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ARTICLE

# Suspected or known neonatal sepsis and neurodevelopmental delay by 5 years

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## Abstract

**Objective** Evaluate impact of known and suspected neonatal sepsis in the term and preterm infant on neurodevelopmental delay by 5 years.

**Study Design** Included infants were born in 2009–2010 and followed for 5 years. Diagnostic codes and at least 5 days of antibiotic use identified suspected sepsis. Laboratory results confirmed known sepsis. Diagnostic codes stratified developmental delay by sub-type. Logistic regression analysis determined odds of developmental delay for sepsis and suspected sepsis.

**Results** Of 65,938 included infants, 190 had sepsis and 3449 had suspected sepsis. After adjustment for known developmental risk factors, sepsis and suspected sepsis were associated with increased risk for any developmental delay, (1.48 (1.05–2.09) and 1.09 (1.01–1.18)), respectively, and multiple developmental delay sub-types.

**Conclusion** Neonatal sepsis and suspected sepsis are associated with neurodevelopmental delay by 5 years of age.

## Introduction

The neonatal period is a crucial time for healthy infant growth and development. Neurodevelopmental delay in children affects 15% of children in the United States, with the prevalence increasing [1]. Complications during the neonatal period have been linked with increased risk of neurodevelopmental delay [2, 3]. Sepsis can occur in both preterm and term infants, and has been linked with neurodevelopmental delay in infants. Previous studies examining effects of sepsis on neurodevelopmental delay have shown considerable variability in outcomes studied, ages of included children, definition of sepsis used, and length of follow-up [4–14].

Most current studies of sepsis focus specifically on preterm and/or very low birth weight (VLBW; <1500 g) infants [4, 11, 13–18]. Studies of infants born preterm and/or VLBW have linked sepsis with increased risk of death, cerebral palsy [4, 8, 15, 19], cognitive delay [4, 19], hearing and vision impairment [4, 18], and neurodevelopmental impairment [8, 19–21]. These studies postulate that an immature immune system places infants at increased risk for infection [22], linking younger gestational age with increased risk of sepsis, brain injury, and adverse clinical outcomes [23]. Researchers further hypothesize that immature white matter is more prone to inflammatory-mediated injury from infection, with subsequent loss of pre-oligodendrocytes leading to neurodevelopmental delay [3, 4, 13, 16]. The preterm and low birth weight (LBW) population, however, is prone to other neonatal complications, including retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), patent ductus arteriosus (PDA), periventricular leukomalacia (PVL), and chronic lung disease (CLD)—all of which can also impact neurodevelopment [4–6, 10, 24].

Research into sepsis in older infants and children has also linked sepsis with impaired cognitive functioning [7, 25–28]. However, research on these older age groups is limited, outcomes are less clearly defined, and many studies limit follow-up observation to a period of 2 years or fewer [4, 9, 10, 13].

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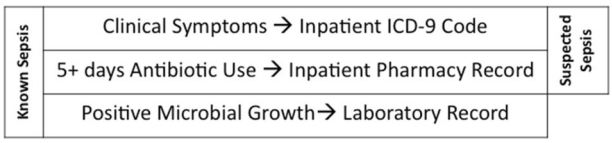


**Fig. 1** Criteria used to define sepsis and suspected sepsis and data sources

Some studies also used sepsis identification criteria that lacked specificity to differentiate known sepsis from suspected sepsis, suggesting the possibility that the risk of neurodevelopmental delay may also be increased with suspected sepsis [8, 14, 26, 27].

Because the definition of sepsis varies, results are difficult to interpret. Some studies define sepsis as clinical symptoms with antibiotic use [5, 9, 10]. Some define sepsis as the presence of specific microbes, such as coagulase-negative staphylococci or *Candida* species [17, 19], whereas others define sepsis as the presence of any positive microbial growth with clinical symptoms [9]. The most robust definition of sepsis used requires the presence of positive microbial growth in blood, urine, or cerebrospinal fluid (CSF) [3, 4, 11, 12, 19] with clinical signs, and use of antibiotics for a defined number of days [4, 11, 16–18].

