Supplementary Online Content

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

eTable 1. Inclusion and Exclusion Criteria for a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
A single course of ACS versus those unexposed		
Children born preterm		
Chawla, 2013 (U.S.)[1] ★★★★★★★★	• GA <28 weeks • BW 400-1000g • Included data on race/ethnicity of children at baseline [ACS group, n=80; unexposed group, n=28] ○ African American in ACS group (n=63) ○ African American in unexposed group (n=26)	• Stillbirths • Congenital infections • Chromosomal or major congenital anomalies • Neonates not resuscitated at birth due to extreme prematurity
Gover, 2012 (Canada)[2] ★★★★★★★½	• GA ≤32 weeks	• Major congenital anomalies • Maternal heroin or cocaine use during pregnancy • Major infant impairment • Infants exposed to a partial course or more than a single course of ACS • Infants on hydrocortisone post-discharge
Chawla, 2016 (U.S.)[3] ★★★★★★★	• BW 401-1000 g/a GA of 22-27 weeks as determined by early ultrasonography or last menstrual period • Included data on race/ethnicity of mothers at baseline [ACS group, n=3630; unexposed group, n=833] ○ White in ACS group (n=1987) ○ African American in ACS group (n=1445) ○ Other in ACS group (n=198) ○ White in unexposed group (n=394) ○ African American in unexposed group (n=399) ○ Other in unexposed group (n=40)	• Infants who died within 12h of birth without aggressive neonatal care
Lee, 2008 (U.S.)[4] ★★★★★★½	• BW 401-1000g • Born at NICHD Neonatal Research Network centers • Included data on race/ethnicity of children followed-up [betamethasone group, n=563; dexamethasone group, n=408; unexposed group, n=153]	• Congenital or chromosomal anomaly • Inborn error of metabolism • Exposure to both dexamethasone and betamethasone • Outborn infants

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
	○ "Non-white" in betamethasone group (56%) ○ "Non-white" in dexamethasone group (70%) ○ "Non-white" in unexposed group (79%)	
Agarwal, 2018 (Singapore)[5] ★★★★★★	• PTB/ VLBW (≤1250 g) • Born at the KK Women's and Children's Hospital (KKH) • Survived until follow-up • Included data on race/ethnicity of all children at baseline [n=165] ○ Chinese (53%) ○ Malay (27%) ○ Indian (15%) ○ "Other" (5%)	• Major congenital malformations
Kim, 2018 (Korea)[6] ★★★★★½	• 21-23 weeks GA (determined by the LMP or crown-rump length on 1st trimester ultrasonography)	• Stillbirth • Voluntary termination of pregnancy or parental elective non-resuscitations • Delayed-interval delivery in twin pregnancies • Major congenital anomalies
Laughon, 2009 (U.S.)[7] ★★★★★½	• GA <28 weeks • Children able to walk independently (Gross Motor Function Classification System)	• NS
McElrath, 2009 (U.S.)[8] ★★★★★½	• <28 weeks GA	• Birth defects and/or aneuploidy
Lardon, 2017 (Spain)[9] ★★★★½	• Preterm infants • BW <1,500 g	• Major malformation detectable in fetus or newborn • Genetic syndromes or metabolic disturbances
Tseng, 2016 (Taiwan)[10] ★★★★½	• GA <35 weeks • BW <1500g	• NS

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
Unspecified number of courses of ACS versus those unexposed		
Children born preterm or at term		
Lamminmaki 2021 (Finland)[11] ★★★★★★★½	• Preterm & term • Matched controls for sex, GA ±6 days, and date of birth ±3 days	• NS
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	• Singletons • Valid maternal and child personal identification codes for register data linkage • Available data on GA at birth • Survived until end of 1st year of life	• NS
Wolford, 2020 (Finland)[13] ★★★★★★★	• Singleton live-born infants • Women with known risk factors for PE and IUGR • Women with no known risk factors	• NS
Children born preterm		

