Original article

doi:10.5633/amm.2026.0424

SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASES: A CASE OF PNEUMOCOCCAL MENINGITIS AND SEROTYPE DISTRIBUTION IN A PRESCHOOL INSTITUTION

Miloš Bogoslović[1], Zorana Deljanin[2], Marina Kostić[2], Vladana Nikolić[3], Milica Jovanović[1]

[1]Primary Health Care Center Doljevac, Department of Child and Adolescent Health Care, Doljevac, Serbia

[2]Institute of Public Health Niš, Niš, Serbia

[3]University Clinical Center Niš, Clinic of Pediatrics, Niš, Serbia

Contact: Bogoslović Miloš

11/67 Romanijska Str., 18000 Niš, Serbia

E-mail: milosbogoslovic@gmail.com

Abstract

Invasive pneumococcal diseases (IPD) remain a significant public health challenge despite routine use of pneumococcal conjugate vaccines. The aim of this study was to analyze a case of pneumococcal meningitis in a preschool setting, including assessment of nasopharyngeal carriage, serotype distribution, vaccination status, and epidemiological implications.

After confirmation of pneumococcal meningitis in a child in December 2025, active epidemiological surveillance was conducted in the preschool institution “Lane” in Pukovac, Municipality of Doljevac. Nasopharyngeal swabs were collected from 44 children and 6 adults (n = 50). Serotyping of isolates was performed at the National Reference Laboratory for Streptococci, Institute of Microbiology and Immunology, Faculty of Medicine, University of Belgrade. Colonization prevalence and 95% confidence intervals (CI) were calculated using the Wilson method. Group comparisons were performed using Fisher’s exact test. The odds ratio (OR) with 95% confidence intervals (CI) was calculated.

Serotype 24B was isolated from both blood and cerebrospinal fluid of the hospitalized child. Among close contacts, serotypes 15B (n=2), 23A (n=2), 21 (n=2), and 29 (n=5) were identified. The overall pneumococcal carriage prevalence was 22% (11/50; 95% CI: 12.6–35.1%). All colonized children had been fully vaccinated with PCV10 and/or PCV13. All detected carriage serotypes were non-vaccine types

(100%; 95% CI: 75.7–100.0%). No statistically significant difference in carriage was observed between children and adults (OR=1.47; 95% CI: 0.15–14.0; p=1.00).

The invasive disease was caused by a non-vaccine serotype (24B), while multiple non-vaccine serotypes were circulating within a highly vaccinated population. These findings support the presence of serotype replacement and underscore the importance of continuous serotype surveillance and consideration of higher-valent pneumococcal vaccines.

Keywords: pneumococcal meningitis, *streptococcus pneumoniae*, serotype replacement, pneumococcal conjugate vaccines, epidemiological surveillance

Originalni rad

doi:10.5633/amm.2026.0424

NADZOR NAD INVAZIVNIM PNEUMOKOKNIM BOLESTIMA: SLUČAJ PNEUMOKOKNOG MENINGITISA I DISTRIBUCIJA SEROTIPOVA U PREDŠKOLSKOJ USTANOVI

Miloš Bogoslović[1], Zorana Deljanin[2], Marina Kostić[2], Vladana Nikolić[3], Milica Jovanović[1]

[1]Dom zdravlja Doljevac, Služba za zdravstvenu zaštitu dece i omladine, Doljevac, Srbija

[2]Institut za javno zdravlje Niš, Niš, Srbija

[3]Univerzitetski klinički centar Niš, Klinika za pedijatriju, Niš, Srbija

Kontakt: Bogoslović Miloš

Romanijska 11/67, 18000 Niš, Srbija

E-mail: milosbogoslovic@gmail.com

Invazivne pneumokokne bolesti (IPB) i dalje predstavljaju značajan javnozdravstveni izazov uprkos rutinskoj primeni konjugovanih pneumokoknih vakcina. Cilj rada bio je analiza slučaja pneumokoknog meningitisa u predškolskoj ustanovi, uz procenu nazofaringealne kolonizacije, serotipske distribucije, vakcinalnog statusa i epidemioloških implikacija.

