

Regular Article

Externalizing behavior in preschool children in a South African birth cohort: Predictive pathways in a high-risk context

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Abstract

Mental health problems often begin in early childhood. However, the associations of various individual and contextual risk factors with mental health in the preschool period are incompletely understood, particularly in low- to middle-income countries (LMICs) where multiple risk factors co-exist. To address this gap, we prospectively followed 981 children in a South African birth cohort, the Drakenstein Child Health Study, assessing pre- and postnatal exposures and risk factors. The predictive value of these factors for child mental health (assessed by the Child Behavior Checklist) was modeled using structural equation modeling. We identified two key pathways to greater externalizing behavior: (1) prenatal exposure to substances (alcohol and smoking) directly predicted increased externalizing behavior ($\beta = 0.24$, $p < 0.001$); this relationship was partially mediated by an aspect of infant temperament (negative emotionality; $\beta = 0.05$, $p = 0.016$); (2) lower socioeconomic status and associated maternal prenatal depression predicted more coercive parenting, which in turn predicted increased externalizing behavior ($\beta = 0.18$, $p = 0.001$). Findings in this high-risk LMIC cohort cohere with research from higher income contexts, and indicate the need to introduce integrated screening and intervention strategies for maternal prenatal substance use and depression, and promoting positive parenting across the preschool period.

Keywords: preschool mental health; externalizing behavior; LMIC; South Africa; birth cohort

(Received 28 May 2021; revised 1 February 2022; accepted 3 February 2022; First Published online 15 March 2022)

Evidence indicates that mental health problems in adolescence and adulthood may be traced to early childhood (Brumley & Jaffee, 2016; Huber et al., 2019), and that as early as the preschool period, psychopathology is identifiable, associated with marked impairment, and stable across time (Barrios et al., 2017). However, for the preschool developmental period, the multiple, complex patterns of individual risk in dynamic interaction with context are incompletely understood (Kostyrka-Allchorne et al., 2020), and arguably form a critical focus for current research (Barrios et al., 2017; Huber et al., 2019). Prospective longitudinal investigation of risk factors in low- to middle-income countries (LMICs) where almost 90% of the world's child population resides (UNICEF, 2005), and where both economic and psychosocial risks tend to be amplified (Grantham-McGregor et al., 2007), is sparse and urgently needed to inform evidence-based early child interventions (Lund, 2014; Mekonnen et al., 2020). We present findings from a population-based birth cohort from a high-risk, LMIC context in the Western Cape, South Africa – the Drakenstein Child Health

Study (DCHS; Donald et al., 2018; Stein et al., 2015; Zar et al., 2014).

Childhood mental health is frequently conceptualized in terms of internalizing and externalizing behavior: internalizing behavior includes signs and symptoms of anxiety, depression and somatic complaints whereas externalizing behavior includes hyperactive, aggressive or oppositional behavior (Dugre et al., 2020). These patterns of behavior are differentiable even in early childhood (Olino et al., 2014; Sterba et al., 2007). Across childhood, they have often been investigated separately, although longstanding evidence indicates that they frequently co-occur (Colder et al., 2013; Cunningham & Ollendick, 2010; Dugre et al., 2020; Weiss et al., 1997). Recent analyses suggest that they may cohere (with psychotic signs) to form a single factor underlying psychopathology across all ages (Caspi & Moffitt, 2018; Patalay et al., 2015). Nonetheless, much of the extant literature seems to indicate that externalizing problems are often detected earlier, and in many children tend to decrease from preschool across the school age period, whereas internalizing difficulties increase, especially during adolescence (Khoury et al., 2018; Leve et al., 2005; Roskam, 2019; Votruba-Drzal & Miller, 2016). There is also, however, clear evidence of specific subgroups where an early onset and persistent trajectory of externalizing problems

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Cite this article: Malcolm-Smith, S., et al. (2023). Externalizing behavior in preschool children in a South African birth cohort: Predictive pathways in a high-risk context. *Development and Psychopathology* 35: 982–999. <https://doi.org/10.1017/S095457942200027X>

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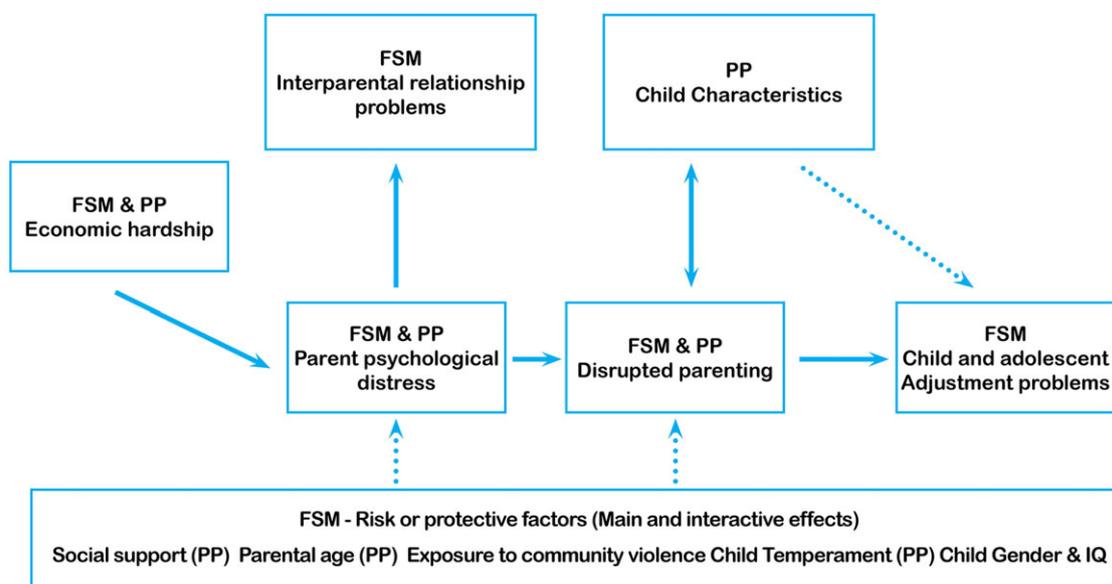


Figure 1. Diagram illustrating important common and unique predictive factors derived from the Family Stress (FSM) and Process of Parenting (PP) models.

presents, often culminating in severe aggressive and antisocial behavior in adolescence and early adulthood (Moffitt, 1993; Odgers et al., 2008; Shaw et al., 2012).

In line with models of development which emphasize dynamic interaction of child characteristics with various levels of contextual factors (Bronfenbrenner, 1979; Bronfenbrenner & Morris, 2006; Sameroff, 2010), extensive research on early childhood mental health has evidenced a range of important predictors of internalizing and externalizing behavior. A comprehensive overview of this literature is beyond the scope of this paper – rather we focus on factors highlighted in pertinent theoretical models (See Figure 1).

First formulated by Conger et al. (1990), the Family Stress Model (FSM) provides an informative theoretical framework for variable selection when modeling child mental health outcomes. A complementary approach is that initially developed by Belsky (1984) – the Process of Parenting (PP) model. Although the latter does not directly concern itself with child outcomes, it is pertinent in the context of clear evidence regarding the negative effects certain parenting styles have on child outcomes (Taraban & Shaw, 2018). In addition to focusing on contextual and parental characteristics' influence on parenting in early childhood, the PP model, very importantly, also includes characteristics of the child – this last factor is not explicitly present in the FSM, and has critical implications for child outcomes.

If we begin at the level of child characteristics (central to the PP model, and potential additional risk or protective factors in terms of the FSM) and their associations with mental health outcomes, gender and general intellectual functioning (IQ; Brumley & Jaffee, 2016; Hastings et al., 2015) are known to be important, with the role of gender becoming more apparent across school age and adolescence (Merikangas et al., 2010). Belsky's (1984) original PP model focused primarily on child temperament, and he considered negative emotionality as particularly important, given the strong associations between difficult temperament and parenting problems, which have been consistently reported over time (Taraban & Shaw, 2018).

Temperament in infancy and early childhood remains an active research focus. The construct is generally understood to

comprise (at least partially or initially) biologically based individual differences in emotional reactivity and self-regulation – the latter being a multifaceted construct that incorporates attentional, behavioral and emotional regulation (Rothbart & Bates, 2006). A great deal of work has shown associations between increased negative emotional reactivity and reduced self-regulation with later internalizing and externalizing difficulties (Cassiano et al., 2019; De Pauw & Mervielde, 2010; Eisenberg et al., 2001; Eisenberg et al., 2005; Whalen et al., 2017) Where inconsistencies are found in these relationships, this may be due to the broad range of negative emotions and forms of regulation these aspects of temperament encompass (Eisenberg et al., 2009).

