List of abbreviations and definitions

english	Psychiatric Disorders	français	Troubles psychiatriques
ANX	**Anxiety Disorders**		**Troubles anxieux**
GAD	Generalized Anxiety Disorder		Trouble anxieux généralisé
OCD	Obsessive Compulsive Disorder	TOC	Trouble obsessionnel-compulsif
PD	Panic Disorder		Trouble panique
PTSD	Post-traumatic Stress Disorder		Trouble de stress post-traumatique
SAD	Separation Anxiety Disorder		Trouble d'anxiété de séparation
SOC	Social Phobia		Phobie sociale
	Agoraphobia		Agoraphobie
SP	Specific Phobia		Phobie spécifique
DBD	**Disruptive Behavior Disorders**		**Troubles du comportement**
ADHD	Attention Deficit Hyperactivity Disorder	TDAH	Trouble du déficit d'attention avec ou sans hyperactivité
ADHD-IA	Attention Deficit Hyperactivity Disorder, inattentive subtype		Trouble du déficit d'attention avec ou sans hyperactivité, sous-type inattention prédominante
CD	Conduct Disorder		Trouble des conduites
ODD	Oppositional Defiant Disorder		Trouble oppositionnel avec provocation
MD	**Mood Disorders**		**Troubles de l'humeur**
BPD	Bipolar Disorder	TB	Trouble bipolaire
OSBARD	Other Specified Bipolar and Related Disorders		
PBD	Pediatric Bipolar Disorder		
MDD	Major Depressive Disorder	TDM	Trouble dépressif majeur
OSDD	Other Specified Depressive Disorder		
ASD	Autism Spectrum Disorder(s)		Troubles du spectre de l'autisme
ED	Eating disorders	TCA	Troubles du comportement alimentaire
SUD	Substance Abuse Disorders		Troubles de l'utilisation de substances psycho-actives
SZA	Schizophrenia		Schizophrénie

Perinatal factors

PNF	perinatal factor
OCs	Obstetric complications

Gestational age (as defined by the WHO)

GA	gestational age
SGA	small (size) for gestational age (<10th percentile)
AGA	appropriate for gestational age
LGA	large for gestational age (>90th percentile)
WGA	weight for gestational age

Preterm birth (as defined by the WHO)

ET	early term, 37-39 weeks of GA
FT	full term, 39-41 weeks of GA
PT	preterm, <37 weeks of GA
VP	very preterm, 28 to <32 weeks of GA
EP	extremely preterm, <28 weeks of GA
Post-term birth	>42 weeks of GA

Birth weight (as defined by the WHO)

BW	birth weight
NBW	normal birth weight
LBW	low birth weight (<2500g)
VLBW	very low birth weight (<1500g)
ELBW	extremely low birth weight (<1000g)

Diagnostic Interviews (DSM- or ICD- criteria)

ADIS-IV	Anxiety Disorders Interview Schedule
CAPA	Child and Adolescent Psychiatric Assessment
CIDI (-Auto)	Composite International Diagnostic Interview
CAS	Child Assessment Schedule
CIS-R	Clinical Interview Schedule-Revised
DAWBA	Developmental and Well-being Assessment DSM-IV-TR and ICD-10 dx)
DIGS	Diagnostic Interview for Genetic Studies
DICA-P	Diagnostic Interview for Children and Adolescents, parent version
DIS	Diagnostic Interview Schedule
DISC	Diagnostic Interview Schedule for DSM-IV for Children
FIGS	Family Interview for Genetic Studies
K-SADS (-E)	Kiddie Schedule for Affective Disorders and Schizophrenia for school-age children, (- Epidemiological version)
SADS-L	Schedule for Affective Disorders and Schizophrenia-Lifetime Version

MINI	Mini International Neuropsychiatric Interview
PAPA	Preschool Age Psychiatric Assessment
SCID-P	Structured Clinical Interview for DSM-IV
SCID-PL	Structured Clinical Interview for DSM-IV for present and lifetime diagnoses
WASH-U K-SADS	Washington University in St. Louis Kiddie-Schedule for Affective Disorders and Schizophrenia

Rating Scales

APSD	Antisocial Process Screening Device
ASSQ	Autism spectrum screening questionnaire
BDI	Beck Depression Inventory
CBCL	Children's Behaviour Check List
CAS	Children Assessment Schedule
CDI	Children Depression Inventory
CESD (-R)	Center of Epidemiological Studies Depression Scale (revised version)
C-GAS	Children's global assessment scale
CSR	Clinician severity rating
CY-BOCS	Children's Yale-Brown Obsessive Compulsive Scale
FH Screen	Family History Screen
GAS	Global Assessment Scale
ITSEA	Infant Toddler Social and Emotional Assessment
ROS	The Rochester Research Obstetrical Scale
SCL	Symptom Check List
SDQ	Strengths and Difficulties Questionnaire
YGTSS	Yale Global Tic Severity Scale

<u>IQ-Tests / measures of intelligence</u>

K-ABC	Kaufman-Assessment Battery for Children
WASI	Wechsler Abbreviated Scale of Intelligence
WISC-III / WISC-R	Wechsler Intelligence Scale for Children, third edition / - revised
FSIQ	Full-scale Intelligence Quotient (measure of general intelligence)

Other abbreviations

btw	between
dx	diagnosis, diagnoses, diagnosed
e.g.	for example
CG	control group
DSM-III, -IV, -5	Diagnostic and Statistical Manual of Mental Disorders third, 4th, 5th edition
ICD-8/-9/-10	International Classification of Diseases 8th, 9th, 10th edition
N	number
NICU	neonatal intensive care unit
NS	not significant
Meta-A	meta-analysis
pts.	Points
RCT	randomized controlled trial
SD	standard deviation
SES	socioeconomic status
SR	systematic review
vs.	versus (→ vs.)
wks.	weeks
mths	months
yrs	years

OR	Odds Ratio
aOR	adjusted Odds Ratio
uOR	unadjusted Odds Ratio
HR	Hazard Ratio
PR / Prev	Prevalence Ratio
RR	Relative Risk

Perinatal Factors

Meta-analysis	Aim	Literature search	Results	Conclusions
Burnett et al. (2011) *Prevalence of psychiatric diagnoses in preterm and full-term children, adolescents and young adults: a meta-analysis* Meta-analysis : 6 studies included (1997-2010)	Synthesis of findings of psychiatric disorders in preterm or LBW individuals. <u>MA 1:</u> prevalence of any psychiatric diagnosis in PT/LBW individuals <u>MA 2:</u> prevalence of anxiety and depressive disorders in PT/LBW individuals	search using PubMed and PsycInfo databases <u>Inclusion criteria:</u> 1) publication btw 1995 - November 2010 2) case-control design, with inclusion of a group of individuals born **preterm/LBW** and a control group of term-born individuals 3) use of a diagnostic instrument to assess a range of psychiatric disorders meeting **DSM-IV, DSM-III-R or ICD-10 criteria** 4) participant ages **btw 10-25 years** 5) did not report on the same cohort as in other publications 6) publication in a peer-reviewed, English-language journal Studies were included if they reported the prevalence of DSM diagnoses in prematurely born and term-born individuals and if they specified the number of participants in each group. No minimum sample size was imposed <u>Studies included:</u> Botting et al (1997,) Elgen et al. (2002), Indredavik et al. (2004), Johnson et al. (2010), Schothorst et al. (2007), Walshe et al. (2008)	The six combined birth cohort studies yielded 734 individuals in the PT/LBW group and 634 individuals in the control group A total of 565 PT/LBW and 533 control individuals in the 5 studies reporting prevalence of 'any diagnosis' A total of 692 PT/LBW and 605 control individuals in the 6 studies that reported rates of anxiety/depression Exclusion of data from the SGA group in the study of Indredavik et al. (2004), as this group wasn't preterm.	Population-based PT/LBW individuals compared with controls were - 3.5 times more likely to receive a psychiatric diagnosis - about 3 times more likely to receive a diagnosis of anxiety or depressive disorder Adjustment: sex, SES <u>Limitation:</u> category "anxiety or depressive disorder" Strengths: → individuals born in "more recent times" (most of the Scandinavian register-based studies participants were born in the 1970s) → all studies were conducted in European countries → Concentration on anxiety and depressive disorders. ADHD rates in PT/LBW individuals were not reported in this study, since increased rates have been widely replicated at diagnostic and dimensional levels
<u>MA 1:</u> prevalence of any **psychiatric diagnosis** in PT/LBW individuals (5 studies)	Increased risk of outcomes for PT/LBW individuals compared with controls: any diagnosis: **OR 3.66, 95% CI 2.57–5.21** (z = 7.42, p <0.00001). Negligible heterogeneity across the study findings I^2 = 0%			Botting et al (1997) Elgen et al. (2002), Indredavik et al. (2004), Johnson et al. (2010), Schothorst et al. (2007)
<u>MA 2:</u> prevalence of **anxiety and depressive disorders** in PT/LBW individuals (6 studies)	Increased risk of outcomes for PT/LBW individuals compared with controls: anxiety or depressive disorder: **OR 2.92, 95% CI 1.82–4.67** (z = 4.46, p <0.00001). Negligible heterogeneity across the study findings I^2 = 8% Some studies (Botting et al (1997) Elgen et al. (2002), Indredavik et al. (2004)) reported the number of anxiety and depressive diagnoses,but did not indicate the number of individuals who received co-morbid anxiety and/or depressive diagnoses. The authors assumed for the purpose of MA that these represented individual cases. However, a second analysis was performed with the assumption that in these studies, individuals with anxiety also had depressive diagnoses in both the PT/LBW and in the control groups. Marginal difference from the original results: OR 2.96, 95% CI 1.70–5.16			Botting et al (1997), Elgen et al. (2002), Indredavik et al. (2004), Johnson et al. (2010), Schothorst et al. (2007), Walshe et al. (2008) *→ OR and 95% CI shown in the text (OR = 2.92, 95% CI: 1.82-4.67) differs from those in the abstract.*

Perinatal Factor: Preterm birth

Studies	Sample			Evaluation	Results				Conclusions
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Rogers et al. (2013) USA *Late Preterm Birth, Maternal Depression, and Risk of Preschool Psychiatric Disorders* Preschool children Longitudinal population-based cohort study	39 Aged btw 3-6 yrs	Late Preterm (GA 34-36 wks.)	Initially, 306 children were recruited in community sites for a study examining the nosology of preschool depression. Oversampling of preschoolers with high depression and disruptive symptoms using the screening checklist, *The Preschool Feelings Checklist* Exclusion criteria: children born <34 wks GA (N=9) (o minimize confounding, resulting from neurodevelopmental deficits), children born >42 wks. (N=19) (exclude confounding through neurodev. effects	PAPA (DSM-IV dx; interview with the caregiver) WASI, Vocabulary and Matrix reasoning subscale, used on the follow-up assessments btw ages 6 and 9 yr FIGS (direct interview with the mother) to assess maternal history of psychiatric disorders Perinatal data:	MDD: NS BPD: not assessed	Any anxiety disorder: aOR = 3.74 (95% CI: 1.59–8.78) p <.01 GAD: aOR = 3.50 (95% CI: 1.03–11.94) p <.0.5 SAD: aOR = 3.04 (95% CI: 1.21–7.63)	ADHD: NS ADHD-inattentive: NS ODD: NS CD: NS	Any axis I psychiatric dx: aOR = 3.18 (95% CI: 1.40-7.27) p <.01 → all aOR shown compare late preterm vs. full term born children	- higher rates of any DSM axis I psychiatric dx, of any ANX, of GAD and SAD in late preterm children compared to full term children - a history of maternal depression mediated the relationship btw late PT birth and ANX - No significant associations btw late preterm birth and MDD, ADHD, CD or ODD - Decreased GA was associated with increased risk for developing any psychiatric disorders and for any ANX (GA analysed as a continuous variable).

			of postmaturity), children with chronic medical or neurological problems, mental retardation or autistic spectrum disorders, missing PAPA data (N=7)	GA: reported by the primary caregiver		p <.0.5 PTSD: NS Maternal depression mediated the relationship btw late PT birth and ANX		GA evaluated as a continuous variable: Any psychiatric disorder: aOR=0.84, (95% CI: 0.72–0.97), p=.019 any ANX: aOR = 0.81, (95% CI: 0.69–0.96), p=.014	However, no significant differences btw ET and FT children for any psychiatric disorders <u>Adjustments:</u> gender, ethnicity, family income, IQ <u>Limitations:</u> - retrospective, maternal report of GA - oversampling of children with disruptive and depressive symptoms
	232 Aged btw 3-6 yrs	N =154 full term N = 78 early term (GA 37-39 wks.)	Control group						
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Burnett et al. (2014) Australia *Extremely preterm birth and adolescent mental health in a geographical cohort born in the 1990s* Young adults Prospective, population-based birth cohort study	215 - *GA:* mean 26.6 wks, SD 2.0 wks, range 23-34 wks - *BW:* mean 889 g, SD 159, range 480-1330 g Average age: 18 yrs	EP (<28 wks of gestation) ELBW (<1'000 g)	Participants were derived from a geographic cohort born in the state of Victoria, Australia, during 1991-1992 (Victorian Infant Collaborative Study Group). Recruited at birth The EP/ELBW group included participants born SGA to facilitate comparisons with previous literature. The EP/ELBW cohort was born largely after exogenous surfactant was introduced into Australian clinical practice in March 1991.	SCID (direct proband interview) SCID-I non-patient version (direct proband interview) Evaluation at average age 18 This cohort has been previously assessed at ages 2, 5 and 8 ChIPS ADHD module Questionnaires : - recent anxiety and depression symptoms : BAI, CESD-R, - personality traits : BIS/BAS, PANAS, APSD - IQ : WASI Perinatal data: collected in infancy and middle childhood (source Doyle, 2001) GA, BW, sex and maternal age at birth, major brain injury on neonatal cranial ultrasound (grade 3/4 intraventricular hemorrhage or cystic periventricular leukomalacia), postnatal corticosteroid treatment or major neonatal surgery Questionnaires in infancy/middle childhood: - externalizing/internalizing problems: BASC, completed by parents - behavioural symptoms: BSI	Any mood disorder: NS To little sample sizes in order to conduct analyses for BPD, MDD (current and past), dysthymia, depressive disorder NOS	Any ANX: NS To little sample sizes in order to conduct analyses for GAD, SOC, SP, PTSD, PD, Agoraphobia, OCD, Anxiety NOS	Any ADHD: aOR = 2.67 (95% CI: 1.08-6.58) P <0.05 ADHD combined type, ADHD inattentive type, ADHD hyperactive/impulsive type: NS	Any SCID psychiatric dx: NS Any anxiety or mood disorder: NS Co-morbid anxiety and mood disorder: NS To little sample sizes in order to conduct analyses for psychotic disorders, ED (current and past) EP/ELBW and control probands were similar concerning to perinatal variables	- the risk for lifetime ADHD was significantly higher in EP/ELBW. ADHD inattentive subtype was the most prevalent subtype in the EP/ELBW and in the control group. - lifetime dx of other psychiatric dx, primarily ANX and mood disorders, were similar btw the EP group and controls - Childhood variables at 8 yrs were more relevant to outcome at 18 yrs than neonatal variables <u>Adjustments:</u> gender, parental education, childhood SES <u>Limitations:</u> - retrospective report of perinatal data? - possible attrition in the CG
	157 Average age: 18 yrs	NBW (>2'499 g)	Controls matched at the group level for mother's country of origin and health insurance status, and sex of the child. Recruited at birth						
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Johnson et al. (2010) UK and Ireland *Psychiatric disorders in extremely preterm children: longitudinal finding at age 11 years in the EPICure study* Children	219 Mean age: 10 yrs and 11 mths (range 121-145 mths)	EP (GA <26 wks.) Children with cognitive and neur-sensory impairment included	All babies born <26 wks. gestation in the United Kingdom and Ireland from March to Dec 1995 admitted for neonatal intensive care. Longitudinal data was available for EP children. *EPICure Study*	DAWBA (DSM-IV dx; administered to parents via telephone or online) at offspring age 11 yrs Previous evaluations at ages 2.5 and 6 yrs At 2.5 yrs: CBCL (parents) At 6 yrs: SDQ (parents and teachers) K-ABC; used to obtain IQ scores from which cognitive impairment was defined	MDD: NS No BPD dx	Any ANX: NS Any emotional disorder" (ANX and MDD): OR = 4.5 (95% CI 1.3-15.8), p= 0.013 ANX: OR = 3.5, (95% CI 1.0-12.4), (p not reported)	Any ADHD: NS Any conduct disorder (ODD and CD): NS Any ADHD: OR = 4.4 (95% CI 1.5-13.4), p= 0.006	Any DSM-IV dx: OR = 3.1 (95% CI 1.6-6.0), p= 0.001 Autism spectrum disorders: 6.4% in EP children vs. 0% in classmates; p= .001 Autistic disorder: 1.8% in EP	- significant higher risk of ASD and of autistic disorder in EP children without neurosensory or cognitive impairment - with EP children with neurosensory or cognitive impairment included, significant higher risk for all psychiatric disorders, any ADHD dx, ADHD inattentive subtype, any emotional disorder (ANX and MDD), any ASD and autistic disorder

