Psychiatric Disorders and General Functioning in Low Birth Weight Adults: A Longitudinal Study

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abstract

OBJECTIVE: To examine psychiatric morbidity and overall functioning in adults born with low birth weight compared with normal birth weight controls at age 26 years and to study longitudinal trajectories of psychiatric morbidity from early adolescence to adulthood.

METHODS: Prospective cohort study wherein 44 preterm very low birth weight (≤1500 g), 64 term small for gestational age (SGA; <10th percentile), and 81 control adults were examined using the MINI-International Neuropsychiatric Interview: M.I.N.I. Plus, Norwegian version, the Global Assessment of Functioning, and questions on daily occupation and level of education. Prevalence of psychiatric disorders from previous follow-ups at age 14 and 19 years were included for longitudinal analysis.

RESULTS: From adolescence to adulthood, the term SGA group had a marked increase in the estimated probability of psychiatric disorders from 9% (95% confidence interval, 4–19) to 39% (95% confidence interval, 28–51). At 26 years, psychiatric diagnoses were significantly more prevalent in the preterm very low birth weight group (n = 16, 36%; P = .003) and the term SGA group (n = 24, 38%; P = .019) compared with the control group (n = 11, 14%). Both low birth weight groups had lower educational level and functioning scores than controls and a higher frequency of unemployment and disability benefit.

CONCLUSIONS: Low birth weight was a substantial risk factor for adult psychiatric morbidity and lowered overall functioning. The results underscore the need for long-term follow-up of low birth weight survivors through adolescence and adulthood, focusing on mental health. The longitudinal increase in psychiatric morbidity in the term SGA group calls for additional investigation.

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Dr Lærum carried out the analyses and interpretation of data, drafted the initial manuscript, and revised the final manuscript; Dr Reitan supervised the diagnostic work and reviewed and revised the manuscript; Drs Evensen, Brubakk, and Skranes participated in conceptualizing and designing the study and reviewed and revised the manuscript; Dr Lydersen carried out the longitudinal statistical analyses, supervised statistical analyses, and reviewed and revised the manuscript; Dr Indredavik participated in conceptualizing and designing the study, coordinated and supervised data collection, supervised the initial analyses and interpretation of data, and critically revised the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Preterm birth and low birth weight involves an increased risk of physical and neurocognitive sequelae of varying severity in childhood and adolescence. Less is known about psychiatric disorders, functional level, education, and occupation in adulthood.

WHAT THIS STUDY ADDS: Low birth weight was a substantial risk factor for adult psychiatric morbidity and lowered overall functioning. The longitudinal increase in psychiatric morbidity in the term small for gestational age group call for additional investigation.

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Preterm birth and low birth weight involves an increased risk of physical and mental health sequelae of varying severity. In childhood, neurodevelopmental disability (including cognition, motor function, hearing, and visual impairments) is reported to be more frequent in preterm born children than in term born peers.[1] In adolescence, associations between low birth weight and/or preterm birth and a range of psychiatric symptoms and disorders are reported, including symptoms of attention-deficit/hyperactivity disorder (ADHD),[2–4] anxiety disorders,[5,6] and autism spectrum disorder,[7] as was also found in our study population at 14 and 19 years of age.[8,9] In late adolescence and into early adulthood, long-term outcome studies are more scarce and somewhat inconsistent. There are a few reports of increased risk of nonaffective psychosis and bipolar disorders in addition to depressive disorders.[10,11] Substance use disorders are reported in individuals born small for gestational age (SGA)[10,12] as opposed to those born preterm who are characterized as low risk takers.[13] Lower cognitive abilities and academic achievement are reported in low birth weight and/or preterm born adolescents and young adults,[4,13] as was also previously found in our project.[14,15] Low socioeconomic status (SES) is found to be associated with both adverse perinatal outcome[16] and increased risk of psychiatric disorders.[17] Results are inconclusive regarding possible sex differences in psychiatric morbidity in low birth weight populations.[5,18]

Thus, studies indicate that consequences of preterm birth and low birth weight extend into early adulthood. However, current knowledge of long-term mental health outcomes in adulthood is still incomplete, and so is knowledge of educational and occupational attainment.

This study aimed to assess psychiatric diagnoses and overall functioning in adults born either preterm at very low birth weight (VLBW) or term but SGA compared with a term born control group with normal birth weight and to explore longitudinal trajectories of psychopathology from adolescence to adulthood.

