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A Qualitative Framework of Cumulative Risk and Protection for Understanding Neurodevelopment and Clinical Progress: A Multiple Case Study Approach

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ABSTRACT

Prenatal substance exposure is a serious public health concern given that such exposure is associated with deficits across various neurodevelopmental domains. Mothercraft's Breaking the Cycle (BTC) is a child maltreatment prevention and early intervention program in Canada for pregnant and parenting women who use substances and their children (0–6 years). Case studies of three substance-exposed sibling groups that received services at BTC are described to depict the spectrum of clinical progress that can be observed. The purpose of this study was to use our clinically and theoretically grounded, cross-domain cumulative risk and protection framework, previously developed for quantitative analyses, to qualitatively describe cumulative risk and protection. Using this framework within a qualitative case study approach yields insights into how contexts of risk and protection contribute to clinical progress. This study offers direction for future research to enhance understanding of the spectrum of clinical progress in substance-exposed families accessing early intervention. We discuss the clinical utility of this qualitative framework for case formulation and treatment planning. Understanding the balance between contexts of risk and protection qualitatively, and the link with neurodevelopment and clinical progress, can inform evidence-based, multisystemic early interventions that target key risk factors and promote salient protective factors.

KEYWORDS

Multiple case studies; substance exposure; cumulative risk; cumulative protection; clinical progress; cross-domain; child maltreatment

Prenatal substance exposure is a serious public health concern given that such exposure is associated with deficits across many domains of functioning (Huizink, 2015; McQueen et al., 2015). Specifically, infants and young children with prenatal substance exposure are considered at high risk for a range of medical, neurodevelopmental, and behavioral problems, as well as later psychopathology (Bandstra et al., 2010). Children exposed prenatally to substances often endure future risks (Layne et al., 2010), including child trauma exposure (Cohodes et al., 2019), as well as broader instability in the family unit (e.g., living in high-risk environments, poor nutrition, family instability and homelessness, limited social supports; Freier, 1994) and parent-child relationship (Johnson et al., 2002).

Adverse consequences of prenatal substance exposure can be exacerbated by risk factors within the perinatal environment (Carta et al., 2001; Conners et al., 2004); these risk factors can be specific to the mother, secondary parent, family, pregnancy, birth period, child, parent-child interactions, social networks, and professional services. The constellation of maternal risk factors that often accompany prenatal substance use include, among others: histories of trauma and abuse, increased exposure to parental and partner violence, mental health concerns, negative life events, intergenerational substance use, and homelessness (Conners et al., 2004; Kettinger et al., 2000; Nair et al., 2003; Slesnick & Erdem, 2012). Additionally, multiple risk factors specific to the child, family context, parent-child relationships, and the larger social networks all contribute to the risks associated with prenatal substance exposure (Carta et al., 2001; LaGasse et al., 1999).

Conversely, the accumulation of protective factors can also occur across perinatal domains (Furstenberg et al., 1999; Ostaszewski & Zimmerman, 2006; Runyan et al., 1998; Spencer, 2005). The primary aim of the present study was to qualitatively describe patterns between cumulative risk and protection and child-specific neurodevelopment and family-specific clinical progress in substance exposed infants and children using our clinically and theoretically grounded,

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cross-domain cumulative risk and protection framework (Bondi et al., 2020c).

Frameworks of cumulative risk and protection

Conceptual frameworks of cumulative risk and protection are relevant considerations for the development of children exposed prenatally to substances. Cumulative risk is a construct used to conceptualize children's exposure to multiple risks and the additive impact on development (Evans et al., 2013). Children 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), specifically children exposed prenatally to substances (Cohodes et al., 2019). Correlations between developmental outcomes and sociodemographic, psychosocial, and biological profiles are often mediated by cumulative risk exposure (Evans et al., 2013; Madigan et al., 2017). Further, cumulative risk exposure accounts for more of the variance in children's developmental trajectories than prenatal substance exposure alone (Carta et al., 2001). There is strong evidence that cumulative 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). Studies that assess the number of domains of cumulative risk to which a child was exposed have indicated larger effect sizes (~22.7% increment in adversity per risk factor) than those found when examining total cumulative risk scores (~5.7% increment in adversity per risk factor; Evans et al., 2013).

There has been a disproportionate research focus on risks or detrimental factors and their impact on development, with only minimal research on the effects of cumulative protective factors (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 development (Crosnoe et al., 2010; Furstenberg et al., 1999; Narayan et al., 2018; Runyan et al., 1998). Some researchers have found that cumulative protection attenuates the negative effects of cumulative risk on child development (Ackerman et al., 1999; Narayan et al., 2018; Ostaszewski & Zimmerman, 2006; Spencer, 2005). Cumulative protective factors are more strongly related to positive development relative to individual protective factors, suggesting that a cumulative conceptualization of protective factors is advantageous to understanding development (Ackerman et al., 1999). Nonetheless, limited research has taken domain-specific protective factors into consideration (Evans et al., 2013). This gap is problematic in that it fails to provide a holistic framework of child development within contexts of both risk and protection.

Additionally, Evans et al. (2013) discussed the importance of grounding cumulative risk and protection research in a theoretical framework that aids in delineating developmentally salient domains of risk and protection. Pepler (2016) has also discussed the need to embed research within clinical and community settings by building trusting relationships. Research designed to establish frameworks of cumulative risk and protection for clinical populations must thus be grounded within the settings that serve them. Therefore, frameworks of cumulative risk and protection must be both clinically and theoretically grounded, with a clinical understanding of the focal population informing the selection of an appropriate theoretical framework.

