Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Epidemiological changes in pediatric community-onset severe bacterial infections in France: A multicenter prospective study

David Malorey
david.malorey@chu-nantes.fr

Centre Hospitalier Universitaire de Nantes
Elise Launay
Centre Hospitalier Universitaire de Nantes
Nicolas Joram
Centre Hospitalier Universitaire de Nantes
Martin Chalumeau
Université Paris Cité
Stéphane Dauger
Hôpital Robert-Debré
Fleur Cour-Andlauer
Hospices Civils de Lyon
Yves Gillet
Hospices Civils de Lyon
Guillaume Mortamet
Centre Hospitalier Universitaire de Grenoble
Gérald Boussicault
Centre Hospitalier Universitaire d'Angers
Jérémie Rousseaux
Centre Hospitalier Universitaire de Lille
Sandrine Jean
Hôpital Armand-Trousseau
Pierre-Louis Léger
Hôpital Armand-Trousseau
Christophe Milési
Hôpital Arnaud de Villeneuve
Julie Toubiana
Hôpital Necker-Enfants Malades
Jean-Michel Roué
Centre Hospitalier Régional Universitaire de Brest
Hugues Patural
Centre Hospitalier Universitaire de Saint-Étienne
Rémy Assathiany
Association Française de Pédiatrie Ambulatoire
Pierre Bourgouin
Centre Hospitalier Universitaire de Nantes
Christèle Gras Leguen
Centre Hospitalier Universitaire de Nantes
Fleur Lorton
Centre Hospitalier Universitaire de Nantes

Research Article

Keywords: bacterial infection, sepsis, children, incidence, morbidity

Posted Date: August 13th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10602894/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Purpose

To describe the epidemiology of pediatric community-onset severe bacterial infections (COSBIs) in France between 2015 and 2018 and evaluate changes over the 2010–2020 decade.

Methods

We conducted a prospective, observational study in 12 French pediatric intensive care units (PICUs) between 2015 and 2018, including children younger than 18 years admitted with a COSBI. Clinical characteristics, microbiological findings, and outcomes were reported. Age-standardized incidence, disability, and mortality rates were estimated in three administrative divisions of western France and compared with those from a 2009–2014 study.

Results

Among 493 children included, the median age (interquartile range [IQR]) was 2.1 (0.4–6.8) years, and 21% had underlying comorbidities. The most frequently identified pathogens were *Neisseria meningitidis* (19%) and *Streptococcus pneumoniae* (19%). Overall in-hospital mortality was 5.3% (95% CI, 3.6–7.8), and 15.8% (95% CI, 12.6–19.5) of survivors had moderate-to-severe disability at PICU discharge. The age-standardized incidence of COSBIs increased from 3.0 (95% CI, 2.7–3.2) to 4.8 (95% CI, 3.8–5.7) per 100,000 child-years between 2009–2014 and 2015–2018 (rate difference, 1.8; 95% CI, 0.8 to 2.8), corresponding to a 60% relative increase. Mortality remained unchanged, whereas the rate of moderate-to-severe disability increased by 270% (rate difference, 0.8; 95% CI 0.3 to 1.2).

Conclusion

The incidence of pediatric COSBIs increased in western France during the 2010–2020 decade, before the implementation of mandatory childhood vaccination. The marked increase in disability among survivors highlights the need for continued epidemiological surveillance and research into the long-term consequences of pediatric severe bacterial infections.

What is known-What is new

What is known?

- Community-onset severe bacterial infections (COSBIs) remain a major cause of childhood mortality and morbidity worldwide, including in high-income countries.
- Continuous epidemiological surveillance is critical to guide vaccination policies and empiric antibiotic strategies.

What is new?

- Among children with COSBIs, mortality was 5.3% and 15.8% of survivors had moderate-to-severe disability at discharge.
- Between 2009–2014 and 2015–2018, the incidence of COSBIs increased by 60% and the rate of moderate-to-severe disability by 270% in western France.

INTRODUCTION

Sepsis remains a leading cause of morbidity and mortality among children worldwide (1–6). It is estimated to affect approximately 25 million children annually and cause 3.3 million deaths (1,6). In high-income countries, sepsis accounts for more than one-quarter of deaths in pediatric intensive care units (PICUs), with bacterial infections responsible for most cases (3,7). A 2018 European study (excluding France) involving 795 children with community-onset severe bacterial infections (COSBIs) reported a mortality rate of 6%, while 31% of survivors had moderate-to-severe sequelae at hospital discharge (8). Reducing the morbidity and mortality associated with COSBIs remains a global priority, as emphasized by the World Health Organization (9).

Achieving this objective requires continuous epidemiological monitoring to assess the impact of public health interventions, including vaccination programs, and to inform healthcare professionals and families about the burden of COSBIs and the importance of early

recognition. Such surveillance also supports early management strategies and timely updates of local and national empiric antibiotic guidelines in response to evolving bacterial epidemiology (7,8).

Over the 2010-2020 decade, the most common presentations of COSBIs have included meningitis and primary bacteremia, particularly invasive meningococcal disease (8,10). In high-income countries, *Streptococcus pneumoniae* and *Neisseria meningitidis* remain the predominant pathogens (3,6,8,10,11). A previous population-based study in western France showed that the incidence of COSBIs declined from 5.8 per 100,000 child-years during 2000–2006 to 3.0 per 100,000 during 2009–2014. During the latter period, in-hospital mortality was 10%, corresponding to 0.3 deaths per 100,000 child-years (10). Since then, major changes have occurred in France, including the progressive introduction of the 13-valent pneumococcal conjugate vaccine and the meningococcal C vaccine from 2009 onward, and the publication of updated pediatric Surviving Sepsis Campaign recommendations in 2012 (12,13).

