



Establishing clinically and theoretically grounded cross-domain cumulative risk and protection scores in sibling groups exposed prenatally to substances

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ABSTRACT

Background: Prenatal substance exposure is associated with neurodevelopmental deficits. Deficits are exacerbated by cumulative risks yet attenuated by cumulative protective factors. Cross-domain relative to intra-domain risk exposure presents more neurodevelopmental challenges. Cumulative risk and protection scores must be clinically and theoretically grounded, with cross-domain considerations.

Objectives: 1) Create clinically and theoretically grounded, cross-domain cumulative risk and protection scores; 2) Describe the benefits of our methodological approach.

Participants & Setting: This study included three sibling groups (N = 8) at Mothercraft's Breaking the Cycle, a child maltreatment prevention and early intervention program for substance using mothers and their children.

Method: We outlined the process of establishing clinically and theoretically grounded, cross-domain cumulative risk and protection scores. Total and cross-domain cumulative risk and protection percentages, and the balance between domains of risk and protection, were explored. **Results:** Clinically and theoretically grounded, cross-domain cumulative risk and protection scores were established. Total percentages were reported. Cross-domain profiles of cumulative risk and protection, and the number of significant domains of risk relative to protection, were reported. The cross-domain profiles facilitated consideration of intra- and inter-domain risk and protection within and between sibling groups.

Conclusions: Emerging patterns indicate the importance of establishing cumulative risk and protection scores that are: 1) clinically and theoretically grounded, 2) cross-domain, and 3) encompass cumulative protection and risk. In understanding profiles of risk and protection, we can inform evidence-based early interventions that address: 1) high-risk children, 2) the full range of risks, 3) vulnerable domains, and 4) protective factors.

1. Introduction

Prenatal substance exposure is a serious public health concern in North America, given that such exposure is associated with

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deficits across many domains of functioning (Huizink, 2015; McQueen, Murphy-Oikonen, & Desaulniers, 2015). Children with prenatal substance exposure are considered at high risk for a range of biological, neurodevelopmental, and behavioural problems, as well as later psychopathology (Bandstra, Morrow, Mansoor, & Accornero, 2010; Kessler, Davis, & Kendler, 1997, 2010). Research has shown that the adverse consequences of prenatal substance exposure can be exacerbated by risk factors across various domains within the perinatal environment (Carta et al., 2001; Conners et al., 2004). The accumulation of protective factors can also occur across domains and attenuate the negative effects of cumulative risk, resulting in more positive developmental outcomes (Ackerman, Schoff, Levinson, Youngstrom, & Izard, 1999; Crosnoe, Leventhal, Wirth, Pierce, & Pianta, 2010; Furstenberg, Cook, Eccles, Elder, & Sameroff, 1999; Ostaszewski & Zimmerman, 2006; Runyan et al., 1998; Spencer, 2005). This study focused on cumulative risk and protective factors in a sample of substance-exposed children, with a focus on domains of risk and protection and their interactions.

1.1. Cumulative risk factors

A risk factor is defined as an endogenous (e.g., mental health challenges) or exogenous (e.g., prenatal substance exposure) factor associated with an increased likelihood of developing negative or undesirable outcomes (Kraemer, Lowe, & Kupfer, 2005). Most children exposed to a single physical or psychosocial risk factor suffer minimal enduring consequences (Evans, Li, & Whipple, 2013; Rutter, 1981). In contrast, children concurrently exposed to multiple risk factors are at high risk for poor developmental outcomes and psychological disorders (Kessler et al., 1997, 2010; Rutter, 1979, 1981; Sameroff, 2006). Therefore, *cumulative risk* is used to conceptualize children's exposure to multiple risks and the additive impact of risk on development (Evans et al., 2013). Correlations between developmental outcomes and sociodemographic, psychosocial, and biological profiles are often mediated by cumulative risk exposure (Evans et al., 2013; Madigan, Wade, Plamondon, Maguire, & Jenkins, 2017). Furthermore, cumulative risk exposure accounts for more of the variance in children's developmental trajectories than prenatal substance exposure alone (Carta et al., 2001). Children growing up in at-risk families often present with constellations of risk rather than isolated instances of adverse circumstances; therefore, assessing cumulative risk exposure yields information about children who are at highest risk for impaired development (Evans et al., 2013).

Cumulative risk models measure the quantity of risk factors rather than the quality of each risk factor, or the degree to which it impacts the outcome of interest (Evans, 2004; Hooper, Burchinal, Roberts, Zeisel, & Neebe, 1998). Two models have been commonly used to conceptualize cumulative risk exposure. First, additive models are based on the number of risk factors experienced overall, with a linear decrease in positive developmental outcomes resulting as the risk exposure increases (Sameroff, Bartko, Baldwin, Baldwin, & Seifer, 1998). Additive cumulative risk models are, therefore, based upon the additivity of risk assumption that implies only a linear relation between the number of risk factors and compromised child developmental outcomes. Two issues with this assumption are that: 1) there is a lack of statistical testing for the additivity assumption in the cumulative risk literature, and 2) risk factors may also interact and increase vulnerability, yet there is a lack of focus on potential nonlinear interactive effects between risk factors using this model (Lamela & Figueiredo, 2015; Sameroff, Seifer, & McDonough, 2004). The second type of model is a threshold model, wherein risk is assessed based on a certain number of risk factors being present and surpassing an arbitrarily assigned level of risk (Appleyard, Egeland, van Dulmen, & Sroufe, 2005). After a certain number of risk factors are experienced, there is said to be an exponentially negative impact on development, with the risk factors potentiating each other such that the effect of all of them together is greater than the sum of their individual effects (Rutter, 1979). Evidence for both additive (i.e., additive model) and exponential (i.e., threshold model) relationships between cumulative risk and developmental outcomes have been reported in the literature (Evans et al., 2013). Nonetheless, the additive cumulative risk models have been found to be more predictive of developmental outcomes over the threshold cumulative risk models (Appleyard et al., 2005). There is, however, a need for further investigation into the potential interactive effects between multiple risks (Evans et al., 2013).