A clinically and theoretically grounded, cross-domain quantitative framework

Mothercraft's Breaking the Cycle (BTC) is a child maltreatment prevention and early intervention program for pregnant and parenting women who use substances and their infants and young children aged 0–6 years in Toronto, Canada (Espinet et al., 2016). Programming at BTC works within an infant mental health framework, supporting the development of substance-exposed young children by addressing maternal addiction problems and the mother-child relationship through a comprehensive, integrated, cross-sectoral model. Given the body of literature on frameworks of cumulative risk and protection in substance-exposed children, a prior study was conducted at BTC in which clinically and theoretically grounded, cross-domain cumulative risk and protective factor measures (Bondi et al., 2020b) were established for quantitative use with substance-exposed children (Bondi et

al., 2020c). The Developmental Model of Transgene rational Transmission of Psychopathology (Hosman et al., 2009) served as the theoretical model to conceptualize salient domains of risk and protective factors in children exposed prenatally to substances and accessing child maltreatment prevention and early intervention services (Bondi et al., 2020c). Cross-domain profiles of cumulative risk and protection, and the number of significant domains of risk relative to protection, were reported, as well as the total percentages of cumulative risk and protection (Bondi et al., 2020c). The cross-domain profiles facilitated consideration of intra- and inter-domain risk and protection within and between three sibling groups accessing services at BTC (Bondi et al., 2020c). Emerging patterns indicated the importance of establishing quantifiable cumulative risk and protection scores that are: 1) clinically and theoretically grounded, 2) cross-domain, and 3) encompass cumulative protection and risk (Bondi et al., 2020c). The present study expanded upon this preliminary quantitative work to explore the framework of cumulative risk and protection in the same substance-exposed sibling groups from a qualitative perspective.

Current study

This study focused on substance-exposed infants and young children in the context of the mother-child relationship. Given the complex histories and contexts of risk that infants and young children exposed prenatally to substances often endure (Layne et al., 2010), these children require multisectoral child maltreatment prevention and early intervention services that support child development, maternal mental health, and substance use discontinuation, as well as the mother-child relationship (Andrews et al., 2018). In the current study, we qualitatively described case studies of three sibling groups at risk for child maltreatment given prenatal polysubstance exposure. Sibling groups had variable clinical progress and received child maltreatment prevention and early intervention services at BTC. These were the same sibling groups involved in the quantitative BTC study (Bondi et al., 2020c). In describing these multiple case studies, we endeavored to illustrate the spectrum of clinical progress that can be observed in families receiving services at BTC. A primary goal of the current study was to qualitatively describe cumulative risk and protection in substance exposed children, and the link with neurodevelopment and clinical progress, using our clinically and theoretically grounded, cross-domain, quantitative framework of cumulative risk and protection. We also explored the link between child-specific neurodevelopment and family-specific clinical progress.

Materials and method

Study design

For this retrospective case study, a comprehensive chart review was conducted and yielded an in-depth qualitative understanding of each sibling group's context of risk and protection, neurodevelopment, and services accessed during their time at BTC. This study was approved by York University's Ethics Review Board.

Setting and participants

This study took place at BTC, focussing on three families with substance exposure histories. Women at BTC have a history of violent and traumatic experiences in the context of relationships which contributed to substance using patterns; therefore, some children within this study were directly exposed to interpersonal violence in the parenting relationship, while others indirectly experienced intergenerational effects of maternal trauma histories. We selected families that included sibling groups in order to compare cumulative risk and protection qualitatively between and within sibling groups. Two families with sibling dyads and one with a sibling quadrad were selected, for a total of eight children aged 0 to 6 years old who had received services at BTC. We selected families that had participated in treatment at BTC for a minimum of 2.5 years and families that included sibling groups in which each child had undergone a developmental assessment at multiple time points. The three families, herein referred to as family A, B, and C, were also selected based on their clinical progress, classified by lead clinicians as good, fair, and poor, respectively. Clinicians assessed overall clinical progress by family, based on the families' participation in programming at BTC, child apprehensions from

parental care during their involvement at BTC, as well as the child custody arrangements and family progression toward goal attainment at the time of ending services at BTC. Three families with variable levels of clinical progress were selected to capture the range of clients seen at BTC. Although several families met this inclusion criteria, only three families were selected as the qualitative nature of this study necessitated extensive chart review. The three families that were selected had the longest involvement time at BTC and were deemed the clearest depictions of each clinical progress status, respectively. 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). Parents within each family are referred to according to family letter (e.g., A, B, C). Informed consent was obtained from all mothers included in the study and mothers consented on behalf of their young children. The sex of the children is not revealed to protect client confidentiality.

Data source and variables

This study utilized archival BTC data collected under a nationally funded study (Espinet et al., 2016]). Data were obtained from clients' charts, which included referral forms, mother and child intake forms, medical notes, correspondence, addiction counseling 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 somewhat across participants. The qualitative case study descriptions encompassed core developmental and relational domains outlined in The Developmental Model of Transgenerational Transmission of Psycho pathology (Figure 1; Hosman et al., 2009), namely: Maternal History, Family Context, Perinatal Course, Early Childhood Course, Child Neurodevelopment, Services Accessed. Each sibling group's context of risk and protection was described across these domains. Each child's neurodevelopment, as well as the services accessed by the families during their time at BTC, were also described.

Neurodevelopment was assessed using age-appropriate measures of cognitive (Bayley Scales of Infant and Toddler Development-Third Edition, Bayley, 2006; Wechsler Preschool and Primary Scale of Intelligence-Fourth Edition; Wechsler, 2012) and social-emotional (Child Behavior Checklist, Achenbach, 2000; Infant-Toddler Social Emotional Assessment, Carter & Briggs-Gowan, 2006) functioning. For a comprehensive 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 et al., 2020b).

