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ORIGINAL ARTICLE

Extremely preterm birth and adolescent mental health in a geographical cohort born in the 1990s

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Background. Preterm birth confers risk for poor outcome, including mental health problems. Survival of extremely preterm (EP; <28 weeks' gestation) or extremely low birthweight (ELBW; <1000 g) infants increased in the 1990s but psychiatric outcomes in older adolescents born preterm since 1990 are not well documented. This study aimed to characterize mental health and personality traits in a prospective geographical cohort of adolescents born EP/ELBW in Victoria, Australia in 1991 and 1992.

Method. At age 18 years, 215 EP/ELBW and 157 normal birthweight (>2499 g) control adolescents completed the Structured Clinical Interview for DSM-IV Disorders, Axis 1 Non-Patient version (SCID-I/NP), the Children's Interview for Psychiatric Syndromes (ChIPS) attention deficit hyperactivity disorder (ADHD) module, and questionnaires assessing recent depression and anxiety symptoms and personality traits.

Results. ADHD prevalence was significantly elevated in EP/ELBW adolescents compared with controls [15% *v.* 7%; odds ratio (OR) 2.67, 95% confidence interval (CI) 1.08–6.58]. Aside from ADHD, however, EP/ELBW and control adolescents reported very similar outcomes, with other lifetime diagnoses identified in 23% of EP/ELBW and 21% of controls. These were predominantly mood and anxiety disorders (21% EP/ELBW, 20% controls). The groups did not differ in recent depression or anxiety symptoms assessed using questionnaires, and personality traits were also similar.

Conclusions. ADHD was more prevalent in EP/ELBW adolescents than controls, which is consistent with some, but not all, reports on preterm survivors born before the 1990s, and younger preterm children born in the 1990s. The high rates of anxiety and mood disorders were similar in both groups, and comparable with population-based estimates.

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Introduction

Preterm birth is associated with an increased risk of poor outcome (Saigal & Doyle, 2008), with extremely preterm (EP; <28 weeks' gestation) and extremely low birthweight (ELBW; <1000 g) survivors generally at higher risk than moderate to late preterm infants (32–36 weeks' gestation) (Johnson, 2007). Although the focus has largely been on physical and cognitive outcomes, growing evidence suggests that preterm survivors may also be more vulnerable to poor mental health and emotional functioning (Crump *et al.* 2010; Nosarti *et al.* 2012).

In the early 1990s, the survival of EP/ELBW infants increased dramatically with the introduction of surfactant therapy, which reduced the severity of hyaline membrane disease, a common cause of death of EP/ELBW infants (Victorian Infant Collaborative Study Group, 1997*a*). Although childhood disability has fallen in comparison with the pre-surfactant era, neurosensory impairments remain more common in EP/ELBW children than in term (>36 weeks) or normal birthweight (>2499 g) controls, indicating that adverse

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sequelae of extreme prematurity continue to affect this population (Doyle *et al.* 2005). The oldest EP/ELBW infants of the 1990s are now in late adolescence, a high-risk period for mental illnesses such as mood and anxiety disorders in the general population (Kessler *et al.* 2005; ABS, 2007). Importantly, assessment in the adolescent period can also identify disorders with earlier onset (e.g. attention deficit hyperactivity disorder, ADHD). Adolescent mental health outcomes for the EP population born in the 1990s have not been well described, and are likely to provide insights relevant to more contemporary EP/ELBW cohorts.

It is well recognized that attention problems and diagnoses of ADHD are more common in preterm children than in their term-born peers (Bhutta *et al.* 2002; Aarnoudse-Moens *et al.* 2009; Johnson *et al.* 2010; Anderson *et al.* 2011). In the general population, ADHD prevalence declines with increasing age (Polanczyk *et al.* 2007), but reports of ADHD diagnoses or symptoms into young adulthood are relatively sparse for preterm samples (Lund *et al.* 2011). In one study of young adults born before the 1990s, 20-year-olds with very low birthweight (VLBW; <1500 g) were similar to controls on both symptoms of ADHD and diagnosis prevalence (Hack *et al.* 2004). Although parents reported more inattentive symptoms among VLBW young men, this difference disappeared after excluding those born small for gestational age (SGA; birthweight $\geqslant 2$ S.D. below the mean for gestational age and gender) (Hack *et al.* 2004). Indeed, some data suggest that preterm young adults who were not SGA have similar levels of ADHD symptoms to controls (Strang-Karlsson *et al.* 2008). However, the prevalence of ADHD in older adolescents born in the 1990s is unknown.

In general, assessment of emotional functioning in preterm children and adolescents has used pencil-and-paper questionnaires and screening measures, such as the Child Behavior Checklist (CBCL). Parent reports of childhood emotional functioning abound, although the effects described in this population are heterogeneous (Aarnoudse-Moens *et al.* 2009). Studies in adolescence allow teenagers to express their own emotional functioning, and indeed, they may have different views to their parents. Our current knowledge of preterm adolescent outcomes by necessity comes from children born before 1990. Some of these studies have found elevated internalizing symptoms by parent report, but not by self-report (Saigal *et al.* 2003; Grunau *et al.* 2004; Indredavik *et al.* 2005; Hallin & Stjernqvist, 2011), although conflicting data exist (Gardner *et al.* 2004; Hille *et al.* 2008). Although parents may perceive more mood and anxiety symptoms in their preterm children, it is less clear whether preterm adolescents themselves endorse such difficulties.