In terms of parental characteristics, research has often focused on mothers, as they remain primary caregivers across many contexts. Parental psychopathology, central to both models, has been associated with problematic child mental health outcomes (Klein et al., 2019). Maternal depression, a common research focus, has been shown to have its greatest impact on parenting during infancy and early childhood (Taraban & Shaw, 2018) and has consistently been linked to increased levels of harsh, negative parenting (Lovejoy et al., 2000). A recent review (Masarik & Conger, 2017) confirmed that, in line with FSM predictions, studies have demonstrated that parent psychological difficulties, mediated by adverse economic conditions, are prospectively associated with poor parenting, including harsh parenting and abuse. This style of parenting is typically associated with poor child mental health outcomes (Cecil et al., 2017; Hastings et al., 2015; Jaffee, 2017). Interestingly, in a US study by Shaw et al. (2012), following 268 boys of low socioeconomic status (SES) from infancy with detailed adolescent follow-up 13–15 years later, univariate analysis implicated a number of factors in boys' later antisocial behavior, including parenting style, interparental aggression, low SES and maternal depression during infancy. However, in multivariate analysis only maternal depression differentiated the high and increasing trajectory of problem behavior which culminated in 79% of this group appearing in juvenile court.

In line with FSM's focus on interparental relationship problems, exposure to intimate partner violence (IPV) has been shown to exert an influence on child mental health outcomes (Koss &

Gunnar, 2018; Laurenzi *et al.*, 2020). In boys particularly, early exposure to such violence can increase the likelihood of behavioral problems and later antisocial behavior (Shaw *et al.*, 2012). A number of studies have suggested that prenatal exposure to IPV is associated with temperament difficulties and increased internalizing and externalizing behaviors in both infancy and across the preschool period (Burke *et al.*, 2008; Levendosky *et al.*, 2016; Martinez-Torteya *et al.*, 2009; Martinez-Torteya *et al.*, 2016).

In both models, economic disadvantage is of prime concern. According to the FSM, economic hardship is the foundational condition which sets in motion many of the key factors and associations that ultimately impact on child mental health. Other contextual factors, however, can also play important roles. For example, exposure to community violence seems to exert a negative influence on both parent and child characteristics (Brumley & Jaffee, 2016; Hastings *et al.*, 2015; Khoury *et al.*, 2018). In contrast, social support may exert a positive influence on parent mental health and parenting: a buffering hypothesis would suggest this effect would be greater in mothers facing increased stressors such as financial or mental health difficulties (Taraban & Shaw, 2018).

A key point is that several of these predictive factors tend to be highly correlated, and may mediate or moderate the effects of others on child mental health, creating complex patterns of association (Leve *et al.*, 2005; Wang *et al.*, 2018). For instance, low SES, maternal mental health difficulties, poor parenting, and increased levels of domestic and community violence frequently co-occur (Parkes *et al.*, 2016; Rotheram-Borus *et al.*, 2015). It is also clear that certain factors such as positive parenting and higher child IQ can protect against the effects of contextual risk factors (Brumley & Jaffee, 2016). The Taraban and Shaw review (2018) emphasizes that contextual factors, particularly SES, impact the strength of association between depression and poor parenting: a meta-analysis revealed a far greater effect size for those of low SES (Lovejoy *et al.*, 2000). Another meta-analysis found that the association between negative emotionality and harsh parenting was stronger in low SES groups, whereas in high SES groups the relationship was reversed (Paulussen-Hoogbeem *et al.*, 2007). Taraban and Shaw (2018) present an updated PP model, where, as in FSM, SES is set apart due to evidence of its role as a moderator exerting an influence on contextual, parental and child characteristics. Developmental cascade models thus emphasize that child, parental, and contextual factors interact via multilevel pathways to impact child mental health (Roubinov *et al.*, 2020).

Research *simultaneously* examining such a broad range of predictors as described above, along with their mediated or interactive effects for the preschool period is relatively limited, even in High-Income Countries (HICs), with most research focusing on a few specific factors (Hastings *et al.*, 2015). In a recent review of evidence for the FSM, Masarik and Conger (2017) stressed the ongoing need for greater investigation of moderating effects in the model, calling especially for longitudinal studies from diverse contexts, examining early development with careful temporal ordering of key variables. Examining a broad and complex range of predictive associations in LMICs, where conditions are often very challenging, is necessary to ascertain which effects may be context specific, or whether those described in HICs also pertain here (Brumley & Jaffee, 2016; Liu *et al.*, 2017).

The DCHS cohort is characterized by high levels of risk related to key factors reviewed above: the cohort features high levels of poverty and low maternal access to education: 73% of mothers are unemployed with 87% of households earning less than USD

350 per month (Zar *et al.*, 2019); only 36.5% of mothers completed high school (Pellowski *et al.*, 2019). Depression prevalence is high (24.2% of mothers met criteria antenatally, decreasing to around 17% at 1 year postpartum, Pellowski *et al.*, 2019). South African studies have previously described high prevalence of depression in disadvantaged communities, where it is strongly linked to lack of social support (Cooper *et al.*, 1999; Tsai *et al.*, 2016). Exposure to IPV is also high: 32% of mothers reported recent exposure at the initial antenatal visit (Okafor *et al.*, 2018). Of particular concern are high rates of problematic alcohol consumption and hence the impact of prenatal alcohol exposure (PAE) on child health outcomes. Prevalence of alcohol consumption and fetal alcohol spectrum disorders (FASDs) in certain communities in the Western Cape is amongst the highest in the world (May *et al.*, 2013). The most recent local prevalence study estimated rates of FAS at 66.7 per 1000, and rates of the full spectrum at 347.6 per 1000 (May *et al.*, 2021). Thirteen percent of mothers in this cohort reported hazardous levels of alcohol use during pregnancy (Myers *et al.*, 2018). Although the models described above do not mention PAE, a recent meta-analytic review confirmed that PAE is associated with increased risk of both internalizing and externalizing behaviors (Khoury *et al.*, 2018). Few population-based cohort studies have sufficiently high rates of prenatal alcohol use to track effects over time.

Our cohort thus offers a unique opportunity to track the role of multiple risk factors in an economically disadvantaged, high-risk, LMIC population-based sample. Here we present the first set of child mental health results, for the children at age 42 months. Our goal was to yield an ecologically valid and theoretically informed representation of risk factors and the nature of their relationships with regard to preschool mental health. We aimed to examine these in relation to both internalizing and externalizing behavior, and their potential co-occurrence at this very early age point. Using structural equation modeling (SEM), we tested the hypothesis that specific contextual and maternal factors (lower SES; exposure to stressors and violence; prenatal substance use; greater mental health difficulties; coercive parenting style) as well as child factors (sex; temperament; reduced IQ) would be associated with reports of greater internalizing and externalizing behavior. We further hypothesized that aspects of child temperament would affect certain relationships: (1) We hypothesized that negative emotionality would mediate positive associations between both prenatal substance use *and* prenatal maternal mental health with adverse child behavioral outcomes. (2) We hypothesized that child self-regulation would interact with both coercive parenting and negative emotionality in predicting adverse child behavioral outcomes.

Methods

Design

The DCHS is a multidisciplinary population-based birth cohort study focused on the early-life determinants of child health and development. Over a three year period (March 2012–March 2015), pregnant women at 20–28 weeks' gestation were enrolled into the cohort during antenatal visits to primary health care clinics; mother-child pairs are followed prospectively until at least child age 8 years. This paper reports on child mental health in the cohort at 42 months, operationalized as internalizing and externalizing behavior. Predictors for statistical modeling were selected *a priori* based on models described above, and existing empirical support, and included prenatal measures of maternal

socioeconomic status (SES); substance use (alcohol and tobacco), mental health, and exposure to IPV; as well as postnatal measures of maternal depression, social support, exposure to community violence, and parenting. Also included were maternal age and child sex (established at birth), and measures of child temperament and child exposure to community violence. Child self-regulation and general cognitive function were assessed directly at 42 months. Although this report does not feature longitudinal analysis of repeated measures, we attempted to include chronology, with maternal data preceding child data where possible, and using measures taken prior to the assessment of child mental health at 42 months.

Population and sample

The DCHS birth cohort is from a peri-urban area 60 km outside of Cape Town, South Africa. The region is characterized as a stable, low SES community with a population of approximately 200,000. The community is characterized by high incidence of a variety of health risk factors such as poverty, depression, IPV, and alcohol use. More than 90% of the population accesses healthcare services via the public health care system (Stein et al., 2015; Zar et al., 2014). Given the abovementioned factors the DCHS cohort can be seen as representative of many peri-urban regions in South Africa, as well as other LMICs.

Pregnant women were recruited from two public sector primary healthcare clinics, one of which serves a predominately black African isiXhosa-speaking community, while the other serves a predominantly mixed ancestry Afrikaans-speaking population. From March 2012–March 2015, all pregnant women were eligible for participation in the study if they were 18 years or older, were within 20–28 weeks of gestation, used either of the two primary healthcare clinics for their antenatal visits, and had no intention of moving away from the district in the coming year. A total of 1225 women were initially enrolled, but due to loss to follow-up over time (see Figure 2), 981 children remained active participants at 42 months.

Procedure

The DCHS adheres to the guidelines set out in the Declaration of Helsinki (2013) and received ethical approval from the Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town (401/2009), from Stellenbosch University (N12/02/0002), and from the Western Cape Provincial Research committee (2011RP45). Mothers provide annually renewed written informed consent in their preferred language (English, Afrikaans, or isiXhosa). All visits take place in a private room at the primary clinics or the central hospital, and all measures are administered by trained research assistants in the mother and child's preferred language.

