

Prenatal Opioid Exposure: Beyond Hospital Discharge

Tammy E. Corr, D.O.

Traci Jennings, MSN, CRNP, NNP-BC

Mandy Haigh Rudy, OTR/L



Part 1

It's Time for School – Neonatal Abstinence Syndrome, Social Drivers of Health, and Academic Achievement

Tammy E. Corr, D.O.

*Associate Professor of Pediatrics, Penn State College of Medicine
Division of Neonatal-Perinatal Medicine*



Disclosures

I have no conflicts of interest or financial disclosures

Objectives

1. Review the latest research on long-term neurodevelopment and academic outcomes in children with a history of NAS
2. Discuss how socioenvironmental factors influence academic achievement in children with prenatal opioid exposure
3. Share recent data on the relationship between prenatal opioid dose and timing and academic success

Women and Opioid Use Disorders

- Opioid fill rates among women are higher than men across all ages¹
- 3% of reproductive-aged women filled an opioid prescription in 2017-2018²
- 2015-2019, 4.3% of women 15-44 reported illicit drug use and 8.8% reported a substance use disorder³
- Women may progress more rapidly than men in addiction and have unique needs⁴



¹ Schieber LZ et al. Variation in Adult Outpatient Opioid Prescription Dispensing by Age and Sex — United States, 2008–2018. MMWR Morb Mortal Wkly Rep 2020;69:298–302

² Elmore AL et al. Prescription opioid use among women of reproductive age in the United States: NHANES, 2003-2018. Prev Med 2021;153:106846

³ Green VR et al. Substance use and treatment characteristics among pregnant and non-pregnant females, 2015–2019. Drug and Alcohol Dependence 2024. 254: 111041

⁴ McHugh RK et al. Epidemiology of substance use in reproductive-age women. Obstet Gynecol Clin North Am 2014;41(2):177–89

Pregnancy and Opioid Use Disorders

- Opioid use disorder (OUD) rates at delivery quadrupled during 1999–2014¹ and more than doubled 2010-2017²
- In 2017, OUD rates at delivery ranged from 1.7 per 1000 deliveries per year (Nebraska) to 47.3 (Vermont)¹
- Analysis of 2019 survey data found that 6.6% of women reported prescription opioid use during pregnancy³
 - 21.2% reported misuse
 - 27.1% wanted or needed to cut down or stop using
 - 31.9% reported not receiving provider counseling about how use could affect an infant

1 Schieber LZ et al. Variation in Adult Outpatient Opioid Prescription Dispensing by Age and Sex — United States, 2008–2018. MMWR Morb Mortal Wkly Rep 2020;69:298–302

2 Hiari AH et al. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. JAMA. 2021 Jan;325(2):146-155

3 Ko JY, D'Angelo DV, Haight SC, et al. Vital Signs: Prescription Opioid Pain Reliever Use During Pregnancy — 34 U.S. Jurisdictions, 2019. MMWR Morb Mortal Wkly Rep 2020;69:897–903

Epidemiology



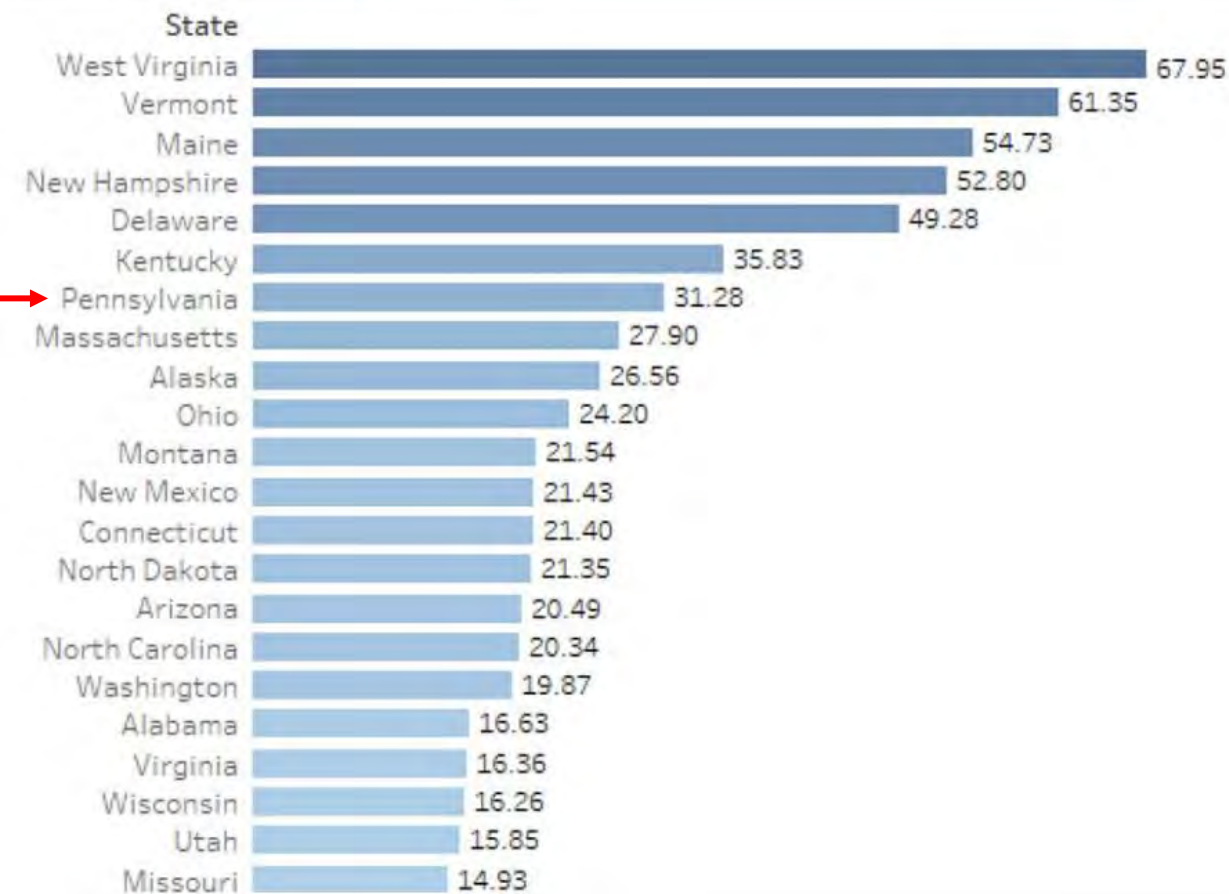
- Opioid epidemic → increased incidence of NAS/NOWS
- 2010 – 2017, maternal opioid-related diagnoses increased from 3.5 to 8.2 per 1000 delivery hospitalizations¹
 - NAS increased from 4.0 to 7.3 per 1000 birth hospitalizations
- NAS affected 12.4 of every 1000 Medicaid birth hospitalizations in 2020²

¹Hiari AH et al. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017. JAMA. 2021 Jan;325(2):146-155

