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Characterizing adverse prenatal and postnatal experiences in children

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Background: Prenatal and postnatal adversities, including prenatal alcohol exposure (PAE), prenatal exposure to other substances, toxic stress, lack of adequate resources, and postnatal abuse or neglect, often co-occur. These exposures can have cumulative effects, or interact with each other, leading to worse outcomes than single exposures. However, given their complexity and heterogeneity, exposures can be difficult to characterize. Clinical services and research often overlook additional exposures and attribute outcomes solely to one factor.

Methods: We propose a framework for characterizing adverse prenatal and postnatal exposures and apply it to a cohort of 77 children. Our approach considers type, timing, and frequency to quantify PAE, other prenatal substance exposure, prenatal toxic stress, postnatal threat (harm or threat of harm), and postnatal deprivation (failure to meet basic needs) using a 4-point Likert-type scale. Postnatal deprivation and harm were separated into early (<24 months of age) and late (≥24 months) time periods, giving seven exposure variables. Exposures were ascertained via health records, child welfare records, interviews with birth parents, caregivers, and/or close family/friends.

Results: Nearly all children had co-occurring prenatal exposures, and two-thirds had both prenatal and postnatal adversities. Children with high PAE were more likely to experience late postnatal adversities, and children with other prenatal substance exposure were more likely to have early postnatal deprivation. Postnatal adversities were more likely to co-occur.

Conclusion: This framework provides a comprehensive picture of a child's adverse exposures, which can inform assessment and intervention approaches and policy and will be useful for future research.

KEYWORDS

abuse, brain development, early childhood adversity, fetal alcohol spectrum disorder, neglect, prenatal alcohol exposure, prenatal and postnatal risks, toxic stress

1 | INTRODUCTION

Many children with complex developmental, behavioral, and mental health problems experience and/or have experienced multiple prenatal and postnatal exposures that might be etiologically linked to their functional difficulties. Pediatricians, psychologists, child welfare workers, and child abuse specialists are faced with determining which adversities in a child's presentation might explain the variance in that child's impairment. On the other hand, researchers are trying to understand how various exposures are associated with child outcomes. Historically, both clinical services and research on adverse child outcomes have focused on single causes. For example, when diagnosing fetal alcohol spectrum

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disorder (FASD), clinicians may assume that prenatal alcohol exposure (PAE) is the sole explanatory cause of a child's neurobehavioral profile, or a child abuse clinic may focus primarily on child maltreatment as an organizing principle for a child's difficulties. However, negative outcomes result from the interplay between multiple risk factors, and it is rare that a child or youth presents for clinical assessment or intervention with a history of only one exposure (Astley, 2010; Gibbard, 2010). See Boxes 1 and 2, for examples, of children characteristic of those who present to clinical and research settings.

Although PAE is a known risk factor for numerous negative outcomes, it is often underrecognized by clinicians, and most children who meet diagnostic criteria for FASD are missed entirely (American Medical Association, 2015; Lange et al., 2017; May et al., 2014). FASD is a complex disorder, originating from organic brain damage caused by PAE, but interacting with genetic and environmental influences (Chudley et al., 2005; Cook et al., 2016). The majority of individuals with PAE have other negative prenatal or postnatal exposures that may impact their developmental or mental health profile (Astley, 2010; Astley, Bailey, Talbot, & Clarren, 2000; Gibbard, 2010; Hyter, 2012; Koponena, Kallandbd, & Autti-Rämöc, 2009). Some FASD diagnostic guidelines encourage clinicians to ascertain the presence of other prenatal or postnatal risks (Astley, 2004; Chudley et al., 2005; Cook et al., 2016) and to adjudicate the impact of exposures beyond PAE. For example, the four-digit diagnostic code for FASD (Astley, 2004) includes categories for PAE, growth, facial dysmorphology, and central nervous system dysfunction, as well as categories for other prenatal risks, and postnatal risks (Astley, 2004). However, other prenatal and postnatal factors are often not described by clinicians in assessment reports or incorporated into treatment recommendations.

Box 1. Cindy (identifying details have been changed)

Anna was a young mother who had been diagnosed with FASD as a child. While pregnant, she had little prenatal care and lived a transient lifestyle, using illicit substances from time to time and drinking alcohol daily until she found out she was pregnant at approximately 5 months. When Anna's daughter Cindy was born at 37 weeks' gestation, the hospital contacted child welfare with significant concerns, as it appeared that there was no preparation for the baby, no support, and Anna admitted to using opioids in the last weeks of her pregnancy. Cindy was placed in foster care while a search for extended family occurred. At 10 months of age, Cindy was placed with her maternal aunt. After 3 years in the aunt's care, Cindy was again placed in foster care. The aunt described Cindy as having severely disrupted sleep, being developmentally delayed in several areas, and with bouts of rage that would last for hours with little response to attempts to comfort. Cindy is now 6 years old and remains in foster care, where her current placement is tenuous given that little positive change has occurred with respect to the challenges that Cindy presents.

