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Research Article

Prenatal Opioid Exposure and Special Education Needs: A Sibling Study

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ABSTRACT

Objective: To determine if prenatal opioid exposure places children at increased risk for using school-based special education services.

Method: Using a sibling-based quasi-experimental design *via* retrospective survey methods, an anonymous survey was distributed to a convenience sample of 2,860 parents/guardians of children with documented prenatal opioid exposure. Data for 720 children from 262 families were collected. The primary outcome was child utilization of special education, 504 plan or school-based behavior services, accounting for biological and environmental determinants *via* the sibling design, as well as 16 confounders including child age, race, biological sex, other substance exposures, birth weight, gestational age, per capita income, city and receipt of early intervention services.

Results: 482 opioid-exposed children were compared to 125 biological and 113 non-biological siblings. Opioid-exposed children had a 2.1 times increased incidence of specialized school-based services use compared to their non-exposed biological siblings (IRR=2.110, 95% CI=1.360-3.273, p<.01) and a 4.1 times increased incidence of service use compared to non-biological siblings (IRR=4.107, 95% CI=2.249-7.499, p<.001), controlling for covariates.

Conclusion: Prenatal opioid exposure is significantly associated with increased use of specialized school-based educational services in children 3 to 18 years of age compared to biological and non-biological siblings without opioid exposure.

Keywords: Opioid exposure; Birth weight; Children; Infant; Pregnancy

INTRODUCTION

Since the late 1990s, the incidence of opioid use during pregnancy has risen precipitously. During 1999-2013, state-specific Neonatal Abstinence Syndrome (NAS) incidence rates increased significantly in 25 of 27 states with at least 3 years of data and by 2017, the estimated NAS rate was 7.3 (95% Confidence Interval (CI), 6.8-7.7) per 1,000 hospital births, with ongoing increases during the Coronavirus Disease 2019 (COVID-19) pandemic [1-3].

Over the past decade, Neonatal Opioid Withdrawal Syndrome (NOWS) has become the preferred diagnosis for infants affected specifically by prenatal opioid exposure. In this paper we will use the term "NAS" since that is the terminology that has been used during the bulk of the opioid epidemic [4-7].

The long-term implications for neurocognitive outcomes of children with prenatal opioid exposure have been recently documented [8]. More specifically, Fill, et al., examined educational disability among children born with NAS, but restricted their subject population to children ages 3 to 8 years and included only those children who had had a diagnosis of NAS [9]. The aim of this study is to determine the relative risk of opioid exposure on the use of school-based services (special education, 504 plan, behavioral services) in children, ages 3 to 18 years, including children with and without a diagnosis of NAS at birth, while addressing potential confounding factors that can influence the need for school-based services.

MATERIALS AND METHODS

Research design

We used a sibling-based quasi-experimental design to achieve our study aim. An anonymous survey of parents/guardians of opioid-exposed children asked for information on the opioid-exposed (focal) child and any biological and non-biological siblings 3 years to 18 years of age living in the home. This approach allowed us to generate one comparison group of non-opioid exposed children (biological siblings) with similar biological and environmental risk

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of requiring school-based services and another comparison group of non-opioid exposed children (non-biological siblings) in the home with similar environmental risk of needing these services [10].

Recruitment

Participants were recruited from two primary sources: a) parents/guardians of at least one child identified with prenatal opioid exposure who joined a lawsuit on the child's behalf ("litigation group," n=2,860 families) and b) parents/guardians of children with prenatal opioid exposure enrolled in community-based behavioral health services who were not involved in the lawsuit ("non-litigation group," n=200 families). To protect participant anonymity, a recruitment email from the investigators with a link to participate in the survey was forwarded to potential participants by either their attorneys or clinicians, respectively. An information sheet specified eligibility as follows: at least 18 years of age, lives in the United States (US), speaks English and the parent or guardian of a child under age 18 identified as exposed to opioids in pregnancy.

