

Common mental disorders in young adults born late-preterm

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Background. Results of adulthood mental health of those born late-preterm (34 + 0–36 + 6 weeks + days of gestation) are mixed and based on national registers. We examined if late-preterm birth was associated with a higher risk for common mental disorders in young adulthood when using a diagnostic interview, and if this risk decreased as gestational age increased.

Method. A total of 800 young adults (mean = 25.3, s.d. = 0.62 years), born 1985–1986, participated in a follow-up of the Arvo Ylppö Longitudinal Study. Common mental disorders (mood, anxiety and substance use disorders) during the past 12 months were defined using the Composite International Diagnostic Interview (Munich version). Gestational age was extracted from hospital birth records and categorized into early-preterm (<34 + 0, *n* = 37), late-preterm (34 + 0–36 + 6, *n* = 106), term (37 + 0–41 + 6, *n* = 617) and post-term (≥42 + 0, *n* = 40).

Results. Those born late-preterm and at term were at a similar risk for any common mental disorder [odds ratio (OR) 1.11, 95% confidence interval (CI) 0.67–1.84], for mood (OR 1.11, 95% CI 0.54–2.25), anxiety (OR 1.00, 95% CI 0.40–2.50) and substance use (OR 1.31, 95% CI 0.74–2.32) disorders, and co-morbidity of these disorders (*p* = 0.38). While the mental disorder risk decreased significantly as gestational age increased, the trend was driven by a higher risk in those born early-preterm.

Conclusions. Using a cohort born during the advanced neonatal and early childhood care, we found that not all individuals born preterm are at risk for common mental disorders in young adulthood – those born late-preterm are not, while those born early-preterm are at a higher risk. Available resources for prevention and intervention should be targeted towards the preterm group born the earliest.

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Introduction

Each year 14.9 million births worldwide are preterm (<37 + 0 weeks + days of gestation) (Blencowe *et al.* 2012). Of these births 70% are late-preterm (34 + 0–36 + 6 weeks + days of gestation) (Davidoff *et al.* 2006; Engle *et al.* 2007). While those born at the most severe end of birth weight and gestational length distribution of preterm birth are at an increased risk of mental

disorders (Johnson & Marlow, 2011; Treyvaud *et al.* 2013; Van Lieshout *et al.* 2015) it remains less clear if this risk also characterizes those born late-preterm. We are aware of only a handful of studies that have examined mental disorders among those born late-preterm (Linnet *et al.* 2006; Moster *et al.* 2008; Talge *et al.* 2010; D'Onofrio *et al.* 2013; Harris *et al.* 2013; Rogers *et al.* 2013; Lahti *et al.* 2014), and only three have extended follow-ups into adulthood (Moster *et al.* 2008; D'Onofrio *et al.* 2013; Lahti *et al.* 2014). These Scandinavian register studies demonstrate an inconsistent pattern of risks. In the first study, late-preterm birth was associated with an increased risk of schizophrenia, disorders of psychological

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development, behaviour and emotion [risk ratios (RR): 1.3–1.5], but not with autism spectrum disorders (Moster *et al.* 2008); in the second study, it was associated with an increased risk of psychotic/bipolar disorder, autism spectrum disorders and attention deficit hyperactivity disorder (ADHD) [hazard ratios (HR): ~1.2 to ~1.3], but not with substance use disorder or suicide attempts (D’Onofrio *et al.* 2013); and in the third study, it was associated with an increased risk of suicide (HR 2.01), but not with substance use, psychotic, mood, anxiety or personality disorders or suicide attempt (Lahti *et al.* 2014).

In all these studies diagnoses of mental disorders were extracted from registers carrying data on inpatient hospitalizations, outpatient care, disability benefits or cause of death. While the severity of mental disorders is highly correlated with receiving treatment, up to 50% of individuals in developed countries with mental disorder go untreated and, hence, remain unidentified by the registers (Demyttenaere *et al.* 2004; Ten Have *et al.* 2013). Furthermore, of those receiving mental health treatment, up to 14% neither meet the criteria for mental disorders nor report other indicators of need for treatment (Bruffaerts *et al.* 2015).

To overcome at least some of the shortcomings related to studies employing registries, we tested if late-preterm birth was associated with increased risk for mood, anxiety and substance use disorders and comorbidity of these disorders defined by the Munich-Composite International Diagnostic Interview (M-CIDI), and if the mental disorder risk decreased according to the degree of prematurity. Our secondary aim was to test if the mental disorder risk varied according to the degree of intrauterine growth restriction.