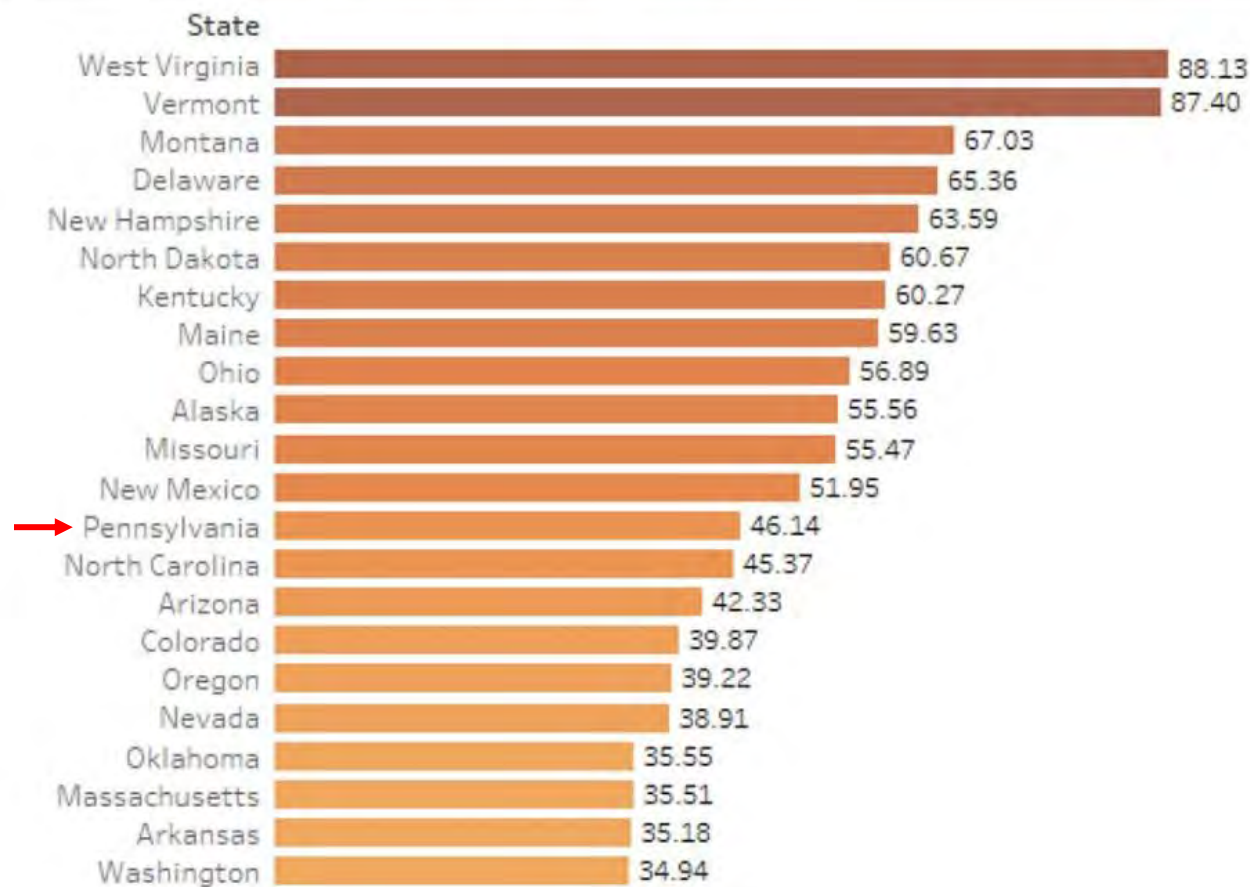
²Ramphul K, Mejias SG, Joynauth J. An update on the burden of neonatal abstinence syndrome in the United States. Hosp Pediatr 2020;10(2):181-184

NAS Rates by State

Cases of NAS in 2020 per 1,000 births



Cases of substance exposure in 2020 per 1,000 births



How Does NAS Occur?

Fetal properties:

Permeable blood-brain barrier

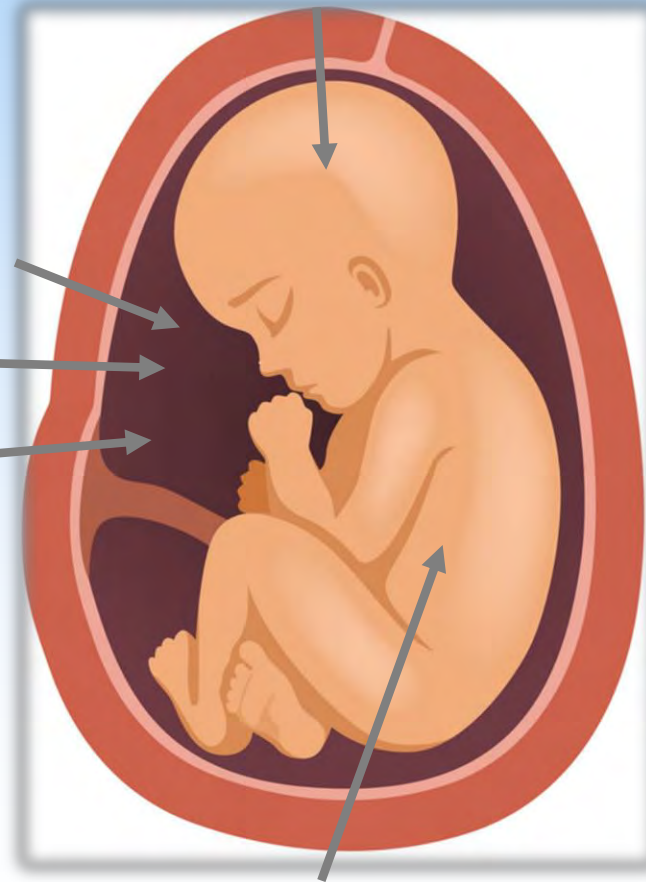
Opioid properties:

Low molecular weight

Water soluble

Lipophilic

*= easily transferable
across the placenta to
the fetus*



Prolonged drug half life in fetus

Increased Transmission:

1. Increasing gestation
2. Synthetic opioids
3. Cocaine or heroin + methadone

Exposure and Fetal Development

- Effects of chronic *in utero* opioid exposure are unclear
- Developing fetal brain is vulnerable¹⁻³
- Effects of drugs on mother can secondarily affect fetus and growth restriction is common⁴
- Prematurity may be as high as 40%⁵



1 Frederick AL, et al. Drugs, Biogenic Amine Targets and the Developing Brain. Dev Neurosci-Basel. 2009;31(1-2):7-22.

2 Money KM, et al. Developmental origins of brain disorders: roles for dopamine. Front Cell Neurosci. 2013 Dec 19;7.

3 Bonnin A, et al. Fetal, Maternal, and Placental Sources of Serotonin and New Implications for Developmental Programming of the Brain. Neuroscience. 2011 Dec 1;197:1-7.

4 Ross EJ, et al. Developmental Consequences of Fetal Exposure to Drugs: What We Know and What We Still Must Learn. Neuropsychopharmacol. 2015 Jan;40(1):61-87.

5 Fajemirokun-Odukeyi O, et al. Pregnancy outcome in women who use opiates. Eur J Obstet Gynecol Reprod Biol. 2006 Jun 01;126(2):170-5.

Academic Achievement

- School achievement is positively associated with:
 1. Adult productivity
 2. Employment
 3. Income
 4. Health

...And negatively correlated with participation in criminal activity
- Important to address the underlying inequities that contribute to poor academic achievement in children to mitigate potential future risks and promote adult success

¹Lochner L. Education and Crime. In: Penelope Peterson EBaBM, ed. International Encyclopedia of Education. Third ed. London, Ontario 2008.

²Berger N. A well-educated workforce is key to state prosperity. Economic Policy Institute. <https://www.epi.org/publication/states-education-productivity-growth-foundations/>. Accessed Sept 20, 2024.

³Lochner L, Moretti E. The effect of education on crime: evidence from prison inmates, arrests, and self-reports. In: University of Western Ontario U, ed. 2003.

⁴Comprehensive Addiction and Recovery Act of 2016. 114th Congress. <https://www.congress.gov/114/plaws/publ198/PLAW-114publ198.pdf>. Accessed Oct 29, 2024.