BTC child maltreatment prevention and early intervention services

BTC supports the development of substance-exposed infants and children through a comprehensive, integrated, cross-sectoral model. BTC operates under formal partnership with nine agencies, including services relating to child protection, addiction treatment, health, corrections and probation, infant and child development, and infant and child mental health. While BTC provides dyadic or relationship-focused services specifically designed to foster the mother-child relationship, maternal and child services are also offered. Given that early engagement in comprehensive, integrated, relationship-focused service is known to support mothers' participation in post-natal services (Andrews et al., 2018), the Pregnancy Outreach Program was developed at BTC to reduce barriers to accessing services that exist for pregnant women with substance use issues (Racine et al., 2009).

Overall, families at BTC are able to participate in a range of services that address addiction, mental health, parenting, mother-child interactional support, and child development. Regular child maltreatment prevention and early intervention services at BTC include: intake assessment and engagement counseling, pediatric medical/health appointments, home visiting dyadic developmental program, individual addiction counseling, case management/service coordination, yearly developmental assessments, and access to a Fetal Alcohol

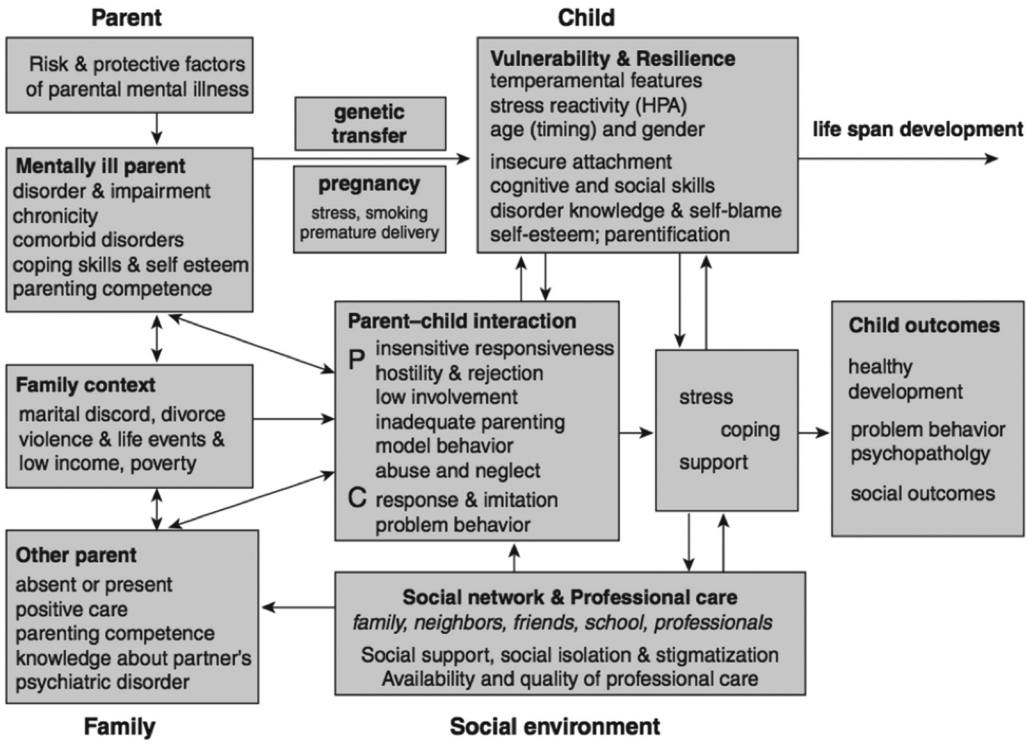

Figure 1. Theoretical Model. Reprinted from Hosman et al. (2009). Prevention of Emotional Problems and Psychiatric Risks in Children of Parents with a Mental Illness in the Netherlands. I. The Scientific Basis to a Comprehensive Approach. *Australian e-Journal for the Advancement of Mental Health*, 8(3),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

Spectrum Disorders (FASD) Diagnostic Clinic. BTC programming also includes the provision of instrumental supports and child-minding.

Various addiction and parenting group interventions are available and recommended to families on the basis of presenting concerns and treatment planning. Groups include: a relapse prevention group (support strategies to manage cravings and pressures to use substances), basic life skills group (support problem solving behaviors to manage life while in recovery), emotion awareness group (support the ability to recognize and make sense of emotions in self and others), *Connections* group (focuses on interpersonal violence and its impact on substance use, parenting, and child development; Mothercraft, 2014), recovery group (support women in identifying and addressing the issues that emerge when substance use is no long a means of coping), mindfulness group (support bringing one's attention to experiences in the present moment), new mom's support group (perinatal education and support around childbirth, parenting, prenatal nutrition, breastfeeding, attachment and bonding, sleeping, and infant development and stimulation), Learning Through Play group (play-based activities using didactic approaches; incorporated Hanen early language intervention programs; Pepper & Weitzman, 2004), Mother Goose Program® parenting group (focus on the pleasure and power of using rhymes, songs, and stories together), and Make the Connection group (designed to strengthen the mother-child relationship through play scenarios and videotape work; Watson & MacKay, 2006).

Family A case study: good clinical progress

Maternal history, family context, and perinatal course

Mother A was very young at the time of A1's birth and had a normal pregnancy with no prenatal substance exposure, followed by a healthy birth. For the first two years of A1's life, A1 lived at home with mother A and father A who had a very unhealthy relationship characterized by conflict and domestic violence (i.e., physical and emotional abuse). Mother A also had a history of sexual abuse in

adolescence. Mother A began using substances after the birth of A1 due to the stress and pressure within her parenting role and intimate relationship. Father A also used substances.