Cindy was referred for an assessment with a query for FASD. However, in thinking about Cindy's story, there are other important risks that she has experienced:

- Maternal prenatal stress—homelessness, lack of prenatal care.
- Prenatal substance exposure—opioids confirmed.
- Multiple placements—2 prior to age 2 years, one between age 3 and 6 years.

Cindy was diagnosed with FASD at 6 years of age.

Box 2. Dustin (identifying details have been changed)

Dustin is a 15-year-old youth with multiple diagnoses: FASD, generalized anxiety disorder, reactive attachment disorder, post-traumatic stress disorder, learning disability in mathematics, attention deficit hyperactivity disorder, dysthymic disorder, and disruptive behavior disorder. Dustin's mother reported regular drinking and occasional marijuana use during her pregnancy.

There are maternal and paternal family histories of substance use (drugs and alcohol), significant mental illness including schizophrenia, and intra-familial sexual abuse. Dustin was severely neglected by his mother and a frequent witness to violence within the home. He became a permanent ward of the government at the age of 5 years. Dustin has had many losses in his life—family members, caregivers, schools, communities, and professional support persons. He has a full-scale IQ of 77, making him ineligible for some adult supports. He is unprepared for adult life and functions poorly without a consistent support person to guide him—a service that will end when he is 18 years old. He has lived with extended family members and within government placements most of his life—none lasting long, with Dustin in the end being "too much to handle". His mother worked hard to stabilize her life and end her drug and alcohol use. She now has Dustin's sister living with her but cannot manage Dustin as well.

Dustin's risks are considerable:

-Prenatal exposure to alcohol and drugs, little to no prenatal care.

-Family history of serious mental illness.

-Multiple losses throughout his life.

-Significant neglect from age 0 to 3 years.

-Multiple caregiver placements.

Attributing functional deficits solely to one etiology is problematic, yet this frequently occurs not only in clinical practice but also in research. To date, very little research has examined the outcomes of children and youth with PAE relative to other prenatal and/or postnatal exposures. A handful of studies demonstrate interactions between PAE and cocaine exposure (Konijnenberg, 2015; Lebel et al., 2013; Richardson & Day, 1994). Other work showed that individuals with FASD who experienced longer durations of postnatal adversities (e.g., exposure to abuse, violence, neglect) had an increased likelihood of poor outcomes relative to individuals with PAE who experienced less postnatal adversity (Streissguth et al., 2004). A recent systematic review found only five studies that clearly addressed the cumulative effect of PAE and postnatal adversity, showing that children with PAE and postnatal exposures were more likely to have deficits in language, attention, memory, intelligence, and behavior than children with only one of these exposures (Henry, Sloane, & Black-Pond, 2007; Price, Cook, Norgate, & Mukherjee, 2017). However, they also noted difficulties making comparisons between studies due to heterogeneity in

study methods and variable definitions of prenatal and postnatal risks (Price et al., 2017).

A cumulative risk conceptual model provides a framework to support risk attribution, diagnostic decision-making, and can guide expectations for developmental trajectory or prognosis, intervention, and prevention (Evans, Li, & Whipple, 2013). The goal of a cumulative risk approach is to determine how multiple factors together may result in negative outcomes. Generally, cumulative risk models assert that the total number of risk factors a child experiences *are more important* than the experience of any one risk factor in particular (Rutter, 1979, 1981). Singular effects may have less explanatory power than a cumulative risk index in explaining child outcomes. Both additive and threshold cumulative risk models have been proposed; both assume that individuals exposed to more risk factors are more likely to experience adverse outcomes (Evans & Kim, 2010). One framework that is increasingly common in research contexts is that of adverse childhood experiences (ACEs), which sums postnatal adverse exposures to provide a cumulative score (Felitti et al., 1998). An increase in the number of adversities, especially in the absence of protective factors, is associated with worse overall brain development (Dufford & Kim, 2017), as well as mental and physical health difficulties across the lifespan (Anda et al., 2009; Felitti & Anda, 2010; Kerker et al., 2015; Oh et al., 2018; Pechtel & Pizzagalli, 2011).

While useful, cumulative risk approaches may obscure differences in frequency, duration, and/or dose of various exposures, as well as the mechanisms of their effects on developmental and behavioral outcomes. To overcome this, it has been suggested that separating different dimensions of environmental experience may be an effective strategy (McLaughlin & Sheridan, 2016). In particular, threat and deprivation have been hypothesized as two core dimensions that have unique effects on emotional, cognitive, and neural development (McLaughlin, Sheridan, & Lambert, 2014; Sheridan & McLaughlin, 2014). Threat, which involves harm or threat of harm, including physical, sexual, and emotional abuse, and exposure to interpersonal violence, is suggested to influence emotional processing (McLaughlin & Sheridan, 2016). On the other hand, deprivation, which represents limited quantity and complexity of cognitive inputs and learning opportunities, including poverty, institutionalization, and neglect, may be more likely to influence cognitive control (McLaughlin & Sheridan, 2016). Recent research suggests that dimensional models, or factor analyses of exposures, better explain outcomes than a cumulative risk model (Brumley, Brumley, & Jaffee, 2018; Dennison et al., 2019; Sheridan, Peverill, Finn, & McLaughlin, 2017).

