Neonatal Abstinence Syndrome in Rural Appalachia

Shannon M. Cain, Anne Conway, Terri Combs-Orme, Sarah L. Bruck, E. Kyle Cook, and Elizabeth Thomas

As the United States faces the repercussions of the current opioid epidemic, it is important for social workers to be able to identify risks for poor birth outcomes in infants with neonatal abstinence syndrome (NAS). Although some studies have identified single risk factors, no studies have tested associations between total amount of risk (that is, cumulative risk) and birth outcomes in infants with NAS. Authors examined 318 mothers who used opioids during pregnancy and their infants' birthweight, length, head circumference, and Apgar scores (which measure overall infant health after birth). All infants were admitted to a neonatal intensive care unit in Appalachia and were diagnosed with NAS. Authors found that high cumulative risk during pregnancy was associated with lower birthweight and Apgar scores one and five minutes after birth as well as shorter length and smaller head circumference at birth. Social workers are encouraged to assess for the quantity of prenatal adversity experienced by the mothers they serve and to consider multicomponent, comprehensive community-based interventions to reduce cumulative risk.

KEY WORDS: *birth outcomes; cumulative risk; neonatal abstinence syndrome; opioids; prenatal adversity*

One of the most tragic consequences of the current opioid crisis is the increase in infants born after exposure to opioids in utero who are diagnosed with neonatal abstinence syndrome (NAS). *NAS* is a withdrawal syndrome that can occur in infants born to mothers who are dependent on substances, such as opioids (for example, heroin, buprenorphine, methadone). During withdrawal from in-utero drug dependence, infants may experience severe symptoms, including sleep–wake (for example fragmented sleep, difficulty remaining alert), movement (such as tremors, jitteriness), autonomic (for example, sweating, fever), stimulation and arousal (for instance, crying, irritability), and feeding and gastrointestinal (such as suck–swallow coordination, gas, loose stool) symptoms (Jansson & Patrick, 2019). Approximately 50 percent to 70 percent of infants with opioid withdrawal symptoms require pharmacological treatment that is most frequently provided in a neonatal intensive care unit (NICU) (Logan, Brown, & Hayes, 2013). Infants are treated using tapered doses of oral morphine or methadone (Jansson & Patrick, 2019). Average length of stay in the hospital for infants with NAS is 16 days (Corr & Hollenbeak, 2017).

From 1999 to 2014, maternal opioid use disorder rates during delivery in the United States increased fourfold to 6.5 out of 1,000 births, and rates of NAS quadrupled (National Institute on Drug Abuse [NIDA], 2019). Costs to treat NAS in 2014 were $563 million (NIDA, 2019). Relative to national rates, there is a significantly higher incidence of infants with NAS in rural and Appalachian counties (Brown, Goodin, & Talbert, 2018). Appalachia is "ground zero" for the current opioid crisis (Erwin, Meschke, Ehrlich, & Lindley, 2017).

A number of risks for NAS have been identified. Use of benzodiazepines (Dryden, Young, Hepburn, & Mactier, 2009; Seligman et al., 2008), marijuana (O'Connor, Kelly, & O'Brien, 2017), or cigarettes (Erwin et al., 2017; Jones et al., 2013) is associated with increased risk of NAS. Relative to mothers of infants without NAS, mothers of infants with NAS are more likely to be older, be non-Hispanic White, have hepatitis C, and use multiple substances (Dryden et al., 2009; Sanlorenzo, Stark, & Patrick, 2018), and are less likely to receive prenatal care and have a Cesarean birth (Erwin et al., 2017; Liu, Jones, Murray, Cook, & Nanan, 2010).

Less attention has been given to examining risks for poor birth outcomes (that is, low birthweight, shorter length, and smaller head circumference) of infants with NAS. It is important to examine risks

for poor birth outcomes because infants with NAS have been shown to have lower birthweight than infants without NAS (Erwin et al., 2017; Patrick et al., 2015). Moreover, although little is known about long-term outcomes of poor birth outcomes in infants with NAS, poor birth outcomes in infants without NAS are associated with childhood diagnosis of attention-deficit hyperactivity disorder (Serati, Barkin, Orsenigo, Altamura, & Buoli, 2017) and lower scores on cognitive tests at age 18 (Odd, Rasmussen, Gunnell, Lewis, & Whitelaw, 2008). Lower weight, smaller head circumference, and shorter length at birth have also been associated with adult type 2 diabetes and impaired glucose regulation in infants without NAS (Xiao et al., 2008).