Haslam, 2018 (Canada)[14] ★★★★★★★★½	• Born at 23-28 weeks GA and admitted to a NICU
	• Included data on race/ethnicity of all children at baseline [n=2187]
	  ○ First Nations (n=77)
	  ○ East Asian (n=60)
	  ○ South Asian (n=144)
	  ○ White (n=1260)
	  ○ "Other/unknown" (n=646)
		• Stillborn
		• Moribund
		• Major congenital anomalies,
		• Admitted to NICU >24h after birth

Aviram, 2021 (Canada)[15] ★★★★★★★★	• Singletons • Live births • 34-36 weeks and 6 days GA	• Multi-fetal gestations • Genetic or major structural abnormalities, • Deliveries complicated by intrapartum asphyxia • No data on exposure to ACS/other variables
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	• Singletons • Valid maternal and child personal identification codes for register data linkage • Available data on GA at birth • Survived until end of 1st year of life	• NS

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
Gentle, 2020 (U.S.)[16] ★★★★★★★	• Born at 22-26 weeks GA • Included data on race/ethnicity of children at baseline [ACS group, n=2752; unexposed group, n=341] ○ "Non-white race" in ACS group (n=1343) ○ "Non-white race" in unexposed group (n=186)	• Major congenital anomaly • Death occurred in first 12h after birth without receiving delivery room resuscitation (no ventilation, intubation or medications)
Hutcheon, 2020 (Canada)[17] ★★★★★★★	• GA 31-36 weeks and 6 days	• Children moved out of province before age 4 • Births with no ultrasound confirmed- or revised-estimate of GA in days •
Bulbul, 2020 (Turkey)[18] ★★★★★★½	• ≤34 weeks GA from participating hospital	• Babies born in other centers and referred to participating hospital • Congenital major anomaly or congenital metabolic disease
Miyazaki, 2015 (Japan)[19] ★★★★★★½	• VLBW neonates born in tertiary perinatal centers •	• Multiple pregnancies • GA >31 weeks • Major congenital malformations • Hospitalization following an out-of-hospital birth • No pathological examination of the placenta
Ushida, 2020a (Japan)[20] ★★★★★★½	• BW ≤1,500g and born at 24-31 weeks GA • Women with complete data about maternal and neonatal characteristics	• <24 weeks GA • Children from higher order multiple births (triplets, quadruplets) • Major congenital abnormalities • Transfer from other facilities • Co-twin fetal death • Incomplete medical records
Ushida, 2020b (Japan)[21] ★★★★★★½	• BW ≤1,500g and born at 24-31 weeks GA	• <24 weeks GA • Multiple pregnancies • Major congenital abnormalities • Out of hospital births • Incomplete medical records

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
Basset, 2018 (France)[22] ★★★★★★	• Born at 24-33 weeks GA • Born in 1 of 24 maternity clinics and hospitalized in 1 of the 3 NICUs • Remaining alive until discharge and enrolled in follow-up program	• Missing data regarding ACS or birth head circumference • Genetic abnormalities or malformations • Extreme birth weight/head circumference (ZS ≤ 3 or >3)
Ishikawa, 2015 (Japan)[23] ★★★★★½	• BW <1500g • SGA	• Multiple pregnancies • >34 weeks GA or uncertain GA • Uncertain administration of ACS • Major congenital malformation • Hospitalization following an out-of-hospital birth
Li, 2019 (China)[24] ★★★★★½	• Extremely preterm (<28 weeks GA)	• NS
Ochiai, 2014 (Japan)[25] ★★★★★½	• Born at 22-24 weeks GA	• NS
Young, 2016 (Canada)[26] ★★★★★½	• Born ≤32 weeks GA • From participating NICU	• Known chromosomal or major congenital abnormality
Kallen, 2015 (Sweden)[27] ★★★★½	• Live-born infants (including multiple births and infants with malformations)	• Stillborn • Infants born outside the country and transferred after birth for neonatal care
Kiechl-Kohlendorfer, 2009 (Austria)[28] ★★★★½	• Born <32 weeks GA • Born at included NICU	• Died before or after discharge • Hospitalization following an out-of-hospital birth • Major congenital anomalies
Sun, 2015 (China)[29] ★★★★½	• Born <32 weeks GA/ birth weight <1,500 g • Respiratory distress syndrome requiring mechanical ventilation less than 24 hours of life	• Genetic or metabolic diseases • Congenital abnormalities • Pneumothorax
Children born at term		
Melamed, 2019 (Canada)[30] ★★★★★★★★	• Singleton infants • Born term (≥37 weeks GA) in Ontario	• Multiple gestations • Cases complicated by intrapartum asphyxia (umbilical artery pH<7.1) • Genetic or major structural abnormalities • Data on exposure to ACS or on other variables were unavailable