Method

The study participants are from the Finnish arm of the Bavarian-Finnish Longitudinal Study (BFLS), also called the Arvo Ylppö Longitudinal Study (AYLS; Wolke *et al.* 1998; Heinonen *et al.* 2008). We identified all 1535 infants (867 boys, 56.5%) born alive in the county of Uusimaa, Finland between 15 March 1985 and 14 March 1986, who were admitted to neonatal wards in obstetric units, or transferred to the Neonatal Intensive Care Unit (NICU) of the Children’s Hospital, Helsinki University Central Hospital within 10 days of their birth. The population ranged from severely ill preterm infants to infants born at term requiring only brief inpatient observation. The gestational age in the hospitalized group ranged from 23 to 43 weeks. Additionally, we identified 658 (326 boys, 49.5%) infants not admitted to neonatal wards or NICU. Infants were prospectively randomly recruited from the three largest maternity hospitals in the study area

and the neonate born after every second hospitalized infant was selected. The gestational age in this control group ranged from 35 to 42 weeks.

Of the 2193 infants of the original cohort, 2086 were identified in adulthood based on Finnish personal identification numbers. During 2009–2012, we invited 1913 (173 participants’ addresses were not traceable, they lived abroad or would have needed accommodation for an overnight stay) for a clinical and psychological follow-up, and 1136 participated (59.4%, 51.8% of the original cohort) [mean age = 25.5, standard deviation (s.d.) = 0.65, range 24.4–27.1 years]. Of these, 957 underwent the M-CIDI interview. We excluded 21 because of organic mental disorder (corresponding to ICD-10 categories F06.0–06.4: mental disorders due to brain damage and dysfunction and to physical disease); two had missing information on the date of last substance use episode; 129 did not have information on gestational age or the information was evaluated as unreliable; five participants had congenital malformations or chromosomal abnormalities. Thus, the analytical sample comprised 800 participants (392 men, 49%) (41.8% of those invited, 36.5% of the initial study cohort) (Supplementary Fig. S1).

Compared to the analytical sample ($n = 800$), those in the initial study cohort ($n = 1393$) but not included in the current study were more often men (49.0% *v.* 57.5%, $p < 0.001$), born preterm [4.6% *v.* 9.3% early-preterm (24 + 0–33 + 6 weeks + days of gestation), 23.3% *v.* 15.0% late-preterm, 77.1% *v.* 71.8% term, and 5.0% *v.* 3.9% post-term, $p < 0.001$], had lower birth weight for gestational age s.d. score [mean difference (MD) = 0.20, $p < 0.001$], were more often admitted to hospital (63.5% *v.* 73.7%, $p < 0.001$), had younger mothers (MD = 0.76 years, $p = 0.001$) who had smoked more often during pregnancy (14.1% *v.* 26.5%, $p < 0.001$) and more often had parents with a lower level of education (8.0% *v.* 15.9% elementary, 21.5% *v.* 28.7% upper secondary, 36.8% *v.* 33.2% lower tertiary, 33.8% *v.* 22.1% upper tertiary, $p < 0.001$). The groups did not differ in 5-min Apgar score ($p = 0.15$). In addition, we compared those included in the current study ($n = 800$) with those excluded due to unreliable, but existing, information on gestational age ($n = 128$). These groups did not differ from each other in gestational age as categorized into early-preterm, late-preterm, term and post-term ($p = 0.44$) or in M-CIDI diagnoses (all p ’s > 0.18).

The study protocol at birth was approved by the ethics committees of the Helsinki City Maternity Hospital, Helsinki University Central Hospital, and Jorvi Hospital and in adulthood by the Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District. The informed consent was obtained from parents (childhood) and participants (adulthood).

Gestational age and fetal growth

Gestational age was categorized as early-preterm ($n = 37$, 16 were born very preterm, $<32 + 0$), late-preterm ($n = 106$), term ($n = 617$) and post-term ($n = 40$). Length of gestation was extracted from medical records. It was based on fetal ultrasound, performed before 24 + 0 weeks of gestation, of 28 (75.7%) of early-preterm, 72 (67.9%) of late-preterm, 395 (64.0%) of term and 20 (50.0%) of post-term participants. If ultrasound was not performed, gestational age was determined from the date of mother's last menstrual period.

Birth weight (g) was extracted from birth records and expressed in S.D. units relative to sex and length of gestation, based on Finnish standards (Pihkala *et al.* 1989). Children born <-2 S.D. of mean birth weight were defined as 'small for gestational age' (SGA), those born ≥ -2 and ≤ 2 S.D. of the mean as 'appropriate for gestational age' (AGA), and those born >2 S.D. of the mean as 'large for gestational age' (LGA).

Mental disorders

Mood, anxiety and substance use disorders (DSM-IV) during the past 12 months were assessed using a Finnish translation of the computerized M-CIDI (Wittchen & Pfister, 1997; Andrews & Peters, 1998; Wittchen *et al.* 1998; Pirkola *et al.* 2005). Mood disorders included major depressive disorder, dysthymia, and bipolar disorder. Anxiety disorders included general anxiety disorder, social phobia, panic disorder with or without agoraphobia, and agoraphobia. Substance use disorders included alcohol use disorder (dependence or abuse) and other substance use disorder (dependence or abuse). Co-morbidity was defined as suffering from any disorder from more than one of the three categories (Pirkola *et al.* 2005). The CIDI interview is valid and reliable (Andrews & Peters, 1998; Wittchen *et al.* 1998; Jacobi *et al.* 2004; Pirkola *et al.* 2005) and has good concordance with the Structured Clinical Interview for DSM Disorders (Haro *et al.* 2006). The interviews were performed by eight master's-level psychology students, trained by a psychiatrist with WHO authorization (S.P.) and supervised by a clinical psychologist (K.H.). The interviewers were blind to all earlier collected information of the participants including gestational age.