We hypothesized that the prevalence of psychiatric disorders at 26 years of age would be higher for the preterm VLBW and term SGA participants compared with controls whereas education, occupation, and daily functioning would be lower, and that IQ and SES, but not sex, would influence the risk of psychiatric morbidity. We expected that the prevalence of psychiatric disorders at 26 years would be stable or increased compared with age 14 and 19 years in all 3 study groups.

METHODS

Design

As part of a prospective cohort study, a preterm VLBW group, a term SGA group and a term control group were examined at 26 years of age. All participants were born between 1986 and 1988. The preterm VLBW participants had all been admitted to the NICU at the University Hospital in Trondheim, Norway. They were either born at this hospital or referred from a local hospital in the region of Mid-Norway. The term SGA and control participants were born to women residing in the Trondheim area and recruited from the Trondheim part of a multicenter study.[19] At enrollment, a 10% sample of these women was randomly selected for participation using a closed envelope procedure. At birth, all children born term but not SGA in this random sample were included as controls for prospective follow-up. Children born term but SGA in this random sample, in addition to all children born term but SGA in the remaining study population, were included in the SGA group.

Participants

The participants in the VLBW group had a birth weight ≤1500 g and all participants in this group were born preterm. This group consisted of 2 cohorts: a geographical cohort restricted to those residing within the hospital catchment area for which data were used to estimate prevalence, and a larger regional cohort, with added participants referred from nearby smaller hospitals in the region of Mid-Norway, used for longitudinal analyses. Numbers are given as catchment area/regional: of the 97/121 VLBW children, 21/33 babies died in the neonatal period. Exclusion criteria at birth were syndromes or congenital malformations, and 2 infants were excluded. In addition, 1/2 children with severe quadriplegia or mental retardation were excluded at follow-up (not testable). Hence, 73/84 individuals were eligible for the study and invited, of whom 44/53 (60%/63%) participated (21/27 males and 23/26 females).

The participants in the SGA group were born at term (week 37–42) with a birth weight <10th percentile adjusted for gestational age, sex, and parity.[19] Among the 1249 eligible women, 104 (9%) gave birth to an SGA infant at term. One participant was excluded according to exclusion criteria at birth and 1 was excluded at follow-up (not testable). Of the 102 eligible participants, 2 could not be reached, and 64 (64% of eligible) participated (32 males, 32 females).

The control group participants were born at term with a birth weight ≥10th percentile. This group comprised 120 infants who were born to mothers in the 10% random sample. Two participants were excluded according to exclusion criteria at birth. Of the 118 eligible participants, 2 could not be reached

and 81 (69% of those eligible) participated (38 males, 43 females).

Data from former psychiatric examinations were available for VLBW/SGA/control participants: 56/60/83 at 14 years[8] and 43/55/75 at 19 years.[9]

Clinical Measures

At the 26 year follow-up, the MINI International Neuropsychiatric Interview: M.I.N.I. Plus, Norwegian version (MINI interview)[20] was used. This is a semistructured interview based on the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), 4th edition, text revision.[21] The MINI interview enables diagnostic assessment of a range of present disorders, with previous or lifetime occurrence for a subset. The examinations were conducted by 6 trained psychiatrists or psychologists and discussed with a senior psychiatrist, all blinded to group adherence and previous diagnostic conclusions. Interviewers also obtained information on education and daily occupation in the interview setting.

The Global Assessment of Functioning-split version, Norwegian version 5.0[22] was used to evaluate general functioning. This assessment is divided into a function score (GAF-F) and a symptom score (GAF-S), both ranging from 0 (worst) to 100 (best). The function scale is based on criteria regarding participation in work and education and coping in everyday and social life. The symptom score is related to the severity of psychiatric symptoms and its impact on cognition, discernment, mood, and behavior. A score ≥81 is considered good functioning.

As previously reported,[8,9] at 14 and 19 years of age, the semistructured psychiatric interview Schedule for Affective Disorder and Schizophrenia for School-Age Children- Present and Lifetime,[23] Norwegian version, was used for diagnostic evaluation according to the DSM-IV.[8,9] For longitudinal analysis, the overall anxiety category was arranged to include the same disorders between the 14-, 19-, and 26-year time points. The Wechsler Adult Intelligence Scale, 3rd edition,[24] was applied to estimate full scale IQ at age 19 years.[14,15] SES (levels 1–5) was calculated according to Hollingshead's Two Factor Index of Social Position, based on information on parents' education and occupation (adapted to today's categories). Parental SES was collected at the 14-year and supplemented at the 19-year time points.