Prospective, population-based birth cohort study	153 Mean age: 10 yrs and 11 mths (range 117-147 mths)	Term-born	Classmates; term-born, same gender and ethnicity matched at the 6 yrs follow-up	Physical examination Perinatal and neonatal data: medical records	→ results of EP children *without* neurosensory or cognitive impairment → results of EP children with children *with* neurosensory or cognitive impairment included	SAD, GAD, SP, SOC, PTSD: NS	ADHD inattentive subtype: OR = 10.5, (95% CI 1.3-82.7), p= 0.006 ADHD combined type: NS	children, vs. 0% in classmates; p=0.009 ASD: 6.4% in EP children vs. 0% in classmates; p= .001 Autistic disorder: 1.8% in EP children, vs. 0% in classmates; p=0.009 Tic disorder: NS Psychiatric disorders in children with cognitive impairment 37% vs. 14% in children without cognitive impairment: OR = 3.5; 95% CI:1.8-6.4), (p = not indicated)	- ANX accounted for most of the emotional disorders (especially SAD and GAD) - Significant association of psychiatric disorders with cognitive impairment - Parent-reported behavioural problems at 2.5 and 6 years were independent predictors of psychiatric disorders at 11 yrs <u>Adjustment:</u> Unadjusted ORs are reported as adjustments for sex and SES had no significant effects according to the authors of the study <u>Limitations:</u> - use of different behavioural scales for assessments at age 2.5 yrs and 6 yrs - children with cognitive impairment included
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Treyvaud et al. (2013) Australia *Psychiatric outcomes at age seven for very preterm children: rates and predictors: Psychiatric outcome for very preterm children* Children Prospective population-based birth cohort study	117 Mean BW 975g (SD 223) GA mean 27.5 weeks (range 1.94) SGA 16% (SD 9)	Very preterm BW BWSDS (birth weight SD score (a measure of growth restriction in utero)) SGA	Families from the Victorian Infant Brain Studies cohort, which included 227 infants born at <30 wks. gestation or with a birth weight <1250 g at the Royal Women's Hospital, Melbourne, Australia, between 2001 and 2003 (VPT group).	DAWBA (DSM-IV TR dx) at age 7 ITSEA and SDQ at ages 2 and 5 "any disorder", "other disorder", eating disorder, tic disorder, ASD Brain MRI: at term corrected age Follow-up assessments: at age 2, 5 and 7 years (all corrected age).			ADHD (any) ADHD combined ADHD inattentive ADHD hyperactive-impulsive ADHD NOS ODD Conduct disorder	Any psychiatric disorder: uOR = 3.13 (95% CI: 1.27-7.71), p=0.01 OR adjusted for social risk = 2.55 (95% CI: 1.01-6.43), p=0.047 OR adjusted for social risk and neurodevelpmental disability = 2.35 (95% CI: 0.92-5.98), p=0.07 Comorbid psychiatric diagnoses: OR = 1.37, (95% CI: 0.37-5.04), p = 0.63). Little evidence for group differences in the likelihood of having comorbid	VPT children had a 3x higher risk of meeting the criteria for any psychiatric diagnosis at age 7. The most common diagnoses were ADs (11% VPT, 8% term), ADHD (10% VPT, 3% term) and ASD (4.5% VPT, 0% term). For VPT children, those with severe global brain abnormalities (p = .02), those who displayed social-emotional problems at age 5 (p = .000) and those with higher social risk at age 7 (p = .001) were more likely to meet criteria for a psychiatric illness at age 7. <u>Adjustments:</u> gender, global brain abnormality, social risk, social-emotional problems at 5 yrs <u>Limitations:</u> - inclusion of neurodevelopmentally disabled children
	65 Mean BW 3320g (SD 499) GA mean 39.1 weeks (range 1.3) SGA 1% (SD 1)	born at term	A comparison group including 77 full term children (>36 weeks' gestation) were recruited at birth from the Royal Women's Hospital maternity wards between 2001 and 2003 (n = 46) or at 2 years from maternal–child health centres in 2004 (n = 31), both in Melbourne, Australia.						

								psychiatric diagnoses	

Perinatal Factor: Low birth weight

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Van Lieshout et al. (2015) Canada *Mental health of extremely low birth weight survivors in their 30s* Adults Prospective, population-based birth cohort study	N = 84 N = 26 SGA (of those, 10 received 2 doses of ACS) N = 58 AGA Born btw 1977-1982 24 mothers of ELBW subjects received a complete course of ACS (2 doses), 14 received a single dose)	ELBW (< 1'000g) SGA (< 10th percentile for GA)	Recruited at birth; Ontario Canada	MINI (current dx), MINI plus (lifetime dx) Selection of common disorders: MDD, BPD, dysthymic disorder, PD, PTSD, alcohol and, substance abuse and dependence, SOC (gernalized, nongeneralized types), GAD, ADHD Assessments at age 3, 5, 8, 14, 22-26, 29-36 yrs Data on BW, GA, gender, ACS-status: Medical charts at birth ACS = antenatal corticosteroids Neurosensory impairment, chronic health problems	<u>MDD: current and lifetime:</u> NS <u>BPD, current and lifetime:</u> NS	<u>GAD:</u> In ACS-exposed ELBW: GAD: OR = 3.42 (95% CI, 1.06–11.06), p = < .05 <u>SOC, generalized type:</u> In ACS-exposed ELBW: OR = 5.80 (95% CI, 1.20–27.99), p = < .05 Panic disorder: NS OCD: NS PTSD lifetime: NS	<u>ADHD, inattentive subtype:</u> In ACS-exposed ELBW: OR = 10.2 (95% CI: 1.61–64.56), p = < .05	<u>Any alcohol or substance use disorder, current:</u> In ELBW, current dx: uOR = 0.38 (95% CI: 0.17-0.86), p = < .05 In ELBW, lifetime dx: aOR = 0.37 (95% CI: 0.18-0.79), p = < .05 In ELBW + SGA, lifetime: aOR = 0.29 (95% CI: 0.09-0.89), p = < .05 In ACS-exposed ELBW: aOR = 0.13 (95% CI: (0.002–1.04), p = < .05 <u>Current non-substance-related psychiatric problems, current:</u> In ELBW: aOR =2.30 (95% CI: 1.01-5.24), p = < .05 In ELBW + SGA: aOR =3.83 (95% CI: 1.21-9.46), p = < .05 In ACS-exposed ELBW: aOR = 3.71 (95% CI, 1.25–10.99), p = < .05	- Decreased risk for alcohol and substance use disorder in ELBW born adults but higher risk for current non–substance-related psychiatric disorders. - the effects were larger for ELBW + SGA born adults - these risks were even higher for ACS-exposed ELBW born adults. They were particularly at risk for GAD, SOC, generalized type and for ADHD, inattentive subtype <u>Adjustment:</u> gender, neurosensory impairment, current total household income, and current marital status <u>Limitations:</u> - attrition, follow-up losses - subjects with neurosensory impairments included - source and recruitment of participants?
	N = 90	NBW, age, gender and SES matched at age 8	Enrolled when both groups were 8 yrs old Ontario Canada						

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Nomura et al. (2007) USA *Low birth weight and risk of affective*	162 offspring of depressed parents	<u>BW:</u> LBW (<2.5kg): 8.2% (n = 20)	Offspring of depressed parents (either parent depressed; recruited in a treatment center)	SADS-L K-SADS-E (for children 6-17 yrs) → lifetime dx	<u>MDD:</u> LBW compared with "high BW": aRR = 2.9, (95% CI 1.4-6.1), p= .004	<u>Any ANX (SAD, overanxious disorder, GAD, OCD, PD, PTSD, phobia):</u>		<u>Suicidal ideation:</u> LBW compared to offspring with "high BW":	→ approx. 3x higher risk of MDD, any ANX, phobia and suicidal ideation in offspring with LBW compared to those with BW > 3.5kg

disorders and selected medical illness in offspring at high and low risk for depression Adults Longitudinal, High-Risk (for MDD) study (Weissman et al.)	82 offspring of nondepressed parents	"mid BW" 2.5-3.5kg: 54.5% (n = 133) "high BW" >3.5kg: 37.3% (n = 91)	Offspring of nondepressed parents recruited in the same community where the treatment center was located Depressed and nondepressed probands were group-matched	Probands were 4x interviewed over a period of 20 yrs Mean age: 33 yrs (SD 8.8 yrs) Birth weight: Extracted from parent's report of the child's developmental history at the baseline assessment C-GAS or GAS completed and information on medical illness collected at each wave	"mid BW" compared with "high BW": aRR = 1.7, (95% CI 1.0-2.7), p= .04 Significant interaction btw BW and parental depression status for MDD (p = .05)	LBW compared to offspring with "high BW": aRR = 3.0, (95% CI 1.4-6.7), p= .006 <u>Any phobia (SP, SOC, agoraphobia):</u> LBW: aRR = 3.1, (95% CI 1.2-8.0), p= .02		aRR = 2.7, (95% CI 1.0-7.2), p= .05	→ significant interaction btw BW and parental depression status for MDD, suggesting that parental depression may increase the impact of LBW on offspring depression → No significant associations btw LBW and psychiatric disorders among offspring of nondepressed parents. <u>Adjustment:</u> sex and preterm birth status of offspring, parental depression, SES, mother's smoking, alcohol and drug use during pregnancy, parity, maternal age at the birth of the offspring <u>Limitations:</u> - small number of offspring with LBW - retrospective report of BW - limited generalizability of the results due to the High-risk sample

Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Elgen et al. (2002) Norway *Population based, controlled study of behavioural problems and psychiatric disorders in low birthweight children at 11 years of age* Children Prospective population-based cohort study	130	LBW (<2kg) Mean BW 1537g LBW and other perinatal factors	All surviving LBW children, born in the count of Hordaland, Norway, btw 1986-1988; without neurosensory handycaps	CAS (dx according to DSM-III TR) at age 11 CBCL (parent's and teacher's report) Yale children's inventory (focus on ADD and ADHD) ASDI WISC-R (subscales) Parental and family characteristics; SCL-90R Total number of diagnosis, enuresis, encopresis Source of pregnancy, perinatal and neonatal data: probably medical records		SAD Phobia	ADHD ODD ADHD aOR = 9.6 (95% CI 1.2-82), p = 0.04	all psychiatric disorders aOR = 2.4 (95% CI: 1.01.-5.5), p = 0.047 40% of LBW children had behavioural problems (defined by abnormal scores on more than four of 32 measures) compared with 7% of NBW children: OR = 8.2, (95% CI 3-25), p = 0001 A psychiatric disorder was diagnosed in 27% of the LBW children compared with 9% of the NBW children: OR = 3.1, (95% CI 1.5-6.5), p = 0.001. Mean prorated IQ was similar in LBW children with normal and abnormal total problem scores.	Psychiatric disorders are 3x more frequent and behavioural problems 8x more present in LBW children. The most common behavioural problems were inattention, social problems and low self-esteem. None of the pre-, neo-,or peri-natal variables in the LBW group were statistically significant predictors of behavioural outcomes or the presence of psychiatric disorders. Behavioural problems and psychiatric disorders were as common in those with BW <1,5kg as in those with BW 1.5-2kg. <u>Adjustement:</u> parental factors <u>Limitations:</u> - Source of pregnancy, perinatal and neonatal data?
	131	Controls: NBW (>3kg), born >37wks. of GA, no requirement for transfer to the neonatal unit	2 sources: - not first born children of mothers of a random sample of women recruited during pregnancy by GPs and obstetricians from the county of Hordaland. - every 40th child born at the regional hospital of Hordaland (in Bergen)						