Nakon potvrde pneumokoknog meningitisa kod deteta u decembru 2025. godine, sproveden je aktivni epidemiološki nadzor u vrtiću „Lane" u Pukovcu, opština Doljevac. Nazofaringealni brisevi uzeti su od 44 dece i 6 odraslih (n=50). Serotipizacija izolata izvršena je u Nacionalnoj referentnoj laboratoriji za streptokok Instituta za mikrobiologiju i imunologiju, Medicinskog fakulteta u Beogradu. Prevalencija kolonizacije i 95% interval poverenja (CI) izračunati su Wilson metodom. Poređenje grupa sprovedeno je Fisher-ovim egzaktnim testom. Izračunat je odds ratio (OR) sa 95% CI.

Serotip 24B izolovan je iz krvi i likvora hospitalizovanog deteta. Kod kontakata su identifikovani serotipovi 15B (n=2), 23A (n=2), 21 (n=2) i 29 (n=5). Prevalencija pneumokoknog kliconoštva iznosila je 22% (11/50; 95% CI: 12,6–35,1%). Sva deca sa izolovanim pneumokokom bila su uredno vakcinisana PCV10 i/ili PCV13 vakcinama. Svi identifikovani serotipovi kod kontakata bili su nevakcinalni (100%; 95% CI: 75,7–100,0%). Nije utvrđena statistički značajna razlika u kolonizaciji između dece i odraslih (OR=1,47; 95% CI: 0,15–14,0; p=1,00).

Invazivna bolest nastala je usled nevakcinalnog serotipa 24B, dok je u kolektivu potvrđena cirkulacija više nevakcinalnih serotipova u visoko vakcinisanoj populaciji. Nalazi ukazuju na prisustvo serotipske zamene i naglašavaju značaj kontinuiranog serotipskog nadzora, kao i razmatranje vakcina proširenog serotipskog obuhvata.

Ključne reči: pneumokokni meningitis, *streptococcus pneumoniae,* serotipska zamena, konjugovane vakcine, epidemiološki nadzor

Introduction

Streptococcus pneumoniae is a Gram-positive, encapsulated diplococcus and one of the leading causes of invasive bacterial infections worldwide, with particular importance in the pediatric population (1). The polysaccharide capsule represents the key virulence factor and the basis for serotype classification of this pathogen. To date, more than 100 serotypes have been identified, however only a limited number account for the majority of invasive pneumococcal diseases (IPD), including bacteremia, pneumonia, and meningitis (2).

Nasopharyngeal colonization with pneumococcus is common among preschool children and constitutes the principal reservoir for community transmission (3). Colonization is most often asymptomatic; however, it is a prerequisite for the development of invasive disease. The progression from colonization to invasive infection depends on the interaction between bacterial virulence factors, host immune status, and environmental determinants. Attendance in collective settings, such as preschool institutions, significantly increases colonization rates and facilitates the circulation of diverse serotypes (4).

Pneumococcal bacterial meningitis remains a medical emergency associated with substantial mortality and a high risk of long-term neurological sequelae, particularly in younger children (5). Despite advances in intensive care and antimicrobial therapy, pneumococcus continues to be one of the predominant causes of bacterial meningitis in the post-Haemophilus influenzae type b (Hib) vaccine era (6). Long-term complications include sensorineural hearing loss, epilepsy, and persistent cognitive impairment.