The few studies that have examined risks for poor birth outcomes in infants with NAS have explored single risk factors. Cigarette smoking (Chisolm et al., 2011) has been associated with lower birthweight, serotonin reuptake inhibitors (SSRIs) have been associated with short length (Jansson et al., 2017), and chronic opioid use has been associated with small head circumference (Towers et al., 2019). No studies have examined whether the accumulation of multiple risks during the prenatal period is associated with the birth outcomes of infants with NAS. Yet, individuals develop and are influenced by multiple and interacting ecological contexts (for example, families, neighborhoods, communities; Bronfenbrenner, 1979). No ecological risk factor exists and operates in isolation, and the accumulation and total number of risks (that is, cumulative risk) to which one is exposed more powerfully predict child outcomes (for a review, see G. W. Evans, Li, & Whipple, 2013). Examples include cognitive development (Sameroff, Seifer, Barocas, Zak, & Greenspan, 1987), social development (Sameroff, Seifer, Zax, & Barocas, 1987), child maltreatment (MacKenzie, Kotch, & Lee, 2011), and problem behavior among children with prenatal substance exposure (Yumoto, Jacobson, & Jacobson, 2008). A cumulative risk approach is particularly relevant for prenatal substance exposure because early risks and adversities among this population co-occur (for example, a pregnant woman who uses heroin may also use additional substances or have a mental health diagnosis; for a review, see Kelty & Preen, 2019).

A few studies have examined the associations between cumulative risk and birth outcomes in infants without NAS. Relative to infants who were not exposed to high cumulative risk (that is, high index of maternal life stressors), those who were had lower birthweight and smaller head circumference (Su et al., 2015). A cumulative risk index of women's exposures to metals, psychosocial stress, and sociodemographic factors also predicted that infants would be small for gestational age at birth (Pao, Harville, Wickliffe, Shankar, & Buekens, 2019).

The purpose of our study was to examine the characteristics of a sample of mothers and infants born with NAS from Appalachia and test links between cumulative risk and birth outcomes (that is, low birthweight, short length, small head circumference, and low Apgar scores, which measure overall infant health after birth). If we found that the overall number of risk factors were associated with birth outcomes, the direct implications of our findings for practice and policy would be that social workers should assess for and attend to the accumulation and quantity of multiple risks experienced by pregnant mothers. A cumulative risk finding could encourage a shift in assessment from a focus on maternal drug use and singular risks to the overall accumulation and totality of risks. It could also affect practice and policy by providing a foundation to test the efficacy of intervention trials and policies targeting the reduction in the accumulation of multiple risks in pregnant women addicted to opioids.

METHOD

Participants

The original sample includes infants who were admitted to the NICU with a diagnosis of NAS during calendar year 2015 and were discharged alive (n = 323); it also includes their mothers. Responses for infant sex and whether mothers received medication-assisted treatment (MAT) were missing for three participants each. Therefore, the final analytic sample includes 318 mothers and infants. The diagnostic code 779.5 in the ninth version of the *International Statistical Classification of Disease and Related Health Problems* (*ICD-9)* (WHO, 1978) was used from January 1, 2015, through September 3, 2015, and the diagnostic code P96.1 in the 10th version of the *IDC* (*IDC-10)* (WHO, 1992) was used from September 4, 2015, onward.

Setting

The Level III NICU of the regional hospital serves a midsize city as well as 16 contiguous rural counties. It has 152 beds (including 46 private rooms and four twin rooms in the NICU) and does not provide delivery services.

Data Collection

After receiving institutional review board approval from East Tennessee Children's Hospital, we abstracted medical record data from 2015 institutional archives. Data were collected from the hospital electronic medical data system linked by medical record identification (ID) numbers from admission and discharge summaries, nursing and social work notes, and family visitation logs. Although records contained personally identifiable data, we did not record these data or hospital ID numbers. We used a code system that was locked on-site and password protected.

