

Supplementary Online Content

Maher GM, O’Keeffe GW, Kearney PM, et al. Association of hypertensive disorders of pregnancy with risk of neurodevelopmental disorders in offspring: a systematic review and meta-analysis. *JAMA Psychiatry*. Published online June 6, 2018. doi:10.1001/jamapsychiatry.2018.0854

eTable 1. Search Strategy for Each Electronic Database

eTable 2. Summary of Characteristics of ASD Studies Included

eTable 3. Summary of Characteristics of ADHD Studies Included

eTable 4. Summary of HDP and Other Neurodevelopmental Disorders

eTable 5. Level of Bias in ASD Studies

eTable 6. Level of Bias in ADHD Studies

eTable 7. Level of Bias in Other Neurodevelopmental Outcome Studies

eFigure 1. ASD Studies With Crude and Adjusted Estimates

eFigure 2. ADHD Studies With Crude and Adjusted Estimates

eFigure 3. ASD Studies That Adjust for Maternal Age and Smoking and Parity/Birth Order

eFigure 4. ADHD Studies That Adjust for Maternal Age and Educational Level

eFigure 5. Funnel Plot of Published HDP and ASD Studies

eReferences.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Search Strategy for Each Electronic Database	
Search terms: For PubMed (1946 - June 7, 2017) LIMIT: humans	
1.	pre eclampsia
2.	preeclampsia
3.	pre-eclampsia
4.	gestational hypertension
5.	hypertensive pregnancy disorder
6.	hypertensive disorders of pregnancy
7.	pregnancy induced hypertension
8.	pregnancy-induced hypertension
9.	pregnancy hypertension
10.	toxaemia
11.	toxemia
12.	maternal metabolic
13.	[#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12]
14.	autism
15.	autism spectrum
16.	autistic
17.	autism spectrum disorders
18.	autism Spectrum Disorder
19.	autistic spectrum disorders
20.	autistic Spectrum Disorder
21.	Asperger
22.	Asperger's
23.	Asperger's Syndrome
24.	autistic Spectrum
25.	pervasive developmental disorder
26.	pervasive developmental disorders
27.	disintegrative disorder
28.	rett syndrome
29.	attention deficit disorder
30.	ADD
31.	ADHD
32.	attention-deficit
33.	attention-deficit/hyperactivity disorder
34.	attention-deficit hyperactivity disorder
35.	attention-deficit-hyperactivity disorder
36.	hyperactivity disorder
37.	hyperactiv*
38.	overactive*
39.	inattent*
40.	hyperkinetic disorders
41.	hyperkinet*
42.	neurodevelopment
43.	specific learning disorder
44.	learning disorder
45.	intellectual disability
46.	mental retardation
47.	communication disorder
48.	motor disorder
49.	conduct disorder
50.	IQ
51.	reading age
52.	school performance
53.	[#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52]
54.	[#13 and #53]

eTable 2. Summary of Characteristics of ASD Studies Included										
Study	Data source	Study design	Region, study period	Sample size and prevalence of exposure	Diagnosis of HDP	Outcome	Assessment method	Confounders adjusted	Matching factors	Confounders identified?
Curran et al, ¹ 2017	Millennium Cohort study	Cohort	UK 2000-01	HDP 983, No HDP 12115 HDP= 7.5%	Doctor-diagnosed self-reported HDP	ASD	Maternal-reported	Smoking during pregnancy, birth order, poverty, maternal ethnicity, age, education, depression, BMI, longstanding diabetes, longstanding HT	n/a	Literature
Walker et al, ² 2015	CHARGE study	Case-control	California 2003-11	ASD 517, Controls 350	PE from medical records or maternal self-reporting in telephone interview. (Diagnostic criteria NR)	ASD	Previous ASD diagnoses were examined using the ADOS and the primary caregiver was administered the ADI-R	Maternal educational level, parity, pre-pregnancy obesity	Age, sex, broad geographic regions within the study catchment areas	Literature and DAG
Polo-Kantola et al, ³ 2014	National registry data	Case-control	Finland 1990-2005	ASD 1036, Controls 4132	Maternal HT: PE and/or PIH from MBR: BP >140/90	ASD	ICD-10	Maternal age, smoking during pregnancy, number of previous births, maternal psychiatric history	Sex, date of birth, place of birth	Literature
Langridge et al, ⁴ 2013	MNS, Registrar General's birth and	Cohort	Western Australia 1984-99	ASD without ID 452, no ASD	Pregnancy hypertension (PE and	ASD	DSM-III-R, DSM-IV, DSM-IV-TR	Birth year, maternal and pregnancy conditions (maternal diabetes, threatened	n/a	NR

	death registrations			376529 Prevalence of HDP: NR	essential hypertension) from MNS. (Diagnostic criteria NR)			abortion, asthma, UTI during pregnancy, placenta praevia, placenta abruption, other antepartum haemorrhage), socio-demographics (parity, maternal and paternal age group, maternal ethnicity, community-level socioeconomic status and community accessibility/remoteness), labour and delivery factors (preterm type, mode of delivery, breech, any complication of labour or delivery), neonatal outcomes (infant gender, resuscitation required at birth, percentage of optimal birthweight and head circumference)		
Mrozek-Budzyn et al, ⁵ 2013	Psychiatric outpatient clinic for children	Case-control	Poland 2006-07	Cases 96, Controls 192	PE and chronic HT from medical records or self-reporting. (Diagnostic criteria NR)	Childhood or atypical autism	ICD-10	No	Year of birth, sex and general practitioners	Only factors associated with ASD in univariate model were included in multivariate model
Nath et al, ⁶ 2012	Neurodevelopment and Early Intervention	Case-control	India 2012	Cases 31, Controls 100	PIH: Self-reported	ASD	DSM IV TR	No	Age	NR

	Clinic									
Lyall et al, ⁷ 2012	Nurses' Health Study II	Cohort	United States 1989-2005	Total 66445, Toxemia 5968, Pregnancy-related HBP 5884 Toxemia = 9% HBP= 8.9%	Toxemia and pregnancy related HBP self-reported in questionnaire	ASD	Maternal-reporting	Race, marital status, income, spouse education, nurse's age at baseline, age at first birth, parity	n/a	Literature
Krakowiak et al, ⁸ 2012	CHARGE study	Case-control	California, 2003-10	Cases 517, Controls 315	Hypertension (chronic, gestational or PE) from medical records or structured interview with the mother. (Diagnostic criteria NR)	ASD	ADI-R and ADOS	Mother's age at delivery, race/ethnicity, education level, delivery payer, calendar time	Age, gender, and regional centre catchment area	DAG
Dodds et al, ⁹ 2011	Administrative Health Databases	Cohort	Nova Scotia, Canada 1990-2002	PIH 11836, No PIH 117897 PIH= 9.1%	PIH from Perinatal Database: ICD-9 and ICD-10	ASD	ICD-9 and ICD-10	No	n/a	Only factors associated with ASD in univariate model were included in multivariate model
Burstyn et al, ¹⁰ 2010	Provincial delivery records and	Cohort	Alberta, Canada 1998-	PE 2774, No PE	PE from APHP delivery	ASD	ICD-9	Maternal age, maternal weight, maternal height, pre-	n/a	NR

	physician billing data		2004	213568 PE= 1.3%	records. (Diagnostic criteria NR)			pregnancy diabetes, gestational diabetes, bleeding, smoking, poor weight gain, parity, mother's SES, presentation (breech etc.), type of labour, caesarean section, gestational age, birthweight, APGAR at 1 min and 5 mins, infant sex, birth year.		
Mann et al, ¹¹ 2010	Birth certificate and Medicaid billing records	Cohort	South Carolina 1996-2002	PE 5531, No PE 82146 PE= 6.3%	PE/ eclampsia from billing records for Medicaid-eligible women, ICD-9	ASD	ICD-9 from Medicaid billing records or children receiving services from the South Carolina DDSN for autism	Maternal age, race, alcohol use, educational attainment, year of birth, child's sex, and diagnosis with a high risk condition (alcohol use, tobacco use, down syndrome, fragile X syndrome, brain anomaly) and birthweight	n/a	NR
Bilder et al, ¹² 2009	Birth certificate records and ADDM	Case-control	Utah, US 1994-2002	Cases 132, Controls 13200	Chronic and PIH from birth certificate records. (Diagnostic criteria NR)	ASD	DSM-IV-TR from ADDM	No	Gender and birth year	NR
Buchmayer et al, ¹³ 2009	Swedish MBR and Hospital Discharge Register	Case-control	Sweden 1987-2002	Cases 1216, Controls 6080	PE and gestational HT from the MBR: ICD-9 and ICD-10	Autistic disorders	ICD-9 and ICD-10	Parity, previous miscarriage, childless years, any maternal infection during pregnancy, season of delivery, diabetes mellitus, maternal age, smoking, maternal	Age, gender, birth year, and birth hospital	Literature

								country of birth, whether the mother lived with the father, maternal schizophrenia		
Larsson et al, ¹⁴ 2005	Danish PCR, Danish MBR and IDA	Case-control	Denmark 1978-90	Cases 698, Controls 17450	PE from MBR. (Diagnostic criteria NR)	Autism	ICD-8 and ICD-10 from PCR	No (information on PE available from 1978-90 only)	Gender, birth year and age	NR
Glasson et al, ¹⁵ 2004	MCHRDB	Case-control	Western Australia 1980-95	Cases 314, Controls 1313	PE: ICD-9	Autism	DSM	No	Sex	NR
Hultman et al, ¹⁶ 2002	Swedish MBR and In-patient Register	Case-control	Sweden 1974-93	Cases 408, Controls 2040	HDP from Medical Birth Register: ICD-8 and ICD-9	Infantile autism	ICD-9 - Discharged from a Swedish psychiatric or general hospital with a main diagnosis of infantile autism	Maternal age, parity, smoking during pregnancy, mother's country of birth, diabetes, pregnancy bleeding, mode of delivery, season of birth, gestational age, birthweight for gestational age, Apgar score at 5 minutes, congenital malformations	Sex, year, and hospital of birth	NR
Eaton et al, ¹⁷ 2001	Danish MBR and Danish PCR	Case-control	Denmark 1973-93	Cases 116, Controls 102905	Eclampsia from MBR. (Diagnostic criteria NR)	Autism	ICD from PCR	Gender and year of birth	NR	Only variables significantly associated with outcome included in multivariate analysis
Matsuishi et al, ¹⁸ 1999	NICU survivors of St. Mary's Hospital,	Case-control	Kurume, Japan 1983-87	Cases 18, Controls 214	Toxemia. (Diagnostic criteria NR)	Autistic disorder	DSM-III-R	No	NR	NR