Previous Studies on Scholastic Outcomes & NAS

Executive Functioning & IQ

- Children exposed to methadone or buprenorphine *in utero* had lower executive-functioning scores¹
- Children exposed to buprenorphine *in utero* had lower IQ scores^{2,3}

Scholastic Performance

- Children with NOWS/NAS were more likely to be referred for disability evaluation, meet criteria for disability, and require classroom therapies⁴
- NOWS/NAS is associated with poor and deteriorating school performance⁵

1 Konijnenberg C, et al.. Mother-child interaction and cognitive development in children prenatally exposed to methadone or buprenorphine. *Early Hum Dev.* 2016;101:91–97

2 Sundelin V, Sarman I. Neurobehavioral development of preschool children born to addicted mothers given opiate maintenance treatment with buprenorphine during pregnancy. *Acta Paediatr.* 2013;102(5):544–549

3 Nygaard E, Moe V, Slinning K, Walhovd KB. Longitudinal cognitive development of children born to mothers with opioid and polysubstance use. *Pediatr Res.* 2015;78(3):330–3352

4 Fill MA, Miller AM, Wilkinson RH, Warren MD, Dunn JR, Schaffner W, et al. Educational Disabilities Among Children Born With Neonatal Abstinence Syndrome. *Pediatrics.* 2018;142(3)

5 Oei JL, Melhuish E, Uebel H et al. Neonatal abstinence syndrome and high school performance. *Pediatrics.* 2017;139(2):e20162651

Longitudinal Academic Performance in Children with a History of Neonatal Abstinence Syndrome

Project Number

1K23DA055096-01

Contact PI/Project Leader

CORR, TAMMY E

Awardee Organization

PENNSYLVANIA STATE UNIV

HERSHEY MED CTR

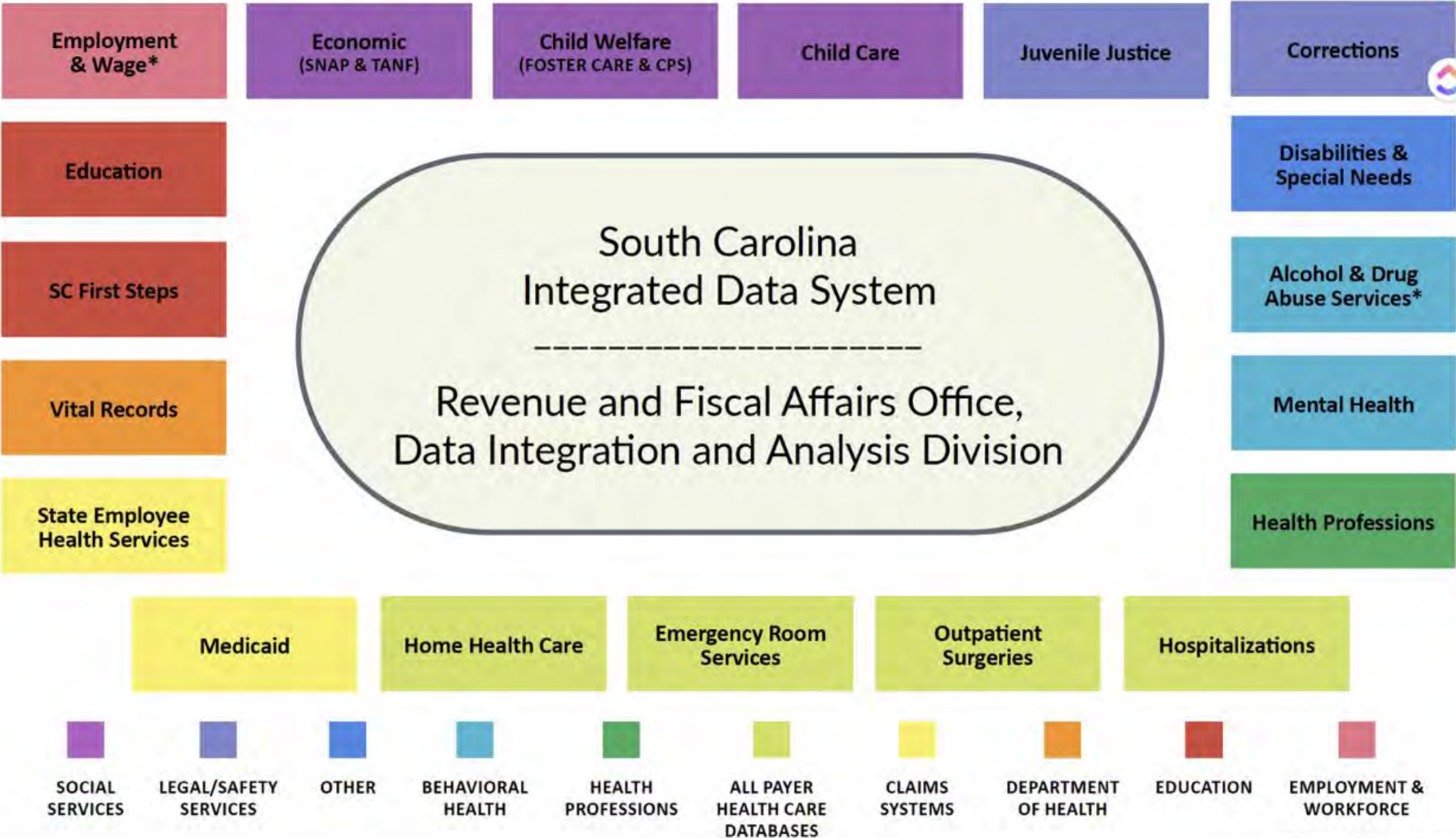
Objective: better understand the relationship between NAS and longitudinal academic performance and determine whether early childhood intervention may be feasible for improving scholastic outcomes

Aim 1. Assess the association between NAS and longitudinal academic performance in school-aged children after controlling for relevant biologic, health, and socioenvironmental variables and examine moderator effects of early childhood interventions on NAS

Aim 2. In children with a history of NAS, evaluate the association between longitudinal academic performance and NAS severity, NAS treatment, and *in utero* drug exposures and explore the moderator effects of early childhood interventions on NAS severity

Aim 3. To augment findings from Aims 1 and 2 by qualitatively exploring how salient variables identified from our quantitative analyses may relate to parents'/guardians' experiences with early interventions and childhood academic performance

FIGURE 1: SOUTH CAROLINA INTEGRATED DATA SYSTEM, REVENUE AND FISCAL AFFAIRS OFFICE, HEALTH AND DEMOGRAPHICS DATA SOURCES



*Limited data available

Inclusion Criteria

- Diagnostic code consistent with NAS with a birth year of 2003-2014
 - *Sensitivity analysis in only children who had supporting indicators in maternal or child records that corroborated their NAS diagnosis (76.4% of original NOWS group)*
- At least one standardized academic achievement test score for **English-Language Arts** or **mathematics** for grades 3-8 (2017-2023) in the SC Department of Education
- Comparison group: children without a diagnostic code for NOWS, frequency matched 3:1 on sex, year of birth, maternal education, and insurance provider

Study Sample

	NOWS ¹ (N=814)	No NOWS (N=2,680)	Total (N=3,494)
Mother's Education, n (%)			
Less than high school	248 (30.5%)	812 (30.3%)	1,060 (30.3%)
High school grad or GED ²	259 (31.8%)	860 (32.1%)	1,119 (32.0%)
Some college	267 (32.8%)	862 (32.2%)	1,129 (32.3%)
College degree or higher	39 (4.8%)	135 (5.0%)	174 (5.0%)
Unknown	1 (0.1%)	11 (0.4%)	12 (0.3%)
Payer, n (%)			
Medicaid/Self-pay	693 (85.1%)	2279 (85.0%)	2,972 (85.1%)
Insurance/HMO ³ /Tricare	121 (14.9%)	401 (15.0%)	522 (14.9%)

¹NOWS=Neonatal Abstinence Syndrome; ²GED=Graduate Equivalency Degree; includes technical school, ³HMO=Health Maintenance Organization