Measures

All self- and parent-report questionnaires were administered in interview-format by trained fieldworkers and research assistants in the mothers' preferred language. This strategy was adopted due to low literacy levels in this context, and enabled mothers to request clarification of questions when needed. Child tasks were administered in the child's home language by trained psychology postgraduate research assistants, and fidelity was maintained via regular site visits by a neuropsychologist. Translation of all questionnaires and measures was completed using standard forward and back-translation processes, with consensus meetings to ensure

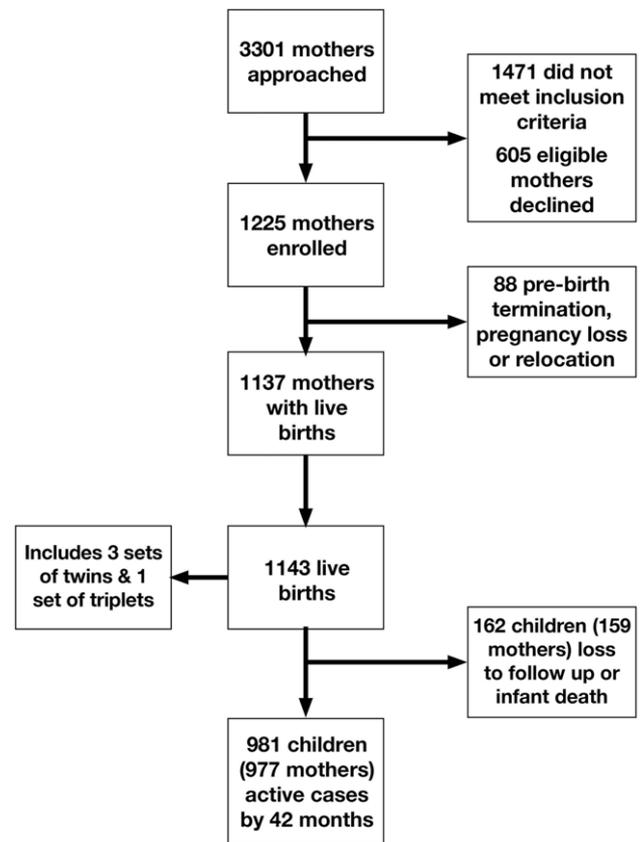


Figure 2. Participant enrolment and current cohort retention.

the original language meaning was retained across all translations. Detailed descriptions of the psychosocial methods and measures employed for this cohort have been provided elsewhere (Donald et al., 2018; Stein et al., 2015). Basic sociodemographic information was obtained at enrollment, and all other prenatal data was acquired at a second visit at 28–32 weeks (see Figure 3 for full timeline).

Below we list all measures we intended to include in modeling. Although most have been used in LMICs including South Africa, their psychometric properties in such contexts are not well-established. We therefore performed reliability and validity checks, described below, to ensure the rigorous demands SEM makes on latent factors were met. Where a measure had to be excluded, explanatory details are provided along with its description.

Measurement reliability and validity checks

We assessed measurement reliability via coefficient omega (ω): measures that demonstrated reliability <0.7 were dropped (Nunnally, 1978; see supplementary materials, Appendix A, Table 1). Construct validity was then assessed using confirmatory factor analyses (CFA; Atkinson et al., 2011). A factor loading of 0.7 or higher is typically considered ideal (Kline, 2016). However, as we included well-established measures, a less stringent cutoff of 0.5 was used: measures were dropped when the majority of factor loadings for a latent variable fell below this (see supplementary materials, Appendix A, Table 2–4). In addition, we assessed local fit by examining standardized residual correlations: high standardized residuals (>0.10) confined to particular latent

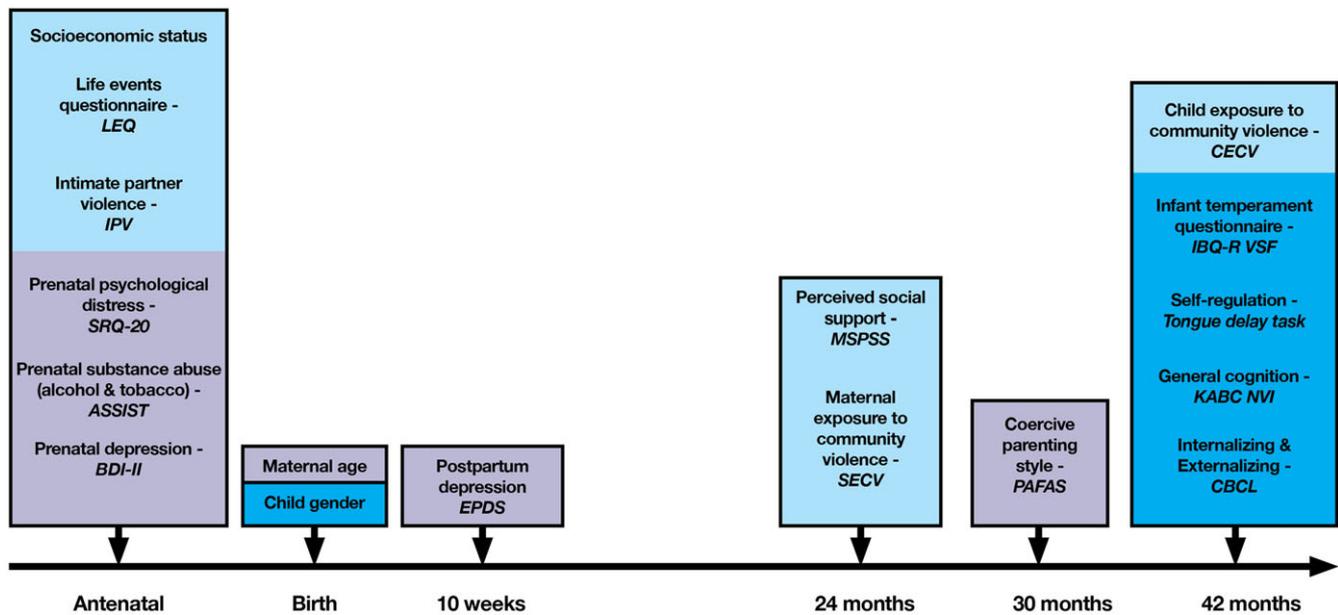


Figure 3. Timeline of measures. Measures highlighted in pale blue identify contextual factors, those in purple identify maternal factors, and those in darker blue identify child measures.

factors were investigated further and considered for removal from the model (Kline, 2016).

Sociodemographic characteristics

Maternal SES was assessed antenatally via questionnaire, and a composite comprising current maternal employment, maternal level of education, household income, and an index of household assets was calculated (based on a measure used in the South African Stress and Health Study; see e.g., Myers et al., 2011). We note that SES is a complex construct, with little consensus regarding exactly which of many indicators should be assessed (Avvisati, 2020). It is generally agreed that multiple indicators provide a better SES estimate (Braveman et al., 2005; Howe et al., 2012), however these indicators may not always be strongly associated with each other. This was the case with our measure, where the individual indicators did not load onto a single factor (See appendix A, Table 5). We thus included SES in modeling as a measured rather than a latent factor. The questionnaire yields a continuous score, which we used in modeling. Quartiles for the sample were derived for descriptive purposes – note that the terms “higher” or “lower” SES are relative to this sample and do not relate to any external benchmark of wealth or poverty.

Maternal age and child gender were established at birth – all births took place at a single central hospital (Zar et al., 2019).

Prenatal measures

Prenatal substance use was determined using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST; Ali et al., 2002). We included scores for alcohol use and smoking (seven items each). The first question is dichotomous (yes/no to lifetime use); questions 2–5 address use in the past 3 months, and are scored on a 5-point Likert scale (0 = Never; 4 = Daily); questions 6 and 7 address friend/family concern regarding use and individual attempts to quit, scored on a 3-point Likert scale (0 = Never; 2 = Yes in past 3 months). Continuous scores were

used in the analyses, with threshold scores given in the descriptive statistics.

Because an extremely low proportion of mothers reported use of any other substances (3%, of which the majority reported cannabis use; Myers et al., 2018), we could not examine any potential effects related to this. A recent local prevalence study confirmed that alcohol and tobacco are the only commonly used substances (May et al., 2021).

Prenatal exposure to IPV was assessed using a questionnaire adapted from the World Health Organization (WHO)’s multi-country study (Jewkes, 2002) and the Women’s Health Study in Zimbabwe (Shamu et al., 2011). Mothers reported frequency of exposure to emotional, physical, or sexual abuse. Responses on the 12-item measure used a Likert scale format (1 = never; 4 = many times). The scale does not yield an overall total score, but subscale scores were expected to load onto a single factor for modeling.

Unfortunately, high residuals were demonstrated between Beck Depression Inventory (BDI) and IPV items, and between ASSIST and IPV items (see supplementary materials; Appendix A, Table 6), whereas the majority of residuals between BDI and ASSIST items were <0.10 (see supplementary materials; Appendix A, Table 7), indicating the necessary removal of the IPV scale from the structural model to improve local fit.