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Elgen et al. (2013) Norway *Psychiatric disorders in low birthweight young adults. Prevalence and association with assessments at 11 years* Young adults Prospective, population based cohort study	136	LBW (<2kg) mean BW 1.5kg	Born in the county of Hordaland, Norway, btw 1986-1988; without neurosensory handycaps	MINI at 19 years Follow-ups at 5, 11 and 19 years of age CAS at 11 years Wechsler Abbreviated Scale of Ability Source of perinatal data: probably medical records	MDD: NS BPD: NS 56% stayed mentally healthy throughout adolescence = half as many as for controls: OR = 0.6, (95% CI: 0.3 to 0.9), p=0.02	ANX = NS At 11 years (with the CAS): 27% of the LBW children were diagnosed with a psychiatric disorder compared to 9% of the NBW children (OR: 3.1; 95% CI: 1.5 to 6.5, p = 0.001).	ADHD: NS	Any psychiatric disorder in LBW young adults: OR = 2.8, (95% CI: 1.1-4.5), p=0.02 Different ORs (table 3) Most common psychiatric disorders among the LBW young adults: affective-, anxiety-, ADHD- and antisocial personality disorders 20% had more than one diagnosis.	Moderate LBW increases more than 2x the risk of psychiatric disorders in young adults The increased risk in for psychiatric disorders continues into young adulthood LBW subjects were significantly less mentally healthy throughout adolescence Adjustment: SES factors, gender, cognitive abilities Limitations: - Source of perinatal data? - LBW not as usually defined (WHO def.: LBW = <2.5kg) resp. <2kg mean 1.5kg / NBW >3kg - use of two different assessment instruments at 11 and at 19 years - categories of dx: "affective", "anxious" or "psychotic" disorders
	132	NBW (>3kg), born >37 GA, no requirement for transfer to the neonatal unit	2 sources: - not first bornchildren of mothers of a random sample of women recruited during pregnancy by GPs and obstetricians from the county of Hordaland. - every 40th child born at the regional hospital of Hordaland (in Bergen)						
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Indredavik et al. (2004) Norway *Psychiatric symptoms and disorders in adolescents with low birth weight* Adolescents Prospective, population-based birth cohort study	56 VLBW 60 SGA Age 14	VLBW SGA (≤ 10th percentile, born at term)	VLBW: recruited from the neonatal intensive care unit at the University Hospital in Trondheim SGA: Trondheim part of a multicenter study	K-SADS ADHD Rating Scale IV (teachers' report) ASSQ (parents' report) Evaluation at age 14; subjects born btw 1986-1988 CGAS WISC-III - evaluation of motor abilities - neuropaediatric examination Source of perinatal data: probably medical records	Mood disorders: NS	ANX VLBW: 8 subjects (14%), p<0.05 OR 4.4 (CI 1.1-17.6) - ≥ 2 diagnoses: 5 (9%), p<0.05 SGA: NS Anxiety disorders: separation anxiety disorder, generalised anxiety disorder, social phobia, or specific phobia.		Any psychiatric dx: VLBW: 14 subjects (25%), (p ≤0.01 vs controls) OR = 4.3 (95% CI: 1.5-12) SGA: 6 subjects (10%) (NS) CG: 6 subjects (7%)	- VLBW adolescents have a high risk of developing psychiatric disorders by the age of 14, especially ANX - VLBW adolescents have a high risk of developing psychiatric symptoms (attention deficit, anxiety symptoms, and relational problems) - SGA adolescents don't have a higher risk than controls → essentially unchanged results when adjusted for confounders Limitations: - Inclusion of adolescents with low IQ (10 VLBW, 4 SGA, 3 controls), cerebral palsy (6 VLBW, 1 SGA) and epilepsy (2 VLBW, 1 control). 4 of the VLBW and the 1 SGA with cerebral palsy had low IQ → essentially unchanged results when adolescents with low IQ were excluded, except a reduction of the prevalence of anxiety symptoms (p=0.09) and disorders (p=0.07) in the VLBW group compared with controls - categories of dx - [sometimes data only in text and not in tables]
	80 Age 14	Term born controls with normal BW	Trondheim part of a multicenter study * * Trondheim and Bergen (Norway); Uppsala (Sweden)						

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Lund et al. (2011) Norway *Psychiatric morbidity in two low birth weight groups assessed by diagnostic interview in young adulthood: Low birth weight and mental health in young adulthood* Young adults Prospective, population-based birth cohort study	43 VLBW (12 VLBW-SGA) 55 SGA Age 20 yrs	VLBW SGA (≤ 10th percentile adjusted for GA, gender and parity)	<u>VLBW:</u> population-based birth cohort; recruited from the neonatal intensive care unit at the University Hospital in Trondheim <u>SGA:</u> Trondheim part of a multicenter study *	Evaluation at age 20; subjects born btw 1986-1988 K-SADS PL SCID II for DSM-IV Personality Disorders ADHD Rating Scale IV; self-report and parent report C-GAS	<u>Mood disorders</u> (MDD, dysthymia, depressive disorders NOS, bipolar disorders): NS	<u>ANX (</u>phobia, OCD, PTSD and GAD): <u>VLBW</u> - AD: 8 (19%), p<0.01 - ADHD: 6 (14%), p<0.01 - more than one dx: 5 (12%), p<0.01 <u>SGA</u> - AD: 7 (13%), p<0.05 - ADHD: 4 (7%), p<0.05 No significant differences for mood and "other" disorders	<u>ADHD</u>: NS	<u>Any psychiatric disorder:</u> <u>VLBW:</u> 14 subjects (33%), (p ≤0.001 vs controls) uOR: 5.6 (CI: 1.9–15.9) p=0.001 aOR for gender: 5.8 (CI: 2–17), p=0.001 aOR for assessment age: 5.6 (CI: 1.9–16.2), p=0.001 aOR for parental SES: 4.2 (CI: 1.4–12.4), p=0.01 VLBW-SGA subgroup: 7 subjects (58%), p=0.04. vs VLBW non-SGA subgroup: 7 (23%) <u>SGA:</u> 14 subjects (26%) (p =0.006 text / p=0.009 table 3 vs controls) uOR 3.9 (CI: 1.4-11), p=0.009 aOR for gender: 4.2 (CI: 1.5–12.1), p=0.008 aOR for assessment age: 3.9 (CI: 1.4–11), p=0.01 aOR for parental SES: 3.1 (CI: 1–9.2), p=0.04 <u>CG:</u> 6 subjects (8%)	- VLBW and SGA subjects were at higher risk for any psychiatric disorder than control subjects - Anxiety disorders and ADHD were the most frequent diagnoses. - The differences were not explained by gender or assessment age. Parental SES reduced the ORs by >20% => confounder <u>Limitations</u>: - use of dx groups
	75 Age 20 yrs	born at term with BW ≥10th percentile adjusted for GA, gender and parity	Trondheim part of a multicenter study * * Trondheim and Bergen (Norway), Uppsala (Sweden)						

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Costello et al. (2007) USA *Prediction from low birth weight to female adolescent depression: a test of competing hypotheses*	1'420 49% female probands Children with behavior problems were	LBW (≤ 2.5 kg), length of gestation, pregnancy difficulties, birth difficulties, adverse	3 cohorts of children aged 9, 11, 13 yr at intake in 1993 Representative sample for rural and urban youth Potential participants were selected among the population of some 20 000 children in North Carolina	CAPA (direct child/adolescent interview; DSM-IV) Annually assessment for all psychiatric disorders in the precedent 3 months btw 9-16 yr	<u>MDD in adolescents with LBW:</u> Girls: OR = 5.0 (95% CI : 1.9-13.1), p = .001 Boys: NS	<u>ANX (social phobia, GAD, symptoms of PTSD) in adolescents with LBW:</u> OR = 4.7 (95% CI, 1.2-18.2). p =.02			- LBW is a predictor of depression in adolescent girls but not in boys - Girls with LBW and NBW with no adversities had no adolescent depression, but each additional adversity increased the risk of depression in girls with LBW more than in girls with NBW

Children, adolescents Prospective population-based cohort study	oversampled (CBCL administered to a parent of the first-stage sample N=3896)	perinatal environment	*"Great Smoky Mountains Study"*	CIDI (parent interview): lifetime parental psychiatric history 13-item version of the Mood and Feelings Questionnaire: current maternal depression Perinatal data: obtained from mothers (retrospectively)	Interaction btw LBW and sex: OR = 0.015 (95% CI: 0.001-0.172, p = .001	→ all of these conditions were comorbid with depression. When depression was included in the model, the effect of the ANX disappeared			- LBW did not predict other psychiatric disorders in either sex. The significant association with ANX disappeared after adjustment for depression <u>Adjustments</u>: perinatal, childhood, and adolescent adversities <u>Limitations:</u> - retrospective recall of perinatal data - no measures of maternal drug use and psychopathology during pregnancy - annual assessment focused on the precedent 3 months, possible episodes of depression in the rest of the yr were therefore not assessed
		No control group							

Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Betts et al. (2013) Australia *The association between lower birth weight and comorbid generalised anxiety and major depressive disorder* Young adults Prospective birth cohort study	N = 2213	LBW	*Mater University Study of Pregnancy (MUSP)* birth cohort Prospective birth cohort started btw 1981-1984	CIDI-Auto, lifetime version, at 21 years Follow-ups at the child's birth and of child aged 6 months and 5, 14 and 21 years Perinatal data (BW, GA, gender): Hospital obstetric records → BW converted into z-scores, internally adjusted for GA and gender	MDD: NS	GAD: NS		Comorbid MDD and GAD: OR = 3.71 (95% CI : 2.08- 6.60)	→ LBW is associated with comorbidity (GAD+MDD) but not with the discrete disorders → inverse linear association: an increase in BW z-score decreased the odds of being diagnosed of comorbid GAD and MDD <u>Adjustments:</u> - GA, gender - maternal smoking and alcohol consumption during pregnancy, maternal antenatal anxiety and depression (assessed by the DSSI), maternal age at birth and parity, offspring work type, income and smoking at 21 years <u>Limitations:</u> - no specification of comorbidity by the primary disorder, or by the severity or recurrence of the depression
	N = 2213	No control group							

Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Westrupp et al. (2011) Australia *Adult Psychiatric Outcomes of Very Low Birth Weight Survivors* Adults Prospective birth cohort study	N = 117	VLBW	Consecutive survivors from two overlapping cohorts born at the Royal Women 's Hospital in Melbourne, Australia. Born 1977-1982 Assessed in early adulthood (24-29 yrs)	SCID (after positive screening) SCL-90-R (Screening) "any diagnosis inclusive / current", eating, drug disorder Perinatal data: Collected at birth SES data: collected at birth	Depressive disorder (current): RR = 1.36, (95% CI : 1.22-1.51), p = < 0.02 Depressive disorder (lifetime): NS Psychotic disorder or BPD: NS	ANX: NS		Any psychiatric disorders (lifetime and current): NS Any psychiatric disorders (current): NS Drug/alcohol disorder: NS ED: NS	VLBW adults were more likely to be diagnosed with a current mood disorder than NBW adults <u>Adjustments :</u> - none? <u>Limitations:</u> - most reported results stem from the SCL-90-R screening - group dx: "psychotic disorder or BPD"
	N = 32	NBW							

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Breslau et al. (1996) USA *Psychiatric sequelae of low birth weight at 6 years of age* Children Cross-sectional, population-based study	473	LBW (< 2'500g)	Randomly selected children from the 1983-1985 newborn lists of an urban and a suburban hospital in Southeast Michigan *Exclusion criteria:* severe neurologic handicaps	DISC-P (DSM-III dx, interview with mothers); evaluation at age 6 btw 1990-1992 Assessment of behavioural problems: TRF (teacher's rating) WISC-R Perinatal data (BW, GA, Apgar score, number of days in the NICU): Medical records	Not assessed	Any ANX: NS SAD: NS SP: NS Overanxious disorder: NS	ADHD: Urban sample: RR = 2.0 (95% CI: 1.4-2.9) Suburban sample: NS ODD: NS		LBW was associated with ADHD in the urban sample, but not in the suburban sample - no significant associations btw LBW and any ANX, SAD, SP, overanxious disorder and ODD Adjustments : - none? Limitations : - no indication about the adjustment of RR - p-values not indicated
	350	NBW							

Other Perinatal Factors

Studies	Sample			Evaluation	Results				Conclusions
	N	PNF	Source		MDD / BPD	ANX	DBD	Other results	
Batstra et al. (2006) The Netherlands *Psychiatric morbidity related to a chain of prenatal and perinatal adversities* Young adults Prospective, population-based, birth cohort study	N = 285 Aged 20-25 yrs	- Obstetric optimality score (OOS; list with 74 items, describing the pre-and perinatal condition of mother and foetus) - BW - t score at 3 min after birth - GA (preterm <37 wks. vs. term >37 wks.) - breast vs. bottle feeding - marital state and SES of the parents at the time of pregnancy	Groningen Perinatal Project (N = 3'162 singleton infants born in the University Hospital Groningen btw 1975-1978) Probands were selected on the basis of their OOS	CIDI (direct interview) Perinatal, obstetric and sociodemographic data collected during the perinatal period Evaluations: - at 5-11 yr: detailed neurological examination, behavioural questionnaires, school performances - at 20-25 yr: emotional and substance use problems in young adulthood	Depressive disorder : Lower OOS: beta-coefficient -0.08 (95% CI: -0.13 – -0.01), p=0.026	ANX/Phobia : Lower OOS : beta coefficient -0.07 (95% CI : -0.15 – -0.00), p=0.055		Substance abuse: LBW: beta-coefficient -1.39 (95% CI: -2.21 – -0.58), p=0.001 Apgar at 3 min : beta-coefficient -0.39 (95% CI: -0.66 – -0.12), p=0.005 (unadjusted) Psychiatric Multimorbidity (≥2 disorders): Lower OOS: beta-coefficient -0.07 (95% CI: -0.14 – -0.006), p=0.030	- lower OOS was significantly associated with depressive disorder, phobia/ANX and psychiatric multimorbidity - LBW, low Apgar at 3min was sign. associated with substance abuse - no association btw LBW, PT, SGA and depression Adjustment: sex and age of probands, whether or not living alone, nationality (Dutch or other), whether or not working or studying at the time of the study, perceived physical health Limitations: - probands born in a university hospital: overrepresentation of probands with OCs -oversampling of subjects with the lowest and the highest OOS → less optimal mean perinatal condition (not possible to generalize results to the general population) - definition of Phobia? Group dx
		No control group							
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Foley et al. (2001) USA *Pregnancy and perinatal*	1806 female twin subjects Aged btw 17-55 years (mean	BW, GA, pregnancy and perinatal complications	All consenting adult female twins registered with the population-based Virginia twin registry for whom prenatal, perinatal and	SCID (DSM-III criteria) DIS, section for SP and SOC → lifetime dx Perinatal data:	MDD: NS	SOC : Prenatal complications : OR = 0.86 (95% CI : 0.75-0.99), p=0.04		Bulimia: Prenatal complications: OR = 1.21 (95% CI : 1.00-1.48), p=0.05	- a shorter GA was significantly associated with increased risk for anorexia nervosa - prenatal complications were associated with a significantly lower