Personality traits, such as temperamental affectivity and sensitivity to reward and punishment, are an important component of individuals' social functioning (Eisenberg *et al.* 2000) and may also be considered risk factors for psychopathology (Krueger, 1999). Differences have been reported on this issue in preterm samples, with very preterm (VP; <30 weeks)/VLBW and ELBW young adults born before the 1990s displaying less extraversion, less openness to experience and more shyness and conscientiousness than controls (Allin *et al.* 2006; Pesonen *et al.* 2008; Schmidt *et al.* 2008). Preterm samples may also engage less in risk-taking behaviors than their peers (Hille *et al.* 2008). This is consistent with reports of greater internalizing and other emotional difficulties outlined previously. Despite this, the picture remains unclear; in a study of youth born <1500 g, the preterm and control groups differed only on some facets of neuroticism and extraversion, but not on those two personality dimensions overall (Pesonen *et al.* 2008). Furthermore, data from the same sample suggested similarities in trait inhibition and at least some aspects of reward sensitivity between preterm and control young adults (Pyhälä *et al.* 2009).

Compared with the many studies using questionnaires, studies using psychiatric diagnostic tools are, to our knowledge, non-existent in EP/ELBW adolescents born in the 1990s. A few studies have assessed younger children born since 1990, and there are some adolescent studies in lower-risk subjects (i.e. those more mature or heavier at birth) who were born pre-1990. At a population level, linkage studies using population-wide registers have indicated an increased risk of hospital admission, out-patient diagnosis and pharmacotherapy prescription in preterm youth and adults for psychiatric diagnoses in Scandinavian countries (Lindström *et al.* 2009; Abel *et al.* 2010; Crump *et al.* 2010; Nosarti *et al.* 2012), but again these subjects were born pre-1990. Meta-analytic evidence from case–control studies of preterm children and youth similarly indicates elevated overall risk [odds ratio (OR) 3.7, 95% confidence interval (CI) 2.7–5.2], including mood or anxiety disorders (Burnett *et al.* 2011). Data from VLBW adults born before the 1990s indicate a smaller (although still significant) increase in current mood disorder (risk ratio 1.4, 95% CI 1.2–1.5), but no difference in other disorders (Westrupp *et al.* 2011). With respect to more recent birth cohorts, parental reports on the Development and Well-Being Assessment (DAWBA) also indicate increased disorder prevalence in preterm children born in the 1990s and 2000s (Johnson *et al.* 2010; Treyvaud *et al.* 2013). In a large UK cohort born in 1995, 11-year-olds born <26 weeks' gestation had higher rates of ADHD and anxiety disorders, based

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on parental report (Johnson *et al.* 2010). Of note, co-morbid disorders were not more common in the preterm children assessed by Johnson *et al.* (2010) and Treyvaud *et al.* (2013). As noted earlier, adolescence is a peak onset period for many mental illnesses and is also a time when self-report becomes more reliable in identifying mental disorders. It is unclear whether preterm children born in the 1990s are more at risk of clinically diagnosable disorders as adolescents, and this represents an important extension to assessment using dimensional measures.

In addition to SGA status, a range of variables have been linked with poor behavioral and emotional outcomes in preterm children and adolescents. In studies of EP and VP children born after 1990, infant brain abnormalities, social risk and earlier behavioral or emotional difficulties have been linked with subsequent psychiatric disorder (Johnson *et al.* 2010; Treyvaud *et al.* 2013). Pre-1990s data also suggest a link between infant brain abnormalities and later psychiatric symptoms or disorder (Whitaker *et al.* 1997, 2011), although not in all reports (Elgen *et al.* 2002). In both pre- and post-1990 cohorts, other infant illness factors seem to be poorer predictors of preterm children's psychiatric outcomes than measures of their behavior and adjustment in the years prior to assessment (Elgen *et al.* 2002; Johnson *et al.* 2010; Treyvaud *et al.* 2013).

Given the paucity of data relating to long-term outcomes for the post-1990 EP/ELBW population, the current study aimed to characterize self-reported psychiatric outcomes in older adolescents born EP/ELBW in the 1990s, including both diagnostic and dimensional information. Consistent with pre-1990 data, and data from younger children born since that time, we hypothesized that the EP/ELBW group would have higher rates of clinically diagnosable disorders and more symptoms (on questionnaires) than controls. We also expected that EP/ELBW adolescents would endorse less sensitivity to reward, more sensitivity to punishment, lower typical positive affect, higher typical negative affect and less antisocial personality traits than controls. Associations of infant, child behavior/cognition and social variables with EP/ELBW adolescent disorders were also examined. We expected that variables from the neonatal period would not be strong predictors of disorders but that poorer childhood functioning would be associated with disorders at age 18 years.