Study sample

In total, 656 surveys had been started when data collection concluded (22.9% response rate total; 22.1% response rate for the litigation group and 33.5% response rate for the non-litigation group). Data cleaning excluded 215 families whose data contained duplicates, blank, unreliable (i.e. did not follow instructions) and other records containing grave errors. Given our research design, we further excluded 179 families with only children or missing information on child relationships, leaving 262 families in the final analysis. Bivariate analyses comparing dropped opioid-exposed children with no siblings to retained opioid-exposed children with siblings revealed that dropped cases were demographically similar to retained cases. However, dropped cases reported higher utilization of school-based services compared to retained cases (68.3% *vs.* 50.1%; χ^2 (1)=16.1, p<0.001).

Any siblings who were exposed to opioids prenatally (n=190 children from 70 families) were categorized as opioid-exposed children for the analysis. The final analytic sample included 720 children from 262 families: 482 opioid-exposed focal children, 125 non-exposed biological siblings and 113 non-exposed non-biological siblings. Internet Protocol (IP) address data indicated that surveys retained for the analysis were completed by respondents in 222 US cities or towns. Bivariate analyses comparing opioid-exposed children in the litigation group to opioid-exposed children in the non-litigation group indicated that litigation group children were demographically similar to the non-litigation group children. The non-litigation group reported higher rates of prenatal nicotine exposure (58.3% *vs.* 27.3%; χ^2 (1)=10.7, p<0.01), alcohol exposure (62.5% *vs.* 19.4%; χ^2 (1)=25.0, p<0.01), marijuana exposure (41.7% *vs.* 12.2%; χ^2 (1)=16.7, p<0.001) and methamphetamine exposure (75.0% *vs.* 14.0%; χ^2 (1)=60.2, p<0.001) as well as more early intervention services utilization (58.3% *vs.* 29.4%; χ^2 (1)=9.0, p<0.01). Based on IP addresses, the non-litigation group respondents were from cities/towns with higher per capita average income ($42,107.58 *vs.* $34,274.05; F (1)=9.28, p<0.01). No bivariate difference in utilization of school-based services was found between the litigation and non-litigation groups of opioid-exposed children.

Measure

Survey description: A survey developed by the authors asked one parent or guardian from each family to answer questions about all children 3 to 18 years of age living in their home including a focal child (child identified as prenatally exposed to opioids) and this focal child's biological or non-biological siblings living in the home. For respondents caring for multiple opioid-exposed children, we asked them to select as focal child the opioid-exposed child about whose social and medical history they knew the most. The survey asked for the first three letters of each child's first name to implement branching logic to increase the chances that questions were answered for each child accurately. After several demographic questions, the survey asked the respondent to report information on each child's birth history including prenatal substance exposure as shown in Table 1, birth outcomes, participation in school-based services and any diagnoses the child may have received.

Dependent variable: The survey asked respondents to indicate which of six types of school-based services the child had received or was currently receiving: early intervention, special education, Individual Education Plan (IEP) assessment, 504 plan, tutoring services, school-based behavioral services and other. School-based services were recoded as 1=yes if the survey indicated a child received either special education, 504 plan or school-based behavioral services.

Independent variable: Child type (0=focal child, 1=biological sibling, 2=non-biological sibling) captured whether the child was prenatally exposed to opioids (focal child) or a "sibling" 3 to 18 years of age living in the same home as the focal child. Biological siblings included full and half siblings (86% full, 14% half). Non-biological siblings included adoptive or foster sibling relationship (7%) and other non-biological relationship (93%).

Control variables: Given their causal relationships with opioid exposure and/or special education needs documented in existing literature, we included 11 covariates in our model. We accounted for three demographic characteristics: biological sex (male *vs.* female), child race (white *vs.* not white) and child age (categorized as 3-7, 8-12 or 13+). To account for gestational and birth confounders we included three dummy variables for other prenatal exposures (alcohol, nicotine and methamphetamine), gestational age in weeks, whether the infant spent time in the Neonatal Intensive Care Unit (NICU) at the time of delivery, whether the child was diagnosed with NAS at birth. We also controlled for whether the child received early intervention services and whether the caregiver who completed the survey was the child's biological parent. To account for socioeconomic status, we used IP address information to collect per capita income for the city/town where the respondent resided from the census' American Communities Survey data (2016-2020). To account for local context, we also controlled for city/town where the respondent resided based on IP address. Finally, we included recruitment source to account for whether the participant was recruited from the litigation group or the non-litigation group.