Both cumulative risks and dimensional models have, to date, been used primarily for characterizing only postnatal adversities. However, the frequent co-occurrence of prenatal and postnatal exposures (Astley, 2010; Astley et al., 2000; Gibbard, 2010; Hyter, 2012; Koponena et al., 2009) suggests that models should incorporate both time periods. In addition to the small number of studies that have examined interactions between PAE and other prenatal exposures (Price et al., 2017), a few studies outside the PAE literature have examined the combined effects of prenatal cocaine exposure and postnatal adversity on development (Eiden, Coles, Schuetze, & Colder, 2014; Eiden, Godleski, Colder, & Schuetze, 2014; Eiden, Granger, Schuetze, & Veira, 2011; Liebschutz et al., 2015) or the differential impacts of stress during prenatal and postnatal periods (Jensen et al., 2015; Jensen et al., 2018). Together, this literature highlights the importance of incorporating information from both prenatal and postnatal periods into the assessment of individual exposure profiles.

This article proposes a method for the characterization of prenatal and postnatal adverse exposures that may be useful for both future research and diagnostic practice. Among youth with PAE, this will allow us to study whether other prenatal and postnatal exposures have major, minor, or modifying effects beyond alcohol exposure. More broadly, this framework provides a starting point for researchers and clinicians to simultaneously consider multiple time points and types of exposures that may contribute to observed child outcomes. The framework presented is widely applicable and will be useful to researchers and clinicians who work with children with FASD, children with PAE (whether or not they have a diagnosis of FASD), and other children with various types of prenatal and postnatal adverse exposures.

1.1 | Development of an exposure framework

A detailed review of prenatal exposures and postnatal adversities is beyond the scope of this article, but the reader is referred to reviews of child outcomes related to PAE (Lebel, Roussotte, & Sowell, 2011; Mattson, Crocker, & Nguyen, 2011; Riley, Infante, & Warren, 2011), prenatal exposure to other drugs (Ackerman, Riggins, & Black, 2010; Addis, Moretti, Ahmed Syed, Einarson, & Koren, 2001; Bublitz & Stroud, 2012; Buckingham-howes & Shafer, 2013; Konijnenberg & Melinder, 2011; Minnes, Lang, & Singer, 2011), maternal mental health problems in pregnancy (Adamson, Letourneau, & Lebel, 2018; Glover, 2014), and postnatal adversity (Bick & Nelson, 2016; Cicchetti, 2013; Danese & Tan, 2014; Edalati & Krank, 2016; Glaser, 2000; Hart & Rubia, 2012). There is robust evidence in the existing literature for the effects of heavy PAE on children's development, and some evidence that lower levels of PAE are also harmful (Cook et al., 2016; Jacobson, Jacobson, Stanton, Meintjes, & Molteno, 2011; Lebel et al., 2011; Mattson et al., 2011). Given the widespread known effects of PAE across a variety of domains, this is a critical exposure to consider on its own. Findings related to other prenatal substance exposures have been mixed, in part because of limited research with well-characterized exposures, which leads to difficulty appropriately attributing risks to prenatal substance exposure versus

PAE or other factors (Konijnenberg, 2015). In general, previous work shows increased externalizing behaviors and risk of mental health problems, and alterations to related brain areas, in children with prenatal substance exposure, including cocaine, methamphetamine, marijuana, opioids, and nicotine (Behnke & Smith, 2013; Derauf, Kekatpure, Neyzi, Lester, & Kosofsky, 2010; Minnes et al., 2011). Given the lack of clear evidence for different substances affecting different domains of functioning, and the fact that exposures commonly co-occur, it makes sense to combine these into a single category of other substance exposures. Prenatal stress (e.g., maternal mental health problems, lack of adequate housing, income, and/or food) has been widely studied and is associated with negative behavioral outcomes in children as well as altered brain development (Bennett, Einarson, Taddio, Koren, & Einarson, 2004; Glover, 2014; Lebel et al., 2016; Sandman, Buss, Head, & Davis, 2015).