Method

Participants

Participants were derived from a geographic cohort comprising 298 consecutive survivors born EP/ELBW in the state of Victoria, Australia, during 1991 and 1992, and 262 normal birthweight (>2499 g) controls, matched at the group level for mother's country of origin (English-speaking or not) and health insurance status, and sex of the child. All participants were recruited at birth. The EP/ELBW cohort was born largely after exogenous surfactant was introduced into Australian clinical practice in March 1991. This cohort has been previously assessed at ages 2, 5 and 8 (Victorian Infant Collaborative Study Group, 1997*b*; Doyle & Victorian Infant Collaborative Study Group, 2001; Anderson & Doyle, 2003; Doyle *et al.* 2010). The participants' average age at the present assessment was 18 years, and 215 (72%) EP/ELBW and 157 (60%) control adolescents provided data for the measures of interest. The EP/ELBW group included participants born SGA to facilitate comparisons with previous literature. The Human Research Ethics Committees of the Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre and Royal Children's Hospital, Melbourne, provided ethical approval for the original and follow-up studies. All participants provided informed consent; if they were aged <18 years, consent was also obtained from their parents.

Measures and procedure

Mental health in late adolescence was assessed using standardized face-to-face clinical interview and questionnaires. The ADHD module of the Children's Interview for Psychiatric Syndromes (ChIPS; Weller *et al.* 1999) was used to assess ADHD (inattentive, hyperactive/impulsive and combined subtypes). The Structured Clinical Interview for DSM-IV Disorders, Axis 1 Non-Patient version (SCID-I/NP; First *et al.* 2002) was used to assess lifetime history of major DSM-IV Axis I disorders (mood, anxiety, substance use, psychotic, eating and adjustment disorders) (APA, 2000), and was administered by five trained interviewers blinded to group. Experienced consultant psychiatrists, also blinded to group, were consulted extensively and consensus diagnoses were reached for all participants. These assessments were supplemented by questionnaires examining recent anxiety and depression symptoms: the Beck Anxiety Inventory (BAI; Beck & Steer, 1990) and the Center for Epidemiologic Studies Depression Scale – Revised (CESD-R; Eaton *et al.* 2004). Personality traits such as sensitivity to reward/punishment [Behavioral Inhibition/Activation Systems (BIS/BAS) scales (Carver & White, 1994)], typical positive and negative affectivity [Positive and Negative Affect Schedule (PANAS; Watson *et al.* 1988)] and antisocial personality traits [a version of the Antisocial Process Screening Device (APSD;

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Frick & Hare, 2001) adapted to self-report] were also assessed. IQ was estimated with the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999).

Data collected in infancy and middle childhood were also included. In addition to gestational age, birthweight, sex and maternal age at birth, neonatal variables included major brain injury on neonatal cranial ultrasound (grade 3/4 intraventricular hemorrhage or cystic periventricular leukomalacia), postnatal corticosteroid treatment or major neonatal surgery, as we previously identified adverse long-term neurosensory outcomes associated with these three variables in this cohort at age 5 (Doyle, 2001). Demographic and other factors that may be associated with behavioral and emotional outcomes were also included. Specifically, at age 8, parents completed the Behavior Assessment System for Children (BASC), which provides indices for internalizing problems, externalizing problems, adaptive skills and behavioral symptoms [the Behavioral Symptoms Index (BSI), reflecting atypical behaviors and social withdrawal]. Parental occupation was used as an indication of family socio-economic status (SES) and dichotomized into lower/higher groups (Congalton, 1969). Parental education was also recorded. Age-8 major disability was defined as any of an IQ < −2 S.D. relative to controls, moderate or severe cerebral palsy, blindness or deafness.

Data analysis

Group comparisons of background variables were analyzed using χ^2 (categorical data) and two-tailed *t* tests, or the Mann–Whitney *U* test, with *z* scores reported where parametric assumptions were violated (continuous data). Disorder prevalence in the EP/ELBW and control groups was compared using logistic regression (univariable and adjusting for sex and demographic differences). Some participants had missing questionnaire items. Where only a few items were missing (BAI: <5; CESD-R: <6; BIS/BAS: <2/subscale; PANAS: <4/subscale), the within-subject mean was substituted for the missing item/s. Group comparisons for these data were also conducted using two-tailed *t* tests, or the Mann–Whitney *U*, with *z* scores reported, as above. Within the preterm group, univariable relationships between historical variables and major disorder classes were examined using logistic regression. Data were analyzed using SPSS version 20 (IBM Corp., USA).

Results

Sample characteristics and loss to follow-up

At age 18, EP/ELBW participants and non-participants were similar on perinatal variables (Table 1). Of the EP/ELBW group, those who participated at age 18 had higher childhood SES (χ^2_1=4.22, p=0.04) but similar parent ratings on BASC indices at age 8 compared with non-participants (all p>0.05). Those who participated also had lower rates of major disability at age 8 than those who did not participate at 18 years (χ^2_1=13.84, p<0.001); some adolescents were unable to complete the interviews because of difficulties understanding the questions (n=5).