	Kurume									
Mason-Brothers et al, ¹⁹ 1990	Survey data and medical records	Case-control	Utah, US 1965-84	Cases 225, Controls 60	Toxemia from medical records. (Diagnostic criteria NR)	Autism	DSM-III from survey	No	Sibling	NR
Deykin et al, ²⁰ 1980	Referral agencies and medical records and interview data	Case-control	Massachusetts, US 1975-77	Cases 118, Controls 246	Toxemia from medical records and interview data. (Diagnostic criteria NR)	Autism	≥1 symptoms of impaired relatedness to the environment, stereopathy and impaired language development	Birth order	Sibling	Excess of first born among cases

ASD=autism spectrum disorder. HDP=hypertensive disorder of pregnancy. n/a=not applicable. CHARGE=Childhood Autism Risks from Genetics and the Environment. PE=pre-eclampsia. NR=not reported. ADOS=Autism Diagnostic Observation Schedule. ADI-R=Autism Diagnostic Interview, Revised. DAG=directed acyclic graph. HT=hypertension. PIH=pregnancy-induced hypertension. MBR=Medical Birth Register. ICD=International Classification of Disease. MNS=Midwives' Notification System. ID=intellectual disability. DSM=Diagnostic and Statistical Manual of Mental Disorders. UTI=urinary tract infection. HBP=high blood pressure. APHP=Alberta Perinatal Health Program. SES=socioeconomic status. DDSN=Department of Disabilities and Special Needs. ADDM=Autism Developmental Disabilities Monitoring Network. PCR=Psychiatric Central Register. IDA=Integrated Database for Longitudinal Labour Market Research. MCHRDB=Maternal and Child Health Research Database. NICU=neonatal intensive care unit.

eTable 3: Summary of Characteristics of ADHD Studies Included										
Study	Data source	Study design	Region, study period	Sample size and prevalence of exposure	Diagnosis of HDP	Outcome	Assessment method	Confounders adjusted	Matching factors	Confounders identified?
Böhm et al, ²¹ 2017	Millennium Cohort study	Cohort	United Kingdom 2001-08	HDP 1069, No HDP 12432 HDP= 7.9%	Self-reported HDP	ADHD	Maternal-reported	Alcohol during pregnancy, maternal education, maternal depression, maternal age, poverty status	n/a	Literature
Silva et al, ²² 2014	MNS and MODDS system	Case-control	Western Australia 1981-2003	Cases 12991, Controls 30071	PE from MNS system. (Diagnostic criteria NR)	ADHD	DSM-IV or ICD-10 Data extracted from MODDS on children and young adults dispensed stimulant medication	Marital status, parity, smoking, complications of pregnancy, onset of labor, augmentation of labor, complications of labor, type of delivery, child characteristics (gestational age, birthweight, average/small/large for gestational age) maternal age, Apgar at five mins.	Year of birth, gender, and socio-economic status	Available from MNS for data analysis
Cak and Gokler, ²³ 2013	NICU hospital records	Cohort	Turkey 2003-08	Total 106, PE 16, HT 22	HT and PE: Self-reported and NICU	ADHD	K-SADS-PL according to DSM-IV	No	n/a	NR

				HT= 20.8% PE= 15.1%	records. (Diagnostic criteria NR)					
Getahun et al, ²⁴ 2013	KPSC medical records	Case- control	Southern California 1995- 2010	Cases 13613, Controls 68065	PE:ICD-9- CM	ADHD	Clinical diagnosis of ADHD using ICD-9-CM on at least 2 separate visits or a diagnosis on 1 visit and at least 2 refills of ADHD- specific medications	Maternal age, education, smoking during pregnancy, parity, prenatal care, household income, psychosocial disorder during pregnancy, child race/ethnicity, and gender	Age at diagnosis	"Chosen a <i>priori</i> "
Golmirzae i et al, ²⁵ 2013	Cluster sampling of preschool children	Case- control	Southern Iran 2012	Cases 208, Controls 196	PE self- reported in quest- ionnaire	ADHD	Conners' parents and teachers rating scale and interview by a child and adolescent psychiatrist using DSM- IV criteria	No	Age	NR
Amiri et al, ²⁶ 2012	Child and Adol- escent Psych- iatric Clinics. Controls from primary school	Case- control	Tabriz, Iran 2009	Cases 164, Controls 166	PE self- reported and medical records when possible. (Diagnostic criteria NR)	ADHD	The ADHD Rating Scale- Parent Version questionnaire according to DSM-IV-TR criteria and K-SADS according to	No	Age	NR

	students						DSM-III-R and DSM-IV			
Halmoy et al, ²⁷ 2012	MBR of Norway	Cohort	Norway 1967-87	Total 1172396, Chronic HT 1570, PE 28495 HT= 0.13% PE= 2.4%	Chronic hypertension and PE from the MBR. (Diagnostic criteria NR)	ADHD	Adult ADHD patients who were approved for stimulant treatment in Norway during 1997–2005, according to ICD-10 criteria, modified to be comparable to DSM-IV	Year of birth, parity, age of mother at birth, educational level of mother and marital status of mother	Born in the same time period	NR
Ketzer et al, ²⁸ 2012	12 public schools in Porto Alegre, Brazil and ADHD outpatient programme	Case-control	Brazil 2001-07	Cases 124, Controls 124	PE/ eclampsia self-reported and medical records when possible. (Diagnostic criteria NR)	ADHD	K-SADS-E and DSM-IV criteria	Agoraphobia (anxiety disorder), maternal ADHD and cigarettes/day during pregnancy	Age, gender	Literature
Gustafsson and Källén, ²⁹ 2011	Swedish MBR and Department of Child and Adolescent Psychiatry Register	Cohort	Sweden 1986-2006	PE 888, No PE 31124 PE= 2.8%	PE from MBR. (Diagnostic criteria NR)	ADHD	DSM-III-R11 before 1994 and DSM-IV12 from 1994 onwards	No	n/a	Only variables with p<0.2 included in multivariate analysis
Mann and McDermo	Medicaid billing	Cohort	South Carolina	PE 4674, No PE	PE/ eclampsia:	ADHD	Diagnosed with ADHD	GU infection, infant race,	n/a	Literature

tt, ³⁰ 2011	records		1996-2002	80047 PE= 5.5%	ICD-9		using ICD-9 by at least two different providers	maternal age and education, alcohol and tobacco use, infant sex, birthweight, and oldest age in Medicaid		
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ADHD=attention deficit/hyperactivity disorder. HDP=hypertensive disorder of pregnancy. n/a=not applicable. MNS=Midwives' Notification System. MODDS=Monitoring of Drugs of Dependence System. PE=pre-eclampsia. DSM=Diagnostic and Statistical Manual of Mental Disorders. ICD=International Classification of Disease. ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification. NICU=neonatal intensive care unit. HT=hypertension. K-SADS-PL=Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version. NR=not reported. KPSC=Kaiser Permanente Southern California. K-SADS-E=Schedule for Affective Disorders and Schizophrenia for School Age Children-Epidemiological Version. MBR=Medical Birth Registry.

eTable 4. Summary of HDP and Other Neurodevelopmental Disorders
Summary of HDP and cognitive functioning/developmental delay studies

Pre-eclampsia								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Warshafsky et al, ³¹ 2016	Offspring, age 1-5 years	Cohort	Kingston and Ottawa, Canada 2003-09	PE 95, No PE 140	Severe PE: BP >140/90 mm Hg and proteinuria >300 mg/24 hours or ≥1+ on repeat dipstick	Neurodevelopmental performance	Failure of Ages and Stages Questionnaire	Severe PE v NT: No significant associations OR and 95% CI: Year 1 follow-up: 0.90 (0.24 to 3.34) Year 2 follow-up: 0.63 (0.19 to 2.09) Year 3 follow-up: 2.31 (0.63 to 8.53)
Walker et al, ² 2015	Offspring, aged 24-60 months	Case-control	20 Californian counties, 2003-11	Developmental delay 138, typical development 277	PE: medical records	Development delay	Vineland Adaptive Behaviour Scales, Mullen Scales of Early Learning, Social Communication Questionnaire	PE (medical records only) v NT: No significant association OR and 95% CI: 1.82 (0.72, 4.64)
Heikura et al, ³² 2013	Offspring, age 11.5 years	Cohort	Oulu and Lapland, Northern Finland 1985-86	PE 267, NT 6897	PE: BP ≥140/90mm Hg and proteinuria	Mild cognitive limitations	IQ between 50 and 85 based on standardised psychometric tests (eg. WISC-R)	PE v NT: No significant association OR and 95% CI: 1.2 (0.5, 2.8)
Tuovinen et al, ³³ 2013	Offspring, 70 years later	Cohort	Helsinki, Finland 1934-44	PE 31, NT 553	PE: proteinuria and SBP ≥140mm Hg or DBP ≥90mm	Self-reported cognitive impairment	CFQ and DEX	PE associated with significantly more

					Hg			complaints of cognitive functioning (MD for total score 0.45 (0.02, 0.87) and more complaints of dysexecutive functioning, but not significant 0.31 (-0.11, 0.73)
Love et al, ³⁴ 2012	All children born to mothers in Aberdeen city between 1995-2008	Cohort	Aberdeen, Scotland 1995-2008	PE 1774, NT 23334	PE: Davey and MacGillivray's classification of HDP	Congenital abnormality, cerebral palsy, autism, ADHD, developmental delay, communication difficulties/learning difficulties and other	Record in SNS	NT v PE: No significant association OR and 95% CI: 0.80 (0.60, 1.07)
Whitehouse et al, ³⁵ 2012	Offspring, age 10 years	Cohort	Western Australia 1989-91	PE 34, NT 1076	PE: gestational HT with proteinuria of $\geq 300\text{mg}/24\text{hr}$.	Neurocognitive development	PPVT-R and RCPM	PE not associated with lower PPVT-R scores (MD for total score -3.35 (-8.41, 1.35) or lower RCPM scores (MD for total score -1.82 (-12.59, 8.95))
Ehrenstein et al, ³⁶ 2009	Men born in 1978-83	Cohort	Northern Denmark 1978-83	PE 604, NT 16566	PE: BP >140/90mm Hg in second half of	Adult cognitive function	BPP group intelligence test	PE v NT: PE associated with increased odds of low

					pregnancy and de novo proteinuria (>0.3g over 24hrs) or edema			cognitive function PR and 95% CI: 1.32 (1.08, 1.62)
Eaton et al, ¹⁷ 2001	Offspring, age <15 years	Case-control	Denmark 1973-93	Learning disorders 580, reference population 102905	Eclampsia from Medical Birth Register	Learning disorders	ICD8	Eclampsia v NT: No significant association RR: 0.9
Seidman et al, ³⁷ 1991	Offspring, age 17 years	Cohort	Jerusalem, Israel 1964-71	PE 428, No PE 33117	PE: After 24 weeks gestation, SBP ≥140mm Hg or DBP ≥90mm Hg or rise in BP of ≥30/15mm Hg (two readings ≥6hrs apart) or proteinuria or oedema of the face and arms or any combination of 2 or more	Intelligence score	Verbal Otis test and nonverbal matrices test transformed into values that correlate with the WAIS	No difference in mean IQ test scores between PE and non PE: mean 109.3 (1.2) v 110.9 (0.1)
Barker and Edwards, ³⁸ 1967	Offspring, age 11 years	Cohort	Birmingham, UK 1950-54	Toxemia 3321, No toxemia 42329	Toxemia: HT or albuminuria during pregnancy	Verbal reasoning	Eleven-plus	Toxemia associated with lower verbal reasoning within sibpairs (MD in unaffected sibs in subsequent birth -0.7 and pre-eding