1.1.1. Cross-domain risk factors

In a review of cumulative risk and child development, Evans et al. (2013) discussed the need to combine single risk factors into domains to examine potential main and interactive effects. Some researchers have, indeed, investigated exposure to risk across different life domains and found that risk exposure across multiple domains presents more challenging adaptive demands on children relative to intense but concentrated intra-domain risk exposure (Ackerman et al., 1999; Brennan, Hall, Bor, Najman, & Williams, 2003; Evans et al., 2013; Whipple, Evans, Barry, & Maxwell, 2010). Studies that assess the number of domains of cumulative risk to which a child was exposed have indicated larger effect sizes (average 22.7 % increment in adversity per risk factor exposure) than those found when examining overall cumulative risk scores (average 5.7 % increment in adversity per risk factor exposure) (Evans et al., 2013). Cross-domain cumulative risk models also enable the examination of main and interactive effects of domain-specific cumulative risk exposure on child development, with several studies indicating interactive effects between domains (Ackerman et al., 1999; Brennan et al., 2003; Carta et al., 2001; Mrug, Loosier, & Windle, 2008; Whipple et al., 2010).

1.2. Cumulative protective factors

Most literature on cumulative risk has focused solely on risks or detrimental factors and their impact on development, with limited focus on the effects of cumulative protective factors as well (Evans et al., 2013). A small number of studies, some of which included populations of at-risk children, have indicated that as protective factors accumulate, their benefits accrue and promote positive developmental outcomes (Crosnoe et al., 2010; Furstenberg et al., 1999; Runyan et al., 1998). Some researchers have even found that cumulative protective factors can attenuate the negative effects of cumulative risk (Ackerman et al., 1999; Ostaszewski &

Zimmerman, 2006; Spencer, 2005). Not only are cumulative protective factor scores associated with more positive developmental outcomes, but cumulative protective factor scores have also been found to interact with cumulative risk scores in predicting developmental outcomes, such that medium and high cumulative protective factor scores have attenuated the relationship between cumulative risk and negative outcomes (Ackerman et al., 1999). Cumulative protective factors are more strongly related to positive developmental outcomes relative to individual protective factors, suggesting that a cumulative conceptualization of exposure to protective factors is advantageous to understanding developmental outcomes (Ackerman et al., 1999). Nonetheless, the accumulation of protective factors, relative to exposure to multiple risk factors, explains minimal variance in developmental outcomes (Gutman, Sameroff, & Cole, 2003; Pollard, Hawkins, & Arthur, 1999; Sameroff & Rosenblum, 2006). Although risk exposure may have a more substantial impact on developmental outcomes relative to protection, it is vital to consider the effects of protection alongside the effects of risk.

1.2.1. Cross-domain protective factors

Similar to risk factors, protective factors can include endogenous (e.g., high IQ, good temperament) or exogenous (e.g., supportive relationships, high socioeconomic status) factors. In the context of children with prenatal substance exposure and histories of risk, early prevention and intervention services for the mother and child can be conceptualized as protective processes designed to promote optimal development (Andrews, Motz, Pepler, Jeong, & Khoury, 2018). Nonetheless, limited work has taken domain-specific protective factors into consideration (Evans et al., 2013). This oversight is problematic in that it fails to provide a holistic perspective of child development within contexts of both risk and protective factors. Combining protective factors into domains allows the potential main and interactive effects of cumulative protective factors to be examined, in addition to allowing the interactive effects between domain-specific risk and protective factors to be examined (Evans et al., 2013).

1.3. Identifying risk and protective domains: a clinically and theoretically grounded approach

Evans et al. (2013) discussed the importance of grounding cumulative risk and protective factor research in a holistic theoretical framework that aids in delineating developmentally salient risk and protective domains. A theoretical foundation provides a rationale to account for the superior predictive power of multiple, relative to singular, risk and protective factor exposure on child developmental outcomes (Evans et al., 2013). Pepler (2016) has discussed the need to embed research within clinical and community settings and build trusting relationships as a preemptive step to fostering co-creation. It is thus essential to ground research establishing cumulative risk and protection scores for focal clinical populations within the settings that serve them. Cumulative risk and protection scores must be both clinically and theoretically grounded, with a clinical understanding of the focal population informing the selection of an appropriate theoretical framework. The Developmental Model of Transgenerational Transmission of Psychopathology (Fig. 1; Hosman, van Doesum, & van Santvoort, 2009) was utilized in this study to conceptualize various domains of risk and protective factors in children exposed prenatally to substances and accessing early intervention services. Although Hosman and colleagues' developmental model outlines the transgenerational transmission of psychopathology, similar developmental and relational domains and processes are relevant to substance-exposed children accessing early intervention.

Hosman and colleagues' model was founded upon practice- and theory-based empirical knowledge, capturing information on the main domains of malleable risk and protective factors (Hosman et al., 2009). This model differentiates multiple interacting domains and systems of influence (i.e., children, parents, family, social network, professionals, community), recognizing that risk and protective factors are linked across domains and each can serve as a relevant intervention focus. The model also differentiates various mechanisms by which risk factors are transmitted (i.e., genetic risk, prenatal influences, parent-child interactions, family processes and conditions, and social influences; Goodman & Gotlib, 1999). Finally, this developmental model differentiates developmental stages in the child's life (e.g., pregnancy, early development, lifespan development), with each stage associated with specific developmental processes and sensitive periods requiring stage-specific intervention (Hosman et al., 2009). The strength of this model is that it comprehensively captures both risk factors and the conditions promoting children's resilience and social-emotional development.

2. Current study

The primary goal of the current study was to create clinically and theoretically grounded, cross-domain cumulative risk and protective factor measures for three sibling groups with prenatal substance exposure participating in a child maltreatment prevention and early intervention program with their mothers. We outlined the process of establishing comprehensive cumulative risk and protective factor measures that build upon a holistic developmental model of domains of risk and protection that is clinically relevant to consider in this population. This domain-specific description of cumulative risk and protective factors facilitated the consideration of both intra- and inter-domain risk and protective factors across the three sibling groups. Through this examination, we also outline the benefits of taking a clinically and theoretically grounded, cross-domain approach to establishing cumulative risk and protection scores in children exposed prenatally to substances. For a comprehensive qualitative case study description of each sibling group's cross-domain context of risk and protection, neurodevelopment, and clinical progress, see Bondi, Pepler, Motz, and Andrews (2020a). For a quantitative description of each child's longitudinal neurodevelopment, and an overview of the patterns between cumulative risk and protection as they relate to neurodevelopment, see Bondi, Pepler, Motz, and Andrews (2020b).