Study (country) [Risk of bias assessment]	Inclusion criteria	Exclusion criteria
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	• Singletons • Valid maternal and child personal identification codes for register data linkage • Available data on GA at birth • Survived until end of 1st year of life	• NS

Legend:
ACS – antenatal corticosteroids; PTB – preterm birth; VLBW – very low birth weight; g – grams; GA – gestational age; LMP – last menstrual period; BW – birth weight; h – hours; NS – not stated/defined; mg – milligrams; NICHD – Eunice Kennedy Shriver National Institute of Child Health and Human Development; IQR – interquartile ratio; PE – preeclampsia; IUGR – intrauterine growth restriction; SD – standard deviation; NICU – neonatal intensive care unit; ZS – z-score; SGA – small for gestational age; RDS – respiratory distress syndrome; PAO2 – partial pressure of oxygen ration; FIO2 – fraction of inspired oxygen ration
Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded

eTable 2. Individual Adjusted Neurodevelopmental/Psychological Outcomes of Included Studies on a Single Course of Antenatal Corticosteroids vs. Non-Exposure in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
Children born preterm						
Chawla, 2016 (U.S.)[3] ★★★★★★★	Neurodevelopmental impairment • moderate to severe cerebral palsy based on the GMFCS levels 3-5, a cognitive score <85 on BSID-III, blindness, or deafness	651/2405	166/419	**Adj OR: 0.70 (0.55-0.89)**	**81 fewer per 1,000** (from 131 fewer to 28 fewer)	Meta-analyzed (Table 2)
	Blindness • bilateral visual acuity of 20/200 or less	12/2402	1/417	Adj OR: 2.73 (0.34-21.76)	4 more per 1,000 (from 2 fewer to 47 more)	Meta-analyzed (eTable 6)
	Deafness • hearing impairment despite amplification or cochlear implants	31/2405	10/418	Adj OR: 0.58 (0.28-1.23)	10 fewer per 1,000 (from 17 fewer to 5 more)	Meta-analyzed (eTable 6)
	Any cerebral palsy	252/2404	73/418	**Adj OR: 0.51 (0.38-0.70)**	**77 fewer per 1,000** (from 100 fewer to 46 fewer)	Meta-analyzed (eTable 6)
	Moderate to severe cerebral palsy • GMFCS levels 3-5	126/2404	26/418	Adj OR: 0.87 (0.55-1.37)	8 fewer per 1,000 (from 27 fewer to 21 more)	Meta-analyzed (eTable 6)

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	BSID-III cognitive score <70	192/2396	53/419	Adj OR: 0.72 (0.51-1.01)	32 fewer per 1,000 (from 58 fewer to 1 more)	⨁◯◯◯ Very low[a]
	BSID-III cognitive score 70-84	423/2396	109/419	**Adj OR: 0.76 (0.59-0.99)**	**49 fewer per 1,000** (from 88 fewer to 2 fewer)	⨁⨁◯◯ Low
	BSID-III cognitive score <85	615/2396	162/419	**Adj OR: 0.69 (0.54-0.87)**	**84 fewer per 1,000** (from 133 fewer to 32 fewer)	Meta-analyzed (eTable 6)
Lee, 2008 (U.S.)[4] ★★★★★½	Neurodevelopmental impairment • cerebral palsy, MDI <70, PDI <70, deafness, or blindness	• *Dex:* 167/408 • *Beta:* 191/563	69/153	• *Dex v none;* Adj OR: 0.74 (0.48-1.15) • *Beta v none;* **Adj OR: 0.63 (0.41-0.97)**	• 73 fewer per 1,000 (from 168 fewer to 35 more) • **110 fewer per 1,000** (from 199 fewer to 8 fewer)	Meta-analyzed (Table 2)