Pre-eclampsia (specific population)								birth -2.2)
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Johnson et al, ³⁹ 2015	Late and moderately pre-term infants	Cohort	East Midlands, United Kingdom 2009-10	638 completed questionnaire at follow-up	PE: self-reported	Cognitive development at age 2	PARCA-R	PE associated with increased risk of cognitive impairment. RR and 95% CI: 2.51 (1.33, 4.70)
Morsing and Maršál, ⁴⁰ 2014	IUGR and very pre-term birth	Cohort	Lund University Hospital, Sweden 1998-2004	PE 11, No PE 23	PE: >90mm Hg on 2 or more occasions and proteinuria >300mg/L	Cognitive impairment	Wechsler scales	IUGR infants exposed to PE had significantly lower full-scale IQ compared to IUGR infants unexposed to PE: PE: 70.1 (±19) Non PE: 83.3 (±14)
Leitner et al, ⁴¹ 2012	IUGR infants	Cohort	Lis Maternity Hospital, Israel 1992-2002	PE 17, NT 78	PE: SBP ≥140mm Hg or DBP ≥90mm Hg developing after 20 weeks gestation with proteinuria >0.3g in 24/hr urine sample or +2 in dipstick urine test, without	IQ and academic achievement	WISC-R95 two-test short form and Kauffman Assessment Battery for Children	No significant differences observed between the groups

					history of previous HT			
Leveresen et al, ⁴² 2011	Children born extremely pre-term (22-27 weeks gestation)	Cohort	Norway 1999-2000	PE 73, No PE 233	PE: Medical Birth Registry of Norway	Cognitive function at age 5	Wechsler Preschool and Primary Scale of Intelligence-Revised	PE associated with lower full-scale IQ MD -7.7 (-12.7, -2.7)
Schlapbach et al, ⁴³ 2010	Pre-term infants <32 weeks gestation	Cohort	University Hospital Zurich, Switzerland 2002-05	PE 33, No PE 33	PE: proteinuria >300mg/d and DBP >90mm Hg in two measurements ≥4 hrs apart after 20th week gestation and regressing after delivery and/or acute spiral artery atherosclerosis on placental histology or placental bed biopsy	Adverse neurodevelopmental outcome	Bayley Scales of Infant Development II: MDI<70 and/or PDI<70	No association: PE v No PE: OR and 95% CI: 1.36 (0.46, 4.04)
Spinillo et al, ⁴⁴ 2009	Pre-term infants (24-33 weeks gestation)	Cohort	Pavia, Italy 1990-2004	PE 185, No PE 569	PE: DBP ≥110mm Hg or ≥90mm Hg in two consecutive measures at any time during pregnancy and proteinuria ≥300mg/day	MDI	Bayley Scales of Infant Development II	PE associated with reduced risk of impairment. OR and 95% CI: 0.52 (0.32, 0.85)
Silveira et al, ⁴⁵ 2007	VLBW infants	Cohort	Hospital de Clínicas de	PE 40, No PE 46	PE: SBP ≥140mm Hg	MDI at 12 and 18 months	Bayley Scales of Infant	Mean MDI scores not

			Porto Alegre, Brazil 2003-05		and/or DBP ≥ 90 mm Hg developing after 20 weeks gestation with proteinuria >300 mg in 24/hr urine sample, without history of previous HT or renal disease		Development II	significantly different. At 12 months: PE: 79.6 (± 0.44) No PE: 79 (± 0.47) At 18 months: PE: 82.9 (± 0.45) No PE: 81.1 (± 0.7)
Cheng et al, ⁴⁶ 2004	VLBW infants <32 weeks gestation	Cohort	Taiwan 1997-99	PE 28, No PE 61	PE: DBP of 110mm Hg once or DBP of ≥ 90 mm Hg twice and proteinuria of ≥ 300 mg in 24/hr	MDI	Bayley Scales of Infant Development II	Median MDI score significantly lower for PE compared to non-PE: PE: 72 (49-116) Non-PE: 86 (49-114) $p=0.04$
Many et al, ⁴⁷ 2003	Children born growth restricted	Cohort	Lis Maternity Hospital, Israel 1992-93	PE 11, No PE 64	PE: persistent BP $\geq 140/90$ mm Hg with proteinuria of 100mg/dL by random urine analysis or >500 mg in 24hr urine collection	Cognitive assessment	Stanford Binnet-IQ	Growth restricted infants exposed to PE had significantly lower IQ scores compared to unexposed growth restricted: PE: 85.5 (± 16) Non PE: 96.9 (± 18)

Szymonowicz et al, ⁴⁸ 1987	VLBW infants	Cohort	Australia 1982-84	PE 35, No PE 35	Severe PE: >140/90mm Hg, persistent proteinuria with UTI and generalised oedema <32 weeks gestation	MDI	Bayley Scales of Infant Development II	PE associated with significantly lower mean MDI PE: 94 No PE: 106
Other HDP								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Heikura et al, ³² 2013	Offspring, age 11.5 years	Cohort	Oulu and Lapland, Northern Finland 1985-86	GH 443, Chronic HT or superimposed PE 564, NT 6897	GH: BP ≥140/90mm Hg Chronic HT or superimposed PE: already using anti-HT medication at the beginning of pregnancy or having blood pressure ≥140/90 mmHg before week 20 classified as having chronic hypertension. With a positive urinary dipstick test (≥0.3 g/L) indicated proteinuria	Mild cognitive limitations	IQ between 50 and 85 based on standardised psychometric tests (eg. WISC-R)	GH v NT: GH associated with increased odds of mild cognitive limitations OR and 95% CI: 2.4 (1.4, 3.9). Chronic HT v NT: No significant association OR and 95% CI: 1.4 (0.8, 2.5)
Tuovinen et al, ³³ 2013	Offspring, 70 years later	Cohort	Helsinki, Finland 1934-44	HT 292, NT 553	Gestational and chronic HT: SBP ≥140mm Hg or DBP ≥90mm	Self-reported cognitive impairment	CFQ and DEX	HT associated with more complaints of cognitive functioning

					Hg at <20 weeks gestation, without proteinuria			(MD for total score 0.12 (-0.04, 0.27) and more complaints of dysexecutive functioning, 0.07 (-0.08, 0.22), but neither result significant
Krakowiak et al, ⁸ 2012	Offspring, age 2-5 years	Case-control	California 2003-10	Developmental delay 64, typical development 172	HT (with or without PE) self-reported or medical records	Developmental delay	Vineland Adaptive Behaviour Scales, Mullen Scales of Early Learning, Social Communication Questionnaire	HT v NT: No significant association OR and 95% CI: 3.58 (0.93, 13.78)
Love et al, ³⁴ 2012	All children born to mothers in Aberdeen city between 1995-2008	Cohort	Aberdeen, Scotland 1995-2008	GH 4092, NT 23334	GH: Davey and MacGillivray's classification of HDP	Congenital abnormality, cerebral palsy, autism, ADHD, developmental delay, communication difficulties/learning difficulties and other	Record in SNS	NT v GH: No significant association OR and 95% CI: 1.16 (0.99, 1.36)
Tuovinen et al, ⁴⁹ 2012	Men (military service), age 20 years	Cohort	Helsinki, Finland 1934-44	HT 449, NT 747	HDP: BP ≥140/90mm Hg at any time during pregnancy	Intellectual abilities at military service	Finnish Defence Forces Basic Ability Test	MD and 95% CI in total intellectual abilities score: -0.12 (-0.24, -0.00)
Tuovinen et al, ⁵⁰ 2012	Men (military service),	Cohort	Helsinki, Finland 1934-44	HT 146, NT 252	HDP: BP ≥140/90mm Hg at any time	Intellectual abilities at military service	Finnish Defence Forces Basic	Men born to HT mothers scored lower

	age 20 and 69 years				during pregnancy		Ability Test	on tests: MD and 95% CI in total intellectual abilities score at age 69: -4.36 (-7.55, -1.17) and in decline in total cognitive ability -2.88 (-5.06, -0.70)
Whitehouse et al, ³⁵ 2012	Offspring, age 10 years	Cohort	Western Australia 1989-91	PE 279, NT 1076	Gestational HT: SBP ≥140mm Hg or DBP ≥90mm Hg in women normotensive at <24 weeks gestation	Neurocognitive development	PPVT-R and RCPM	HT associated with lower PPVT-R scores (MD for total score -1.71 (-3.39, -0.03) but not associated with lower RCPM scores (MD for total score 0.15 (-3.60, 3.90)
Ehrenstein et al, ³⁶ 2009	Men born in 1978-83	Cohort	Northern Denmark 1978-83	GH 287, NT 16566	GH: BP >140/90mm Hg in second half of pregnancy	Adult cognitive function	BPP group intelligence test	GH v NT: GH associated with increased odds of low cognitive function PR and 95% CI: 1.34 (1.01, 1.77)
Lawlor et al, ⁵¹ 2005	Offspring, age 7, 9 and	Cohort	Aberdeen, Scotland	PIH 1977, No PIH 9702	PIH: PE or GH from Aberdeen	Childhood intelligence	Age 7: Moray House Picture	PIH v No PIH: MD in IQ