Among the controls, females were more likely to participate than males (χ^2_1=7.02, p=0.008), as were those whose parents had completed high school (mothers: χ^2_1=11.90, p=0.001; fathers: χ^2_1=8.58, p=0.003). Participants had lower rates of major disability in childhood than non-participants (χ^2_1=5.46, p=0.02). Participants had older mothers (t_{260}=2.89, p=0.004) and better childhood emotional/behavioral functioning (internalizing: t_{213}=−3.17, p=0.002; externalizing: z=−1.92, p=0.05; adaptive: t_{213}=3.18, p=0.002; BSI: z=−2.45, p=0.01) than non-participants.

Among those who participated at age 18, the EP/ELBW and control groups had similar sex distributions and ages. Compared with controls, EP/ELBW teenagers had a lower mean IQ at 18 years (z=−6.78, p<0.001), and more often had lower childhood SES (χ^2_1=5.76, p=0.02) and parents who had not completed secondary schooling (mothers: χ^2_1=12.55, p<0.001; fathers: χ^2_1=19.29, p<0.001). At age 8, the EP/ELBW group had more parent-reported internalizing symptoms, poorer adaptive skills and more behavioral symptoms than controls (t_{349}=3.49, p=0.001; t_{347}=−3.26, p=0.001; and z=2.70, p=0.007 respectively).

Disorder prevalence (Table 2)

ADHD was more frequent among EP/ELBW adolescents than controls but group differences in specific subtypes did not reach significance, probably because subgroup numbers were small. More than 20% of participants met criteria on the SCID-I/NP for a lifetime diagnosis of one or more mental illnesses, and this overall prevalence was similar across the two groups. Mood and anxiety disorders were most frequent, identified in around a fifth of each group, but individual diagnoses within those categories were less common. Although expected sex differences were apparent (i.e. more females meeting criteria than males; 25% *v.* 14%, p=0.009), there was no group-by-sex interaction (interaction p=0.81). Substance use, psychotic and eating disorders were infrequent in both groups. Co-morbid disorders were not more frequent among EP/ELBW adolescents than controls (44% *v.* 42% of those with any diagnosis, χ^2_1=0.06, p=0.80). ADHD was frequently co-morbid

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Table 1. *Characteristics of EP/ELBW and control participants and non-participants*[a]

	EP/ELBW		Control	
	Seen (n=215)	Not seen (n=83)	Seen (n=157)	Not seen (n=105)
Perinatal				
Gestational age (weeks), mean (S.D.), range	26.6 (2.0), 23–34	26.9 (1.7), 23–32	39.2 (1.5)[d], 35–42	39.2 (1.4), 35–42
Birthweight (g), mean (S.D.), range	889 (159), 480–1330	885 (166), 430–1458	3408 (460)[d], 2515–4320	3341 (409), 2545–4150
Female, % (n)	55 (119)	49 (41)	59 (92)	42 (44)[e]
Singleton, % (n)	68 (146)	73 (61)	99 (155)[d]	94 (99)
Major neonatal brain injury[b] % (n)	10 (22)	12 (10)	0 (0)[d]	0 (0)
SGA, % (n)	16 (34)	14 (12)	0.6 (1)[d]	0 (0)
Postnatal corticosteroids, % (n)	31 (67)	37 (31)	0 (0)[d]	0 (0)
Neonatal surgery, % (n)	26 (55)	27 (22)	0 (0)[d]	0 (0)
Maternal age (years), mean (S.D.)	28.9 (6.0)	27.7 (5.3)	29.9 (4.9)	28.0 (5.5)[e]
Mother completed high school, % (n)	50 (104/208)	41 (25/61)	69 (105/153)[d]	44 (30/68)[e]
Father completed high school, % (n)	44 (84/193)	33 (18/55)	68 (98/145)[d]	46 (29/63)[e]
Age 8 years				
BASC Internalizing, mean (S.D.)	49.6 (10.9)	52.0 (12.2)	45.7 (9.5)[d]	50.6 (12.1)[e]
BASC Externalizing, mean (S.D.)	49.8 (11.9)	50.9 (9.9)	47.7 (9.1)	51.8 (13.3)[e]
BASC Adaptive skills, mean (S.D.)	48.7 (10.5)	45.7 (10.7)	52.2 (9.5)[d]	47.4 (11.4)[e]
BASC Behavioral symptoms, mean (S.D.)	50.8 (12.1)	52.5 (10.4)	47.2 (10.1)[d]	52.1 (13.7)[e]
Major disability, % (n)	13 (28)	32 (25)[c]	2 (3)[d]	8 (7)[e]
Higher SES, % (n)	60 (124/207)	45 (28/62)[c]	72 (111/154)[d]	66 (46/70)
Age 18 years				
Age at assessment (years), mean (S.D.); corrected for prematurity	17.9 (0.9)	N.A.	18.1 (0.8)	N.A.
Full-scale IQ, % (n)	96 (16)	N.A.	107 (13)[d]	N.A.