English/Language Arts & Math Vertical Scale Scores

Vertical Scale Scores						
Parameter	English Language Arts			Mathematics		
	Mean difference (SE ¹)	95% CI	p-value	Mean difference (SE)	95% CI	p-value
Intercept	357.5 (48.2)	(263.1, 451.9)	<0.001	421.9 (43.9)	(335.9, 507.9)	<0.001
Grade						
3 (ref ²)						
4	62.3 (1.8)	(58.8, 65.8)	<0.001	28.7 (1.7)	(25.3, 32.1)	<0.001
5	101.1 (2.1)	(97.1, 105.2)	<0.001	73.5 (2.0)	(69.6, 77.4)	<0.001
6	112.2 (2.5)	(107.3, 117.2)	<0.001	69.7 (2.5)	(64.8, 74.5)	<0.001
7	152.7 (2.9)	(147.1, 158.3)	<0.001	88.3 (2.8)	(82.9, 93.7)	<0.001
8	179.7 (3.3)	(173.2, 186.2)	<0.001	122.9 (3.2)	(116.7, 129.1)	<0.001

¹SE=standard error; ²ref=reference group; ³NOWS=Neonatal Opioid Withdrawal Syndrome

Vertical Scale Scores by Grade and Neonatal Opioid Withdrawal Syndrome Diagnosis

	Grade 3 (N=2,341)	Grade 4 (N=2,015)	Grade 5 (N=1,797)	Grade 6 (N=1,491)	Grade 7 (N=1,245)	Grade 8 (N=979)
ELA¹ VSS²						
NOWS ³ , mean (SD)	416 (115)	473 (111)	515 (106)	532 (110)	575 (114)	601 (116)
No NOWS, mean (SD)	416 (111)	481 (112)	517 (107)	529 (112)	565 (105)	594 (110)
→ State, mean (SD)	442 (117)	503 (120)	538 (111)	554 (117)	596 (115)	623 (116)
Math VSS						
NOWS, mean (SD)	429 (113)	450 (100)	493 (97)	497 (102)	523 (87)	552 (92)
No NOWS, mean (SD)	428 (105)	456 (103)	500 (99)	496 (102)	513 (87)	551 (97)
→ State, mean (SD)	456 (119)	484 (112)	529 (113)	527 (112)	546 (103)	581 (107)

¹ELA=English/Language Arts, ²VSS=Vertical Scale Scores, ³NOWS=Opioid Withdrawal Syndrome

Maternal Profile

	NOWS ¹ (N=814)	No NOWS (N=2,680)	Total (N=3,494)
Covariates			
Maternal age at delivery, years			
N	814	2680	3494
Mean (SD ²)	27.7 (5.32)	25.0 (5.56)	25.6 (5.63)
Median	27.0	24.0	25.0
IQR ³	24.0, 31.0	21.0, 28.0	21.0, 29.0
Range	15.0, 43.0	14.0, 46.0	14.0, 46.0
Maternal race/ethnicity, n (%)			
White, non-Hispanic	694 (85.3%)	1182 (44.1%)	1876 (53.7%)
Black, non-Hispanic	102 (12.5%)	1148 (42.8%)	1250 (35.8%)
White, Hispanic	13 (1.6%)	293 (10.9%)	306 (8.8%)
Other	5 (0.6%)	57 (2.1%)	62 (1.8%)
Adequacy of prenatal care⁶, n (%)			
Inadequate	375 (46.7%)	624 (23.4%)	999 (28.6%)
Intermediate	68 (8.5%)	179 (6.7%)	247 (7.1%)
Adequate	132 (16.4%)	677 (25.3%)	809 (23.2%)
Adequate plus	228 (28.4%)	1192 (44.6%)	1420 (40.9%)
Missing	11	8	19

¹NOWS=Neonatal Abstinence Syndrome, ²SD=standard deviation, ³IQR=interquartile range,

⁶Kotelchuck index

Socioenvironmental Profile

	NOWS ¹ (N=814)	No NOWS (N=2,680)	Total (N=3,494)
Covariates			
Maternal WIC² recipient, n (%)			
Yes	498 (62.6%)	1856 (71.1%)	2354 (69.1%)
No	283 (35.6%)	721 (27.6%)	1004 (29.5%)
Unknown	14 (1.8%)	35 (1.3%)	49 (1.4%)
Missing	19	68	87
Foster care placement, n (%)			
Yes	167 (20.5%)	113 (4.2%)	280 (8.0%)
No	647 (79.5%)	2567 (95.8%)	3214 (92.0%)
Maternal criminal conviction, n (%)			
Yes	118 (14.5%)	44 (1.6%)	162 (4.6%)
No	696 (85.5%)	2636 (98.4%)	3332 (95.4%)

¹NOWS=Neonatal Abstinence Syndrome, ²WIC=Women Infants Children supplemental nutrition program/

School Profile

	NOWS ¹ (N=814)	No NOWS (N=2,680)	Total (N=3,494)
Covariates			
School rating², n (%)			
Unsatisfactory	42 (5.3%)	189 (7.3%)	231 (6.8%)
Below average	101 (12.8%)	430 (16.5%)	531 (15.6%)
Average	245 (30.9%)	971 (37.3%)	1216 (35.8%)
Good	200 (25.3%)	573 (22.0%)	773 (22.8%)
Excellent	204 (25.8%)	442 (17.0%)	646 (19.0%)
Missing	22	75	97
School poverty index³			
N	792	2606	3398
Mean (SD ³)	66.7 (17.97)	70.1 (17.57)	69.3 (17.72)
Median	69.5	73.2	72.4
IQR ⁴	56.3, 79.8	59.8, 84.1	58.5, 83.6
Range	9.3, 97.0	9.6, 97.6	9.3, 97.6
Preschool participation⁴, n (%)			
Yes	372 (48.8%)	1531 (59.6%)	1903 (57.1%)
No	390 (51.2%)	1039 (40.4%)	1429 (42.9%)
Missing	52	110	162
Individualized Education Plan, n (%)			
Yes	288 (35.4%)	654 (24.4%)	942 (27.0%)
No	526 (64.6%)	2026 (75.6%)	2552 (73.0%)

¹NOWS=Neonatal Abstinence Syndrome, ²School rating results based on child's first year of data in SC Department of Education, ³Percent of school students meeting criteria for living in poverty; poverty index results based on child's first year of data in SC Department of Education, ⁴Preschool participation=preschool and/or pre-kindergarten

English/Language Arts & Math Vertical Scale Scores

	English Language Arts			Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Grade						
3 (ref ³)						
4	62.2 (1.8)	(58.7, 65.7)	<0.0001	28.5 (1.7)	(25.1, 31.9)	<0.0001
5	101.3 (2.0)	(97.3, 105.3)	<0.0001	73.5 (2.0)	(69.7, 77.4)	<0.0001
6	113.0 (2.5)	(108.1, 117.9)	<0.0001	70.4 (2.5)	(65.6, 75.2)	<0.0001
7	153.8 (2.8)	(148.3, 159.3)	<0.0001	89.4 (2.7)	(84.0, 94.7)	<0.0001
8	180.9 (3.2)	(174.5, 187.2)	<0.0001	124.1 (3.1)	(118.0, 130.2)	<0.0001
NOWS⁴ group						
No NOWS (ref)						
NOWS	-6.3 (4.5)	(-15.1, 2.5)	0.16	-8.9 (4.1)	(-16.9, -0.9)	0.030
Sex						
Male (ref)						
Female	24.5 (3.1)	(18.4, 30.5)	<0.0001	-3.2 (2.8)	(-8.7, 2.3)	0.24

¹SE=standard error, ²CI=confidence interval, ³ref=reference group, ⁴NOWS=neonatal opioid withdrawal syndrome