	11 years		1950-56		Maternal and Neonatal Database		Intelligence 1&2. Age 9: Schonell and Adams Essential Intelligence form A&B. Age 11: battery of Moray House Tests (2 verbal reasoning, arithmetic and English)	points and 95% CI: 2.35 (1.56, 3.14) Results attenuated towards the null when adjusted for parental characteristics
Other HDP (specific population)								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Leitner et al, ⁴¹ 2012	IUGR infants	Cohort	Lis Maternity Hospital, Israel 1992-2002	GH 25, NT 78	GH: SBP ≥140mm Hg or DBP ≥90mm Hg developing after 20 weeks gestation without history of previous HT	IQ and academic achievement	WISC-R95 two-test short form and Kauffman Assessment Battery for Children	No significant differences observed between the groups
Many 2005	Children born with severe growth restriction	Cohort	Israel Date: NR	HDP 22, No HDP 70	HDP: NR	IQ at age 6	Wechsler Preschool and Primary Scale of Intelligence	No significant difference in mean IQ HDP: 106 (±11) No HDP: 101 (±14)
McCowan et al, ⁵² 2002	SGA children (birthweight)	Cohort	New Zealand 1993-97	HDP 88, No HDP 132	HDP: BP ≥140/90mm Hg with an	MDI	Bayley Scales of Infant Development II	HDP associated with higher

	<10th centile)				increase of ≥ 15 mm Hg in DBP on 2 occasions >4hrs apart after 20 weeks gestation and/or proteinuria of >300mg/24hr and/or at least +2 proteinuria on repeated testing with urine dipsticks, without UTI			MDI scores. Mean MDI: HDP: 98.6 No HDP: 93.7
Gray et al, ⁵³ 1998	Very pre-term infants (24-32 weeks gestation)	Cohort	Mater Mother's Hospital, Brisbane, Australia 1992-93	Maternal HT 107, No maternal HT 107	Maternal HT: Australasian Society for the Study of Hypertension in Pregnancy	Developmental delay	Griffith's Infant Ability Scale	Maternal HT not associated with developmental delay OR and 95% CI: 1.33 (0.61, 2.99)
Spinillo et al, ⁵⁴ 1994	Pre-term infants (24-35 weeks gestation)	Cohort	Italy 1986-90	HDP 92, No HDP 184	HDP: Davey and MacGillivray	Minor neurodevelopmental impairment	Bayley Scale of Infant Development	HDP associated with increased risk of minor impairment OR and 95% CI: 3.1 (1.41, 6.88)
Winer et al, ⁵⁵ 1982	SGA infants (<10th centile)	Cohort	USA 1973-76	HDP 20, No HDP 35	HDP: American College of Obstetricians	Verbal IQ, performance IQ and full-scale IQ	Wechsler Preschool and Primary Scales of Intelligence	HDP associated with higher verbal IQ

					and Gynaecologists		or WISC-R and Raven's Coloured Progressive Matrices	score Mean and SD: HDP: 105.75 (13.50) No HDP: 93.68 (12.84) No significant differences observed for performance or full-scale IQ
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Summary of HDP and other behavioral outcome studies

Pre-eclampsia

Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Robinson et al, ⁵⁶ 2009	Offspring at age 2, 5, 8, 10 and 14 years	Cohort	Western Australia 1989-91	PE: 80 NT: 2119	PE: BP ≥140/90mm Hg after 24 weeks gestation and proteinuria (≥0.3g/24hr)	Behavioural problems in childhood and adolescence	CBCL	No significant association between PE and overall behavioural problems. Protective relationship observed between PE and internalising behaviour problems at age 5 and 8. OR and 95% CI: 0.22 (0.05,

								0.97) 0.33 (0.11, 0.98)
Wu et al, ⁵⁷ 2009	All singletons born in Denmark between 1978 and 2004	Cohort	Denmark 1978-2004	PE 46384, No PE 1499059	PE: ICD8 and ICD10	Disease specific hospitalisations	Hospitalisation as a result of mental and behavioural disorders	PE not associated with increased risk of hospitalisation IRR and 95% CI: 1.1 (1.0, 1.2)
Glasson et al, ¹⁵ 2004	Western Australia, born between 1980 and 1995	Case-control	Western Australia 1980-95	PDD-NOS 84, controls 1313, siblings of cases 481	PE: ICD9	PDD-NOS	DSM	No association between PE and PDD-NOS: OR and 95% CI: 1.2 (0.5, 2.6)
Glasson et al, ¹⁵ 2004	Western Australia, born between 1980 and 1995	Case-control	Western Australia 1980-95	Asperger's 67, controls 1313, siblings of cases 481	PE: ICD9	Asperger's	DSM	No association between PE and Asperger's: OR and 95% CI: 1.3 (0.6, 3.0)
Eaton et al, ¹⁷ 2001	Offspring, age <15 years	Case-control	Denmark 1973-93	Asperger's Syndrome 279, reference population 102905	Eclampsia from Medical Birth Register	Asperger's Syndrome	ICD	Eclampsia v NT: No significant association RR: 1.06
Other HDP								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Böhm et al, ²¹ 2017	Millennium Cohort, age 7	Cohort	United Kingdom 2001-08	HDP 1069, No HDP 12431	HDP: self-reported (includes	Behavioural difficulties	SDQ	No association between HDP and abnormal

					raised BP, eclampsia, PE or toxemia).			SDQ: OR and 95% CI: 0.94 (0.69, 1.29)
Polo-Kantola et al, ³ 2014	Singleton births in Finland between 1990-2005	Case-control	Finland 1990-2005	PDD 1602, Controls 6371	Maternal HT: (includes PE and pregnancy induced HT) $\geq 140/90$ mm Hg	PDD	ICD9 and ICD10	No association when results adjusted for SGA, other birth factors or neonatal treatment
Polo-Kantola et al, ³ 2014	Singleton births in Finland between 1990-2005	Case-control	Finland 1990-2005	Asperger's syndrome 1466 Controls 5839	Maternal HT: (includes PE and pregnancy induced HT) $\geq 140/90$ mm Hg	Asperger's syndrome	ICD9 and ICD10	No association OR and 95% CI: 1.03 (0.8, 1.4)
Robinson et al, ⁵⁶ 2009	Offspring at age 2, 5, 8, 10 and 14 years	Cohort	Western Australia 1989-91	GH: 605 NT: 2119	GH: BP $\geq 140/90$ mm Hg after 24 weeks gestation	Behavioural problems in childhood and adolescence	CBCL	GH associated with increased risk of overall behavioural problems at age 8 and 14. OR and 95% CI: 1.40 (1.03, 1.91) 2.07 (1.35, 3.17) Also associated with increased risk of externalising behavioural problems at age 10 OR and 95%

								CI: 1.63 (1.13, 2.33)
Summary of HDP and intellectual disability studies								
Pre-eclampsia								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Griffith et al, ⁵⁸ 2011	Live births in South Carolina between 1996-2002	Cohort	South Carolina 1996-2002	PE 5169, No PE 75697	PE or eclampsia: ICD9	Intellectual disability	Whether a child received special education or ID-related services from DDSN	PE associated with an increased risk of ID OR and 95% CI: 1.38 (1.16, 1.64)
Eaton, et al, ¹⁷ 2001	Offspring, age <15 years	Case-control	Denmark 1973-93	Mental retardation 201, reference population 102905	Eclampsia from Medical Birth Register	Mental retardation	ICD	Eclampsia associated with statistically significant increased risk of mental retardation RR: 3.03
Other HDP								
Study	Population	Study design	Region, study period	Sample size	Diagnosis of HDP	Outcome measure	Assessment method	Main findings
Langridge et al, ⁴ 2013	All singleton births in Western Australia	Cohort	Western Australia 1984-99	Mild-moderate ID 4339, severe ID 237, unaffected children 376529	Pregnancy HT: PE and essential HT from MNS	Mild-moderate ID and severe ID	American Association on Mental Retardation classification system	Pregnancy HT associated with increased risk of mild-moderate ID: OR and 95% CI: 1.39 (1.25, 1.54) but not severe ID: 1.01 (0.64,

								1.59)
Leonard et al, ⁵⁹ 2006	Children born in Western Australia between 1983-92	Cohort	Western Australia 1983-92	HT 1379, No HT 238450	HT: ICD9	Intellectual disability	Mild-moderate ID: IQ 35 to 40 to 69 Severe ID: IQ<35 or 40 based on DSM-IV	No significant association. Mild-moderate ID: OR and 95% CI: 0.99 (0.58, 1.68) Severe ID: OR and 95% CI: 2.48 (0.79, 7.77)
Salonen, et al ⁶⁰ 1984	Children age 9-10 years living in one Finnish county (Kuopio)	Case-control	Eastern Finland 1979 and 1981	Mental retardation 136, Controls 122	HT during pregnancy: confirmed by a physician	Mental retardation	Screened using a standardised set of tests for mental performance	HT during pregnancy associated with increased risk of mental retardation RR and 95% CI: 6.1 (1.3, 28.9)

HDP=hypertensive disorder of pregnancy. PE=pre-eclampsia. BP=blood pressure. NT=normotensive. CFQ=Cognitive Failures Questionnaire. DEX=Dysexecutive Questionnaire. MD=mean difference. SNS=Support Needs System. PPVT-R=Peabody Picture Vocabulary Test-Revised. RCPM=Ravens Colored Progressive Matrices. BPP=Boerge Prien Prove. ICD=International Classification of Disease. WAIS=Wechsler Adult Intelligence Scale. HT=hypertension. PARCA-R=Parent Report of Children's Abilities-Revised. IUGR=Intrauterine growth restricted. WISC-R=Wechsler Intelligence Scale for Children-Revised. DBP=diastolic blood pressure. MDI=Mental Developmental Index. PDI=Psychomotor Developmental Index. VLBW=Very low birthweight. GH=gestational hypertension. NT=normotensive. SBP=systolic blood pressure. PIH=pregnancy-induced hypertension. NR=not recorded. SGA=small for gestational age. UTI=urinary tract infection. CBCL=Child Behaviour Checklists. PDD-NOS=Pervasive Developmental Disorder-Not Otherwise Specified. DSM=Diagnostic and Statistical Manual of Mental Disorders. SDQ= Strengths and Difficulties Questionnaire. ID=intellectual disability. DDSN=Department of Disabilities and Special Needs. MNS=Midwives' Notification System.

