# Mental Health of Extremely Low Birth Weight Survivors in Their 30s

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abstract

**OBJECTIVE:** To determine the risk for psychiatric disorders among extremely low birth weight (ELBW) survivors in their early to mid-30s and to determine whether those born small for gestational age or those exposed to a full course of antenatal corticosteroids (ACS) were at particularly high risk.

**METHODS:** A prospective, longitudinal, population-based cohort of 84 ELBW survivors and 90 normal birth weight (NBW) control participants born in Ontario, Canada from 1977 to 1982 were assessed by interviewers naive to birth weight status using the Mini-International Neuropsychiatric Interview.

**RESULTS:** ELBW survivors had lower odds of an alcohol or substance use disorder but higher odds of current non–substance-related psychiatric problems (odds ratio [OR] = 2.47; 95% confidence interval [CI], 1.19–5.14). Those born ELBW and SGA exhibited the same patterns with larger effects. ACS-exposed ELBW survivors had even higher odds of any current non–substance-related psychiatric disorder (OR = 4.41; 95% CI, 1.65–11.82), particularly generalized anxiety disorder (OR = 3.42; 95% CI, 1.06–11.06), the generalized type of social phobia (OR = 5.80; 95% CI, 1.20–27.99), and the inattentive subtype of attention-deficit/hyperactivity disorder (OR = 11.45; 95% CI, 2.06–63.50).

**CONCLUSIONS:** In their early to mid-30s, ELBW survivors were less likely to have alcohol or substance use disorders but may be at greater risk for other psychiatric problems. Those exposed to ACS were at especially high risk and manifested no reduction in alcohol or substance use disorders. ELBW survivors exposed to ACS may be a special group at risk for psychopathology in adulthood.

FREE

**WHAT'S KNOWN ON THIS SUBJECT:** Little is known about the mental health of extremely low birth weight survivors in their 30s. It is also unclear whether being born small for gestational age or being exposed to antenatal corticosteroids increases risk in this group.

**WHAT THIS STUDY ADDS:** In their 30s, extremely low birth weight survivors are less likely to have substance problems but are at elevated risk for other psychiatric disorders. Those born small for gestational age are at higher risk, but those exposed to antenatal corticosteroids are at the greatest risk of all.

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Advances in neonatal care have resulted in more infants born at extremely low birth weight (ELBW, <1000 g) surviving into adulthood.[1] Although many ELBW survivors are not affected by significant disabilities,[2] they are at elevated risk for developing psychiatric problems in childhood and adolescence, particularly attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, and social difficulties.[3–7] However, little is known about the extent to which these risks persist into adulthood. Previous studies of very low birth weight (VLBW, <1500 g) survivors in their 20s suggest that they may be at elevated risk for ADHD, mood disorders, anxiety, and social problems[8–12] but are less likely to have alcohol and substance use disorders.[13–16] Although few data exist on the adult mental health of ELBW survivors, these individuals may also be at elevated risk for depression, anxiety, and avoidant personality problems in their early to mid-20s.[17]

Recent data suggest that people born at VLBW or ELBW may not be a homogeneous group in terms of risk. Indeed, studies suggest that VLBW or ELBW survivors born small for gestational age (SGA; birth weight <10th percentile for gestational age) may be at especially high risk for psychopathology, particularly ADHD, depression, and anxiety problems.[17–19] Moreover, despite the fact that antenatal corticosteroid (ACS) administration reduces the risk of morbidity and mortality in premature infants,[20] steroids do cross the placenta and have consequences for brain function in survivors.[21] Although observational studies suggest that fetal exposure to repeated courses of ACS is associated with an elevated risk of ADHD symptoms in childhood,[22,23] randomized controlled trials of ACS have not linked antenatal steroid exposure to mental health problems in the third or fourth decades of life.[24,25] However, these studies contained very few ELBW infants, had high rates of attrition, and relied on self-report questionnaires to ascertain psychiatric outcomes, making it difficult to generalize their findings to those born at ELBW.