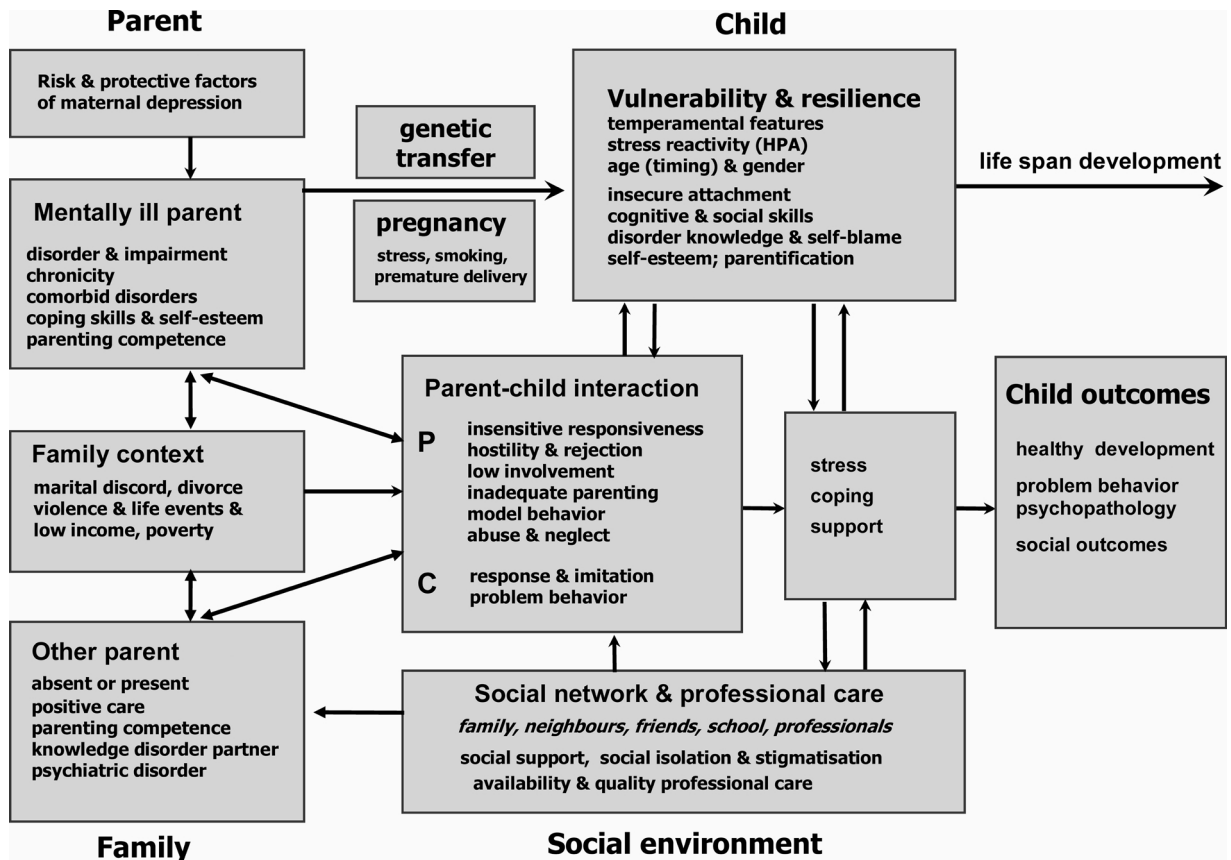


Fig. 1. Theoretical Model. Reprinted from Hosman et al. (2009). Prevention of Emotional Problems and Psychiatric Risks in Children of Parents with a Mental Illness in the Netherlands. I. The Scientific Basis to a Comprehensive Approach. *Australian e-Journal for the Advancement of Mental Health*, 8(3), 250-63. Copyright 2009 by the Taylor & Francis Ltd (<https://www.tandfonline.com>). Reprinted with permission.

3. Material and method

3.1. Study design and setting

This was a retrospective study conducted at Mothercraft's Breaking the Cycle (BTC). BTC is a child maltreatment prevention and early intervention program for substance using mothers and their children from birth to 6 years old in Toronto, Canada. In addition to prenatal substance use, women at BTC have histories of trauma, mental health issues, interpersonal violence, and family instability, making BTC a unique context to evaluate cumulative risk and protective factors in children exposed prenatally to substances. The program supports the development of children with prenatal substance exposure by providing maternal (e.g., addiction counseling), child (e.g., early intervention services), and mother-child relationship-focused (e.g., home-based dyadic developmental services) services. Embedding the present study within a clinical setting that serves this vulnerable population and co-creating research with highly experienced clinicians was essential. These professionals offered a deep understanding and grounded perspectives about developmental processes and change through maltreatment prevention. Attending bi-monthly case formulation team meetings at BTC contributed to a comprehensive clinical understanding of the families accessing services at BTC, enabling us to establish clinically and theoretically grounded cumulative risk and protection scores.

3.2. Sample characteristics

Three pediatric (aged 0–6 years) sibling groups were included in this study: two sibling dyads and one sibling quadrad ($N = 8$). All sibling groups had substance exposure histories and had received long-term treatment at BTC for a minimum of 2.5 years. The three families, herein referred to as family A, family B, and family C, were selected based on their clinical progress, which lead clinicians at BTC classified as good, fair, and poor, respectively. Clinicians assessed overall clinical progress based on the families' participation in programming at BTC, child apprehensions from parental care during their involvement, and status at closing. Families with variable levels of clinical progress were included to capture the range of clients seen at BTC. Individual children within each sibling group are referred to according to family letter (e.g., A, B, C) and birth order (e.g., 1–4).

To ensure client privacy and confidentiality, the sex of the children, and other highly identifiable sample characteristics, will not be disclosed. A1 entered BTC programming at age 3.5 years and spent 44 % of life in BTC services. A2 entered BTC programming at birth and spent 94 % of life in BTC services. B1 and B2 entered BTC programming at 2 years and spent 64 % of their lives in BTC services. B3 entered BTC programming at 1 year and B4 entered at birth. B3 and B4 spent 77 % and 94 % of life in BTC programming, respectively. C1 spent 39 % of life in BTC programming and C2 spent 46 % of life in BTC programming. Notably, both C1 and C2 entered BTC at older ages relative to the children in the other sibling groups, entering at ages 5 and 4 years, respectively. For comprehensive case studies and qualitative descriptions of each child's clinical progress, see (Bondi et al., 2020a).

3.3. Study design and development of cross-domain cumulative risk and protective factor scales

This study used archival BTC data collected under a CIHR-funded, multi-year study (Espinete, Motz, Jeong, Jenkins, & Pepler, 2016). Data were obtained from clients' charts, which include: referral forms, mother and child intake forms, progress notes, medical notes, correspondence, addiction counselling notes, mother-child interactional support notes, clinical team review notes, child developmental assessment measures and reports, and service ending forms. Clients differed in their use of services and their length of involvement with BTC; therefore, available information varied slightly across participants. The study was approved by York University's Ethics Review Board (Approval #: STU2018-134).