Association of Socioenvironmental Factors and Academic Achievement

Parameter	English Language Arts			Mathematics		
	Mean difference (SE ¹)	95% CI ²	<i>p</i> -value	Mean difference (SE)	95% CI	<i>p</i> -value
Mother's race/ethnicity						
White, non-Hispanic (ref ³)						
Black, non-Hispanic	-49.1 (3.8)	(-56.5, -41.7)	<0.0001	-46.5 (3.5)	(-53.3, -39.7)	<0.0001
White, Hispanic	-4.5 (6.2)	(-16.7, 7.7)	0.47	-0.5 (5.7)	(-11.6, 10.6)	0.93
Other	33.6 (11.7)	(10.5, 56.6)	0.0043	44.1 (10.6)	(23.2, 64.9)	<0.0001

¹SE=standard error, ²CI=confidence interval, ³ref=reference group, ⁴HMO=Health Maintenance Organization, ⁵WIC=Women Infant Children supplemental nutrition program

Association of Socioenvironmental Factors and Academic Achievement

	English Language Arts			Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Mother's race/ethnicity						
White, non-Hispanic (ref ³)						
Black, non-Hispanic	-49.1 (3.8)	(-56.5, -41.7)	<0.0001	-46.5 (3.5)	(-53.3, -39.7)	<0.0001
White, Hispanic	-4.5 (6.2)	(-16.7, 7.7)	0.47	-0.5 (5.7)	(-11.6, 10.6)	0.93
Other	33.6 (11.7)	(10.5, 56.6)	0.0043	44.1 (10.6)	(23.2, 64.9)	<0.0001
Maternal education						
Less than high school (ref)						
High school grad	12.5 (4.0)	(4.7, 20.4)	0.0017	14.2 (3.6)	(7.1, 21.3)	0.0001
Some college	36.1 (4.2)	(27.8, 44.3)	<0.0001	33.6 (3.8)	(26.1, 41.1)	<0.0001
Graduated from college	82.2 (8.2)	(66.1, 98.3)	<0.0001	79.3 (7.4)	(64.8, 93.9)	<0.0001
Unknown	-16.3 (25.9)	(-67.1, 34.5)	0.52	-2.6 (23.4)	(-48.5, 43.3)	0.91

¹SE=standard error, ²CI=confidence interval, ³ref=reference group, ⁴HMO=Health Maintenance Organization, ⁵WIC=Women Infant Children supplemental nutrition program

Association of Socioenvironmental Factors and Academic Achievement

	English Language Arts			Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Mother's race/ethnicity						
White, non-Hispanic (ref ³)						
Black, non-Hispanic	-49.1 (3.8)	(-56.5, -41.7)	<0.0001	-46.5 (3.5)	(-53.3, -39.7)	<0.0001
White, Hispanic	-4.5 (6.2)	(-16.7, 7.7)	0.47	-0.5 (5.7)	(-11.6, 10.6)	0.93
Other	33.6 (11.7)	(10.5, 56.6)	0.0043	44.1 (10.6)	(23.2, 64.9)	<0.0001
Maternal education						
Less than high school (ref)						
High school grad	12.5 (4.0)	(4.7, 20.4)	0.0017	14.2 (3.6)	(7.1, 21.3)	0.0001
Some college	36.1 (4.2)	(27.8, 44.3)	<0.0001	33.6 (3.8)	(26.1, 41.1)	<0.0001
Graduated from college	82.2 (8.2)	(66.1, 98.3)	<0.0001	79.3 (7.4)	(64.8, 93.9)	<0.0001
Unknown	-16.3 (25.9)	(-67.1, 34.5)	0.52	-2.6 (23.4)	(-48.5, 43.3)	0.91
Payer						
Insurance/HMO ⁴ /Tricare (ref)						
Medicaid/Self-pay	-10.7 (4.8)	(-20.0, -1.3)	0.025	-7.4 (4.3)	(-15.9, 1.0)	0.08
Maternal WIC⁵ recipient	-8.6 (3.7)	(-15.8, -1.4)	0.020	-10.7 (3.3)	(-17.2, -4.2)	0.0014

¹SE=standard error, ²CI=confidence interval, ³ref=reference group, ⁴HMO=Health Maintenance Organization, ⁵WIC=Women Infant Children supplemental nutrition program

Association of Socioenvironmental Factors and Academic Achievement

	English Language Arts			Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Mother's race/ethnicity						
White, non-Hispanic (ref ³)						
Black, non-Hispanic	-49.1 (3.8)	(-56.5, -41.7)	<0.0001	-46.5 (3.5)	(-53.3, -39.7)	<0.0001
White, Hispanic	-4.5 (6.2)	(-16.7, 7.7)	0.47	-0.5 (5.7)	(-11.6, 10.6)	0.93
Other	33.6 (11.7)	(10.5, 56.6)	0.0043	44.1 (10.6)	(23.2, 64.9)	<0.0001
Maternal education						
Less than high school (ref)						
High school grad	12.5 (4.0)	(4.7, 20.4)	0.0017	14.2 (3.6)	(7.1, 21.3)	0.0001
Some college	36.1 (4.2)	(27.8, 44.3)	<0.0001	33.6 (3.8)	(26.1, 41.1)	<0.0001
Graduated from college	82.2 (8.2)	(66.1, 98.3)	<0.0001	79.3 (7.4)	(64.8, 93.9)	<0.0001
Unknown	-16.3 (25.9)	(-67.1, 34.5)	0.52	-2.6 (23.4)	(-48.5, 43.3)	0.91
Payer						
Insurance/HMO ⁴ /Tricare (ref)						
Medicaid/Self-pay	-10.7 (4.8)	(-20.0, -1.3)	0.025	-7.4 (4.3)	(-15.9, 1.0)	0.08
Maternal WIC⁵ recipient	-8.6 (3.7)	(-15.8, -1.4)	0.020	-10.7 (3.3)	(-17.2, -4.2)	0.0014
School rating						
Unsatisfactory	↑ -26.3 (4.1)	(-34.3, -18.3)	<0.0001	↑ -37.4 (4.1)	(-45.4, -29.3)	<0.0001
Below average	-19.9 (3.1)	(-26.0, -13.8)	<0.0001	-28.2 (3.1)	(-34.3, -22.0)	<0.0001
Average	-11.0 (2.5)	(-16.0, -6.0)	<0.0001	-17.9 (2.5)	(-22.9, -12.9)	<0.0001
Good	-5.7 (2.4)	(-10.4, -1.0)	0.018	-9.6 (2.4)	(-14.3, -4.9)	0.0001
Excellent (ref)						

¹SE=standard error, ²CI=confidence interval, ³ref=reference group, ⁴HMO=Health Maintenance Organization, ⁵WIC=Women Infant Children supplemental nutrition program

Conclusions

- In a sample of children with comparable socioenvironmental backgrounds, we found similar English and math academic achievement test scores between children with and without a history of NAS (*and those scores are less than the state averages across grades*)
- Results of our confounder analysis emphasize the importance of socioeconomic circumstances and environment in childhood outcomes

Within children with a history of NAS, does amount of timing of prenatal opioid exposure make a difference?