The aim of this study was to explore the impact of neonatal sepsis or suspected sepsis in both term and preterm infants on neurodevelopmental delay in children by the age of 5 years.

## Methods

A retrospective cohort was formed using the Military Healthcare System (MHS) database. The MHS provides healthcare to nearly 9.5 million military members, retirees, and spousal and child dependents in the United States and abroad. The MHS database includes records of inpatient hospitalizations, outpatient care, and outpatient prescriptions provided at military treatment facilities (MTF) and civilian facilities, as well as pharmacy and laboratory records associated with inpatient care provided at MTFs. All infants born in a MTF between October 1, 2008 and September 30, 2010, who had follow-up care within the MHS for at least 5 years following birth were included. Children born at civilian facilities and those transferred to civilian facilities for higher level Neonatal Intensive Care Unit care in the first month of life were excluded due to the lack of inpatient pharmacy records and laboratory test results for inpatient treatment at civilian facilities.

Cases of sepsis were identified using data from the inpatient medical, pharmacy, and laboratory records. The criteria for sepsis required that infants have documented clinical symptoms, five or more days of antibiotic use, and a positive laboratory screening test (positive microbial growth in the blood, urine, or CSF). We defined suspected sepsis as clinical symptoms of sepsis and five or more days of antibiotic use without a positive laboratory screening test, consistent with other studies' definition of suspected sepsis (Fig. 1) [5, 9, 10]. Clinical symptoms of sepsis were operationalized as any International Classification of Disease-9$^{th}$ Edition (ICD-9) code for sepsis or suspected sepsis during any inpatient hospitalization within the neonatal period—the first 28 days of life (Supplemental Table 1). Five or more days of antibiotic use was identified in the inpatient prescription record. Positive microbial growth was defined as any inpatient laboratory record of a positive screening test for a bacterial infection in the blood, urine, or CSF.

Common neonatal conditions that have been associated with neurodevelopmental delay in childhood were identified as potential confounders. Diagnoses for preterm birth, LBW, ROP, CLD, PDA, IVH, PVL, hypoxic ischemic encephalopathy (HIE), and hearing loss were identified by ICD-9 codes in the inpatient neonatal record as well as the outpatient records during the first 5 years of life. Preterm birth and birth weight were sub-divided into gestational age and weight categories.

The dependent variable was identified by ICD-9 diagnostic code for neurodevelopmental delay in the outpatient treatment care record at military or civilian facilities within the first 5 years of life. The Agency for Healthcare Quality and Research (AHQR) Clinical Classification System (CCS) categorizes ICD-9 diagnosis codes into 17 clinical categories, including sub-categories for developmental disorders and disorders usually diagnosed in infancy, childhood, or adolescence. Neurodevelopmental delay was defined as diagnosis within these two CCS subcategories within the first 5 years of life. Care for neurodevelopmental delay is typically provided in the community and, as such, often only the initial diagnosis is documented in the medical record. Secondary outcomes included neurodevelopmental delay sub-types of communication delay, intellectual disabilities, motor delay, pervasive developmental disorders (PDD), learning delay, and developmental delay not otherwise specified (NOS). This last category, developmental delay NOS, includes reading and communication issues such as developmental dyslexia, reading disorder, and receptive-expressive reading disorder. It also includes general developmental difficulties, including mixed developmental disorder and developmental delay not elsewhere classified [29].

Chi-squared analysis and nonparametric equality-of-medians tests determined group differences between children with and without sepsis. Logistic regression analysis determined adjusted and unadjusted odds of neurodevelopmental delay and its subtypes by sepsis and suspected sepsis. Logistic regression also was used to determine

adjusted and unadjusted odds of neurodevelopmental delay for the subset of children born preterm and the subset of children born term. Adjusted models controlled for common neonatal complications that have been associated with neurodevelopmental delay including preterm birth, LBW, ROP, CLD, PDA, IVH, PVL, HIE, and hearing loss. Stata Intercooled 13 (Stata Corp, College Station, TX) software was used for statistical analysis; $p$-values of <0.05 were considered statistically significant. The study was reviewed and approved by the appropriate institutional review boards.