EP, Extremely preterm; ELBW, extremely low birthweight; S.D., standard deviation; SGA, small for gestational age (birthweight $\geqslant$2 S.D. below the mean for gestational age and gender); BASC, Behavior Assessment System for Children; SES, socio-economic status; N.A., not applicable.

[a] Group ns vary because of missing data.

[b] Grade 3/4 intraventricular hemorrhage/cystic periventricular leukomalacia.

[c] Within the EP/ELBW group, participants and non-participants significantly different.

[d] Within participants, EP/ELBW group and controls significantly different.

[e] Within controls, participants and non-participants significantly different.

Significance level: $p<0.05$.

with other diagnoses, although this was similar in the EP/ELBW and control groups (interaction p=0.16). Adjustment for gender, parental education and childhood SES did not alter the pattern of results for the key outcomes.

Dimensional measures of emotional functioning (Table 3)

The adolescents' self-reports on dimensional measures of recent depression, recent anxiety and personality traits were similar across groups (all $p>0.05$), although scores reflecting antisocial personality traits were lower in the EP/ELBW group than controls (p=0.047).

Associations of 18-year EP/ELBW outcomes with neonatal and childhood variables (Table 4)

There was little evidence that neonatal medical morbidity was related to disorder at age 18. Childhood variables at 8 years were more relevant to outcome at 18 years; parent-rated externalizing, atypical behaviors

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Table 2. *Disorder prevalence in EP/ELBW and control adolescents*

Disorder	EP/ELBW (n=205)	Control (n=154)	OR (95% CI)	Adjusted OR (95% CI)
Any ADHD diagnosis	15 (30[a])	7 (11[a])	2.23 (1.08–4.60)*	2.67 (1.08–6.58)*
ADHD combined type	3 (7)	1 (2[a])	2.67 (0.55–13.03)	4.90 (0.56–43.24)
ADHD inattentive type	11 (22[a])	6 (9[a])	1.93 (0.86–4.33)	2.09 (0.78–5.63)
ADHD hyperactive/impulsive type	0.5 (1)	0 (0[a])	–	–
Any SCID-I/NP diagnosis	23 (47)	21 (32)	1.39 (0.86–2.24)	1.16 (0.67–2.04)
Any anxiety or mood disorder	21 (43)	20 (31)	1.05 (0.63–1.77)	1.08 (0.61–1.91)
Any mood disorder	16 (33)	15 (23)	1.09 (0.61–1.95)	0.96 (0.51–1.84)
Major depressive disorder	14 (28)	12 (19)		
Current major depressive episode	4 (8)	2 (3)		
Past major depressive episode	13 (26)	12 (18)		
Bipolar disorder	0.5 (1)	0.6 (1)		
Dysthymic disorder[b]	3 (6)	2 (3)		
Depressive disorder NOS	0.5 (1)	0 (0)		
Past mood disorder due to GMC	0 (0)	0.6 (1)		
Any anxiety disorder	11 (23)	10 (16)	1.09 (0.56–2.14)	1.11 (0.53–2.33)
Generalized anxiety disorder[b]	5 (10[a])	4 (6)		
Social phobia	1 (2)	1 (2)		
Specific phobia	4 (8[a])	0.6 (1)		
Post-traumatic stress disorder	1 (3[a])	2 (3)		
Panic disorder	2 (5)	0.6 (1)		
Agoraphobia	0.5 (1)	0.6 (1)		
Obsessive–compulsive disorder	2 (4)	3 (4)		
Anxiety NOS	1 (3)	0 (0)		
Co-morbid anxiety and mood disorder	6 (13)	5 (8)	1.24 (0.50–3.06)	0.90 (0.34–2.41)
Current/past substance use disorder	4 (9[a])	3 (5)		
Psychotic disorders	0 (0)	0.6 (1)		
Current eating disorder	2 (4[a])	0.6 (1)		
Past eating disorder	0.5 (1[a])	0.6 (1)		

EP, Extremely preterm; ELBW, extremely low birthweight; ADHD, attention deficit hyperactivity disorder; SCID-I/NP, Structured Clinical Interview for DSM-IV Disorders, Axis I Non-Patient version; NOS, not otherwise specified; GMC, general medical condition; OR, odds ratio; CI, confidence interval.

Adjusted model includes sex, parental education and childhood socio-economic status (SES) as covariates.

[a] Data missing for n=1.

[b] Current disorder only. No diagnoses of: current mood disorder due to GMC; current/past substance-induced mood disorder; anxiety disorder due to GMC; substance-induced anxiety disorder; adjustment disorder.

Final solution not possible for ADHD hyperactive/impulsive type because of small numbers.

Data given as percentage of group (n).