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Blindness • 20/200 visual acuity or less	• *Dex:* 4/408 • *Beta:* 5/563	1/153	• *Dex v none;* Adj OR: 1.51 (0.17-13.61) • *Beta v none;* Adj OR: 1.36 (0.16-11.77)	• 110 fewer per 1,000 (from 199 fewer to 8 fewer) • 2 more per 1,000 (from 5 fewer to 65 more)	Meta-analyzed (eTable 6)
	Deafness • use of hearing aids in both ears	• *Dex:* 13/408 • *Beta:* 5/563	5/153	• *Dex v none;* Adj OR: 0.85 (0.28-2.59) • *Beta v none;* **Adj OR: 0.22 (0.06-0.82)**	• 5 fewer per 1,000 (from 23 fewer to 48 more) • **25 fewer per 1,000** (from 31 fewer to 6 fewer)	Meta-analyzed (eTable 6)
	Cerebral palsy	• *Dex:* 55/408 • *Beta:* 56/563	20/153	• *Dex v none;* Adj OR: 0.91 (0.46-1.80) • *Beta v none;* Adj OR: 0.67 (0.34-1.33)	• 10 fewer per 1,000 (from 66 fewer to 82 more) • 39 fewer per 1,000 (from 82 fewer to 36 more)	Meta-analyzed (eTable 6)

Study (country) [Risk of bias assessment]	Neurodevelopmental/psychological outcomes (with definitions when available)	Single course of ACS (n/N)	Unexposed group (n/N)	Reported relative effect (95% CI)	Absolute effect (95% CI)	GRADE certainty
	Moderate or severe cerebral palsy	• *Dex:* 29/408 • *Beta:* 30/563	10/153	• *Dex v none;* Adj OR: 0.86 (0.34-2.15) • *Beta v none;* Adj OR: 0.61 (0.25-1.51)	• 9 fewer per 1,000 (from 42 fewer to 65 more) • 24 fewer per 1,000 (from 48 fewer to 30 more)	Meta-analyzed (eTable 6)
	BSID-II MDI <70	• *Dex:* 135/408 • *Beta:* 163/563	58/153	• *Dex v none;* Adj OR: 0.73 (0.46-1.15) • *Beta v none;* Adj OR: 0.70 (0.45-1.09)	• 71 fewer per 1,000 (from 160 fewer to 33 more) • 80 fewer per 1,000 (from 164 fewer to 20 more)	⊕◯◯◯ Very low[a] ⊕◯◯◯ Very low[a]
	BSID-II PDI <70	• *Dex:* 98/408 • *Beta:* 107/563	31/153	• *Dex v none;* Adj OR: 1.25 (0.71-2.18) • *Beta v none;* Adj OR: 0.89 (0.51-1.55)	• 38 more per 1,000 (from 50 fewer to 154 more • 18 fewer per 1,000 (from 88 fewer to 80 more)	⊕◯◯◯ Very low[a] ⊕◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Unimpaired • the absence of the following: cerebral palsy, blindness, deafness, MDI ≥85, PDI ≥85	• *Dex:* 106/408 • *Beta:* 225/563	32/153	• *Dex v none;* Adj OR: 1.50 (0.91-2.48) • *Beta v none;* **Adj OR: 2.42 (1.49-3.91)**	• 75 more per 1,000 (from 15 fewer to 187 more) • **181 more per 1,000** (from 74 more to 299 more)	⨁◯◯◯ Very low[a] ⨁⨁◯◯ Low
Laughon, 2007 (Unspecified)[7] ★★★★★½	BSID-II PDI score <55	71/588	4/93	**Adj OR: 2.3 (1.5-3.5)**	**51 more per 1,000** (from 20 more to 93 more)	⨁◯◯◯ Very low[a,b]
Lardon, 2017 (Spain)[9] ★★★★½	Visual sensory disorder • myopia, loss of vision or strabismus	17/134	4/37	Adj OR: 1.08 (0.28-4.17)	8 more per 1,000 (from 75 fewer to 228 more)	Meta-analyzed (eTable 6)
	Auditory sensory disorder • sensorineural deafness	10/134	2/37	Adj OR: 1.19 (0.22-6.26)	10 more per 1,000 (from 42 fewer to 209 more)	Meta-analyzed (eTable 6)
	Behavioral/conduct disorder • autism spectrum disorder	6/134	2/37	Adj OR: 0.72 (0.13-4.01)	15 fewer per 1,000 (from 47 fewer to 132 more)	⨁◯◯◯ Very low[a,b]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Motor disorder • mild neuromotor disorder, diparesis, hemiparesis or tetraparesis	25/134	7/37	Adj OR: 0.59 (0.25-1.38)	68 fewer per 1,000 (from 134 fewer to 54 more)	⨁◯◯◯ Very low[a,b]
	Cognitive delay	62/134	18/37	Adj OR: 0.84(0.28-2.46)	43 fewer per 1,000 (from 277 fewer to 213 more)	⨁◯◯◯ Very low[a,b]
	Multiple deficiency • profound intellectual deficiency associated with more or less severe motor disturbances or sensory or behavioral disturbances	5/134	1/37	Adj OR 1.60 (0.14-18.3)	16 more per 1,000 (from 23 fewer to 310 more)	⨁◯◯◯ Very low[a,b]