After extensive training and practice, three social work students who were supervised by the social work faculty investigators abstracted 2015 data from hospital computers on-site from February 2018 to January 2019. Reliability testing was conducted with IBM SPSS Statistics for Windows, Version 25, on a random 10 percent of the sample (stratified according to early, midway, and later in the data collection process) and demonstrated all Cohen's kappa coefficients (calculated for nominal/categorical variables) to be above .61, indicating substantial or perfect agreement. All intraclass reliability coefficients (calculated for continuous and count variables) were greater than .75, suggesting excellent agreement.

Variables

Demographic. Maternal age and race (1 = Black, 2 = White, 3 = Latina) and infant sex (1 = boy, 2 = female) were recoded from the NICU discharge summary. Consistent with the demographics of the region, only 1.6 percent of our sample was Black and 0.3 percent was Latina. Therefore, we had to code maternal race as "White" and "non-White" and use this race variable in the analysis. Infant sex was recoded into "0 = boy" and "1 = girl" for analysis.

Predictor: Cumulative Risk. Based on identified risks for NAS previously described, we selected 17 exposures listed in Table 1. Mothers reported whether they had custody issues with other children; had other children born substance exposed in the past; and had depression, anxiety, or other mental health diagnoses. Responses to each question (0 = no, 1= yes) were obtained from the social work notes. The number of children in the home was also obtained from social work notes. Mothers reported whether they had received MAT (that is, methadone or buprenorphine prescribed and monitored by a physician; American College of Obstetricians and Gynecologists [ACOG] & American Society of Addiction Medicine [ASAM], 2017). Mothers also reported other substances (for example, psychotropic medications, alcohol, marijuana, heroin, cocaine, methamphetamine) to which their infant was been exposed. Responses and the total number of substances were extracted from administrative data.

From the NICU discharge summary, we obtained information regarding the presence or absence of hepatitis C (no/yes) or HIV (no/yes); delivery (1 = vaginal, 2 = cesarean); prenatal care status assessed by the health care provider (0 = no prenatal care, 1 = late/inadequate/insufficient, 2 = adequate care); and cigarette smoking (0 = none reported, 1 = smoke less than a half pack a day, 2 = smoke more than a half pack a day). For each risk variable, a score of "1" was given if the infant had been exposed and "0" if they had not been exposed. Criteria for exposure for each variable and percentage exposed are listed in Table 1. Scores for all 17 variables were summed to create a cumulative risk exposure index.

Dependent: Birth Outcomes. Birthweight (grams), birth length (centimeters), birth head circumference (centimeters), and Apgar score at one and five minutes after birth were obtained from the NICU discharge summary.

Empirical Strategy

First, we examined the characteristics of opioid-dependent mothers in our sample and their infants who were diagnosed with NAS using descriptive statistics. For ease of interpretation and to ensure that all coefficients would be equal to effect sizes, birth outcomes were standardized to have a mean of 0 and a standard deviation of 1. This would allow us to evaluate the degree to which an increase in cumulative risk is associated with a standard deviation change in birth outcomes. Cumulative risk scores were also standardized with a mean of 0 and a standard deviation of 1 to produce standardized estimates.

Because removing participants with missing data can significantly bias results, we addressed

Table 1: Means, Standard Deviations, Ranges of Study Variables, and Percentage Missing

Variable	%	*M* (*SD*)	Range	Percentage Missing
Covariates				
Child race/ethnicity				0
African American		1.6		
European American		97.2		
Non-White Hispanic	0.3			
Medication-assisted treatment during pregnancy				0.6
Yes	70			
No	29.4			
Predictors				
Child sex				0
Male	49.7			
Female		50.3		
Prenatal: Early adversity/cumulative risk score		4.8 (2.0)	0–11	16.7
Maternal age (36 years and older)	7.2			0.9
Previous custody issues	39			3.5
Other children in the home	45.6			3.8
Inadequate/no prenatal care	32			5.7
Other children exposed to substances	15.4			9.7
Maternal depression disorder	9.1			0.3
Maternal anxiety disorder	8.8			0.3
Maternal other mental health problem	11			0.3
Cannabis use	22.5			0.01
Benzodiazepine use	22			0.6
Selective serotonin reuptake inhibitor use	4.7			0.6
Cigarette smoking	61.9			0.3
Vaginal birth	65			2.2
Gestational diabetes	11.9			0
Maternal human immunodeficiency virus	0			1.9
Maternal hepatitis C	47.2			0.6
Polysubstance use	68.6			0.9
Outcomes				
Birthweight (grams)		2,981.4 (498.8)	841–4,400	0.3
Birth length (cms)		48.6 (2.7)	34–54	14.8
Birth head circumference (cms)		33 (1.9)	23.5–46.9	18.6
Apgar 1 minute after birth		8.1 (1.2)	2–9	3.1
Apgar 5 minutes after birth		8.9 (0.6)	4–10	3.8