* p<0.05.

and adaptive skills, in addition to major disability, were associated with ADHD diagnosis, although not mood or anxiety disorders. Higher paternal education was associated with higher odds of mood/anxiety disorders at 18 years, although this was not the case for maternal education or family SES.

Discussion

This study describes mental health outcomes in a cohort of EP/ELBW and NBW control adolescents born in 1991 and 1992. As predicted, ADHD was more prevalent among EP/ELBW adolescents, who were around twice as likely to receive this diagnosis as controls. In the EP/ELBW group, childhood behavior ratings and disability were related to 18-year ADHD diagnoses. Other diagnoses identified were predominantly mood and anxiety disorders, but in contrast to previous reports, the EP/ELBW and control groups had similar rates. Both groups had low rates of substance use, eating and psychotic disorders, and rates of co-morbidity did not differ between EP/ELBW and control adolescents. Assessment of recent depression and anxiety symptoms and personality traits did not reveal group differences, with the exception of fewer antisocial personality traits in EP/ELBW adolescents than controls.

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Table 3. *Dimensional measures of emotional functioning in EP/ELBW and control adolescents*

	Possible range	EP/ELBW		Control		Statistics
		n	Mean (S.D.)	*n*	Mean (S.D.)	
Beck Assessment Inventory (BAI)[a]	0–63	194	8.5 (9.6)	146	7.6 (8.2)	$z=-0.16$
Center for Epidemiologic Studies Depression Scale – Revised (CESD-R)[a]	0–80	191	11.2 (13.5)	148	10.1 (9.4)	$z=-0.54$
Behavioral Inhibition System (BIS)	7–28	192	19.8 (3.8)	148	19.8 (3.6)	$t_{338}=-0.03$
Behavioral Activation System (BAS)						
Drive	4–16	193	9.7 (2.6)	148	10.2 (2.3)	$t_{339}=-1.86$
Reward responsiveness	5–20	192	16.8 (2.2)	148	16.6 (2.2)	$t_{338}=1.10$
Fun-seeking[a]	4–16	192	11.5 (2.3)	148	12.1 (1.9)	$z=-1.92$
Positive and Negative Affect Schedule (PANAS)						
Positive affect[a]	10–50	191	34.3 (7.7)	146	34.5 (6.6)	$z=-0.07$
Negative affect[a]	10–50	191	19.1 (7.7)	146	18.5 (5.9)	$z=-0.21$
Antisocial Process Screening Device (APSD) total	0–40	188	9.4 (4.6)	145	10.4 (4.7)	$t_{331}=-2.00$*

EP, Extremely preterm; ELBW, extremely low birthweight; S.D., standard deviation.
[a] *z* scores for the Mann–Whitney *U* test.
* $p<0.05$.

The elevated ADHD prevalence found here is consistent with findings in preterm children born pre-1990 (Bhutta *et al.* 2002), and extends the limited data on ADHD in older EP/ELBW adolescents. The 15% prevalence identified is in accordance with data from VLBW 20-year-olds born pre-1990 (Lund *et al.* 2011), suggesting that this may be a stable finding among preterm youth despite differences in neonatal medical care, and the higher survival rate of EP/ELBW adolescents. With regard to subtypes, diagnoses were predominantly inattentive-type ADHD. Group differences did not reach significance for subtypes, possibly because of the small subtype samples. Our findings were also similar to other post-1990 cohorts assessed in childhood, including Johnson *et al.*'s (2010) report of primarily inattentive-type ADHD among EP 11-year-olds. Importantly, the increased prevalence identified in our sample was not predicted by SGA status. This suggests that EP/ELBW survivors born in the surfactant era remain at risk for attention problems, despite having appropriate birthweight for their gestational age.

ADHD in preterm children may differ qualitatively from ADHD in the general population, with less co-morbidity with conditions such as conduct disorder and reports of relationships between infant brain injuries, such as diffuse white matter injury, ventricular enlargement and parenchymal lesions, and later diagnosis (Anderson & Doyle, 2004; Johnson, 2007). In the present study, major neonatal brain injury diagnosed by ultrasound was not associated with ADHD at age 18. However, ultrasound is less sensitive to pathologies such as diffuse white matter injury and parenchymal lesions than neonatal magnetic resonance imaging (MRI) (Woodward *et al.* 2006), which was unavailable to this 1991–1992 cohort. In addition, EP/ELBW adolescents who had major childhood disability had around three times the odds of ADHD at age 18. This may reflect the neurodevelopmental sequelae of subtler neuropathology than could be detected in infancy using ultrasound. Furthermore, higher externalizing and behavioral symptoms and lower adaptive skills in childhood were associated with ADHD diagnosis in adolescence for the EP/ELBW group. This is consistent with evidence that childhood behavior and emotional problems predict later psychiatric diagnosis in preterm children (Johnson *et al.* 2010), and suggests a persistent profile of difficulties likely to affect social and cognitive development in this population.