Legend:
ACS – antenatal corticosteroids; SD – standard deviation; CI – confidence interval; BSID – Bayley Scales of Infant and Toddler Development; NS – not stated/defined; adj – adjusted; OR – odds ratio; GMFCS – Gross Motor Function Classification System; MDI – mental development index; PDI – psychomotor development index; Dex – dexamethasone; Beta – betamethasone; v – versus

Newcastle-Ottawa Scale: ★ – point awarded, ½ – half point awarded

GRADE Assessment: Low rating indicates no serious concerns in GRADE domains and no other considerations were made; a–serious rating for imprecision due to small sample size/wide 95% CI's; b–serious rating for risk of bias due to low Newcastle-Ottawa scale rating (i.e., <6 stars).

Green font– a statistically significant beneficial outcome, grey highlighting – not measured/reported, **red font**– a statistically significant harmful outcome

eTable 3. Individual Unadjusted Neurodevelopmental/Psychological Outcomes of Included Studies on a Single Course of Antenatal Corticosteroids vs. Non-Exposure in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N) or Mean (SD)	**Unexposed group** (n/N) or Mean (SD)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Children born preterm					
Chawla, 2013 (U.S.)[1] ★★★★★★★★	Neurodevelopmental impairment • moderate to severe cerebral palsy based on the GMFCS levels 3-5, a cognitive score <85 on BSID-III, blindness, or deafness	16/51	3/8	p=0.08	Meta-analyzed (eTable 6)
	Blindness • bilateral visual acuity of 20/200 or less	0/51	0/8	p=0.15	Meta-analyzed (eTable 6)
	Deafness • the need for bilateral amplification or cochlear implants	3/51	0/8	p=0.47	Meta-analyzed (eTable 6)
	Any cerebral palsy	13/51	3/8	p=0.27	Meta-analyzed (eTable 6)
	Moderate/severe cerebral palsy • GMFCS levels 3-5	7/51	1/8	p=0.82	Meta-analyzed (eTable 6)
	BSID-III MDI/cognitive score <70	14/51	3/8	p=0.68	⊕◯◯◯ Very low[a]
	BSID-III MDI/cognitive score <85	27/51	5/8	p=0.13	Meta-analyzed (eTable 6)
Agarwal, 2018[5] (India) ★★★★★★	Neurodevelopmental impairment • presence of neurosensory impairment (cerebral palsy, deafness, or blindness) or with BSID-III score <70 in any domain	NS	NS	Lack of ACS: **unadjusted OR: 2.91 (1.21-7.00)**	⊕◯◯◯ Very low[a]
	Abnormal cognition significant delay: <70 on the BSID-III cognitive scores	1/122	8/43	Lack of ACS: **unadjusted OR: 41.5 (3.5-485.7)**	⊕◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N) or Mean (SD)	**Unexposed group** (n/N) or Mean (SD)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
	Abnormal language significant delay: <70 on the BSID-III language score	15/122	14/43	Lack of ACS: **unadjusted OR: 2.8 (1.1-7.4)**	⊕◯◯◯ Very low[a]