To establish the cumulative risk factor score, risk elements were extracted from clients' charts based on prior measures, including: 1) items from a cumulative risk measure utilized in prior BTC research, 2) measures used clinically at BTC to assess maternal mental health, addiction, and parenting capacity, 3) a measure utilized in studies on adverse childhood experiences, and 4) the Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood, specifically Axis IV on Psychosocial Stressors (Anda et al., 2006; Mothander, 2016; Motz et al., 2011). A cumulative protective factor score was then established based on: 1) existing early intervention components of services at BTC, 2) clinical measures assessing maternal mental health, addiction, and parenting capacity, and 3) known protective factors outlined in the literature. The cumulative risk and cumulative protective factor scores were categorized by domains based on Hosman et al.' (2009) theoretical model, which was selected based on our clinical understanding of these substance-exposed children undergoing intervention (Fig. 1). Specifically, the following domains of both risk and protective factors were assessed: mother, secondary parent, family, pregnancy, birth, child, parent-child interactions, social networks, and professional services.

3.4. Total and cross-domain cumulative risk and cumulative protection scores

Each risk element was coded dichotomously, with exposure = 1 and no exposure = 0. Risk assignment was accomplished with statistical criteria (e.g., upper quartile of risk exposure = 1; all others = 0) or based on *a priori* theoretical and conceptual categorization (e.g., being below the poverty line, single parenthood) and pre-existing clinical classifications on the clinical measures used at BTC (e.g., clinically significant anxiety), when appropriate. Similarly, each protective element was coded dichotomously, with exposure = 1 and no exposure = 0. Again, assignment was accomplished with statistical criteria (e.g., lower quartile of risk exposure = 1; all others = 0) or based on *a priori* theoretical and conceptual categorization (e.g., accessing early intervention services), when appropriate. The sum of the dichotomous elements within each domain was calculated to yield domain-specific cumulative risk and protective factor scores. Total cumulative risk and cumulative protective factor scores were computed by adding the scores across each domain for each child within the three sibling groups. These total scores were converted into percentages to ensure that the denominator was dependent on the number of applicable items per child, with unknown elements removed.

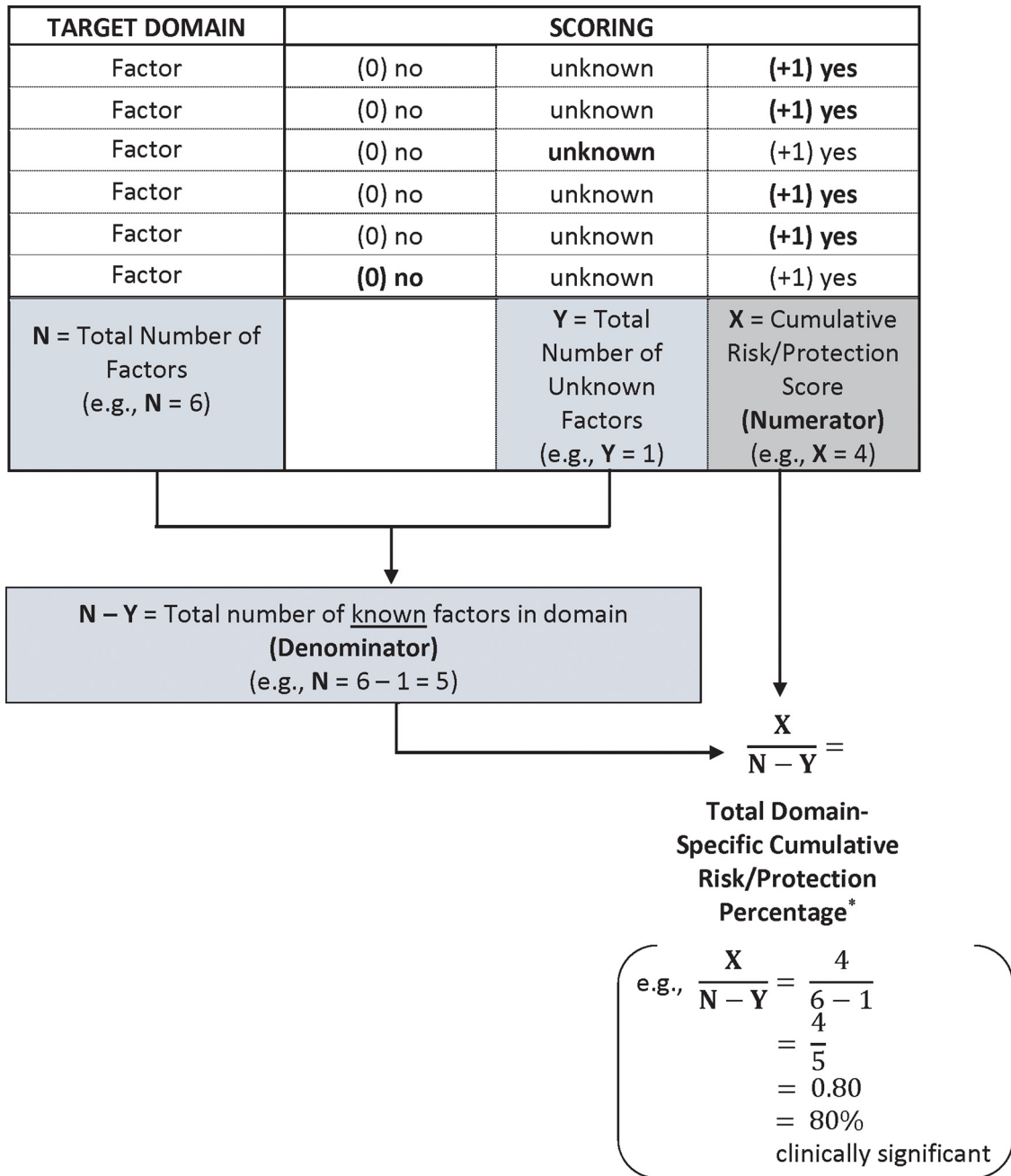
Domain-specific cumulative risk and protective factor scores were also converted to percentages to ensure that the denominator reflected the number of applicable items per domain, with unknown elements removed (see Fig. 2). As an example: in a domain with 7 factors, an individual was coded as having risk exposure on 3 factors and unknown on 2 factors. Using the formula $3/(7-2)$ results in a domain risk percentage score of 0.60, or 60 %. Domain-specific cumulative risk and protective factor percentages > 25 % were considered clinically significant. Thus, in the example above, the individual would be classified as having clinically significant risk in that domain. The number of clinically significant domains of risk and protection (Fig. 3A) were also subtracted to quantify the balance between cross-domain cumulative risk and protection, with positive numbers (highlighted) indicating more risk domains relative to protection domains (i.e., Net Risk Score; Fig. 3B).