Early childhood course

At the age of 2 years old, A1 was apprehended from the home by child protective services because of parental substance misuse, and was placed into kinship care with the maternal grandparents for one year. While A1 was in kinship care, mother A terminated a pregnancy with twins, which caused her much emotional distress and heightened her substance misuse. After the pregnancy termination, she became pregnant with A2. The relationship between mother A and father A continued to be characterized by substance misuse and interpersonal violence throughout the pregnancy. After a domestic violence incident late in the pregnancy, mother A decided to leave the relationship and move in with her parents, who were caring for A1. A2 was born experiencing neonatal abstinence syndrome and required postnatal interventions (A2 had prenatal polysubstance exposure across all three trimesters; i.e., nicotine, opioids, opiates, prescribed and non-prescribed methadone, cocaine). By the time of A2's birth, mother A had been involved in BTC's Pregnancy Outreach Program for 5 months. Across her substance use recovery at BTC, mother A struggled with methadone misuse.

Mother A continued to maintain boundaries with her ex-partner after their separation, during which time he was incarcerated several times. After the separation, father A maintained inconsistent involvement in A1's life; however, was not involved in A2's life. Although mother A, as well as A1 and A2, had extended family supports in the form of maternal grandparents, there was much family conflict within the home and problematic alcohol use by the maternal grandfather. There was a family history of mental illness on the maternal side and mother A struggled with anxious and depressive symptoms. Given A1's time in kinship care, A1 perceived family A's grandparents as the primary caregivers, rather than mother A, which led to a challenging parent-child relationship between A1 and mother A which was characterized by struggles with limit setting, praise, and the allocation of quality time. A2 and mother A, however, had a very close relationship and mother A found it easier to engage with and care for A2. According to mother A, both A1 and A2 had easy temperaments.

Child neurodevelopment

A1 was diagnosed with Attention-Deficit/Hyperactivity Disorder – Combined Presentation at age 6 years old and exhibited social-emotional and behavioral challenges at home. These problematic behaviors were not reported at school or at BTC, but were specific to the relationships between A1 and A1's caregivers. A1 demonstrated strong cognitive abilities (i.e., average to above average). In contrast, A2 showed no social-emotional or behavioral difficulties and demonstrated average to high average cognitive abilities. A2 had some early expressive language difficulties; with early intervention services these resolved over time. Both A1 and A2 were in childcare and accessed speech and language supports, as well as psychological assessments at BTC. A1 and A2 also had access to physician follow-up.

Specific services accessed at BTC

In addition to regular BTC intervention programming, mother A attended various support groups at BTC, including the *Connections* program (Mothercraft, 2014), as well as the Parent-Child Mother Goose Program® parenting group. Additionally, Mother A participated in urine screens and substance use treatment in other community services. Given family A's financial strain, they received governmental financial assistance. At the end of her involvement at BTC, mother A was in recovery for substance use.

Within-family overview of cross-domain cumulative risk and protection

A1 and A2 had numerous risks in the maternal, other parental figure, and family domains (Supplementary Table S1). A2 had more risks in the prenatal/pregnancy and birth/postnatal domains relative to A1. Contrastingly, A1 had more risks in the child and parent-child interaction domains relative to A2, who had no risks in these domains. Neither A1 or A2 had risks in the social network/professional services

domain. A1 and A2 both had notable protection in the maternal, child, and social network/professional services domains (Supplementary Table S2). Relative to these domains, A1 and A2 showed less protection in the family and parent-child interaction domains. A2 had more protection in the prenatal/pregnancy domain relative to A1, who had no protection in that domain. Neither A1 or A2 had protection in the other parental figure and birth/postnatal domains. For a quantitative within- and between-family comparison of total and cross-domain cumulative risk and protection, see (Bondi et al., 2020c).

Family B case study: fair clinical progress

Maternal history, family context, and perinatal course

Mother B had a long history of substance use, which resulted in her oldest child (not followed at BTC) from a previous relationship being apprehended early in life. Mother B also had a history of sexual, physical, and emotional abuse across development. Mother B had an eating disorder history and a family history of mental illness. Mother B was in a substance using relationship that she described as dysfunctional and characterized by blame, guilt, and differing parenting styles. The couple's first pregnancy together was with B1 and B2, identical twins who were exposed to prenatal polysubstance use across all three trimesters (i.e., nicotine, alcohol, prescribed methadone). The twins were diagnosed with twin-to-twin transfusion syndrome, which resulted in an early cesarian delivery. Born prematurely and at a low birth weight, the twins exhibited neonatal abstinence syndrome and required postnatal interventions. After the birth of B1 and B2, mother B experienced post-partum depression. The family was under extreme financial distress and moved to a family support shelter.

At this time, mother B was struggling with parenting stress. Her substance use with her first child many years prior occurred while she was living in a shelter. As such, residing in a shelter created a sense of imprisonment and a lack of freedom that triggered her heightened substance use. During the family's stay at the shelter, she was pregnant with B3, who was also exposed to prenatal polysubstance use across all three trimesters (i.e., consistent nicotine, few occasions of alcohol and cocaine use). B3 was born only one year after B1 and B2 by cesarean delivery and tested positive for substance exposure at birth; however, mother B reported that B3 did not required postnatal interventions. B3 demonstrated very early limitations in mobility due to being bow-legged. Soon after the birth of B3, mother B became pregnant again with B4, who was also exposed to prenatal polysubstance use across all three trimesters (i.e., consistent nicotine and cocaine, few occasions of alcohol use), and received minimal prenatal care. B4 was born prematurely, one year after B3. B4 tested positive for substance exposure at birth and showed irregular heartbeats, thus requiring postnatal interventions. Mother B's pregnancies with B3 and B4 were high risk due to her advanced age.