Note: cms = centimeters.

missingness using multiple imputation (Graham, 2012). We examined the percentage of missing data depicted in Table 1. We used Stata 13 (StataCorp, 2013) to generate 40 datasets and conducted multivariate regression on the pooled estimates. Specifically, we examined the association between cumulative risk and birth outcomes (weight, length, head circumference, and Apgar scores one and five minutes after birth) on the pooled estimates controlling for infant sex and maternal race.

RESULTS

What Are the Characteristics of Opioid-Dependent Mothers and Infants with NAS in Appalachia?

The average age of mothers was 27.5 years. As shown in Table 1, almost all of the mothers received

some prenatal care as judged by health providers. Smoking was common, and 70 percent of mothers reported using more than one substance (for example, MAT, psychotropic medications, alcohol, marijuana, heroin, cocaine, methamphetamine.) Seventy percent of mothers were receiving MAT at delivery. Many mothers had other children at home, issues with child protective services, mental health conditions, and hepatitis C infections.

Does Cumulative Risk Predict Poor Birth Outcomes for Infants with NAS?

Results are presented in Table 2. Findings from multivariate regression analyses showed that cumulative risk was associated with all birth outcomes. Specifically, higher cumulative risk was associated with lower (1) birthweight ($B = -.13$, $p = .04$), (2) birth length ($B = -.14$, $p = .03$), (3) head circumference ($B = -.18$, $p = .00$), (4) Apgar one minute after birth ($B = -.16$, $p = .01$), and (5) Apgar five minutes after birth ($B = -.14$, $p = .03$).

Table 2: High Cumulative Risk Is Associated with Poor Birth Outcomes in Infants with NAS (n = 318)

Variable	*B* (*SE*)	*t* Test	*p*
Birthweight (grams)			
Sex	−.29 (.11)**	−2.67	.00
Race	.13 (.33)	0.41	.68
Cumulative risk	−.13 (.06)*	−1.99	.04
Birth length (cm)			
Sex	−.30 (.11)**	−2.68	.00
Race	.24 (.35)	0.70	.48
Cumulative risk	−.14 (.06)*	−2.12	.03
Head circumference (cm)			
Sex	−.33 (.11)**	−2.94	.00
Race	.08 (.35)	0.23	.81
Cumulative risk	−.18 (.06)**	−2.74	.00
Apgar (1 minute after birth)			
Sex	.08 (.11)	0.75	.45
Race	.34 (.33)	1.04	.30
Cumulative risk	−.16 (.06)*	−2.57	.01
Apgar (5 minutes after birth)			
Sex	.06 (.11)	0.53	.59
Race	.15 (.33)	0.45	.65
Cumulative risk	−.14 (.06)*	−2.15	.03

Notes: Model controls for infant sex (male = reference) and maternal race/ethnicity (White = reference). NAS = neonatal abstinence syndrome; *B* = unstandardized beta, *SE* = standard error; cm = centimeters.
*$p < .05$. **$p < .01$.

DISCUSSION

Our findings revealed similarities, but also differences, with other samples from Appalachia. Consistent with other studies, many mothers had mental health conditions (for example, depression). Rates of hepatitis C, however, were nearly double in our sample relative to another study (Erwin et al., 2017). The majority of mothers in our sample used numerous substances, including benzodiazepines, SSRIs, and cannabis, and, although more than half of mothers smoked cigarettes, this rate is lower than rates of 75 percent to more than 80 percent reported in other studies (Baxter, Nerhood, & Chaffin, 2009; Burnette, Chernicky, & Towers, 2019). More mothers in our study received adequate prenatal care than mothers in another study conducted in Huntington, West Virginia (Baxter et al., 2009). Consistent with Burnette et al. (2019), the majority of mothers had MAT at delivery. Yet, this rate was higher than that of mothers in other studies (Baxter et al., 2009; Erwin et al., 2017) and may have also been influenced by state policy. If mothers were involved in treatment in 2015, they were less likely to be prosecuted if their baby were harmed or born with an addiction (Shearer, Erwin, Davis, Anderson, & Lindley, 2019). Therefore, services required to meet the needs of infants and families could vary between communities based on severity, region, and so forth.