Prenatal maternal mental health: We included a number of indicators of maternal mental health. Prenatal depression was assessed via the Beck Depression Inventory-II (BDI-II; Beck et al., 1996). A four-point Likert response format (0 = no symptoms; 3 = severe symptoms) is used for 21 items. Scores increasing above 20 indicate moderate – severe depression. Prenatal distress and exposure to stressful events were assessed using the Self-Reporting Questionnaire (SRQ-20) and the WHO Life Events questionnaire (LEQ) respectively. The SRQ-20 is a WHO endorsed measure of psychological distress, where 20 items assessing signs of anxiety and depression are scored as present or not. The LEQ yields a maximum score of 17, asking whether or not mothers had experienced a range of stressful events in the past year. CFA however

showed that only 35% of SRQ items (7 of 20) and 18% of LEQ items (3 of 17) demonstrated sufficient factor loadings (see supplementary materials Appendix A, Tables 2 and 3). These measures were therefore not included in modeling.

Postnatal measures

Postnatal maternal depression was assessed at 10 weeks postpartum using the Edinburgh Postnatal Depression Scale (Cox et al., 1987), where 10 items assess recent symptoms of depression. Item responses are scored on a 4-point Likert scale (0 = no never; 3 = yes, most of the time), yielding a maximum score of 30. Continuous scores were used for analyses, with clinical ranges presented for descriptive purposes.

Postnatal maternal social support was assessed at 24 months using the Multidimensional Scale of Perceived Social Support (MSPSS; Zimet et al., 1988). The 12-item scale assesses support from family, friends, and significant others, using a 5-point Likert scale (1 = strongly disagree; 5 = strongly agree). These subscales load onto a single factor for modeling.

Postnatal maternal exposure to community violence was assessed at 24 months using the Survey of Exposure to Community Violence (SECV; Richters & Salzman, 1990). Twelve items ask about witnessing of violence in the past year, and responses are scored on a 4-point Likert scale (0 = never; 3 = many times), yielding a total score that was used for analyses.

Parenting was assessed at 30 months using the Parenting and Family Adjustment Scales (PAFAS; Sanders et al., 2014). This instrument was designed as a brief assessment of parenting practices and family adjustment, using easy to read language to ensure applicability in low literacy samples. Only the parenting practices subscales were considered directly relevant to our focus, and given the extant evidence of the elevated risk that coercive parenting presents (Brumley & Jaffee, 2016; Leve et al., 2005), we decided to include only this subscale. Five items are scored on a 4-point Likert scale (0 = not at all; 3 = very much).

Child temperament was assessed at 42 months via the very short form of the revised Infant Behavior Questionnaire (IBQ-R-VSF; Putnam et al., 2014) reported retrospectively. This questionnaire assesses three overarching domains of temperament – surgency, negative emotionality, and effortful control. Thirty-seven questions ask about very specific behaviors, and mothers respond regarding frequency of observing the behavior on a 7-point Likert scale (0 = never; 6 = always). A "not applicable" response is also available, where opportunities for the behavior are not present. We chose to focus on the effortful control subscale as an indicator of self-regulation, and on negative emotionality. However, the Effortful Control subscale demonstrated inadequate reliability ($\omega = 0.67$; see supplementary materials Appendix A, Table 1) and was excluded from analysis.

We must note that detailed measures of child socioemotional development were only introduced to the DCHS protocol at the 42-month timepoint. Given that a slow rate of cognitive and language development was evident in the cohort (Donald et al., 2019; Wedderburn et al., 2019), no doubt due to adverse socioeconomic context, we decided that the temperament questionnaire usually administered from 36 months, the Child Behavior Questionnaire, would be more appropriate at a slightly older age, and that we would attempt to obtain retrospective reporting of infant characteristics from mothers at 42 months. Mothers were asked to think back to the period when their child was 6 months to around 1 year old, and report on their behavior during this time. We assessed

mothers' confidence in their retrospective reporting as an indication of whether this choice was viable or not. A large majority of active case mothers (86%) indicated high confidence in their responses regarding infant temperament with only 3.9% indicating low confidence in their responses.

Child exposure to community violence was assessed at 42 months using the Child Exposure to Community Violence Checklist (CECV; Amaya-Jackson, 1998). Thirty-five items asking about exposure to various kinds of community violence and violence in the home are coded using a 4-point Likert scale (0 = never; 3 = very often). However, this measure demonstrated inadequate reliability ($\omega = 0.66$) and was excluded from modeling (see supplementary material Appendix A, Table 1).

Child assessment measures

At the 42-month timepoint, the children were individually assessed to evaluate self-regulation and general cognitive function.

Self-regulation was assessed via a gratification delay task based on the Tongue Snack Delay task (Kochanska et al., 2000), where the child must hold a small candy on their tongue without chewing and eating it, across 3 delay trials (20s, 30s, 15s). Summed latency scores across trials (i.e., seconds before candy was consumed) were calculated.

General cognitive function was assessed via the Nonverbal Index of the Kaufman Assessment Battery for Children (KABC-2; Kaufman & Kaufman, 2004), which provides a global index of general cognitive function where the effect of language on test performance is reduced (Greenop et al., 2012) – a concern given the multilingual nature of our cohort. For this age point, the Nonverbal Index is comprised of 4 subtests: Hand Movements; Triangles; Conceptual Thinking, and Face Recognition. There are concerns that exclusion of verbal abilities leads to over-estimation of intelligence (Scheiber & Kaufman, 2015), but given the very early stage of language development in our cohort, we decided that the Nonverbal Index would be a fair measure to administer.

Outcome measure

Child mental health was assessed at 42 months, using the parent-report version of the Child Behavior Checklist for children aged 1.5–5 years (CBCL; Achenbach, 2009). Ninety-nine items ask about various signs of mental health using a 3-point Likert scale (0 = not true; 2 = often or very true), from which various subscale scores can be derived. We used the scores for Internalizing and Externalizing behavior subscales. Most unfortunately, CFA indicated that only 14% of CBCL Internalizing subscale items loaded ≥ 0.50 (supplementary materials; Appendix A, Table 4) – given this, the internalizing subscale had to be dropped from consideration in our modeling.

Data analysis

This study relied on multigroup hierarchical covariance-based SEM to assess the nature of relationships between several risk factors and externalizing child behavior. Due to inadequate psychometric properties we could not model internalizing behavior as originally intended (see above and Discussion). All hierarchical SEMs were conducted using R's lavaan package. Full information maximum likelihood estimation was applied to all models – this has the benefit of enabling model fit estimation of an entire available sample with the inclusion of incomplete data, and has been reported to produce unbiased estimates

