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Mood and anxiety disorders in very preterm/very low birth weight individuals from six to 26 years

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Abstract

Background. Very preterm (<32 weeks gestational age; VP) or very low birth weight (<1500g; VLBW) birth has been associated with increased risk for anxiety and mood disorders and less partnering in adulthood. The aim was to test if (1) VP/VLBW are at increased risk of any anxiety or mood disorders from 6 to 26 years of age compared to term-born individuals; (2) whether social support from romantic partners is associated with protection from anxiety and mood disorders; and (3) whether VP/VLBW adults' lower social support mediates their risk for any anxiety and mood disorders.

Methods. Data are from a prospective geographically defined longitudinal whole population study in South Bavaria (Germany). 200 VP/VLBW and 197 term individuals were studied from birth to adulthood. Anxiety and mood disorders were assessed at 6, 8, and 26 years with standardized diagnostic interviews and social support via self-report at age 26.

Results. At age 6, VP/VLBW children were not at increased risk of any anxiety or mood disorder. At age 8, VP/VLBW more often had any anxiety disorder than term comparisons (11.8% vs. 6.6%, $OR=2.10$, 95% CI [1.08-4.10]). VP/VLBW adults had an increased risk for any mood (27.5% vs. 18.8%, $OR=1.65$ [1.02-2.67]) but not for any anxiety disorder (33.0% vs. 28.4%, $OR=1.27$ [0.82–1.96]). None of the significant differences survived correction for multiple testing. Social support was associated with a lower risk of anxiety or mood disorders in both groups ($OR=0.81$ [0.68-0.96]) and mediated the association of VP/VLBW birth with any anxiety or any mood disorders at age 26.

Conclusions. This study does not show a persistently increased risk for any anxiety or mood disorder after VP/VLBW birth. Low social support from a romantic partner mediates the risk for anxiety or mood disorders after VP/VLBW birth.

Keywords: preterm birth, clinical diagnoses, anxiety disorder, mood disorder, social support, protection

Abbreviations: Very preterm: VP; very low birth weight: VLBW; gestational age: GA; attention-deficit/hyperactivity disorder: ADHD; small for gestational age: SGA; Bavarian Longitudinal Study: BLS; socioeconomic status: SES; Mannheimer Parent Interview: MEI; Diagnostic and Statistical Manual of Mental Disorders: DSM; Munich Composite International Diagnostic Interview: DIA-X/M-CIDI; risk ratio: RR;

About 15 million babies worldwide are born preterm (<37 weeks gestational age (GA)) every year (March of Dimes, PMNCH, Save the Children, & WHO, 2012). Of these, ~2 million (1-2%) are born very preterm (VP; <32 weeks GA) or with very low birth weight (VLBW; <1500g) (Zeitlin et al., 2013). Survival rates for VP/VLBW have increased over the last decades (Ancel et al., 2015). The prevalence of psychiatric symptoms after VP/VLBW birth is significantly higher than that of term-born individuals (2-4 times increased odds for symptoms in the clinical range compared with the general population) during childhood and adolescence (Johnson & Marlow, 2011, 2014; Johnson & Wolke, 2013), and anxiety or mood problems, in particular, may be more prevalent in VP/VLBW adults (Mathewson et al., 2017; Pyhälä et al., 2017). VP/VLBW children show increased symptoms of autism spectrum and attention-deficit/hyperactivity disorders (ADHD) (D'Onofrio et al., 2013), and ADHD type problems have been shown to continue more often into early adulthood in VP/VLBW than term controls (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015). In contrast, findings of increased risk for anxiety or mood disorders have been mixed (Johnson & Marlow, 2011; Johnson & Wolke, 2013). While VP/VLBW individuals are more often diagnosed with anxiety disorders in childhood, adolescence, and adulthood (Lærum et al., 2017; Lund, Vik, Skranes, Brubakk, & Indredavik, 2011; Van Lieshout, Boyle, Saigal, Morrison, & Schmidt, 2015), the evidence for increased mood disorders is inconsistent. Two studies reported that small for gestational age (SGA) adults who were VLBW (Raikkonen et al., 2008) or term-born (Lærum et al., 2017) may have an increased risk for mood disorders.