4. Results

Comprehensive, domain-specific, clinically and theoretically grounded cumulative risk and protective factor measures were established (see Bondi, Pepler, Motz, & Andrews, 2020c). These scores were used to conceptualize the histories of risk experienced by children in the three focal families, both across and within the sibling groups. Additionally, these scores highlighted the protective factors experienced by each child to help promote resilience and healthy development.

4.1. Cross-family comparison of cumulative risk and protection scores

The cross-domain and total cumulative risk and protective factor percentages for each child in the three sibling groups are outlined in Table 1. An overview of the total cumulative risk and protective factor percentages for each child is shown in Fig. 4, indicating the children with the highest and lowest cumulative risk and protection, both within and between the sibling groups.



*Cumulative risk/protection percentage > 25% classified as clinically significant

Fig. 2. Calculating Cross-Domain Cumulative Risk and Protection Percentage.

Family B had the highest total cumulative risk percentages, particularly B1 and B2 who had notably higher total percentages compared to B3 and B4. Relative to family B, family A and family C had lower total cumulative risk percentages, with fairly stable total percentages found within and between these two sibling groups. Family B also had the highest total cumulative protection percentages, with consistent total percentages within the sibling group. Relative to family B, family A had slightly lower total cumulative protection percentages; however, there was discrepancy within this sibling group, with A2 having a notably higher total percentage relative to A1. Family C had the lowest total cumulative protection percentages, with consistent total percentages within the sibling group. Notably, even within sibling groups, children had differing domains of risk and protection given the changing circumstances across their family's involvement at BTC.

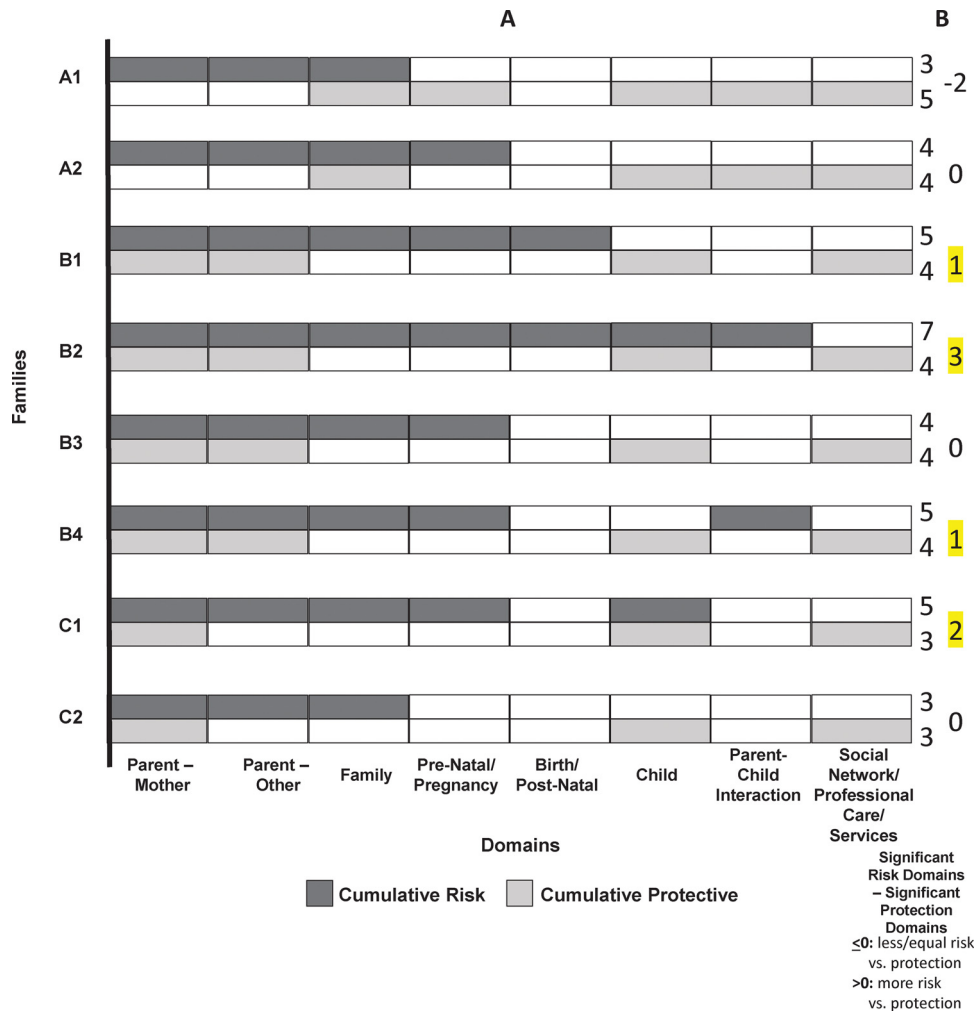


Fig. 3. Cross-Domain Cumulative Risk and Protection **Panel A:** Clinically Significant Cumulative Risk and Protection Domains; **Panel B:** Net Risk Score.

4.2. Child-specific description of cumulative risk and protection scores

4.2.1. Family A

A1 and A2 both had high cumulative risk scores in the maternal, other parental figure, and family domains (see Table 1, Fig. 3A). Relative to these domains, A1 and A2 had slightly lower cumulative risk scores in the pre-natal/pregnancy, birth/post-natal, child, and parent-child interaction domains, despite differing degrees of cumulative risk between A1 and A2. A1 and A2 both had low cumulative risk scores in the social network/professional services domain. A1 and A2 both had high cumulative protection scores in the child and social network/professional services domains; relative to these domains, both children had lower cumulative protection scores in the maternal and family domains. A1 and A2 had differing degrees of cumulative protection in the pre-natal/pregnancy and parent-child interaction domains. Both A1 and A2 had low cumulative protection scores in the other parental figure and birth/post-natal domains.