complications associated with risks for common psychiatric disorders in a population-based sample of female twins Adults Prospective, population-based female twin study	29.5 years, SD 7.4 y)		psychiatric interview data were available. The data was collected as part of a longitudinal study of the genetic and environmental risk factors for common psychiatric disorders in women (Kendler et al., 1992)	retrospectively collected in parent and subject interviews; birth certificates noting BW were obtained for 182 cases. (Data hierarchy: birth certificates over maternal report over paternal report) *Prenatal complications:* premature contractions, swelling of face/hands/ankles, high blood pressure, vaginal bleeding, seizures or toxaemia, german measles, labor lasting more than 24hr, serious physical injury, other serious illness, any other complication, any prenatal complications *Perinatal complications:* breech delivery, caesarean delivery, forceps delivery, other delivery complications, cord wrapped around neck, blue at birth, failure to breath at first, convulsions, jaundice, blood transfusion, required an incubator, other perinatal complications, any perinatal complication		PD : NS GAD : NS		Anorexia nervosa: Prenatal complications: OR = 1.43 (95% CI : 1.25-1.64), p<0.0001 Anorexia nervosa: Shorter GA : OR = 0.82 (95% CI : 0.70-0.96), p=0.02 Alcoholism: NS	risk for social phobias and with an increased risk for anorexia and bulimia nervosa - no significant association with alcoholism, SP, GAD, PD and MDD - no significant associations with BW Adjustments: zygosity, age at interview, years of education of the primary breadwinner in the twin's family of origin (as an estimate of SES) Limitations: - no definition of "shorter GA" - only female twins - wide age spectrum (17-55 years) - composite indexes of pregnancy and perinatal complications - twin samples may be viewed as naturally enriched for prenatal and perinatal complications
		No control group							
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Nosarti et al. (2012) Sweden *Preterm Birth and Psychiatric Disorders in Young Adult Life* Young adults Retrospective, population-based register study	PT: N = 47'864 VP: N = 5'125 Post-term birth: N = 221'022 BW for GA SD score: SGA (< -2): N = 43'334 LGA (> 2): N = 29'579 Agpar score at 5min: 4-6 pts.: N = 8'837 0-3 pts.: N = 2'264	Preterm birth: - PT 32-36 wks. - VP <32 wks. Post-term birth: ≥ 42 wks. BW for GA SD score (non-optimal fetal growth) Agpar score at 5 min.: <7 pts	All live-born individuals registered in the Swedish Medical Birth Register btw 1973-1985, living in Sweden at age 16 years by Dec 2002 (N = 1'301'522) Age of probands: 16-29 yrs → mean age 23.0 yrs (SD 4.1) → age at first hospitalization for all dx: mean age 20.9 yrs (SD 3.01)	Psychiatric hospitalization, dx according to the ICD-8-10; only first dx included (eg. MDD for someone first developing MDD and afterwards BPD); registers Perinatal data: registers → all data from the National Board of Health and Welfare, Stockholm, Sweden, and Statistics Sweden, which provided individually linked data in 3 population-based registers - the Swedish Medical Birth Register - the Swedish National Hospital Discharge Register - the Swedish Multi-Generation Register	Depressive disorder : Preterm birth 32-36 wks.: aHR = 1.3 (95% CI : 1.1-1.7) < 32 wks.: aHR = 2.9 (95% CI : 1.8-4.6) Post-term birth: aHR = 1.1 (95% CI : 1.0-1.2) Apgar sore 0-3 pts. : aHR = 2.2 (95% CI : 1.2-4.0) Bipolar affective disorder: Preterm birth 32-36 wks.: aHR = 2.7 (95% CI : 1.6-4.5) < 32 wks. : aHR = 7.4 (95% CI : 2.7-20.6)			Drug dependency: Preterm birth 32-36 wks.: aHR = 1.2 (95% CI: 1.0-1.4) SGA (SD score < -2): aHR = 1.4 (95% CI: 1.2-1.6) Alcohol dependency: Preterm birth 32-36 wks.: aHR = 1.3 (95% CI: 1.1-1.5) Post-term birth: aHR = 1.1 (95% CI : 1.0-1.2) SGA (SD score < -2): aHR = 1.2 (95% CI: 1.0-1.4) Eating disorders: Preterm birth <32 wks.: aHR = 3.5 (95% CI: 1.3-9.6)	Significantly associated with psychiatric hospitalization for: - depressive disorder: preterm birth (<32 wks., 32-36 wks.), post-term birth (≥ 42 wks) and Apgar score at 5min 0-3pts - BPD: preterm birth (<32 wks., 32-36 wks.) - drug dependency: preterm birth (<32-36 wks.), and SGA (SD score < -2) - alcohol dependency: preterm birth (32-36 wks.), post-term birth (≥ 42 wks) and SGA (SD score < -2) - ED: preterm birth (<32 wks.) - nonaffective psychosis: preterm birth (<32 wks., 32-36 wks.) Adjustments: other variables (GA, BW or Apgar score), sex, parity, maternal age at delivery, maternal education, maternal psychiatric family history Limitations: - only more severe cases (outcome criterion: "psychiatric hospitalization") - no control group with psychiatric disorders habitually not requiring hospitalization (e.g. ANX, depressive disorders) - ANX aren't included - no p-values indicated
	Early term and full-term: N = 1'022'431 Normal BW for GA: N = 1'219'783 Agpar score at 5 min: 7-10 pts. N = 1'271'464	Early and full-term birth: 37-41 wks. Normal BW for GA (SD score -2 to 2) Agpar score at 5 min: 7-10 pts.							

								Nonaffective psychosis : Preterm birth 32-36 wks.: aHR = 1.6 (95% CI: 1.1-2.3) < 32 wks.: aHR = 2.5 (95% CI: 1.0-6.0)	
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	N	**PNF**	**Source**		**MDD / BPD**	**ANX**	**DBD**	**Other results**	
Allen et al. (1998) USA *Prenatal and perinatal influences on risk for psychopathology in childhood and adolescence* Adolescents Longitudinal, population-based cohort study	N = 579 58% female Mean age: 16.4 yrs (SD 1.2 yrs)	Prenatal, perinatal and neonatal complications	Initial pool of participants was randomly selected in 3 cohorts from 9 senior high schools (approx. 10'200 students) representative of urban and rural districts in western Oregon The analysed sample was restricted to 579 subjects who completed the T2 assessment Data collection at T1 and T2 (1987-1989) T1: N = 1'709 T2: N = 1'507	T1: K-SADS and additional items of the DSM-III-R T2: Longitudinal Interval Follow-up Evaluation (Keller et al., 1987) → lifetime dx Prenatal, perinatal, neonatal data: reported by biological mothers <u>prenatal complications:</u> - *maternal physical health:* bleeding from vagina, premature contractions, swelling of face and hands, high blood pressure, seizures and convulsions, rubella, any other infectious diseases, diabetes mellitus, anemia, serious injury, X rays - *maternal emotional health:* depression or anxiety during depression - *use of prescribed drugs:* morning sickness, pain, high blood pressure, hormones, Valium, thyroid medication - *maternal substance use:* cigarettes, alcohol, coffee/tea, marijuana - *maternal obstetric history;* previous miscarriage or stillbirth, medications to prevent miscarriage <u>perinatal and neonatal complications:</u> *Intrapartum:* - surgical delivery: caesarean delivery, general anesthesia - difficult delivery: local anesthesia, breech birth, forceps used *Early neonatal:* - Prematurity: LBW, premature birth, baby required incubator - acute anoxia/hypoxia: cord around neck, blue baby, slow heart beat, baby did not breathe, baby had convulsions, baby required oxygen - hematological problems: rhesus incompatibility, baby had jaundice, baby required blood transfusion *Late neonatal:* - illness in the first year: fever, infection - breast feeding	MDD: NS BPD: not assessed	ANX (PD, agoraphobia, SP, SOC, OCD, SAD, overanxious disorder): NS	DBD (ADHD, CD, ODD): Birth complications (anoxia/hypoxia) aOR = 3.20 (1.36–7.55), p = <.05	Alcohol and other drug abuse / dependence: NS	- birth complications (anoxia/hypoxia) increased 3 times the risk of DBD - no other perinatal and neonatal complication was significantly associated with a psychiatric disorder - several significant association btw prenatal complications and psychiatric disorders <u>Adjustments:</u> For other adolescent psychiatric disorders, maternal depression, family cohesion, family conflict, adolescent physical symptoms <u>Limitations:</u> - perinatal data: retrospective recall - entities of psychiatric dx - psychiatric evaluation: different instruments at T1 and T2 - mean age relates to T1 or T2?
		No controls							

Bipolar Disorder

Systematic review and meta-analysis	Aim	Literature search	Results	Conclusions
Scott et al. (2006) UK *Exposure to obstetric complications and subsequent development of bipolar disorder* 21 studies included (1965-2003)	Systematic review of studies comparing exposure to OCs in cases of BPD vs. non-psychiatric controls and vs. unipolar disorder cases or vs. schizophrenia cases.	Search in Medline (1966 to January 2004), PreMedline (to January 2004), PsychINFO (1967 to January 2004), Cochrane Library (up to October 2003), Best Evidence (1991 to September 2003) and EMBASE (1980 to January 2004). Hand searches of reference lists and raw data received from researchers. Inclusion criteria: 1) method used for measuring OCs stated: according to the *Lewis scale*, *Parnas scale*, *McNeil, Sjostrom scale*, *Mirdal scale* or maternal recall, medical notes, checklist applied to case notes 2) method of psychiatric evaluation specified: psychiatric assessment, interview with psychiatrist, DSM-IV, SCID, chart review, discharge diagnosis, medical records, interview with reliable informants (control group) Exclusion criteria: 1) insufficient information to allow identification of a distinct subgroup of cases of BPD with OCs that met the operational criteria defined; 2) insufficient information to allow OCs to be distinguished from other early developmental abnormalities or adverse events; 3) review papers with no new empirical data. Included studies: Brown et al. (2000), Browne et al. (2000), Byrne et al. (1996), Cannon et al. (1996), Cannon et al. (2002a), Dalen et al. (1965), Gunduz et al. (1999), Guth et al. (1993), Kinney et al. (1993), Kinney et al. (1998), Lewis & Murray (1987), Machon et al. (1997), Ogendahl et al. (2002), Schwarzkopf et al. (1989), Sigurdsson et al. (1999), Stober et al. (1977),Taylor & Abrams (1981), Verdoux & Bourgeois (1993a), Vocisano et al. (1996), Wals et al. (2003); Zornberg et al. (2000).	Pooled odds ratio for exposure to OCs and subsequent development of BPD in comparison to: BPD cases vs healthy controls (8 studies): pooled OR = 1.01 (95% CI: 0.76-1.35) BPD cases vs unipolar disorder cases (5 studies) : pooled OR = 1.13 (95% CI: 0.64-1.99) BPD cases vs schizophrenic individuals (6 studies): pooled OR = 0.61 (95% CI: 0.39-0.95)	There is no robust evidence that exposure to obstetric complications increases the risk of developing bipolar disorder. Albeit the range of events regarded as OCs and methodological inadequacies make definitive conclusions difficult. Limitations: - scales with sum scores: only OCs "yes" or "no", do not permit any association btw specific obstetric/perinatal factors and psychiatric diagnostics - relevant data were not reported in many studies in order to analyse confounders - no specification for age of onset of BPD

Study	Sample			Evaluation	Results				Conclusions
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Martelon et al. (2012) USA *Are obstetrical, perinatal, and infantile difficulties associated with pediatric bipolar disorder* Children, adolescents Prospective population-based family study	N = 120 Mean age 12 ± 3.37 yrs *Exclusion criteria:* Neurosensory impairment, cognitive impairment, ASD, adopted infants where the nuclear family was not available for evaluation	PBD	2 family studies with N = 327 families *"Juvenile Bipolar Disorder and Substance Use Disorder" (BPD/SUD)* 10-18 yrs old probands *"Childhood Mania"* 4-18 yrs old probands	KSADS-E: parent interview + child and sibling interview if >12 yrs SCID for probands >18 yrs WISC-IV Perinatal data: DICA-P module (mother report) - *obstetrical complications*: breech delivery, caesarean section, and other difficulties (e.g. cord around the neck, or labor greater than 24 hours) - *perinatal difficulties*: placement in an incubator, weight of less than 5 lbs, required hospital stay, and needed surgery	Not assessed	Obstetrical complications: NS aOR = 1.19 (95% CI: 0.62-2.31), p = 0.59	Perinatal difficulties: NS aOR = 0.43 (95% CI: 0.66-0.85), p = 0.10	Infantile difficulties: aOR = 6.6 (95% CI: 3.0-14.6), p <0.001 - "stiffened infant": OR = 7.2 (95% CI: 1.1-47.1), p = 0.04 - "other" infantile difficulties (incl. acting colicky: OR = 4.9 (95% CI: 1.3-18.8), p = 0.02	- significant association of PBD with infantile difficulties (especially "stiffened infant", "other" infantile difficulties) - no significant association between obstetrical or perinatal difficulties with PBD. - when CD or maternal BPD was added to the model, no association gained or lost significance. Adjustement: - age Limitations: - retrospective report of perinatal data (possible recall bias)
	N = 98 healthy controls without	controls	*"BPD/SUD":* non-mood-disordered controls						

	any mood disorder N =120 siblings of affected children (siblings >18y were excluded)		*"Childhood Mania"* Recruitment strategies for all probands (children, adolescents): Community advertisement, clinical referral (only for Childhood Mania participants) and internal posting in the extended hospital system.	- *infant behavior*: need to switch formulas 3 times or more, crying day and night, unusually quiet infant, stiffened infant, floppy infant, and any other issues that seemed unique to the mother, including acting colicky, vomiting, and thrashing about.				BPD probands were more likely: - to be male and have a lifetime history of ADHD and CD (vs nonaffected siblings) - to be younger, have a parental history of BPD, and have a lifetime history of ADHD and CD (vs healthy controls)	
Study	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Chudal et al. (2014) Finland *Perinatal factors and the risk of bipolar disorder in Finland* Adolescents Nested-case-control study; retrospective population-based register study	N = 724 born bw 1987-1998, dx and/or treated for BPD by December 31, 2008 Mean age of dx 16.9 yr (SD 2.6)	BPD	*"Finish Prenatal Study of Bipolar Disorders" (FIPS-B):* derived from all singleton live births in Finland btw 1983-1998) BPD cases were identified from the Finnish Hospital Discharge Register	Clinical dx ICD-8, -9, -10; Finnish Hospital Discharge Register Maternal educational level data: Register of Education at Statistics Finland Perinatal data: Finnish Medical Birth Register Classification of perinatal risk factors into two categories: - indicators of fetal growth: BW, GA and weight for gestational age (SGA, AGA, LGA) - OCs: . maternal risk factors: high blood pressure, uterine bleeding . birth factors: birth presentation (cephalic, breech, other presentation) . birth type: vaginal cephalic, suction+forceps, planned C-section, Emerg+other C-section, unknown . induced labor . hypoxia related factors: Apgar score at 1min . neonatal treatment: monitoring / NICU	BW, weight for gestational age: NS	post-term birth (GA ≥42 weeks): uOR = 1.7 (95% CI: 1.08-2.66), p = 0.02 aOR= 1.52, (95% CI: 0.93-2.45), p = 0.09 other GA categories: NS Birth presentation other than cephalic or breech (i.e. transverse, oblique, upper or lower limb): uOR = 5.31 (95% CI: 1.06-26.77), p = 0.01 aOR= 5.12, (95% CI: 0.95-27.54), p = 0.06 cephalic or breech presentation: NS Planned cesearean section: aOR = 2.51 (95% CI: 1.32-4.78), p <0.01 birth types vaginal cephalic, suction+forceps, Emerg+other C-section, unknown: NS Induced labor: NS	Hypoxia related factors (Apgar score at 1min): NS Monitoring / NICU: NS	. neonatal treatment: monitoring / NICU	- 2.5x increased risk of BPD in children delivered by planned caesarean section - Significant association btw post-term birth and birth presentations other than cephalic or breech and BPD in the unadjusted analysis - No significant associations for other GA categories, BW and their combinations, other perinatal factors and BPD <u>Adjustments:</u> maternal age, psychiatric history and educational level, place of birth, number of previous births and maternal smoking during pregnancy. <u>Limitations:</u> - study based on register data - only treated children included - inclusion into the study via hospital based clinical diagnosis - low power to detect associations for certain exposures including the lowest BW category and PT birth
	N = 1'419	Matched controls (sex, date of birth, residence in Finland on the first date of diagnosis of the case), not diagnosed with BPD or psychotic disorder	Finnish Central Population Register						