Consistent with our hypothesis, higher cumulative risk/prenatal adversity was associated with lower weight, shorter length, smaller head circumference, and lower Apgar scores one and five minutes after birth. Our study is the first to demonstrate that prenatal cumulative risk is associated with poor birth outcomes in infants with NAS. Our findings support more than 50 years of research on cumulative risk demonstrating that the overall quantity and accumulation of multiple risks are most predictive of child outcomes (for a review, see G. W. Evans et al., 2013). We build on this literature to show that associations extend to birth outcomes in infants with NAS.

Comparable to the demographics of the region, our sample was predominately White, and findings may not generalize to other racial and ethnic groups. Many variables were based on maternal re-

port, and substance use behaviors may be underreported. Future studies should include multiple sources of data. Despite these limitations, our study has many strengths. Our study builds on prior research by examining infants who required pharmacological treatment in a Level III NICU (for NAS symptoms) and were given *ICD-9* or *ICD-10* diagnoses for NAS (779.5, drug withdrawal syndrome in newborn for *ICD-9*, or P96.1, neonatal withdrawal symptoms from maternal use of drugs of addiction for *ICD-10*; WHO, 1978, 1992). We also examined mothers without regard to insurance status; infants with severe withdrawal symptoms; and infants who were exposed to nonprescription opioids, which are dominant in the region (Erwin et al., 2017).

Our findings suggest that social workers should assess and identify the accumulation and quantity of risks a pregnant mother may have. It is also important to develop and test comprehensive interventions and policies to reduce cumulative risk. Recognizing that the integration of multiple ecological levels of influence and systems that serve mothers, infants, and families may have a cumulative effect, the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Administration for Children and Families (SAMHSA, 2016) offer guidelines for collaboration across child welfare, service, and medical fields. Future research should examine the effectiveness of risk reduction and multicomponent, comprehensive approaches.

ADDITIONAL CONSIDERATIONS FOR SOCIAL WORK PRACTICE AND POLICY

Treatment for women who are pregnant and opioid dependent involves MAT, an evidence-based intervention, to help avoid fluctuating levels of opiates that can cause maternal and fetal withdrawal and minimize the use of illicit substances (ACOG & ASAM, 2012). MAT should not be stopped during pregnancy because it disrupts opioid levels and could result in preterm labor or fetal distress and death (Patrick, Schiff, & Committee on Substance Use and Prevention, 2017).

Psychosocial interventions and supports may be also helpful. Although it has not been tested in pregnant women using opioids, evidence from 13 randomized control trials has demonstrated the potential effectiveness of behavior change techniques for alcohol use (for a review, see Fergie et al., 2019), such as action planning, behavioral contract, problem solving, and goal setting. To prevent substance use in young adults, effective intervention components include cognitive restructuring; community mobilization; education campaigns; screening and brief intervention; and others (for a review, see SAMHSA, 2019). For women of childbearing age, it may also be helpful to connect them with medical providers who can address family planning needs (Heil et al., 2011) and provide treatment for underlying health conditions like hepatitis C infection (Erwin et al., 2017).

Other interventions include Parents Under Pressure (Dawe & Harnett, 2007), a program in which therapists teach parenting and mindfulness skills to enhance parents' ability to manage their emotions, and Relational Psychotherapy Mothers' Group (RPMG) (Luthar & Suchman, 2000), which is a group-based psychotherapy intervention and also has a methadone counseling component. Both interventions have been effective in reducing child abuse potential, and mothers in RPMG have shown reductions in opioid use over time. Trauma-informed approaches (Hemsing, Greaves, Poole, & Schmidt, 2016) may also be beneficial because women with opioid use disorders report high rates of childhood adversity (E. A. Evans, Goff, Upchurch, & Grella, 2020), and mothers who abuse opioids often report experiencing shame (Stone, 2015).