## Results

There were a total of 65,938 infants born in 2009–2010 at a MTF who had five or more years of MHS follow-up. Of the included children, 190 (0.29%) met criteria for known sepsis and 3449 (5.23%) infants met criteria for suspected sepsis. The remaining 62,299 (94.48%) had no sepsis and were used as controls (Supplemental Fig. 1). In the cohort of children that did not have sepsis, 13,802 (22.2%) had a diagnosis of developmental delay. In those with suspected sepsis, 971 (28.2%) children had developmental delay; in those with known sepsis, 96 (50.5%) children had developmental delay (Table 1). The median age of first visit for developmental delay in those without sepsis was 2.0 years (IQR 1.5–3.0), and the median age of oldest visit within the study period was 3.4 years (IQR 2.1–4.6). Age of first developmental delay visit was younger in those with suspected sepsis and sepsis, but the age of the last visit was not (Table 1). Children had a median of five developmental delay visits (IQR 1–35). Of all included children, 3626 (5.5%) were born preterm (<37 weeks estimated gestational age) and 2316 (3.5%) were born LBW (<2500 g; Table 1).

In unadjusted analysis, suspected sepsis was associated with a 38% increased odds of developmental delay of any type, and known sepsis was associated with over 3.5 times the odds of any developmental delay. When broken into neurodevelopmental delay sub-types, all sub-types were associated with suspected and known sepsis in unadjusted analysis with the exception of intellectual delay in children with known sepsis, which was non-significant (Table 2).

After adjusting for common neonatal comorbidities including preterm birth (divided into categories 32–37 weeks, 28–32 weeks, and <28 weeks gestational age), LBW, ROP, CLD, PDA, IVH, PVL, HIE, and hearing loss, children with suspected sepsis as infants had a 9% increased odds of any developmental delay. In adjusted analysis, children with suspected sepsis had significantly increased odds of delays in communication, development delay NOS, learning, and PDD. Intellectual and motor delays were not significantly associated with suspected sepsis (Fig. 2). After adjusting for the same neonatal comorbidities, children with known sepsis during the neonatal period had a 48% increased odds of any developmental delay. Children with known neonatal sepsis were at increased odds of having developmental delay NOS, learning delay, and PDD. Communication, intellectual, and motor delays were not significantly associated with sepsis in adjusted analysis (Fig. 2).

In subgroup-adjusted analysis of preterm infants only, suspected sepsis was associated with an 18% increased odds of any developmental delay. In preterm infants sepsis was associated with a 33% increased odds of communication delay and a 20% increased odds of developmental delay NOS. Suspected sepsis in preterm infants was not associated with PDD, intellectual, learning, and motor delay.

**Table 1** Comparison of Infants with Sepsis and Suspected Sepsis to those without Sepsis on Neurodevelopmental Delays by 5 Years of Age and on Associated Neonatal Conditions