Postnatal adversities have variable effects depending on the timing and duration of exposure, but generally are associated with increased behavioral problems, increased risk of substance use, and mental health disorders (Heim, Shugart, Craighead, & Nemeroff, 2010; Oh et al., 2018), and alterations to limbic and prefrontal brain structures (De Bellis & Zisk, 2014). Threat and deprivation have been hypothesized as two core dimensions that tend to have unique effects on emotional and cognitive development, respectively (McLaughlin et al., 2014; Sheridan & Mclaughlin, 2014), and recent research evidence supports this distinction (Brumley et al., 2018; Dennison et al., 2019; Sheridan et al., 2017). Furthermore, evidence shows differential effects of maltreatment in the early postnatal period (i.e., <2 years) versus later childhood (≥2 years) on outcomes across multiple domains (Fox, Nelson, & Zeanah, 2017; Kaplow & Widom, 2007; McDermott et al., 2013; Nelson et al., 2007; Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012; Smyke, Zeanah, Fox, Nelson, & Guthrie, 2010), suggesting that it is useful to separate these time frames.

With perspectives from experts in diagnosis, assessment, child welfare, child development and psychopathology, and neuroscience, we developed an adverse exposure reporting and ranking framework to ascertain key prenatal and postnatal adverse exposures. The framework is a hybrid cumulative risk/dimensional model that builds on the four-digit code for diagnosing FASD (Astley, 2004). Using a Likert-type scale from 1 to 4 similar to the four-digit code, this framework ranks exposures in seven categories (i.e., dimensions of risk): PAE, other prenatal substance exposure, other prenatal toxic stress, early postnatal threat (<age 24 months), early postnatal deprivation (<age 24 months), late postnatal threat (≥age 24 months), and late postnatal deprivation (≥age 24 months). Thresholds and case definitions were constructed following social sciences guidelines (Plews, 2010), best practices for diagnosing FASD (Cook et al., 2016), and the literature on early adverse exposures and negative outcomes in children (Almas et al., 2015; Bick et al., 2015; Buss, Entringer, Swanson, & Wadhwa, 2012; Coles & Li, 2011; Eckstrand et al., 2012; Lebel et al., 2011; Lebel et al., 2013; Lebel et al., 2016; McDonald & Tough, 2013; Pampel, Krueger, & Denney, 2010; Sandman et al., 2015; Warner et al., 2006; Wozniak et al., 2006; Wozniak & Muetzel, 2011). Each variable is ranked based on the amount of exposure (similar to cumulative risk scores), where 1 = no exposure (confirmed absence), 2 = unknown exposure (insufficient information), 3 = some exposure, and 4 = high exposure. Table 1 details our criteria for each score.

This is not an exhaustive list that covers every early adverse event, so it is worth noting other exposures that might be useful in the process of characterization prenatal and postnatal risks. Some examples may include various forms of physical trauma to the fetus, other forms of postnatal brain injury (e.g., concussion), or adverse social experiences, such as bullying, unhealthy continued contact with biological parents after safe placement, and/or neighborhood violence. Furthermore, as more research is conducted and new evidence arises, it may make sense to combine certain variables or further separate them into domains that may affect child development in different ways.

2 | METHODS

2.1 | Participants

Our sample included 77 children aged 2.8–15.9 years (7.2 ± 3.0 years; 43 males/34 females) recruited for an ongoing study of prenatal and postnatal exposures, and brain and mental health outcomes. Children and youth were recruited from various settings across Alberta, Canada: Calgary and Area Child Services (CT, Associate Director), the Cumulative Risk Diagnostic Clinic in Calgary (BG, Medical Lead); online advertisements, parent groups, and word of mouth. To be enrolled in the study, children were required to be in a stable placement (same home for 6 months or more), have at least one confirmed prenatal and/or postnatal adverse exposure, and be free from contraindications to magnetic resonance imaging (MRI).

2.2 | Characterization

Characterization of prenatal and postnatal exposure was done by consensus in a group consisting of a developmental pediatrician with expertise in FASD diagnosis, a child welfare manager, a child clinical psychologist, and a neuroscientist. Information pertaining to early prenatal and postnatal exposures was obtained from each participant's child welfare file (which contained information from birth families, social workers, police records, and medical files), and semistructured interviews with foster/adoptive parents and birth

TABLE 1 Exposure definitions and criteria for scores. Adverse exposures were assessed on a Likert-type scale from 1 to 4. Specific criteria for Ranks 3 and 4 are shown below for each variable. Criteria for Ranks 1 and 2 are not shown, as they were the same for all variables. Scores of 1 represent a confirmed absence of any exposure, whereas 2 represents unknown exposure (generally due to insufficient information)