Covariates and confounders

All covariates and confounders were *a priori* selected on the basis of earlier literature. Covariates associated with either prematurity or mental health extracted from hospital records, included sex, multiple pregnancy (singleton/multiple), parity (primiparous *v.*

multiparous), Apgar score at 5 min (0–7, >7), length of stay in neonatal ward (no hospitalization, ≤ 7 days, 8–14 days, >14 days). Confounders associated with both prematurity and mental health, extracted from hospital records, included maternal pre-pregnancy body mass index (kg/m^2) (BMI), hypertensive disorder during pregnancy (hypertension, pre-eclampsia, normotension), diabetes during pregnancy (gestational diabetes, type 1 diabetes, no diabetes; none had type 2 diabetes), and maternal age at delivery (<20 , 20–40, >40 years). Other confounders included maternal smoking during pregnancy (0, 1–10, or >10 cigarettes per day; reported at maternity ward) reported by the child's mother at study baseline, highest educational attainment of the either parent (elementary, upper secondary, lower tertiary, upper tertiary) reported by the child's mother when the child was 56 months old, maternal mental disorders (no *v.* yes) reported by the child's mother in conjunction with the adulthood follow-up, and self-reported highest completed or ongoing educational attainment (elementary, upper secondary, lower tertiary, upper tertiary).

Statistical analysis

Logistic regression analyses with odds ratios (OR) and 95% confidence intervals (CI) were used to test if late-preterm birth, in relation to (a) term birth, (b) early-preterm birth, and (c) post-term birth increased the risk of mental disorders. Linear regression analysis tested if co-morbidity of mental disorders was higher in those born late-preterm than those born at term, early-preterm and post-term. The above analyses were re-run with length of gestation as a continuous variable to test if the prevalence of mental disorders and co-morbidity decreased according to the degree of prematurity. These analyses were further specified by comparing the early-term group with term-born and post-term groups. Early-preterm/late-preterm *v.* term birth \times SGA *v.* AGA interaction tested if intrauterine growth restriction modified the associations.

In all analyses, we made adjustments for all covariates and confounders, except for maternal mental disorders (model I), and then for all of them (model II). Missing information in covariates and confounders were dummy-coded as a separate category. We considered two-tailed p values <0.05 as statistically significant.

Results

Twelve-month prevalence of any common mental disorder was 34.8%, and of mood, anxiety and substance use disorders 13.1%, 9.3% and 23.4%, respectively;

25.5%, 7.5% and 1.8% had suffered from a disorder in one, two or three categories, respectively. Women had more often mood, anxiety and less often substance use disorders, but their co-morbidity did not differ by sex (Table 1). There were no sex differences in covariates or confounders (p values >0.06).

Table 2 presents covariates and confounders by gestational age categories. Those born late-preterm differed from those born at term such that they were hospitalized more often and for a longer period after birth and their mothers had smoked more, had more often hypertensive disorders and diabetes during pregnancy; They also differed from those born early-preterm such that they were hospitalized less often and for a shorter period after birth and more often had Apgar score >7 at 5 min, and from those born post-term such that they were hospitalized more often and for a longer period after birth, were more often men, and born from multiple, multiparous or hypertensive pregnancies. Differences between those born early-preterm and post-term from the term group and from each other are presented in Table 2.

Supplementary Table S1 presents these characteristics by mental disorders.

Late-preterm birth and mental disorders

Table 3 shows that those born late-preterm did not differ from those born at term in their risk for any common mental disorder, for mood, anxiety or substance use disorders, or their co-morbidity (β 's <0.04 , p 's >0.38 for models I and II).

When compared to those born early-preterm, those born late-preterm had lower odds for any common mental disorder (OR 0.37, 0.15–0.94, $p=0.04$ for model I, $p=0.04$ for model II) and mood disorders (OR 0.27, 0.08–0.92, $p=0.04$ for model I, $p=0.04$ for model II). Rates of mental disorders did not vary between those born late-preterm and those born post-term (all p values >0.10).

Degree of prematurity and mental disorders

The prevalence of mood disorders ($p=0.03$, Fig. 1) and co-morbidity for mental disorders ($p=0.045$, Fig. 2) decreased as the length of gestation increased. When we excluded those born post-term, prevalence for substance use disorders decreased as gestational age increased ($p=0.04$) (Fig. 1).