Inclusion Criteria

- Diagnostic code consistent with NAS with a birth year of 2003-2014
- At least one standardized academic achievement test score for ***English-Language Arts*** or ***mathematics*** for grades 3-8 (2017-2023) in the SC Department of Education
- Medicaid insurance (85% of cohort) with at least one claim

Type of Prescription Opioids

Type of opioid prescriptions during pregnancy period Excluding birth month

	Total (N=496)
Type of opioid prescription, n (%) [Patients could have multiple]	
Hydrocodone	186 (37.5%)
Oxycodone	101 (20.4%)
Buprenorphine	79 (15.9%)
Codeine	57 (11.5%)
Tramadol	41 (8.3%)
Methadone	17 (3.4%)
Propoxyphene	17 (3.4%)
Hydromorphone	13 (2.6%)
Morphine	12 (2.4%)
Meperidine	4 (0.8%)
Fentanyl	4 (0.8%)
Dihydrocodeine	1 (0.2%)
Oxymorphone	1 (0.2%)
Pentazocine	1 (0.2%)

Calculating Morphine Milliequivalents (MME)

Opioid	mg per day	Conversion factor	Morphine equivalents
Benzhydrocodone		1.22	
Buprenorphine film* (mcg)		0.03	
Buprenorphine transdermal* (mcg/hr)		1.8	
Butorphanol (nasal)		7	
Codeine		0.15	
Dihydrocodeine		0.25	
Fentanyl transdermal (mcg/hr)		2.4	
Fentanyl buccal tablet (mcg)		0.13	
Fentanyl nasal spray (mcg/spray)		0.16	
Fentanyl oral spray (mcg/spray)		0.18	
Hydrocodone		1	
Hydromorphone		5	
Levomethadyl		8	
Levorphanol		11	
Meperidine (IM, IV)		0.3	
Meperidine (oral)		0.1	
Methadone		**	
Morphine		1	
Oxycodone		1.5	
Oxymorphone		3	
Pentazocine		0.37	
Propoxyphene		0.23	
Tapentadol		0.4	
Tramadol		0.2	
TOTAL MME			0

Study Sample

Matching variables		Total (N=496)
Year of Birth, n (%)		
2003		12 (2.4%)
2004		26 (5.2%)
2005		26 (5.2%)
2006		34 (6.9%)
2007		29 (5.8%)
2008		31 (6.3%)
2009		47 (9.5%)
2010		46 (9.3%)
2011		65 (13.1%)
2012		70 (14.1%)
2013		69 (13.9%)
2014		41 (8.3%)
Child's Sex, n (%)		
Male		264 (53.2%)
Female		232 (46.8%)
Mother's Education, n (%)		
Less than high school		156 (31.5%)
High school <u>grad</u> or GED ¹		169 (34.1%)
Some college		158 (31.9%)
College degree or higher		12 (2.4%)
Unknown		1 (0.2%)
Payer, n (%)		
Medicaid/Self-pay/Indigent		496 (100.0%)

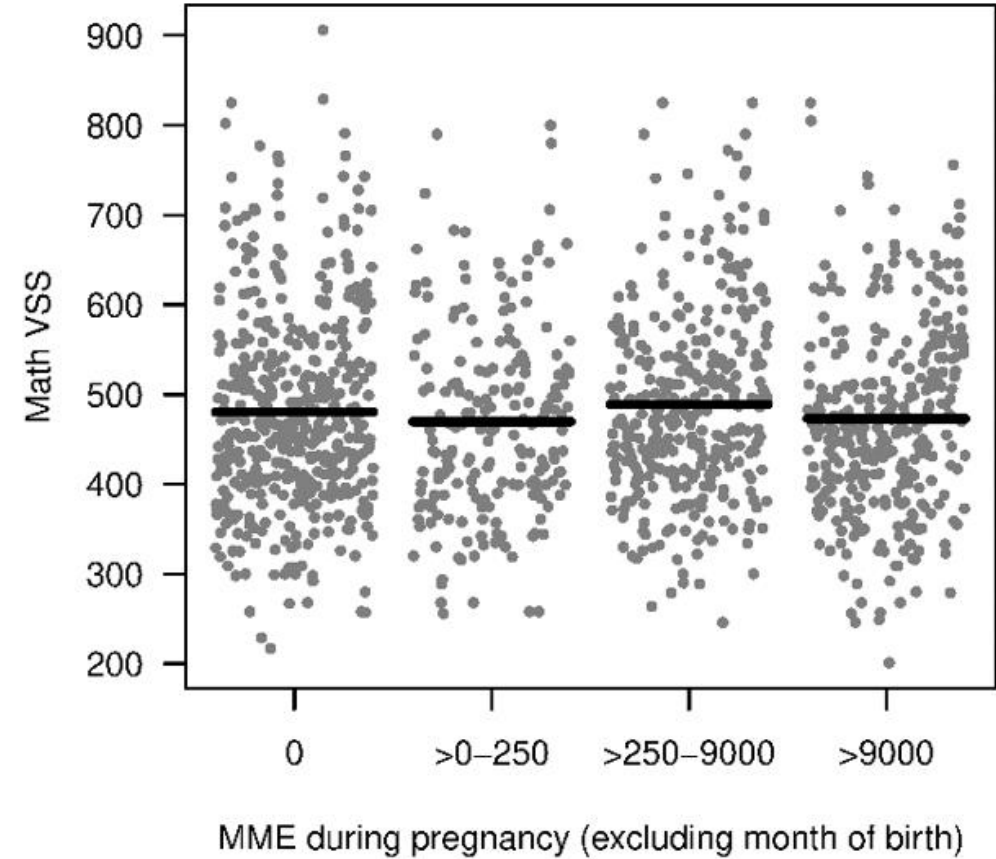
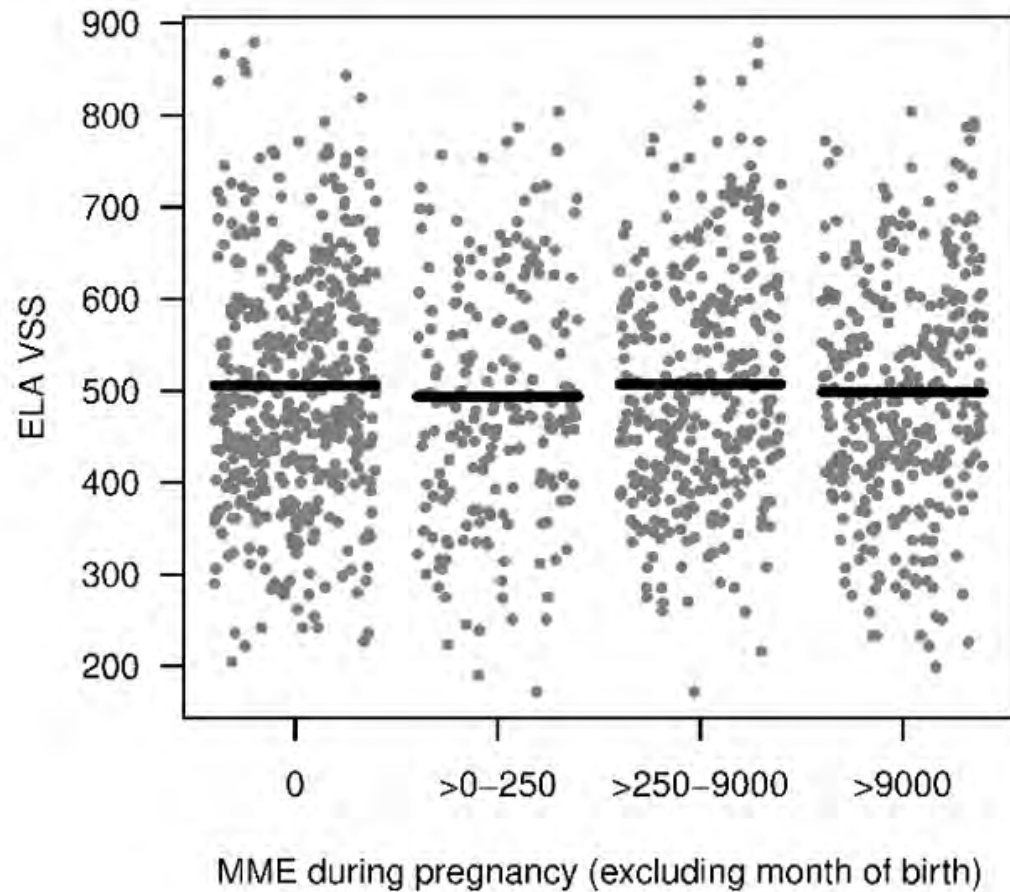
¹GED=Graduate Equivalency Degree; includes technical school