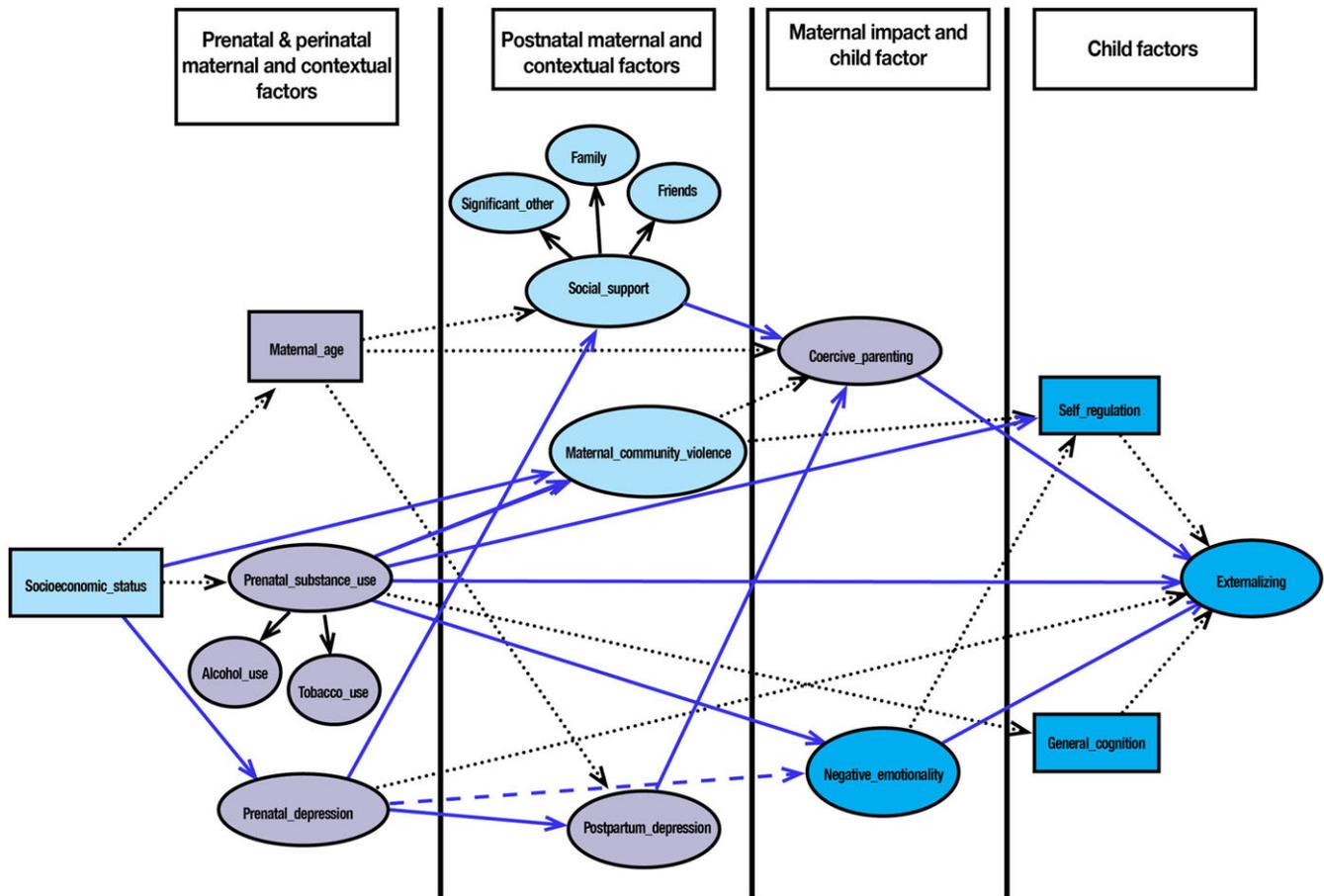


Figure 4. Final baseline hierarchical structural model. Structural model exclusively presented (measurement model not displayed). Latent factors are represented as ovals, and observed variables are represented as squares. Pale blue ovals indicate contextual factors, purple ovals indicate maternal factors and darker blue ovals indicate child factors. Blue lines represent: $p < 0.05$; Black dotted lines: $p = 0.05$; Dotted blue line: $p = 0.07$ (trend-level).

under missing at random and missing completely at random assumptions (Enders & Bandalos, 2001). In order to account for any non-normally distributed data, bootstrapped 95% confidence intervals are reported alongside regression coefficients (Mooney & Duval, 1993).

Broadly speaking, the initial SEM aimed to represent how prenatal maternal and contextual in combination with postnatal maternal, contextual and child risk factors may impact child externalizing behavior at 42 months. Risk factors were segmented into four roughly chronologically ordered stages: prenatal & perinatal maternal and contextual factors; postnatal maternal and contextual factors; maternal and contextual impact on child; and child-only factors (see Figure 4). This chronological ordering of variables formed the basis of the rationale behind the direction of predicted relationships between risk factors, with prenatal factors preceding postnatal factors, and maternal factors preceding maternal-child relationship factors, with child-only factors following from maternal influences in the model. Thus, chronology of measurements as well as previous literature were used to inform the selection of regression paths.

In order to redress the presence of any further model misspecifications, the CFA was re-run with additional cross-item correlations that were systematically selected using the approach proposed by Saris et al. (2009). Where modification indices could not fix additional poorly fit indicators of the included latent factors, items were only considered for exclusion if factor loadings fell

≤ 0.2 ; this criterion was chosen to ensure conservative selection of items for potential exclusion (Maskey et al., 2018; see supplementary materials, Appendix B).

The final confirmatory factor model was assessed for global fit using chi-squared test (X^2), robust Comparative Fit Index (CFI), robust Tucker-Lewis Index (TLI), robust Root Mean Square Error of Approximation (RMSEA) and Standard Root Mean Square Residual (SRMR), where $CFI \geq 0.90$, $TLI \geq 0.90$, $RMSEA \leq 0.05$, $SRMR \leq 0.08$ indicate adequate global fit (Cheng, 2011). The inclusion of cross-item correlations were considered where necessary to improve model fit with the use of modification indices according to the approach proposed by Saris et al. (2009)

Of the models tested, a multigroup hierarchical SEM was run to test for structural invariance of predictive pathways between male and female children (Sass & Schmitt, 2013). Results indicated that these did not differ according to child sex (see Table 1). Thus, a baseline SEM excluding child sex was accepted.

Baseline SEMs were run against a series of alternate mediation and moderation models, where model selection was based on chi-square difference test for nested models, as well as Akaike Information Criterion and Bayesian Information criterion estimates of global fit (Kline, 2016).

We tested two mediation effects: infant negative emotionality as a mediator between prenatal substance use and externalizing behavior (mediation model 1), and infant negative emotionality

Table 1. Global model fit and model comparison estimates

Model	Global model fit estimates						Model comparisons						
	AIC	^a BIC	Robust CFI	Robust TLI	RMSEA	SRMR	^b χ^2	Df	p	Model comparison	$\Delta \chi^2$	Δdf	p
Multigroup baseline model 1	174136	175270	0.860	0.856	0.034	0.074	11,897	8452	<0.001	v. Constrained multigroup model	128.02	103	0.952
Alternate baseline model 2	212582	213301	0.888	0.885	0.025	0.060	9628	7080	<0.001				
Mediation model 1	212596	213314	0.887	0.884	0.025	0.061	9641	7081	<0.001	v. Alternate baseline model 2	14.21	1	<0.001
Mediation model 2	212583	213301	0.887	0.885	0.025	0.061	9631	7081	<0.001	v. Alternate baseline model 2	2.42	1	0.120
Moderation model 1	212583	213304	0.888	0.885	0.025	0.060	9628	7079	<0.001	v. Alternate baseline model 2	0.89	1	0.346
Moderation model 2	212582	213303	0.888	0.885	0.025	0.060	9627	7079	<0.001	v. Alternate baseline model 2	2.13	1	0.144

^aSample-size adjusted BIC. ^bYuan-Bentler corrected chi-squared statistic for non-normally distributed data.

as a mediator between prenatal maternal depression and externalizing behavior (mediation model 2). Moreover, we tested two moderation effects: child self-regulation moderating the impact of coercive parenting on externalizing behavior (moderation model 1); and child self-regulation moderating the impact of child negative emotionality on externalizing behavior (moderation model 2). However, no moderation effects emerged (Table 1).

Lastly, in order to check that these factors did not impact on our model, we ran additional SEMs: The SEM findings including only HIV unexposed participants ($n = 765$) remained consistent with those found in the larger sample (see supplementary materials; Appendix C, Table 8). Findings were also consistent for the subsample ($n = 939$) excluding participants who utilized substances other than alcohol and tobacco (supplementary materials; Appendix C, Table 9).

Results

Descriptives

Of the 1143 children enrolled in the DCHS, 86% of the total birth cohort was retained as part of the analytic sample (981 child participants), and represented the active participant group at 42 months, with the outstanding 14% representing confirmed withdrawn participants (162 child participants). Active participants did not differ from withdrawn participants on any major sociodemographic or psychosocial risk factors (supplementary materials; Appendix D).

Within the analytic sample, there appeared to be a relatively even distribution across child sex, with a marginally higher percentage of dyads residing at Site 1 (Table 2). Mothers were on average 27 years of age when they gave birth, delivering an infant weighing on average 3034 grams at 38 weeks of gestation. Approximately 20% of mothers were identified as depressed (BDI-II). Approximately 29% of mothers were at moderate to high risk of tobacco use disorder, while a lower 11% of mothers were at risk for alcohol use disorder (ASSIST). Eighty-six percent indicated high confidence in their retrospective responses regarding infant temperament as measured on the IBQ-R-VSF. Children averaged 3.5 years (i.e., 42 months; $SE = 0.08$; $min = 3.1$; $max = 4.4$) at the time of the CBCL mental health assessment; 6.2% displayed clinically relevant levels of externalizing behavior.

The final CFA demonstrated an adequate global model fit in terms of absolute fit measures, where robust RMSEA = 0.027 [0.026:0.028] and SRMR = 0.059. With respect to incremental fit measures, the measurement model demonstrated a sufficiently sized robust CFI of 0.918 and robust Tucker-Lewis Index of 0.915. Furthermore, the majority of model residuals (93.5%) fell below 0.10 (See supplementary materials; Appendix E).

Negative infant emotionality partially mediated the relationship between maternal prenatal substance use and externalizing behavior ($B = 0.05$, $p = 0.016$; Table 3; Figure 5), but interestingly, there was also a relatively stronger direct effect ($B = 0.24$, $p < 0.001$) between maternal prenatal substance use and externalizing behavior. Other major pathways of interest included the complex relationships between SES, maternal depression, maternal social support, coercive parenting risk factors and child externalizing behavior, where two pathways emerged. The strengths of relationships between variables were small and varied between -0.18 and 0.37 (standardized coefficients), with the exception of the relationship between maternal prenatal depression and postpartum depression, which was a moderate size of 0.53.

Interestingly, neither child self-regulation nor general cognition were significantly related to externalizing behavior. Moreover, maternal age at birth did not appear to be related to any other proposed risk factor.

Discussion

Our results define two pathways to increased externalizing behavior at 42 months in this cohort: one highlighting primarily biological risk factors, and the other, contextual factors involving mothers. Maternal prenatal substance use (alcohol and tobacco) was directly associated with increased externalizing behavior at 42 months, and this relationship was partially mediated by infant temperament (negative emotionality). Coercive parenting was also associated with increased externalizing behavior – links between prenatal maternal lower SES and increased depression preceded this association. No child sex differences in these patterns of association were apparent.

