assess relative change rather than absolute change pre/post vaccination, a fixed percentage of "missed" visits does not confound a comparison between an intervention and control group or alter a percentage improvement/worsening.

Due to the distributed nature of care among patients in our cohort,

Table 2
Changes in healthcare encounters and antibiotic courses.

Encounters (mean [95 % CI])		Antibiotic Prescriptions (mean [95 % CI])	
Pre-Vaccine (n = 628)	2.70 [2.29–3.10]	Pre-Vaccine (n = 600)	2.58 [2.17–2.98]
Post-Vaccine (n = 287)	1.23 [1.00–1.46]	Post-Vaccine (n = 274)	1.18 [0.93–1.42]
% Change (per model)	51.1 %* [42.9–58.2]	% Change (per model)	51.3 %* [42.9–58.6]

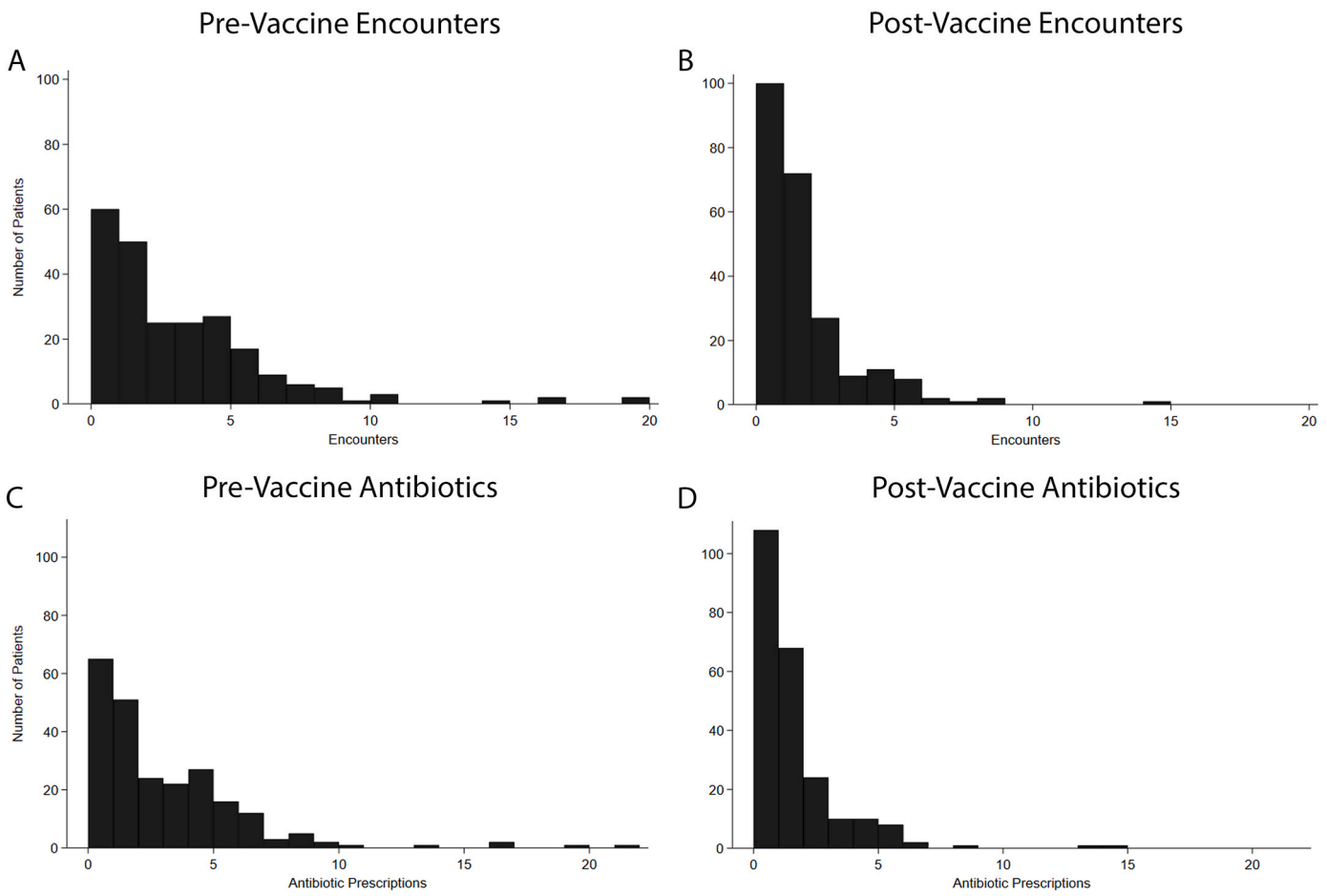

Fig. 1. Healthcare Encounters (A, B) and Antibiotic Prescriptions (C, D) before and after PPSV23 vaccination.

limited data granularity, and the retrospective nature of our study, no consistent criteria were utilized to diagnose sinusitis, distinguish between type of sinusitis, or prescribe medication. While this may limit the precision of our study, we believe it more accurately reflects the real-world conditions in which clinical decisions are being made, particularly in primary and urgent care settings. While the effects of pneumococcal vaccination on sinonasal symptoms beyond those required to meet the precise diagnostic standards of acute and chronic rhinosinusitis are not known, we assert that the association between PPSV23 provision in children diagnosed with "sinusitis" and reduced health care utilization is worthy of reporting, even if incompletely understood.