Anxiety disorders have their onset in childhood (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003) whereas mood disorders usually have a later onset with prevalence rising rapidly from early adolescence into young adulthood (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). However, we do not know if the findings from general population studies can be generalized to VP/VLBW individuals. Trajectories of anxiety and mood disorder may be different in VP/VLBW compared to the general population because disturbances to brain

development (Meng et al., 2016) may alter the presentation of disorders. Moreover, VP/VLBW infants often spent months in hospital and underwent intensive medical treatment that involved significant pain (Puchalski & Hummel, 2002; Valeri, Holsti, & Linhares, 2015). Many of their early social contacts involved intrusive interventions. Thus, early life experiences may be related to increased psychiatric risk.

An alternative to prospective follow-up studies is the use of registries of medical records. These indicate more frequent diagnoses of anxiety or mood problems (Moster, Lie, & Markestad, 2008; Nosarti, Reichenberg, Murray, & et al., 2012), more hospital admissions for mood disorders (Lindstrom, Lindblad, & Hjern, 2009) and higher rates of antidepressant medication (Crump, Winkleby, Sundquist, & Sundquist, 2010) in VP/VLBW compared to term-born adults. VP/VLBW individuals often require social benefits (D'Onofrio et al., 2013) and are in frequent contact with health and social services (Petrou, Johnson, Wolke, & Marlow, 2013), which may partly explain registry-reported increased diagnosis rates and bias findings (Mooney, 2017). Thus, there is a need for prospective study of VP/VLBW in comparison to term-born individuals using standard diagnostic instruments unbiased by service use or inaccuracies in diagnosis (O'Malley et al., 2005) to understand prevalence and trajectories of anxiety and mood disorders from childhood into adulthood (Copeland, Shanahan, Costello, & Angold, 2011).

Recent studies have found that VP/VLBW young adults often have poor social support and are less likely to engage in romantic relationships than term-born adults (D'Onofrio et al., 2013; Darlow, Horwood, Pere-Bracken, & Woodward, 2013; Männistö et al., 2015). A supportive partner relationship can provide protection against the development of psychiatric problems (La Greca & Harrison, 2005; Ozbay, Fitterling, Charney, & Southwick, 2008). Potentially protective effects of having a supportive romantic partner on VP/VLBW adults' mental health have not been investigated. Unknown is whether VP/VLBW adults may be at particular risk for anxiety or mood disorders because of their lower success in partnering.

The aim of this prospective study was to assess anxiety and mood disorders from six to 26 years and social support at age 26 in VP/VLBW and healthy term comparison individuals.

1. Are VP/VLBW at higher risk for anxiety and mood disorders than term-born participants in childhood and adulthood?
2. Is VP/VLBW and term comparison adults' social support from romantic partners associated with a lower risk of having any anxiety or mood disorder at 26 years?
3. Does VP/VLBW adults' lower social support mediate their risk for any anxiety and mood disorders?

Methods

Data were collected as part of the prospective Bavarian Longitudinal Study (BLS) (Wolke & Meyer, 1999), a geographically defined whole-population sample of VP/VLBW and term-born individuals in Germany.

Design and Participants

Of 70,600 children born in South Bavaria during a 15-month period in 1985/86, 682 were VP or VLBW infants, or both, born alive and admitted to neonatal care within the first ten days of life (0.97%). Of these, 411 were eligible for longitudinal follow-up (Figure S1), 15 had severe disability and were unable to be interviewed, and 200/396 (51%) participated in full clinical interviews at 26 years. The BLS VP/VLBW participants did not differ from adults who dropped out in terms of GA, BW, duration of hospitalization, gender, maternal age, parental marital status, and childhood cognitive scores, but had fewer prenatal complications and were of higher socioeconomic status (SES) (Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015).

Healthy term infants who were born in the same obstetric hospitals were recruited as comparisons. Of the initial 916 children alive at 6 years, 350 were randomly selected within

the stratification variables sex and family SES. Of these, 308 were eligible for longitudinal follow-up, and 197 (64%) participated in clinical interviews at 26 years.

Clinical diagnostic interviews were conducted at 6 (preschool), 8, and 26 years. In total, data on anxiety and mood disorder diagnoses were available for 200-232 (184 assessed longitudinally) VP/VLBW and 197-229 (197 longitudinally) term comparisons across the three time points. Among those lost to follow-up between 8 and 26 years, 16% had had an anxiety and/or mood disorder diagnosis at 6 or 8 years, compared to 19% among those who participated at 26 years.