The objectives of this study were to describe the clinical characteristics and bacterial epidemiology of COSBIs in France and evaluate temporal trends between 2010 and 2020.

MATERIALS AND METHODS

Study design and participants

We conducted a prospective, observational, multicenter study in 12 PICUs across France (Figure S1, Supplement), representing 35% (110/334) of all French PICUs beds. The study was designed to characterize the clinical and microbiological features of pediatric COSBIs and to develop a predictive tool for assessing the optimality of patient management. This study was approved by the local ethics committee (*Groupe Nantais d'Ethique dans le Domaine de la Santé)* on June 10, 2014, in accordance with the Declaration of Helsinki, was registered on ClinicalTrials.gov (NCT02167802), and oral informed consent was obtained from parents or legal guardians. This report adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (table S6, Supplement).

Children younger than 18 years with a diagnosis of COSBI were prospectively enrolled between March 2015 and July 2018. According to the 2005 International Pediatric Sepsis Conference definitions (14), COSBIs were defined as bacterial sepsis that was either microbiologically confirmed by a positive culture from a normally sterile site or diagnosed as a clinical syndrome with a high probability of bacterial infection following review by a pediatric infectious diseases specialist, and requiring PICU admission or resulting in death before PICU admission. Community-acquired infections were defined as infections acquired outside a healthcare facility or within 48 hours of hospital admission in children without recent hospitalization or healthcare exposure. Children with healthcare-associated infections, viral infections, Kawasaki disease, or hemolytic uremic syndrome were excluded. Patients with pertussis were analyzed separately in a prespecified ancillary analysis because of their distinct pathophysiology. Patients with missing data regarding the primary diagnosis were also excluded because eligibility could not be confirmed.

Data collection and outcome definitions

Clinical data were collected through interviews with parents and treating physicians during the PICU stay and supplemented by review of the medical records. Data were entered into a standardized electronic case report form and included sociodemographic characteristics, underlying medical conditions, clinical presentation, and microbiological findings. Significant comorbidities were defined as conditions predisposing to severe bacterial infection, including genetic or congenital disorders, prematurity in infants younger than one year, a history of severe infection, primary or acquired immunodeficiency, and severe neurological or neuromuscular disorders.

Disease severity was assessed using blood lactate concentration, the Pediatric Index of Mortality 2 (PIM2) score at PICU admission, the requirement for inotropic support, and PICU length of stay.

Outcomes were classified according to in-hospital mortality and functional status at PICU discharge using the Pediatric Overall Performance Category (POPC) score (15). A POPC score of 1 or 2 was considered no or mild disability, corresponding to normal function or minor physical impairment compatible with normal daily life. Moderate-to-severe disability was defined as a POPC score of 3 to 5, ranging from moderate disability to coma or a vegetative state, while a score of 6 indicated brain death (15).

Statistical analysis

The sample size was originally calculated for the development of a predictive model evaluating the optimality of the care pathway. Baseline characteristics, clinical diagnoses, and outcomes were summarized for all included patients and according to clinical outcome. Bacterial

pathogens were described according to the clinical diagnosis. Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables as counts and percentages.

To estimate the incidence, mortality, and disability rates of COSBIs during 2015–2018, analyses were restricted to three French administrative divisions (Loire-Atlantique, Vendée, and Maine-et-Loire), where consecutive enrollment of all eligible cases was ensured. This catchment area represented approximately 5% of the French pediatric population (Figure S1, Supplement). Regional healthcare organization ensured referral of all children requiring PICU admission to one of the two participating university hospitals. The completeness of case ascertainment for fatal COSBIs was verified using the French Epidemiology Centre on Medical Causes of Death (16) and the National Observatory for Sudden Infant Death Syndrome (17). Incidence rates were calculated by dividing the total number of cases by the corresponding number of child-years, derived from the average pediatric population between 2016 and 2018 obtained from the French National Institute of Statistics and Economic Studies (18).

To evaluate changes in the epidemiology of COSBIs over approximately one decade, data from the 2015–2018 cohort were compared with those from a previous population-based study conducted between 2009 and 2014 in 15 French administrative divisions, including the three divisions common to the present study (Figure S2, Supplement) (10). Because the previous study included children aged 1 month to 16 years, analyses were restricted to the same age group to ensure comparability.

Age-standardized incidence rates (SIRs) were calculated using direct standardization based on the 2014 French population aged 1 month to 16 years. Differences in incidence, mortality, and morbidity between the two study periods were estimated with corresponding 95% confidence intervals (95% CIs) (19). As the geographical coverage differed between studies, SIRs were also calculated separately for the three administrative divisions included in both cohorts as a complementary analysis. Finally, age-standardized incidence rates were estimated according to the identified bacterial pathogen and compared between the two study periods. All statistical analyses were performed using R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was defined as a p value < 0.05.

Results

Study population

Between March 2015 and July 2018, 524 children with suspected COSBIs were identified, of whom 493 were included in the final analysis (Figure 1). Two patients (0.4%) were excluded because of missing data on the primary diagnosis.

The clinical characteristics of the study population according to hospital discharge outcome are presented in Table 1. The median age was 2.1 years (IQR, 0.4–6.8), including 15 neonates (3%), and the male-to-female ratio was 1.36. Thirty-one children (6%) had been born preterm, 31 (6%) had a genetic or congenital disorder, and 24 (5%) had a history of severe bacterial infection.

The most common clinical diagnoses were meningitis (190/493, 39%), respiratory infections (83/493, 17%), and invasive meningococcal disease (47/493, 10%). Among children with respiratory infections, 42 of 83 (21%) had parapneumonic empyema and 41/83 (49%) had severe pneumonia.