eTable 5. Level of Bias in ASD Studies							
Study	Selection bias	Exposure bias	Outcome bias	Confounding	Analytic bias	Attrition bias	Overall risk of bias
Curran et al, ¹ 2017	Minimal: Sample selected from general population rather than a select group (Sample is representative of children born in the UK in 2000-01)	Low: Recall < 1 year after birth	Minimal: Direct question to mother about outcome (doctor diagnosed maternal reporting)	Low: Certain confounders assessed - smoking during pregnancy, birth order, poverty, maternal ethnicity, age, education, depression, BMI, longstanding diabetes, longstanding HT	Low: Sample size calculation not performed, but all available eligible patients studied	Moderate: >20% attrition	Low
Walker et al, ² 2015	Low: Sample from select group of population - only births in California who lived in catchment areas	Minimal: Direct questioning supplemented with medical records	Minimal: Previous ASD diagnoses were examined with validated measures	Low: Certain confounders assessed - maternal educational level, parity, pre-pregnancy obesity, age, sex, broad geographic regions within the study catchment areas	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Minimal: Little to no attrition	Low
Polo-Kantola et al, ³ 2014	Minimal: Sample selected from general population rather than a select group	Low: Assessment of exposure from a dataset	Low: Assessment from administrative database	Low: Certain confounders assessed - maternal age, maternal smoking during pregnancy, number of previous births, maternal psychiatric history, sex, date of birth, place of birth	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Langridge et al, ⁴ 2013	Minimal: Consecutive unselected population	Low: Assessment of exposure from a dataset - Midwives' Notification System	Low: Assessment from administrative database	Low: Certain confounders assessed - birth year, maternal and pregnancy conditions (maternal diabetes, threatened abortion, asthma, UTI during pregnancy, placenta praevia, placenta abruption, other	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for (Registry data)	Low

				antepartum haemorrhage), socio-demographics (parity, maternal and paternal age group, maternal ethnicity, community-level socioeconomic status and community accessibility/remoteness), labour and delivery factors (preterm type, mode of delivery, breech, any complication of labour or delivery), neonatal outcomes (infant gender, resuscitation required at birth, percentage of optimal birthweight and head circumference)			
Mrozek-Budzyn et al, ⁵ 2013	Low: Sample from select group of population - cases from the one psychiatric outpatient clinic for children in the area. Controls identified through outpatient clinic records	Moderate: Medical records and/or interview with trained nurse 2-15 years after birth	Minimal: Cases identified using medical records from a psychiatric outpatient clinic for children	Moderate: Not assessed for confounders (but matched by year of birth, sex and general practitioners)	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Moderate
Nath et al, ⁶ 2012	Moderate: Sample selection ambiguous but sample may be representative	Moderate: Recall 1-5 years after birth	Minimal: DSM IV-TR	Moderate: Not assessed for confounders (but matched age)	Moderate: Sample size estimation unclear	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Moderate

Lyall et al, ⁷ 2012	Low: A select group of population - nurses only, high education status	Low: Indirect assessment - mailed questionnaire	Moderate: Assessment from "close-ended" questions	Low: Certain confounders assessed - race, marital status, income, spouse education, nurse's age at baseline, age at first birth, parity	Low: Sample size calculation not performed, but all available eligible patients studied	Moderate: >20% attrition	Moderate
Krakowiak et al, ⁸ 2012	Low: A select group of population - born in California, residing in specific catchment area	Minimal: Direct questioning supplemented with medical records	Minimal: Cases confirmed by trained clinician	Low: Certain confounders assessed - mother's age at delivery, race/ethnicity, education level, delivery payer, calendar time, age, gender, and regional centre catchment area	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: Little to no attrition	Low
Dodds et al, ⁹ 2011	Minimal: Consecutive unselected population - all live births	Low: Assessment of exposure from a dataset - Perinatal Database	Low: Assessment from administrative database	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Burstyn et al, ¹⁰ 2010	Minimal: Sample selected from general population rather than a select group	Low: Assessment of exposure from a dataset - delivery records held by Alberta Perinatal Health Programme	Low: Assessment from administrative database - ICD-9 codes linked to billing records	Low: Certain confounders assessed - maternal age, maternal weight, maternal height, pre-pregnancy diabetes, gestational diabetes, bleeding, smoking, poor weight gain, parity, mother's SES, presentation (breech etc.), type of labour, caesarean section, gestational age, birthweight, APGAR at 1 min and 5 mins, infant	Low: Sample size calculation not performed, but all available eligible patients studied	Moderate: >20% attrition	Low

				sex, birth year.			
Mann et al, ¹¹ 2010	Low: A select group of population - Medicaid Social Healthcare Programme	Low: Assessment of exposure from a dataset	Low: Assessment from administrative database	Low: Certain confounders assessed - maternal age, race, alcohol use, educational attainment, year of birth, child's sex, and diagnosis with a high risk condition (alcohol use, tobacco use, down syndrome, fragile X syndrome, brain anomaly) and birthweight	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Bilder et al, ¹² 2009	Low: A select group of population - 8 year olds, vast majority white	Low: Birth certificate data	Low: Assessment from administrative database	Moderate: Not assessed for confounders for prenatal factors (but matched by gender and birth year)	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Buchmayer er et al, ¹³ 2009	Low: A select group of population - overrepresentation of severe cases as inpatient care data available only	Low: Assessment of exposure from a dataset - Medical Birth Register	Low: Assessment from administrative database - Hospital Discharge Register	Low: Certain confounders assessed - parity, previous miscarriage, childless years, any maternal infection during pregnancy, season of delivery, diabetes mellitus, maternal age, smoking, maternal country of birth, whether the mother lived with the father, maternal schizophrenia, age, gender, birth year, and birth hospital	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Larsson et al, ¹⁴ 2005	Minimal: Rational for case and control selection explained	Low: Assessment of exposure from	Low: Assessment from	Moderate: Not assessed for confounders (but matched by gender, birth	Minimal: Analyses appropriate for	Minimal: All subjects from initiation of	Low

		a dataset - Danish Medical Birth Register	administrative database - Danish Psychiatric Register	year and age)	type of sample - conditional logistic regression	study to final outcome assessment were accounted for	
Glasson et al, ¹⁵ 2004	Minimal: Sample selected from general population rather than a select group	Low: Assessment of exposure from a dataset - Maternal and Child Health Research Database	Low: Assessment from administrative database - Diagnosis and Service Delivery Records	Moderate: Not assessed for confounders (but matched by sex)	Minimal: Sample size calculation performed and adequate sample studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Hultman et al, ¹⁶ 2002	Low: A select group of population - overrepresentation of severe cases as inpatient care data available only	Low: Assessment of exposure from a dataset - Swedish Medical Birth Register	Low: Assessment from administrative database - Swedish Inpatient Register	Low: Certain confounders assessed - maternal age, parity, smoking during pregnancy, mother's country of birth, diabetes, pregnancy bleeding, mode of delivery, season of birth, gestational age, birthweight for gestational age, Apgar score at 5 minutes, congenital malformations, sex, year, and hospital of birth	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Eaton et al, ¹⁷ 2001	Low: A select group of population - cases were hospitalised (more severe)	Low: Assessment of exposure from a dataset - Medical Birth Register	Low: Assessment from administrative database - Danish Psychiatric Register	Low: Certain confounders assessed - gender and year of birth	Low: Sample size calculation not performed, but all available eligible patients studied (Does not provide 95% CI)	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low

Matsuishi et al, ¹⁸ 1999	Low: A select group of population - NICU survivors in a Japanese hospital	Minimal: Medical records	Minimal: Diagnosis confirmed by two paediatric neurologists who used DSM-III-R	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Low: <10% attrition	Low
Mason-Brothers et al, ¹⁹ 1990	Low: Epidemiological Survey of Utah	Minimal: Medical records	Minimal: Diagnosed by at least 2 clinicians using DSM-III	Moderate: Not assessed for confounders (but matched by sibling)	Moderate: Sample size estimation unclear	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Moderate
Deykin et al, ²⁰ 1980	Low: A select group of population - Massachusetts, referred by 19 medical and educational facilities	Minimal: Medical records	High: Assessment from non-validated sources - parent-reported symptoms by age 6	Low: Certain confounders assessed - birth order, sibling	Moderate: Sample size estimation unclear	Low: Medical records located for 81% cases and 75% controls	Moderate

eTable 6. Level of Bias in ADHD Studies							
Study	Selection bias	Exposure bias	Outcome bias	Confounding	Analytic bias	Attrition bias	Overall risk of bias
Böhm et al, ²¹ 2017	Minimal: Sample selected from general population rather than a select group (when weighted, sample is representative of children born in the UK in 2000-01)	Low: Recall < 1 year after birth	Minimal: Direct question to mother about outcome (doctor diagnosed maternal reporting)	Low: Certain confounders assessed - alcohol during pregnancy, maternal education, maternal depression, maternal age, poverty status	Minimal: Analyses appropriate for type of sample - multivariate analysis	Moderate: >20% attrition	Low
Silva et al, ²² 2014	Minimal: Consecutive unselected population	Low: Assessment of exposure from a dataset - Midwives Notification System	Low: Assessment from administrative database - subjects dispensed stimulant medication from Monitoring of Drugs of Dependence System	Low: Certain confounders assessed - year of birth, gender, and socioeconomic status, marital status, parity, smoking, complications of pregnancy, onset of labor, augmentation of labor, complications of labor, type of delivery, child characteristics (gestational age, birthweight, average/small/large for gestational age) maternal age, Apgar at five	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low

				minutes			
Cak and Gokler, ²³ 2013	Low: Sample from select group of population (30-36 weeks gestation in one hospital)	Minimal: Medical records	Minimal: Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version semi-structured interview	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Moderate: >20% attrition but reasons for loss of follow up explained	Moderate
Getahun et al, ²⁴ 2013	Minimal: Rational for case and control selection explained	Low: Assessment of exposure from a dataset - Perinatal Service System and inpatient/outpatient records	Minimal: Clinically diagnosed (1CD9) on at least 2 separate visits or 1 visit and 2 refills of ADHD medication	Low: Certain confounders assessed - age at diagnosis, maternal age, education, smoking during pregnancy, parity, prenatal care, household income, psychosocial disorder during pregnancy, child race/ethnicity, and gender	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Golmirzaei et al, ²⁵ 2013	Low: A select group of population - sample of 4-11 year old school children, Southern Iran	High: Recall >5 years after birth	Minimal: Conner's Scales (those positive for ADHD were interviewed by psychiatrist using DSM-IV criteria)	Moderate: Not assessed for confounders (but matched by age)	Moderate: Sample size estimation unclear	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	High
Amiri et al, ²⁶ 2012	Moderate: Sample selection ambiguous but	Moderate: Recall >5 years after birth but supplemented with medical	Minimal: Direct question to parent about outcome using	Moderate: Not assessed for confounders (but matched by	Moderate: Sample size estimation unclear	Minimal: All subjects from initiation of study to final outcome	Moderate