Prenatal substance use, negative emotionality, and externalizing behavior. The biological pathway indicates a direct relationship between prenatal exposure to substances (alcohol and

Table 2. Analytic sample characteristics

Variable	Active participants, N = 981 ^a	
	Mean (SD), n (%)	Median [IQR]
Socio-economic status (SES)		
lowest SES	238 (24%)	
low-mod SES	264 (27%)	
mod-high SES	253 (26%)	
higher SES	226 (23%)	
Site		
Mbekweni	535 (55%)	
TC Newman	446 (45%)	
Maternal age at birth	27.0 (5.7)	26.3 [22.4–31.1]
Child Gender		
Female	480 (49%)	
Male	501 (51%)	
HIV exposure		
HIV exposed	216 (22%)	
HIV unexposed	765 (78%)	
Gestational age (weeks)	38.52 (2.67)	39.00 [38.0–40.0]
Birth weight (grams)	3034 (582)	3100 [2710–3410]
Prenatal depression (BDI)		
Probable subthreshold	705 (81%)	
Probable moderate/severe clinical	163 (19%)	
Prenatal tobacco use (ASSIST)		
Low risk	618 (71%)	
Moderate risk	206 (24%)	
High risk	46 (5.3%)	
Prenatal alcohol use (ASSIST)		
Low risk	772 (89%)	
Moderate risk	68 (7.8%)	
High risk	29 (3.3%)	
Postpartum depression (EPDS)		
Probable subthreshold	531 (83%)	
Probable moderate/severe clinical	105 (17%)	
Maternal exposure to community violence (SECV)	13 (7)	13.00 [7.0–18.0]
Coercive parenting (PAFAS)	5.7 (3.6)	5.0 [3.0–8.0]
Negative emotionality (IBQ-R-VSF)	2.91 (1.24)	3.00 [2.0–3.8]
Perceived social support (MSPSS)	5.58 (1.25)	5.80 [5.0–6.7]
Family	6.10 (1.49)	7.00 [5.8–7.0]
Friends	4.44 (2.17)	4.80 [2.5–6.8]
Significant other	6.23 (1.44)	7.00 [6.0–7.0]
Self-regulation		
Gratification delay task (seconds)	56 (15)	65.00 [53.0–65.0]
Nonverbal Index (KABC)	77 (15)	78.0 [68.0–87.0]
Externalizing (CBCL)		
Healthy	831 (94%)	
Borderline clinical	29 (3.3%)	
Clinical	26 (2.9%)	

^aStatistics presented. Categorical: n (%). Continuous: Mean (SD); Median [IQR].

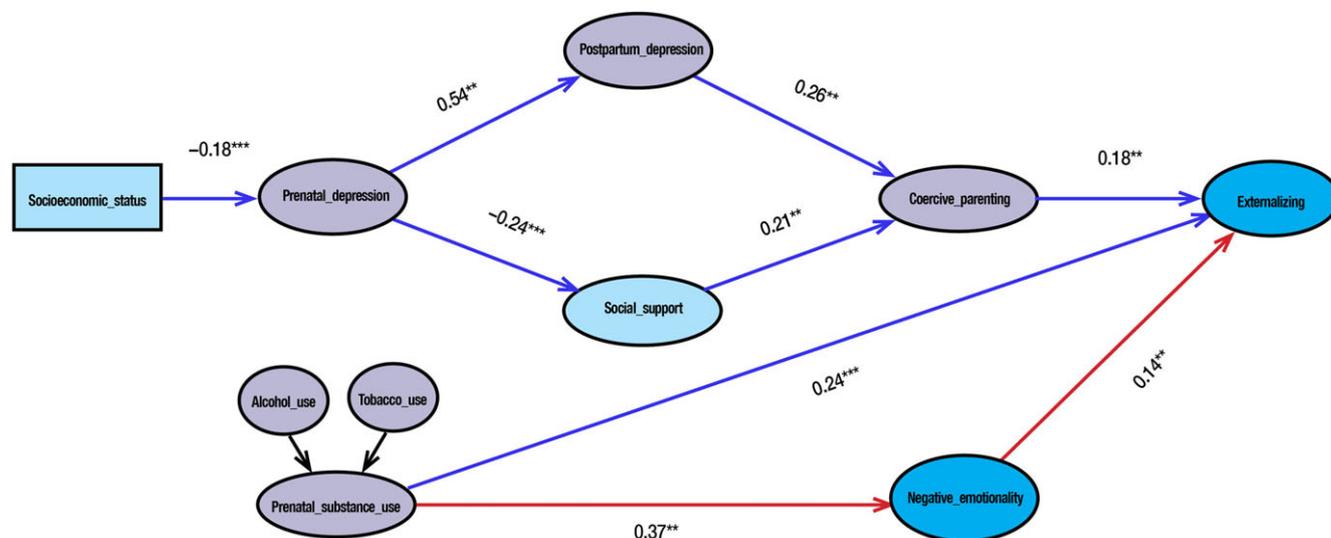


Figure 5. Significant pathways to externalizing behavior (with dark blue lines representing direct effects and red lines representing mediation effect). Standardized estimates presented. * $p < 0.05$; ** $p < 0.01$.

tobacco) and greater externalizing behavior at 42 months. In terms of the standardized coefficients, this was the strongest predictor in our model. This finding is consistent with that of a recent meta-analytic review focused on the effects of PAE on child mental health (Khoury et al., 2018), which found that in the 65 studies reviewed, PAE was strongly associated with externalizing behavior, with a large effect size ($d = 0.90$), in comparison to unexposed children from the same communities. An early study found 91% of children with heavy PAE had clinically significant levels of externalizing behavior, compared to 27% of demographically matched controls (Mattson & Riley, 2000). A more recent review of neuro-behavioral outcomes concurs that psychiatric disorders, especially those characterized by externalizing behaviors, occur at elevated rates in FASD (Mattson et al., 2019). Another recent systematic review indicates that even at low to moderate levels of use, PAE is associated with poor child mental health outcomes (Easey et al., 2019). Proposed mechanisms underlying the effect of PAE include the direct toxic effect of alcohol on the developing fetus, less direct effects via placental insufficiency and pro-inflammatory effects, as well as indirect effects through consequences of altered maternal behavior such as food insecurity or nutrition choices, micronutrient deficiencies, smoking, maternal mental health problems, and increased exposure to violence (Behnke et al., 2013).

There is also substantive literature indicating that prenatal exposure to tobacco is associated with elevated levels of externalizing behavior from early childhood onward, as well as disruptive behavior disorders including ADHD, Oppositional Defiant Disorder and Conduct Disorder (Brannigan et al., 2020; Robinson et al., 2010; Sutin et al., 2017; Wakschlag et al., 2011; Wakschlag et al., 2006). Prenatal tobacco exposure has long been known to impact fetal growth and development (above and beyond the influence of other risk factors; Lassen & Oei, 1998); and the associated low birth weight is a known risk factor for development of psychiatric disorders (Talati et al., 2017). Research in this area is demonstrating that prenatal tobacco exposure results in hyperactive behavior in animal studies (Tien et al., 2020), and in humans it effects motivational self-regulation; with self-regulation difficulties being thought to underly many behavioral disorders (Cao et al., 2020; Wiebe et al., 2015).

It is important to note, that in Western Cape communities where PAE is prevalent, the only other substance consistently consumed alongside alcohol is tobacco, and mothers of children with FASD smoke at a far higher rate than do mothers of unaffected children (May et al., 2021) – this is consistent with patterns of concurrent use of alcohol and tobacco seen in our cohort. We must emphasize that to date few studies have been able to look at relationships other than associations, whereas in the DCHS we are able to track patterns of prenatal maternal alcohol use to child behavioral outcomes at age 3 years in a population-based birth cohort from a high-risk community, and demonstrate the effects of alcohol and tobacco use over and above other highly salient concurrent risk factors.

This direct association between prenatal substance use and externalizing behavior at 42 months was partially mediated, with small effect, by infant negative emotionality, an aspect of child temperament. Notably, prenatal substance use strongly predicted this aspect of child temperament, so although negative emotionality's mediation effect was small, the direct association between PAE and negative emotionality also speaks to the need for interventions to limit prenatal alcohol and tobacco use. Negative emotionality has repeatedly been shown to be associated with increased mental health problems, including externalizing behavior, in very young children (Cassiano et al., 2019; De Pauw & Mervielde, 2010), as well as over time and into adolescence (for review, see Kostyrka-Allchorne et al., 2020).

Maternal prenatal depression also showed a trend towards predicting infant negative emotionality, a relationship described in other studies (Howland et al., 2020; Werner et al., 2007), and one to follow-up on in future assessments of the DCHS cohort. Both prenatal substance use and depression appear to be associated with increased negative emotionality in infants, via different mechanisms. Genetic predisposition may underly this facet of temperament in children of prenatally depressed mothers (Koss & Gunnar, 2018), whereas teratogenic effects on the developing fetus may account for increased negative emotionality and "difficult" temperament in infants with PAE (Alvik et al., 2011; O'Connor, 2001).