Procedure and Ethical Considerations

Perinatal details have been described elsewhere (Wolke & Meyer, 1999) and are briefly outlined here. Participating parents were approached within 48 hours of infants' hospital admissions and were included after giving written consent. Initial ethical approval was obtained from the University of Munich Children's Hospital Ethics committee and in 2009 from the University Hospital Bonn Ethical Board (#159/09). All adult participants gave fully informed written consent. At 6, 8, and 26 years, participants were assessed with detailed clinical interviews with the parents (6 and 8 years) and the participants themselves (26 years). Assessors were qualified experienced psychologists trained in the interview administration and blind to group membership.

Measures

Biological variables. Gestational age was determined from maternal reports of the last menstrual period and serial ultrasounds during pregnancy. Birth weight was documented in birth records. Infants were classified as SGA if they weighed less than the sex specific 10th percentile for their gestational age according to national standard weight charts (1985-1986).

Socioeconomic status. Information was obtained by standardized interviews within the first 10 days of life. Family SES was coded into three predefined categories (1=lowest to 3=highest) (Eryigit Madzwamuse et al., 2015).

Diagnosis of anxiety and mood disorders at 6 and 8 years. Depressive mood and anxiety disorder diagnoses (including phobias) were obtained with the structured Mannheimer Parent Interview (MEI) (Esser, Blanz, Geisel, & Laucht, 1989), a gold standard interview in Germany allowing for 100% concordant clinical Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnosis (El-Faddagh, Laucht, Maras, Vöhringer, & Schmidt, 2004; Esser, Fischer, Wyschkon, Laucht, & Schmidt, 2007) and inter-rater reliabilities of *Cohen's Kappa* = .71 (Esser et al., 1989).

Diagnosis of anxiety and mood disorders at 26 years. Detailed anxiety and mood disorder diagnoses (including phobias) were obtained according to DSM-IV criteria using a computer-assisted version of the Munich Composite International Diagnostic Interview (DIA-X/M-CIDI) that assessed symptoms in the last six months before the interview (Wittchen et al., 1995). Our definitions of any anxiety or mood disorders included all DSM-IV defined subtype diagnoses (please see supplementary materials Table S1 and Figure S2 for details on specific prevalence). The DIA-X/M-CIDI is a fully structured clinical interview, supplemented by a separate respondent booklet including cognitive aids to assist with questions about symptom onset, duration, recency, and severity (Carter, Wittchen, Pfister, & Kessler, 2001). The DIA-X/M-CIDI DSM-IV diagnostic categories' procedural validity (*kappa* = .50-.96) (Reed et al., 1998) is acceptable and in concordance with the Structured Clinical Interview for DSM-IV (SCID) (Haro et al., 2006).

Social support from relationships with romantic partners. Information on romantic relationships was obtained using a standardized Life Course Interview and the Young Adult Self-Report (Achenbach, 1997). We extracted critical items from these assessments that covered romantic partner relationships (Table S2) and summed these into a cumulative *z*-standardized index score (Wolke, Copeland, Angold, & Costello, 2013) of 'social support from romantic partner'.

Statistical analyses

Data were analyzed with SPSS 22. Group comparisons of any anxiety or mood disorders were carried out with binary logistic regressions (Table 2), adjusted for multiple testing using the M_{eff} method that controls the error-rate of correlated multiple testing (Li & Ji, 2005), thereby balancing the risk for false-positive and false-negative results. Analyses were repeated including additional $n=89$ of the original participants (57 VP/VLBW and 32 term comparisons) who had agreed to answer DSM-IV oriented screening questionnaires for anxiety and mood disorders but not full clinical interviews at 26 years. All logistic regressions were adjusted for family SES at birth.

The cumulative risk (summing any anxiety and mood disorder diagnoses across time) at 6, 8, and 26 years and stability of diagnoses over time were calculated for both groups. Direct associations of VP/VLBW and term individuals' social support from romantic partners with anxiety or mood disorders were evaluated. Mediation of risks for any anxiety and any mood disorders by social support at age 26 were tested using 10,000 bootstrap samples in the SPSS PROCESS macro (Hayes, 2013).

Results

Table 1 shows that VP/VLBW participants were more often born SGA. There were no group differences with regard to sex, however, VP/VLBW adults had been born into lower SES families than term comparisons. VP/VLBW had lower levels of social support from romantic partners than term comparison adults.

- Tables 1 and 2 about here -

At 6 years (preschool), VP/VLBW children were not at increased risk of any anxiety or mood disorders. At 8 years, VP/VLBW more often had anxiety disorders than term comparisons. At 26 years, VP/VLBW adults were diagnosed with mood but not with anxiety disorders more often (Table 2). Adjusting for multiple testing using the M_{eff} method (Li & Ji,

2005) resulted in an alpha-level of $p < 0.01$ for any disorder, none of the group differences survived this correction.