At PICU admission, the median blood lactate concentration was 2.1 mmol/L (IQR, 1.3–3.4). Among the 337 children with available data, the median Glasgow Coma Scale score was 15 (IQR, 13–15). During the PICU stay, 120 of 492 children (24%) required invasive mechanical ventilation, and 89 of 492 (18%) received vasoactive support.

Among patients with available outcome data, 26 of 489 children (5.3%; 95% CI, 3.6–7.8) died during hospitalization. Among the 463 survivors with available follow-up data, 73 (15.8%; 95% CI, 12.6–19.5) had moderate-to-severe disability at PICU discharge.

Table 1. Clinical characteristics of 493 children with community-onset severe bacterial infections, overall and according to hospital outcome

Variable	MD	Overall (n=493)	No or mild disability (n=391)	Moderate-to-severe disability* (n=73)	Death (n=26)
Sex	0				
Female		209 (42)	159 (41)	35 (48)	13 (50)
Male		284 (58)	232 (59)	38 (52)	13 (50)
Age (years)	0	2.1 (0.4 - 6.8)	2.3 (0.5-6.8)	1.6 (0.3-6.2)	1.0 (0.3-7.3)
0 - 23 months		241(49)	186 (48)	38 (52)	17 (65)
2 - 4 years		103 (21)	85 (22)	16 (22)	1 (4)
5 - 10 years		69 (14.0)	54 (14)	10 (14)	4 (15)
11 - 18 years		80 (16)	66 (17)	9 (12)	4 (15)
≥ 1 underlying condition	1	105 (21)	82/390 (21)	12/73 (16)	10/26 (38)
Preterm birth		31 (6)	25 (6)	2 (3)	4 (15)
Genetic or congenital defect		31 (6)	26 (7)	2 (3)	3 (12)
History of severe infection		24 (5)	22 (6)	2 (3)	0
Immunodeficiency		21 (4)	12 (3)	5 (7)	3 (12)
Severe neurological or neuromuscular disorder		10 (2)	9 (2)	1 (1)	0 (0)
Severity at PICU admission					
Lactate levels (mmol/L)	133	2.1 (1.3 - 3.4)	2.0 (1.2-3.1)	2.1 (1.2-3.9)	3.4 (2.4-5.7)
PIM2 score	72	2.8 (1.1 - 10.0)	2.2 (1.0-8.3)	5.1 (1.8-13.5)	9.5 (2.9-22.2)
Vasoactive support	1	89 (18)	56/391 (14)	20/73 (27)	11/25 (44)
PICU length of stay, deaths excluded (days) (N=467)	8	4 (2 - 8)	3 (2-6)	9 (4-15)	-
Clinical diagnosis	0				
Meningitis		190 (39)	139 (36)	36 (49)	15 (58)
Respiratory infection		83 (17)	75 (19)	6 (8)	1 (4)
Invasive meningococcal disease		47 (10)	34 (9)	10 (14)	3 (12)
Skin infection / toxic shock		43 (9)	39 (10)	3 (4)	0
Sepsis without an identified source		46 (9)	36 (9)	5 (7)	4 (15)
Other		84 (17)	68 (17)	13 (18)	3 (12)

Data are presented as n (%) or median (interquartile range [IQR]).

* Corresponding to a Pediatric Overall Performance Category (POPC) score of 3–5.
MD: missing data, PIM2: pediatric index of mortality, PICU: pediatric intensive care unit

Bacterial findings

Microbiological findings according to clinical presentation are summarized in Table 2 and Table S1 (Supplement). Among children with meningitis, the most frequently identified pathogens were *Streptococcus pneumoniae* (75/190, 39.5%) and *Neisseria meningitidis* (51/190, 26.8 %).

Among children with severe respiratory infections, *Staphylococcus aureus* was identified in 17 of 83 cases (20.5%), *Streptococcus pyogenes* in 15 (18.1%), and *S. pneumoniae* in 15 (18.1%).

The distribution of pneumococcal and meningococcal serotypes is shown in Table S2 (Supplement). Among the 67 pneumococcal COSBI isolates with available serotype data, 10 (15%) were covered by the 13-valent pneumococcal conjugate vaccine (PCV13); 15 (22%) by PCV15; 40 (60%) by PCV20, and 42 (63%) by the 23-valent pneumococcal polysaccharide vaccine

(PPSV23).

Table 2. Bacterial etiology according to clinical diagnosis

Bacterium, No. (%)	Meningitis (N = 190)	Respiratory infection (N = 83)	Invasive meningococcal disease (N = 47)	Skin infection / toxic shock (N = 43)	Brain abscess (N = 25)	Pyelonephritis (N = 25)	Sepsis of unknown origin (N = 46)
Streptococcus pneumoniae	**75 (40)**	15 (18)	0 (0)	0 (0)	1 (4)	0 (0)	2 (4)
Neisseria meningiditis	51 (27)	0 (0)	**40 (85)**	0 (0)	0 (0)	0 (0)	3 (7)
Staphylococcus aureus	0 (0)	17 (21)	0 (0)	**22 (51)**	1 (4)	0 (0)	8 (17)
Streptococcus agalactiae (Group B)	34 (18)	0 (0)	1 (2)	0 (0)	2 (8)	0 (0)	5 (11)
Streptococcus pyogenes (Group A)	1 (1)	15 (18)	1 (2)	10 (23)	1 (4)	0 (0)	2 (4)
Escherichia coli	10 (5)	2 (2)	0 (0)	0 (0)	0 (0)	**17 (68)**	6 (13)
Other gram negative bacteria	5 (3)	4 (5)	0 (0)	0 (0)	1 (4)	4 (16)	**10 (22)**
Other streptococcus	3 (2)	4 (5)	0 (0)	1 (2)	**13 (52)**	0 (0)	0 (0)
Other bacteria	7 (4)	9 (11)	0 (0)	0 (0)	0 (0)	2 (8)	3 (7)
No positive identification	5 (3)	**17 (21)**	5 (11)	10 (23)	6 (24)	2 (8)	7 (15)

Evolution of incidence, mortality, and disability rates

During the 2015–2018 study period, 97 COSBI cases were identified among children aged 1 month to 16 years in the three administrative divisions of western France included for population-based analyses (Figure S1, supplement), representing an average pediatric population of 2.1 million child-years.