In this economically disadvantaged cohort, prenatal substance use was not predicted by SES. The Khoury et al review (2018)

Table 3. Final SEM regression coefficients

Outcome	Predictors	Standardized coefficient	Standard error	Confidence interval	Z statistic	p
<i>Externalizing</i>	Self-regulation	-0.03	0.055	-0.14: 0.07	-0.60	0.548
	General cognition	0.02	0.043	-0.07: 0.10	0.45	0.657
	Coercive parenting	0.18	0.055	0.08: 0.29	3.40	0.001
	Negative emotionality	0.14	0.057	0.03: 0.25	2.52	0.012
	Community violence	0.01	0.059	-0.11: 0.12	0.09	0.925
	Prenatal depression	0.07	0.048	-0.02: 0.17	1.51	0.132
	Prenatal substance use	0.24	0.075	0.09: 0.39	3.25	0.001
<i>Self-regulation</i>	Coercive parenting	0.11	0.049	0.01: 0.21	2.23	0.025
	Negative emotionality	-0.06	0.055	-0.17: 0.04	-1.17	0.241
	Community violence	0.01	0.059	-0.10: 0.13	0.20	0.843
	Prenatal substance use	-0.14	0.069	-0.27: -0.01	-2.05	0.041
<i>General cognition</i>	Prenatal substance use	-0.03	0.050	-0.13: -0.06	-0.66	0.506
<i>Negative emotionality</i>	Prenatal substance use	0.37	0.076	0.22: 0.52	4.94	<0.001
	Prenatal depression	0.13	0.066	-0.01: -0.25	1.91	0.056
<i>Coercive parenting</i>	Social support	0.21	0.075	0.06: -0.36	2.85	0.004
	Community violence	0.07	0.050	-0.02: 0.17	1.48	0.139
	Postpartum depression	0.26	0.054	0.16: 0.37	4.91	<0.001
	Maternal age	0.06	0.049	-0.03: 0.16	1.21	0.225
<i>Social support</i>	Maternal age	-0.01	0.048	-0.10: 0.08	-0.25	0.801
	Prenatal depression	-0.24	0.065	-0.37: -0.12	-3.76	<0.001
<i>Community violence</i>	Socioeconomic status	-0.10	0.047	-0.19: -0.01	-2.10	0.036
	Prenatal substance use	0.55	0.072	0.41: 0.69	7.66	<0.001
<i>Postpartum depression</i>	Maternal age	0.06	0.043	-0.03: 0.14	1.32	0.185
	Prenatal depression	0.54	0.070	0.40: 0.67	7.67	<0.001
<i>Maternal age</i>	Socioeconomic status	0.05	0.030	-0.01: 0.11	1.64	0.101
<i>Prenatal substance use</i>	Socioeconomic status	-0.03	0.036	-0.10: 0.04	-0.96	0.336
<i>Prenatal depression</i>	Socioeconomic status	-0.18	0.036	-0.25: -0.11	-5.07	<0.001
<i>Externalizing</i>	Mediation effect: Infant negative emotionality on prenatal substance use	0.05	0.024	0.01: 0.10	2.28	0.023

highlights a specific gap in the literature, where clarification is required regarding the role of SES in the relationship between PAE and externalizing behavior. It may be that in our low SES cohort, minor variations in economic disadvantage were insufficient to elucidate this relationship, although SES did display sufficient variation to be associated with prenatal maternal mental health. We did not model prenatal substance use as possibly following from prenatal mental health problems (we chose to examine the effects of these predictors separately); this is a pathway that should be examined in future studies.

SES, prenatal depression, coercive parenting (30 months) and externalizing behavior at 42 months. Maternal prenatal SES was strongly and inversely associated with prenatal depression in mothers in this cohort. This path culminated in higher reported levels of coercive parenting at 30 months, which predicted increased externalizing behavior at 42 months. These associations are strongly consistent with predictions from both the FSM and the PP model.

The path between prenatal depression and coercive parenting followed two alternate routes: (1) A positive association between prenatal and postnatal depression was followed by increased coercive parenting. (2) An inverse association between prenatal depression and postnatal perceived social support was seen; and a positive association between social support and coercive parenting followed. Inspection of zero order correlations (see Table 4) further indicated that postnatal depression and perceived social support were inversely correlated.

We thus interpret the split in the path between maternal prenatal depression and coercive parenting as essentially meaningless: mothers who remain depressed postnatally have less social support and go on to use coercive parenting; mothers who are no longer depressed postnatally have better social support but also use coercive parenting. We must note that physical disciplining of children and the authoritarian parenting style continue to be practiced as normative in many South African communities (Marcus *et al.*, 2020; Ward, Gould, *et al.*, 2015; Ward, Makusha, *et al.*, 2015),

Table 4. Bivariate correlations

Variable	1	2	3	4	5	6	7	8	9	10	11	12
Socioeconomic status [1]	1											
Maternal age at birth [2]	0.049	1										
Prenatal substance use [3]	-0.035	-0.002	1									
Prenatal depression [4]	-0.178 ^a	-0.009 ^a	0.006 ^a	1								
Social support [5]	0.042 ^a	-0.010	-0.001	-0.241 ^a	1							
Community violence [6]	-0.102 ^a	-0.005	0.488 ^a	0.018 ^a	-0.004	1						
Postpartum depression [7]	-0.083 ^a	0.046	0.003	0.480 ^a	-0.116 ^b	0.008	1					
Coercive parenting [8]	-0.020	0.066	0.040	0.087 ^a	0.172 ^a	0.081 ^a	0.263 ^a	1				
Negative emotionality [9]	-0.033	-0.002	0.350 ^a	0.121 ^a	-0.029	0.173 ^a	0.058	0.024	1			
Self-regulation [10]	0.003	0.008	-0.159 ^a	0.001	0.022	-0.059	0.027	0.111 ^a	-0.114 ^a	1		
General cognition [11]	0.001 ^a	0.000	-0.032 ^a	0.000	0.000	-0.016	0.000	-0.001	-0.011	0.005	1	
Externalizing [12]	-0.029	0.011 ^a	0.302 ^a	0.100 ^a	0.011	0.162 ^a	0.088 ^a	0.200 ^a	0.239 ^a	-0.063	0.005	1

^ap < 0.05.^bp = 0.05.

so seeing this in both groups of mothers, and at similar strengths of association, should not be particularly surprising. Physical discipline and less positive parenting styles are also widely associated with the stressors attendant on low SES (Cluver et al., 2020; Hastings et al., 2015). What is perhaps most important to emphasize, is that coercive parenting is associated with increased externalizing behavior, and that even though coercive parenting may be common in this setting, lower maternal SES and prenatal depression appear to drive an increase in its use, as predicted by FSM and PP theory.

The direction of the association between coercive parenting and externalizing behavior is one that has been open to question. Bidirectional associations have been documented previously (Leve et al., 2005), and the possibility that children who act out elicit increased harsh parenting responses is certainly credible (Roskam, 2019). A meta-analysis of 1435 studies examined cross-lagged effects in order to assess whether externalizing behavior can elicit increased harsh parenting over time – the analysis showed this was indeed the case, although the effect was very small (Pinquart, 2017). This bidirectional relationship over time as been confirmed in a Brazilian cohort (Bauer et al., 2021). Our assessment of parenting occurred prior to the assessment of externalizing behavior, lending some support to the direction of association assumed above, but future examinations of child mental health in our cohort, using longitudinal data from later timepoints, will be able to assess whether the effects of child behavior on parenting are evident in our cohort as well.

Implications and interventions

The results of our SEM indicate that maternal drinking patterns, embedded in this region in cultural practices around weekend drinking (May et al., 2013), remain a primary driving force implicated in problematic child behavior and development. Additionally, as has been repeatedly evidenced across multiple contexts (Brumley & Jaffee, 2016; Cecil et al., 2017; Ward, Gould, et al., 2015), coercive parenting also predicts increased behavior problems in these young children. Evidence from other contexts around early developing trajectories of problematic

behaviors (Odgers et al., 2008; Shaw et al., 2012), often culminating in violent antisocial behavior in adolescence and early adulthood, is of grave concern given the problems South Africa experiences regarding youth violence, gangsterism and violent crime (Pinnock, 2016; S.A.P.S., 2020; Ward et al., 2013). Psychosocial risk factors are deeply inter-connected, hence the urgency of implementing effective prenatal interventions for at risk mothers, targeting multiple factors (e.g., use of tobacco as well as alcohol, and maternal mental health) cannot be overstated. Support for parents with implementation of positive parenting programs is also critical, and has been shown to be effective in various LMICs (Cluver et al., 2020; Ward et al., 2020), improving parenting practices and child mental health outcomes.

Limitations: Variables not examined due to statistical considerations

It may seem conservative to exclude measures of key constructs from modeling based on poor psychometric performance. However, many statisticians argue strongly that SEM will produce misleading results if the soundness of the measures underlying the latent constructs is not thoroughly investigated for each sample (Kline, 2016; Morrison et al., 2017; Vize et al., 2018). Reliability and validity are not inherent properties of questionnaire measures – they reflect the pattern of responses obtained, which may vary across different socio-cultural and demographic contexts (Knekt et al., 2019). This was very much evident in our data.