Data analysis

We first performed bivariate analyses to examine demographic and service characteristics of children across the three groups. Next, model variables were examined for multi-collinearity; no correlation rose above r=0.578 (NICU and NAS diagnosis). Data for gestational age and birth weight were missing for 24.3% of children. All other model variables' missingness was below 2% so addressed with list wise deletion. To address missing data on gestational age and birth weight, we used multiple imputation with chained equations (using Stata/Standard Error (SE) 16.1) [11]. We then developed a multivariate negative binomial regression model to test the incidence of school-based services controlling for covariates. Compared to logistic regression, binomial regression provides unbiased estimates of Incidence Rate Ratios (IRR) when estimating prevalence for an outcome that occurs in more than 10% of the population, as is the case with special education [12,13]. A priori significance levels were p<0.05 using two-sided hypothesis tests. All research activities were approved by the University of Connecticut Institutional Review Board.

RESULTS

Descriptive characteristics

Table 1 presents characteristics of the analytic sample as a whole and for each group. Opioid-exposed children were younger than their siblings, more likely to have a NICU stay and NAS diagnosis at birth, concurrent exposures to alcohol and methamphetamine, utilize early intervention services, have shorter gestational age and lower birth weight. Regarding school-based services, 50.1% of opioid-exposed children used at least one service (special education, 504 plan or behavior service), compared to 27.9% of biological siblings and 11.6% of non-biological siblings. For the specific school-based services, opioid-exposed children were enrolled in special education (34.4%) and received 504 plan (12.2%) or behavioral services (28.3%) at significantly higher rates than non-exposed biological or non-biological siblings.

Multivariate analysis

Table 2 summarizes findings from the negative binomial regression. Opioid-exposed children were significantly more likely to use school-based services compared to biological siblings. The IRR indicates that opioid-exposed children had a 2.1 times increased incidence of utilization of school-based services compared to biological siblings controlling for covariates (IRR=2.11, 95% CI=1.36-3.27, p<0.0001). The only covariates significantly associated with the outcome were age (older children use school-based services at higher rates), biological sex (males used school-based services at higher rates) and early intervention service receipt (recipients of 0-3 years' early intervention services used school-based services at higher rates). Not reported in Table 2, switching the reference group to non-biological siblings revealed that opioid-exposed children had 4.1 times increased incidence (IRR=4.107, 95% CI=2.249-7.499, p<.001) of utilizing school-based services compared to their non-biological siblings.

Table 1: Descriptive characteristics of convenience sample of opioid-exposed children and non-opioid-exposed siblings in 222 United States cities (n=720).

	Total		Opioid-exposed children		Biological siblings		Non-biological siblings		Statistical test	
	(n=720)		(n=458)		(n=103)		(n=110)			
	n	%	n	%	n	%	n	%		
Child age category									χ^2 (4)=162.68	***
3 to 7 years	285	39.8	246	51.3	20	16.1	19	16.8		
8 to 12 years	241	33.6	163	34	45	36.3	33	29.2		
13 to 17 years	191	26.6	71	14.8	59	47.6	61	54		
Child male (yes)	399	55.5	280	58.2	61	48.8	58	51.3	χ^2 (2)=4.50	
White (yes)	587	82.4	396	82.9	97	80.2	94	83.2	χ^2 (2)=0.53	
NICU (yes)	353	49	324	67.2	20	16	9	8	χ^2 (2)=194.64	***
NAS diagnosis (yes)	261	36.8	259	54.2	1	0.8	1	0.9	χ^2 (2)=191.03	***
Prenatal exposures										
Nicotine	194	26.9	139	28.8	29	23.2	26	23	χ^2 (2)=2.66	
Alcohol	120	16.7	104	21.6	12	9.6	4	3.5	χ^2 (2)=26.88	***
Marijuana	99	13.8	66	13.7	21	16.8	12	10.6	χ^2 (2)=1.92	
Meth	93	12.9	82	17	9	7.2	2	1.8	χ^2 (2)=23.30	***
Early intervention services	171	24.1	147	30.8	19	15.6	5	4.5	χ^2 (2)=40.28	***
School-based service	286	40.2	239	50.1	34	27.9	13	11.6	χ^2 (2)=65.26	***
Special education	186	26.2	164	34.4	18	14.8	4	3.6	χ^2 (2)=54.5	***