The SIR of COSBIs increased from 3.0 (95% CI, 2.7–3.2) per 100,000 child-years during 2009–2014 to 4.8 (95% CI, 3.7–5.5) during 2015–2018 (incidence rate difference [IRD], 1.8; 95% CI, 0.8–2.8), corresponding to a relative increase of 60% (95% CI, 30–100) (Table 3). This increase was particularly pronounced among children aged 1–23 months (IRD, 7.1; 95% CI, 0.5–13.6) and adolescents aged 11–16 years (IRD, 1.6; 95% CI, 0.4–2.6) (Figure S3 and Table S3, Supplement). The age-standardized rate of moderate-to-severe disability at PICU discharge increased from 0.3 (95% CI, 0.2–0.4) to 1.0 (95% CI, 0.6–1.5) per 100,000 child-years between the two study periods (IRD, 0.8; 95% CI, 0.3–1.2), representing a relative increase of 270% (95% CI, 150–440) (Table 3). In contrast, mortality remained stable. The mortality SIR was 0.3 (95% CI, 0.2–0.4) per 100,000 child-years during 2009–2014 and 0.2 (95% CI, 0.0–0.3) during 2015–2018 (IRD, −0.2; 95% CI, −0.4 to 0.04).

Table 3. Comparison of age-standardized incidence, disability, and mortality rates of community-onset severe bacterial infections between 2009-2014 and 2015-2018 (per 100,000 child-years)

Outcome	2009-2014* SIR (95% CI)	2015 - 2018** SIR (95% CI)	Rate difference (95% CI)
COSBI incidence	3.0 (2.7 - 3.2)	4.8 (3.8 - 5.7)	1.8 (0.8 to 2.8)
Moderate-to-severe disability	0.3 (0.2-0.4)	1.0 (0.6-1.5)	0.8 (0.3 to 1.2)
Mortality	0.3 (0.2-0.4)	0.2 (0-0.3)	-0.2 (-0.4 to 0.04)

* Fifteen administrative divisions in western France
** Three administrative divisions (Loire-Atlantique, Vendée, Maine-et-Loire) in western France
COSBI: community-onset severe bacterial infection, SIR: age-standardized incidence rate, 95% CI: 95% confidence interval

A complementary analysis restricted to the three administrative divisions common to both cohorts yielded similar findings, although the increase in incidence was no longer statistically significant (IRD, 0.8; 95% CI, −0.5 to 2.0) (Table S4, Supplement).

The incidence of COSBIs without microbiological confirmation declined from 0.8 (95% CI, 0.6–1.0) per 100,000 child-years during 2009–2014 to 0.2 (95% CI, 0.0–0.4) during 2015–2018 (IRD, −0.6; 95% CI, −0.9 to −0.3). Pathogen-specific analyses demonstrated a significant increase in *S. pyogenes* COSBIs, with the SIR rising from 0.2 (95% CI, 0.1–0.2) to 0.5 (95% CI, 0.2–0.8) per 100,000 child-years (IRD, 0.4; 95% CI, 0.1–0.7) (Figure S4 and Table S5, Supplement).

DISCUSSION

This prospective study of 493 children admitted to French PICUs between 2015 and 2018 provides updated insights into the epidemiology of COSBIs following the implementation of meningococcal and pneumococcal vaccination programs, including changes in incidence, causative pathogens, and clinical outcomes.

In western France, the age-standardized incidence of COSBIs increased from 3.0 to 4.8 per 100,000 child-years between 2009–2014 and 2015–2018, contrasting with the decline observed since the early 2000s, particularly among infants (10). The increase occurred in a context of suboptimal vaccine uptake and immediately preceded the introduction of mandatory childhood vaccination in France in 2018, which substantially improved vaccine coverage (20,21). Reported incidence rates vary from 10 to 50 per 100,000 child-years, and several studies have reported increasing pediatric sepsis incidence over the past two decades (2,3,7). Schlapbach *et al.* similarly reported an increase in invasive infections from 10 to 16 per 100,000 child-years in Australia and New Zealand between 2002 and 2013 (3). However, comparisons should be interpreted cautiously because of heterogeneity in case definitions, age ranges, and inclusion criteria, particularly regarding neonates and healthcare-associated infections.

The increased incidence may also reflect improved recognition of COSBIS and changes in PICU admission practices following the expansion of pediatric intermediate care units in France (22). Although lactate concentrations were similar between the 2009–2014 and 2015–2018 cohorts (23), higher rates of vasoactive support and invasive mechanical ventilation reported elsewhere suggest that the later cohort may have included less severely ill children (7,24).

Our cohort was consistent with previous studies from high-income countries, with a median age of 2.1 years, 58% males, and underlying conditions in one-fifth of children (8,10,24).