| | No Sepsis ($N = 62,299$) | Suspected Sepsis ($N = 3449$) | Known Sepsis ($N = 190$) | $p$-value |
|---|---|---|---|---|
| Gestational age | | | | |
| Over 37 weeks | 59,635 | 2583 | 94 | <0.001 |
| 32–37 weeks | 2418 | 635 | 17 | |
| 28–32 weeks | 180 | 176 | 30 | |
| <28 weeks | 66 | 55 | 49 | |
| Birth weight | | | | |
| Over 2500 g | 60,667 | 2858 | 97 | <0.001 |
| 1500–2499 g | 1483 | 455 | 28 | |
| 1000–1499 g | 101 | 109 | 23 | |
| <1000 g | 48 | 27 | 42 | |
| SGA | 470 | 56 | 3 | <0.001 |
| IUGR | 110 | 36 | 2 | <0.001 |
| Any Developmental Delay | 13,802 (22.2%) | 971 (28.2%) | 96 (50.5%) | <0.001 |
| Communication | 7479 (12.0%) | 520 (15.1%) | 46 (24.2%) | <0.001 |
| Developmental | 10,969 (17.6%) | 819 (23.8%) | 87 (45.8%) | <0.001 |
| Intellectual | 56 (0.1%) | 7 (0.2%) | 0 (0%) | =0.10 |
| Learning | 1270 (2.0%) | 132 (3.8%) | 25 (13.2%) | <0.001 |
| Motor | 675 (1.1%) | 65 (1.9%) | 15 (2.0%) | <0.001 |
| PDD | 1591 (2.6%) | 143 (4.2%) | 14 (7.4%) | <0.001 |
| First Developmental Delay Visit Age —Median (IQR) | 2.02 (1.50–3.031) | 1.70 (1.24–2.55) | 1.17 (0.54–2.02) | <0.001 |
| Last Developmental Delay Visit Age —Median (IQR) | 3.41 (2.05–4.58) | 3.54 (2.08–4.65) | 3.86 (2.42–4.71) | =0.22 |

*SGA* small for gestational age, *IUGR* intrauterine growth restriction, *PDD* pervasive developmental disorder

**Table 2** Unadjusted Odds Ratios of Neurodevelopmental Delays with Suspected Sepsis or Known Sepsis Compared to Healthy Controls

| | Suspected Sepsis OR (95% CI) | Known Sepsis OR (95% CI) |
|---|---|---|
| Any Developmental Delay | 1.38 (1.28–1.49) | 3.59 (2.70–4.77) |
| Communication | 1.30 (1.18–1.43) | 2.34 (1.68–3.27) |
| Developmental NOS | 1.46 (1.34–1.58) | 3.95 (2.97–5.26) |
| Intellectual | 2.26 (1.02–4.96) | —* |
| Learning | 1.91 (1.59–2.30) | 7.28 (4.76–11.13) |
| Motor | 1.75 (1.36–2.27) | 7.83 (4.59–13.33) |
| PDD | 1.65 (1.39–1.97) | 3.04 (1.76–5.24) |

*Omitted due to small number of infants with known sepsis and intellectual disability

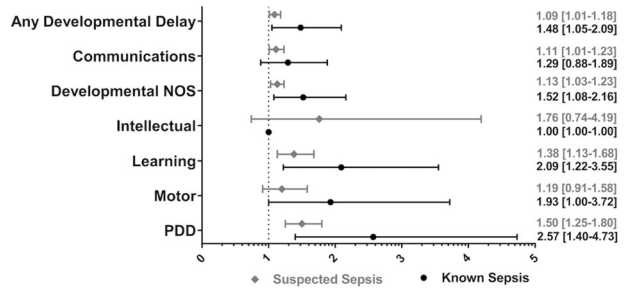


**Fig. 2** Adjusted[1]Odds Ratio with 95% Confidence Interval of Neurodevelopmental Delays by 5 Years of Life in Infants with Suspected and Known Sepsis Compared to Healthy Infants
[1]Model adjusted for preterm birth (32–37 weeks, 28–32 weeks, and less than 28 weeks gestational age), low birth weight, retinopathy of prematurity, chronic lung disease, patent ductus arteriosus, intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, and hearing loss

Known sepsis in preterm infants was associated with an 80% increased odds of any developmental delay and a 65% increased odds of developmental delay NOS (Table 3).

In subgroup adjusted analysis of term infants, suspected sepsis was not associated with increased odds of the composite measure of developmental delay. Suspected sepsis was associated with a 14% increased odds of developmental delay NOS, a 46% increased odds of learning delay, and a 50% increased odds of PDD in term infants. Known sepsis in term infants was associated with a 71% increased odds of the composite measure of developmental delay, a 91% increased odds of delay in communication, a 96% increased odds of developmental delay NOS, and over four times the odds of learning delay, motor delay, and PDD (Table 3).