The current study uses the oldest longitudinally followed cohort of ELBW survivors in the world and a structured diagnostic interview administered by trained assessors naive to participant birth weight status to compare rates of current and lifetime psychiatric disorders in a cohort of ELBW survivors and normal birth weight (NBW) control participants in their early to mid-30s, determine whether those born ELBW and SGA are at particularly elevated risk, and compare rates of psychiatric disorders in those born at ELBW and exposed to a full course of ACS to NBW control participants.

## METHODS

### Sample

The study cohort consisted of ELBW survivors recruited at birth and NBW control participants enrolled when both groups were 8 years old. A total of 397 mainly Caucasian infants born at <1000 g between 1977 and 1982 in central-west Ontario, Canada were recruited. Of these, 179 (45%) survived to hospital discharge and have been followed longitudinally, with assessments at age 3, 5, 8, 14, 22 to 26, and 29 to 36 years. At age 22 to 26, 142 of 166 survivors participated. Of these individuals, 84 (59.2%) participated in our structured psychiatric interview at the current data collection sweep.

ELBW survivors who had birth weights <10th percentile for gestational age were classified as SGA ($n$ = 26),[26] and the remainder ($n$ = 58) were born at an appropriate weight for gestational age (AGA). Data on ACS status were collected from the medical charts of ELBW survivors at birth. A complete course of steroids was defined as a mother receiving 2 doses of betamethasone (12 mg) administered intramuscularly within a 24-hour period. The mothers of 24 ELBW participants received a complete course of steroids, and 14 received a single dose of betamethasone. We focus in this work on those who received a complete course. Ten participants who were born ELBW and SGA also received ACS.

The age-, gender-, and socioeconomic status (SES)-matched NBW control group consisting of 145 children born at NBW (≥2500 g) has been assessed in tandem with the ELBW cohort at ages 8, 14, 22 to 26, and 29 to 36. Of these, 133 participated at age 22 to 26, and 90 (67.7%) completed the Mini-International Neuropsychiatric Interview (MINI) at age 29 to 36.

### Outcome: Mini International Neuropsychiatric Interview

The MINI is a structured diagnostic interview used to assess psychiatric disorders in a manner consistent with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) and the *International Classification of Diseases, 10th Revision.* It demonstrates very good agreement with the Structured Clinical Interview for DSM-IV disorders and World Health Organization Composite International Diagnostic Interview. Strong interrater reliability is also noted.[27]

We selected disorders common enough to yield reliable comparisons between the birth weight groups, and so some problems assessed by the MINI were omitted (eg, psychotic and eating disorders, antisocial personality disorder, suicidality). Because the main focus of the MINI is current psychiatric disorders, we used a select number of modules from the more comprehensive MINI-Plus.[27] Our final MINI interview assessed the lifetime prevalence of 9 disorders: major depressive disorder (MDD), bipolar disorder, dysthymic disorder, panic disorder, posttraumatic stress disorder, alcohol

abuse and dependence, and substance abuse and dependence. It also assessed current diagnoses of all these lifetime disorders plus social phobia (generalized and nongeneralized types), obsessive–compulsive disorder, generalized anxiety disorder (GAD), and ADHD.

High levels of comorbidity between alcohol and substance abuse and dependence in our sample led us to collapse these conditions into a single category we called "any alcohol or substance use disorder." Because ELBW survivors may have lower rates of alcohol or substance use but elevated rates of other psychiatric problems, we created an additional variable called "any non–substance use disorder" to capture the presence of disorders other than alcohol and substance use problems for both current and lifetime periods.

A minimum prevalence threshold was set for analyzing psychiatric disorders in this work: ≥5 cases total (ELBW plus NBW) were required for study inclusion. This resulted in analyses being conducted for lifetime MDD, bipolar disorder, posttraumatic stress disorder, any alcohol or substance use disorder, and any non–substance use disorder. Current diagnoses of MDD, GAD, generalized social phobia (gSP), panic disorder, inattentive subtype of attention-deficit/hyperactivity disorder (iADHD), any alcohol or substance use disorder, and any non–substance use disorder were also examined. Two trained psychology graduate students naive to participant birth weight group status administered the MINI in a private room in the Psychology Department at McMaster University. The McMaster University Health Sciences Research Ethics Board approved all study procedures.