Statistical Analyses

Pearson's χ^2 test was used for comparing dichotomous outcomes between groups. In 2 × 2 tables with small counts, we used the exact unconditional version of this test.[25] Ordinal and continuous outcomes between groups were compared using nonparametric tests. To preserve the familywise error rate due to comparisons between the 3 groups, we reported the maximum *P* values of the 3-group comparison and pairwise comparisons.[26] To assess the effect of possible confounders, we used logistic regression with any psychiatric diagnosis as the dependent variable, birth weight group as covariate, and adjusted separately for each possible confounder (Table 1). The longitudinal development of diagnosis was analyzed using general estimating equations (GEEs). We report 95% confidence intervals (CI) where relevant. In addition, *P* values <0.05 were considered statistically significant. Analyses were carried out by using SPSS version 22 (IBM SPSS Statistics, IBM Corporation), except the GEE analyses, which were carried out by using Stata version 13 (Stata Corp, College Station, TX) and the unconditional Pearson's test in www4.stat.ncsu.edu/~boos/exact/. The interrater reliability was examined in 30 randomly drawn participants and details of the analyses are given in the Supplemental Materials, including Supplemental Tables 5 and 6. Briefly, the participants were rerated by the 6 interviewers based on recorded interviews. The intraclass correlation coefficient for the GAF-F and GAF-S scores were 0.71 and 0.72, respectively (linear mixed model with subject and rater as random factors). For total disorders, Cohen's $\kappa = 0.71$, indicating good agreement. There was no tendency for the second rating to be higher or lower than the first one.

Ethics

The Regional Committee for Medical and Health Research Ethics of Central Norway approved the study protocols for each follow-up (No. 78-May 00, 2000; 4.2005.2605; 2013/636/REK midt). Participation was based on written informed consent, including written consent from the parents at the 14-year follow-up. There was a protocol for referral.

RESULTS

Clinical Characteristics

Clinical characteristics are presented in Table 2. Birth weight, gestational age, and head circumference at birth in the 3 groups differed by study design. All participants were white. Mean and range of parental SES was similar in the 3 study groups. In the subsample with available IQ data, mean IQ score was significantly lower in the VLBW ($P < .001$) and SGA group ($P = .002$) compared with the control group. Seven participants (2 VLBW, 5 SGA) were referred to appropriate health services.

Nonparticipant Analysis

Sex, birth weight, head circumference at birth, and gestational age did not differ between participants and nonparticipants in each group (Supplemental Table 7). There was

a significantly lower mean parental SES score for VLBW nonparticipants, a tendency toward a lower mean IQ score for SGA nonparticipants, and a significantly lower mean IQ score for control nonparticipants compared with the respective participant groups.

Prevalence of Psychiatric Disorders at 26 Years of Age

The VLBW group had a significantly higher overall prevalence of psychiatric disorders (n = 16, 36%) compared with the control group, including anxiety (n = 12, 27%), mood (n = 8, 18%), and somatoform disorders (n = 4, 9%) (Table 3). Of the 8 participants with mood disorders, 4 had bipolar disorder. All participants with somatoform disorders had body dysmorphic disorder. The higher prevalence of ADHD in the VLBW group (n = 4, 9%) did not reach significance. No participants had a substance use disorder. Analyzing by degree of prematurity and degree of growth restriction showed no significant differences in the proportion of any present psychiatric disorder (data not shown). Of the 3 participants with cerebral palsy, 1 had a psychiatric diagnosis. In the subsample with available IQ data, neither of the 2 participants with an IQ <70 had a psychiatric disorder.

The SGA group had a significantly higher overall prevalence of psychiatric disorders (n = 24, 38%) compared with the control group, including anxiety (n = 13, 20%), mood (n = 9, 14%), and somatoform disorders (n = 6, 9%) (Table 3). Of the 9 participants with a mood disorder, 3 had bipolar disorder. Of the 6 participants with somatoform disorder, 3 had body dysmorphic disorder. Seven participants (11%) had a substance use disorder.