Exposure type	Description	Rank 3	Rank 4
Prenatal alcohol exposure	Consumption of any form of alcohol during pregnancy	Exposure to prenatal alcohol not meeting criteria for a score of 4 or confirmed exposure of unknown amount	High exposure of ≥7 drinks/week or ≥ 2 binge episodes (≥4 drinks on one occasion) at some point in pregnancy
Other prenatal substance exposure	Exposure to harmful substances including marijuana, nicotine, cocaine, methamphetamines, and opioids during pregnancy.	Exposure to nicotine or marijuana of any amount; low frequency use of other substances, or confirmed use of unknown amount	High frequency use (≥5 times in pregnancy) of an illicit substance (cocaine, methamphetamines, opioids, etc.)
Other prenatal toxic stress	Harm or threat of harm to the mother and fetus during pregnancy; lack of prenatal care, housing, food, or income to meet needs; maternal mental health problems.	Symptoms of a mental health problem (undiagnosed), lack of prenatal care, housing/food/income insecurity <3 months, OR a single instance of domestic violence or sex trade work	DSM 5 diagnosis of mental health disorder, domestic violence or sex trade work at least twice during pregnancy, housing/food/income insecurity ≥3 months, or multiple exposures
Early postnatal deprivation (<24 months)	The basic needs of the child not being met or a risk of needs not being met, including attachment needs.	One care transition (excluding from hospital), housing/food/income insecurity, or loss of caregiver (e.g., death, incarceration)	Multiple care transitions (≥2), neglect, or multiple exposures
Late postnatal deprivation (≥24 months)	Same as above	Same as above	Same as above
Early postnatal threat	Harm or threat of harm, including physical, emotional, sexual abuse; or witnessing violence, substance abuse, or criminal activity in the home.	Witnessing substance use or domestic violence, caregiver with mental illness	Abuse of any kind, or multiple exposures
Late postnatal threat (≥24 months)	Same as above	Same as above	Same as above

families where possible. Each child was scored on the 7 exposure variables (outlined earlier).

2.3 | Data analysis

The number of participants and proportion of our sample with each level of each exposure in each category was calculated. Exposure scores were examined for relationships with one another using χ^2 analyses. For PAE (because all participants had this exposure), we compared some exposure (Rank 3) versus high exposure (Rank 4); all other variables were dichotomized to absence (Rank 1 or 2) versus presence (Rank 3 or 4) of the exposure.

3 | RESULTS

3.1 | Exposure profiles

Table 2 shows the number and proportion of our sample ($n = 77$) that scored at each level for each variable. All children had confirmed PAE, 95% had other prenatal substance exposure, and 86% experienced prenatal stress. More children in our sample experienced postnatal deprivation (61% experienced early deprivation; 19% experienced late deprivation) than postnatal threat (36% early; 17% late). More children experienced postnatal adversity before 2 years of age (36% threat; 61% deprivation) than after 2 years of age (17% threat; 19% deprivation). Box 3 shows the exposure assessments for the two children whose stories are presented in Boxes 1 and 2.

Table 3 shows similar information to Table 2 but separated into groups of children who had some alcohol exposure (PAE Rank 3) or high alcohol exposure (PAE Rank 4, defined according to the Canadian guidelines for FASD diagnosis; Cook et al., 2016). Most children with Rank 3 or Rank 4 PAE had other prenatal substance exposure (96% vs. 94%) and/or exposure to prenatal toxic stress (84% vs. 88%). Generally, more of the children with high levels of PAE experienced other prenatal and postnatal adverse exposures compared to the children with some PAE; χ^2 analysis showed that high PAE significantly predicted the presence (Rank 3 or 4) of late postnatal threat exposure ($p = 0.034$) and late postnatal deprivation ($p = 0.008$).

3.2 | Relationships between risk variables

As described above, χ^2 analysis showed that high PAE (Rank 4) significantly predicted the presence (Rank 3 or 4) of late postnatal threat exposure ($p = 0.034$) and late postnatal deprivation ($p = 0.008$). Other confirmed prenatal substance exposure (Rank 3 or 4) predicted early postnatal deprivation ($p = 0.02$); other prenatal toxic stress did not significantly predict any other exposures. The presence of early postnatal threat significantly predicted every other postnatal variable: early postnatal deprivation ($p < 0.001$), late postnatal threat ($p = 0.001$), and late postnatal deprivation ($p = 0.007$). Early postnatal deprivation also predicted late postnatal deprivation ($p = 0.037$). Late postnatal threat and deprivation were significantly associated ($p < 0.001$); see Table 4 for summary.

TABLE 2 Exposure profiles across the whole sample. Table lists the number (percentage) of children with each level of exposure for each variable. Some columns do not add to 100% due to rounding

Rank	Prenatal alcohol exposure N (%)	Other prenatal substance exposure	Other prenatal toxic stress	Postnatal threat (<24 months)	Postnatal deprivation (<24 months)	Postnatal threat (≥24 months)	Postnatal deprivation (≥24 months)
1 (none)	0 (0)	1 (1)	0 (0)	34 (44)	24 (31)	55 (71)	54 (70)
2 (unknown)	0 (0)	3 (4)	11 (14)	16 (21)	6 (8)	9 (12)	8 (10)
3 (some)	45 (58)	46 (60)	30 (39)	5 (7)	17 (22)	2 (3)	4 (5)
4 (high)	32 (42)	27 (35)	26 (47)	22 (29)	30 (39)	11 (14)	11 (14)