Lastly, our cohort included a large percentage of immunocompromised patients, likely secondary to broad inclusion criteria and our center's referral pattern. This may limit the generalizability of our results. However, our general cohort and immunocompromised subpopulation had similar response rates to vaccination. Given that we would expect immunocompromised patients to have reduced vaccination response relative to a healthy peer, we hypothesize that the general population may have a more robust vaccination response and that our study population would be biased towards the null hypothesis.

5. Conclusions

Booster vaccination with PPSV23 among pediatric patients with sinusitis may be associated with a decrease in sinusitis related healthcare encounters and antibiotic use by up to 51 %. Among immunocompromised patients, PPSV23 may also be associated with decreased sinus related healthcare encounters and antibiotic use. Future studies should involve a randomized, prospective trial of PPSV23 booster vaccination in this cohort to more precisely assess its effects.

CRediT authorship contribution statement

William G. Cohen: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Chau Phung:** Writing – review & editing, Investigation. **Dominick Rich:** Writing – review & editing, Investigation. **Fengling Hu:** Writing – review & editing, Methodology, Formal analysis. **Jana Bradley:** Writing – review & editing, Investigation. **Mark D. Rizzi:** Writing – review & editing, Methodology. **Adva Buzi:** Conceptualization, Methodology, Supervision, Writing - review & editing.

Funding

No financial support

Declaration of competing interest

The authors have no conflicts to disclose.

Acknowledgements

None.

References

[1] S.J. Alter, N.K. Vidwan, P.O. Sobande, A. Omoloja, J.S. Bennett, Common childhood bacterial infections, Curr. Probl. Pediatr. Adolesc. Health Care 41 (10) (2011) 256–283, https://doi.org/10.1016/j.cppeds.2011.06.001.