The prevalence of psychiatric morbidity was nonsignificantly higher among females versus males

TABLE 1 OR for Any Psychiatric Disorder in the VLBW and the SGA Group Versus the Control Group, Adjusted Separately for Each Variable

	Preterm VLBW	*P*	Term SGA	*P*
Sex, OR (95% CI)[a]				
Unadjusted	3.6 (1.5–8.8)	.004	3.8 (1.7–8.6)	.001
Adjusted	3.7 (1.5–8.9)	.004	3.9 (1.7–8.8)	.001
Maternal age, OR (95% CI)[b]				
Unadjusted	3.9 (1.6–9.6)	.003	4.5 (1.9–10.7)	.001
Adjusted	4.1 (1.6–10.5)	.003	4.8 (2.0–11.5)	<.001
Maternal smoking, OR (95% CI)[c]				
Unadjusted	—	—	4.5 (1.9–10.7)	.001
Adjusted	—	—	4.2 (1.8–10.1)	.001
SES, OR (95% CI)[d]				
Unadjusted	3.8 (1.4–10.2)	.007	3.6 (1.5–8.9)	.006
Adjusted	3.8 (1.4–10.1)	.008	3.5 (1.4–8.8)	.006
IQ, OR (95% CI)[e]				
Unadjusted	4.6 (1.6–13.2)	.005	5.5 (2.1–14.9)	.001
Adjusted	2.4 (0.7–7.2)	.150	4.5 (1.6–12.3)	.004
GSI, mother, OR (95% CI)[f]				
Unadjusted	2.8 (1.0–7.7)	.055	2.7 (1.1–6.9)	.034
Adjusted	2.7 (1.0–7.7)	.056	2.7 (1.1–6.9)	.034
GSI, father, OR (95% CI)[g]				
Unadjusted	2.6 (0.9–7.6)	.087	3.6 (1.3–9.6)	.011
Adjusted	2.5 (0.8–7.5)	.113	3.6 (1.4–9.7)	.010

GSI, Global Severity Index, from Symptom Checklist-90-Revised. —, no information.
[a] Sex (n = 44 VLBW; 64 SGA; 81 control).
[b] Maternal age at birth in a subsample (n = 44 VLBW, 55 SGA, 78 control).
[c] Maternal smoking at conception in a subsample (n = 0 VLBW, 55 SGA, 78 control).
[d] Parental SES in a subsample (n = 36 VLBW, 52 SGA, 70 control).
[e] IQ scaled score at 19 years in a subsample (n = 33 VLBW, 44 SGA, 63 control).
[f] GSI, mother at 14 years in a subsample (n =31 VLBW, 50 SGA, 61 control).
[g] GSI Father at 14 y in a subsample (n = 30 VLBW, 40 SGA, 56 control).

TABLE 2 Clinical Characteristics Among Participants in the 3 Study Groups

	Preterm VLBW (n = 44)	Term SGA (n = 64)	Control (n = 81)
Birth characteristics, mean (SD)			
Birth weight, g	1196 (265)	2936 (199)	3710 (447)
Gestational age, weeks	30.0 (2.7)	39.6 (1.2)	39.8 (1.2)
Head circumference, cm[a]	26.9 (2.5)	33.8 (1.1)	35.5 (1.1)
Maternal age at birth, y[b]	28.5 (4.8)	28.8 (3.9)	30.7 (4.5)
Maternal smoking at conception, n (%)	— (—)	32/55 (58)	31/78 (40)
Parental SES, mean (SD)[c]	3.6 (1.3)	3.6 (1.2)	3.8 (1.1)
GSI, mother, mean (SD)[d]	0.23 (0.19)	0.28 (0.27)	0.28 (0.22)
GSI, father, mean (SD)[e]	0.35 (0.50)	0.14 (0.13)	0.17 (0.17)
IQ, mean (SD) [f]	87.5 (13.0)	95.8 (9.4)	102.4 (12.4)
Twins, No. (%)	7[g]/44 (16)	0 (0)	0 (0)
CP, n (%)	3/44 (7)	0 (0)	0 (0)
Boy, n (%)	21/44 (48)	32 /64 (50)	38 / 81 (47)
Age at participation, mean (SD), y	26.3 (0.7)	26.5 (0.5)	26.5 (0.5)

CP, cerebral palsy; GSI, Global Severity Index from Symptom Checklist-90-Revised. —, no information.
[a] Head circumference at birth in a subsample.
[b] Maternal age at birth in a subsample (n = 44 VLBW, 55 SGA, 78 control). P value VLBW versus control = .014; P value SGA versus control = .012.
[c] Parental SES in a subsample (n = 36 VLBW, 52 SGA, 70 control), collected at 14 years for 34 VLBW, 50 SGA, and 68 control participants, supplemented at 19 years for 2 VLBW, 2 SGA, and 2 control participants.
[d] Information on GSI, mother in a subsample (n = 31 VLBW, 50 SGA, 61 control).
[e] Information on GSI, father in a subsample (n = 30 VLBW, 40 SGA, 56 control).
[f] IQ scaled score at 19 years in a subsample (n = 33 VLBW, 44 SGA, 63 control).
[g] From 6 pairs.

in both the VLBW and the SGA groups (data not shown).