## Covariates

### *Sociodemographic Variables*

Sociodemographic variables assessed included current self-reported total household income, marital status, and number of years of education. Income was rounded to the nearest 1000 Canadian dollars, marital status was defined as currently having a partner or no partner, and number of years of education was summed.

### *Chronic Health Problems*

Current nonpsychiatric health problems were self-reported and analyzed as a count of illnesses lasting ≥6 months. These were drawn from a list of 16 disorders that included asthma, hypertension, and heart disease.

### *Neurosensory Impairment*

Neurosensory impairment was defined as the presence or absence of ≥1 of cerebral palsy, blindness, deafness, mental retardation, and microcephaly diagnosed in childhood by a developmental pediatrician.

### *Birth Variables*

Data on gender at birth, birth weight, and gestational age were drawn from participants' medical charts.

## Data Analysis

Statistical comparisons of group differences (ELBW versus NBW; ELBW and SGA versus NBW, and ELBW and complete course of ACS versus NBW) used $\chi^2$ tests for categorical variables and independent Student's $t$ tests for continuous variables. Logistic regression was used to estimate the strength of associations between group status and psychiatric diagnoses.

Unadjusted and adjusted statistical models were examined. Unadjusted models contained a group status variable and each psychiatric disorder. This resulted in us comparing ELBW versus NBW, ELBW and SGA versus NBW, and ELBW and ACS versus NBW groups for each psychiatric outcome.

Although ELBW and NBW groups were matched on age, gender, and parental SES at age 8, sample attrition and emerging SES differences between groups could result in confounding. Accordingly, we compared sociodemographic variables between participants and nonparticipants at age 8 (ie, predictors of attrition) and differences between ELBW and NBW participants on similar variables at age 29 to 36. We also compared participants and nonparticipants at this occasion on clinically significant levels of depression, anxiety, antisocial personality, and avoidant personality problems collected at our previous data collection sweep (ie, at age 22 to 26) by using the Young Adult Self-Report measure.[28] Taking into account observed differences in participants and nonparticipants and in birth weight groups at ages 29 to 36 led us to adjust for gender, neurosensory impairment, current total household income, and current marital status in these models. We conducted analyses by using IBM SPSS Statistics 22 (IBM SPSS Statistics, IBM Corporation), and all statistical tests were 2-tailed, with significance levels set at $\alpha = 0.05$.

We imputed missing data for all covariates in our adjusted models by using the fully conditional specification multiple imputation. Ten imputation data sets were generated, and the results of these imputations were integrated into 1 final estimate for each outcome.

## RESULTS

Table 1 contains a summary of the sample characteristics. Eighty-four ELBW survivors and 90 NBW control participants contributed data. Birth weight and gestational age differed between ELBW and NBW groups, and more ELBW participants had neurosensory impairments. Mean household income was higher in NBW control participants than in ELBW survivors and participants with ELBW and ACS. More control participants also had a current partner.