4.2.2. Family B

B1, B2, B3, and B4 all had high cumulative risk scores in the maternal and other parental figure domains; relative to these domains, they had slightly lower cumulative risk scores in the family and pre-natal/pregnancy domains (Table 1, Fig. 3A). B1, B2, B3, and B4 had differing degrees of cumulative risk in the birth/post-natal, child, and parent-child interaction domains. B1, B2, B3, and B4 all had low cumulative risk scores in the social network/professional services domain. B1, B2, B3, and B4 all had high cumulative protection scores in the maternal, other parental figure, child, and social network/professional services domains; relative to these domains, they had slightly lower levels of cumulative protection in the family and parent-child interaction domains. B1, B2, B3, and B4 all had low cumulative protection scores in the pre-natal/pregnancy and birth/post-natal domains.

Table 1
Cross-Family Comparison of Cumulative Risk and Protective Factor Scores.

Domain/Factor	n(%)							
	Family A		Family B				Family C	
	A1	A2	B1	B2	B3	B4	C1	C2
PARENT - MOTHER								
Cumulative Risk (n = 20)	11(55)	11(55)	9(45)	9(45)	9(45)	9(45)	8(42) ^a	8(42) ^a
Cumulative Protective (n = 18)	4(22)	4(22)	11(61)	11(61)	11(61)	11(61)	8(44)	8(44)
PARENT - OTHER								
Cumulative Risk (n = 6)	3(50)	4(67)	3(50)	3(50)	3(50)	3(50)	3(50)	3(50)
Cumulative Protective (n = 6)	0(0)	0(0)	3(50)	3(50)	3(50)	3(50)	0(0)	0(0)
FAMILY								
Cumulative Risk (n = 25)	14(56)	10(40)	8(32)	8(32)	8(32)	8(32)	12(48)	11(44)
Cumulative Protective (n = 7)	2(29)	2(29)	1(14)	1(14)	1(14)	1(14)	0(0)	0(0)
PRE-NATAL/PREGNANCY								
Cumulative Risk (n = 27)	1(4)	10(37)	8(30)	8(30)	9(33)	9(33)	7(26)	3(11)
Cumulative Protective (n = 2)	0(0)	1(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
BIRTH/POST-NATAL								
Cumulative Risk (n = 22)	1(5)	4(18)	8(36)	8(36)	2(9)	3(14)	0(0) ^a	0(0)
Cumulative Protective (n = 1)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
CHILD								
Cumulative Risk (n = 31)	5(16)	1(3)	7(23)	10(32)	7(23)	5(16)	9(29)	7(23)
Cumulative Protective (n = 8)	4(50)	5(63)	6(75)	6(75)	5(63)	6(75)	4(50)	7(88)
PARENT-CHILD INTERACTION								
Cumulative Risk (n = 15)	3(20)	0(0) ^a	3(20)	6(40)	3(20)	5(33)	2(13)	3(20)
Cumulative Protective (n = 15)	4(27)	7(47) ^a	3(20)	3(20)	3(20)	3(20)	2(13)	1(7)
SOCIAL NETWORK/ PROFESSIONAL CARE/SERVICES								
Cumulative Risk (n = 3)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
Cumulative Protective (n = 5)	2(40)	2(40)	3(60)	3(60)	3(60)	3(60)	2(40)	2(40)
TOTAL								
Cumulative Risk (n = 149)	38(26)	40(27) ^a	46(31)	52(35)	41(28)	42(28)	41(29) ^a	35(24) ^a
Cumulative Protective (n = 62)	16(26)	22(37) ^a	27(44)	27(44)	26(42)	27(44)	16(26)	18(29)

^a Adjusted denominator due to removed unknown factors.

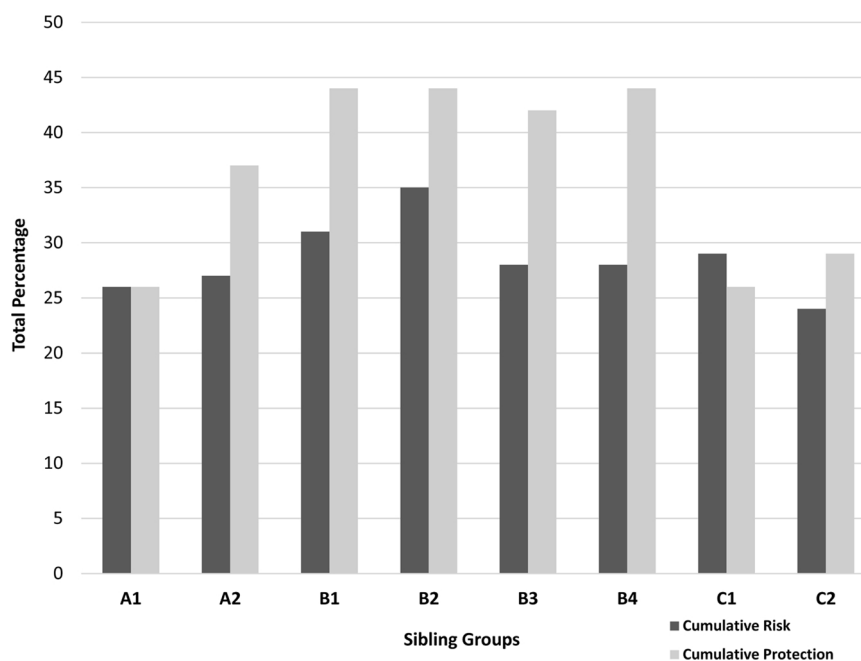


Fig. 4. Total Cumulative Risk and Protection Percentage.

4.2.3. Family C

C1 and C2 both had high cumulative risk scores in the maternal, other parental figure, and family domains; relative to these domains, C1 and C2 had slightly lower cumulative risk scores in the child domain (Table 1, Fig. 3A). C1 and C2 had differing degrees of cumulative risk in the pre-natal/pregnancy and parent-child interaction domains. Both C1 and C2 had low cumulative risk scores in the birth/post-natal and social network/professional services domains. Both C1 and C2 had their highest cumulative protection score in the child domain, despite differing degrees of cumulative protection. Both C1 and C2 had high cumulative protection scores in the maternal and social network/professional services domains; relative to these domains, C1 and C2 had lower cumulative protection scores in the parent-child interaction domains, despite differing degrees of cumulative protection between C1 and C2. C1 and C2 both had low cumulative protection scores in the other parental figure, family, pre-natal/pregnancy, and birth/post-natal domains.