Analyses were repeated including $n=89$ participants with DSM-IV oriented screening data. Inclusion of these additional cases did not change the risk for any mood (22.6% vs. 17.5%, $OR=1.38$, 95% CI [0.88-2.16]) or anxiety disorder (26.5% vs. 24.9%, $OR=1.09$, 95% CI [0.72-1.63]) in $n=257$ (65%) VP/VLBW versus $n=229$ (74%) term comparisons.

There were no group differences with regard to SGA birth (Table S2), adjusting for SGA birth in main analyses did not result in a significant effect of SGA birth nor alter any of the prevalence rates (not shown). Comparing only those that were born VP/VLBW and SGA ($n=69$) with healthy term AGA adults ($n=179$) did not show any group differences, even before correction for multiple testing. In addition to clinically significant diagnoses, we also investigated prevalence rates including sub-threshold symptoms of any anxiety or mood disorders and found no differences between VP/VLBW and term comparisons that survived correction for multiple testing (Table S3).

We summed any anxiety and mood disorder diagnoses across time. This cumulative risk was not significantly increased in VP/VLBW compared with term-born participants ($\chi^2=1.69$, $p=.219$) (Figure 1). Similarly, the pattern of diagnostic persistence was not statistically different between groups (Figure 2), e.g., those VP/VLBW and term individuals diagnosed with any anxiety or mood disorder in childhood were not at increased risk for diagnosis in adulthood (VP/VLBW risk ratio (RR)=1.18, 95% CI [0.76 to 1.84]; term comparison $RR=0.78$ [0.52 to 1.16]).

Figures 1 and 2 about here -

Having social support from a romantic partner was associated with a lower risk for any anxiety or mood disorder in both VP/VLBW and term comparisons ($OR=0.81$ [0.68 to 0.96]) at 26 years. Finally, social support from romantic partners mediated the relationship of

VP/VLBW birth with any anxiety (*indirect effect* $B=.13$ ($SE=.06$), 95% CI [0.04-0.26]) and any mood disorder (*indirect effect* $B=.09$ ($SE=.06$), 95% CI [0.00-0.22]; Figure S3).

Discussion

This prospective, whole population longitudinal study from birth to adulthood found that VP/VLBW survivors were not at persistently increased risk for anxiety and mood disorders. Although odds ratios indicated a higher prevalence of anxiety at age 8 and a higher prevalence of mood disorders at 26 years in VP/VLBW compared with healthy term-born comparison individuals, no differences remained significant after correction for multiple testing. Moreover, the cumulative prevalence of anxiety and mood disorders at 6, 8, and 26 years was not higher in VP/VLBW than term-born controls. Both VP/VLBW and term-born individuals showed the universally found rapid increase in anxiety and mood disorders from childhood into adulthood. Having a romantic partner in adulthood was associated with protection from anxiety and mood disorders in both VP/VLBW and term comparisons. Although there was no direct effect of VP/VLBW birth, social support from romantic partners mediated the relationship of VP/VLBW birth with anxiety and mood disorders (i.e., indirect effect).

Our findings suggest that, contrary to cross-sectional questionnaire studies (Johnson & Marlow, 2014; Johnson & Wolke, 2013; Mathewson et al., 2017; Pyhälä et al., 2017), clinically significant anxiety and mood problems may not be a persistent characteristic of the preterm phenotype. We also investigated sub-threshold symptoms of anxiety and mood disorders (Cuijpers & Smit, 2004) but did not find differences between VP/VLBW and term comparisons. Similarly, no differences in the cumulative risk and diagnostic persistence of anxiety and mood disorders were found. This suggests that despite their neurodevelopmental challenges VP/VLBW survivors' may not have a significantly increased risk for anxiety and mood disorders.