[2] N.F. Ray, J.N. Baraniuk, M. Thamer, et al., Healthcare expenditures for sinusitis in 1996: contributions of asthma, rhinitis, and other airway disorders, J. Allergy Clin. Immunol. 103 (3) (1999) 408–414, https://doi.org/10.1016/S0091-6749(99)70464-1.
[3] K. Revai, L.A. Dobbs, S. Nair, J.A. Patel, J.J. Grady, T. Chonmaitree, Incidence of acute otitis media and sinusitis complicating upper respiratory tract infection: the effect of age, Pediatrics 119 (6) (2007) e1408–e1412, https://doi.org/10.1542/peds.2006-2881.
[4] D.J. Shapiro, R. Gonzales, M.D. Cabana, A.L. Hersh, National trends in visit rates and antibiotic prescribing for children with acute sinusitis, Pediatrics 127 (1) (2011) 28–34, https://doi.org/10.1542/peds.2010-1340.
[5] C.C. Nocon, F.M. Baroody, Acute rhinosinusitis in children, Curr. Allergy Asthma Rep. 14 (6) (2014) 443, https://doi.org/10.1007/s11882-014-0443-7.
[6] M.J. Cunningham, E.J. Chiu, J.M. Landgraf, R.E. Gliklich, The health impact of chronic recurrent rhinosinusitis in children, Arch Otolaryngol Neck Surg 126 (11) (2000) 1363, https://doi.org/10.1001/archotol.126.11.1363.
[7] D.J. Kay, R.M. Rosenfeld, Quality of life for children with persistent sinonasal symptoms, Otolaryngol Neck Surg 128 (1) (2003) 17–26, https://doi.org/10.1067/mhn.2003.41.
[8] E.O. Meltzer, Quality of life in adults and children with allergic rhinitis, J. Allergy Clin. Immunol. 108 (1) (2001) S45–S53, https://doi.org/10.1067/mai.2001.115566.
[9] E.F. Rudnick, R.B. Mitchell, Improvements in quality of life in children after surgical therapy for sinonasal disease, Otolaryngol Neck Surg 134 (5) (2006) 737–740, https://doi.org/10.1016/j.otohns.2005.12.033.
[10] S. Sawada, S. Matsubara, Microbiology of acute maxillary sinusitis in children, Laryngoscope 131 (10) (2021), https://doi.org/10.1002/lary.29564.
[11] G.P. DeMuri, E.R. Wald, Acute bacterial sinusitis in children, N. Engl. J. Med. 367 (12) (2012) 1128–1134, https://doi.org/10.1056/NEJMcp1106638.
[12] J. Gwaltneyjr, W. Scheld, M. Sande, A. Sydnor, The microbial etiology and antimicrobial therapy of adults with acute community-acquired sinusitis: a fifteen-year experience at the University of Virginia and review of other selected studies, J. Allergy Clin. Immunol. 90 (3) (1992) 457–462, https://doi.org/10.1016/0091-6749(92)90169-3.
[13] H.A.S. Ingels, B. Kantsø, H.C. Slotved, Serologic response to pneumococcal vaccination in children experiencing recurrent invasive pneumococcal disease, BMC Infect. Dis. 18 (1) (2018) 366, https://doi.org/10.1186/s12879-018-3267-6.
[14] H. Hidalgo, C. Moore, L.E. Leiva, R.U. Sorensen, Preimmunization and postimmunization pneumococcal antibody titers in children with recurrent infections, Ann. Allergy Asthma Immunol. 76 (4) (1996) 341–346, https://doi.org/10.1016/S1081-1206(10)60035-X.
[15] L. Sanders, G. Rijkers, W. Kuis, et al., Defective antipneumococcal polysaccharide antibody response in children with recurrent respiratory tract infections, J. Allergy Clin. Immunol. 91 (1) (1993) 110–119, https://doi.org/10.1016/0091-6749(93)90303-W.
[16] D. Tuerlinckx, F. Vermeulen, V. Pékus, et al., Optimal assessment of the ability of children with recurrent respiratory tract infections to produce anti-polysaccharide antibodies, Clin. Exp. Immunol. 149 (2) (2007) 295–302, https://doi.org/10.1111/j.1365-2249.2007.03409.x.
[17] O. Ruuskanen, A. Nurkka, M. Helminen, M.K. Viljanen, H. Käyhty, L. Kainulainen, Specific antibody deficiency in children with recurrent respiratory infections: a controlled study with follow-up, Clin. Exp. Immunol. 172 (2) (2013) 238–244, https://doi.org/10.1111/cei.12053.