The introduction of pneumococcal conjugate vaccines (PCV10 and PCV13) has led to a significant reduction in the incidence of invasive disease caused by vaccine serotypes, accompanied by a pronounced herd immunity effect (7,8). However, extended epidemiological surveillance has identified the phenomenon of serotype replacement, characterized by an increasing prevalence of non-vaccine serotypes in the etiology of invasive disease (9,10). These shifts have prompted the development of expanded-valency vaccines (PCV15 and PCV20), representing a new phase in pneumococcal disease prevention (11–13). In addition to changes in serotype distribution, the growing antimicrobial resistance of pneumococcus constitutes a major global public health challenge. Resistance to penicillin, macrolides, and third-generation cephalosporins has been documented in numerous regions worldwide (14). The interaction between vaccination and antimicrobial resistance is complex: while vaccination reduces the circulation of certain resistant vaccine serotypes, it may simultaneously allow expansion of non-vaccine serotypes with diverse susceptibility profiles (15).

Within our setting, the analysis of invasive pneumococcal disease in a local collective environment, combined with parallel assessment of nasopharyngeal colonization and serotype distribution, represents a valuable epidemiological model for evaluating the effectiveness of immunization programs and guiding future public health interventions.

Materials and Methods

An observational, cross-sectional epidemiological study was conducted in a preschool institution, kindergarten “Lane” in Pukovac, Municipality of Doljevac, following laboratory confirmation of a case of pneumococcal meningitis in a child in December 2025. The investigation was designed as an active epidemiological surveillance study within a collective setting, aiming to identify nasopharyngeal colonization with Streptococcus pneumoniae and to assess serotype distribution.

A total of 50 participants were included, comprising 44 children and 6 adult staff members employed at the preschool facility. Nasopharyngeal swabs were collected using standard microbiological sampling techniques in accordance with current respiratory tract sampling guidelines. Data on vaccination status were obtained from official medical records. Isolation of Streptococcus pneumoniae was performed using standard bacteriological methods. Serotyping of confirmed isolates was performed at the National Reference Laboratory for Streptococci, Institute of Microbiology and Immunology, Faculty of Medicine,

University of Belgrade, using validated serological methods. The results were analyzed in the context of coverage provided by currently available pneumococcal conjugate vaccines. The prevalence of nasopharyngeal colonization was calculated as the proportion of positive findings relative to the total number of participants. A 95% confidence interval (95% CI) was estimated using the Wilson method for binomial proportions. Differences in colonization rates between children and adults were analyzed using Fisher's exact test due to the small sample size in one subgroup. The odds ratio (OR) with a 95% CI was calculated using the Woolf method. Statistical significance was defined at the level of $p < 0.05$.

This study has several methodological limitations. The relatively small sample size—particularly in the adult group—reduces statistical power and results in wide confidence intervals. The single-center design, limited to one preschool institution, may restrict external validity and generalizability of the findings. Incomplete antimicrobial susceptibility analysis represents an additional limitation, as phenotypic resistance testing was not performed for all isolates, thereby limiting detailed assessment of the local antimicrobial resistance profile. The cross-sectional design precludes longitudinal follow-up of colonization dynamics and assessment of carriage duration. Furthermore, potential external transmission factors—such as household contacts, prior respiratory infections, and other determinants influencing transmission—were not systematically analyzed.

Despite these limitations, the study provides valuable local epidemiological data and contributes to sentinel surveillance of invasive pneumococcal disease in a highly vaccinated population.

Results

Within the epidemiological surveillance framework, the immunization status of 12 individuals with isolated Streptococcus pneumoniae was analyzed (11 children and 1 adult – a preschool teacher). In the hospitalized child (D.M., born in 2022), invasive pneumococcal disease was confirmed, with Streptococcus pneumoniae serotype 24B isolated from both blood and cerebrospinal fluid. According to available medical records, the child had been fully vaccinated in accordance with the national immunization schedule: PREVENAR13 – 18 August 2022, PREVENAR13 – 22 October 2022, PREVENAR13 – 15 March 2023, SYNFLORIX – 11 June 2024. The child received complete primary immunization and an age-appropriate booster vaccination. Serotype 24B is not included in PCV10 (Synflorix) or PCV13 (Prevenar13). This finding confirms the occurrence of invasive disease caused by a non-vaccine serotype rather than vaccine failure. Analysis of the immunization status of colonized individuals showed that all 11 colonized children had been appropriately vaccinated with PCV10 and/or PCV13 vaccines. The single colonized adult (preschool teacher) had not received pneumococcal vaccination (Table 1).