Study	Sample			Evaluation	Results				Conclusions
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Ogendahl et al. (2006) Denmark *Indicators of fetal growth and bipolar disorder: a Danish national register-based study* Adolescents, young adults Nested population-based case-control study (retrospective, register-based)	N = 196 Probands were born btw 1973-1983 admitted and diagnosed 1987-1999: aged btw 12-26 yrs 55.6% females *Exclusion criteria*: lifetime dx of SZA or depressive disorders	BPD	Danish Psychiatric Central Register	Admission to a Danish psychiatric facility (until 1995: only inpatient. From 1995: also inpatients) Clinical dx using ICD-8 and -10 criteria Perinatal data: Danish Medical Birth Register (BW, birth length, GA, number of previous pregnancies in the mother) SES data: Integrated Database for Longitudinal Labour Market Research Register and the Danish Civil Register		Premature birth (GA <37 wks.): only in females OR = 2.91, (95% CI: 1.10-7.73), p = ? → this analysis was based on only 6 exposed cases and 5 of these exposed cases also had a BW <2.5kg: OR = 3.70, (95% CI 1.35-10.15), p = ? Trend towards an increased risk of BPD: Preterm birth (GA <37 weeks): OR = 1.58, (95% CI: 0.67-3.75), (p=0.295) = NS Combination of LBW and preterm birth (BW <2.5kg and GA <37 weeks): OR = 2.10, (95% CI: 0.86-5.15), (p=0.106) = NS		Trend towards a lower risk of BPD: Length <49 cm: OR = 0.64, (95% CI: 0.34-1.22), (p=0.177) = NS	The only significant association: higher risk in females with preterm birth (GA <37 weeks) and LBW (<2.5kg) <u>Adjustments:</u> parental psychiatric illness, parental age at birth and SES, eventual previous admission and time since the first admission <u>Limitations:</u> - the significant association was based on only 6 cases - p-values for sex-specific analyses not shown - only inpatients until 1995 - clinical dx and not diagnostic interviews
	N = 25 *Exclusion criteria*: lifetime dx of BPD; SZA or depressive disorders	controls	Danish Medical Birth Register; time-, age- and sex- matched controls						

Study	Sample			Evaluation	Results				Conclusions
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Pavuluri et al. (2006) USA *Biological Risk Factors in Paediatric Bipolar Disorder* Children, adolescents Retrospective, cross-sectional, population-based study	N = 37 probands with BPD type I N = 33 probands with BPD type I combined with ADHD Mean age 11.5 ± 3.3 yrs	PBD	Recruited through the community and by the paediatric mood disorders clinic at the University of Illinois at Chicago *Exclusion criteria for all probands:* active substance abuse, IQ <70 (WASI) or presence of another DSM-IV Axis 1 dx that required use of any concomitant therapy other than for ADHD	WASH-U K-SADS (child interview and interview of at least one of the parents) Family psychiatric history obtained by interviewing the parents and by the FHS Perinatal data: Reported by parents - Computation of a numeric perinatal risk index from the sum of perinatal risk factors <u>Assessed perinatal risk factors:</u> in-utero exposure to medications prescribed for medical reasons, excessive use of unprescribed medications and/or illegal drugs, and birth complications (toxemia of pregnancy, peri-partum hemorrhage, prolonged labor, difficult delivery requiring additional intervention, low apgar score, oxygen requirement after birth, and neonatal jaundice) - Computation of a numeric index of developmental milestones, of a numeric variable of the presence and the number of physical illnesses requiring medical intervention and/or		Perinatal Risk index : OR = 6.23 (95% CI : 1.81-21.01), p <.01 Birth complications: NS Birth complications = toxemia of pregnancy, peri-partum hemorrhage, prolonged labor, difficult delivery requiring additional intervention, low apgar score, oxygen requirement after birth, and neonatal jaundice)		First degree relative with BPD: OR = 15.39 (95% CI: 1.83-129.85), p <.05	- the risk of PBD dx increased 6x for every additional perinatal risk factor such as prenatal exposure to drugs or birth complications (= only an additive effect) - birth complications were not significantly associated with a higher risk of BPD - 15x higher risk for BPD when first degree relative with BPD <u>Adjustment:</u> none <u>Limitations:</u> - perinatal data were retrospectively reported by parents - small sample size - cross-sectional
	N = 28	Healthy controls: demographically matched	Recruited through the community and by the paediatric mood disorders clinic at the University of Illinois at Chicago						

				hospitalization for medical illnesses from birth till the time of study entry - Inclusion of an indicator variable representing a history of traumatic brain injury					
Study	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Goldstein et al. (2010) USA *Clinical, Demographic, and Familial Correlates of Bipolar Spectrum Disorders Among Offspring of Parents with Bipolar Disorder* Children, adolescents High-Risk study, cross-sectional (offspring of parents with BPD)	N = 41 offspring with BPD Female 61% Mean age: 12.8 ± 3.1 yrs	9 with BPD-I 5 with BPD-II 27 with BPD-NOS* * In order to avoid dx youth with "soft" BPD symptoms, an operationalized and stricter DSM BPD-NOS dx was used	*Pittsburgh Bipolar Offspring Study* Parents with BPD were recruited through advertisement (53%), adult BPD studies (31%), outpatient clinics (16%) *Exclusion criteria:* current or lifetime dx, of SZA, mental retardation, mood disorders secondary to substance abuse, medical conditions, or medications, and living more than 200 miles away from Pittsburgh. 233 parents with BPD-I or BPD-II with N = 388 offspring, aged 6-17 years 119 offspring had no siblings in the study, whereas 269 were members of a sibling group	KSADS-PL, lifetime version (direct offspring interview) SCID (parent interview): for parental psychiatric history Perinatal data: medical history questionnaire used in research protocols at the Western Psychiatric Institute and Clinic (items: e.g. BW; drugs, smoking, psychotropic medication during pregnancy; normal delivery, trouble at birth, trouble breathing, other troubles) SES: Hollingshead scale FH-RDC: psychiatric history of second-degree relatives, biological coparents not seen for direct interview, and siblings of offspring that were >18 yrs at intake and therefore to old to participate in the study Nomi Pubertal Development: the Petersen Pubertal Developmental Scale	Weight at birth: NS	Normal delivery: NS Trouble at birth: NS	Trouble breathing: NS	Other troubles: NS	- no significant association of obstetric variables with BPD among offspring - no significant association of parental clinical variable with BPD in offspring - Significant associations of BPD in offspring and: . older age, more likely to be female, comorbid ANX and ODD/CD, exposure to stimulants and antidepressants and a history of physical and/or sexual abuse . younger parent age at birth, lower parental SES and biological coparent with BPD <u>Adjustment:</u> Sibling correlation <u>Limitations:</u> - retrospective recall of obstetric history, eventually mood-related bias - young mean age of offspring; before the period of greatest risk for onset for BPD - cross-sectional study
	N = 347 offspring without BPD Female 47% Mean age: 11.9 ± 3.7 yrs	Non BPD							

Major Depressive Disorder

Systematic review and meta-analysis	**Aim**	**Literature search**	**Results**	**Conclusions**
Loret de Mola et al. (2014) *Low birth weight, preterm birth and small for gestational age association with adult depression: systematic review and meta-analysis*	Assessment of the relationship of LBW, SGA and PT birth with **adult** depression.	Search in PsycINFO, Medline, LILACS, the Cochrane Library and SciELO databases. No limit for language or year of publication (final search 10 Sept 2013). <u>Inclusion criteria:</u> 1) original studies assessing the risk of depression according to birth weight, gestational age or intrauterine growth 2) age of participants: **>18 years** 3) measure of depression with **self-rating scales or diagnostic interview** <u>Exclusion criteria:</u>	Grouped into birth weight (14 studies, 21 estimates), premature birth (7 studies, 8 estimates), SGA (4 studies, 5 estimates): Significant association btw **low birth weight** (≤ 2.5 kg / 14 studies, 21 estimates) and adult depression: • pooled OR = 1.39, 95% CI 1.21-1.60 • adjusted pooled OR (among studies that controlled for SES and GA) = 1.35, 95% CI 1.15–1.60 • pooled OR (in studies using interviews as depression measure) = 1.47, 95% CI 1.13–1.89	Significant association btw LBW and adult depression No significant associations btw PT birth, SGA and adult depression <u>Limitation:</u> only 4 studies used diagnostic interviews: Batstra et al. (2006), Gudmundsson et al. (2011), Preti et al. (2000), Vasiliadis et al. (2008) → *according to the authors, the assessment of the outcome was not a source of heterogeneity (the pooled estimates were not biased*

15 population-based studies included (2000-2011)		outcome definition as psychological distress, common mental disorders and mood disorders, 'depression and/or anxiety' or any diagnosis that did not specifically identify the participant as having depression Included studies: Alati et al. (2007), Batstra et al. (2006), Dalziel et al. (2007), Fan et al. (2001), Gale et al. (2004), Gale et al. (2011), Gudmundsson et al. (2011), Herva et al. (2008), Mallen et al. (2008), Preti et al. (2000), Raikkonen (2007), Raikkonen (2008), Thompson (2001), Vasiliadis et al. (2008), Westrupp et al. (2011)	Premature birth (7 studies, 8 estimates): No significant association btw adult depression and **premature birth** or **SGA**	Adjustment: studies adjusted for BW, GA and/or SES / or no adjustment at all

Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Patton et al. (2004) Australia *Prematurity at birth and adolescent depressive disorder* Adolescents Population-based nested case-control design within a prospective cohort study	N = 63 N = 112	Depressive disorder controls	*Victorian Adolescent Health Cohort Study* conducted btw 1992-1996 in six waves (this sub-study took place btw waves 2 and 6). Participants were recruited in schools CIS-R (computerised assessment): identification of putative episodes of MDD in 2032 participants of the cohort study Identification of cases (using the CIS-R) Mean age at wave 2: 15.0 yrs (SD 0.4) Mean age at wave 6: 17.4 yrs (SD 0.4) Selection of non-cases (according to the CIS-R) from participants of the same school in a 2:1 ratio to the cases	CIDI (adolescent interview) for lifetime dx of MDD - "Threatening Experiences Questionnaire", adapted list: identification of recent life events - PBI (administered to the probands immediately before the CIDI) CIDI (parent interview) for the assessment of parental lifetime psychiatric disorders; six months after completion of wave 6 Perinatal data (BW and GA): parental report (mostly from mothers)	LBW (<2'500g): uOR = 2.9 (95% CI: 0.6-1.4)	Preterm birth (<37 wks. of gestation): uOR = 5.7 (95% CI: 1.4-2.3)		PT birth or LBW: - aOR = 11.6 (95% CI: 2.2-62) adjusted for: background factors (gender, parental education, parental separation, parental history of MDD, maternal smoking in pregnancy, maternal age at birth and serious illness in the first year of life) - aOR = 6.2 (95% CI: 0.8-48) adjusted for: background factors (described above), parenting style, negative life events and level of earlier depressive and anxiety symptoms Lifetime rates of MDD were 1.0% (95% CI: 0.8-1.3) in PT/LBW males and 15.2% (95% CI: 11.1-20.5)	- PT birth increased approximately 6x and LBW approximately 3x the risk of MDD in adolescents - the risk for depressive disorder was 11x higher in adolescents born LBW or PT, but clear reduction of the risk with the adjustment for negative life events but primarily with the adjustment for pre-existing depressive and anxiety symptoms - substantially higher rates of lifetime MDD in PT/LBW female adolescents than in male adolescents Adjustments: See below "other results" Limitations: - retrospective recall of perinatal data - no p-values indicated - sample badly described

Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Loret de Mola et al. (2015) Brazil *The Effect of Fetal and Childhood Growth over Depression in Early Adulthood in a Southern Brazilian Birth Cohort*	N = 282 N = 3'294	MDD No MDD	*The Pelotas Birth cohort study* Recruitment of individuals born 1982 in the maternity hospital in Pelotas, southern Brazil (N = 5914) In 2012/2013 N = 3'576 individuals aged 30 yrs of the cohort study were evaluated concerning the	MINI for MDD dx at age 30 yrs BDI-II for depression intensity Perinatal data measured at birth: GA (estimated from the last menstrual date), family income, maternal age, marital status,	LBW: NS SGA : NS SGA + "stunted in childhood": aPR = 1.87 (95% CI: 1.06-3.29), p = 0.09 (p value for heterogeneity)	PT birth: NS			- Higher risk of adult depression in individuals born SGA and who were "stunted in childhood" - Preterm birth, SGA and LBW were not significantly associated with adult MDD Adjustments: Skin color, mother's age, schooling, previous gestations, pregnancy risk factors, C-section, smoking and income at birth Models including variables at 2 and 4 yrs were further adjusted for assets index, mother "nerve" problems,

Adults Longitudinal population-based birth cohort study			presence of depression: prevalence of MDD = 7.9% Female 52 % Mean BW: 3222 g (SD 526 g) Mean GA: 39.4 wks of GA (SD 1.8) SGA: 14.2% (N = 410) "stunted" at 2 yrs: 12.7% (N = 416) "stunted" at 4 yrs: 10.5% (N = 337)	maternal schooling, pregnancy risk factors, prenatal visits, type of delivery, child's sex, number of siblings Childhood data: follow-up evaluations in 1984 and 1986 LBW: <2'500g SGA: >1.28 SD below the mean in the Williams reference "stunted": length/height for age z-score >2 SD below the mean of the WHO references PT birth: GA <37 wks.					father live together and history of psychiatric illness, parent's alcoholism and breastfeeding <u>Limitations:</u> - unusual definitions of perinatal factors - p-values? - p-value for heterogeneity? *Further description of methodology in Barros, 2008*
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Osler et al. (2005) Denmark *Birth dimensions and risk of depression in adulthood: cohort study of Danish men born in 1953* Adults Longitudinal, population-based cohort study (only men)	N = 151 men with MDD N = 39 men with BPD Age range for first psychiatric hospitalization for depression: 16-49 yrs	MDD, BPD	Danish birth register 10'753 Male singletons born in Copenhagen in 1953 *Danish longitudinal study (Project Metropolit)* (1965-2002) No controls	First psychiatric hospitalization with discharge diagnosis of depression (ICD-8 and -10). Entry in 1969 and end of follow-up with the first psychiatric hospitalization for MDD or BPD (Data source: Danish Psychiatric Central Register) Perinatal data: Birth certificates LBW ≤ 2'499g LBW 2'500-3499g Ponderal Index: BW (kg) / birth length (m) and divided in quintiles	LBW ≤ 2'499g: NS LBW 2'500-3499g: NS Ponderal Index: NS				- no significant association btw LBW and depression in adult men <u>Adjustments</u>: Maternal marital status, paternal occupation <u>Limitations:</u> - "first psychiatric hospitalization for depression"; inclusion of subjects later developing BPD - only subjects treated in an inpatient setting - only men - gestational age not included - no information available for possible confounders like parental psychopathology (e.g. maternal depression)
Studies	**Sample**			**Evaluation**	**Results**				**Conclusions**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Vasiliadis et al. (2008) USA *Fetal growth restriction and the development of major depression* Adults Prospective, population-based cohort study	N = 1101 47.3% female	LBW SGA Ponderal Index GA NBW	The subjects of this study were offspring of participants in the Providence, RI, site of the *National Collaborative Perinatal Project (NCPP)* At 12 US academic medical centers, 53'000 pregnant women were enrolled btw 1959-1966 and followed during labor and delivery. The Providence, RI, site enrolled 4140 pregnant women. Recruitment: Of the 4184 resulting births, a stratified random sample was selected for participation in one of two adult re-interview studies (in 1984 with offspring aged 18-27	DIS (direct structured interview), lifetime dx (DSM) Perinatal data: Obstetric summary and delivery report. Medical reports of the newborn included data concerning foetal growth indicators: LBW: <2.5kg SGA: BW <10th percentile ot the Providence NCPP cohort Ponderal Index: BW (kg) / length (m) Preterm birth: ≤37 wks. GA Post-term birth: ≥42 wks. GA Other information collected during pregancy: women's past reproductive	<u>MDD:</u> LBW: NS SGA: NS Ponderal Index: NS Preterm birth: NS Post-term birth: NS			Overall rate of MDD: 23.7%	- no association btw LBW, SGA, ponderal index, gestational age and adult depression <u>Adjustment :</u> Parental factors at subject's birth: mother's age, marital status, mother's and father's lifetime history of mental illness (yes/no; illness requiring hospital care or psychiatric treatment), mother's and father's employment status Subject's age and race at interview Pregnancy/delivery complications (yes/no), potential learning disabilities at age 7 (yes/no) <u>Limitations:</u> - parent's psychiatric history was based on parental self-report of "nervous problem", requiring hospital care or psychiatric treatment

			yrs and in 1996 with offspring aged 30-39 yrs) on the relation between early life factors and adult psychiatric disorders.	and gynecological history, past and recent medical history, SES and medical family history.					