In the control group, 11 (14%) participants had a psychiatric disorder, of whom 7 had anxiety disorders and 5 had substance use disorders (Table 3). None of the participants in the control group had mood disorders. There were no significant sex differences in the prevalence of psychiatric morbidity (data not shown).

The odds ratio (OR) of having any psychiatric disorder in the VLBW and SGA groups versus the control group is displayed in Table 1. The unadjusted OR for the VLBW group was 3.6 (95% CI: 1.5–8.8; $P = .004$), and was 3.8 for the SGA group (95% CI: 1.7–8.6; $P = .001$). The ORs were practically unchanged in both the VLBW and the SGA group after adjusting for possible confounders; however, adjusting for IQ (subsample) reduced the OR in the VLBW group from 4.6 (95% CI: 1.6–13.2; $P = .005$) to 2.4 (95% CI: 0.7–7.2, $P = .150$).

Education, Occupation, Living Situation, and Functioning Scores at 26 Years of Age

Present functioning in terms of daily occupation is available in Table 4. The number of participants who were unemployed or receiving disability benefit was 8 (19%) for the preterm VLBW group, 9 (14%) for the term SGA group, and 4 (5%) for the control group. In the preterm VLBW group, 6 (14%) participants received disability benefits.

As shown in Fig 1, the VLBW group had lower levels of education compared with controls, a higher prevalence of having not completed high school, and a lower prevalence of having completed a master's degree or above ($P < .001$). The SGA group displayed corresponding, but less pronounced, results ($P = .017$).

There were no significant study group differences in living situation, or between those with or without a psychiatric disorder within the study groups (data not shown).

Function scores as estimated by GAF-F and GAF-S at 26 years of age are shown in Table 3. Both the VLBW and the SGA group had significantly lower function scores than the control group. No significant sex differences were found (data not shown).

TABLE 3 Prevalence of Psychiatric Diagnoses and Functioning Scores in the 3 Study Groups at 26 Years of Age

	Preterm VLBW ($n = 44$)	P	Term SGA ($n = 64$)	P	Control ($n = 81$)
Any psychiatric diagnosis, *n* (%)	16 (36)	.003	24 (38)	.002	11 (14)
Anxiety disorders	12 (27)	.020	13 (20)	.043	7 (9)
Panic disorder	1 (2)	—	3 (5)	—	0 (0)
Agoraphobia	2 (5)	—	8 (13)	—	0 (0)
Social phobia	3 (7)	—	3 (5)	—	3 (4)
Specific phobia	5 (11)	—	1 (2)	—	3 (4)
GAD	3 (7)	—	1 (2)	—	1 (1)
OCD	2 (5)	—	2 (3)	—	1 (1)
PTSD	0 (0)	—	1 (2)	—	0 (0)
Adjustment or mixed anxiety depressive disorder	0 (0)	—	0 (0)	—	0 (0)
Mood disorders	8 (18)	.001	9 (14)	.001	0 (0)
Depressive or dysthymic disorder	4 (9)	—	6 (9)	—	0 (0)
Bipolar disorder	4 (9)	—	3 (5)	—	0 (0)
Substance related disorders	0 (0)	.296	7 (11)	.301	5 (6)
Alcohol dependence or abuse	0 (0)	—	7 (11)	—	4 (5)
Drugs dependence or abuse	0 (0)	—	1 (2)	—	3 (4)
ADHD	4 (9)	.081	2 (3)	.581	1 (1)
Psychotic disorders	1 (2)	—	0 (0)	—	0 (0)
Eating disorders	0 (0)	—	0 (0)	—	0 (0)
Somatoform disorders	4 (9)	.019	6 (9)	.019	0 (0)
Somatization disorder	0 (0)	—	2 (3)	—	0 (0)
Hypochondria	0 (0)	—	1 (2)	—	0 (0)
Body dysmorphic disorder	4 (9)	—	3 (5)	—	0 (0)
Pain disorder	0 (0)	—	0 (0)	—	0 (0)
Comorbidity; ≥2 disorders	10 (23)	—	9 (14)	—	2 (2)
Comorbidity; ≥3 disorders	3 (7)	—	6 (9)	—	0 (0)
Functioning scores; mean (SD)					
GAF-F score at 26 y	78.5 (18.4)	.018	83.5 (11.8)	.047	87.4 (8.7)
GAF-S score at 26 y	79.3 (16.1)	.016	80.8 (13.5)	.010	86.4 (10.3)