4.3. Balance between domains of cumulative risk and protection

The domains with clinically significant percentages of cumulative risk and/or protection for each child are displayed in Fig. 3A, as well as a quantitative depiction of the number of clinically significant domains of risk relative to protection (i.e., Net Risk Score; Fig. 3B). Four children, namely B1, B2, B4, and C1, experienced more significant risk domains relative to significant protection domains (i.e., highlighted Net Risk Scores in Fig. 3B). All eight children showed clinically significant levels of risk across the mother, other parental figure, and family domains; however, their scores differed across the other domains. The six children who had clinically significant levels of risk in the pre-natal/pregnancy domain were also exposed to substances prenatally, whereas the two children who did not show clinically significant levels of risk in this domain did not have substance exposure. The four children who experienced more significant risk domains relative to significant protection domains, were also the only children who showed significant levels of risk in the birth/post-natal, child, and parent-child interaction domains. The children in family A were the only children who had clinically significant levels of protection within the family and parent-child interaction domains.

5. Discussion

Within this study, cumulative risk and protective factor measures were established with domains relevant to neurodevelopment in substance-exposed children accessing a child maltreatment prevention and early intervention program. The case study approach in developing the measures enabled an in-depth and clinically grounded analysis of each child and family's situation. This theoretically grounded domain-specific conceptualization of risk and protective factors facilitated the consideration of both intra- and inter-domain risk and protection within and between three sibling groups. The patterns that emerged indicate the importance of establishing cumulative risk and protection scores: 1) with clinical and theoretical grounding, 2) across domains, and 3) with consideration of cumulative protection in addition to risk.

5.1. Clinically and theoretically grounded cumulative risk and protection

Although cumulative risk and protection measures are often established for use with clinical populations, they are not typically established within the context of clinical and community settings. Notably, in the current study, cumulative risk and protection measures were grounded within a clinical setting that serves the focal population. Another limitation in previous studies using established cumulative risk and protection measures is the lack of theoretical foundation in determining which factors to include in the measures (Evans et al., 2013). In general, key risk factors for the outcome of interest are included in research, as well as risk factors related to proximal processes and salient mediating processes. Additionally, the degree of stability in what constitutes a risk or protective factor may differ across samples, with concerns for the generalizability of the operational definitions for risk and protection (Evans et al., 2013). Given the limited research on measures of cumulative risk and protection for children exposed prenatally to substances, it was essential to take a clinically grounded approach in establishing the cumulative risk and protection measures for children at BTC. Further, given the highly vulnerable population at BTC, the established cumulative risk and protection measures are comprehensive measures applicable for use with lower-risk populations.

The cumulative risk and protection scores were theoretically grounded using the Developmental Model of Transgenerational Transmission of Psychopathology (Hosman et al., 2009; Fig. 1). Our clinical understanding of the clinical profiles of risk and protection that are incorporated into case formulation at BTC was essential in selecting this model and in delineating the salient domains of risk and protection for children exposed prenatally to substances and accessing a child maltreatment prevention and early intervention program. This clinically and theoretically grounded approach aided us in identifying the specific factors to incorporate into each domain in these measures. Therefore, although recent literature has outlined the need to establish theoretically grounded cumulative risk and protection measures, the results of this study emphasize the importance of first grounding the research clinically, and using that knowledge to aid in selecting an appropriate theoretical model, as well as relevant domains and factors to be included. Our clinically grounded approach to establishing cumulative risk and protection measures, in addition to ensuring that the measures aligned with clinical case formulation at BTC, also ensured that the completed measures provided clinically accurate scores for each child. In the present study, we attempted to overcome shortcomings in the cumulative risk and protection research, including a lack of information on: contextual factors, risk and protective factor intensity, and the degree of risk and protective factor exposure (Evans et al., 2013; Lima, Caughy, Nettles, & O'Campo, 2010). The present research supports the need to establish cumulative risk and protection measures within a clinically and theoretically grounded framework that is unique to the focal population prior to use in

larger samples.

5.2. Cross-domain cumulative risk and protection

In the field of cumulative risk, there has been a recent shift towards classifying singular risk factors into domains, given that risk exposure across multiple domains presents more challenging adaptive demands on children relative to intense but concentrated intra-domain risk exposure (Ackerman et al., 1999; Brennan et al., 2003; Evans et al., 2013; Whipple et al., 2010). Limited work has taken domain-specific protective factors into consideration, despite findings that prevention and early intervention services across various domains (i.e., mother and child) can promote optimal child development (Andrews et al., 2018; Evans et al., 2013). Therefore, in this study, cumulative risk and protection were explored across domains relevant to substance exposed children accessing a child maltreatment prevention and early intervention program, grounded in a theoretical model (Hosman et al., 2009; Fig. 1). In comparison to the total cumulative risk and protection scores, the cross-domain scores provided a more nuanced understanding of each child's context, also distinguishing key differences within sibling groups. The cross-domain scores, relative to total scores, also aligned more accurately with each child's clinical profile. Therefore, understanding the full range of risk and protective factors and domains that a child must contend can aid in implementing individualized maltreatment prevention and early intervention programming.

A cross-domain examination of risk and protection provided insight into baseline levels of risk in this sample of children, given that all eight children showed clinically significant levels of risk across the mother, other parental figure, and family domains. In exploring the differences between clinically significant domains of cumulative risk across all children, the results of this study suggest that ongoing risk in the postnatal environment, specifically within the birth/post-natal, child, and parent-child interaction domains, appears to have more influence on clinical progress relative to risk in the maternal and family history domains. However, given that this study involved mothers in the context of treatment, the influence of maternal risk on clinical progress may be underestimated relative to what would be expected in similar populations without access to treatment. Similarly, clinically significant levels of protection in the family and parent-child interaction domains appeared to be unique aspects of protection in family A that may have contributed to the children's strong clinical progress. A cross-domain examination of cumulative risk and protection thus enables exploration of unique domains of risk and protection in children with developmental challenges who are growing up in vulnerable families experiencing challenges.