Table 1. Distribution of Serotypes Among Vaccinated Children

Serotype	Number of cases (n)	Vaccinated	Unvaccinated
15B	2	2	0
21	2	2	0
23A	1 child	1	0
29	5	5	0
23A	1 adult	0	1

Among children, PREVENAR13 (PCV13) and SYNFLORIX (PCV10) were administered. Most children received a combination of PCV10 and PCV13 according to the national immunization schedule and vaccine availability at the time of birth. Importantly: Serotype 15B → not included in PCV10/PCV13,

Serotype 21 → not included in PCV10/PCV13, Serotype 23A → not included in PCV10/PCV13, Serotype 29 → not included in PCV10/PCV13, Serotype 24B → not included in PCV10/PCV13, Serotype 15B → included in PCV20.

Epidemiological interpretation indicates high vaccine coverage within the collective and absence of immunization gaps. The circulation of non-vaccine serotypes clearly reflects the phenomenon of serotype replacement. Notably, 100% of children with isolated pneumococcus were fully vaccinated, and the invasive case occurred due to a serotype not covered by currently used pediatric vaccines.

Out of 50 tested individuals (44 children and 6 adults), nasopharyngeal colonization with Streptococcus pneumoniae was detected in 11 participants (22.0%; 95% CI: 12.6–35.1%). Specifically, 10/44 children (22.7%) and 1/6 adults (16.7%) were colonized. No statistically significant difference in colonization rates was observed between children and adults (OR = 1.47; 95% CI: 0.15–14.0; $p > 0.05$) (Figure 1).

In addition to S. pneumoniae, other respiratory pathogens were identified: Moraxella catarrhalis – 9 cases (18.0%), Haemophilus influenzae – 2 cases (4.0%). Negative findings – 30 participants (60.0%) (Figure 2).

Regarding serotype distribution among contacts, the following serotypes were identified: Serotype 29 – 5 isolates (45.5%), Serotype 15B – 2 isolates (18.2%), Serotype 23A – 2 isolates (18.2%), Serotype 21 – 2 isolates (18.2%) (Figures 3 and 4). All serotypes isolated among contacts were non-vaccine serotypes in relation to PCV10 and PCV13 (100%; 95% CI: 75.7–100.0%). In the context of expanded-spectrum vaccines: Serotype 15B is included in PCV20, PCV21, and PPV23. Serotype 23A is included in PCV21 (for adults ≥18 years). Serotypes 21 and 29 are not covered by PCV13. The dominant serotype within the collective was serotype 29 (45.5%), which is not covered by the standard PCV13 vaccine.

Epidemiological indicators in our study demonstrate that the hospitalized meningitis case (serotype 24B) differed from the serotypes isolated in the collective. High serotype heterogeneity was observed among isolates. Importantly, 100% compliance with mandatory childhood immunization was confirmed. Statistical analysis and epidemiological surveillance findings confirm that pneumococcal colonization prevalence in the collective was 22%, the dominant serotype was 29 (45.5%), no statistically significant difference existed between children and adults (OR 1.47; $p > 0.05$), the isolated serotypes were largely not covered by PCV13, and the recommendation for implementation of broader-spectrum vaccines (PCV20) is epidemiologically justified (Table 2).