Early childhood course

During and following the birth of four children within three years, family B was experiencing immense stress and financial strain. All four children were exposed to extended periods of neglect during their early years. Six weeks after the birth of B4, all four children were apprehended from the home by child protective services (at the ages of 2 years old, 1 year old, and 6 weeks old, respectively) and placed into foster care, where they remained together for nine months. While the children were in foster care, the foster parents expressed concerns about B1 and B2's development, and both of them received developmental assessments that indicated broad developmental concerns. All four children underwent occupational therapy assessments, with B1 and B2 found to have speech, language, and fine-motor delays. The children received supervised therapeutic access with their parents throughout their time in foster care. No additional information was available surrounding foster care conditions or the separation and reunification process. During this time, mother B became involved with BTC and began her recovery process. Mother B left the shelter, finding confined housing with her partner (the biological father of all four children). Mother B was very distressed by child protective services' involvement in her life and was concerned about the children's return to her and her parnter's care given the

associated lifestyle and regulations. Upon the children's return to their care, the family was still under immense financial distress. All four children were immediately enrolled into full-time childcare; however, the twins, B1 and B2, experienced many childcare transitions over the next few years. B3 and B4 remained in stable childcare placements. Mother B was very motivated and committed to her recovery process at BTC, prioritizing her return to school and employment. She struggled, however, to prioritize her children's social and emotional needs. Despite the unhealthy relationship between mother B and father B, which involved threats related to the custody of the children and conflicting parenting styles, mother B chose to remain in the relationship to avoid legal custody challenges from father B. Father B took on the primary caregiving role in the children's lives as mother B focused on her return to school and work.

Child neurodevelopment

B1 and B2 were rated by mother B as having difficult temperaments and their developmental assessments at BTC indicated significant speech and fine motor delays. The twins had a one-year delayed entry into kindergarten in the hopes that they would be more developmentally ready. Both twins were diagnosed with FASD, specifically Alcohol Related Neurodevelopmental Disorder. B2 was seen as the more challenging twin and mother B reported having a very challenging relationship with B2 relative to B1, given that B2 exhibited externalizing behaviors, whereas B1 was more likely to demonstrate internalizing behaviors. B2 had selective eating problems, whereas B1 had challenges with peer relationship formation, thus relying on B2 for most social interactions. Both children demonstrated extensive social-emotional and behavioral challenges, struggling with transitions and routines, as well as emotion regulation. They both showed low average to average cognitive and academic functioning. Overall, B1 and B2 were able to function better in their small childcare setting with one-on-one support relative to a large classroom setting at school. B1 and B2 received speech and language as well as occupational therapy support in the school setting. B1 and B2 also received psychological assessments at BTC. Although recommendations were made for intensive therapeutic supports for both children in the child care and school, the children did not receive such support in either setting, despite advocacy from the parent-child therapist at BTC.

B3 and B4 were rated by mother B as having an easy temperament and generally better emotion regulation relative to the twins. B3 had some challenges with emotional reactivity, but had average cognitive and academic abilities. Mother B reported a strong relationship with B3. In contrast, mother B had a very challenging relationship with B4, which she attributed to the early apprehension at 6 weeks of age, causing her to feel disconnected and emotionally challenged by B4. B4 was diagnosed with low upper body muscle tone in the first year. B4 also showed minimal socialization with peers and increasing social-emotional challenges with age. Mother B reported more social-emotional concerns regarding B4 at home relative to the reports at school or at childcare. B4 demonstrated average to high average cognitive and academic abilities. B3 and B4 both received occupational therapy support and psychological assessments. All the children in family B also had access to physician follow-up.

Specific services accessed at BTC

In addition to regular intervention programming, mother B attended various support groups at BTC, including the *Connections* program (Mothercraft, 2014), Basic Life Skills groups, Relapse Prevention group, and New Mom Support group. Additionally, Mother B accessed urine screens as well as substance use and addictions treatment through other community services. Father B also accessed external addictions treatment. Given family B's financial strain, they received governmental financial assistance. At the end of family B's involvement at BTC, mother B and father B were both in recovery for substance use.

Within-family overview of cross-domain cumulative risk and protection

B1, B2, B3, and B4 all had many risks in the maternal and family domains; relative to these domains, they had slightly fewer risks in the

other parental figure domain (Supplementary Table S1). B1 and B2 had more risks in the prenatal/pregnancy, birth/postnatal, and child domains relative to B3 and B4. B2 and B4 had more risks in the parent-child interaction domain relative to B1 and B3. No child in family B had risks in the social network/professional services domain. B1, B2, B3, and B4 all had much protection in the maternal, other parental figure, child, and social network/professional services domains; relative to these domains, they had slightly less protection in the family and parent-child interaction domains (Supplementary Table S2). No child in family B had protection in the prenatal/pregnancy or birth/postnatal domains.

Family C case study: poor clinical progress

Maternal history, family context, and perinatal course

Mother C had a family history and long personal history of pervasive mental health concerns, including depression with related somatic symptoms and anxiety. Both mother C and father C had an unhealthy substance using relationship characterized by a lack of support throughout mother C's substance use recovery process, as well as anger and aggression when father C was using substances (i.e., emotional and physical abuse). Mother C also had a history of emotional and physical abuse in prior relationships. The couple's first pregnancy was with C1, who was exposed to prenatal polysubstance use within the first trimester (i.e., nicotine, alcohol, cannabis, ecstasy). Mother C also experienced pre-eclampsia; however, C1 had a normal birth. Soon after, she became pregnant with C2, who was reportedly only exposed to nicotine within the first trimester. Mother C again experienced pre-eclampsia during this pregnancy and was overweight prior to the pregnancy, which intensified the risks; however, C2 had a normal birth and was born approximately one year after C1.