Kim, 2018 (Korea)[6] ★★★★★½	Neurodevelopmental impairment • cerebral palsy GMFCS level ≥ II, MDI<70 on BSID-II or cognitive score <85 on BSID-III, suspicion of developmental delay on Denver Developmental Screening test, blindness or use of cochlear implant	24/25	15/16	p=0.197	Meta-analyzed (eTable 6)
	Cerebral palsy • Any level using the GMFCS	14/27 ≥ level III: 0/26	9/18 ≥ level III: 1/18	p=0.659 ≥ level III: p=0.171	Meta-analyzed (eTable 6)
	Developmental delay by BSID or Denver Developmental Screening test	24/25	14/17	p=0.162	⊕◯◯◯ Very low[a,b]
Laughon, 2007 (Unspecified)[7] ★★★★★½	BSID-II MDI score <55	71/588	10/93		⊕◯◯◯ Very low[a,b]
	BSID-II MDI score of 55-59	65/588	8/93		⊕◯◯◯ Very low[a,b]
	BSID-II PDI score of 55-59	88/588	14/93		⊕◯◯◯ Very low[a,b]
McElrath, 2009 (U.S.)[8] ★★★★★½	Quadriparesis	6/681	8/113		⊕◯◯◯ Very low[a,b]
	Diparesis	4/681	4/113		Meta-analyzed (eTable 6)
	Hemiparesis	2/681	0/113		Meta-analyzed (eTable 6)
Lardon, 2017 (Spain)[9] ★★★★½	Mild motor disorder	16/134	3/37		⊕◯◯◯ Very low[a,b]
	Diparesis	4/134	1/37		Meta-analyzed (eTable 6)

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Single course of ACS** (n/N) or Mean (SD)	**Unexposed group** (n/N) or Mean (SD)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
	Hemiparesis	3/134	1/37		Meta-analyzed (eTable 6)
	Tetraparesis	2/134	2/37		⊕◯◯◯ Very low[a,b]
	Mild cognitive delay	55/134	15/37		⊕◯◯◯ Very low[a,b]
	Moderate cognitive delay	6/134	3/37		⊕◯◯◯ Very low[a,b]
	Serious cognitive delay	1/134	0/37		⊕◯◯◯ Very low[a,b]
Tseng, 2016 (Taiwan)[10] ★★★★½	BSID-II MDI score	90.38 (3.31)	79.94 (3.58)	p=0.043	⊕◯◯◯ Very low[a,b]
	BSID-II PDI score	78.17 (3.81)	76.13 (4.51)	p>0.05	⊕◯◯◯ Very low[a,b]
	MDI <70 on the BSID-II scale	3/24	3/16	p>0.05	Meta-analyzed (eTable 6)

Legend:
ACS – antenatal corticosteroids; SD – standard deviation; CI – confidence interval; BSID – Bayley Scales of Infant and Toddler Development; NS – not stated/defined; adj – adjusted; OR – odds ratio; GMFCS – Gross Motor Function Classification System; MDI – mental development index; PDI – psychomotor development index; Dex – dexamethasone; Beta – betamethasone; v – versus

Newcastle-Ottawa Scale: ★ – point awarded, ½ – half point awarded

GRADE Assessment: Low rating indicates no serious concerns in GRADE domains and no other considerations were made; a–serious rating for imprecision due to small sample size/wide 95% CI's; b–serious rating for risk of bias due to low Newcastle-Ottawa scale rating (i.e., <6 stars). For pooled outcomes refer to eTable 6.