Internalizing behavior. Confirmatory Factor Analysis of this CBCL subscale in this cohort yielded results indicating that it did not provide a valid representation of the latent construct. Thus, despite the fact that it was intended to be a key focus of our investigation, we were obliged to omit internalizing behavior from analysis. The version of the CBCL for very young children has been shown to be psychometrically sound in many studies (Achenbach et al., 1987; Neo et al., 2021), including some LMICs (Dang et al., 2017; Rescorla et al., 2020) but this was not the case in our cohort. There are a number of reasons that may underlie this difficulty: (1) Internalizing behavior tends to develop, or at least be reported, at a later age than externalizing behavior.

We note, for example, that in a study by Barrios *et al.* (2017), parental hostility at a similar age to our cohort (3 years) was only associated with externalizing behavior at that timepoint, whereas increases in both internalizing and externalizing behavior were reported later in the preschool period. Externalizing behavior problems are far more commonly diagnosed in early childhood, whereas internalizing problems emerge later in childhood (Miller & Votruba-Drzal, 2017). Thus, the absence or extremely low rates of occurrence of internalizing behavior in our very young children may have led to odd patterns of parent responses to items. (2) Internalizing behavior is not as easily noticeable as externalizing behavior. Whereas externalizing behavior features acting out, internalizing behavior features social withdrawal, anxiety or depression, and somatic complaints (Huber *et al.*, 2019). The very young age of the children, and the early stage of their language development (Donald *et al.*, 2019; Wedderburn *et al.*, 2019), also means that the children were unlikely to be sufficiently able to verbalize their internal states, and thus reporting would rely entirely on mothers' behavioral observations. Our unanticipated results with this well-established scale should alert researchers working in contexts which differ markedly from those in which measures were developed, to the necessity of examining psychometric properties for their samples. We do not necessarily advocate the development of new measures or major adaptations for differing countries or communities, as this would render research incomparable across contexts. Rather, it is our opinion that use of standard, well-established measures is good practice; however the commonly made assumption that these measures will be psychometrically sound in diverse populations is not tenable, and researchers should check their measures before placing confidence in their results.

Prenatal exposure to IPV. This measure was omitted from analysis due to high residual covariance between items measuring maternal prenatal substance use and prenatal depression. The co-occurrence of exposure to IPV, substance use and depression is well documented (Rotheram-Borus *et al.*, 2015; Stein *et al.*, 2015). It is, however, unfortunate that we were not able to examine the potentially unique predictive effects of IPV in our model.

Child exposure to community violence. This measure demonstrated inadequate reliability in our cohort. This may be due, in part, to the children's young age. At 42 months, their main context is that of the family, inside the home (Hastings *et al.*, 2015; Zeanah & Lieberman, 2016). Independent exposure to the community context will increase as the children get older, and examination of this factor at older timepoints will be key.

Other limitations and future directions

Our model identified a number of key variables associated with increased externalizing behavior in cohort children; nonetheless it must be acknowledged that this model in no way comprises a complete explanation of this outcome. Although our objective was to capture a complex set of relationships between multiple predictors and externalizing behavior, for which purpose SEM is uniquely suited, even this technique has limits in terms of the number of factors it can manage. Our inclusion of predictors was guided by theory and prior literature, but we were unable to include every variable or pathway of interest – the tension between wanting to model complexity versus difficulties around overly complex structural equation models (Kline, 2016) resulted in having to make decisions about variable inclusion and specified pathways that are to some extent subjective. A level of complexity remains apparent in our final model, and the inadvertent possibility that

the variance partialling that is central to regression methods along with the shared method variance (most of our data is derived from maternal reports) may have resulted in inflated estimates must be acknowledged (Lynam *et al.*, 2006). The concern regarding the effects of partialling is particularly pertinent when highly related constructs with a great deal of shared variance are being modeled (see Vize *et al.*, 2018). We faced this difficulty in the instance described above, where, although conceptually distinct, prenatal maternal depression, substance use and exposure to IPV residuals were correlated to moderate degrees; hence we decided to exclude the IPV scale to address this difficulty. Nonetheless, this might not have been sufficient correction, and we remain mindful of the dangers that partialling methods pose to construct composition (Lynam *et al.*, 2006).

In our modeling, directly observed self-regulation abilities were not associated with externalizing behavior. This was unexpected, given the strong associations often reported in the literature (Cassiano *et al.*, 2019; De Pauw & Mervielde, 2010; Kostyrka-Allchorne *et al.*, 2020). The fact that self-regulation and child mental health were assessed at the same timepoint may have had some role in this negative finding. The use of direct assessment of self-regulation rather than parent-report of temperament may also be a factor. Psychometric considerations precluded the use of parent-report data on infant self-regulation in the model – it is possible that retrospective reporting may have contributed to this problem. We do note that the meta-analytic review of prospective longitudinal studies by Kostyrka-Allchorne *et al.* (2020) found that predictive effects of infant temperament (parent-reported) for later psychopathology were significant, but small. It will be important to track the role of this factor in future assessments of the cohort, particularly as we saw bivariate associations between both coercive parenting and maternal prenatal substance use with directly observed self-regulation at 42 months (see Table 4).

Although not a predictor of externalizing behavior in this model, maternal exposure to community violence was inversely associated with SES, and strongly associated with prenatal substance use (see Table 4). This thus remains an important variable to consider in future studies.

We acknowledge that this set of results does not assess the potential impact of genetic variables. This should be explored in future papers, as several important mechanisms may influence our variables of interest. For example, Since Caspi *et al.*'s (2002) work, we have known that genetics influence externalizing behavior. Furthermore, the concept of differential susceptibility proposes that some children are more reactive to their environments, and hence do worse or better than others given high-risk or optimal contexts respectively. Genetic mechanisms may underlie this variability: for example, studies have shown that temperament and candidate gene \times environment interactions, as well as polygenic susceptibility scores may underlie differential susceptibility to parenting interventions (Belsky & van IJzendoorn, 2017; Overbeek, 2017). Research is also beginning to show the role of risk and protective genes, gene \times environment interactions, and epigenetic regulation mechanisms, in the variable effects of PAE on the developing fetus and later outcomes (Kaminen-Ahola, 2020; Ungerer *et al.*, 2013). Including genetic variables in future models will strengthen our understanding of important mechanisms underlying phenotypes.

One of the chief strengths of the DCHS is the antenatal recruitment and longitudinal follow-up of a birth cohort from a socio-economically disadvantaged, high-risk LMIC context. Critically, this cohort provides a rare opportunity to examine the effects of

PAE on child mental health longitudinally, and to elucidate explicit relationships with comorbid use of other substances, in the presence of multiple other measured psychosocial risk factors.

Conclusion

The patterns of association described above are largely consistent with those from HICs, and confirm important targets for intervention in our context, that may also be relevant for other LMICs. Prenatal use of alcohol and tobacco, lower SES associated with prenatal depression and later coercive parenting style predicted greater externalizing behavior at 42 months in our cohort. Early externalizing behavior is established as a major public health problem, frequently resulting in negative outcomes into adolescence and adulthood (Brumley & Jaffee, 2016; Moffitt, 1993). It is noteworthy that no sex differences in patterns of predictive associations emerged at this early timepoint, and it will be important to establish whether this changes over time in the cohort. The variables identified as critical in this study are largely consistent with predictions from theory, and reflect the most relevant child context at this age – those relating to individual, maternal and family characteristics (Koss & Gunnar, 2018). The impacts of the broader context are likely to become more influential as the children grow older and have increased exposure to their peers and community. What is already clear from this initial work, is that supportive multifaceted prenatal interventions for mothers, targeting not only use of alcohol, but also tobacco, as well as mental health, are essential to avoid negative consequences in early childhood. Implementation of positive parenting programs can change community practices, and promote positive child mental health outcomes. Far broader sustainable development goals, aimed at improving socioeconomic conditions across LMICs such as South Africa, have not yet been achieved but should remain a critical focus in the strategy to improve child developmental and mental health outcomes overall.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S095457942200027X>

Acknowledgements. We would like to thank Prof Colin Tredoux, Dept of Psychology, UCT for his invaluable guidance regarding the statistical analyses. We thank the study staff and the staff at Paarl Hospital, and at Mbekweni and TC Newman clinics for their support of the study. We thank the families and children who participated in this study.

Funding statement. Support for this study was provided by the Bill and Melinda Gates Foundation [HJZ; OPP 1017641] and by the National Institute of Mental Health Brain Disorders in the Developing World: Research Across the Lifespan program (DJS; grant number R21 MH098662). DJS and HJZ are supported by the Medical Research Council of South Africa. Further support for aspects of this work was provided by grants from the National Institute on Alcohol Abuse and Alcoholism (KAD: R21AA023887), US Brain and Behaviour Foundation (KAD; 24467), Collaborative Initiative on Fetal Alcohol Spectrum Disorders (KAD; U24 AA014811), Newton Fund (KAD; NAF002\1001), Medical Research Council of SA Self-Initiated Research grant (KAD); and National Research Foundation of South Africa Thuthuka grants (SMS; TTK150624120738; KAD; TTK160525166241).

Conflicts of interest. None.

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