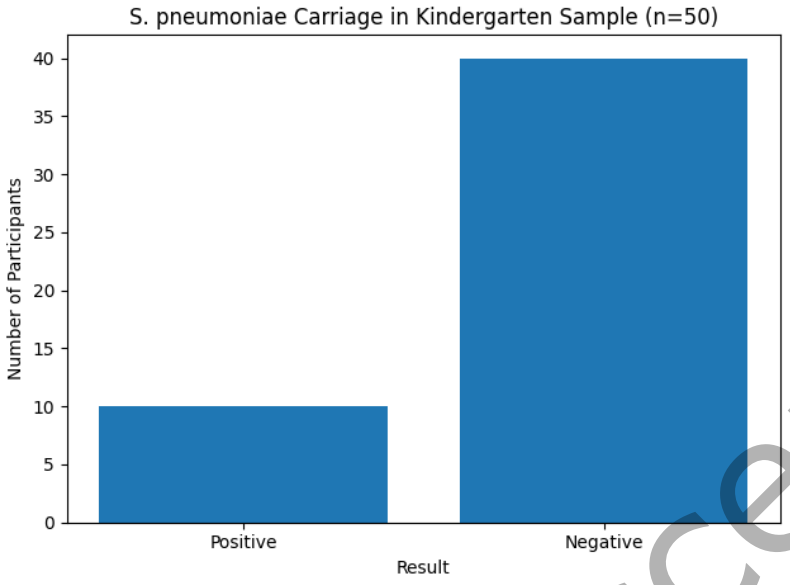

Figure 1. Prevalence of Carriage in the Preschool Sample

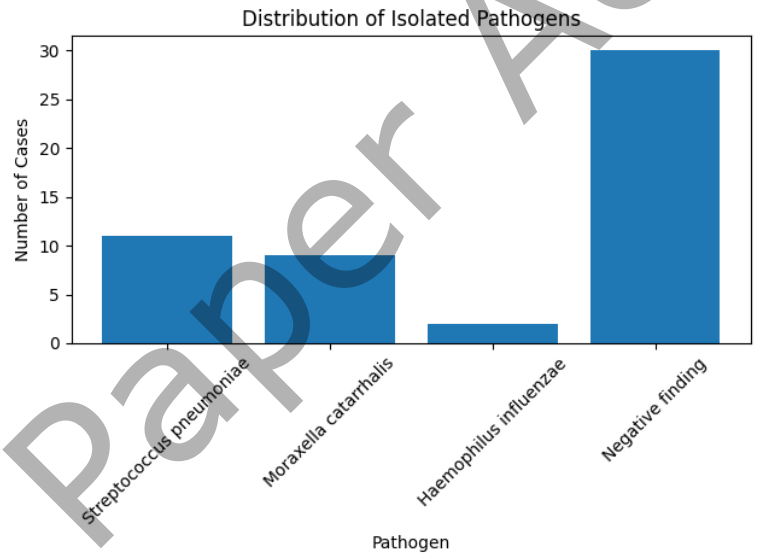

Figure 2. Distribution of Isolated Pathogens

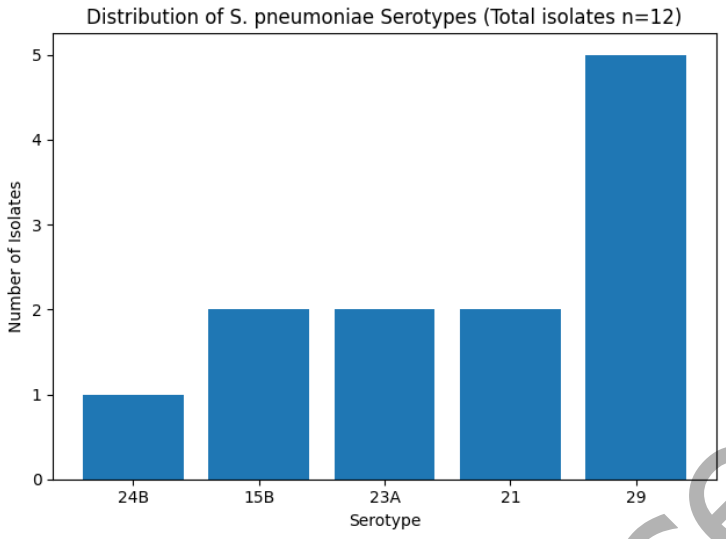

Figure 3. Distribution of Streptococcus pneumoniae Serotypes Among Isolates

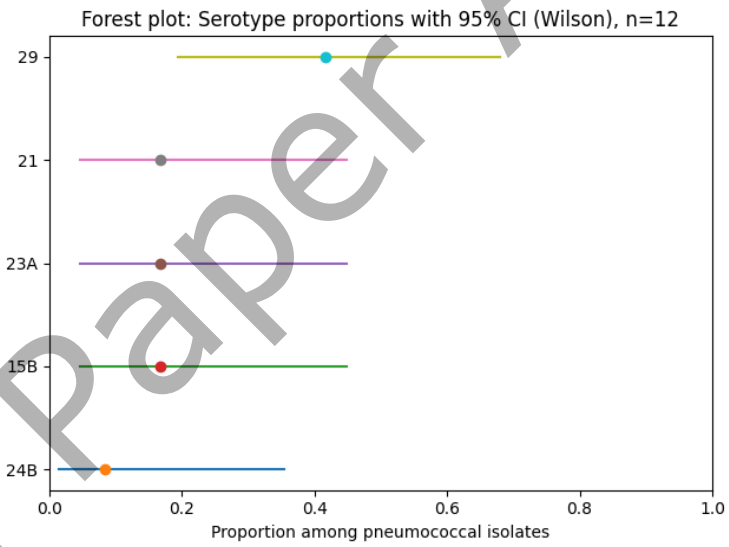

Figure 4. Proportion of Serotypes Among Pneumococcal Isolates

Table 2. Key Epidemiological Indicators

Sample (n)	50
Positive for S. pneumoniae (n)	11
Prevalence (%)	22,0
95% CI (%)	12,6–35,1
Total isolates (n)	12
Non-vaccine serotypes (%)	100,0
95% CI for 100% (%)	75,7–100,0

Discussion

The findings of this study confirm the occurrence of invasive pneumococcal disease caused by a non-vaccine serotype in a population with high vaccination coverage, consistent with the globally documented phenomenon of serotype replacement (16). The identification of serotype 24B in the hospitalized child, alongside the simultaneous circulation of multiple non-vaccine serotypes within the collective (15B, 21, 23A, and 29), reflects contemporary epidemiological trends described in the post-PCV13 era (17,18). Following the widespread implementation of PCV10 and PCV13, most European countries have reported a substantial decline in invasive pneumococcal disease (IPD) caused by vaccine serotypes, accompanied by a proportional increase in non-vaccine serotypes (19,20). This redistribution represents an expected ecological response of the pneumococcal population to vaccination-induced selective pressure (16). According to data from the European Centre for Disease Prevention and Control, the incidence of IPD in the European Union ranges between 