Early childhood course

During their early years, C1 and C2 were exposed to significant dysfunction in the home: domestic violence in the parental relationship, an unsafe home environment, neglect, and parental and non-parental substance use. At the age of 5 and 3 years old respectively, C1 and C2 were apprehended and placed into foster care for three months, then transitioned into kinship care with a maternal aunt for four months. During this time, mother C became involved with BTC; however, due to her inconsistent attendance and her need for external mental health supports, her file was temporarily closed. Despite mother C's inconsistent engagement in community mental health services, her file was opened again at BTC several months later. Prior to the children being returned to parental care, mother C told her partner to leave the home given his continued substance use and the stipulations by child protective services. Upon the children's return, mother C was parenting independently with financial strain. At this time, she had feelings of guilt around the children's apprehension history and was struggling to enforce limit-setting and routines. C1 struggled with routines and separations. C1 and C2 both experienced chronic colds and respiratory problems. Both children were involved with some extracurricular activities for a short period of time. Mother C had many negative conversations regarding the children's biological father in front of the children, which remained a consistent problem throughout her involvement with BTC. Father C was inconsistent with his visitations with the children, which impacted the children emotionally, especially C1. After a few years of child protective service involvement and mother C's withdrawal from both mental health and BTC services, mother C disclosed her substance use relapse and her reunification with her partner in the home. The children were apprehended and placed for adoption at this time (ages 7 and 8 years, respectively).

Child neurodevelopment

C1 demonstrated social-emotional concerns that manifested through negative externalizing behaviors. C1 was rated by mother C as having a difficult temperament and mother C noted a challenging mother-child relationship. C1 showed aggressive behaviors both at home and at school, and clinicians were concerned for C1's risk of mental health problems. C1 had

average to high average cognitive abilities. C2 was not reported by mother C or at school to be showing social-emotional or behavioral concerns; however, clinicians were concerned about C2 experiencing unreported internalizing behaviors. C2 endorsed symptoms of deprivation, a lack of safety, as well as loss and separation. C2 was seen as a compliant child who engaged in desirable behaviors to please adults, rated by mother C as having an easy temperament. C2 lacked strong peer relationships and had some speech articulation concerns, for which speech and language supports were received. C2 showed average cognitive and academic achievement. Given these difficulties, clinicians were concerned that C2 would be at high risk for future mental health problems. Both C1 and C2 were in daycare and received psychological assessment at BTC. C2 also accessed speech and language supports. C1 and C2 had access to physician follow-up.

Specific services accessed at BTC

In addition to regular intervention programming, mother C attended the Relapse Prevention group at BTC and some external mental health and substance use treatment supports. Given family C's financial strain, they received governmental financial assistance.

Within-family overview of cross-domain cumulative risk and protection

C1 and C2 both had many risks in the maternal and family domains; relative to these domains, they had slightly less risk in the other parental figure and parent-child interaction domains (Supplementary Table S1). C2 had slightly more risks in the prenatal/pregnancy domain relative to C1 but C1 had slightly more risks in the child domain relative to C2. Neither child in family C had risks in the birth/postnatal or social network/professional services domains. C1 and C2 showed minimal protection in the maternal and social network/professional services domains (Supplementary Table S2). C2 had more protection in the child domain relative to C1. Neither child in family C had protection in the other parental figure, family, prenatal/pregnancy, birth/postnatal, or parent-child interaction domains.

Discussion

This qualitative study focused on case studies of three substance-exposed sibling groups that received services at BTC. The three families, referred to throughout this study as family A, B, and C, differed in their clinical progress. These multiple case studies illustrate the spectrum of clinical progress that can be observed in families receiving services at BTC. We expanded upon our clinically and theoretically grounded, cross-domain cumulative risk and protection framework, initially developed for quantitative analyses, to qualitatively describe cumulative risk and protection, and neurodevelopment, in substance exposed infants and children. This framework yielded insights into how contexts of cumulative risk and protection may have contributed to neurodevelopment and clinical progress within and between the sibling groups. Further, this framework revealed potential links between child-specific neurodevelopment and family-specific clinical progress. The clinical utility of this qualitative framework for case formulation and treatment planning is discussed in the context of dynamic programing and monitoring to maximize clinical progress.

BTC spectrum of clinical progress

Families accessing services at BTC are highly vulnerable, with mothers struggling with substance use and trauma histories, and children exposed prenatally to substances. Clinically, we are aware that families who access services at BTC differ in their clinical progress through service delivery. A prior study conducted at BTC outlined women's use of services and examined how early engagement of pregnant women related to postnatal service use (Andrews et al., 2018). In this prior study, the differing circumstances in which women ended their service relationship with BTC were reported (e.g., service goals met, stable in terms of addiction and parenting and moved to other counseling services, woman's parental rights terminated, etc.), suggesting variability in clinical progress (Andrews et al., 2018). Additionally, custody at service ending (i.e., 60% with mother, 20% kin placement, 20% foster placement) and the overall change in custody status (i.e., 52% moved to maternal custody, 48% moved away from maternal custody) further suggest

variability in clinical progress (Andrews et al., 2018) in families at BTC.

The current study is the first investigation into the spectrum of clinical progress that can be observed in families accessing services at BTC. Given the preliminary nature of this investigation, a clinically based, multiple case study approach was taken. Families A, B, and C were classified by BTC clinicians as having good, fair, and poor clinical progress, respectively during their time at BTC, thus capturing the range of clinical progress that is generally observed. Progress was assessed clinically and qualitatively based on families' participation in programming at BTC, child apprehensions from parental care during their involvement, as well as their situation and progression toward goal attainment at the time of ending services at BTC. Therefore, we believe that the assessment of clinical progress for the sibling groups included in this study is accurate and reliable.

Qualitative framework of cumulative risk and protection

To best understand the spectrum of clinical progress that can be observed at BTC, it was important to qualitatively describe the sibling groups' perinatal contexts of risk and protection. Our qualitative framework enabled a comprehensive understanding of the variations in risk and protective processes that may contribute to variability in neurodevelopment and clinical progress. It is well known that the adverse consequences of prenatal substance exposure can be exacerbated by the accumulation of risk factors across perinatal domains (Carta et al., 2001; Conners et al., 2004). Additionally, the accumulation of protective factors can attenuate the negative effects of cumulative risk, resulting in more positive development (Ackerman et al., 1999; Crosnoe et al., 2010; Furstenberg et al., 1999; Ostaszewski & Zimmerman, 2006; Runyan et al., 1998; Spencer, 2005). In formulating and examining the spectrum of clinical progress at BTC, it was vital to consider the complex interplay between contexts of risk and protection, and neurodevelopment, in a comprehensive, qualitative manner.