P values versus controls. GAF-F and GAF-S score normal/preferable level: ≥81. GAD, global anxiety disorder; OCD, obsessive compulsive disorder; PTSD, posttraumatic stress disorder; —, not applicable.

TABLE 4 Daily Occupation in the 3 Study Groups

	Preterm VLBW ($n = 44$)	Term SGA ($n = 64$)	Control ($n = 81$)
In education, *n* (%)	7/44 (16)	14/ 64 (22)	23/81 (28)
Employed, *n* (%)	29/44 (66)	41/ 64 (64)	54/81 (67)
Receiving disability benefits, *n* (%)	6/44 (14)	2/64 (3)	0 (0)
Unemployed, *n* (%)	2/44 (5)	7/64 (11)	4/81 (5)

Longitudinal Analysis

A summary of cross-sectional prevalence at 14 and 19 years is presented in Supplemental Table 8. The main results are previously published.[8,9] The longitudinal development of the probability (%) of any psychiatric disorder is shown in Fig 2 (and Supplemental Table 9). From 14 to 26 years of age, the probability of any psychiatric

disorder increased slightly in the VLBW and the control groups, but markedly in the SGA group.

DISCUSSION

In this study, adults born preterm VLBW or term SGA had a higher prevalence of psychiatric disorders than controls. In addition, they were less likely to complete higher education and more likely to be unemployed or receiving disability benefits. They had lower function scores, indicating less coping abilities in everyday and social life. Overall, there were no, or small, sex differences. Parental SES, maternal age at birth, maternal smoking at conception (SGA and control groups only), and parental psychological distress did not influence results, whereas lower IQ was associated with psychiatric morbidity in the VLBW group. The longitudinal analyses indicated a high risk of psychiatric morbidity in the VLBW group at all 3 time points, and, importantly, the term born SGA group had a striking rise of psychiatric morbidity into adulthood.

At 26 years, mood disorders were significantly more prevalent in both the VLBW and SGA groups compared with control participants, who had a lower prevalence than the general population.[27] Interestingly, a quite large proportion of participants in the VLBW and SGA groups had bipolar disorder. Body dysmorphic disorder was the most frequent of the somatoform disorders. To our knowledge, body dysmorphic disorder is not previously demonstrated in low birth weight populations, and the prevalence was higher than the prevalence rate of 2% to 3% reported in the general population.[28,29] Body dysmorphic disorder shares some features with obsessive compulsive disorder and is in fact categorized as such in DSM-V. Body dysmorphic disorder also shares features with psychotic disorders, such as schizophrenia.[30] Body dysmorphic and bipolar disorders are considered severe psychiatric disorders and the long-term development and clinical implications in low birth weight individuals is uncertain.