Green font– a statistically significant beneficial outcome, grey highlighting – not measured/reported, **red font**– a statistically significant harmful outcome

eTable 4. Individual Adjusted Neurodevelopmental/Psychological Outcomes of Included Studies on an Unspecified Number of Courses of Antenatal Corticosteroids vs. Non-Exposure in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
Children born preterm or at term						
Lamminmaki 2021 (Finland)[11] ★★★★★★★½	Pre-school Activities Inventory Score • Psychometric scale to discriminate gender-typical behavior within and between sexes	Mean (SD): *Male:* 68.5 (10.6), n=171 *Female:* 27.5 (11.3), n=166	Mean (SD): *Male:* 68.6 (9.9), n=213 *Female:* 28.2 (10.0), n=186	β=0.3, (−1.7 to 2.3); p=0.75 β = 1.3 (−1.1 to 3.6); p=0.29		⊕⊕◯◯ Low
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Any mental and behavioral disorder in all children born preterm/term • *all consecutive sibling pairs discordant for treatment-exposure vs concordant for non-exposure* • *younger treatment-exposed and older non-exposed vs both younger and older non-exposed* • *all consecutive sibling pairs with first sibling pair discordant for treatment-exposure for each mother versus first sibling pair concordant for non-exposure for each mother*	1785/14868	42243/655229	• **Adj HR: 1.38 (1.21-1.58)** • **Adj HR: 1.53 (1.29-1.81)** • **Adj HR: 1.36 (1.17-1.57)**		⊕⊕◯◯ Low ⊕⊕◯◯ Low ⊕⊕◯◯ Low
	Psychological development disorders	956/14868	19089/655229	**Adj HR: 1.31 (1.21-1.42)**	**89 more per 10,000** (from 60 more to 120 more)	⊕⊕◯◯ Low

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Autism spectrum disorders	96/14868	2807/655229	Adj HR: 1.25 (0.99-1.58)	11 more per 10,000 (from 0 fewer to 25 more)	⨁⨁◯◯ Low
	Attention-deficit/hyperactivity or conduct disorders	216/14868	6773/655229	**Adj HR: 1.18 (1.01-1.38)**	**18 more per 10,000** (from 1 more to 39 more)	⨁⨁◯◯ Low
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	181/14868	6350/655229	**Adj HR: 1.20 (1.02-1.42)**	**19 more per 10,000** (from 2 more to 40 more)	⨁⨁◯◯ Low
	Other behavioral and emotional disorders	345/14868	8049/655229	**Adj HR: 1.16 (1.02-1.32)**	**19 more per 10,000** (from 2 more to 39 more)	⨁⨁◯◯ Low
	Psychotic**,** mood, neurotic, stress-related, or somatization disorders	71/14868	2241/655229	Adj HR: 1.28 (0.98-1.67)	10 more per 10,000 (from 1 fewer to 23 more)	⨁⨁◯◯ Low
	Eating disorders	6/14868	243/655229	Adj HR: 0.67 (0.31-1.47)	1 fewer per 10,000 (from 3 fewer to 2 more)	⨁◯◯◯ Very low[a]
	Sleep disorders	79/14868	2110/655229	**Adj HR: 1.52 (1.18-1.96)**	**17 more per 10,000** (from 6 more to 31 more)	⨁⨁◯◯ Low
	Mild, moderate, unspecified intellectual disability	101/14868	2259/655229	**Adj HR: 0.66 (0.52-0.83)**	**12 fewer per 10,000** (from 17 fewer to 6 fewer)	⨁⨁◯◯ Low