4 and 15 cases per 100,000 population annually, with the highest rates observed among children under five years of age and adults aged 65 years and older (21). In several countries, post-PCV13 surveillance has documented increases in serotypes 8, 12F, 22F, 15A, and 23B, underscoring the dynamic adaptation of circulating strains (19). Our results, demonstrating 100% prevalence of non-vaccine serotypes among colonized individuals, align with this broader European pattern. Although serotypes 24B, 21, and 29 are not among the most common global invasive types, their presence in a highly vaccinated population further confirms that vaccination-driven selective pressure influences serotype structure (17,18). The World Health Organization emphasizes that pneumococcus remains a leading cause of vaccine-preventable mortality among children under five years of age in low- and middle-income countries (22). While European countries have achieved significant reductions in mortality, regional differences in serotype distribution and vaccine coverage persist. The issue of antimicrobial resistance adds further complexity. Streptococcus pneumoniae has been designated a priority pathogen within global antimicrobial resistance strategies (22). According to the European Centre for Disease Prevention and Control, macrolide resistance in certain European countries exceeds 25%, while reduced susceptibility to penicillin ranges between 5% and 20%, depending on the region and prevailing serotypes (21). The interaction between serotype replacement and antimicrobial resistance may complicate therapeutic management, particularly in severe invasive infections such as bacterial meningitis (23).