	sample may be representative	documents where possible	ADHD Rating Scale - Parent Version	age)		assessment were accounted for	
Halmoy et al, ²⁷ 2012	Minimal: Sample selected from general population rather than a select group	Low: Assessment of exposure from a dataset - Medical Birth Registry of Norway	Low: Assessment from administrative database - Adult patients who were approved for stimulant treatment in Norway during 1997-2005	Low: Certain confounders assessed - born in the same time period, year of birth, parity, age of mother at birth, educational level of mother and marital status of mother	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Ketzer et al, ²⁸ 2012	Minimal: Rational for case and control selection explained	Moderate: Recall >5 years after birth (however supplemented with medical records in 38% of sample)	Minimal: Three stage process at outpatient clinic	Low: Certain confounders assessed - age, gender, agoraphobia (anxiety disorder), maternal ADHD and cigarettes/day during pregnancy	Minimal: Analyses appropriate for type of sample - conditional logistic regression	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Gustafsson and Källén, ²⁹ 2011	Minimal: Sample selected from general population rather than a select group	Low: Assessment of exposure from a dataset - Swedish Medical Birth Register	Low: Assessment from administrative database - Department of Child and Adolescent Psychiatry	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Mann and McDermott, ³⁰ 2011	Low: A select group of population - Medicaid eligible women	Low: Assessment of exposure from a dataset - Medicaid billing data	Low: Assessment from administrative database - Medicaid billing	Low: Certain confounders assessed - GU infection, infant race, maternal age and education,	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted	Low

			data	alcohol and tobacco use, infant sex, birthweight, and oldest age in Medicaid		for	
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eTable 7. Level of Bias in Other Neurodevelopmental Outcome Studies

Study	Selection bias	Exposure bias	Outcome bias	Confounding	Analytic bias	Attrition bias	Overall risk of bias
Warshafsky et al, ³¹ 2016	Low: Sample from select group of population, based on residence	Minimal: Direct measurement of exposure from chart	Low: Indirect assessment (mailed questionnaire)	Low: Certain confounders assessed - MgSO4 usage, smoking, SES, sex, parity, breastfeeding, gestational age, IUGR	Moderate: Sample size estimation unclear	High: >20% attrition	Moderate
Johnson et al, ³⁹ 2015	Low: Sample from four maternity centres, a midwife led unit and homebirths	Minimal: Exposure from maternity records	Low: Direct question to mother about outcome using Parent Report of Children's Abilities-Revised	Low: Certain confounders assessed - ethnic group, SES, sex, ethnic group, SES, sex, received breastmilk at discharge	Low: Sample size calculation not performed, but all available eligible patients studied	High: >20% attrition	Moderate
Morsing and Maršál, ⁴⁰ 2014	Low: A select group of population - (pre-term infants, Lund University Hospital)	Minimal: Exposure from clinical data	Minimal: Standardised test - Wechsler Scales IQ Test	Low: Matched for gestational age, gender and age at examination only	Moderate: Sample size estimation unclear	Minimal: Little to no attrition	Low
Heikura et al, ³² 2013	Low: All maternal healthcare centres in Oulu and Lapland, Northern Finland	Minimal: Structured questionnaire near time of exposure	Minimal: Psychometric tests collected from hospitals, institutions for children with intellectual disability, family counselling centres and school psychologists	Low: Certain confounders assessed - child's gender, family SES, maternal age, pre-pregnancy BMI, parity, birthweight	Low: Sample size calculation not performed, but all available eligible patients studied	Low: <10% attrition and reasons for loss of follow up not explained	Low
Tuovinen et al, ³³ 2013	Low: Sample from select group of population,	Minimal: Exposure from hospital records	Low: Self-reported Cognitive Failures	Low: Certain confounders assessed - sex, length of gestation, weight, head circumference at birth,	Moderate: Sample size estimation unclear	Moderate: >20% attrition but reasons for	Moderate

	based on residence (Maternity Hospital, Helsinki, Finland)		Questionnaire and Dysexecutive Questionnaire	father's occupation in childhood, parity, mother's age, BMI at delivery, age at completion of questionnaire		loss of follow up explained	
Leitner et al, ⁴¹ 2012	Low: A select group - (IUGR) born at one medical centre	Minimal: Direct questioning about exposure and medical records	Minimal: Assessed by paediatric neurologists and psychologists	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Low: All subjects from initiation of study to final outcome assessment were accounted for. (Not definite however as N only given for those with full data)	Low
Love et al, ³⁴ 2012	Low: A select group of population - Aberdeen Grampian	Low: Assessment of exposure from a dataset (Aberdeen Maternity and Neonatal Databank)	Low: Assessment from administrative database (Support Needs System)	Low: Certain confounders assessed -maternal SES, induced labour, placental abruption, gestational age, birthweight	Minimal: Sample size calculation performed and adequate sample studied	Minimal: Little to no attrition	Low
Tuovinen et al, ⁴⁹ 2012	Low: A select group of population - Maternity Hospital, Helsinki, Finland (Men only)	Minimal: Exposure from hospital records	Low: Administrative database - Finnish Defence Forces Basic Ability Test	Low: Certain confounders assessed - gestational age, weigh, head circumference at birth, year of birth, childhood SES, parity, mother's age and BMI at delivery, age and height at military service	Moderate: Sample size estimation unclear	Moderate: Only had data on 1196 out of 2786	Moderate
Tuovinen et al, ⁵⁰ 2012	Low: A select group of	Minimal: Exposure from	Low: Administrative	Low: Certain confounders assessed - length of	Moderate: Sample size	Moderate: Only had	Moderate

	population - Maternity Hospital, Helsinki, Finland (Men only)	hospital records	database - Finnish Defence Forces Basic Ability Test	gestation, weight and head circumference at birth, father's occupational status in childhood, parity, mother's age and BMI at delivery, age at testing, cognitive ability at 20 years, time interval between tests from 20-68 years, height at testing in late adulthood and blood pressure medication	estimation unclear	data on 398 out of 931	
Whitehouse et al, ³⁵ 2012	Low: A select group of population based on residence - Public antenatal clinic or surrounding private clinics in Perth, Western Australia. Sample may be over representative of lower SES group	Minimal: Exposure from the chart and confirmed by obstetricians and midwives	Minimal: Standardised tests - verbal ability and non-verbal reasoning ability	Low: Certain confounders assessed - maternal age at conception, maternal education at pregnancy, household income during pregnancy, maternal smoking and alcohol, maternal essential hypertension, maternal use of anti-hypertensive medication, spontaneous labour, parity, gestational age, birthweight, APGAR score, offspring sex, scores on McMaster Family Assessment device at 3 or 5 years of age	Moderate: Sample size estimation unclear or only sub-sample of eligible patients studied (Unclear what percentage of eligible participants included)	High: >20% attrition but reasons	Moderate
Griffith et al, ⁵⁸ 2011	Low: A select group of population based on residence and SES - South Carolina Medicaid data	Low: Assessment of exposure from a dataset - Medicaid billing files	Low: Assessment from administrative database - Dept. of Education and Dept. of Disabilities and Special Needs	Low: Certain confounders assessed - maternal age, white race, education, birth year, female sex, preterm status	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: Little to no attrition	Low
Leversen et al, ⁴²	Low: All	Low:	Minimal:	Low - Certain confounders	Low: Sample	Low: 11-20%	Low

2011	extremely preterm births in Norway	Assessment of exposure from a dataset - Medical Birth Registry of Norway and registration forms	Assessment by paediatrician at age 5	assessed - gestational age, gender, illness severity score, small for gestational age, chorioamnionitis, prenatal steroids, multiple births, caesarean section, use of postnatal steroids, persistent ductus arteriosus, necrotizing enterocolitis, oxygen requirement at 36 weeks gestational age, retinopathy of prematurity, pathology on cerebral ultrasound, and high maternal education	size calculation not performed, but all available eligible patients studied	attrition	
Schlapbach et al, ⁴³ 2010	Low: A select group of population - Zurich, preterm infants	Low: Assessment of exposure from a dataset - University Hospital Zurich neonatal database	Minimal: Performed routinely by paediatricians at age 2 years	Low: Certain confounders assessed - gestational age, birthweight, postnatal growth, mechanical ventilation, bronchopulmonary dysplasia	Low: Sample size calculation not performed, but all available eligible patients studied (small sample however: n=33 in each group)	Minimal: Little to no attrition	Low
Ehrenstein et al, ³⁶ 2009	Low: A select group of population - Danish men who presented for mandatory army fitness evaluation in the Fifth District	Low: Assessment of exposure from a dataset - Danish National Registry of Patients	Minimal: Direct assessment using Boerge Prien Group Intelligence Test, converted to IQ scale	Low: Certain confounders assessed - small for gestational age, maternal age, parity, marital status, history of diabetes, conscript's year of birth, county of birth, birthweight, large for gestational age	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: Little to no attrition	Low
Robinson et al, ⁵⁶ 2009	Low: A select group of population - Public antenatal clinic or	Minimal: Exposure from the chart by obstetricians and midwives in	Low: Parent Reported Child Behaviour Checklist	Low: Certain confounders assessed - gestational age, birthweight, maternal smoking in pregnancy, child sex, maternal	Low: Sample size calculation not performed, but all available eligible patients	High: >20% attrition - teenage and young mothers,	Low

	surrounding private clinics in Perth, Western Australia.	research team		experience of stressful events during pregnancy, maternal age at conception, maternal education in pregnancy, family income in pregnancy, presence of biological father during pregnancy, family functioning score	studied	those who did not live with child's father at birth, those who experienced high stress, those whose children had lower gestational age were less likely to remain in study	
Spinillo et al, ⁴⁴ 2009	Low: A select group of population - preterm infants, single centre, Pavia, Italy	Minimal: Exposure from hospital records	Minimal: Bayley Scales of Infant Development by child neuropsychiatrist	Low: Certain confounders assessed - gestational age, proportion of expected birthweight, sex, umbilical artery, antenatal steroids	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Minimal: <10% attrition	Low
Wu et al, ⁵⁷ 2009	Minimal: Consecutive unselected population - all singleton born in Demar between 1978-2004	Low: Assessment of exposure from a dataset - Danish National Hospital Register	Low: Assessment of exposure from a dataset - Danish National Hospital Register	Low: Certain confounders assessed - infant sex, gestational age, parity, maternal age, maternal education, marriage status at birth, calendar year	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Silveira et al, ⁴⁵ 2007	Low: A select group of population - very low birthweight infants in Hospital de Clinicas de Porto	Minimal: Exposure from the chart	Minimal: Bayley Scales of Infant Development	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients studied	Moderate: >20% attrition but reasons for loss of follow up explained	Moderate