Additional analyses where early-preterms were compared to those born at term demonstrated that early-preterms had higher odds for any common mental disorder (OR 3.00, 1.25–7.21, $p=0.01$ for model I, $p=0.02$ for model II), for mood (OR 4.03, 1.30–12.51, $p=0.02$ for model I, $p=0.02$ for model II) and substance use disorders (OR 3.12, 1.15–8.48, $p=0.03$ for model I,

$p=0.03$ for model II), and were more likely to suffer from mental disorder co-morbidity (p values <0.03 for models I and II). Compared to post-terms, those born early-preterm had higher odds for mood disorders (OR 7.14, 1.47–33.33, $p=0.02$ for model I, $p=0.02$ for model II) and were more likely to suffer from mental disorder co-morbidity (p values <0.04 for models I and II).

Intrauterine growth patterns and mental disorders

Finally, analyses testing moderation by SGA/AGA status among those born late-preterm and term, and among those born early- to late-preterm and term did not reveal any significant interactions (all p values >0.75). Compared to those born AGA, those born SGA did not have an increased risk for mental disorders with or without controlling for gestational age (all p values >0.08).

Discussion

Using a validated diagnostic interview, the current study demonstrates that 33.0% of adults born late-preterm had suffered from any common mental disorder during the previous 12 months, compared to 34.2% of those born at term. For specific disorders, the rates were also similar: 17.4% *v.* 16.1% had a history of a mood, 10.1% *v.* 13.1% of anxiety, and 26.8% *v.* 25.0% of substance use disorders. Rates of co-morbidity of these disorders were also equivalent between those born late-preterm and at term, 21.7%, 9.4% and 1.9% of those born later preterm and 25.8%, 6.6% and 1.8% of those born at term had suffered from one disorder or two or three co-morbid disorders, respectively. These findings concur with previous studies that have not either identified differences in risks for mood, anxiety or substance use disorders in adulthood when these diagnoses are derived from registers (Moster *et al.* 2008; D'Onofrio *et al.* 2013; Lahti *et al.* 2014). Our findings thus add to the previous literature by showing that even when mental disorders are identified using a diagnostic interview, adults born late-preterm and at term do not differ from each other in the 12-month prevalence and co-morbidity rates of common mental disorders.

However, our study revealed that the risk for these disorders decreased as gestational age increased. Indeed, compared to those born early-preterm, those born late-preterm had lower risks for any common mental disorder and mood disorders, those born at term had lower risks for any common mental disorder, mood and substance-use disorders and mental disorder co-morbidity, and those born post-term had lower risk for mood disorders and mental disorder

Table 1. 12-month prevalence of M-CIDI DSM-IV mood, anxiety, and substance use disorders

Mental disorder	Men (<i>n</i> = 392)	Women (<i>n</i> = 408)	Men <i>v.</i> women χ^2 test, <i>p</i>
Any common mental disorder	134 (34.2%)	144 (35.3%)	0.74
Mood disorders	35 (8.9%)	72 (17.2%)	0.003
Dysthymia or major depressive disorder ^a	28 (7.1%)	59 (14.5%)	0.003
Bipolar disorder	7 (1.8%)	11 (2.7%)	0.38
Anxiety disorders	24 (6.1%)	50 (12.3%)	0.006
Social phobia	11 (2.8%)	15 (3.7%)	0.48
Generalized anxiety disorder	4 (1.0%)	8 (2.0%)	0.27
Other anxiety disorder	16 (4.1%)	38 (9.3%)	0.006
Substance use disorders	115 (29.3%)	72 (17.6%)	0.005
Alcohol use disorder (dependence or abuse)	111 (28.3%)	70 (17.2%)	0.006
Other substance use disorder	13 (3.3%)	4 (1.0%)	0.03
Co-morbidity			0.16
One disorder	103 (26.3%)	101 (24.8%)	
Two disorders ^b	22 (5.6%)	38 (9.3%)	
Three disorders	9 (2.3%)	5 (1.2%)	

Categories have co-morbidity with each other.

^a Of total 10.0% (6.6% men, 13.2% women, $p = 0.005$) had major depressive disorder.

^b Mood and anxiety disorder $n = 19$ (31.7%), mood and substance use disorder $n = 26$ (43.3%), anxiety and substance use disorder $n = 15$ (25.0%).

co-morbidity. Hence the decreasing trend of mental disorder risk was driven by a higher risk for mental disorders in those born the earliest. Strikingly, nearly half of those born early-preterm had suffered from any common mental disorder during the past 12 months. While not the direct focus of our study, these findings deserve some attention as they concur with previous studies (Indredavik *et al.* 2010; Johnson *et al.* 2010; Johnson & Marlow, 2011; Nosarti *et al.* 2012; D'Onofrio *et al.* 2013; Van Lieshout *et al.* 2015) and hence increase both internal and external validity of our findings. However, of note is that in some previous studies those born the earliest/smallest have been less likely to suffer from alcohol and substance use disorders than those born at term (Strang-Karlsson *et al.* 2008; Lindström *et al.* 2009; D'Onofrio *et al.* 2013; Van Lieshout *et al.* 2015). In our study, the number of participants was, however, too small to examine more extreme groups, such as those born very preterm, separately. Thus, combining them may have masked any potential protective effects and may explain this slight controversy. This was supported by a *post-hoc* analyses in this sample which showed that those born very preterm did not differ (p values >0.39) from those born at term, whereas those born moderately preterm (32+0–33+6 weeks of gestation) had a significantly higher risk (p values <0.03) for substance use disorders.