[18] C.A. Makary, P.R. Purnell, D. O'Brien, R. Chaiban, Y.Y. Demirdağ, H. Ramadan, Antibody deficiencies are more common in adult versus pediatric recurrent acute rhinosinusitis, Am. J. Otolaryngol. 42 (5) (2021) 103004, https://doi.org/10.1016/j.amjoto.2021.103004.
[19] A. Keswani, N.M. Dunn, A. Manzur, et al., The clinical significance of specific antibody deficiency (SAD) severity in chronic rhinosinusitis (CRS), J. Allergy Clin. Immunol. Pract. 5 (4) (2017) 1105–1111, https://doi.org/10.1016/j.jaip.2016.11.033.
[20] T.F. Carr, A.P. Koterba, R. Chandra, et al., Characterization of specific antibody deficiency in adults with medically refractory chronic rhinosinusitis, Am J Rhinol Allergy. 25 (4) (2011) 241–244, https://doi.org/10.2500/ajra.2011.25.3653.
[21] S. Kashani, T.F. Carr, L.C. Grammer, et al., Clinical characteristics of adults with chronic rhinosinusitis and specific antibody deficiency, J. Allergy Clin. Immunol. Pract. 3 (2) (2015) 236–242, https://doi.org/10.1016/j.jaip.2014.09.022.
[22] M. Alqudah, S.M. Graham, Z.K. Ballas, High prevalence of humoral immunodeficiency patients with refractory chronic rhinosinusitis, Am J Rhinol Allergy. 24 (6) (2010) 409–412, https://doi.org/10.2500/ajra.2010.24.3532.
[23] A.K. Bareiss, N. Kattar, R. Tivis, et al., Health-care utilization for sinusitis after pneumococcal vaccination in patients with low antibody titers, Int Forum Allergy Rhinol 12 (8) (2022) 1018–1024, https://doi.org/10.1002/alr.22954.
[24] R.U. Sorensen, L.E. Leiva, P.A. Giangrosso, et al., Response to a heptavalent conjugate Streptococcus pneumoniae vaccine in children with recurrent infections who are unresponsive to the polysaccharide vaccine, Pediatr. Infect. Dis. J. 17 (8) (1998) 685–691, https://doi.org/10.1097/00006454-199808000-00005.
[25] C. Li, T. Peng Hwa, E. Schussler, A.N. Pearlman, Immunologic evaluation of pediatric chronic and recurrent acute rhinosinusitis, Am J Rhinol Allergy 34 (1) (2020) 93–99, https://doi.org/10.1177/1945892419875088.
[26] K. Snidvongs, M. Sangubol, O. Poachanukoon, Pediatric versus adult chronic rhinosinusitis, Curr. Allergy Asthma Rep. 20 (8) (2020) 29, https://doi.org/10.1007/s11882-020-00924-6.
[27] Child and Adolescent Immunization Schedule by Age. Published online November 16, 2023. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html.
[28] L. Olarte, K.G. Hulten, L. Lamberth, E.O. Mason, S.L. Kaplan, Impact of the 13-valent pneumococcal conjugate vaccine on chronic sinusitis associated with Streptococcus pneumoniae in children, Pediatr. Infect. Dis. J. 33 (10) (2014) 1033–1036, https://doi.org/10.1097/INF.0000000000000387.
[29] S. Ben-Shimol, N. Givon-Lavi, E. Leibovitz, S. Raiz, D. Greenberg, R. Dagan, Impact of widespread introduction of pneumococcal conjugate vaccines on pneumococcal and nonpneumococcal otitis media, Clin. Infect. Dis. 63 (5) (2016) 611–618, https://doi.org/10.1093/cid/ciw347.
[30] I. Brook, A.E. Gober, Frequency of recovery of pathogens from the nasopharynx of children with acute maxillary sinusitis before and after the introduction of vaccination with the 7-valent pneumococcal vaccine, Int. J. Pediatr. Otorhinolaryngol. 71 (4) (2007) 575–579, https://doi.org/10.1016/j.ijporl.2006.10.025.
[31] W. Orenstein, P. Offit, K. Edwards, S. Plotkin, Pneumococcal polysaccharide vaccines, in: Vaccines, eighth ed., Elsevier, 2024, pp. 869–889.