The development of expanded-valency vaccines represents a strategic response to these epidemiological shifts. PCV15 includes additional serotypes 22F and 33F, whereas PCV20 provides broader coverage, including serotype 15B. In our study, serotype 15B—covered by PCV20—was identified among colonized contacts, suggesting potential benefits of broader-spectrum vaccines in specific epidemiological contexts. Nevertheless, even PCV20 does not include all emerging serotypes, such as 24B, highlighting

that complete elimination of pneumococcal disease remains an unrealistic objective at present (24). Despite its local scope, our study has broader epidemiological relevance, as it demonstrates that global trends in serotype redistribution are mirrored at the community level. Local sentinel surveillance data are essential for national immunization programs, enabling timely assessment of the need for vaccine policy adjustments and optimization of surveillance strategies.

Conclusion

In this study, invasive pneumococcal disease was identified in a fully vaccinated child and was caused by a non-vaccine serotype, confirming the presence of serotype replacement in a population with high vaccination coverage. Analysis of immunization records revealed no deficiencies in the implementation of the mandatory national immunization program and no evidence of declining vaccine uptake. The concurrent identification of nasopharyngeal carriage of non-vaccine serotypes within the collective further indicates dynamic serotype redistribution in the post-PCV10/PCV13 era. These findings underscore the importance of continuous serotype surveillance, integrated with antimicrobial resistance monitoring, as a critical tool for evaluating the effectiveness of immunization strategies. In light of the identified serotypes, consideration of introducing expanded-valency vaccines, such as PCV20, may represent a rational public health measure aligned with the local epidemiological context.

References

1.O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009;374(9693):893–902. doi:10.1016/S0140-6736(09)61204-6

2.Hausdorff WP, Bryant J, Paradiso PR, Siber GR. Which pneumococcal serogroups cause the most invasive disease? Implications for conjugate vaccine formulation. Clin Infect Dis. 2000;30(1):100–121. doi:10.1086/313608

3.World Health Organization. Pneumococcal vaccines WHO position paper – 2019. Wkly Epidemiol Rec. 2019;94(8):85–104.

4.Balsells E, Guillot L, Nair H, Kyaw MH. Serotype distribution of invasive pneumococcal disease in children before and after conjugate vaccine introduction: global review. PLoS One. 2017;12(4):e0177113. doi:10.1371/journal.pone.0177113

5.Thigpen MC, Whitney CG, Messonnier NE, Zell ER, Lynfield R, Hadler JL, et al. Bacterial meningitis in the United States, 1998–2007. N Engl J Med. 2011;364(21):2016–2025. doi:10.1056/NEJMoa1005384

6.Metcalf BJ, Gertz RE Jr, Gladstone RA, Walker H, Sherwood LK, Jackson D, et al. Strain features and distributions in pneumococcal meningitis before and after PCV13 introduction. Clin Infect Dis. 2016;63(6):718–725. doi:10.1093/cid/ciw390

7.Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med. 2003;348(18):1737–1746. doi:10.1056/NEJMoa022823

8.Moore MR, Link-Gelles R, Schaffner W, Lynfield R, Lexau C, Bennett NM, et al. Effect of use of 13-valent pneumococcal conjugate vaccine in children on invasive pneumococcal disease in children and adults in the USA. Lancet Infect Dis. 2015;15(3):301–309. doi:10.1016/S1473-3099(14)71081-3