Several mechanisms may underlie the detected associations, including brain immaturity, and severity of

neonatal illnesses and complications, which decrease as gestational age increases. Although abnormalities in brain structure and function are also detected among those born late-preterm (Munakata *et al.* 2013; Rogers *et al.* 2014; Kelly *et al.* 2015), brain changes have been reported to be wide among those born earliest (Bäumler *et al.* 2014). Moreover, existing studies have shown associations between brain abnormalities and behavioural and psychiatric problems in preterm children (Skranes *et al.* 2007; Rogers *et al.* 2012, 2014; Treyvaud *et al.* 2013). Further, neonatal complications and illnesses related to preterm birth may amplify the risk for neurodevelopmental adversities (Whitaker *et al.* 1997; Indredavik *et al.* 2010). The risk for neonatal illnesses and complications generally decrease as gestational age increases (Milligan, 2010; Engle, 2011; Laptok, 2013). Moreover, severe complications, e.g. intracranial haemorrhage, are less common among those born late than among those born earlier (Laptok, 2013). Further, in our sample, the length of stay in neonatal intensive care was longest and 5-min Apgar score more often <7 in those born early-preterm suggesting more severe illnesses/complications in this group. However, as we lack neuroimaging data, we cannot determine the extent to which any potential differences in brain structure and function according to the severity of preterm birth underlie our findings.

Moreover, also less mature regulatory and communicative abilities of those born preterm (Voegtline &

Table 2. Characteristics of the study sample by gestational age

Variable	Gestational age			
	Early-preterm 24+ 0–33+6 weeks (n = 37) n (%) / mean (s.d.)	Late-preterm 34+0– 36+6 weeks (n = 106) n (%) / mean (s.d.)	Term 37+0–41+6 weeks (n = 617) n (%) / mean (s.d.)	Post-term ≥42+0 weeks (n = 40) n (%) / mean (s.d.)
Sex (men)	23 (62.2%) ^a	59 (55.7%)	299 (48.5%)	11 (27.5%) ^{b,c}
Pre- and neonatal period				
Intrauterine growth				
SGA	9 (24.3%) ^{a,b}	18 (17.0%)	27 (4.4%)	1 (2.5%)
AGA	27 (73.0%)	82 (77.4%)	568 (92.1%)	36 (90.0%)
LGA	1 (2.7%)	6 (5.7%)	22 (3.6%)	3 (7.5%)
Multiple pregnancy	3 (8.1%) ^b	12 (11.3%)	14 (2.3%)	0 (0.0%) ^c
Parity (primiparous)	25 (67.6%) ^b	59 (55.7%)	305 (49.4%)	33 (82.5%) ^{b,c}
Maternal prepregnancy, BMI	22.3 (3.72)	22.0 (2.53)	22.2 (3.36)	21.8 (3.05)
Maternal hypertensive disorder				
Hypertension	3 (8.1%) ^{a,b}	9 (8.5%) ^b	108 (17.5%)	4 (10.0%) ^c
Pre-eclampsia	7 (18.9%)	15 (14.2%)	14 (2.3%)	0 (0.0%)
Normotension	27 (73.0%)	82 (77.4%)	495 (80.2%)	36 (90.0%)
Maternal diabetes				
No OGTT	33 (89.2%)	81 (76.4%) ^b	494 (80.1%)	36 (90.0%)
Normal OGTT	4 (10.8%)	14 (13.2%)	84 (13.6%)	4 (10.0%)
Gestational diabetes	0 (0.0%)	3 (2.8%)	30 (4.9%)	0 (0.0%)
T1 diabetes	0 (0.0%)	8 (7.5%)	9 (1.5%)	0 (0.0%)
Maternal smoking during pregnancy				
No	27 (73.0%) ^b	86 (81.1%) ^b	542 (87.8%)	32 (80%)
1–10/day	7 (18.9%)	18 (17.0%)	54 (8.8%)	6 (15.0%)
>10 /day	3 (8.1%)	2 (1.9%)	21 (3.4%)	2 (5.0%)
Maternal age at delivery				
<20 years	1 (2.7%)	1 (0.9%)	8 (1.3%)	0 (0.0%)
20–40 years	36 (97.3%)	103 (97.2%)	598 (96.8%)	40 (100.0%)
>40 years	0 (0.0%)	2 (1.85)	11 (1.8%)	0 (0.0%)
Apgar score 5 min ^d				
0–7	8 (22.2%) ^{b,c}	9 (8.8%)	44 (7.3%)	7 (17.9%) ^b
>7	28 (77.8%)	93 (91.2%)	560 (92.7%)	32 (82.1%)
Length of stay in hospital				
No hospitalization	0 (0.0%) ^{b,c}	6 (5.7%) ^{b,a}	275 (44.6%)	11 (27.5%) ^c
≤7 days	13 (35.1%)	84 (79.2%)	318 (51.5%)	29 (72.5%)
8–14 days	7 (18.9%)	15 (14.2%)	15 (2.4%)	0 (0.0%)
>14 days	17 (45.9%)	1 (0.9%)	9 (1.5%)	0 (0.0%)
Childhood				
Parental education				
Elementary	2 (5.4%)	11 (10.4%)	47 (7.6%)	4 (10.0%)
Upper secondary	10 (27.0%)	27 (25.5%)	127 (20.6%)	8 (20.0%)
Lower tertiary	13 (35.1%)	35 (33.0%)	229 (37.1%)	17 (42.5%)
Upper tertiary	12 (32.4%)	33 (31.1%)	214 (34.7%)	11 (27.5%)
Young adulthood				
Age	25.0 (0.65)	24.7 (0.68)	24.8 (0.70)	24.6 (0.71)
Own education ^e				
Elementary	2 (5.4%)	3 (2.9%)	26 (4.3%)	2 (5.1%)
Upper secondary	11 (29.7%)	37 (35.6%)	192 (31.6%)	11 (28.2%)
Lower tertiary	8 (21.6%)	28 (26.9%)	168 (27.7%)	12 (30.8%)
Upper tertiary	16 (43.2%)	36 (34.6%)	221 (36.4%)	14 (35.9%)
Mother's self-reported mental illness ^f	10 (31.3%)	14 (17.5%)	107 (20.8%)	5 (16.1%)