Apart from our analysis of primary outcomes, any anxiety and/or mood disorder, exploration of specific disorder prevalence rates (Table S1, Figure S2) suggests that VP/VLBW individuals may have a persistently elevated risk for specific blood and injection phobia. VP/VLBW infants usually spend their early months in hospital and experience invasive and painful medical procedures (e.g., intubation, setting catheters, blood taking) (Puchalski & Hummel, 2002). Research on pain memory suggests different pathways how pain experiences from the neonatal period may be remembered later in life including dynamic interactions of nervous system alterations with cognitive and social development (Noel, Palermo, Chambers, Taddio, & Hermann, 2015; Puchalski & Hummel, 2002). There is further evidence that neonatal pain exposure beyond neonatal complications is related to alterations in cerebral thickness, especially in frontal and parietal areas and the cerebellum (Ranger et al., 2015), and to down regulation of the HPA axis and stress responses (Grunau et al., 2013). In the last decades there have been changes in neonatal care including treatment of pain and less invasive procedures (Roofthoof, Simons, Anand, Tibboel, & van Dijk, 2014). However, there is still a need for blood taking and enteral feeding by gastric tubes. Future studies with potentially higher statistical power to test specific diagnoses over time should explore whether recently born cohorts have increased rates of blood and injection phobia.

We found an elevated risk for mood disorders in VP/VLBW adults that did not survive correction for multiple testing. With an OR of 1.65 this risk was lower than previously reported (Nosarti et al., 2012; Westrupp, Northam, Doyle, Callanan, & Anderson, 2011) but consistent with others (Lund et al., 2011; Natalucci et al., 2013; Van Lieshout et al., 2015). Our findings suggest that higher rates of psychiatric problems and antidepressant medication could be partly explained by VP/VLBW adults' higher risk of being without a romantic partner rather than due to increased depression symptomatology. This is consistent with repeated findings that VP/VLBW have higher scores for socially withdrawn personality traits (Eryigit Madzwamuse et al., 2015; Waxman, Van Lieshout, Saigal, Boyle, & Schmidt, 2013)

and romantic relationship problems (Männistö et al., 2015; Saigal et al., 2016). In accordance with recent findings (Van Lieshout et al., 2015), our supplementary data suggest an increased prevalence of social phobia in VP/VLBW adults. Unclear is whether these social difficulties may reflect alterations in their brain development and processing of social information or adverse experiences in school and early working life, or both.

Few studies have investigated factors in VP/VLBWs' environments that may protect from the development of psychiatric disorders (Westrupp, Northam, Doyle, Callanan, & Anderson, 2012a). Social support from romantic partners is associated with lower risk for anxiety and mood disorders in both VP/VLBW and term born adults. However, as VP/VLBW often have social difficulties (Ritchie, Bora, & Woodward, 2015), there may be merit of investing in social competence training after VP/VLBW birth.

Some studies have reported that intrauterine growth patterns (i.e., SGA birth) may increase VP/VLBW individuals' risk for anxiety and mood disorders (Lærum et al., 2017; Lund et al., 2011; Raikkonen et al., 2008) but our results do not confirm such effects.

This is the first longitudinal investigation of anxiety and mood disorders in childhood and adulthood using clinical diagnoses in a large whole-population sample of VP/VLBW individuals and term comparisons. In total, 56% of the eligible VP/VLBW and term comparisons recruited at birth could be assessed with full psychiatric interviews at 26 years, however, the dropout was not random as low SES families were less likely to continue participation. Social factors are a major reason for dropout in most longitudinal studies (Hille, Elbertse, Gravenhorst, Brand, & Verloove-Vanhorick, 2005) and analyses were controlled for SES at birth. Our sample represents one of the largest longitudinal studies of psychiatric risk after VP/VLBW birth ever reported. For comparison, other well-respected cohort studies of VP/VLBW survivors reported sample sizes and cross-sectional follow-up rates in adulthood of N=44, 60% (Lærum et al., 2017), N=174, 51% (Van Lieshout et al., 2015), and N=79, 56% (Westrupp, Northam, Doyle, Callanan, & Anderson, 2012b), respectively. Despite this, the