In addition to baseline levels of risk across all three families, each family displayed unique contexts of risk and protection with specific challenges that were primarily linked to clinical progress. Family A primarily struggled with interpersonal violence within the parental relationship. Family B primarily struggled with a long history of maternal addiction and substance use, as well as significant financial distress. Family C primarily struggled with pervasive maternal mental health challenges and child neglect. Although the case studies represent unique families with distinct challenges and clinical trajectories, the three families illustrate the spectrum of clinical progress that can be seen at BTC. The results of this study indicate that our framework of cumulative risk and protection can extend beyond quantitative analyses to inform a holistic qualitative understanding of risk and protection in sibling groups exposed prenatally to substances.

Within-family balance between cumulative risk and protection

Family A

Both A1 and A2 had comparable risk and protection in the maternal, other parental figure, and family domains. A1 and A2 both had more risks than the other in two domains, but comparable levels of protection; therefore, given this balance between risk and protection across these domains, we would expect A1 and A2 to have comparable neurodevelopmental and clinical outcomes. Yet, A2 had fewer neurodevelopmental concerns than A1. This discrepancy may be due to the early intervention that A2 received by entering therapeutic programming at BTC at birth, relative to A1 who was older at age of entry (i.e., 3.5 years old).

Family B

B1, B2, B3, and B4 had comparable risk and protection in the maternal, other parental figure, and family domains. B1 and B2 (i.e., identical twins) had substantially more risk relative to B3 and B4 across several domains; however, all four children had comparable protection within these domains. Therefore, the heightened levels of risk alongside minimal to no protection may explain why B1 and B2 had more neurodevelopmental concerns relative to B3 and B4. It is also vital to note that B3 and B4 received intervention at an earlier age (i.e., 1 year old and birth, respectively) relative to B1 and B2 (i.e., 2 years old). B2 and B4 showed risk in the parent-

child interaction domain due to challenging relationships with mother B, alongside comparable levels of protection in this domain across all children. This heightened level of risk in the absence of heightened protection may explain why B2 showed slightly more neurodevelopmental concerns relative to B1, despite being identical twins. Similarly, such heightened risk in the mother-child relationship, alongside an early apprehension history, may explain why B4 showed slightly more neurodevelopmental concerns relative to B3.

Family C

C1 and C2 had comparable risk and protection in the maternal, other parental figure, family, and parent-child interaction domains. C1 and C2 both had more risks than the other in one domain; however, C1 had lower levels of protection relative to C2. C2 received earlier intervention relative to C1 (i.e., entered programming at 4 years of age relative to 5 years); however, both children entered BTC programming at an older age relative to the other children in this study (i.e., entered programming between birth and 3.5 years of age). Given the heightened risk alongside minimal to no protection in these domains, we would expect C1 and C2 to have relatively comparable neurodevelopmental and clinical outcomes, with C1 potentially experiencing slightly poorer outcomes. Notably, C1 did appear to have more neurodevelopmental concerns relative to C2. These results suggest a link to the lack of early intervention that C1 received. Similarly, although C2 was exposed to lower levels of risk, C2 also experienced neurodevelopmental concerns which were not mitigated with early intervention opportunities. The poor outcomes for both C1 and C2 were likely due to the lack of protection experienced by family C overall.

Between-family cumulative risk and protection and links with clinical progress

In exploring the patterns between qualitative contexts of risk and protection between the three families, we can begin to understand how such contexts impact the spectrum of clinical progress observed at BTC. All three families had comparable risks across the maternal, other parental figure, and family domains, suggesting a potential baseline level of risk in this sample. Family B had the most cumulative risk, while family A and C had relatively less cumulative risk. All three families showed notable protection across the child and social network/professional services domains. Family B also had the most cumulative protection, while family A had slightly less cumulative protection and family C had the least cumulative protection. Therefore, families B, C, and A can be classified as high, medium, and low risk families, respectively. Contrastingly, families B, A, and C can be classified as high, medium, and low protection families, respectively.

This multiple case study indicates that clinical progress appears to be linked with the balance between contexts of risk and protection. Although family B had the most risk exposure, family B also had the most protective factors. 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. Relative to family B, families A and C had slightly less risk exposure alongside notably fewer protective factors; however, families A and C differed substantially in their clinical progress, classified as good and poor, respectively. Notably, family A had slightly more protective factors relative to family C, alongside a relatively comparable level of risk exposure. This balance between contexts of risk and protection may have contributed to family A having better clinical progress relative to family C. Therefore, heightened contexts of risk, in the absence of heightened contexts of protection, can result in notable differences in clinical progress.

Across all the families, B1, B2, B4, and C1 had relatively more risk exposure relative to the other children. Notably, these four children also had heightened neurodevelopmental challenges, suggesting that risk exposure may be linked with neurodevelopmental deficits. Domain-specific investigation reveals salient domains of risk and protection when considering neurodevelopment. These four children with notable neurodevelopmental concerns and risk exposure showed overall heightened levels of risk in the birth/postnatal, child, and parent-child interaction domains. These results suggest that ongoing risk in the postnatal environment may be more indicative of neurodevelopmental deficits and clinical progress compared to maternal or family history risks, or risks within the prenatal period (i.e., potential baseline level of risk in this sample). Notably, family A had exposure to

protective factors within various domains relative to family B and C, suggesting that said domains may have been an important aspects of protection, or early intervention, that contributed to family A's superior clinical progress. Again, these qualitative results align strongly with and supplement the quantitative findings regarding total percentages of cross-domain cumulative risk and protection (Bondi et al., 2020c) and neurodevelopment (Bondi et al., 2020b) previously reported in these three sibling groups.