Consistent with the results from the present study, the balance between each sibling group's context of risk and protection has been found to be linked with clinical progress (Bondi et al., 2020a). Specifically, family B's high risk exposure, when balanced with high protective factors, contributed to fair, rather than poor, clinical progress (Bondi et al., 2020a). Relative to family B, families A and C had slightly fewer risk exposures alongside notably fewer protective factors; however, families A and C differed substantially in their clinical progress, classified as good and poor, respectively (Bondi et al., 2020a). Family A had slightly more protective factors relative to family C, alongside relatively comparable risk exposure (Bondi et al., 2020a). This balance between risk and protection contributed to family A having better clinical progress relative to family C (Bondi et al., 2020a). Therefore, heightened contexts of risk, in the absence of heightened contexts of protection, can result in notable differences in clinical progress (Bondi et al., 2020a). Further consistent with the present study, such balance between contexts of risk and protection, in addition to early intervention, has been found to impact neurodevelopment (Bondi et al., 2020b). Specifically, children who experienced more significant risk domains relative to significant protection domains demonstrated clinically significant neurodevelopmental deficits during their time at BTC (Bondi et al., 2020b).

5.3. Cumulative protection in addition to risk

Given the potential importance of cumulative protective processes in attenuating the negative effects of cumulative risk, cross-domain cumulative protective factors were also examined within this study (Ackerman et al., 1999; Ostaszewski & Zimmerman, 2006; Spencer, 2005). The results highlight the importance of the balance between the number of clinically significant domains of risk and protection; however, it is also important to consider the balance between overall cumulative risk and protection. The results indicate that heightened levels of cumulative risk, in the absence of heightened levels of cumulative protection, can result in notable differences within sibling groups. Although family B was classified as having the highest overall cumulative risk scores, family B was also classified as having the highest overall cumulative protection scores. This balance between risk and protection may have contributed to family B being classified as having fair, rather than poor, clinical progress despite being the highest risk family. Families A and C showed slightly lower levels of cumulative risk alongside notably lower levels of cumulative protection relative to family B; however, families A and C differed substantially in their clinical progress, classified as good and poor progress, respectively. Notably, family A had slightly higher levels of protection relative to family C, alongside relatively comparable levels of risk. This balance between risk and protection may have contributed to family A having better clinical progress relative to family C. These results indicate that clinical progress is linked with the balance between cumulative risk and protection; however, a cross-domain consideration is essential for a more nuanced understanding.

Overall, comparisons between sibling groups indicated that the balance between cross-domain levels of cumulative risk and protection can impede or contribute to clinical progress. The common domains found to have significant levels of risk in this sample (i.e., mother, other parental figure, and family) seem to portray the baseline level of risk present within this sample, including maternal risk factors and proximal risk factors within the home environment. The presence of significant risk within the pre-natal/pregnancy domain for children with substance exposure indicates that the established measure of cumulative risk was able to distinguish prenatal substance exposure histories. Given that the four children who experienced more significant risk than protection

domains also were the only children with significant levels of risk in the birth/post-natal, child, and parent-child interaction domains, these results suggest that ongoing risk in the postnatal environment may be more substantial compared to maternal or family history risks, or risks within the prenatal period. However, the clinically significant levels of risk within the parent-child interaction domain across all children in this study is likely an underestimation given that many of the factors within this domain were dependent on maternal self-report at entry into BTC programming, rather than clinical reports across each child's time at BTC. Therefore, the children who showed clinically significant levels of risk in the parent-child interaction domain likely had extreme levels of risk in this domain. Given that family A's children were the only children with clinically significant levels of protection within the family and parent-child interaction domains, these two domains may be an important aspect of protection, or early intervention, that contributed to family A's superior clinical progress amongst the three families. Overall, our cross-domain approach to considering cumulative protection in addition to risk has allowed us to delineate salient protective factors that can be incorporated into child maltreatment prevention and early intervention services.

5.4. Strengths and limitations

The major strengths of this study include the clinically and theoretically grounded, and cross-domain consideration of both cumulative risk and protection within a vulnerable sample of children exposed prenatally to substances and accessing child maltreatment prevention and early intervention services through BTC. The case study approach in developing the measures enabled an in-depth analysis of each child and family's situation. Despite these strengths, this study is limited by a lack of generalizability. The study involved a small sample of moderate to high risk children embedded within a child maltreatment prevention and early intervention program. Specifically, given mothers' and children's participation in child maltreatment prevention and early intervention services through BTC, all participants had exposure to protective factors that other families struggling with prenatal substance exposure and concurrent contexts of risks may not. As such, results may not generalize to other clinical and typically developing populations; however, this study has yielded comprehensive cumulative risk and protection measures that are capable of capturing the wide range of risk factors typical in this vulnerable population, and protective factors contextualized within prevention and intervention services. Moreover, this study has opened the door for future research on risk and protective factors with other vulnerable populations. Additionally, given that maternal disclosure of substance use and risk were obtained through self-report, results may be limited by respondent bias. That is, mothers may have been reticent to disclose substance use and other risks such as family violence and challenging parent-child relationships. Although the BTC clinicians are highly skilled at getting to know a woman and her life history, mothers' self-reported cumulative risk exposure is likely higher than reported. The potential underestimation of cumulative risk in this sample may impact interpretations of the efficacy of our established measures, as well as the impact of our methodological approach. Despite these limitations, this study offers novel information regarding the establishment of comprehensive measures of cumulative risk and protection.

5.5. Implications and conclusion

In conclusion, cumulative risk and protective factor measures with domains relevant to substance-exposed sibling groups accessing child maltreatment prevention and early intervention services at BTC were established. This domain-specific conceptualization of risk and protective factors facilitated the consideration of intra- and inter-domain risk and protection both within and between sibling groups. The present research highlights the importance of a clinically and theoretically grounded, and cross-domain consideration of both risk and protective processes. The measures of cumulative risk and protection established in this study will inform future quantitative research validating these measures in larger samples of children at BTC or other similar programs. Overall, this study provides evidence and direction for future research that can enhance understanding of the risk and protective profiles of children exposed prenatally to substances and at risk for child maltreatment and neglect, when they are able to access services such as BTC. The present research also enhances understanding of how risk and protective processes interact, and points to domains of risk and protection that may be most salient in this population.

In delineating profiles of risk and protection, these findings and future research can begin to inform evidence-based child maltreatment prevention and early interventions that: 1) serve children identified as having high-risk profiles, 2) address the full range of risk factors impacting child development, 3) provide individualized interventions for children that are specific to vulnerable risk domains, and 4) incorporate the most effective protective factors into practice. Overall, this research contributes to enhancing the clinical services for this highly vulnerable population of children exposed prenatally to substances and at risk for child maltreatment and neglect. Providing individualized, client-centered maltreatment prevention and early intervention can be an important step to improve these children's development and reduce the social and economic costs for society.

Authorship statement

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Bianca Bondi. The first draft of the manuscript was written by Bianca Bondi and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Declarations of Competing Interest

None.

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