## Discussion

After adjustment for common risk factors, neonatal sepsis in both term and preterm infants was associated with neurodevelopmental delay in children by 5 years of age. Sepsis and suspected sepsis appear most strongly associated with PDD. While sepsis and suspected sepsis were associated with neurodevelopmental delays in both term and preterm infants, the pattern of delay appears to differ with gestational age. This study explored the relationship between sepsis and neurodevelopmental delay using a robust definition of known sepsis (clinical diagnoses, antibiotic use, and positive microbial growth), follow-up extended to 5 years, a model that controlled for confounders, and a neurodevelopmental delay measure that included both an overall indicator of neurodevelopmental delay and delay sub-types. With known benefit of early intervention programs on cognitive and motor delay in infancy and childhood [30, 31], the findings of this study underline the importance of including children with a history of known or suspected sepsis as being at risk for neurodevelopmental delay, and thus also underlines the importance of early counseling for these children.

Our findings are consistent with many previous studies that have linked neonatal sepsis with neurodevelopmental delays [4–6, 8–12, 17, 19]. Similar to a meta-analysis which identified neurodevelopmental delay sub-types across multiple studies, we found neonatal sepsis was associated with multiple categories of neurodevelopmental delay [6]. Unlike the meta-analysis, we adjusted for multiple comorbidities common in the preterm infant and found that the link between sepsis and multiple types of neurodevelopmental delay endured after adjustment. Schlapbach et al. [11] also adjusted for multiple confounders and found a significant association between proven sepsis and neurodevelopmental delay. However, these studies only considered the impact of sepsis on premature infants.

With our relatively large sample, we were able to separately analyze the impact of known and suspected sepsis on term and preterm infants. Some previous studies of sepsis have used a definition of sepsis more consistent with our measure of suspected sepsis—clinical signs of sepsis and antibiotic use in the absence of a confirmed positive culture [5, 9, 10]. These studies generally referred to "clinical infection" or "clinical sepsis" in describing the criteria for sepsis, illustrating the inconsistency among clinicians and researchers in describing suspected sepsis. In our study, while suspected sepsis did not appear to confer as great a risk as known sepsis, suspected sepsis was significantly associated with multiple categories of neurodevelopmental delay in unadjusted and adjusted models, illustrating the need to be aware of suspected sepsis as a risk for neurodevelopmental delay in children, especially in children born preterm. Our study differs from previous findings, which found a link only between known sepsis and neurodevelopmental delay, but not suspected sepsis and neurodevelopmental delay [11]. In contrast, Ferreira et al. [9] found

**Table 3** Adjusted Odds Ratio of Neurodevelopmental Delay and Delay Sub-types by 5 Years of Life by Suspected and Known Sepsis in Preterm and Term Infants[a]

| | Preterm Infants $N = 3626$ | | Term Infants $N = 62{,}312$ | |
|---|---|---|---|---|
| | Suspected Sepsis OR (95% CI)[b] | Known Sepsis OR (95% CI)[b] | Suspected Sepsis OR (95% CI)[c] | Known Sepsis OR (95% CI)[c] |
| Any Developmental Delay | **1.18 [1.00–1.40]** | **1.80 [1.09–2.98]** | 1.08 [0.98–1.19] | **1.71 [1.10–2.65]** |
| Communication | **1.33 [1.09–1.62]** | 1.05 [0.62–1.79] | 1.04 [0.92–1.18] | **1.91 [1.15–3.18]** |
| Developmental | **1.20 [1.01–1.42]** | **1.65 [1.01–2.70]** | **1.14 [1.03–1.26]** | **1.96 [1.24–3.09]** |
| Intellectual | 1.08 [0.10–11.17] | 1.00 [1.00–1.00] | 2.25 [0.95–5.32] | 1.00 [1.00–1.00] |
| Learning | 1.26 [0.89–1.77] | 1.55 [0.78–3.07] | **1.46 [1.15–1.85]** | **4.92 [2.42–10.02]** |
| Motor | 0.97 [0.61–1.53] | 1.71 [0.79–3.72] | 1.39 [0.99–1.94] | **4.27 [1.55–11.75]** |
| PDD | 1.39 [0.94–2.04] | 1.02 [0.34–3.05] | **1.50 [1.22–1.84]** | **4.64 [2.37–9.07]** |