statistical power to detect differences in diagnosis of specific anxiety or mood disorders was not sufficient. We utilized gold-standard diagnostic interviews and our overall prevalence rates are in accordance with what has been reported by normal population studies before (Polanczyk et al., 2015). Our findings suggest that rates of anxiety and mood disorders may have been over-estimated by previous studies (Lærum et al., 2017; Van Lieshout et al., 2015), potentially due to false positive findings. Larger sample sizes or pooling of prospective VP/VLBW studies are needed to investigate longitudinal mechanisms of specific psychiatric risks and resilience. Furthermore, our estimate of cumulative anxiety and mood disorders at 6, 8, and 26 years was purely made to compare VP/VLBW and controls assessed at the same time points. It should not be interpreted as an estimate of total burden of psychiatric disorder in either group which would require additional assessments during adolescence (Copeland et al., 2011). Social support from romantic partners was assessed in adulthood, thus causality of romantic relationships as protective factors for anxiety and mood disorders cannot be inferred. We confirmed mediation (i.e., significant indirect effects) of VP/VLBW birth on the risk for anxiety and mood disorders via low social support at age 26, although the direct effects of VP/VLBW birth on anxiety and mood disorders (path 'c' in the mediation model) were not or only marginally significant (see Figure S3). Current statistical recommendations do however not require significance of path 'c' to confirm mediation (Kenny & Judd, 2014; Rucker, Preacher, Tormala, & Petty, 2011). Finally, interview instruments changed from childhood to adulthood, however, this is consistent with clinical practice as questions have to be age-appropriate while applying DSM criteria.

Conclusion

This prospective study was not able to show a persistently increased risk for anxiety and mood disorders in VP/VLBW compared to healthy term-born comparison individuals.

Having a romantic partner appears to be associated with protection from anxiety and mood disorders for both VP/VLBW and term adults.

What's Known

- Very preterm/very low birth weight birth is associated with increased anxiety disorders into adulthood. In contrast, there are controversial findings regarding increased mood disorders.
- Little is known about factors that may protect against anxiety and mood disorders in preterm adults.

What's new

- Very preterm/very low birth weight individuals may not have a persistently increased risk of anxiety or mood disorders from childhood into adulthood.
- Having social support from a romantic partner is associated with protection from anxiety and mood disorders.

What's clinically relevant

- Adults without support from romantic partners may need additional social support to prevent the development of anxiety and mood disorders.

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Table 1. Background characteristics of the VP/VLBW and term participants at 26 years

	VP/VLBW (<i>n</i> = 200)	Term comparisons (<i>n</i> = 197)	Mean difference (95% CI)	<i>p</i>	
Birth weight (g)	1319 (322)	3371 (452)	2052 (1975 – 2130)	<.001	
Gestational age (weeks)	30.39 (2.05)	39.67 (1.16)	9.28 (8.95 – 9.61)	<.001	
Small for gestational age (SGA) birth (%)	34.5	9.1	5.24 (2.98 – 9.22)	<.001	
Sex (% male)	53.0	47.7	0.81 (0.55 – 1.20)	.316	
Family SES at birth	Low %	29.6	22.8	7.74 ^a	.021
	Medium %	47.7	42.1		
	High %	22.6	35.0		
Social support from romantic partner ^b	-0.50 (1.27)	0.02 (1.01)	0.51 (0.29 – 0.74)	<.001	

Please note: Data are presented as mean (standard deviation) if not indicated otherwise; ^a χ^2 -value; ^b *z*-standardized index score; VP=very preterm, VLBW=very low birth weight

Table 2. Prevalence of DSM-IV emotional disorder diagnoses (%) comparing VP/VLBW and term individuals at age 6, 8, and 26 years

<i>DSM IV Diagnoses</i>	Age 6 years				Age 8 years				Age 26 years			
	VLBW/VP		Term		VLBW/VP		Term		VLBW/VP		Term	
	(n=218)	(n=229)	OR ^a	95% CI	(n=232)	(n=229)	OR ^a	95% CI	(n=200)	(n=197)	OR ^a	95% CI
Any Mood Disorder	0.0	1.7	-	-	0.9	0.0	-	-	27.5	18.8	1.65	(1.02–2.67)
Any Anxiety Disorder	10.0	11.4	0.85	(0.47–1.56)	11.8	6.6	2.10	(1.08–4.10)	33.0	28.4	1.27	(0.82–1.96)

Please note: All available participants with full clinical interviews assessed at 6, 8, and 26 years were included; ^a adjusted for SES at birth; VP=very preterm, VLBW=very low birth weight

Figure 1. Cumulative prevalence of any DSM-IV emotional disorder diagnosis comparing VP/VLBW and term comparison individuals at age 6, 8, and 26 years

Please note: Longitudinal participants with full clinical interviews assessed at 6, 8, and 26 years were included ($N=381$); VP=very preterm, VLBW=very low birth weight

Figure 2. Persistence and change of DSM-IV emotional disorder diagnoses in VP/VLBW and term comparison individuals from childhood to age 26 years

Please note: Longitudinal participants with full clinical interviews assessed at 6, 8, and 26 years were included ($N=381$); VP=very preterm, VLBW=very low birth weight