Table 2 (cont.)

Variable	Gestational age			
	Early-preterm 24+ 0–33+6 weeks (n = 37) n (%) / mean (s.d.)	Late-preterm 34+0– 36+6 weeks (n = 106) n (%) / mean (s.d.)	Term 37+0–41+6 weeks (n = 617) n (%) / mean (s.d.)	Post-term ≥42+0 weeks (n = 40) n (%) / mean (s.d.)
CIDI DSM-IV mental disorders				
Any common disorder	17 (45.9%)	35 (33.0%)	211 (34.2%)	15 (37.5%)
Mood disorder	8 (28.6%)	15 (17.4%)	78 (16.1%)	4 (13.8%)
Anxiety disorder	4 (16.7%)	8 (10.1%)	61 (13.1%)	1 (3.8%)
Substance use disorder	13 (39.4%)	26 (26.8%)	135 (25.0%)	13 (34.2%)

SGA, Small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; BMI, body mass index; OGTT, Oral glucose tolerance test.

^a $p < 0.05$ for difference between early-preterm and post-term groups.

^b $p < 0.05$ for difference against the term born group.

^c $p < 0.05$ for difference against the late-preterm born group.

^d Data missing from 1 early-preterm, 4 late-preterm, 13 term and 1 post-term participants.

^e Data missing from 2 late-preterm, 10 term, and 1 post-term participants.

^f data missing from 5 early-preterm, 26 late-preterm, 102 term and 9 post-term participants.

Table 3. Risk of common mental disorders during the past 12 months in young adults born late-preterm (n = 106) compared to those born at term (n = 617)

	Mental disorder ^a											
	Any common			Mood			Anxiety			Substance use		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Term v. late-preterm												
Model I	1.11	0.67–1.84	0.68	1.11	0.54–2.25	0.78	1.00	0.40–2.50	0.99	1.31	0.74–2.32	0.36
Model II	1.08	0.66–1.80	0.75	1.08	0.53–2.21	0.83	1.00	0.40–2.49	0.99	1.30	0.73–2.29	0.37

OR, Odds ratio; CI, confidence interval.

Of those born at term 406 and of those born late-preterm 71 did not have any mental disorders and were used as a comparison group.

Model I: Controlling for sex, age and maximum educational level of either parent(s), own educational level, maternal age, and pre-pregnancy body mass index, multiple pregnancy, parity, small for gestational age (SGA), large for gestational age (LGA), 5-min Apgar score, smoking during pregnancy, maternal diabetes, hypertension, and pre-eclampsia, length of hospitalization after birth.

Model II: Further controlling for mother's self-reported mental health.

Stifter, 2010; Wolke *et al.* 2014) may add to the risk for later mental health problems of the offspring (Hemmi *et al.* 2011). Further, although observed parenting sensitivity does not differ between those born preterm and term (Bilgin & Wolke, 2015), findings suggest that those born preterm are more susceptible to parenting effects (Shah *et al.* 2013; Jaekel *et al.* 2014). Evidence that especially those born the earliest (Shah *et al.* 2013) are most affected, may potentially also explain

the increased risk of mental disorders among those born early-preterm, but not among those born late-preterm. Finally, a common, not yet known, genetic or environmental risk factor may also be involved.