Although the age-standardized mortality rate remained stable, the case-fatality rate decreased from 11% during 2009–2014 to 5.3% during 2015–2018 (10). The lack of a statistically significant reduction may reflect limited statistical power rather than an absence of clinical improvement. Mortality rates reported elsewhere are generally higher (6–20%), likely because they include healthcare-associated infections, which are associated with greater comorbidity and poorer outcomes (2,4,6,25). The decline in case fatality is consistent with advances in pediatric critical care, implementation of the pediatric Surviving Sepsis Campaign recommendations, and the widespread introduction of meningococcal and pneumococcal vaccination (3,7,8,26–28).

In contrast, 15.8% of children experienced moderate-to-severe disability at PICU discharge. Although this proportion was lower than the 24% reported in the European EUCLIDS cohort, supporting the inclusion of less severely ill children (8), the age-standardized disability rate increased by 270% between the two study periods. Improved survival after severe sepsis may have increased the number of survivors with residual disability, while changes in discharge practices or disability assessment may also have contributed (10,23).

These findings highlight the growing burden of post-sepsis morbidity. Improved diagnostics, personalized approaches, and pediatric quality-improvement are needed to optimize early recognition and treatment (28,29). High-quality acute care remains a key determinant of outcome,

as suboptimal management has been independently associated with severe sequelae at PICU discharge (30).

Structured follow-up pathways are also needed, particularly for children at high risk of long-term disability and mortality (29,31). Although French national recommendations for post-sepsis care were published in 2025 (32), medium- and long-term outcomes remain poorly characterized, and standardized follow-up protocols are lacking. Future interventional studies should therefore include long-term functional outcomes in addition to mortality and early morbidity (29,33,34).

Consistent with previous studies, *S. pneumoniae* and *N. meningitidis* remained the leading pathogens, each accounting for approximately 19% of COSBI cases (8,10). The incidence of pneumococcal COSBIs remained stable, suggesting that the decline observed between 2000–2006 and 2009–2014 has been sustained following the introduction of PCV7 and PCV13 (10). PCV13 coverage remained high in France, increasing from 89% in 2010 to 92% in 2022 (20). Among typed pneumococcal isolates, only 15% were covered by PCV13 compared with 50% previously, consistent with serotype replacement following widespread pneumococcal conjugate vaccination (35).

Serogroup B remained the predominant cause of invasive meningococcal disease, accounting for 68% of meningococcal COSBIs (10). Following the resurgence of invasive meningococcal disease after the COVID-19 pandemic, France expanded mandatory infant vaccination in January 2025 to include serogroups A, B, W, and Y, in addition to serogroup C (13). This policy is expected to further reduce the burden of meningococcal disease, which remains associated with social inequalities (13,36).

Finally, S. aureus accounted for 11% of COSBIs during 2015–2018, compared with 6% previously (10). We also observed increases in *S. pyogenes* and *S. agalactiae* infections. These changes may partly reflect improved microbiological diagnosis, as evidenced by the decline in microbiologically undocumented COSBIs. Advances in molecular diagnostics, including PCR and next-generation sequencing, have substantially improved pathogen detection (37). Continued epidemiological surveillance remains essential to inform empiric antimicrobial treatment guidelines for pediatric community-acquired sepsis (38).

Limitations

This study has several limitations. First, because data collection was not exhaustive across all French PICUs during the study period, selection bias cannot be excluded, potentially limiting the generalizability of our findings. Although participating centers accounted for 35% of all French PICU beds, caution is warranted when extrapolating these results to the national population.

Second, the absence of a dedicated registry made it challenging to ensure complete case ascertainment within the population used for incidence estimates. Although national mortality databases were consulted to identify fatal cases, some COSBIs may have been missed, potentially leading to an underestimation of incidence. However, this limitation is unlikely to explain the observed increase incidence unless a similar degree of under-ascertainment occurred in the 2009–2014 study. Furthermore, the increase may partly reflect changes in PICU admission practices, with less severely ill children being admitted during the later study period rather than a true increase in disease incidence.

Third, the observed increase in the incidence of specific bacterial pathogens may partly be explained by improvements in microbiological diagnostics, including molecular techniques, as reflected by the marked decline in microbiologically undocumented COSBIs.

Finally, comparisons between the two study periods involved different geographical catchment areas. To account for differences in population structure, age-standardization was performed. In addition, incidence estimates were recalculated after restricting the analysis to the three administrative divisions common to both cohorts, thereby minimizing geographical variations and reducing potential ascertainment bias.

CONCLUSION

In this prospective multicenter study, approximately one in five children with a COSBI either died or experienced moderate-to-severe disability at PICU discharge. Meningitis remained the most frequent clinical presentation, and the incidence of COSBIs increased in western France between 2009–2014 and 2015–2018. Although mortality remained stable, the substantial increase in disability among survivors highlights the growing burden of post-sepsis morbidity. These findings underscore the importance of continued epidemiological surveillance, optimization of acute sepsis management, and the development of structured long-term follow-up strategies for survivors. They also support ongoing efforts to strengthen preventive measures, particularly vaccination programs, to further reduce the burden of pediatric COSBIs.

Abbreviations

95% CI
95% confidence interval
COSBIs
community-onset severe bacterial infections, **IQR**:interquartile range
IRD
incidence rate difference
PCV
pneumococcal conjugate vaccine
PICU
pediatric intensive care unit
PIM2
pediatric index of mortality 2
POPC
pediatric overall performance category
SIR
standardized incidence rate
WHO
World Health Organization

Declarations

Conflict of interest disclosure:

The authors declare that they have no competing interests.

Funding:

This study was supported by the French national hospital research program (DGOS PREPS-IQ 2013, grant no. 13–0041).