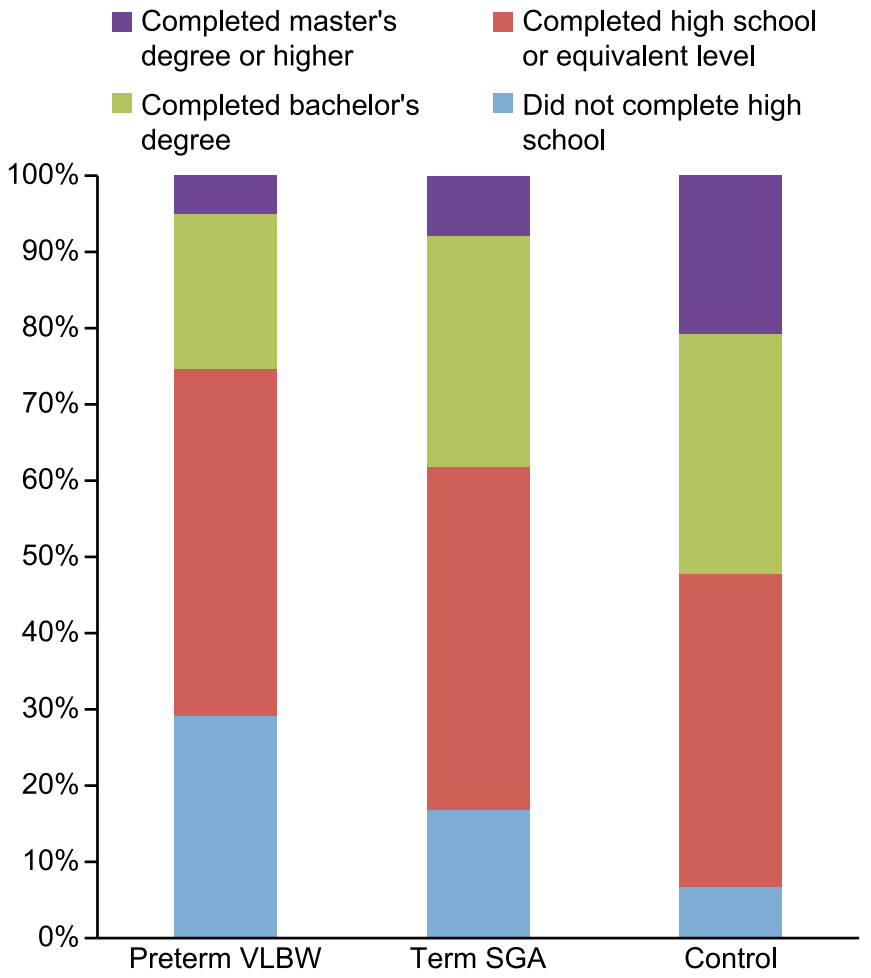

FIGURE 1
Completed educational level.

As expected, the previously reported high prevalence of anxiety disorders continued into adulthood in both the VLBW and SGA groups. Anxiety disorders have a multifactorial etiology; still, low birth weight seems to imply increased vulnerability. Brain development deviations[31] and disturbances in the neuroendocrine axis[32] may both contribute to this vulnerability.

Although the decreasing prevalence of ADHD into adulthood seen in this study is consistent with population data,[33] according to Breeman et al,[34] VLBW/very preterm individuals showed more stability in both attention problems and prevalence of ADHD into adulthood compared with their term born peers.

The prevalence of substance use disorders differed between the VLBW and the SGA groups; in the SGA group, these disorders accounted for nearly one-third of the overall prevalence of psychiatric disorders, but were absent in the VLBW group. This finding might represent a predisposition to substance use disorders specific to the SGA group. Furthermore, substance use may also serve as "self-medication" of potentially underlying psychopathology.[35] For

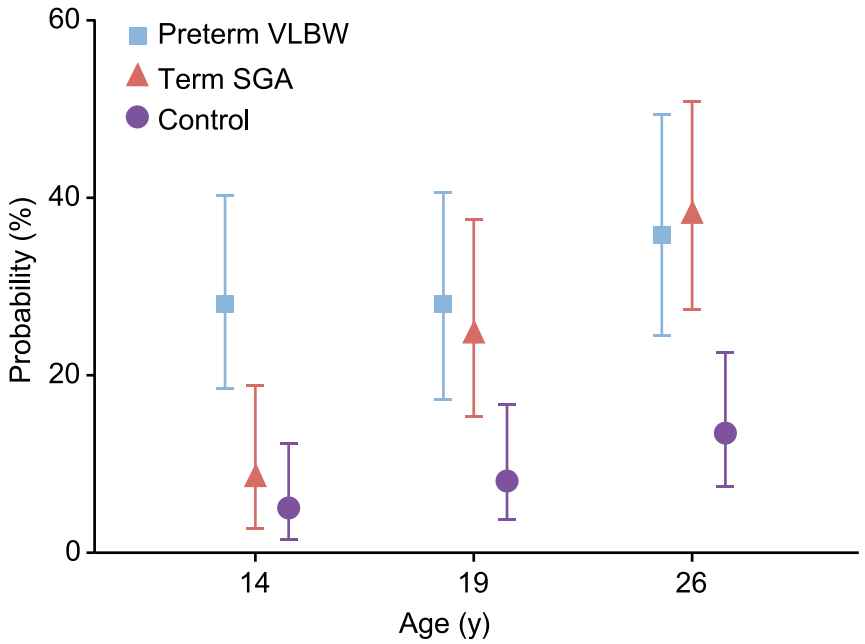

FIGURE 2
Probability of psychiatric disorders from adolescence to adulthood. Estimates and 95% CIs from GEEs.

both groups, the results on substance use disorders are in line with other studies.[10,12,13]

According to our longitudinal analysis, the probability of psychiatric disorders in the term SGA group increased substantially into adulthood. Although the pre- and perinatal differences between the VLBW and the SGA are most apparent, we speculate, in line with Barker's hypothesis of developmental origins of health and disease,[36] that the 2 groups may share some prenatal exposure, contributing to their similar overall adult morbidity and similar profile of non–substance use disorders.