3.3 | Co-occurring exposures

All children had at least one confirmed adverse exposure and most had multiple exposures. No children had high exposure (Rank 4) in every category. Eight percentage of children had at least some confirmed exposure (Rank 3 or 4) in every category. Figure 1 shows Venn diagrams depicting children who had overlapping exposures (with exposure defined as Rank 3 or 4) for prenatal (A) and postnatal (B) categories separately, as well as prenatal and postnatal together (C). To reduce variables for part C, we collapsed the two separate time periods for threat and deprivation categories. All children had confirmed PAE, while 99% also had other prenatal substance exposure and/or prenatal toxic stress; 70% of children had at least one confirmed postnatal adversity, while 23% had a confirmed absence of postnatal adversity (most of these children were adopted at birth), and 7% had unknown postnatal exposures (i.e., Rank 2).

Box 3. Adverse exposure assessments

Cindy:

Prenatal alcohol exposure (PAE): 4 (confirmed high exposure).

Other prenatal substance exposure: 3 (confirmed opioid use; unknown amount).

Other prenatal toxic stress: 4 (little prenatal care; housing, income, and food insecurity).

Postnatal deprivation (early): 3 (one care transition at 10 months).

Postnatal threat (early): 1 (no evidence of abuse or violence in the home).

Postnatal deprivation (late): 3 (one care transition at age 3 years).

Postnatal threat (late): 1 (no evidence of abuse or violence in the home).

Dustin:

Prenatal alcohol exposure: 4 (confirmed high exposure).

Other prenatal substance exposure: 3 (marijuana and cocaine exposure of unknown amount).

Other prenatal toxic stress: 4 (confirmed maternal mental illness; lack of prenatal care).

Postnatal deprivation (early): 4 (neglect).

Postnatal threat (early): 4 (witness to domestic violence and criminal activity).

Postnatal deprivation (late): 4 (neglect to age 3 years; multiple caregiver transitions).

Postnatal threat (late): 4 (witness to domestic violence and criminal activity).

4 | DISCUSSION

Here, we present a novel hybrid cumulative risk/dimensional model for ranking and reporting prenatal and postnatal adverse exposures in children and youth. Applying this framework to a cohort of children recruited for research, we show that children with a history of PAE frequently have other co-occurring exposures. In our cohort, PAE co-occurred with other prenatal exposures in 99% of cases. Co-occurring PAE and postnatal adversity were seen in two-thirds of our sample, and high PAE was a significant predictor of late postnatal exposure to threat or deprivation. The presence of one postnatal adversity was significantly related to the presence of other postnatal adversities. These results highlight the importance of considering additional prenatal and postnatal adverse exposures in clinical assessment, intervention, and research.

Prenatal and postnatal exposures rarely occur in isolation (Astley, 2010; Astley et al., 2000; Gibbard, 2010; Hyter, 2012; Koponena et al., 2009); however, negative child outcomes are commonly attributed to a single cause. For FASD, clinicians and researchers have primarily focused on understanding child negative outcomes related to PAE. In doing so, the field has overlooked other co-occurring exposures that may also contribute to a child's cognitive, behavioral, social–emotional, and neurological development. Furthermore, the interaction between PAE and other prenatal and postnatal factors may also contribute to negative outcomes in children. It is this overlap and interplay of early adverse exposures that necessitates the development of a framework to better identify and understand the complex profiles of children and youth. The framework presented here, based on a hybrid cumulative risk approach and dimensional model, considers the role of key early exposures a child may experience in relation to one another.

While all children had at least one confirmed prenatal exposure (and 99% had multiple risks), fewer children had postnatal adversities, likely because of adoption or placement into stable homes. In some cases (23%), where children had been adopted from hospital, the absence of postnatal

TABLE 3 Exposure profiles across the subset of participants with some alcohol exposure (PAE Rank 3) and high alcohol exposure (PAE Rank 4). Table lists number (percentage) of participants with each category of exposure. Some columns do not add to 100% due to rounding

	Rank	Other prenatal substance exposure N (%)	Other prenatal toxic stress	Postnatal threat (<24 months)	Postnatal deprivation (<24 months)	Postnatal threat (≥24 months)	Postnatal adversity (≥24 months)
Children with some alcohol exposure (PAE Rank 3; $n = 45$)	1 (none)	0	0	19 (42)	12 (27)	33 (73)	34 (76)
	2 (unknown)	2 (4)	7 (16)	13 (29)	5 (11)	8 (18)	7 (16)
	3 (some)	30 (67)	15 (33)	2 (4)	13 (29)	1 (2)	0 (0)
	4 (high)	13 (29)	23 (51)	11 (24)	15 (33)	3 (7)	4 (9)
Children with high alcohol exposure (PAE rank 4; $n = 32$)	1 (none)	1 (3)	0 (0)	15 (47)	12 (38)	22 (69)	20 (63)
	2 (unknown)	1 (3)	4 (13)	3 (9)	1 (3)	1 (3)	1 (3)
	3 (some)	16 (50)	15 (47)	3 (9)	4 (13)	1 (3)	4 (13)
	4 (high)	14 (44)	13 (41)	11 (34)	15 (47)	8 (25)	7 (22)

adverse exposures could be confirmed. Similarly, the decrease in proportion of children with late postnatal adversities compared to early postnatal adversities reflects the fact that many children entered stable homes before the age of 2 years and thus did not experience significant exposures after that age. It is important to note that some children in our sample may still go on to experience postnatal adversities, and thus the numbers presented here may not reflect exposure in a group of adults.