Author Contribution

The study was conceived and designed by E.L., M.C., and C.G. Funding was acquired by E.L and C.G. All authors participated in the study investigation. Data curation and formal analysis were performed by D.M., E.L., and F.L. The first draft of the manuscript was written by D.M. All authors commented on previous versions of the manuscript, read and approved the final manuscript.

Acknowledgement

We sincerely thank the children and their families for participating in this study. We are grateful to the French National Reference Center for Pneumococcal Diseases and its director, Dr. Emmanuelle Varon, for their valuable support. We also thank Dr. Florence Moulin (Pediatric Intensive Care Unit, Necker–Enfants Malades University Hospital, AP-HP, Université Paris Cité, Paris, France), Pr. Thierry Debillon (Neonatal Intensive Care Unit, Grenoble Alpes University Hospital, Grenoble, France), Pr. Gilles Cambonie (Pediatric Intensive Care Unit, Arnaud de Villeneuve Hospital, Montpellier University Hospital, Montpellier, France), Pr. Étienne Javouhey (Pediatric Intensive Care Unit, Hôpital Femme Mère Enfant, Lyon, France), and Pr. Stéphane Leteurtre (Pediatric Intensive Care Unit, Univ. Lille Nord de France, CHU Lille, Lille, France), as well as all study investigators and clinical research assistants, for their invaluable contributions to this study and their commitment to patient care at their respective institutions.The authors thank Sophie Domingues for proofreading the manuscript and Thomas Nedelec for creating the maps included in the Supplementary Material.

Data Availability

Individual participant data (including the data dictionary) underlying the results reported in this article will be shared upon request after de-identification. The study protocol, and informed consent form will also be made available. Data will be accessible 12 months after publication and will remain available for up to 36 months following publication. Data will be shared for any analysis by researchers who

submit a methodologically sound proposal, subject to approval by the ethics committee at the institution of the corresponding author. Requests should be directed to the corresponding author of the article, and a data-sharing agreement must be signed to gain access.

References

1. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR et al (2020) Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet Lond Engl 395(10219):200–211. 10.1016/S0140-6736(19)32989-7 PubMed PMID: 31954465; PubMed Central PMCID: PMC6970225
2. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N (2018) The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respir Med 6(3):223–230. 10.1016/S2213-2600(18)30063-8
3. Schlapbach LJ, Straney L, Alexander J, MacLaren G, Festa M, Schibler A et al (2015) Mortality related to invasive infections, sepsis, and septic shock in critically ill children in Australia and New Zealand, 2002–13: a multicentre retrospective cohort study. Lancet Infect Dis 15(1):46–54. 10.1016/S1473-3099(14)71003-5
4. Tan B, Wong JJM, Sultana R, Koh JCJW, Jit M, Mok YH et al (2019) Global Case-Fatality Rates in Pediatric Severe Sepsis and Septic Shock: A Systematic Review and Meta-analysis. JAMA Pediatr 01(4):352–362. 10.1001/jamapediatrics.2018.4839 PubMed PMID: 30742207; PubMed Central PMCID: PMC6450287
5. Zimmerman JJ, Banks R, Berg RA, Zuppa A, Newth CJ, Wessel D et al (2020) Trajectory of Mortality and Health-Related Quality of Life Morbidity Following Community-Acquired Pediatric Septic Shock*. Crit Care Med 48(3):329–337. 10.1097/CCM.0000000000004123
6. Watson RS, Carrol ED, Carter MJ, Kissoon N, Ranjit S, Schlapbach LJ (2024) The burden and contemporary epidemiology of sepsis in children. Lancet Child Adolesc Health 8(9):670–681. 10.1016/S2352-4642(24)00140-8
7. Agyeman PKA, Schlapbach LJ, Giannoni E, Stocker M, Posfay-Barbe KM, Heininger U et al (2017) Epidemiology of blood culture-proven bacterial sepsis in children in Switzerland: a population-based cohort study. Lancet Child Adolesc Health 1(2):124–133. 10.1016/S2352-4642(17)30010-X PubMed PMID: 30169202
8. Boeddha NP, Schlapbach LJ, Driessen GJ, Herberg JA, Rivero-Calle I, Cebey-López M et al Mortality and morbidity in community-acquired sepsis in European pediatric intensive care units: a prospective cohort study from the European Childhood Life-threatening Infectious Disease Study (EUCLIDS). Crit Care Lond Engl 2018 31;22(1):143. 10.1186/s13054-018-2052-7 PubMed PMID: 29855385; PubMed Central PMCID: PMC5984383.
9. Reinhart K, Daniels R, Kissoon N, Machado FR, Schachter RD, Finfer S (2017) Recognizing Sepsis as a Global Health Priority - A WHO Resolution. N Engl J Med 377(5):414–417. 101056/NEJMp1707170 PubMed PMID: 28658587
10. Lorton F, Chalumeau M, Martinot A, Assathiany R, Roué JM, Bourgoin P et al (2020) Epidemiology of Community-Onset Severe Bacterial Infections in Children and Its Evolution: A Population-Based Study in France. Pediatr Crit Care Med J Soc Crit Care Med World Fed Pediatr Intensive Crit Care Soc. 12. 10. 1097/PCC.0000000000002300 PubMed PMID: 32224829
11. Ikuta KS, Swetschinski LR, Robles Aguilar G, Sharara F, Mestrovic T, Gray AP et al (2022) Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 400(10369):2221–2248. 10.1016/S0140-6736(22)02185-7
12. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al (2013) Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock. Crit Care Med 41(2):580–637. 10.1097/CCM.0b013e31827e83af
13. Haute Autorité de Santé [Internet] [cited 2025 Jan 3]. Stratégie de vaccination contre les infections invasives à méningocoques: Révision de la stratégie contre les sérogroupes ACWY et B. Available from: https://www.has-sante.fr/jcms/p_3460601/fr/strategie-de-vaccination-contre-les-infections-invasives-a-meningocoques-revision-de-la-strategie-contre-les-serogroupes-acwy-et-b
14. Goldstein B, Giroir B, Randolph A (2005) International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*: Pediatr Crit Care Med. ;6(1):2–8. 10.1097/01.PCC.0000149131.72248.E6
15. Fiser DH (1992) Assessing the outcome of pediatric intensive care. J Pediatr 121(1):68–74. 10.1016/s0022-3476(05)82544-2 PubMed PMID: 1625096
16. Causes de décès - Inserm-CépiDc [Internet]. [cited 2023 Feb 7]. Available from: https://opendata-cepidc.inserm.fr/
17. OMIN Observatoire national des morts inattendues du nourrisson [Internet] [cited 2023 Feb 7]. OMIN Observatoire national des morts inattendues du nourrisson. Available from: https://www.omin.fr/
18. Institut national de la statistique et des études économiques Population et structure de la population [Internet]. [cited 2021 May 15]. Available from: https://www.insee.fr/fr/statistiques
19. Xu Y, Cheung YB, Lam KF, Tan SH, Milligan P (2010) A Simple Approach to the Estimation of Incidence Rate Difference. Am J Epidemiol 172(3):334–343. 10.1093/aje/kwq099