9.Ladhani SN, Collins S, Djennad A, Sheppard CL, Borrow R, Fry NK, et al. Rapid increase in non-vaccine serotypes causing invasive pneumococcal disease in England and Wales after PCV13 introduction. Lancet Infect Dis. 2018;18(4):441–451. doi:10.1016/S1473-3099(18)30052-5

10.Gladstone RA, Devine V, Jones J, et al. Impact of pneumococcal conjugate vaccines on antimicrobial resistance and serotype replacement. Lancet Microbe. 2021;2(10):e459–e468. doi:10.1016/S2666-5247(21)00138-3

11.Senders S, Klein NP, Lamberth E, et al. Safety and immunogenicity of a 15-valent pneumococcal conjugate vaccine in infants. Pediatrics. 2021;148(5):e2021051407. doi:10.1542/peds.2021-051407

12.Essink B, Sabharwal C, Xu X, et al. Pivotal phase 3 randomized study of a 20-valent pneumococcal conjugate vaccine in adults. Clin Infect Dis. 2022;75(3):390–398. doi:10.1093/cid/ciab990

13.Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent and 20-valent pneumococcal conjugate vaccines among adults: updated ACIP recommendations. MMWR Morb Mortal Wkly Rep. 2022;71(4):109–117. doi:10.15585/mmwr.mm7104a1

14.European Centre for Disease Prevention and Control (ECDC). Antimicrobial resistance surveillance in Europe – Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; latest edition.

15.Kim L, McGee L, Tomczyk S, Beall B. Biological and epidemiological features of antibiotic-resistant Streptococcus pneumoniae. J Clin Microbiol. 2016;54(5):1079–1086. doi:10.1128/JCM.02498-15

16.Weinberger DM, Malley R, Lipsitch M. Serotype replacement in disease after pneumococcal vaccination. Lancet. 2011;378(9807):1962–1973. doi:10.1016/S0140-6736(10)62225-8

17.Ouldali N, Varon E, Levy C, Angoulvant F, Georges S, Ploy MC, et al. Emergence of pneumococcal serotype 24F invasive disease after introduction of the 13-valent conjugate vaccine in France. Clin Infect Dis. 2021;73(9):e3000–e3007. doi:10.1093/cid/ciaa1810

18.Waight PA, Andrews NJ, Ladhani SN, Sheppard CL, Slack MPE, Miller E. Effect of the 13-valent pneumococcal conjugate vaccine on invasive pneumococcal disease in England and Wales. Lancet Infect Dis. 2015;15(5):535–543. doi:10.1016/S1473-3099(15)70044-7

19.Hanquet G, Krizova P, Valentiner-Branth P, et al. Effect of childhood pneumococcal conjugate vaccination on invasive disease in Europe. Euro Surveill. 2019;24(47):1900301. doi:10.2807/1560-7917.ES.2019.24.47.1900301

20.Savulescu C, Krizova P, Lepoutre A, et al. Effect of high-valency pneumococcal conjugate vaccines on serotype distribution and antimicrobial resistance in Europe. Vaccine. 2017;35(45):5858–5867. doi:10.1016/j.vaccine.2017.09.041

21.European Centre for Disease Prevention and Control (ECDC). Surveillance of invasive pneumococcal disease in Europe – 2022 report. Stockholm: ECDC; 2023.

22.World Health Organization. Global antimicrobial resistance and use surveillance system (GLASS) report. Geneva: WHO; latest edition.

23.Richter SS, Heilmann KP, Dohrn CL, Riahi F, Beekmann SE, Doern GV. Changing epidemiology of antimicrobial-resistant Streptococcus pneumoniae in the United States. Clin Infect Dis. 2014;59(3):354–361. doi:10.1093/cid/ciu285

24.Gladstone RA, Devine V, Jones J, et al. Impact of pneumococcal conjugate vaccines on serotype replacement and antimicrobial resistance. Lancet Microbe. 2021;2(10):e459–e468. doi:10.1016/S2666-5247(21)00138-3