Anxiety Disorders

SR and Meta-A	Aim	Literature search	Results	Remarques / Limitations
Sømhovd et al. (2012) *Anxiety in adolescents born preterm or with very low birthweight: a meta-analysis of case-control studies* 6 studies included (1997-2010)	Assessment of the relationship **of VP birth and/or VLBW** with **adolescent** clinically significant anxiety problems	Search in ISI Web of Knowledge, PubMed, PsycNET, Educational Resources Information Center (ERIC), Latin American and Caribbean Literature on the Health Sciences (LILACS), and Virtual Health Library (VHL) databases. Screening of references lists of identified articles (final search June 2011). Inclusion criteria: 1) case–control studies of **adolescents** 11 to 20 years old who were born VP and/or with VLBW, with a matched reference group born at normal GA and with normal BW 2) use of **validated anxiety outcome measures.** By default, Sømhovd et al**.** accepted the validity of the cut-offs selected by the authors of the original papers. All types of informants were accepted; self-reports were the a priori preference. Exclusion criteria: 1) children with neurodevelopmental impairment (severe learning disability, cerebral palsy) or major psychiatric disorders (to reduce confounding by comorbidity to severe neurodevelopmental impairment) 2) studies published only as abstracts, conference proceedings, studies involving <30 children or adolescents and studies of low methodological quality (<5 stars on the Newcastle–Ottawa scale) Included studies: Botting et al. (1997), Indredavik et al. (2004), Johnson et al. (2010), Farooqi et al. (2007), Grunau et al. (2004), Hack et al. (2004)	General risk of developing clinically significant anxiety problems in the very preterm/VLBW population (unadjusted OR): OR = 2.27, (95% CI: 1.15-4.47), (p<0.05)	- 2x higher risk of anxiety problems in VPT/VLBW born adolescents Estimates are unadjusted Limitations: - "anxiety problems" and not dx of ANX - only 3 of 6 studies used psychiatric diagnostic interviews: Botting: CAPA Indredavik: K-SADS Johnson: DAWBA *Farooqi: CBCL-P* *Grunau: CBCL-P* *Hack: YABCL*

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Hirshfeld-Becker et al. (2004) USA *Pregnancy complications associated with childhood anxiety disorders* Children	138 children with parents with PD and MDD 26 children with parents with PD and without MD 47 children with parents with MDD and	ANX	Children of parents with PD (with or without comorbid MDD); Children of parents with MDD (without comorbid PD or agoraphobia) Recruitment from clinical referral and advertising Participants had been recruited for a study of temperament and psychopathology in children who were	K-SADS-E - completed by mothers for children >5 yrs - interviews with mothers and direct interviews with children >12 yrs SCID: with each parent Perinatal data: DICA-P (developmental history module), administered to parents:	Not assessed	Total number of delivery complications: OR = 1.63 (95% CI: 0.9-2.0) NS Total number of delivery complications and multiple (≥2) ANX: OR = 1.3 (95% CI: 0.9-2.0)	Not assessed	Total number of pregnancy complications and multiple (≥2) ANX: aOR = 1.6 (95% CI: 1.4-2.0), p <.001 Significant associations btw specific pregnancy complications and specific childhood ANX (→ table 3)	- children with or without multiple ANX did not differ significantly on number of delivery problems - Number of delivery problems significantly predicted multiple childhood ANX. Adjustments: parental psychopathology, child age, maternal smoking Limitations:

Cross-sectional, retrospective High-Risk-study (parents with PD and with or without MDD)	without PD or agoraphobia		at risk for ANX because of having at least one parent with PD	- pregnancy complications: spotting or light bleeding, heavy bleeding requiring bed rest, excessive nausea or vomiting lasting more than 3 months, weight gain >25 lbs., weight loss >10 lbs., infection requiring medical attention, high blood pressure and/or excessive fluid retention, convulsions, accidents requiring medical care, emotional problems for which counselling was sought, serious family problems that were upsetting, taking any medication, smoking a pack a day for at least 3 months, drinking alcohol daily or going on binges, or taking drugs not prescribed by a doctor - delivery complications: breech delivery, caesarean section, or other difficulties (e.g. cord around the neck, labor >24h) Childhood anxiety disorders: child PD, agoraphobia, childhood avoidant disorder (DSM-III), SAD		NS			- perinatal data was reported retrospectively - the DICA-P module does not quantify for intensity of pregnancy and delivery problems - statistical analyses limited by low reported rates of some risk factors
	95 children with parents without a lifetime dx of mood disorder or ANX ..... → N = 306 children: mean age 6.8 ± 2.4 yrs (5–25 yrs, 9 children were >12 yrs) Exclusion criteria in the proband and the control group: - families in which a parent had a psychotic disorder, was suicidal or in which a parent or a child was mentally retarded. - participants who would not cooperate, could not understand, or could not communicate sufficiently. - children with events at birth resulting in brain damage (brain bleeds, severe anoxia, seizures)	Controls	Children of comparison parents without PD, agoraphobia, SOC, OCD, MD Recruitment from hospital personnel and through community advertisements						
Study	**Sample**			**Evaluation**	**Results**				**Comments**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Freed et al. (2014) USA *Early risk factors for psychopathology in offspring of parents with bipolar disorder: the role of obstetric complications and maternal comorbid anxiety* Adolescents Cross-sectional retrospective High-Risk study (parents with BPD)	206 offspring of 119 parents with BPD Age of offspring: 13.6 ± 6.1 (4–33) yrs No exclusion criteria described	BPD I, BPD II, depressive disorder, ANX, ADHD, CD, ODD	Recruitment of possible participant parents through advertisements posted in waiting rooms of Massachusetts General Hospital psychiatry units, letter to clinicians and advertisements to the general public Inclusion of parents with a positive BPD dx according to the SCID Data stems from 2 studies examining characteristics of and risk factors for offspring of BPD parents.	- K-SADS with children btw 12-18 yrs - SCID with offspring >18 yrs + K-SADS modules for the assessment of childhood dx - SCID with parents Lifetime dx for parents and offspring, grouped in the following categories: - BPD (I or II) - depressive disorder (MDD and/or dysthymic disorder) - ADHD - DBD (ODD and/or CD) - ANX (PD, agoraphobia, SOC, SP, OCD, GAD, PTSD, SAD) Perinatal data: selected items of the DICA-P developmental history module, administered to parents: - pregnancy complications: heavy bleeding requiring bed rest, excessive nausea or vomiting lasting more than 3 months, weight loss >10 lbs., infection	Weight less than 5 lbs: NS	Offspring ANX and delivery complications: β = .27, (p<.01), R^2 = .07 controlled for parental lifetime ANX: β = .24, p <.01, R^2 = .10 In offspring of BPD mothers, but not fathers, offspring ANX were significantly associated with delivery complications: β = .33, (p<.01), R^2= .11 *vs*. β = .18, p = .29 , R^2 = .03	Neonatal characteristics: NS	Offspring lifetime ANX and OC history: β = .25, (p<.01), R^2 = .06 Controlled for parental lifetime ANX: β = .21, p < .05, R^2 = .08	- significant association of a history OCs (pregnancy and delivery complications, neonatal characteristics) only with offspring ANX, even when controlled for parental lifetime ANX - significant association btw delivery complications and offspring ANX, even when controlled for parental lifetime ANX - no significant associations btw offspring ANX and the other OCs (pregnancy complications and neonatal characteristics) or LBW - no associations btw OCs and mood disorders Adjustments: parental lifetime ANX Limitations: - no information concerning the psychiatric history of the unaffected (non-BPD) parent was collected
	No controls								

				requiring medical attention, high blood pressure and/or excessive fluid retention, convulsions, accidents requiring medical care, other illnesses requiring medical care - <u>delivery complications:</u> breech delivery, caesarean section, other delivery complications (e.g. born 2 weeks early/late, forceps delivery, cord wrapped around neck, labor >24h) - <u>neonatal characteristics:</u> Put in incubator, weight less than 5 lbs, long stay in hospital		- significant association btw maternal ANX comorbidity and OCs - delivery complications act as a mediator in the relationship btw comorbid maternal ANX (and not paternal) and offspring ANX			- perinatal data was collected by retrospective self-report - the DICA-P module is not primarily used for the assessment of OCs and does not assess OCs severity
Study	**Sample**			**Evaluation**	**Results**				**Comments**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Johnco et al. (2016) USA *Adverse Prenatal, Perinatal and Neonatal Experiences in Children with Anxiety Disorders* Children, preadolescents Cross-sectional, population-based study	N = 107 Aged 7-13 yrs <u>Exclusion criteria</u>: dx of BPD, SZA, schizoaffective disorder; significant or unstable medical condition, clinically significant suicidality	ANX	Treatment-seeking children and their parents form 3 community mental health sites Recruited during the baseline assessment for a child anxiety treatment trial.	ADIS-IV (child and parent interviewed separately) + CSR CIS, parent version Perinatal data: The "Perinatal and Medical Questionnaire" of the KSADS-E, a parent self-report measure, contains items about complications during pregnancy, birth, early temperament and development and family psychiatric history Outcome: "all anxiety disorders" (ANX)	LBW (<2.5kg): NS	Preterm birth, higher rates: 29.0% compared to 11.5%, $X^2 = 31.81$, p<.001 Overall birth complications: NS - induced labor, lower rates: 11.2% compared to 23.0%, $X^2 = 8.45$, p=.003 - vacuum delivery, higher rates: 7.5% compared to 2.8%, $X^2 = 8.52$, p <.01 Forceps, breech birth, caesarean delivery, cord around neck, other (e.g., placenta previa, hypertension, long labor): NS In children with birth complications, higher rates of comorbid ADHD: $X^2 = 5.74$, p =.017 This was largely the result of increased rates of umbilical cord: $X^2 = 9.56$, p=.002 In children whose mothers experienced illness or injury during pregnancy (requiring medical care), higher rates of comorbid depressive disorder: p=.006	Overall neonatal complications, higher rates: 43.9% compared to 14.0%, $X^2 = 13.05$, p <.001 - NCIU, higher rates: 15.0% compared to 7.8%, $X^2 = 7.56$, p <.01 - Formula switched >3 times, higher rates: 17.8% compared to 0%, $X^2 = 9.91$, p <.01 - UV lights, baby in hospital > mother, surgery >1 mth. old: NS	Prevalence of ANX in this sample: - 41.12% GAD - 24.3% SOC - 24.3% SAD - 7.48% SP - 0.93% PD - 1.87% OCD 78.5% of the children with ANX had first degree relatives with a psychiatric history Overall prenatal/pregnancy complications, lower rates: 33.6% compared to 78.0%, $X^2 = 25.98$, p =.001 - significant higher rates of substance use during pregnancy (cigarettes, alcohol, recreational drugs), of prescription medication use and of maternal illness requiring medical care - significant lower rates of assisted conception/fertility treatment Multiple birth, adoption: NS Infant temperament (excessive crying, sleeping problems, severe reactivity to environmental changes): NS Overall developmental problems: higher rates: 57.0% compared to 13.8%, $X^2 = 24.95$, p=.001 - significant higher rates of delayed walking - developmental consultation sought, delayed speech, delayed toilet training: NS	- youth with ANX had been significantly more exposed to preterm birth, vacuum delivery, NCIU stay and had higher overall neonatal complications (more NCIU admissions probably due to preterm births) - no increased rates of LBW or overall birth complications in youth with ANX - youth with ANX had lower rates of complications during pregnancy and lower rates of induced labor No adjustments <u>Limitations:</u> - no control group, comparisons with population base-rates - retrospective recall of perinatal complications - only "treatment-seeking children" → sufficiently representative? Selection bias - statistical analyses limited by low prevalence rates of many complications
	No controls		Perinatal data was compared to base rates of perinatal complications in the general population						

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Kingston et al. (2015) Canada *Predictors of Childhood Anxiety* Children Cross-sectional, population-based register study	N = 591 Age: 5 yrs *Exclusion criteria:* first nation mothers living on the reserve, child not living with the biological mother	"childhood anxiety"	Provincial administrative data from Manitoba, Canada (Families First Program)	Data source: administrative databases linked with personal health identification numbers: Lifetime dx of "childhood anxiety" till age 5; def childhood anxiety - Physician visits with dx of ANX (ICD-9 CM) *or* - prescription of anxiolytic medication *or* - hospitalization for "childhood anxiety" Perinatal data: hospital discharge abstracts, medical claims file (physician visits) SES data: vital statistics, population registry (demographics), Manitoba Family Services, Healthy Child Manitoba)	SGA: NS LBW: not assessed	Preterm birth (<37 wks.): aOR = 0.67 (95% CI: 0.45-0.999), p<.05 Cesarean delivery: NS Apgar score at 5 min of ≤7 pts.: aOR = 1.76 (95% CI 1.20-2.58), p<.05	Breast-feeding initiation	Prevalence of "childhood anxiety" from birth to age 5: 3.1% Of those children: - 73,8% had ≥1 physician visits for anxiety - 24.9% prescription of an anxiolytic - 1.3% had both - no children had been hospitalized	Increased risk for "childhood anxiety" by age 5: - Apgar score at 5 min of ≤7, maternal psychological distress from birth-12 months and from 13 months to 5 years post-delivery Decreased risk for "childhood anxiety" by age 5: - preterm birth multiple parity, maternal age <20 yrs No significant associations with "childhood anxiety" by age 5: - SGA, cesarean delivery <u>Adjustments:</u> Variables adjusted for all other variables in the model <u>Limitations:</u> - umbrella term "childhood anxiety" - register based
	N = 18'725 Age: 5 yrs	without "childhood anxiety"	Provincial administrative data from Manitoba, Canada (Families First Program)						