20. SPF Accueil [Internet]. [cited 2021 Jul 24]. Available from: https://www.santepubliquefrance.fr/
21. de Figueiredo A, Simas C, Karafillakis E, Paterson P, Larson HJ (2020) Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study. Lancet 396(10255):898–908. 10.1016/S0140-6736(20)31558-0
22. Thiriez G, Lefebvre A (2010) Estimation des besoins en lits d'unité de surveillance continue pédiatrique, résultats d'une enquête sur 3 régions françaises. Arch Pédiatrie 17(8):1147–1152. 10.1016/j.arcped.2010.04.005
23. Malorey D, Lorton F, Chalumeau M, Bourgoin P, Boussicault G, Chantreuil J et al (2023) Distribution, Consequences, and Determinants of Time to Antibiotics in Children With Community-Onset Severe Bacterial Infection: A Secondary Analysis of a Prospective Population-Based Study. Pediatr Crit Care Med 24(9):e441–e451. 10.1097/PCC.0000000000003306
24. Long E, Borland ML, George S, Jani S, Tan E, Phillips N et al (2025) Epidemiology of community acquired sepsis in children in Australia and New Zealand: a multicentre prospective cohort study. Lancet Reg Health - West Pac 60:101608. 10.1016/j.lanwpc.2025.101608
25. Giuliano JS, Markovitz BP, Brierley J, Levin R, Williams G, Lum LCS et al (2016) Comparison of Pediatric Severe Sepsis Managed in U.S. and European ICUs*. Pediatr Crit Care Med 17(6):522–530. 10.1097/PCC.0000000000000760
26. Borrow R, Alarcón P, Carlos J, Caugant DA, Christensen H, Debbag R et al (2017) The Global Meningococcal Initiative: global epidemiology, the impact of vaccines on meningococcal disease and the importance of herd protection. Expert Rev Vaccines 16(4):313–328. 10.1080/14760584.2017.1258308
27. Cohen R, Cohen JF, Chalumeau M, Levy C (2017) Impact of pneumococcal conjugate vaccines for children in high- and non–high-income countries. Expert Rev Vaccines 16(6):625–640. 10.1080/14760584.2017.1320221
28. Carter MJ, Carrol ED, Ranjit S, Mozun R, Kissoon N, Watson RS et al (2024) Susceptibility to childhood sepsis, contemporary management, and future directions. Lancet Child Adolesc Health 8(9):682–694. 10.1016/S2352-4642(24)00141-X
29. De Souza DC, Paul R, Mozun R, Sankar J, Jabornisky R, Lim E et al (2024) Quality improvement programmes in paediatric sepsis from a global perspective. Lancet Child Adolesc Health 8(9):695–706. 10.1016/S2352-4642(24)00142-1
30. Lorton F, Chalumeau M, Martinot A, Assathiany R, Roué JM, Bourgoin P et al (2022) Prevalence, Characteristics, and Determinants of Suboptimal Care in the Initial Management of Community-Onset Severe Bacterial Infections in Children. JAMA Netw Open 5(6):e2216778. 10.1001/jamanetworkopen.2022.16778
31. Dervan LA, Hartman M, Fink EL, Fitzgerald JC, Hall TA, Laux K et al (2025) Eight PICU Follow-Up Programs in the United States Established From 2013 to 2022: Report From the Pediatric Outcomes Studies After PICU (POST-PICU) Investigators. Pediatr Crit Care Med 26(10):e1296–e1306. 10.1097/PCC.0000000000003804
32. Haute Autorité de Santé [Internet] (2025) Dec 3]. Prise en charge du sepsis du nouveau-né, de l'enfant et de l'adulte: recommandations pour un parcours de soins intégré. Available from: https://www.has-sante.fr/jcms/p_3587144/fr/prise-en-charge-du-sepsis-du-nouveau-ne-de-l-enfant-et-de-l-adulte-recommandations-pour-un-parcours-de-soins-integre
33. Gayat E, Cariou A, Deye N, Vieillard-Baron A, Jaber S, Damoisel C et al (2018) Determinants of long-term outcome in ICU survivors: results from the FROG-ICU study. Crit Care 22(1):8. 10.1186/s13054-017-1922-8
34. Long E, Williams A, George S, Hearps S, Yock-Corrales A, Pavlicich V et al (2025) Protocol for a multi-country retrospective observational paediatric sepsis epidemiological study (SENTINEL International). BMJ Open 15(10):e101332. 10.1136/bmjopen-2025-101332
35. Hanquet G, Krizova P, Dalby T, Ladhani SN, Nuorti JP, Danis K et al (2022) Serotype Replacement after Introduction of 10-Valent and 13-Valent Pneumococcal Conjugate Vaccines in 10 Countries, Europe. Emerg Infect Dis 28(1):137–138. 10.3201/eid2801.210734
36. Taha MK, Weil-Olivier C, Bouée S, Emery C, Nachbaur G, Pribil C et al (2021) Risk factors for invasive meningococcal disease: a retrospective analysis of the French national public health insurance database. Hum Vaccines Immunother 17(6):1858–1866 PubMed PMID: 33449835; PubMed Central PMCID: PMC8115611
37. Sinha M, Jupe J, Mack H, Coleman TP, Lawrence SM, Fraley SI (2018) Emerging Technologies for Molecular Diagnosis of Sepsis. Clin Microbiol Rev 31(2):e00089–e00017. 10.1128/CMR.00089-17
38. Paul M, Zemer-Wassercug N, Talker O, Lishtzinsky Y, Lev B, Samra Z et al (2011) Are all beta-lactams similarly effective in the treatment of methicillin-sensitive Staphylococcus aureus bacteraemia? Clin Microbiol Infect 17(10):1581–1586. 10.1111/j.1469-0691.2010.03425.x