Morphine Milliequivalents

Morphine Milliequivalents during Pregnancy ¹	
	Total (N=496)
Number of prescriptions	
N	496
Mean (SD ²)	4.5 (6.27)
Median	2.0
IQR ³	0.0, 7.0
Range	0.0, 59.0
Number of prescriptions (group), n (%)	
0	<u>169 (34.1%)</u>
1	67 (13.5%)
2 to 5	106 (21.4%)
6 to 10	88 (17.7%)
11 or more	66 (13.3%)
Cumulative morphine milliequivalents⁴	
	N=327
Median	3810.0
IQR	270.0, 21675.0
Range	25.0, 2341050.0
Cumulative morphine milliequivalents (group), n (%)	
0	169 (34.1%)
>0 to ≤250	76 (15.3%)
>250 to ≤9000	126 (25.4%)
>9000	125 (25.2%)

¹Excluding birth month, ²SD=Standard Deviation, ³IQR=Interquartile Range, ⁴Among those with prescriptions

English and Math Vertical Scale Scores

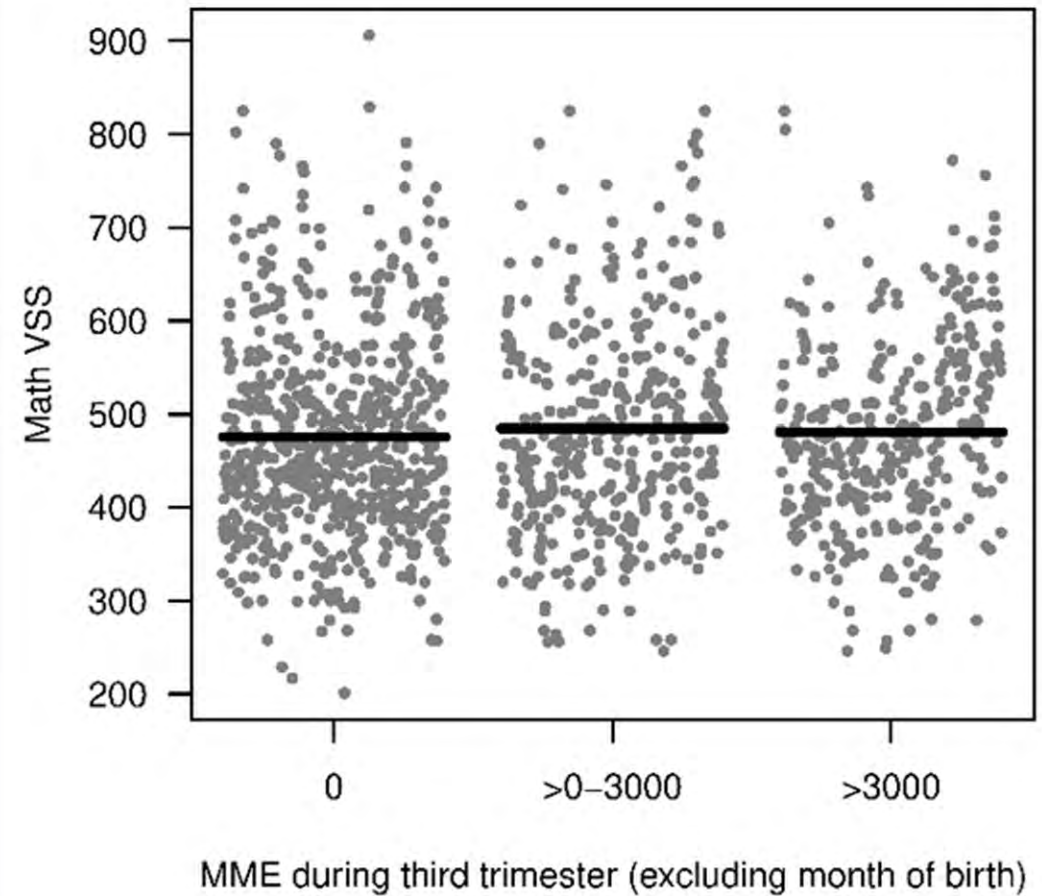
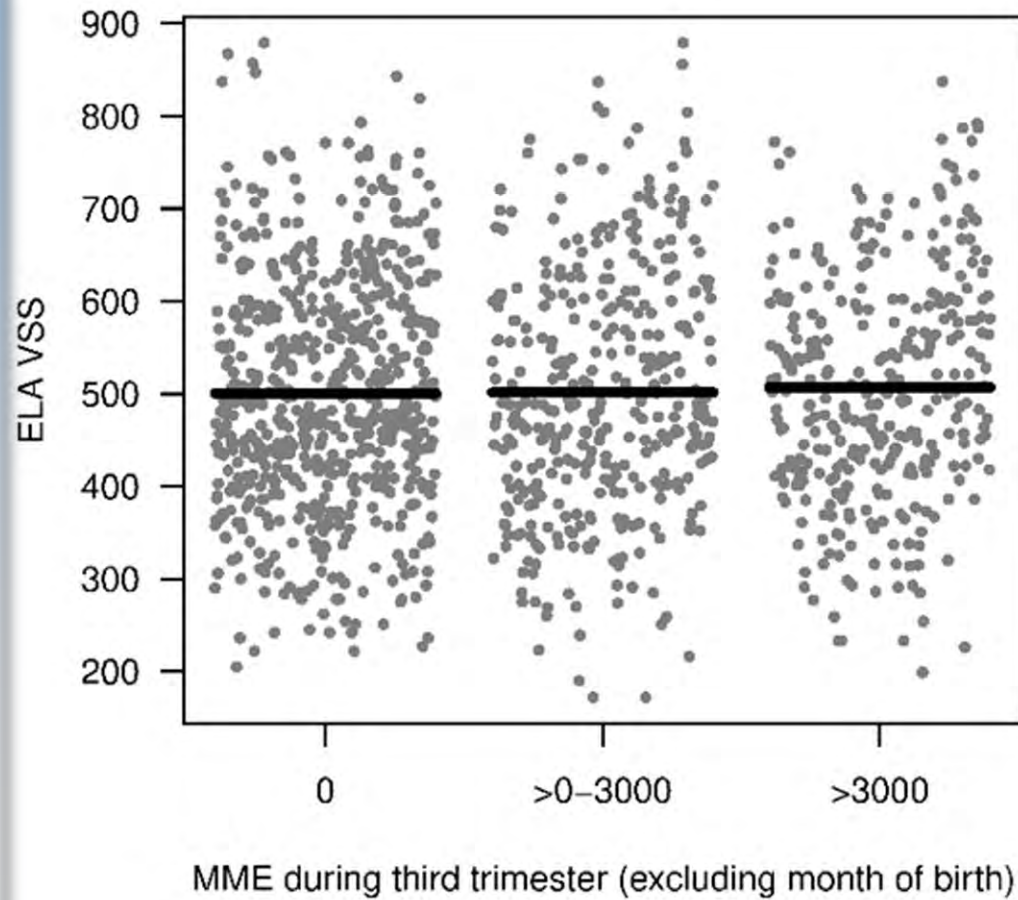