Clinical utility of a qualitative framework of cumulative risk and protection

Given our case study approach, we have discussed the retrospective utility of our qualitative framework for understanding cumulative risk and protection, and the link with neurodevelopment and clinical progress. The findings also provide insight into the clinical utility of this framework in the dynamic process of case formulation and treatment planning to support clinical progress in the context of child maltreatment prevention and early intervention.

A quantitative approach can be advantageous in conceptualizing cumulative risk and protection as it enables children's exposure to multiple risks, alongside multiple protective factors, to be quantified and yields information about children who are at highest risk for impaired development (Cohodes et al., 2019; Evans et al., 2013; Layne et al., 2010). Qualitative assessments complement quantitative metrics in capturing information regarding: contextual factors, risk and protective factor intensity, domains of risk and protection, the degree of risk and protective factor exposure, and interactive effects (Evans et al., 2013; Lima et al., 2010). Our quantitative framework addressed some of the aforementioned shortcomings of crude metrics of cumulative risk and protection, and has strong utility when working with samples of substance- and trauma-exposed children (Bondi et al., 2020c). Nonetheless, a limitation of our quantitative framework was the lack of comprehensive and holistic information on contexts and intensities of risk and protection, and the interplay across risk and protective domains at a client-specific level.

Within the context of child maltreatment prevention and early intervention service delivery with marginalized populations of women and children, or other clinical populations, comprehensive client-specific information is essential for effective case formulation and treatment planning. Our proposed qualitative framework of cumulative risk and protection enables quantifiable differences between levels of cumulative risk and protection across key perinatal domains to be conceptualized comprehensively. Further, our qualitative approach demonstrates that salient risk (e.g., family A: interpersonal violence; family B: addiction and substance use; family C: pervasive mental health concerns, child neglect) and protective (e.g., Pregnancy Outreach Program) factors impacted neurodevelopment and clinical progress, thus demonstrating the nuances of differential intensities of experiences of risk and protection. Lastly, our qualitative framework for cumulative risk and protection demonstrates the complex interplay between contexts of risk and protection and provides insight into how the balance between risk and protection impacts neurodevelopment and contributes to clinical progress.

Overall, this qualitative framework can contribute to comprehensive case formulation and treatment planning for evidence-based, multisystemic early interventions that target key risk factors while incorporating salient protective factors. Our proposed framework for clinical formulation and treatment planning can support clinical practice by encouraging a strengths-based approach to clinical interventions with families and in writing letters of support and advocacy. This framework can also enable a better understanding of what additional supports for families may be required, and allow targeted recommendations to be made and implemented in clinical practice. In combining the clinical applicability of this qualitative framework for case formulation and treatment planning with the retrospective utility for understanding the contribution of cumulative risk and protection on neurodevelopment and clinical progress, case formulation and treatment planning can be adapted dynamically to maximize client-specific clinical progress over time.

Conclusions and implications

In this study, we used a qualitative, case study approach with three substance-exposed sibling groups, with the aim of illustrating the spectrum of clinical progress that can be observed in families accessing services at BTC. We used our clinically

and theoretically grounded, cross-domain cumulative risk and protection framework, initially developed for quantitative analyses, to describe cumulative risk and protection in substance exposed infants and children, and the link with neurodevelopment and clinical progress. This framework provides the basis for a strong qualitative description of the contexts of risk and protection that families at BTC often endure, offering insights into how such contexts of risk and protection may contribute to the observed child-specific neurodevelopment and family-specific clinical progress. This qualitative framework is useful in dynamically identifying cumulative risk and protection for case formulation and treatment planning to maximize clinical progress over time. By including sibling groups in this evaluation, we were able to compare contexts of risk and protection within and between families with differential prenatal exposure to substances. Further, the qualitative examination of sibling groups provided a more nuanced depiction of the complex family profiles that exist at BTC, where families often include multiple children with unique risk exposure histories dependent on the time of entry at BTC and clinical trajectories.

Despite these strengths, this study is limited by a lack of generalizability. The study involved a small case study sample of moderate to high risk children embedded within a child maltreatment prevention and early intervention program. 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 risk may not. As such, results may not generalize to other clinical populations. Quantitative analyses of the impact of cumulative risk and protection on neurodevelopment and clinical progress is also warranted to supplement our qualitative descriptions.

Overall, this study provides preliminary evidence and direction for future research that can enhance understanding of the spectrum of clinical progress observable in families with substance exposure and trauma histories accessing services at BTC, or other comparable early intervention programs. Supplementing our quantitative framework for conceptualizing cumulative risk and protection through a qualitative case study approach highlights the need for a holistic consideration of neurodevelopment and clinical progress that encompasses contexts of risk and protection from quantitative and qualitative perspectives. Further, this qualitative framework of risk and protection specifically provides direction for future quantitative studies to establish means of quantifying the nuanced balance between contexts of risk and protection (see also Bondi et al., 2020c).

Overall, the present study enhances understanding of how the balance between contexts of risk and protection may contribute to neurodevelopment and clinical progress in a highly vulnerable population, which can inform evidence-based, multisystemic early interventions that target key risk factors and promote the most salient protective factors in practice. Ultimately, understanding contexts of risk and protection within the perinatal period, and the link with neurodevelopment, clinical progress, and clinical practice when working with vulnerable infants, children, and their families, is essential within an infant mental health framework.

Authorship statement

All authors contributed to the study conception and design. Material preparation, data collection and analyses 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 mothers who were included in the study and mothers consented on behalf of their young children.

Disclosure statement

No conflicts of interest to report.

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