Figures

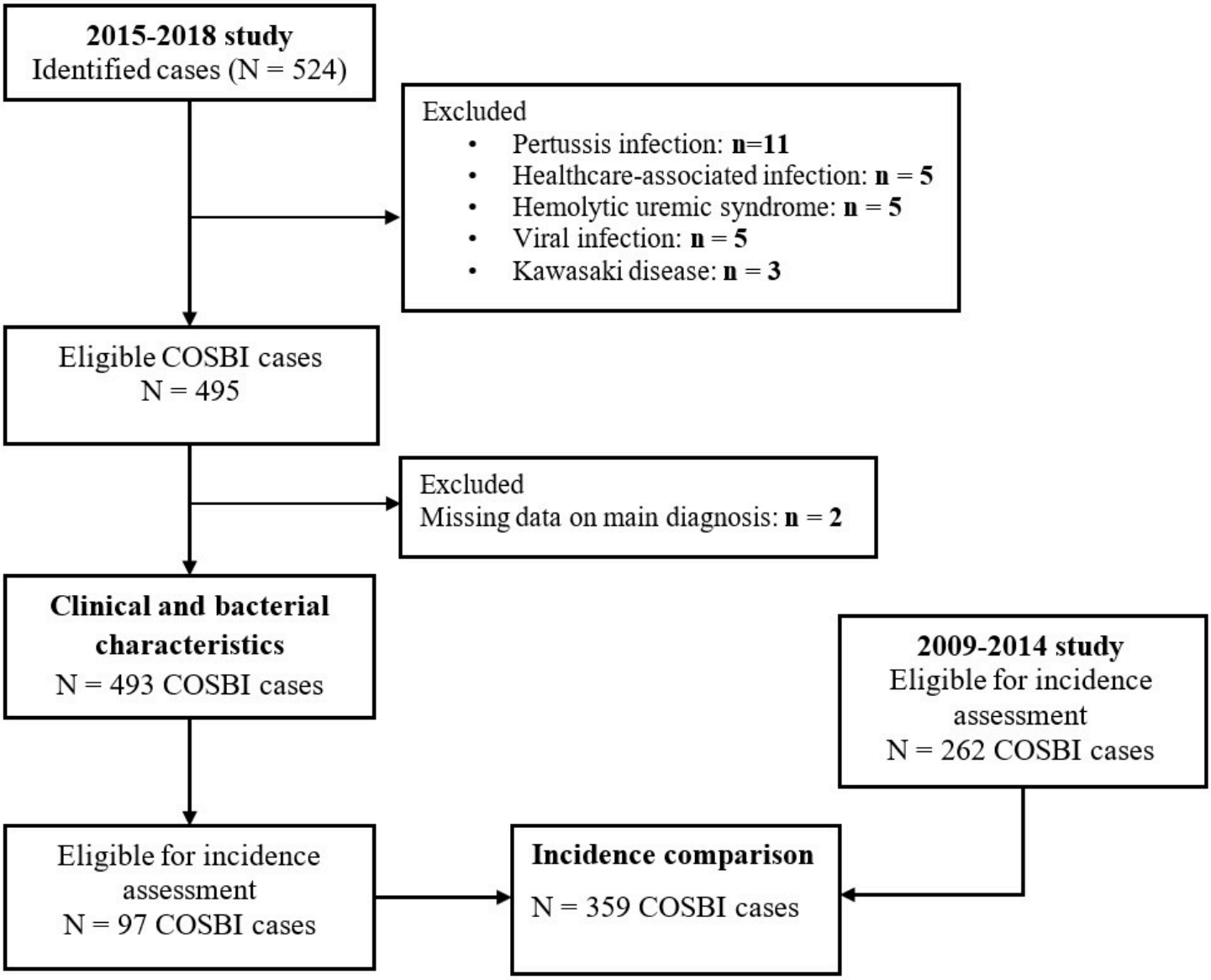


Figure 1

Flowchart of the study population.

COSBI: community-onset severe bacterial infection

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- DIABACTIVSupplementalMaterialEJPE.docx