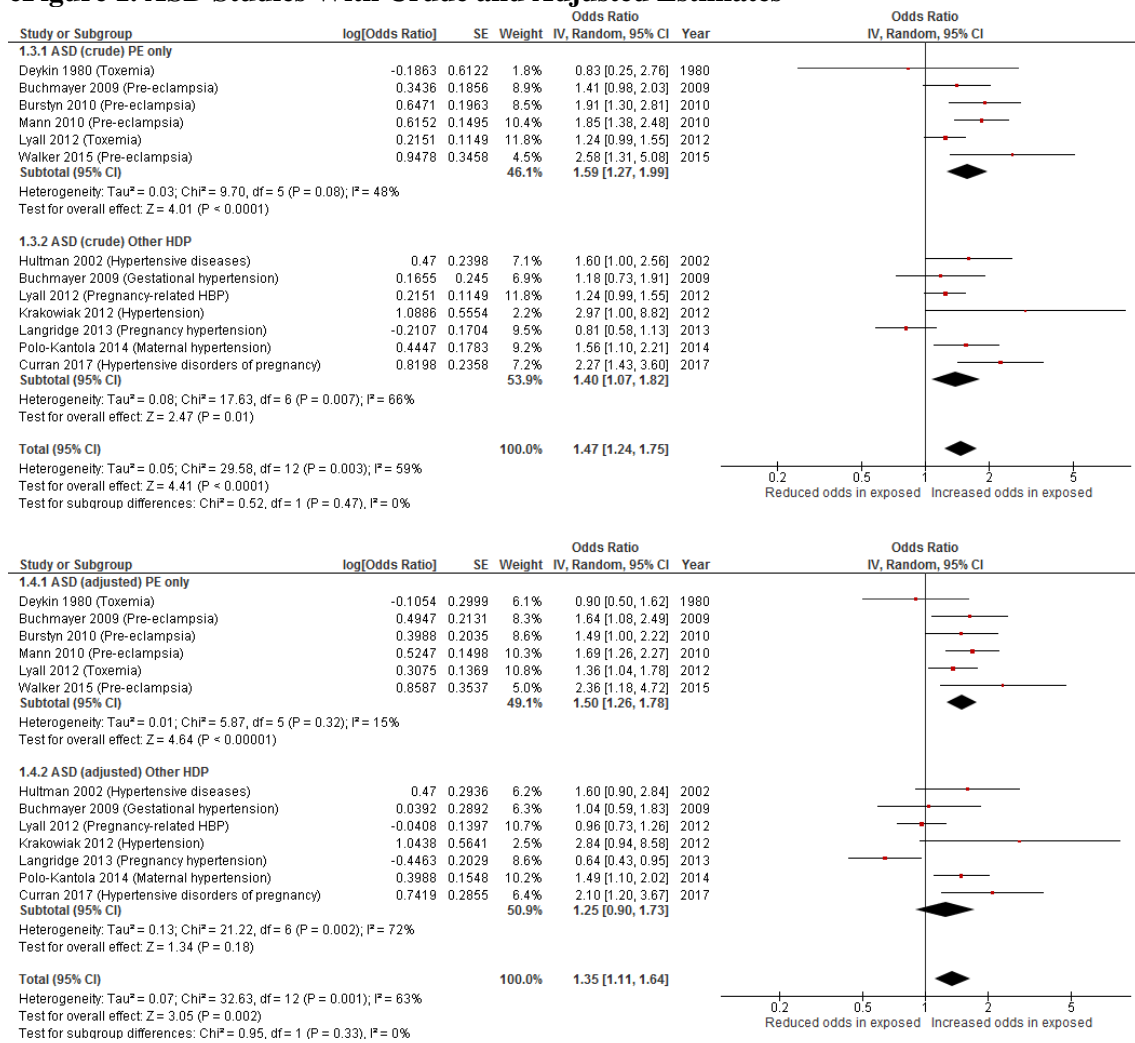
	Alegre, Brazil						
Leonard et al, ⁵⁹ 2006	Minimal: Consecutive unselected population - Western Australia	Low: Assessment of exposure from a dataset - birth registry	Low: Assessment of exposure from a dataset - Disability Services Commission and education sources	Low: Aggregate SES measures	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: All subjects from initiation of study to final outcome assessment were accounted for	Low
Many 2005	Low: A select group of population - severe growth restriction	Minimal: Direct questioning (interview)	Minimal: Wechsler Preschool and Primary Scale of Intelligence	Moderate: Not assessed for confounders	Moderate: Sample size estimation unclear	Moderate: 11-20% attrition but reasons for loss of follow up not explained	Moderate
Lawlor et al, ⁵¹ 2005	Low: A select group of population - primary school attenders in Aberdeen, Scotland	Low: Assessment of exposure from a dataset - Maternal and Neonatal Database	Low: Assessment from administrative database - Aberdeen Childhood Development Survey linked to routine intelligence tests in primary schools	Moderate: Not assessed for confounders (not for HDP estimates, but associations between all complications of pregnancy and IQ attenuated towards the null when adjusted for parental characteristics)	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: Little to no attrition	Low
Cheng et al, ⁴⁶ 2004	Low: A select group of population - very low birthweight, delivery before 32 weeks gestation	Minimal: Exposure from the chart	Minimal: Evaluated by psychiatrist - Bayley Scales of Infant Development	Low: Certain confounders assessed - parental education (unclear if there are others)	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Minimal: Little to no attrition	Low
Many et al, ⁴⁷	Low: A select	Minimal:	Minimal:	Low: Certain confounders	Low: Sample	Low: 11-20%	Low

2003	group of population - Lis Maternity Hospital, Israel (children born growth restricted)	Exposure from the chart	Standardised IQ test	assessed - gestational age, birthweight, neonatal complications	size calculation not performed, but all available eligible patients may have been studied	attrition	
McCowan et al, ⁵² 2002	Low: A select group of population - small for gestational age infants at Auckland Hospital, New Zealand	Minimal: Direct questioning (interview) by midwife	Minimal: Assessed by trained psychologist	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Moderate: >20% attrition but reasons for loss of follow up explained	Moderate
Gray et al, ⁵³ 1998	Low: A select group of population - very preterm infants, Mater Mother's Hospital, Brisbane, Australia	Minimal: Exposure from the chart	Minimal: Griffiths' Infant Ability Scale	Moderate: Not assessed for confounders	Minimal: Sample size calculation performed and adequate sample studied	Minimal: <10% attrition	Low
Spinillo et al, ⁵⁴ 1994	Low: A select group of population - one clinical setting in Italy	Low: Assessment of exposure from a dataset	Low: Assessment from administrative database	Low: Certain confounders assessed - social class and maternal education	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Minimal: <10% attrition	Low
Seidman et al, ³⁷ 1991	Low: A select group of population - 17 year olds during assessment for drafting to Israel Defence Forces	Low: Assessment of exposure from a dataset - Jerusalem Perinatal Study	Low: Assessment from administrative database - Israel Defence Force records	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Minimal: Little to no attrition	Low

Szymonowicz et al, ⁴⁸ 1987	Low: A select group of population - very low birthweight infants at one centre	Low: Assessment of exposure from a dataset	Minimal: Bayley Scales	Moderate: Not assessed for confounders	Moderate: Sample size estimation unclear	Minimal: Little to no attrition	Moderate
Salonen et al, ⁶⁰ 1984	Low: A select group of population - All 9-10 year olds in one Finnish county in 1979-81	Minimal: Confirmed by physician during pregnancy	Low: Assessment from administrative database - records in local Developmental Defect Registries or screening in schools	Low: Certain confounders assessed- mother's age at birth, sibling with mental retardation or birth defect, parity, mode of birth, mother's smoking status during pregnancy	Low: Sample size calculation not performed, but all available eligible patients studied	Low: <10% attrition and reasons for loss of follow up not explained	Low
Winer et al, ⁵⁵ 1982	Moderate: Sample selection process unclear	Minimal: Exposure from the chart	Minimal: Psychological testing (carried out blinded)	Moderate: Not assessed for confounders	Low: Sample size calculation not performed, but all available eligible patients may have been studied	Moderate: >20% attrition but reasons for loss of follow up explained	Moderate
Barker and Edwards, ³⁸ 1967	Low: A select group of population - children in Birmingham who took the 'Eleven Plus' exam	Minimal: Exposure from the chart	Moderate: Eleven Plus exam (However, those in special schools or those in mainstream school but assessed as "borderline subnormal" excluded)	Moderate: Not assessed for confounders (but matched by sibpairs)	Low: Sample size calculation not performed, but all available eligible patients studied	Minimal: <10% attrition	Moderate

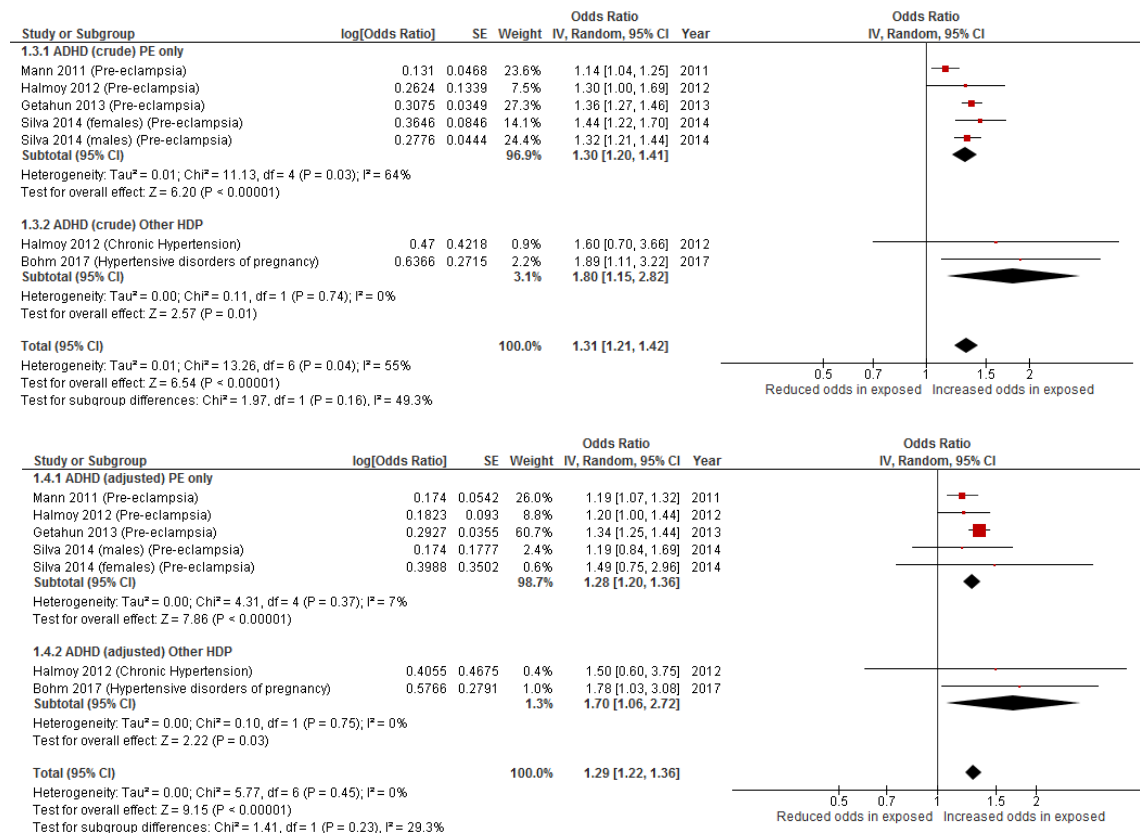
Additional forest plots displaying results of studies that provide both a crude and adjusted estimates for the association between HDP-ASD and HDP-ADHD