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Bandelow et al. (2002) Germany *Early traumatic life events, parental attitudes, family history, and birth risk factors in patients with panic disorder* Adults Cross-sectional study	N = 115 Mean age: 38.1 yrs (SD 10.6) 59.1% women *Exclusion criteria :* history of other mental disorders (MDD, BPD, GAD, SOC, OCD, PTSD, SUD, personality disorders) .	Panic Disorder (without any other current or past mental disorder)	Outpatients treated at the AD Unit at the Department of Psychiatry, University of Göttingen	SCID Questionnaire containing items concerning - birth risk factors: age of mother at childbirth in years, age of father at childbirth in years, percentage of Caesarean sections or premature birth, week of premature birth, or birth complications - traumatic life events during childhood - parental attitudes towards the subjects - psychiatric disorders in family members	NS Trend toward more reports of LBW in patients, p = .064	Birth risk factors: NS OR = 0.85, p = .38			- birth risk factors did not differ significantly btw patients and controls - LBW is more frequent in patients (p = .064) <u>Adjustments:</u> Not stated <u>Limitations:</u> - summary score for "birth risk factors" - perinatal data was retrospectively reported by the proband - the methodology applied in this study may not be appropriate to exclude influences of birth risk factors Missing: 95% CI
	N = 124 Mean age: 36.8 yrs (SD 11.6) 57.3% women	Healthy controls	Controls without a history of psychiatric disorders (according to the SCID interview). Recruitment in official buildings (e.g. hospitals, city halls) Matched for sex, age, school, education, social class						

Study	Sample			Evaluation	Results				Comments
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Bandelow et al. (2004) Germany *Early traumatic life events, parental rearing styles, family history of mental disorders, and birth risk factors in patients with social anxiety disorder* Adults Cross-sectional study	N = 50 Mean age: 39.9 yrs (SD 10.4) *Exclusion criteria:* Severe medical illness or history of mental disorder (MDD, BPD, GAD, PD, OCD, PTSD, SUD, personality disorders), except avoidant personality disorder)	Social Anxiety Disorder	Patients treated at the Department of Psychiatry and Psychotherapy at the University of Göttingen	SCID Questionnaire containing items concerning - birth risk factors: age of mother > 35, Caesarean section, low birth weight, premature birth, perinatal complications (e.g. asphyxia), congenital defects - traumatic life events during childhood - parental rearing styles and attitudes towards the subject - psychiatric disorders in family members	NS	Birth risk factors: NS OR = 1.23, 95% CI: 0.6-2.5, p = 0.56			- birth risk factors did not differ significantly btw patients and controls <u>Adjustments:</u> Not stated <u>Limitations:</u> - perinatal data was reported retrospectively by probands - summary score for "birth risk factors" - interviewers weren't blind whether they were interviewing patients or controls
	N = 120 Mean age: 40.1 yrs (SD 13.5)	Healthy controls	Controls without a history of psychiatric disorders (according to a SCID interview). Recruitment in official buildings (e.g. hospitals and city halls) Matched for sex and age						
Study	**Sample**			**Evaluation**	**Results**				**Comments**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Betts et al. (2011) Australia *The association between birth weight and anxiety disorders in young adults* Young adults Prospective birth cohort study	N = 2210 Age: 21 yrs *Exclusion criteria:* Non-caucasian mother/offspring pairs	PD, GAD, agoraphobia, SOC, SP, PTSD	*Mater University Study of Pregnancy birth cohort (MUSP)* All variables of interest were available for 2210 mother/offspring pairs	CIDI-Auto, lifetime version, at 21 years Follow-ups at the child's birth and of child aged 6 months and 5, 14 and 21 years Hospital obstetric records: BW, GA, gender → BW converted in to z-scores, internally adjusted for GA and gender	Within the smallest BW quintile group: Lifetime dx of PTSD after exposure to a traumatic event: OR = 1.96 (95% CI: 1.10, 3.52), *p for linear* = 0.03 No gender interaction btw BW and PTSD	Not assessed	Not assessed	No significant associations btw perinatal variables and PD, GAD, agoraphobia, SOC or SP in young adults Prevalence rates of discrete disorders in this sample → table 2	- almost two-fold increased odds for PTSD after an traumatic event within the smallest BW quintile group compared to the largest group - BW z-score was linearly and inversely associated with life time PTSD dx at 21 years in fully adjusted analysis <u>Adjustments:</u> maternal smoking and alcohol consumption during pregnancy, maternal antenatal anxiety (assessed by the DSSI), maternal age at birth and parity, offspring work type, income and smoking at 21 yr and for attrition <u>Limitations:</u> -
			Participants with PTSD were compared with participants of other BW quintiles groups						
Study	**Sample**			**Evaluation**	**Results**				**Comments**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Vasiliadis et al. (2010) Canada *Fetal Growth and the lifetime risk of Generalized Anxiety Disorder* Adults	N = 682 Mean age 33.3 years (SD 2.5)	GAD Lifetime dx	Offspring of participants in the *Collaborative Prenatal Project (CPP).* The Providence, Rhode Island, site enrolled 4'140 pregnant women btw 1959- 1966 (of a total of >53'000, enrolled at 12 US academic medical centers)	DIS, lifetime dx Indicators of fetal growth (BW and ponderal index): collected by CPP study personnel *(probably in medical records)* Analysis of BW as 4-category (<2.5, 2.5-3.0, >3.0-3.5, >3.5 kg) and as	<u>BW/PI</u>: The lifetime risk of GAD differed between infants in the highest category of BW, PI, and all others: - infants with BW <3.5 kg: HR = 2.38,	<u>Preterm birth:</u> - males born <37 weeks vs males born 38-41 weeks: HR = 4.66 (95% CI: 2.16-10.04), (p=.04) - among females: NS			- In general, the heaviest born infants had the lowest lifetime risks of GAD as adults - no linear association btw BW, PI, GA and lifetime risk of GAD - higher lifetime risk of GAD for males born preterm <u>Adjustments:</u> - maternal factors at subjects' birth: age, marital status, self-reported history of

Prospective birth cohort study		controls	Other participants in the *CPP*	dichotomous variable (≤ 3.5 vs >3.5 kg) z-scores, standardized for sex and GA and split into quintiles; analysis as ordinal variable and as dichotomous variable (quintiles 1-4 vs quintile 5) Ponderal Index (PI) = BW (kg) / (birth length in m)^2 Analysis as 5-category variable (in quintiles) and as dichotomous variable (quintiles 1–4 versus quintile 5).	95% CI: 1.25-4.55), (p=.004) - infants in the lowest 4 BW Z-score quintiles: HR = 2.49 (95% CI: 1.14-5.45). (p=.01) - infants with a PI in the thinnest 4 quintiles: HR = 2.33 (95% CI: 104-5.00), (p=.02)				treated mental illness and employment status - offspring sex, race and age at interview, potential learning disability at age 7 - for BW categories, PI and GA - MDD episode prior to onset of GAD Limitations: - self-reported history of treated mental illness of the mother - LBW is generally def. as < 2.5 kg → the significant associations btw lower BW and adult GAD are evt. not an effect of LBW, as a higher risk of adult GAD was also observed in subjects born at normal BW >2.5-3.5 kg kg), relative to those born in the highest BW category (>3.5 kg) - lifetime dx: based on retrospective recall of GAD symptoms

Obsessive Compulsive Disorder

Study	**Sample**			**Evaluation**	**Results**				**Comments**
	Characteristics	**Dx**	**Source**		**BW**	**Birth**	**Post-natal**	**Other results**	
Brander et al. 2016 Sweden *Association of Perinatal Risk Factors with Obsessive-Compulsive Disorder* Adults Longitudinal population-based cohort study	N = 17'305 Dx during the studied period (1973-2013) Born btw 1973-1996 Mean age at first dx of OCD 23.4 years (SD 6.5)	OCD	N = 2'421'284 individuals in the cohort Swedish Medical Birth Register Swedish Multigeneration Register Swedish Nationa Patient Register Migration Register Cause of Death Register	Clinical dx of OCD (ICD-10). Source: Swedish National Patient Register Perinatal data from the Swedish Medical Birth Register: maternal smoking during pregnancy, labor presentation, obstetric delivery, GA, BW, BW in relation to GA, 5-min Apgar score, head circumference	LBW 1.5-2.5kg): aHR = 1.30; (95%CI: 1.05-1.62) BW 2.5-3.5kg: aHR = 1.08 (95% CI: 1.01-1.16) Large for GA: aHR = 1.23; 95%CI, 1.05-1.45	Preterm: aHR = 1.24 (95%CI: 1.07-1.43) Apgar score 4-6 at 5min: aHR = 1.50; (95%CI: 1.07-2.09) Breech presentation: aHR = 1.35 (95%CI: 1.06-1.71) Cesarean section: aHR = 1.17 (95%CI: 1.01-1.34) Number of perinatal events: 1 event: aHR = 1.11 (95% CI: 1.07-1.15) ≥ 5 events: aHR = 1.51 (95% CI: 1.18-1.94)		Prevalence of OCD: 1.32% at age 40 years; 41.1% men; more comorbid disorders among those with OCD: 37.95 vs 5%, (p=<.001)	- U-shaped curve for the association btw BW and OCD - significant association with lifetime OCD: BW categories, preterm, breech presentation, caesarean section, Apgar score at 5min, smoking ≥10 cigarettes/day - dose-response association btw the number of adverse perinatal events (from 1 to ≥5) and increased risk for OCD Adjustments: Adjustment for shared familial confounders and measured covariates (incl. sex, year of birth, maternal and paternal age at birth, and parity) Limitations: - perinatal data was reported retrospectively - p-values?
	N = 2'403'979 Sibling subsample: 743'885 families with ≥2 full siblings	controls	Swedish Medical Birth Register For the sibling comparison analysis: Swedish Multi-genration Register						

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Geller et al. (2008) USA *Perinatal factors affecting expression of obsessive-compulsive disorder in children and adolescents* Children Longitudinal controlled family study	N = 130 Mean age 11.5 yr (± 3.1) mean age at onset of OCD 7.6 years (SD 3.1) 59% males <u>Exclusion criteria:</u> diagnosis of autism or pervasive developmental disorder, psychosis, or schizophrenia, eating disorder, major sensorimotor handicaps (deafness, blindness), or inadequate English language	OCD	Pediatric OCD study, longitudinal family study	<u>Pediatric OCD study:</u> K-SADS-E clinical assessment including the CY-BOCS <u>Family study of ADHD:</u> K-SADS-E Perinatal data: the KSADS-E, administered to the mother as indirect informant, includes questions about the pregnancy, including drug and alcohol use, delivery and obstetric information, perinatal history, and early developmental history		Birth difficulties (induced labor, forceps delivery, nuchal cord, prolonged labor): $X^2 = 7.51$, (p=0.006) significant associations btw adverse perinatal events and earlier age at onset, increased OCD severity, and increased risk for comorbid ADHD, chronic tic disorder, AD and MDD. Comorbid psychopathology was predicted by specific perinatal risk factors among children with OCD: - higher rates of illness requiring medical care in pregnancy in mothers of children with a positive immediate family history of OCD ("familial" OCD): $X^2 = 7.56$, (p=0.006) - need for an incubator in the postnatal period, need to stay in hospital after mother was discharged werel associated with an increased risk for comorbid ADHD - perinatal jaundice in infancy requiring treatment predicted comorbid chronic tic disorder - sleeping problems in infancy predicted a later comorbid AD - severe irritability in infancy predicted lifetime comorbid MDD	Among OCD children: - perinatal jaundice in infancy predicted comorbid chronic tic disorder: $X^2 = 10.93$, (p=0.001) Needed more formula changes in infancy (> 3 formula switches): $X^2 = 7.95$, (p=0.005)	Maternal illness during pregnancy requiring medical care: $X^2 = 8.61$, (p=0.003) Lifetime rates of comorbid disorders: 42% ADHD, 22% Tourette's syndrome, 50% MDD 4.6% BD, 49% GAD Several significant associations btw adverse perinatal experiences and earlier age at onset, increased OCD severity, and increased risk for comorbidities	- significantly higher rates of birth difficulties in children with OCD <u>Adjustments:</u> - none <u>Limitations:</u> - perinatal data was reported retrospectively
	N = 49 Mean age = 11.7 ± 3.1	controls	Matched controls: siblings of non-ADHD control probands from a contemporaneous family case control study of ADHD						

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Grisham et al. (2011) Australia *Risk factors prospectively associated with adult obsessive-compulsive symptom and obsessive-compulsive disorder* Adults Longitudinal birth cohort study	N = 36	OCD	*Dunedin Multidisciplinary Health and Development Study* (New Zealand; 23-year birth cohort study, children born 1972-1973) N = 972 (96% of the living cohort members)	DIS at ages 26 and 32 Follow-ups: at ages 5,7, 9,11, 13,15, 18, 21, 26, 32 years of age WISC-R One or more perinatal insults (12 prenatal and 12 neonatal problems recorded by clinicians during the mother's pregnancy): epilepsy, moderate or severe hypertension, antepartum hemorrhage, delivery other than spontaneous or breech birth, SGA (<10th percentile), preterm (<37 weeks GA), idiopathic respiratory distress syndrome, minor or major neurological signs, non-hemolytic hyperbilirubinemia, Rhesus incompatibility		Number of perinatal insults: NS		OCD prevalence: 2.3% at age 26 1.8% at age 32	The number of perinatal insults was not associated with significantly increased risk for OCD at ages 26 or 32 Significant risk factors for adult OCD dx: social isolation, retrospectively reported physical abuse and negative emotionality <u>Adjustments:</u> - sex and SES <u>Limitations:</u> - outcome « number of perinatal insults", no results for individual insuls
	N = 613 healthy controls N = 310 ANX controls	Healthy and ANX controls							

Study	Sample			Evaluation	Results				Comments
	Characteristics	Dx	Source		BW	Birth	Post-natal	Other results	
Vasconcelos et al. (2007) Brazil *Prenatal, Perinatal, and Postnatal Risk Factors in Obsessive–Compulsive Disorder* (Young) adults Retrospective cross-sectional study	N = 68 Mean age: 24.93 yr (range 11-44)	OCD	PROTOC: Obsessive–Compulsive Disorder Spectrum Program at the Institute of Psychiatry of the Clinical Hospital of the University of São Paulo Medical School (FMUSP)	K-SADS (5-15 yrs) SCID (> 15 yrs) supplemented with additional modules designed by the PROTOC staff for the DSM-IV dx of Tourette syndrome and tics Y-BOCS YGTSS Perinatal data: Medical and Risk Factor Questionnaire based on translations and adaptations of the Modified Schedule for Risk and Protective Factors developed by the Yale Child Study Center of the Yale University School of Medicine		Protracted labor: aOR = 13.408, (95% CI: 2.368-75.920), (p=.003)		Higher prevalence in OCD patients of: - prolonged labor (p<.001) - nuchal cord entanglement (p=.05) - cesarean section (p=.005) - born in hospitals (p=.014) - perinatal complications: premature rupture of membranes (p=.013) - longer periods in incubators (p=.01) - preterm birth and jaundice (p <.001) - delayed bladder control (p=.026)	- the development of OCD was significantly associated with protracted labor. <u>Adjustments:</u> SES, schooling <u>Limitations:</u> - perinatal data was reported retrospectively
	N = 70 Mean age: 24.2 yr (range 11-43)	controls	Gender- and age- matched individuals without OCD Recruitment at the FMUSP Orthopedics Institute						