Bolded values are those that show statistical significance.

[a]Model adjusted for low birth weight, retinopathy of prematurity, chronic lung disease, patent ductus arteriosus, intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, and hearing loss

[b]Reference is preterm infants without sepsis

[c]Reference is term infants without sepsis

neuromotor developmental delay to be almost twice as likely in infants with neonatal "clinical sepsis" (consistent with our suspected sepsis), and found no significant association between confirmed neonatal sepsis and neurodevelopmental delay. Similar to our findings, Stoll et al. [5] found neonates with "clinical infection" and those with confirmed sepsis had similar levels of neurodevelopmental delay.

Although blood culture is typically the gold standard to diagnose sepsis, some studies suggest blood cultures are not sufficiently sensitive [9], which may explain the statistically significant findings of neurodevelopmental delay in neonates with suspected sepsis. Blood cultures can be unreliable with maternal intra-partum antibiotic administration and insufficient collection of inoculated blood from neonates [32]. One milliliter of blood from septic neonates is shown to produce reliable positive growth from blood cultures, however insufficient blood negatively impacts results [33]. The absence of positive cultures can create a false negative for sepsis, especially when it may be difficult to obtain one milliliter of blood from some preterm and term neonates [9]. While cases of suspected sepsis may include false negatives due to laboratory issues, these infants also may not have microbial infection. Other conditions in the perinatal period may initially look like sepsis due to neurologic symptoms, cardiorespiratory issues, or temperature instability, thus resulting in extended antibiotic administration. These conditions may include, but are not limited to, hypoglycemia, transient tachypnea of the newborn, and congenital adrenal hyperplasia. The more general inclusion criteria in the suspected sepsis group may decrease homogeneity in this group and contribute to the striking findings linking suspected sepsis with neurodevelopmental delay. While it is unlikely that all infants with clinical symptoms have undocumented infection, the inclusion of the suspected sepsis category in analysis of the impact of sepsis is important to gauge effects of sepsis on neurodevelopmental delay, compare findings with previous research, and formulate clinical guidelines for referral for early intervention for those with a history of suspected sepsis.

Also important to note is the increasing understanding of the impact of antibiotic use on the gut microbiome as a potential risk factor for neurodevelopmental delay in infants and children [34]. Length and type of antibiotic prescribed to children with suspected and known sepsis may differ, potentially impacting inflammation, injury, and respiratory morbidities differently.

Our study differed from previous research in our inclusion of term infants. In our study, term infants with confirmed neonatal sepsis appeared to have increased risk of neurodevelopmental delay in almost all sub-types of delay examined. While previous research has linked sepsis and neurodevelopmental delay in term infants and children, it focused on outcomes following infection and examined those with high risk illnesses or congenital conditions [7]. In studies of older, largely school-aged children, associations between an episode of sepsis and cognitive or intellectual deficits or general diminished functional status have been reported [25–28]. Our research builds on these findings to support the idea that sepsis can impact neurodevelopment in the absence of prematurity. Findings illustrate the importance of identifying, treating, and providing long term monitoring to infants with sepsis regardless of gestational age.