Our study also showed that intrauterine growth (SGA/AGA), did not add to the risk for common mental disorders at any degree of gestational age. Earlier studies among adults born with extremely or very low birth weight have suggested that SGA birth

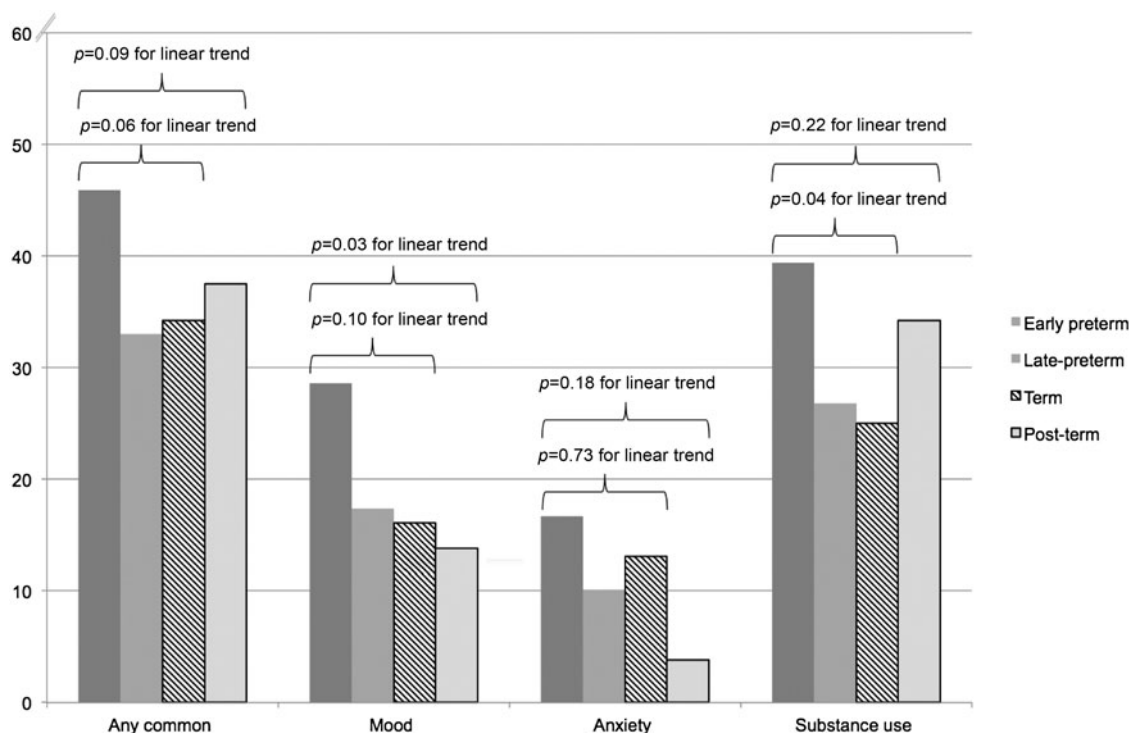


Fig. 1. The prevalence (%) of common mental disorders during the past 12 months by gestational age. p values are for linear trend after controlling for sex, age, highest education level of either parent, own educational level, maternal age, and pre-pregnancy body mass index, multiple pregnancy, parity, growth velocity (small, appropriate or large for gestational age), 5-min Apgar score, smoking during pregnancy, maternal diabetes, hypertension, and pre-eclampsia, length of hospitalization after birth, and mother's self-reported mental health (model II).

increases the risk for any non-substance use disorder (Van Lieshout *et al.* 2015) and depression (Raikonen *et al.* 2008). Further, SGA have been shown to be associated with risk for mental disorders at any length of gestation (Mathiasen *et al.* 2011). A difference explaining the lack of moderation by intrauterine growth pattern in our study may relate to the relatively moderate degree of SGA in our sample in comparison to the earlier studies that by design have included those born at the extreme end of birth weight and gestational age distribution in their samples.

Strengths of our study include a validated diagnostic interview. Although the prevalence rates of mental disorders in the current study may seem relatively high (Table 1), especially for any substance use disorders, they correspond earlier reported twelve-months prevalence rates among young adults which for any substance-use disorder is 30.5%, and for any mood and anxiety disorders are 11.3% and 12.4%, respectively (Blanco *et al.* 2008). Further, we had reliable and verified information on gestational age, available data on important covariates and confounders, a relatively large sample, and a long follow-up to adulthood.

There are also limitations. Two thirds of the infants participating in the AYLS were admitted to neonatal

wards in obstetric units or NICU after birth. However, the majority of the admitted infants had no diagnosed illness and were on the wards for observation or because of common problems of neonatal adaptation. Moreover, those with congenital malformations or chromosomal abnormalities potentially affecting gestational age and/or mental health, were excluded. While the eligibility criteria related to hospitalization after birth enriched the number of preterm births in our sample, it is also a study limitation that restricts generalizations from our findings to samples that may vary from ours in neonatal health characteristics. Loss of follow-up may also inevitably cause selection bias and impact generalizability of the findings further. Of the original sample, 33.1% of the hospitalized infants and 44.4% of the non-hospitalized infants participated in the follow-up in adulthood. Moreover, participation rates in this adulthood follow-up increased according to gestational age: of the original sample 22.3%, 33.7%, 38.2% and 42.6% of those born early-preterm, late-preterm, term and post-term participated in the adulthood follow-up, respectively. Furthermore, those who did not participate in the adulthood follow-up had more often younger mothers who had smoked more often during pregnancy, and more often had