Disruptive behaviour disorders

Systematic Rev.	Aim	Literature search	Results	Comments / Limitations
Serati et al. (2017) *Research Review: The role of obstetric and neonatal complications in childhood attention deficit and hyperactivity disorder – a systematic review* Systematic Review : 40 studies included (1987-2016)	Review of the literature related to obstetric and neonatal complications and the risk of developing **ADHD from birth up until 12 years of age**	search 3 databases. Searches limited to references published between 1987 – Dec 2016 <u>Inclusion criteria:</u> 1 keywords: ADHD + Pregnancy, delivery, perinatal complications, obstetric complications, preterm birth, low birth weight, bleeding, asphyxia, small for gestational age, abnormal foetal presentation, Apgar 2 **OCs defined as those reported in the Lewis-Murray rating scale with particular attention to labour, birth weight, asphyxia, Apgar score** 3 studies considering maternal non-obstetric complications (e.g. obesity, smoking or alcohol abuse during pregnancy) weren't taken into consideration 4 only articles in English <u>Exclusion criteria:</u> 1. Animal studies 2. studies with a different diagnosis 3. adult ADHD 4. physiology studies 5. Researches about ADHD comorbidity (e.g. diabetes, smoking) 6. R. aimed to investigate generic attention problems	Results have been <u>grouped into six sections:</u> labour, birth weight, preterm birth, asphyxia, Apgar score, neonatal seizures	in several studies: parent reports, dx not according to ICD or DSM criteria
Labour (6 studies)	**<u>Oxytocin-induced labour</u>** - No association / oxytocin-induced labour HR 1.42; CI: 1.12–1.80 (N = 546'146 / Henriksen et al., 2015) - Association (p < .001) / perinatal pitocin exposure (N = 172 / Kurth and Haussmann, 2011) **<u>Complicated labour</u>** - Significant higher risk for ADHD-Inattentive subtype OR = 1.25; CI 1.1–1.5 (N = 124/124 / Ketzer, Gallois, Martinez, Rohde and Schmitz, 2012) **<u>Cord prolapse</u>** - Significant associated with a higher risk of ADHD in females than in the control group OR 2.83 (N = 12'991/30'071 / Silva, Colvin, Hagemann & Bower, 2014) **<u>Mode of birth</u>**			

	- Emergency delivery: no association OR: 1.28; CI: 0.61–2.66 (N = 18'827 / The Millennium cohort study / Curran, Cryan et al., 2016) - Emergency caesarean delivery: significant association HR: 1.16; CI: 1.12–1.20 (N = 1'772'548 / Curran, Khashan et al., 2016)	
Birthweight (LBW 13 studies, VLBW 7 studies, ELBW 5 studies)	**Low birth weight** (<2'500g) - Association with ADHD particularly in children living in urban areas than in sub-urban ones (Breslau et al., 1996) - Increased risk OR: 3.1; CI: 1.03–9.3 (Mick, Biederman, Prince, Fischer and Faraone, 2002) - 3.6 times more frequent in ADHD cases respect to subjects with normal birth weight (p = .03) (Sasaluxnano and Kaewpornsawan, 2005) - no significantly higher rates of neonatal complications (including LBW) in children with ADHD compared with their unaffected siblings (p = .99) (Ben Amor et al., 2005) - increased risk for ADHD in moderately LBW children compared to children with normal birth weight: OR: 1.77; CI: 1.07–2.9 (Stein, Siegel and Bauman, 2006) - LBW is a risk factor for ADHD symptoms also after controlling for genetic influence / effect size d = 1.64, OR: 19.6; CI: 1.44–266 (N = 1480 / prospective twin study / Hultman et al., 2007) - Differences in birth weight in discordant twins for ADHD (p = .031) (Lehn et al., 2007) - association btw LBW and ADHD (p < .01) / (Martel, Lucia, Nigg and Breslau, 2007), - higher risk of ADHD for children with LBW combined to SGA: OR: 3.60; CI: 1.63–7.95 (Heinonen et al., 2010) - higher risk of ADHD for children with LBW and/or preterm birth compared to controls (p = .003) (Chu et al., 2012) - higher risk of ADHD for children with LBW XR 1.54; CI: 1.44–1.65) (Class, Rickert, Larsson, Lichtenstein & D'Onofrio, 2014) - association btw LBW and ADHD in a British (OR: 2.29; CI: 1.09–4.8) but not in a Brazilian sample (OR: 0.78; CI: 0.34–1.8) (Murray et al., 2016) - **no** association btw LBW and ADHD (p = .40) (Langley, Holmans, van den Bree and Thapar, 2007*) → a low quality study according to Serati* **Very low birth weight** (<1'500g) - at 5 years 31% of children born with VLBW had ADHD (Astbury, Orgill & Bajuk, 1987) - at 12 years 23% of children born with VLBW had ADHD compared with 6% of matched peers (p < .0001) (Botting, Powls, Cooke & Marlow, 1997) - 1.7x higher risk (CI: 1.13–2.47) (National Survey of Children's Health, Singh et al., 2013) - Increased risk OR: 2; 1.3–2.8 (Boulet, Schieve & Boyle, 2011) - higher risk for ADHD-IA but not for hyperactive-impulsive subtype prospective study in VLBW and very preterm (<32 weeks) children: RR 2.76; CI: 1.46–5.19 (Jaekel, Wolke, & Bartmann, 2013) - the combination of VP birth and VLBW is significantly associated with a higher risk of ADHD-IA and ADHD combined type (ADHD-C): XR 2.8; CI: 1.6–5 (The Bavarian Longitudinal Study; Breeman, Jaekel, Baumann, Bartmann & Wolke, 2016). - the combination of VLBW and preterm birth is significantly associated with ADHD: RR: 1.6; (CI: 1.2– 2.3) (Schieve et al., 2016) **Extremely low birth weight** (<1'000g) - 16% of ELBW had ADHD compared with 6.9% of controls (p = .04) (Szatmari, Saigal, Rosenbaum, Campbell & King,1990) - higher prevalence of ADHD in ELBW children compared to offspring with normal weight: OR: 4.2; CI: 1.9–9.1 (Hack et al., 2009) - increased risk for ADHD in ELBW infants with mechanical ventilation for ≧15 days even without significant neonatal brain damage: AHR: 1.95; CI: 1.02–3.76 (Tsai et al., 2014) - increased risk for ADHD-IA for children with ELBW and SGA age combined: AOR: 4.98; CI: 0.72–34.69 (Van Lieshout, Boyle, Saigal, Morrison and Schmidt, 2015) - no association between ADHD and perinatal adversities in ELBW children (O'Callaghan & Harvey, 1997)	
Preterm birth (4 studies)	**Preterm birth** (<35 weeks) - higher risk OR: 3.42; CI: 1.41–8.32 (El Marroun et al., 2012) **Very preterm birth** (<32 weeks) - higher risk OR: 3.05; CI: 1.39–6.71) (Gustafsson & Källen, 2011) - children at 7 years reporting borderline statistically significant difference in the prevalence of ADHD between children born VP versus controls (10% vs. 3%; UOR: 4.09; CI: 0.93–18 (medium- large effect size d = .76) (N = 242Treyvaud et al., 2013) **Extreme preterm birth** (≤28 weeks) - higher risk OR: 3.3; CI: 1–10.5 (Lindström, Lindblad, & Hjern, 2011)	Preterm birth (<35 wks.) is not defined according to the WHO
Asphyxia (2 studies)	**Perinatal cyanoses** - association with ADHD (p = .05) (Perna and Cooper, 2012) in utero exposure to **ischemic-hypoxic conditions** - higher risk for ADHD: OR: 1.16; CI: 1.11–1.21 (Getahun et al., 2013)	
Apgar score (4 studies)	**low Apgar score** - from 1 to 4 at 5 min: higher risk for ADHD AHR: 1.75; CI: 1.15–2.66 (Li, Olsen, Vestergaard & Obel, 2011)	

	- <7 at 5 min: significantly associated with ADHD OR: 2.17; CI: 0.93–5.06 (Gustafsson & Källen, 2011) - A low Apgar score = highest predictive perinatal risk factor for ADHD onset in males (Hanc et al., 2016). - Low apgar scores were not identified as a risk factor for ADHD (Silva et al., 2014)	
Neonatal seizures (1 study)	Association between neonatal seizures and ADHD in a genetic high-risk group for this disorder (adjusted OR: 5.6; CI: 1.4–22.5) (Pineda et al., 2007)	

Systematic Rev.	**Aim**	**Literature search**	**Results**	**Comments / Limitations**
Latimer et al. (2012) *Disruptive behaviour disorders: a systematic review of environmental antenatal and early years risk factors* Systematic Review : 47 studies included (1993-2008)	Review of the evidence for risk factors (environmental, psychosocial, protective) associated with five operationally defined disruptive behaviour disorders: ADHD, CD, ODD, DAMP, RAD DAMP: deficits of attention, motor control and perception RAD: reactive attachment disorder	6 databases. Searches limited to references published between Jan 1966 – April 2009 Inclusion criteria: 1 Human study population. 2 Study measures/outcomes include at least one **diagnosis** of CD, ODD, ADHD, DAMP, RAD [based on **ICD-10, DSM-IV** or earlier versions of these manuals, (in the case of DAMP…)]. 3 Study includes assessment of factors (social, physical, temperamental, behavioural, interactional) **present antenatally and in the first 4 years of life** 4 Factors measured prospectively or retrospectively. 5 Study design is one of the following: case-control study, including nested case-control study, cohort study, or controlled trial. Exclusion criteria: 1 Paper published before 1966. 2 Paper not published in a peer-reviewed journal. 3 Paper not published in English.	Results have been grouped into three sections: Perinatal: Maternal smoking, alcohol and drug use during pregnancy / Maternal illness during pregnancy Post-natal: Birthweight / Post-natal complications Infancy: Parenting styles and parental stress / Early deprivation / Adoption and separation	Despite the understanding that there is sharing of risk factors between the DBDs, there has been a disproportionate focus on the role of certain risk factors at the expense of others and the field is weakened by difficulties in controlling for all potential confounding variables ADHD "overrepresented", other DBD "underrepresented" → Studies in young children have demonstrated that DBDs overlap in both presentation and aetiology (Costello *et al.* 2005) Age at time of dx?
Post-natal Birthweight (11 studies)	**Perinatal risk factors:** (LBW = < 2.5 kg, moderate LBW = 1.5-2.49 kg) Significant association between **low birthweight** and **ADHD** / ADD / hyperkinetic disorder (Knopik, 2005 ; Stein, 2006 ; Linnet, 2006 ; Lehn, 2007 ; Breslau, 1996 ; Botting, 2007 ; Indredavik, 2005 ; Sasaluxnanon & Kaewpornsawan, 2005) - Mick, 2002b: 3x more likely - Sasaluxnanon & Kaewpornsawan, 2005: 3.6x more ADHD in the low birthweight than in the control group No association between low LBW and **ADHD** (Langley, 2007) Other **DBD**s than ADHD (Stein, 2006) Significant association between **extremely preterm** (<29 gestational weeks)(compared to full term) and **ADHD** (Stejernqvist and Svenningsen, 1999)			
Post-natal Complications (7 studies)	Association between **perinatal complications** (= ?) and **ADHD** (Sprinchbuckminster, 1993 ; Milberger, 1997 ; Bhat, 2005). No association between **low Apgar scores** and **ADHD** or **DAMP** (Krebs, 2001) Significant Association between **DBDs** and **acute anoxia/hypoxia** (Allen, 1998) **Neonatal complications:** Association between **neonatal hypoglycaemia** and long-term neurological dysfunction and **DAMP** (Stenninger, 1998). Higher rates of **neonatal complications** in children with **ADHD** (Ben-Amor, 2005 / Maternal smoking and alcoholism did not result in significant differences between patients and their unaffected siblings) → The children with ADHD had significantly higher rates of neonatal complications compared with their unaffected siblings ($F_{4,196} = 3.67$, $p < 0.006$).			

Meta-Analysis	Aim	Literature search	Results	Remarques / Limitations
Momany et al. (2017) *A Meta-Analysis of the Association Between Birth Weight and Attention Deficit Hyperactivity Disorder* 88 population-based studies included (1968-2017)	Assessment of the association of BW and ADHD	Search in the following databases: Medline (PubMed), PsychInfo, and ProQuest Dissertation and Theses (through march 2016) Inclusion criteria: 1) studies were empirical and published in the English language in a peer-reviewed journal or were a component of a dissertation or thesis (literature reviews, meta-analyses, and case studies were not included), (2) studies included a measure of birth weight, (3) studies included a measure of ADHD symptoms or diagnosis (parent report of previous diagnosis, diagnosis from a medical record, diagnostic interview, or questionnaire assessing ADHD symptoms), (4) studies examined the relationship between birth weight and ADHD in human subjects. Exclusion criteria: excluded if the 1) participants in the study were part of a specific medical population (e.g., fetal alcohol syndrome, velo-cardio-facial syndrome), 2) study population had already been reported on in another study (the study with the largest sample size was retained), 3) the study did not provide sufficient data to calculate an effect size.	Individuals born at lower BW manifested greater symptoms of ADHD (r = −0.15) (95% CI: −0.16, −0.13) Significant heterogeneity was detected (Q (92) = 8673.9.0, p < 0.0001 and I2 = 98.9) Sample type, mean birth weight of the sample, geographic region, the informant of ADHD symptoms, ADHD symptom measurement method, and race were all found to contribute significantly to heterogeneity in effect sizes. Several early life risk factors previously found to be associated with both ADHD and BW, GA and prenatal smoking exposure, were not found to contribute to heterogeneity in effect sizes.	All ages Studies using diagnostic interviews and rating scales included
Zhu et al. (2016) *Association Between Perinatal Hypoxic-Ischemic Conditions and Attention-Deficit/Hyperactivity Disorder: A Meta-Analysis* 10 population based studies included (1992-2014)	Assessment of the association btw perinatal hypoxic-ischemic conditions and ADHD	Search in the following databases: PsycINFO, EMBASE, Web of Science, and PubMed. A further manual search was performed (before Sept 2015). Inclusion criteria: 1) the article's status was published and written in English; (2) cases were individuals with ADHD regardless of age; (3) individuals without ADHD were the controls; (4) and risk factors which were akin to those of the in this study included article by Getahun: placental abruption, an Apgar score <7 at 5 minutes, neonatal resuscitation, breech/transverse presentations or delivery, prolapsed/nuchal cord, preeclampsia respiratory distress syndrome, and fetal dystocia. 5) use of validated scales or criteria to assess ADHD. 6) the country of origin, study design, subjects' ethnicity, and the number of patients/control subjects were reported Exclusion criteria: Studies that attempted to identify the risk factors for a broader definition of an adverse outcome that may include ADHD, or the co-occurrence of ADHD and other impairments.	Significant associations with ADHD: Preeclampsia: OR = 1.31, (95% CI: 1.26-1.37) Apgar score <7 at 5 minutes: OR = 1.31, (95% CI; 1.12-1.54) breech/transverse presentations: OR = 1.14, (95% CI: 1.06-1.23) prolapsed/nuchal cord: OR = 1.10, (95% CI: 1.06-1.15)	All ages Studies used diagnostic interviews to establish the dx or were based on registers (ICD or DSM codes).