The similar prevalence of lifetime mood and anxiety disorders between EP/ELBW and control groups is in contrast with much of the published literature, although studies vary in their methodologies (Walshe *et al.* 2008; Johnson *et al.* 2010; Lund *et al.* 2011; Nosarti *et al.* 2012). Nevertheless, our findings are not without precedent, particularly with respect to questionnaire data (Saigal *et al.* 2003; Hallin & Stjernqvist, 2011). Limited self-report data exist for preterm young people, and anxiety and mood disorder prevalence changes substantially from childhood to young adulthood in the general population. In a recent follow-up of 19-year-olds born <2000 g, overall disorder prevalence was elevated relative to controls, although specific disorder subgroups (e.g. mood or

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Table 4. *Association of EP/ELBW 18-year outcomes with historical variables*

	Any ADHD		Any mood/anxiety disorder	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Perinatal				
Gestational age (weeks)	1.00 (0.83–1.21)	0.99	1.09 (0.93–1.28)	0.28
Birthweight (100-g units)	0.91 (0.71–1.17)	0.47	1.06 (0.86–1.30)	0.60
Major neonatal brain injury[a]	1.10 (0.30–4.02)	0.89	1.01 (0.32–3.20)	0.99
SGA	1.00 (0.35–2.83)	>0.99	1.45 (0.62–3.39)	0.39
Postnatal corticosteroids	1.95 (0.88–4.32)	0.10	0.75 (0.35–1.60)	0.46
Neonatal surgery	1.94 (0.85–4.41)	0.11	1.01 (0.47–2.19)	0.97
Maternal age (years)	0.95 (0.89–1.02)	0.15	0.99 (0.94–1.05)	0.84
Mother completed high school	0.81 (0.37–1.75)	0.58	1.37 (0.69–2.72)	0.37
Father completed high school	1.06 (0.47–2.42)	0.89	2.46 (1.19–5.12)	0.02
Age 8 years				
BASC Internalizing	1.03 (0.99–1.07)	0.12	1.03 (0.999–1.063)	0.06
BASC Externalizing	1.07 (1.03–1.10)	<0.001	1.01 (0.99–1.04)	0.33
BASC Adaptive skills	0.94 (0.90–0.97)	0.001	1.02 (0.98–1.05)	0.36
BASC BSI	1.06 (1.02–1.09)	0.001	1.02 (0.99–1.05)	0.29
Major disability	3.21 (1.18–8.70)	0.02	0.84 (0.27–2.64)	0.77
Higher SES	0.50 (0.23–1.10)	0.09	1.31 (0.64–2.69)	0.47

EP, Extremely preterm; ELBW, extremely low birthweight; ADHD, attention deficit hyperactivity disorder; SGA, small for gestational age (birthweight ⩾2 S.D. below the mean for gestational age and gender); BASC, Behavior Assessment System for Children; BSI, Behavioral Symptoms Index; SES, socio-economic status; OR, odds ratio; CI, confidence interval.

Lower scores on BASC adaptive skills reflect poorer skills.

[a] Grade 3/4 intraventricular hemorrhage/cystic periventricular leukomalacia.

anxiety disorders) did not reach significance (Elgen *et al.* 2012). In Lund *et al.*'s (2011) study, 20-year-olds born <1500 g had more anxiety than controls, with rates of 19% in the VLBW group. Subjects in both of these studies were born pre-1990. In the present study, prevalence rates were broadly consistent with population estimates from Australia and comparable nations, with about a fifth of control participants meeting criteria for a current or lifetime mood or anxiety disorder (Hankin *et al.* 1998; Patton *et al.* 1999; Slade *et al.* 2009; Merikangas *et al.* 2010). This suggests that our control group was not abnormally symptomatic. In addition, most studies in preterm samples have focused on recent disorder histories. However, dimensional assessment of recent depression and anxiety symptoms also revealed similarities between groups. It is therefore unlikely that the groups' similar disorder prevalence is masking a difference in subthreshold symptoms. The limited relationships between historical variables and mood and anxiety disorders were expected, given previous reports of the limited predictive value of these variables as preterm children age (Johnson *et al.* 2010). It was notable, however, that childhood BASC scores were not significantly associated with later mood and anxiety disorder in the preterm group, suggesting that further research is required to identify precursors to depression and anxiety in this population.

These mood and anxiety findings also contrast with those of Scandinavian register studies suggesting that decreasing birthweight is associated with higher psychiatric morbidity (Lindström *et al.* 2009; Abel *et al.* 2010; Nosarti *et al.* 2012). Although linkage studies have many strengths, a limitation is the reliance on gross outcomes. Moreover, the birth periods for these linkage studies were all pre-1990. Young people are often unlikely to seek treatment for mental health difficulties (Reavley *et al.* 2010), suggesting that community prevalence is higher than hospital admissions or treatment records indicate. Some have speculated that preterm survivors may have better awareness of medical conditions or more often interact with clinicians who recognize psychiatric problems, and may therefore be over-represented in health records (Nosarti *et al.* 2012). The similarities in mood and anxiety disorder prevalence reported here are encouraging findings for the preterm group. Nonetheless, it remains to be seen whether these data are characteristic of broader self-reported mood/anxiety outcomes for adolescents born since the 1990s.