ELBW and NBW participants and nonparticipants at age 29 to 36 were

**TABLE 1** Comparison of Demographic Factors Between Groups at Current Sweep (Age 29–36)

| Characteristic | NBW | ELBW | ELBW and SGA | ELBW and Steroids |
|---|---|---|---|---|
| Number of subjects | 90 | 84[a] | 26[b] | 24 |
| Gender (male), no. (%) | 36 (40) | 31 (37) | 6 (23) | 9 (38) |
| Birth wt, mean (SD), g | 3411 (473) | 829 (132)*** | 823 (133)*** | 825 (119)*** |
| Gestational age, mean (SD), wk | 40 | 27.05 (2.29)*** | 29.58 (1.75)*** | 27.42 (2.17)*** |
| Age, mean (SD), y | 32.46 (1.34) | 32.02 (1.60) | 31.98 (1.53) | 31.21 (1.17)*** |
| Education, mean (SD), y | 16.63 (3.21) | 16.24 (2.78) | 16.29 (3.18) | 16.88 (3.03) |
| Median total household income | $81 104 | $55 000*** | $60 652 | $54 090*** |
| Nonpsychiatric health problems, no. | | | | |
| 0 | 46 | 37 | 10 | 11 |
| 1 | 25 | 25 | 8 | 5 |
| 2+ | 14 | 19 | 7 | 8 |
| Married or common-law, no. (%) | 52 (58) | 34 (40)*** | 12 (46) | 9 (38) |
| Neurosensory impairment, no. (%) | 1 (1) | 23 (27)*** | 4 (15)*** | 5 (21)*** |

[a] 4 ELBW survivors received postnatal steroids.
[b] 10 ELBW and SGA survivors also received ACS.
***$P < .05$ compared with NBW control participants.

compared on variables assessed when these groups were first matched (age 8). Male gender was a predictor of nonparticipation among control participants, and SGA status predicted better participation among ELBW survivors (Table 2). Levels of clinically significant mental disorders at age 22 to 26 did not differ between participants and nonparticipants at the current sweep, although more ELBW survivors than NBW control participants had anxiety problems at that time.

## Current Psychiatric Disorder

In unadjusted models, ELBW survivors had higher odds for any current non–substance use disorder (OR = 2.47; 95% CI, 1.19–5.14) but lower odds of any current alcohol or substance use disorder (OR = 0.38; 95% CI, 0.17–0.86). After adjustment, the ELBW group still had elevated odds for any non–substance use disorder (OR = 2.30; 95% CI 1.01–5.24) and were less likely to have any alcohol or substance use disorder (OR = 0.41; 95% CI, 0.16–1.04; Table 3).

The higher odds of any non–substance use disorder and lower odds of alcohol or substance use disorders were mirrored in comparisons involving ELBW survivors born at SGA and NBW control participants but were of greater magnitude (OR = 3.82; 95% CI, 1.46–10.04 and OR = 0.11; 95% CI, 0.01–0.88). Participants born at ELBW and AGA were not at higher or lower odds for any current disorders (data not shown).

ELBW infants who received a complete course of ACS had higher odds of having any current non–substance use disorder (OR = 4.41; 95% CI, 1.65–11.82), GAD (OR = 3.42; 95% CI, 1.06–11.06), the generalized subtype of social phobia (gSP: OR = 5.80; 95% CI, 1.20–27.99), and iADHD (OR = 11.45; 95% CI, 2.06–63.50). After adjustment, all ELBW and ACS findings remained statistically significant except for GAD. The ELBW and ACS group was not protected against substance or alcohol use disorders, although those born ELBW and not exposed to ACS did have a lower risk (OR = 0.20; 95% CI, 0.08–0.48).

Finally, for ELBW survivors exposed to any dose of steroids (ie, 1 or 2 doses of betamethasone) the odds of having a current disorder were between those of NBW control participants and ELBW survivors receiving a complete antenatal steroid course (eg, OR = 4.39, 95% CI, 0.99–19.43 for gSP; OR = 8.16, 95% CI 1.57–42.50 for iADHD; and OR = 3.79, 95% CI, 2.93–4.92 for any non–substance use disorder), raising the possibility of a dose–response effect. Only 4 ELBW survivors received postnatal steroids, and none of the ELBW and ACS GAD, gSP, or iADHD case participants received these.