eFigure 1. ASD Studies With Crude and Adjusted Estimates



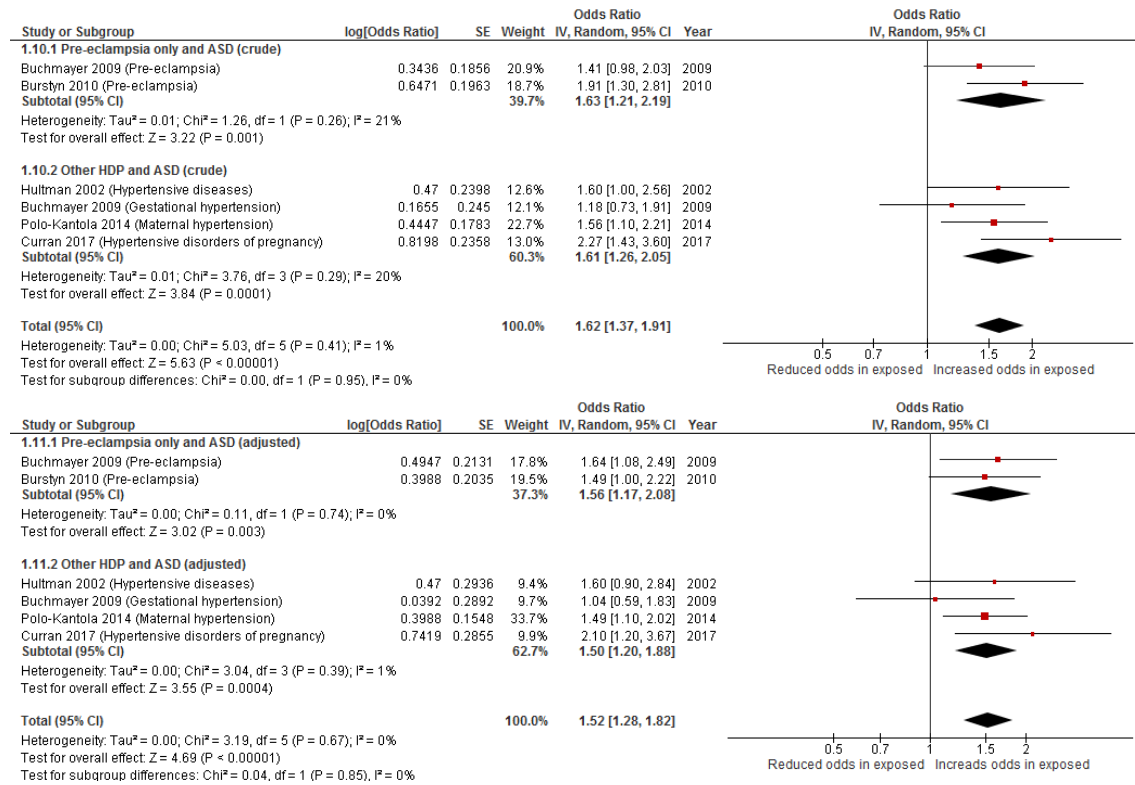
Forest plots displaying crude and adjusted estimates examining the association between HDP and ASD in the offspring.

eFigure 2. ADHD Studies With Crude and Adjusted Estimates



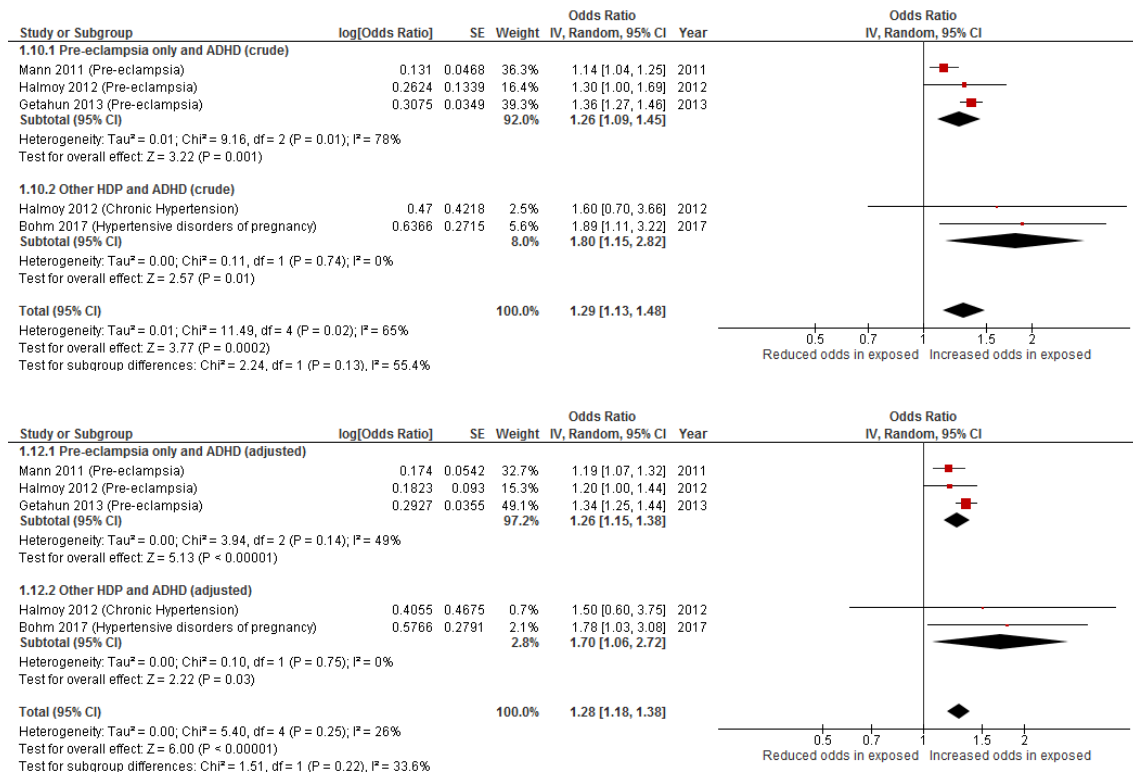
Forest plots displaying crude and adjusted estimates examining the association between HDP and ADHD in the offspring.

Figure 3. ASD Studies That Adjust for Maternal Age and Smoking and Parity/Birth Order



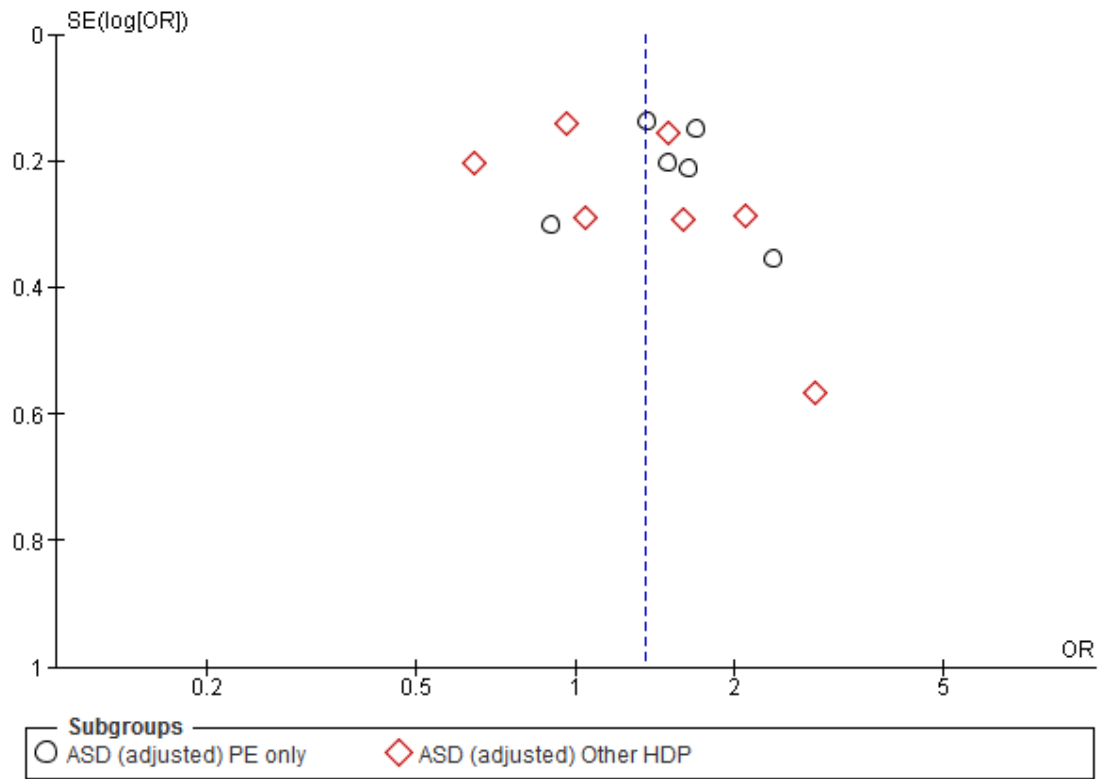
Forest plots displaying crude and adjusted estimates examining the association between HDP and ASD in the offspring.

eFigure 4. ADHD Studies That Adjust for Maternal Age and Educational Level



Forest plots displaying crude and adjusted estimates examining the association between HDP and ADHD in the offspring.

eFigure 5. Funnel Plot of Published HDP and ASD Studies



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