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Consistent with the SCID-I/NP results, the two groups self-rated similarly on most personality trait measures. The EP/ELBW group reported similar sensitivity to reward and punishment to the control group, and did not differ in their endorsement of positive and negative trait affectivity. These findings are in contrast to some in the literature, which have identified marked personality differences between preterm and control youth (Allin *et al.* 2006; Pesonen *et al.* 2008). However, they are also not without precedent from pre-1990 samples; in a study of ELBW and control young adults, BIS/BAS score differences did not reach significance, despite group differences on other measures of personality (Schmidt *et al.* 2008). Although Pyhälä *et al.* (2009) found lower BAS Fun-Seeking scores in their preterm group, there were no differences on the other BIS/BAS scales. This may reflect the particular methodologies used and conceptual distinctions made between different aspects of personality and emotional functioning. Despite higher ADHD prevalence in the EP/ELBW group than controls, group differences on BAS subscales were not significant. This is not entirely unexpected, given that inattentive-type ADHD predominated in this sample and high BAS scores have been linked with the hyperactive and impulsive symptoms of ADHD (Mitchell & Nelson-Gray, 2006; Hundt *et al.* 2008). In the present study, the EP/ELBW group did endorse fewer antisocial personality traits than controls, in accordance with evidence of greater 'agreeableness' in preterm young adults from an earlier birth cohort (Pesonen *et al.* 2008).

Given the importance of subjective emotional experience in diagnosing the disorders of interest, this study focused on self-reported outcomes. However, it has been suggested that preterm samples may lack insight into their own well-being, which may explain discrepancies between, for instance, self-reported and other measures of quality of life (Zwicker & Harris, 2008). In one study, VP young adults tended to portray themselves in more socially desirable ways than their peers, a difference largely driven by males (Allin *et al.* 2006). By contrast, others have reported that ELBW and control teenagers self-rated similarly on depressive symptoms, and although parental ratings differed between groups, teenagers of both groups reported more symptoms than their parents (Saigal *et al.* 2003). Although it would have been useful to have a structured parent interview in the present study, the adolescents' self-report is important in assessing psychopathology, particularly internalizing difficulties (Cantwell *et al.* 1997).

This study has notable strengths, including a large geographical sample and prospective design with contemporaneously recruited controls. Moreover, it reports data from the oldest survivors born in the 1990s, providing important contemporary information about outcomes after extreme prematurity. Further replication of these findings in other recent adolescent cohorts will extend our understanding of the impact of medical care improvements in the early 1990s. In addition, we were able to explore outcomes diagnostically and dimensionally, revealing a consistent picture. We also acknowledge the limitations of this study. As mentioned, retention rates were 72% and 60% for the EP/ELBW and control groups respectively. The EP/ELBW participants reflected the original cohort in neonatal morbidities and childhood behavioral ratings. However, we cannot reject the potential influence of attrition in the control group; the disproportionate loss of males, those with more childhood emotional/behavioral symptoms, and those with less educated parents from this group may suggest a higher true disorder prevalence among controls. Importantly, however, group differences in ADHD prevalence persisted when accounting for gender, parental education and SES. Furthermore, attrition does not seem to account for the groups' similarity in mood and anxiety disorders. Although female sex was associated with mood/anxiety disorders, the EP/ELBW and control groups had similar sex ratios. Some aspects of social disadvantage were over-represented in non-participants from both groups. Of the participants, however, the EP/ELBW group more often had lower childhood SES and their parents had less often completed high school than controls. Although paternal education was associated with disorder in the EP/ELBW group, controls with less-educated fathers were also lost to follow-up more often; this suggests that this loss to follow-up is more likely to have decreased the observed mood/anxiety disorder prevalence in controls than the reverse.

The present study could not explore potential contributions of stressful life events, or of parental mental health to outcome, which may relate to the risk of preterm birth (Dole *et al.* 2003; Grote *et al.* 2010). However, evidence does exist that maternal anxiety and depression, at least during pregnancy, do not fully account for depressive symptoms in early adulthood (Alati *et al.* 2007). Nonetheless, we could not account for genetic risk for psychiatric disorder, which may have differed across the groups. This is an important avenue for future research.

This study examined mental health in a large, contemporary geographical cohort of EP/ELBW adolescents born post-1990, finding similar lifetime prevalence of self-reported mood and anxiety disorders and dimensional ratings of mood, anxiety and personality to controls. However, elevated ADHD prevalence indicates that EP/ELBW teenagers self-identify attention

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difficulties that affect their everyday functioning. These findings have important clinical implications and extend the limited data on preterm outcomes into the high-risk adolescent period. Although prematurity was not associated with mood and anxiety disorders, these were relatively common, as was ADHD. Many preterm survivors maintain involvement with clinical services, which provides an opportunity to identify at-risk adolescents. Future research is needed to assess whether these outcomes are maintained as EP/ELBW adolescents transition into adulthood.

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Declaration of Interest

None.

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