**TABLE 2** Demographic Factors of Participants and Nonparticipants at Current Sweep

| Characteristic | Birth Wt Group | Participants | Nonparticipants |
|---|---|---|---|
| Number of participants | Overall | 174 | 150 |
| | NBW | 90 | 55 |
| | ELBW | 84 | 95 |
| Gender (male) | NBW | 36 | 30 |
| | ELBW | 31 | 53* |
| Birth wt, mean (SD), g | NBW | 3411 (473) | 3311 (511) |
| | ELBW | 829 (132) | 844 (114) |
| Gestational age, mean (SD), wk | NBW | 40 | 40 |
| | ELBW | 27.1 (2.3) | 27.0 (2.2) |
| Neurosensory impairment | NBW | 1 | 2 |
| | ELBW | 23 | 28 |
| SGA | NBW | 0 | 0 |
| | ELBW | 26 | 17* |
| Prenatal steroids | NBW | 0 | 0 |
| | ELBW | 46 | 39 |
| Socioeconomic status of household at 8 years of age | NBW | 3 | 3 |
| | ELBW | 3 | 4 |
| Depression at age 22–26 y | NBW | 7/90 | 3/43 |
| | ELBW | 13/84 | 8/59 |
| Anxiety at age 22–26 y | NBW | 5/90 | 3/43 |
| | ELBW | 14/84* | 8/59 |
| Antisocial behavior at age 22–26 y | NBW | 8/90 | 7/43 |
| | ELBW | 7/84 | 6/59 |
| Avoidant personality problems at age 22–26 y | NBW | 11/90 | 2/43 |
| | ELBW | 17/84 | 8/59 |

*$P < .05$ compared with NBW control participants.

**TABLE 3** Current Psychiatric Disorder Risk

| Outcome | No. of Cases | | ELBW | | ELBW and SGA | | ELBW and Steroids | |
|---|---|---|---|---|---|---|---|---|
| | NBW | ELBW | Unadjusted OR (CI) | Fully Adjusted OR (CI) | Unadjusted OR (CI) | Fully Adjusted OR (CI) | Unadjusted OR (CI) | Fully Adjusted OR (CI) |
| Major depressive disorder | 2 | 6 | 3.39 (0.66–17.26) | 1.71 (0.26–11.08) | 1.76 (0.15–20.22) | 1.12 (0.09–13.93) | 2.44 (0.33–18.03) | 1.95 (0.21–18.47) |
| Generalized anxiety disorder | 8 | 9 | 1.23 (0.45–3.35) | 0.90 (0.28–2.90) | 1.34 (0.33–5.45) | 1.10 (0.23–4.52) | 3.42 (1.06–11.06)* | 2.34 (0.58–9.52) |
| Social phobia (generalized subtype) | 3 | 6 | 2.23 (0.54–9.22) | 2.32 (0.52–10.27) | 1.16 (0.12–11.65) | 1.02 (0.10–10.74) | 5.80 (1.20–27.99)* | 5.90 (1.05–33.03)* |
| Panic disorder | 1 | 6 | 6.78 (0.80–57.57) | 6.56 (0.69–62.12) | 3.48 (0.21–57.65) | 2.98 (0.17–52.76) | 7.91 (0.69–91.25) | 6.41 (0.50–81.63) |
| Obsessive–compulsive disorder | 3 | 4 | 1.45 (0.32–6.68) | 0.91 (0.14–6.16) | 0 | 0 | 1.61 (0.26–10.05) | 0.78 (0.06–10.84) |
| ADHD (inattentive subtype) | 2 | 8 | 4.58 (0.94–22.22) | 7.37 (0.80–68.11) | 5.67 (0.90–35.99) | 4.98 (0.72–34.69) | 11.45 (2.06–63.50)* | 10.20 (1.61–64.56)* |
| Any alcohol or substance use disorder | 23 | 10 | 0.38 (0.17–0.86)* | 0.41 (0.16–1.04) | 0.11 (0.01–0.88)* | 0.13 (0.02–1.04)* | 0.74 (0.25–2.22) | 0.74 (0.22–2.46) |
| Any non–substance use disorder | 14 | 27 | 2.47 (1.19–5.14)* | 2.30 (1.01–5.24)* | 3.82 (1.46–10.04)* | 3.83 (1.21–9.46)* | 4.41 (1.65–11.82)* | 3.71 (1.25–10.99)* |

*$P < .05$ compared with NBW control participants.