It is important to note that pregnant women and mothers experience many barriers to treatment. First, women who give birth to infants with NAS often live in rural and Appalachian areas, which are far from opioid treatment facilities and are less likely to offer treatment tailored to the unique needs of pregnant women and mothers (Brown et al., 2018; Terplan, Longinaker, & Appel, 2015). Second, this lack of access to specialized services is problematic because treatment retention is increased for this population when programs are geared toward the needs of pregnant women and mothers, help them maintain child custody, and provide for psychosocial needs (for example, parenting, transportation) (Staudt, 2018). Third, state policies may also affect mothers' engagement in, and level of, treatment participation. For example, the Tennessee Fetal Assault Law 2014 (2015) allowed for the criminal prosecution of women if they used substances during pregnancy (only in effect until July 1, 2016, when it was allowed to sunset), whereas policies that reduced criminalization

if women engaged in substance use treatment, like the Safe Harbor Act, may have facilitated participation (Shearer et al., 2019).

Notably, there has been an increase in punitive policies at the state level from 1970 to 2016 (Thomas, Treffers, Berglas, Drabble, & Roberts, 2018), yet there is no evidence that punitive approaches encourage mothers to seek treatment or help them achieve recovery (Staudt, 2018). Criminalizing substance use during pregnancy appears to lead to higher rates of NAS (Faherty et al., 2019) and lower rates of prenatal care (Patrick et al., 2017; Stone, 2015). Social workers should advocate to repeal state laws and policies that punish pregnant women instead of providing and connecting them to treatment.

For infants born with symptoms of NAS, evidence suggests that family-focused interventions, such as encouraging parental presence on the unit and rooming-in, are effective at improving symptoms and treatment course (Holmes et al., 2016; Wachman et al., 2018). *Rooming-in* involves providing a private hospital room to each infant that allows the parent to stay with them. It encourages the mother or parent to stay and provide all nonmedical care (that is holding, feeding, changing) for their infant. This allows mothers to be able to also engage in skin-to-skin care (that is, the infant is placed on the mother's chest), which supports breastfeeding (Moore, Bergman, Anderson, & Medley, 2016). For some infants, however, NAS symptoms may not emerge until four weeks postdischarge (Kandall & Gartner, 1974). Therefore, social workers should monitor infants who have been exposed to opioids in utero and assist their mothers with connection to medical treatment should NAS symptoms present.

Little is known about the long-term outcomes for infants with NAS who have poor birth outcomes. Programs have been developed to improve the growth and nutrition of infants and young children without NAS, such as the Special Supplemental Nutrition Program for Women, Infants and Children (Black et al., 2004). Other programs focus on supporting child well-being and healthy development, such as home visiting programs (Sweet & Appelbaum, 2004). These programs may help to prevent developmental delays or challenges in children with poor birth outcomes.

In conclusion, social workers encounter and serve mothers, infants, and families experiencing repercussions of the opioid epidemic, such as NAS, in medical, school, child welfare, and behavioral health care settings. Social workers can be creative and innovative; these skills are needed to work with these families because of the myriad of risks they encounter and the need to mitigate adversity. Social workers can offer their expertise in prenatal settings. Social work has an unrealized potential in the areas of practice, policy, and research to improve clinical services and advocate for better policies for pregnant mothers, infants with NAS, and their families. **SW**

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Shannon M. Cain, MSW, *is doctoral student and graduate research assistant;* ***Anne Conway, PhD,*** *is associate professor; and* ***Terri Combs-Orme, PhD,*** *is professor emeritus, College of Social Work, University of Tennessee, Knoxville.* ***Sarah L. Bruck, MSSW,*** *is outpatient therapist, Camelot Care Centers, Knoxville, TN.* ***E. Kyle Cook, MSN, NNP-BC,*** *is neonatal nurse practitioner, Pediatrix Medical Group, East Tennessee Children's Hospital, Knoxville.* ***Elizabeth Thomas, PhD,*** *is assistant professor, College of Social Work, University of Tennessee, Knoxville. Address correspondence to Shannon Cain, College of Social Work, University of Tennessee, Knoxville, 1618 Cumberland Avenue Knoxville, TN 37996; e-mail: scain7@utk.edu.*

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