The current Canadian guidelines for diagnosis of FASD encourage clinicians to obtain histories related to other exposures, although these exposures are not quantified (Cook et al., 2016). Our current data, along with limited previous studies (Astley, 2010; Price et al., 2017), highlight the importance of a multidisciplinary approach in which clinicians collaborate and integrate assessment findings related to individual profiles of adverse exposures, protective factors, and outcomes. Diagnostic processes and measures from all relevant disciplines must also take into account other etiologically relevant exposures or moderating factors (occurring prenatally or postnatally) to integrate these into a coherent diagnostic profile. By considering prenatal and postnatal adverse exposures other than just PAE, clinicians can understand the child in their environment, potentially leading to more accurate diagnoses. Furthermore, treatment and intervention recommendations may be made that are consistent with the child's history. Recognizing the co-occurrence of adversities is critical to gaining a more complete understanding of the child and assessing frequency and severity of these experiences may help to better predict developmental outcomes.

Implementing a common framework across child-serving sectors (in particular between child welfare and health) will be important to document exposure profiles for future assessment needs, when required. Furthermore, considering *all* factors of a child's prenatal and postnatal history along with their strengths and deficits will aid in determining what interventions are most appropriate for a child's needs, and how they should to be modified for that individual to promote success. Services and interventions that address multiple exposures and functional domains have the potential to have a greater influence on child outcomes. Increased support during childhood and adolescence has a direct impact on successful outcomes in adulthood, as long as it is understood that targeted strategies will continue to be required for vulnerable adults (Pecora et al., 2006; Spohr & Steinhausen, 2008; Streissguth et al., 2004). The co-occurrence of adverse exposures highlights the need for services that begin as early as possible (including prenatally) and continues to support the child and family throughout development.

TABLE 4 Chi-squared tests of relationships among variables. For prenatal alcohol exposure (since all children had confirmed exposure), we tested whether Ranks 3 versus 4 predicted the presence of other exposures. For all other exposures, we tested the absence of confirmed exposure (Rank 1 or 2) versus presence (Rank 3 or 4). *P*-values are given below

	Prenatal alcohol exposure	Other prenatal substance exposure	Other prenatal toxic stress	Postnatal threat (<24 months)	Postnatal deprivation (<24 months)	Postnatal threat (≥24 months)
Other prenatal substance exposure	NS					
Other prenatal toxic stress	NS	NS				
Postnatal threat (<24 months)	NS	NS	NS			
Postnatal deprivation (<24 months)	NS	0.02	NS	<0.001		
Postnatal threat (≥24 months)	0.034	NS	NS	0.001	NS	
Postnatal deprivation (≥24 months)	0.008	NS	NS	0.007	0.037	<0.001

NS = not significant ($P > 0.05$)