### Lifetime Psychiatric Disorder

In our unadjusted models, ELBW survivors (OR = 0.32; 95% CI, 0.17–0.61) and those born SGA (OR = 0.23; 95% CI, 0.08–0.66) had lower odds than NBW control participants of any lifetime alcohol or substance use disorder (Table 4). Those born at ELBW or AGA (OR = 0.42; 95% CI, 0.18–0.97) and ELBW survivors not exposed to ACS (OR = 0.25; 95% CI, 0.10–0.68) were also at lower risk. These findings persisted despite adjustment for covariates (Table 4). These lower odds were not seen in the ELBW and ACS group. The absence of an elevated lifetime risk for any non–substance use disorder was probably a result of the fact that the disorders in this category (current ADHD, current anxiety disorders) were not assessed by the MINI for the lifetime period.

## DISCUSSION

Assessing the oldest known longitudinally followed cohort of ELBW survivors using structured psychiatric diagnostic interviews, we report that the odds of people born at ELBW having a clinically significant psychiatric problem were twice as high as those of NBW control participants. However, ELBW survivors had lower odds of having a current or lifetime alcohol or substance use disorder. The only ELBW subgroup that was not protected against substance use disorders was the one exposed to a full course of ACS. This ELBW and ACS group also had higher odds of a current psychiatric disorder and 3 times the odds of a current diagnosis of GAD, were 6 times more likely to have gSP, and had 11 times the odds of having iADHD.

Our findings are consistent with studies that have shown that VLBW or ELBW survivors are less likely to develop problems with alcohol and other substances.[13–16] This risk reduction may result from their cautious, shy, risk-avoidant personality style,[11,29] higher parental monitoring earlier in life,[16] or a later manifestation of their tendency to show lower levels of externalizing behavior in childhood and adolescence.[9,15,30]

The finding that ELBW survivors were more likely to have a current non–substance use related psychiatric disorder is also in keeping with studies of VLBW survivors in adulthood.[8–12] The etiologic factors contributing to this finding are complex and multifactorial, and they probably interact. These factors include prenatal insults leading to preterm birth and exposure to stressful neonatal experiences, both of which could lead to brain changes and dysregulation of the hypothalamic–pituitary–adrenal axis.

Although we did find that ELBW survivors born SGA were at elevated odds of any psychiatric disorder, they were not at especially high risk of any 1 disorder except iADHD. Though at odds with previous studies that have suggested that VLBW or SGA survivors may be at elevated risk of depression,[19] these studies did not use structured diagnostic interviews. However, our lack of statistically significant risks for specific psychiatric disorders may result from the small number of SGA survivors in our study.

Our most novel findings were those of ELBW survivors whose mothers received a complete course of ACS. We are the first to report that not only are steroid-exposed ELBW survivors not protected against alcohol and substance use disorders, but they may have higher odds of developing GAD, gSP, and iADHD. Interestingly, these odds increased with increasing steroid exposure (eg, risks for a complete ACS course > any ACS exposure > NBW control participants). Although our findings appear to be at odds with the results of randomized controlled trials of people exposed to ACS or placebo,[24,25] those studies contained