Few others have used diagnostic interviews or presented longitudinal diagnostic data on preterm VLBW and term SGA individuals. Van Lieshout et al[37] reported significant differences only in the total prevalence of non–substance use disorders, using the MINI interview when assessing extremely low birth weight (<1000 g) individuals at age 30 years. Vasiliadis et al[38] reported a protective effect of high birth weight in the risk of adult generalized anxiety disorder, using the Diagnostic Interview Schedule at a mean age of 33 years, and Westrupp et al[18] reported a higher risk of mood disorders in VLBW individuals using the Structured Clinical Interview at age 24 to 29 years. In line with our results, Heinonen et al[39] reported for the early preterm group an OR of any common mental disorder of 3.0 (95% CI: 1.25–7.21). The prevalence of psychiatric disorders in the control group was comparable with data from the Norwegian Institute of Public Health, reporting a prevalence of mental health problems of 10.4% in the age group of 25 to 44 years (Hopkins Symptom Check List-25 score >1.75).[40]

Although there were differences in maternal age at birth and maternal smoking (SGA and control group only) at conception, adjusting for these factors had no effect on the risk for psychiatric disorders at 26 years of age. In addition, sex, parental SES, and parental psychological distress measured during adolescence did not alter the OR for any psychiatric disorder in the regression analysis. Thus, we speculate that low birth weight or preterm birth override the potential modifying effect of these variables.

Despite the overall prevalence of psychiatric disorders being quite similar in the 2 low birth weight groups, our results indicate that the term SGA group managed better than the preterm VLBW group in everyday life, both in academic performance and general functioning. This finding may be related to the observed lower IQ and the association between psychiatric disorders and IQ in the VLBW group. The difference in functioning may also be explained by the different pattern of disorders in the 2 groups, because substance use disorders might be compatible with an approximately normal function level at this young age. In addition, the SGA group had less comorbidity than the VLBW group, suggesting less total strain.

Study limitations include the limited sample size, which may influence the external validity of our findings. In addition, due to the small sample size, random findings may occur and negative findings should be interpreted with caution. The nonparticipant analysis of IQ and parental SES may indicate higher attrition of those with lower functioning across birth weight groups. Age-specific diagnostic interviews were used in adolescence (Schedule for Affective Disorder and Schizophrenia for School-Age Children- Present and Lifetime at 14 and 19 years of age) and adulthood (MINI interview at 26 years of age), and equivalent diagnostic categories were applied for longitudinal comparison. The 26-year assessment was performed by several interviewers, thus, despite acceptable results in the interrater analysis, misclassification bias cannot be ruled out. We did not have information on child neglect or maltreatment, including prenatal

exposure to alcohol or drugs. These are all known risk factors for later somatic and mental health problems, and may confound the results. Thus, the lack of influence by SES on risk of psychiatric disorders cannot exclude social factors as contributors.

CONCLUSIONS

The higher psychiatric morbidity and poorer functioning in adults born preterm VLBW and term but SGA emphasize the obvious importance of primary prevention of preterm birth and low birth weight and continual improvement of perinatal treatment. Furthermore, secondary prevention and early intervention is crucial to promote optimal health trajectories throughout life. Still, many adults with low birth weights were health and well-functioning and their high rate of employment is encouraging. The longitudinal development of psychiatric morbidity in the term SGA group calls for additional investigation because this part of the population receives no special attention or health care, and yet may have unrecognized challenges.

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ABBREVIATIONS

ADHD: attention-deficit/hyperactivity disorder
CI: confidence interval
DSM: *Diagnostic and Statistical Manual of Mental Disorders*
GAF-F: Global Assessment of Functioning: function score
GAF-S: Global Assessment of Functioning: symptom score
GEE: general estimating equation
MINI interview: MINI International Neuropsychiatric Interview: M.I.N.I. Plus, Norwegian Version
OR: odds ratio
SES: socioeconomic status
SGA: small for gestational age
VLBW: very low birth weight

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