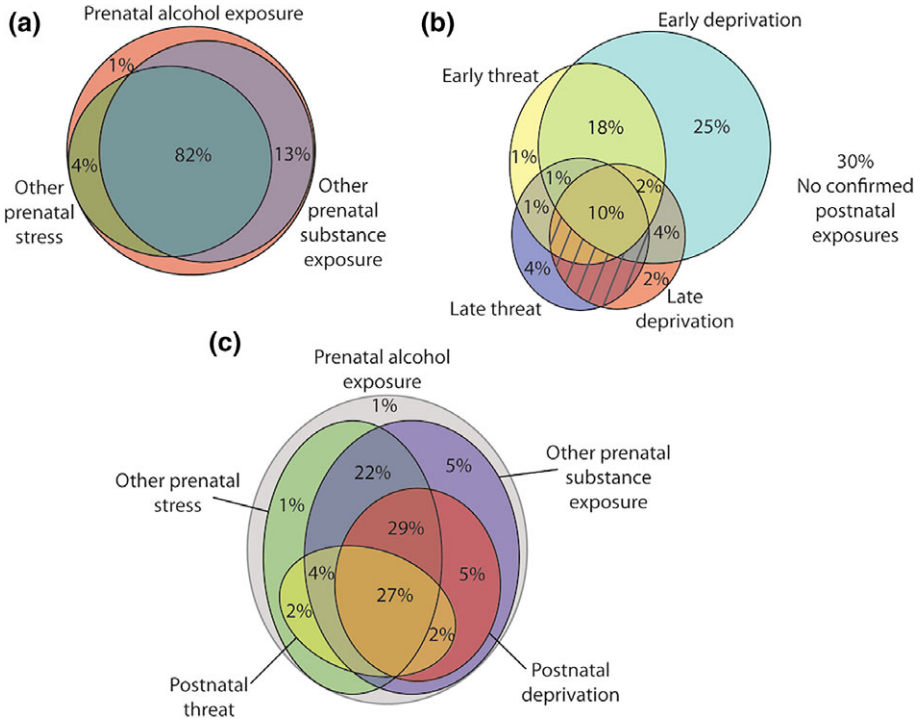

FIGURE 1 Venn diagrams of exposures. (a) Overlapping prenatal exposures are shown. Only one child (1% of the sample) had confirmed prenatal alcohol exposure (PAE) without other prenatal substance exposure or toxic stress. The vast majority (82%) of children had all three types of prenatal adverse exposures. (b) Overlapping postnatal exposures are shown. Most children (70%) had at least one confirmed postnatal adverse exposure; 44% had only early exposures (<24 months), 6% had only late exposures (≥24 months), and 18% had both early and late adversities. (c) Overlapping prenatal and postnatal exposures are shown, with postnatal exposures collapsed across time into one category for each of threat and deprivation. All children had PAE, and only 1% of those had no confirmed additional exposures. All children with postnatal exposures had PAE and additional prenatal exposures. Presence of an exposure was defined as Rank 3 or 4. Note that an absence of exposure on this diagram merely denotes an absence of *confirmed* exposure (Rank 1 or 2), rather than a confirmed absence of exposure, due to some missing information. Percentages may not add to 100% due to rounding

Adequately and appropriately serving individuals with FASD requires a multidisciplinary approach and collaboration across health, education, child and family service, and criminal justice. Given the heterogeneity of outcomes of this population, there is no "one size fits all" approach to treating co-occurring developmental, mental health and behavioral outcomes. Consequently, an individualized approach to treatment and prevention across the lifespan will be essential for individuals who experience multiple early adverse exposures.

The proposed framework for characterizing early adverse exposures may also be an important approach for future research. Much of the existing literature on adverse child outcomes has focused on single etiologic variables (i.e., PAE or maltreatment alone) or single time periods (e.g., ACEs focuses only on postnatal variables), although the majority of children experience multiple exposures. Furthermore, negative outcomes may result from the complex interplay between these exposures (Green et al., 2010; McLaughlin et al., 2012), which need to be considered in research both statistically and when creating research methodologies. Future research should document additional exposures and incorporate them into statistical analyses of developmental, neurological, and/or cognitive outcomes in children, considering both unique and cumulative effects of the different variables. Research on children with early adversities is complex, but appropriate consideration of different exposures is essential for properly assessing, treating, and promoting optimal outcomes for these children and their families.

It is important to recognize that obtaining detailed, comprehensive information on children with early adversities can be challenging, particularly for prenatal exposures (Konijnenberg, 2015; Lebel & Sowell, 2011). Our approach deals with this in two ways. First, we combine exposures that are likely to co-occur and have little evidence of distinct outcomes (e.g., other prenatal substance exposure), to reduce the need for specific information about each variable, and also to reduce complexity of interpretation of the data. Second, as in the four-digit code for FASD diagnosis (Astley, 2004), a Rank 2 can be used to designate unknown information. Postnatal exposure may be more easily obtained if child welfare, medical, or legal records are available. Implementing a common risk assessment and documentation framework across child-serving sectors (in particular between child welfare and health) will be important to record exposure profiles for future assessment needs.

A limitation of our current approach is that its validity and reliability have not yet been assessed with respect to child outcomes. Furthermore, this framework must be

assessed in the context of broader clinical assessments and service delivery, including interventions. Future work will be essential to validate this framework, including examining how specific prenatal and postnatal exposures, and their interactions with each other, relate to child development outcomes. This framework provides an important new way in examining prenatal and postnatal exposures together, and it is easily adaptable to include additional exposures that capture unique effects or to collapse exposure categories to simplify the model. This may be particularly important as further research emerges on the unique effects of various adverse exposures.

In conclusion, we present a novel and innovative approach to understanding and documenting the multiple early adverse exposures of children and youth. This framework provides a comprehensive and systematic approach to characterize numerous important factors that can contribute to negative developmental, behavioral, cognitive, and mental health outcomes. The current framework quantifies prenatal and postnatal adverse exposures in terms of dosage, frequency, and timing based on existing literature on individual risks and extensive clinical experience. Applying this framework to a cohort of children recruited for research demonstrated that co-occurrence of exposures is common. Determining the interplay between multiple exposures a child experiences prenatally and postnatally is essential to completing valid and reliable research, conducting comprehensive assessments, determining effective intervention, and ensuring appropriate policies are in place to serve these vulnerable children and youth.

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