**TABLE 4** Lifetime Psychiatric Disorder Risk

| Outcome | No. of Cases | | ELBW | | ELBW and SGA | | ELBW and Steroids | |
|---|---|---|---|---|---|---|---|---|
| | NBW | ELBW | Unadjusted OR (CI) | Fully Adjusted OR (CI) | Unadjusted OR (CI) | Fully Adjusted OR (CI) | Unadjusted OR (CI) | Fully Adjusted OR (CI) |
| Major depressive disorder | 23 | 21 | 1.02 (0.51–2.03) | 0.71 (0.32–1.57) | 1.35 (0.51–3.55) | 0.78 (0.30–2.03) | 1.06 (0.45–2.53) | 0.81 (0.27–2.45) |
| Bipolar disorder | 10 | 8 | 0.84 (0.32–2.25) | 0.78 (0.25–2.41) | 1.04 (0.27–4.11) | 0.94 (0.21–4.23) | 1.14 (0.29–4.53) | 1.05 (0.23–4.80) |
| Posttraumatic stress disorder | 3 | 6 | 2.23 (0.54–9.22) | 2.10 (0.43–10.33) | 0 | 0 | 2.49 (0.48–12.91) | 2.53 (0.35–18.36) |
| Any alcohol or substance use disorder | 45 | 21 | 0.32 (0.17–0.61)* | 0.37 (0.18–0.79)* | 0.23 (0.08–0.66)* | 0.29 (0.09–0.89)* | 0.57 (0.23–1.45) | 0.68 (0.24–1.91) |
| Any non–substance use disorder | 32 | 34 | 1.03 (0.55–1.92) | 0.71 (0.34–1.47) | 1.11 (0.45–2.74) | 0.83 (0.32–2.16) | 1.27 (0.51–3.19) | 0.84 (0.31–2.32) |

*$P < .05$ compared with NBW control participants.

very few ELBW participants. However, observational studies of infants born at VLBW have also not shown an effect of ACS on mental disorders up to 14 years of age,[31] and so our findings must be replicated.

The brains of people born preterm are marked by widespread alterations in regions known to be altered in those with psychiatric disorders including the frontal cortex,[32] hypothalamic–pituitary–adrenal axis,[33] and hippocampus.[34] Corticosteroids administered antenatally cross the placenta, and receptors for glucocorticoids are highly expressed in the limbic region (particularly the hippocampus), making it especially susceptible to ACS effects.[35,36] These areas play a vital role in the development of emotion, behavior, and cognition,[35,37] and they may be where ACS act to amplify brain changes present in ELBW survivors.

Previous research has also shown that fetuses treated prenatally for congenital adrenal hyperplasia early in gestation with dexamethasone manifest reduced sociability and increased shyness in childhood.[38] ACS has also been linked to volume reductions in neuroanatomical regions known to be altered in ADHD (eg, the corpus callosum).[39,40] A recent study of 2-year-olds exposed to repeated courses of ACS has also found an elevated risk of attention problems,[22] and levels of distractible and hyperkinetic behavior were elevated in a separate study of children exposed to multiple courses of ACS at both 3 and 6 years of age.[23] Thirty-two percent of children who received ≥3 courses of ACS scored above the 90th percentile on these scales, compared with 12% of those who were not, suggesting that the impact of ACS on ADHD may be dose-dependent.[23]

It is important that our findings be interpreted with the following limitations in mind. First, although our ELBW and NBW samples were age, gender, and SES matched at age 8, and the participants in the current sweep are not very different from those lost to follow-up, our sample has undergone attrition over the past 30 years. Moreover, although our sample size is adequate to highlight a number of important findings, it does limit the statistical power available to detect other clinically important differences between groups in adulthood. Furthermore, our sample was born at a time when the survival rate of ELBW infants was lower and when SGA survivors, on average, had a higher gestational age and therefore a better chance of survival. Finally, they were born before the use of surfactant and grew up in a developed country (Canada) where medical care and education are universally available.

## CONCLUSIONS

Unfortunately, ELBW survivors who may benefit significantly from ACS at birth and in the neonatal period may be at an elevated risk of psychopathology in later life. However, it is important to stress that ACS is a lifesaving intervention, and even if our findings are replicated, we would advocate for close follow-up of these individuals rather than avoidance of ACS by women presenting with threatened preterm birth.

Future work is needed to replicate our ELBW and ACS survivors' results in adulthood and to elucidate the psychosocial and biological pathways underlying our findings. Understanding the specific types of problems ELBW survivors are at risk for can help us better predict, detect, and treat mental disorders in this group and provide us with valuable insights into the pathogenesis of these conditions.

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