504 Plan	74	10.4	58	12.2	11	9	5	4.5	χ^2 (2)=6.07	*
Behavior services	159	22.4	135	28.3	16	13.1	8	7.1	χ^2 (2)=30.64	***
	M	SD	M	SD	M	SD	M	SD		
Average per capita income	34361.74	11614.11	34664.91	12385.31	33666.59	9076.63	33835.52	10710.35	F (2)=0.50	
Gestational age	37.49	2.98	37.14[a]	3.06	37.89[b]	2.74	38.51[b]	2.66	F (2)=9.16	***
Birthweight	6.67	1.52	6.47[a]	1.52	6.86[b]	1.44	7.24[b]	1.45	F (2)=10.70	***

Note: NICU: Neonatal Intensive Care Unit; NAS: Neonatal Abstinence Syndrome; M: Mean; SD: Standard Deviation; [ab] Pairwise comparisons interpreted as follows: different superscripts indicate statistically significant difference at p<0.05. For example, gestational age for the opioid-exposed group is significantly different from both non-opioid-exposed sibling groups, but the sibling groups are not different from one another; *:p<0.05; ***: p<0.001; F(19,0.000)=4.39; χ^2: Chi square test.

Table 2: School-based services[a] use among convenience sample of opioid-exposed children and non-opioid-exposed siblings in 222 United States cities (n=690)

					95% Confidence interval	
	IRR	SE	t	p	Lower limit	Upper limit
Child (referred to biological sibling)						
Opioid-exposed	2.11	0.47	3.34	**	1.36	3.27
Adoptive sibling	0.51	0.17	-1.96	*	0.26	1
Child Age (referred to 3-7 years old)						
8 to 12 years old	1.66	0.24	3.54	***	1.25	2.2
13 years and older	1.67	0.3	2.9	**	1.18	2.37
Male (yes)	1.37	0.18	2.44	*	1.06	1.77
White (yes)	0.94	0.16	-0.37		0.68	1.3
NICU (yes)	0.93	0.15	-0.47		0.68	1.26
NAS (yes)	1.03	0.16	0.17		0.76	1.39
Nicotine exposure	0.89	0.14	-0.75		0.64	1.22
Alcohol exposure	1.07	0.19	0.35		0.75	1.52
Marijuana exposure	0.73	0.16	-1.43		0.48	1.12
Methamphetamine exposure	1.15	0.23	0.68		0.77	1.7
Early intervention services (yes)	1.6	0.22	3.49	***	1.23	2.09
Income	1	0	0.6		1	1
Gestational age	1.01	0.03	0.48		0.96	1.07
Birthweight	0.96	0.05	-0.69		0.86	1.07
Recruitment source	0.94	0.27	-0.21		0.54	1.65
Biological parent reporter	0.78	0.12	-1.64		0.57	1.05
City/town	1	0	0.44		1	1
Constant	0.12	0.12	-2.15	*	0.02	0.82

Note: IRR: Incidence Rate Ratios; NICU: Neonatal Intensive Care Unit; NAS: Neonatal Abstinence Syndrome; t: true value of population parameter; P: Probability; SE: Standard Error; [a]School-based services defined as special education, 504 plan or behavior service. List wise deletion on eight model variables reduced the sample size by 30 cases. Missing data on two variables with most missingness (birthweight and gestational age) addressed using multiple imputation with chained equations. Negative binomial regression model with imputed data provided above estimates; Model specifications: Number of observations: 690; Imputations: 20; F (19,0.000): 4.39; *: p<0.05; **: p<0.01, ***: p<0.001.