In this analysis of the impact of sepsis on different types of neurodevelopmental delay, learning delay and PDD were most noticeably associated with known and suspected sepsis. However, in models analyzing the impact of known

and suspected sepsis on preterm and term infants separately, we found that the link between sepsis and diagnoses of PDD and learning delay was stronger in children born at term. The strength of this relationship may be due to the fact that we controlled for factors associated with sepsis in preterm infants, but did not control for factors associated with sepsis in the term infant (aside from HIE), as risk factors for sepsis in term infants have not been identified clearly. Findings still warrant close attention during follow-up care for all children with a history of neonatal sepsis.

This study has many strengths. We included analysis of the impact of sepsis on all children and on the term and the preterm infant independently, and we assessed known and suspected sepsis separately. We had a large population of included children overall and a fairly large number of children with known and suspected sepsis, both of which are rare. We also assessed neurodevelopmental delay as a global indicator and divided neurodevelopmental delay into sub-types that were assessed at up to age 5 years, extending the follow-up period from previous studies. The military population studied was geographically, socioeconomically, and racially diverse, increasing generalizability. Using a population of children born and treated in the MHS, we ensured that all included children had access to healthcare through Tricare for the full course of the study, decreasing access-to-care bias.

Our study was limited by issues inherent to health claims database research. Because of the use of ICD-9 codes, we were dependent on coding data, which can be affected by provider coding inconsistencies. We also were only able to include infants born and initially cared for in MTFs, which may not be representative of the larger military population or the national population. Because MTFs do not all have a level three neonatal intensive care unit, the percentage of preterm infants in our study is lower than average, even for the MHS, which already has lower preterm birth rates than the national average [35]. In contrast, the rate of neurodevelopmental delay in our military population was higher than national averages, possibly due to access to free and comprehensive care, and more universal neurodevelopmental delay screening. In addition, parents of children with neurodevelopmental delay may stay in the military longer to access the free unlimited healthcare benefit for their children, decreasing military and therefore study attrition for this sub-population. The use of diagnostic codes as an indicator of neurodevelopmental delay also may contribute to our elevated rate, as children were included if they ever had a condition within the first 5 years. Children with milder neurodevelopmental delay may have been diagnosed formally in the MHS to ensure their family was located at a base where developmental services could be accessed. Another limitation to our study is there are no military-wide uniform laboratory indicator of significant sepsis findings in laboratory results. As such, we relied on text fields in the data files in some instances to identify known sepsis in the absence of a clear laboratory value. As text fields were not always populated, this method increased the possibility that some cases of sepsis were misclassified as suspected sepsis. Another limitation is that, with the exception of HIE, most of the risk factors included in our adjusted analyses are complications that mainly affect the preterm and not the term infant. In our study, we could not control for maternal complications, such as chorioamnionitis, preterm labor, and maternal antibiotics because of the unavailability of corresponding maternal data; maternal chorioamnionitis has been linked to early onset sepsis and mental developmental delay [36]. Similarly, factors that occur outside of the neonatal period including growth, nutrition, trauma, and accidental injury may impact child development, and these factors were not controlled for in our study.

Results of this study corroborate research indicating the importance of providing early counseling about neurodevelopment to parents of children with known sepsis and suspected sepsis. Diagnosis of suspected or known neonatal sepsis alone, especially in term infants, would not typically merit immediate referral for developmental services. In contrast, depending on the gestational age, prematurity alone often justifies referral to early intervention. This study suggests that a history of known and suspected sepsis in term and preterm infants warrants close examination, and potentially a lower threshold for referral for early intervention services after developmental screening.

## Conclusion

Building on previous research, this study strengthens the understanding that both known and suspected sepsis are associated with neurodevelopmental delay. Among the different subtypes of neurodevelopmental delay, the strongest and most consistent association with sepsis and suspected sepsis were developmental delay NOS, PDD, and learning delay. These findings suggest the need for practitioners to be vigilant in assessing possible neurodevelopmental delay in children with a history of neonatal sepsis and provide interventions as early as possible.

## Disclaimers

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government. Some authors are a military service member or a U.S. Government employee. This work was prepared as part of their official duties. Title 17 U.S.C. 105

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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