English and Math Vertical Scale Scores: Total Dose

Parameter Estimates for Vertical Scale Scores						
English Language Arts				Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Intercept	405.2 (8.9)	(387.8, 422.6)	<0.001	431.6 (7.9)	(416.2, 447.1)	<0.001
Grade						
3 (reference)						
4	66.2 (5.0)	(56.4, 76.0)	<0.001	22.7 (4.7)	(13.4, 32.0)	<0.001
5	114.6 (5.5)	(103.7, 125.4)	<0.001	65.8 (5.3)	(55.5, 76.1)	<0.001
6	126.5 (6.4)	(113.9, 139.2)	<0.001	61.4 (6.3)	(49.1, 73.7)	<0.001
7	168.7 (6.8)	(155.5, 182.0)	<0.001	82.6 (6.6)	(69.7, 95.6)	<0.001
8	200.1 (7.3)	(185.7, 214.5)	<0.001	112.8 (7.1)	(98.9, 126.8)	<0.001
Morphine milliequivalents in pregnancy			0.54			0.63
0 (reference)						
>0 to ≤250	-8.2 (14.8)	(-37.2, 20.9)	0.58	-11.6 (13.0)	(-37.1, 13.8)	0.37
>250 to ≤9000	9.7 (12.6)	(-15.0, 34.3)	0.44	5.5 (11.0)	(-16.1, 27.1)	0.62
>9000	11.2 (12.5)	(-13.3, 35.8)	0.37	-4.1 (10.9)	(-25.6, 17.3)	0.70

¹SE=Standard Error, ²CI=Confidence Interval

Opioid Exposure by Trimester



English and Math Vertical Scale Scores: Trimester Timing

Parameter Estimates for Vertical Scale Scores						
English Language Arts				Mathematics		
Parameter	Mean difference (SE ¹)	95% CI ²	p-value	Mean difference (SE)	95% CI	p-value
Intercept	404.6 (8.1)	(388.6, 420.6)	<0.001	430.4 (7.3)	(416.0, 444.7)	<0.001
Grade						
3 (reference)						
4	66.1 (5.0)	(56.3, 75.9)	<0.001	22.6 (4.7)	(13.4, 31.9)	<0.001
5	114.7 (5.5)	(103.8, 125.5)	<0.001	65.7 (5.3)	(55.4, 76.1)	<0.001
6	126.7 (6.4)	(114.0, 139.3)	<0.001	61.4 (6.3)	(49.1, 73.7)	<0.001
7	169.0 (6.7)	(155.7, 182.2)	<0.001	82.9 (6.6)	(69.9, 95.8)	<0.001
8	200.2 (7.3)	(185.8, 214.6)	<0.001	112.9 (7.1)	(99.0, 126.9)	<0.001
Morphine milliequivalents during first trimester			0.61			0.83
0 (ref)						
>0 to ≤2000	-10.1 (15.2)	(-40.0, 19.8)	0.50	-6.4 (13.4)	(-32.6, 19.9)	0.63
>2000	-14.6 (17.0)	(-48.0, 18.8)	0.39	-7.1 (15.0)	(-36.5, 22.3)	0.63
Morphine milliequivalents during second trimester			0.22			0.87
0 (ref)						
>0 to ≤2000	12.0 (13.3)	(-14.1, 38.1)	0.36	-6.2 (11.7)	(-29.3, 16.8)	0.59
>2000	29.6 (17.9)	(-5.6, 64.7)	0.09	-3.1 (15.8)	(-34.0, 27.9)	0.84
Morphine milliequivalents during third trimester			0.64			0.79
0 (ref)						
>0 to ≤3000	-9.2 (12.1)	(-32.9, 14.5)	0.44	4.8 (10.7)	(-16.1, 25.7)	0.65
>3000	4.2 (16.0)	(-27.2, 35.6)	0.79	9.1 (14.1)	(-18.6, 36.8)	0.51

¹SE=Standard Error, ²CI=Confidence Interval

Conclusions and Next Steps

- In a sample matched on biologic and socioenvironmental factors, we found similar ELA and math academic achievement test scores between children with and without a history of NOWS *and those scores are less than the state averages across grades*
 - Results of our covariate analysis emphasize the importance of socioeconomic circumstances and environment in childhood outcomes
- Total dose of opioids and trimester of opioid exposure are not associated with differences in academic achievement
- Next steps
 - Interview parents/guardians of children with a history of NOWS to explore how salient variables identified from our quantitative analyses may relate to parents'/guardians' experiences with childhood academic performance

Neonatal Abstinence Syndrome (NAS) and School Performance

If you are a parent or legal guardian of a child born with NAS you may be eligible to participate in this research study.

ABOUT THIS STUDY

Research suggests that children with a history of Neonatal Abstinence Syndrome (NAS), also known as Neonatal Opioid Withdrawal Syndrome (NOWS), may have more difficulties in school. However, looking at past data from a large group does not consider all items that may contribute to a child's academic success. Therefore, we are conducting 40 interviews with parents/guardians of children with a history of NAS in infancy to gain a better understanding of the many factors that may support or hinder academic success.

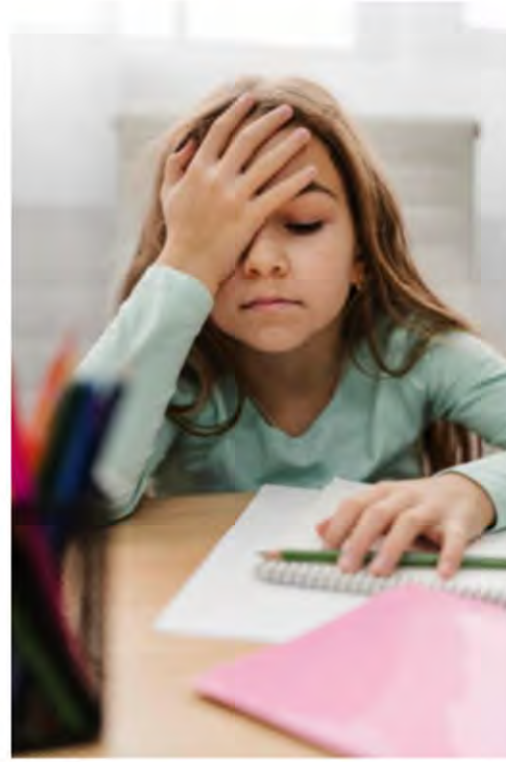
WHO CAN PARTICIPATE?

- Parents/legal guardians of elementary school students that were born with a history of NAS

WHAT WILL PARTICIPANTS DO?

- A short 5-minute demographic survey
- A virtual 45-minute interview discussing your child's education

To compensate you for your time, you will receive a \$25 Amazon gift card.



FOR MORE INFORMATION

Study Coordinator:

Gabrielle Lang
glang@pennstatehealth.psu.edu
(717) 531-5656

Principal Investigator:

Tammy Corr, DO
Department of Pediatrics

For more information and to choose to participate, use the link or QR code below.

<https://redcap.ctsi.psu.edu/surveys/>

Access Code: WTL3FFJKX



Moving Forward

- Support women with substance use disorders
- Investigate interventions at family level
 - Enhancing Permanency in Children and Families (EPIC), Children and Recovering Mothers (CHARM) Collaborative, hub-and-spoke care for OUD
- Early interventions and supports for children
 - Routine care with PCP, referrals to Early Intervention Services, follow-up in NICU or Developmental Care Clinics

¹Freisthler, B., Maguire-Jack, K., Yoon, S. et al. Enhancing Permanency in Children and Families (EPIC): a child welfare intervention for parental substance abuse. BMC Public Health 21, 780 (2021). <https://doi.org/10.1186/s12889-021-10668-1>

²Mills-Huffnagle SL, Sullivan RE, Corr TE, Nyland JE. Call to Action: Standardizing Follow-Up Care for Infants Prenatally Exposed to Opioids. Hosp Pediatr. 2025 Mar 1;15(3):e121-e125. doi: 10.1542/hpeds.2024-008094. PMID: 39914459.



Thank you

Funding

National Institute on Drug Abuse K23DA055096

Contact Information

Phone: 717-531-8413

Email: tcorr@pennstatehealth.psu.edu

Part 2

NAS Neurodevelopmental Follow-Up Clinic – Outcomes and Challenges

Traci Jennings, CRNP

Mandy Haigh Rudy, OTR/L