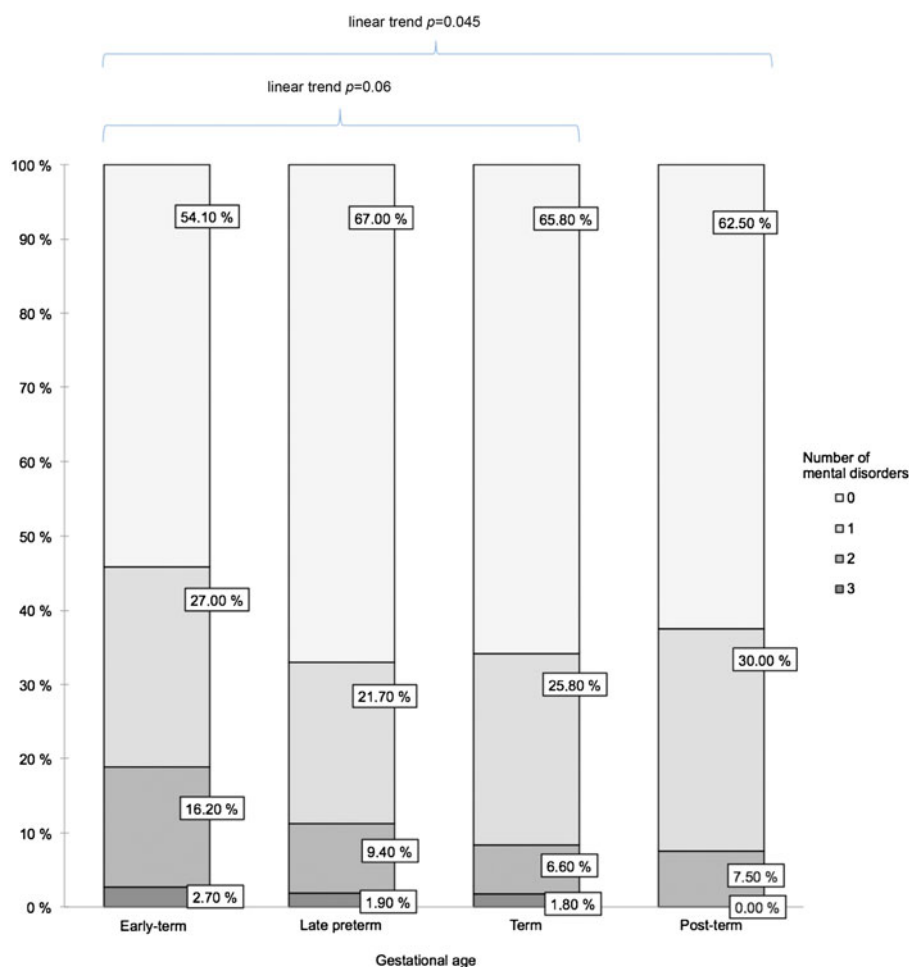


Fig. 2. Co-morbidity of common mental disorders during the past 12 months (%) by gestational age. *p* values are for linear trend after controlling for sex, age, highest education level of either parent, own educational level, maternal age, and pre-pregnancy body mass index, multiple pregnancy, parity, growth velocity (small, appropriate or large for gestational age), 5-min Apgar score, smoking during pregnancy, maternal diabetes, hypertension, and pre-eclampsia, length of hospitalization after birth, and mother's self-reported mental health (model II).

parents with a lower level of education. All these characteristics have been related to preterm birth. Hence, the preterm group that participated in the adulthood follow-up might be healthier than those born preterm in general. Whether our results generalize to samples exposed to less advanced neonatal and early childhood medical care remains also unknown. As we examined the most common mental disorders in adulthood, we cannot either determine the extent to which our findings agree with previous studies, which have shown that late-preterm birth increased the risk of other mental disorders, such as schizophrenia. Moreover, our findings do not either inform of the lifetime mental disorder risk. Finally, although we did not find any statistically significant associations, ORs for those born late-preterm were 1.11 and 1.31 for mood and substance use disorders compared to those born at term. To detect significant association with these

ORs the sample size should have been >36 000 and >5000, respectively. Thus, future studies detecting mental disorders using structured interviews should be conducted in at least 5000 individuals to either confirm or refute the null associations found in this study. Moreover, the sample size of the current study also precluded us to study the less common mental disorders, such as psychotic disorders, autism spectrum disorders or adult ADHD.

Conclusions

Using a cohort born during the advanced neonatal and early childhood care we found that not all individuals born preterm are at risk for common mental disorders in young adulthood – those born late-preterm are not, while those born early-preterm are at higher risk. Available resources of prevention and intervention of

common mental disorders should be targeted towards the preterm group born the earliest.

Supplementary material

For supplementary material accompanying this paper visit: <http://dx.doi.org/10.1017/S0033291716000830>.

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Declaration of Interest

None.

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