DISCUSSION

Nationally, over 13% of all students receive special education services [14]. However, in the present sample, approximately 34% of children born opioid-exposed had been or currently were enrolled in special education classes in school. By comparison, 15% of their non-opioid-exposed biological siblings were enrolled in special education services, similar to the national prevalence.

Prenatal opioid exposure can cause permanent neurodevelopmental damage to the developing fetal brain [15-17]. A 2019 meta-analysis of 26 studies, involving 1,455 children ages 6 months to 18 years, found that children with prenatal opioid exposure were significantly more likely to have a severe intellectual disability and that the neurodevelopment of these children did not improve after preschool but rather worsened by school age [8]. Further, in a 2017 study of 6,664 children with NAS, the children with NAS were more likely to fail to meet educational standards and the gap between children with NAS and other children widened as the children progressed to higher grades [18].

Fill, et al., conducted a population incidence study utilizing Tennessee birth and education records to ascertain the need for special education services among 1,815 children ages 3 to 8 years who had been diagnosed with NAS as compared to 5,441 children who had not been diagnosed with NAS. Approximately 15% of children with a history of NAS met criteria for a qualifying educational disability and were eligible for services, compared with 11.6% of children without a history of NAS [9].

Some important points emerge in comparing our study to the Fill, et al. study. For one, our treatment condition included opioid-exposed children with and without NAS diagnoses. Based on our data, which found that less than half of the opioid-exposed children in our sample had a confirmed NAS diagnosis, it is likely that children in the Fill, et al., control condition had prenatal opioid exposure but did not meet criteria for an NAS diagnosis or were otherwise misdiagnosed. This is meaningful because, as observed in our multivariate model, it was the opioid exposure, not the NAS diagnosis, per se, that was associated with special education and other school-based service utilization. In addition, our sample included children from 22 states and an age range of 3-18. Our data, similar to the Oie, et al., study, demonstrate that risk for requiring specialized educational services increases as the child ages [18].

The fact that Fill, et al., is a population-based study is one of its strongest design elements, thus protecting against the threat of selection bias. To explore whether our sample was "higher risk" than the general population of children with prenatal opioid exposure, perhaps reflecting selection bias where parents of children with more problems opted in to participate in litigation, receive community-based services or participate in a survey, we conducted a post-hoc analysis using methods that approximately replicated the Fill, et al., study. We examined likelihood of special education services (excluding 504 plans and behavior services) with a restricted sample of children ages 3-8 with *vs.* without NAS diagnosis (excluding children with diagnosis unknown). Our negative binomial regression (n=205) controlling for similar confounders as Fill, et al., as well as litigation status found that children with NAS had a 1.4 times increased incidence of special education as compared to children with no NAS diagnosis (IRR=1.44, 95% Confidence Interval (CI)=0.63-3.30, p=0.392). This outcome is similar to that of Fill, et al., which estimated effects of NAS on special education services between 1.3 and 1.4.

In sum, the divergence in findings between our study and prior literature appears explained by the different approaches to measurement, including the age of the targeted population and the inclusion of children with prenatal opioid exposure who had not received a diagnosis of NAS. Based on our findings, the Fill, et al., study and the clinical diagnostic criteria for NAS, NAS may be more appropriately considered a proxy for severity of prenatal opioid exposure and a mediator on the path from prenatal opioid exposure to school-based service needs.

Previous studies have demonstrated the role of prenatal alcohol exposure in increasing risk for special education enrollment [19]. We found that opioid exposure conferred a greater risk for special education service use compared to alcohol exposure. This is corroborated with other recent research on the relative effects of prenatal alcohol *vs.* opioid exposure in over 3,000 children, which showed that children with prenatal opioid exposure had the highest risk (2.2 times increased) for receiving a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) [20]. After adjusting for other substances, neither cannabis (0.28) nor alcohol (0.28) was associated with an ADHD diagnosis [21-25].

CONCLUSION

Early intervention through special education services is considered the most effective means of changing the developmental trajectory of infants and children with or at risk of, developmental delays or disabilities. This is meaningful because the economic and social costs of disabilities are considerable. In purely economic terms, scholars estimate that these costs per child per year range from $ 450-69,500. Caregiver burden may also be considerable depending on the specific disability and the family's social situation and larger societal context.

One factor critical in ensuring access to services, improving child outcomes and relieving caregiver burden, is IDEA part C, which mandates automatic eligibility for early intervention services on the basis of diagnoses or conditions known to cause developmental delays. As noted, states may expand eligibility to include children "at risk" of these delays in the absence of early intervention services. Nearly half of states include NAS in the list of qualifying conditions.

The purpose of these policies is to reduce the social and economic costs to individuals, families and states associated with unmitigated delays stemming from NAS. Based on our study's findings, however, limiting eligibility to prenatal opioid exposure that results in an NAS diagnosis is excluding nearly half of children with exposure who are at considerable risk of requiring special education services. Moreover, our estimate is likely conservative since we measured receipt of services, which requires identification, screening, referral and uptake. The proportion of our sample who needed services but did not receive them is unknown.

In summary, remedial measures offered through the school system serve a crucial role in enabling children to adapt to the neurodevelopmental deficits caused by prenatal opioid exposure. Expanding access to early intervention services offered through IDEA part c to include children with prenatal opioid exposure but who do not meet criteria for NAS may reduce the burden on schools to address these children's needs over the longer term. This information is important for policymakers and state and federal education agencies as they prepare to address the developmental and academic needs of children with prenatal opioid exposure.

Limitations

Although this study advances knowledge on the relationship between prenatal opioid exposure and school-based services by both corroborating and expanding upon previous population-based research, some limitations must be noted. First, the majority of the sample were recruited from a group of families engaged in litigation. Although the survey recruitment materials specified that the study was conducted by researchers, not attorneys and that the law firm who partnered in recruitment efforts did not represent any of the potential participants (and therefore respondents had no financial interest in the outcome of the study), the opioid-exposed children in the lawsuit could have had sufficiently notable clinical or behavioral problems that would motivate their guardians' involvement in litigation. However, our sample is nearly identical to children receiving school-based services in the U.S. according to five key metrics: 1) our findings on the effect of NAS on special education services receipt reflect the population-based findings documented in Fill, et al., 2) the non-exposed biological siblings in our data set demonstrated similar rates of special education service use (14.8%) compared to the general U.S. population (13%), 3) the percentage of prenatal alcohol-exposed children among biological and non-biological siblings (6.7%) reflects the general population of prenatal alcohol-exposure in the time frame that our sample of children were born (8.5%), 4) the average per capita income for settings where our sample lived ($34,361.74) is similar to the average U.S. per capita income (($35,384) and 5) the litigation-involved participants in our study reported statistically similar or lower risk characteristics compared to the non-litigation involved participants. Nonetheless, future replication studies with random sampling approaches are needed.

Second, other unmeasured factors may have contributed to the likelihood of receiving school-based education services. Although we accounted for many important factors including prenatal alcohol, nicotine and illicit drug exposure; birth characteristics; gender; age; income; and geographic location, there may be other factors that would further our understanding of causal effects. Moreover, our measure of socioeconomic status, an important predictor in special education needs, was an approximation (i.e. per capita income for the respondent's city/town).

Third and finally, we relied on self-reported medical, educational and social histories. Although this approach offered a clear advantage in terms of capturing opioid-exposed children who did not receive an NAS diagnosis at birth, future sibling-based replication studies corroborating self-report with administrative records may further our understanding of this problem.

COMPETING INTERESTS

In the past, the authors provided expert consultation regarding opioid litigation for Mehri & Skalet PLLC, who represent public school districts. The law firm does not represent any of the families included in this study. The law firm was not involved in the research design, data analysis, interpretation of results or development of the manuscript.

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