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Severe, profound intellectual disability	18/14868	219/655229	Adj HR: 1.15 (0.63-2.12)	1 more per 10,000 (from 1 fewer to 4 more)	⨁⨁◯◯ Low
Wolford, 2020 (Finland)[13] ★★★★★★★	Disorders of psychological development	19/117	238/4591	**Adj OR: 3.57 (1.94-6.59)**	**1,115 more per 10,000** (from 441 more to 2,130 more)	⨁◯◯◯ Very low[a]
	Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	14/117	184/4591	**Adj OR: 2.66 (1.30-5.46)**	**599 more per 10,000** (from 114 more to 1,456 more)	⨁◯◯◯ Very low[a]
Children born preterm						
Haslam, 2018 (Canada)[14] ★★★★★★★★½	Severe neurodevelopmental impairment at least one of the following: GMFCS 3-5, BSID-III <-2 SD, hearing aid or cochlear implant, bilaterally blind	276/1963		**Adj OR: 0.62 (0.39-0.98)**	N/A	Meta-analyzed (Table 2)
	Severe neurodevelopmental impairment at least one of the following: GMFCS 4-5, BSID-III cognitive or language composite score <-3 SD, bilaterally blind	64/1963		Adj OR: 0.83 (0.40-1.73)	N/A	⨁◯◯◯ Very low[a]
Aviram, 2021 (Canada)[15] ★★★★★★★★	Investigation for suspected neurocognitive disorder • any physician service claim with a diagnosis code related to a suspected neurocognitive disorder • after removing NICU admitted infants and BW <10th percentile from model	1156/2689	8581/22979	**Adj HR: 1.12 (1.05-1.20)** **Adj HR: 1.14 (1.07-1.22**	**342 more per 10,000** (from 145 more to 559 more)	⨁⨁◯◯ Low

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Visual testing • any consultations or assessments from an ophthalmologist or optometrist. • after removing NICU admitted infants and BW <10th percentile from model	1860/2689	15483/22979	**Adj HR: 1.06 (1.01-1.11)** **Adj HR: 1.06 (1.01-1.12)**	**212 more per 10,000** (from 36 more to 378 more)	⨁⨁◯◯ Low
	Audiometry testing • physician service claim for hearing deficits (i.e., outside of the routine provincial infant screening program) • after removing NICU admitted infants and BW <10th percentile from model	627/2689	4559/22979	**Adj HR: 1.20 (1.10-1.31)** **Adj HR: 1.21 (1.11-1.32)**	**347 more per 10,000** (from 175 more to 531 more)	⨁⨁◯◯ Low
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Psychological development disorders	687/8138	1095/20472	Adj HR: 0.96 (0.86-1.08)	21 fewer per 10,000 (from 73 fewer to 42 more)	⨁⨁◯◯ Low
	Autism spectrum disorders	68/8138	123/20472	Adj HR: 1.12 (0.78-1.61)	7 more per 10,000 (from 13 fewer to 36 more)	⨁◯◯◯ Very low[a]
	Attention-deficit/hyperactivity or conduct disorders	132/8138	325/20472	Adj HR: 0.82 (0.64-1.05)	28 fewer per 10,000 (from 57 fewer to 8 more)	⨁◯◯◯ Very low[a]
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	94/8138	273/20472	Adj HR: 0.84 (0.63-1.11)	21 fewer per 10,000 (from 49 fewer to 15 more)	⨁◯◯◯ Very low[a]
	Other behavioral and emotional disorders	230/8138	466/20472	Adj HR: 0.83 (0.69-1.00)	38 fewer per 10,000 (from 70 fewer to 0 fewer)	⨁◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Psychotic, mood, neurotic, stress-related, or somatization disorders	47/8138	98/20472	Adj HR: 1.01 (0.66-1.54)	0 fewer per 10,000 (from 16 fewer to 26 more)	⨁◯◯◯ Very low[a]
	Eating disorders	5/8138	19/20472	Adj HR: 0.35 (0.11-1.10)	6 fewer per 10,000 (from 8 fewer to 1 more)	⨁◯◯◯ Very low[a]
	Sleep disorders	38/8138	82/20472	**Adj HR: 1.64 (1.05-2.57)**	**26 more per 10,000** (from 2 more to 63 more)	⨁⨁◯◯ Low
	Mild, moderate, unspecified intellectual disability	76/8138	166/20472	**Adj HR: 0.60 (0.44-0.83)**	**32 fewer per 10,000** (from 45 fewer to 14 fewer)	⨁⨁◯◯ Low
	Severe, profound intellectual disability	15/8138	22/20472	Adj HR: 1.17 (0.37-3.69)	2 more per 10,000 (from 7 fewer to 29 more)	⨁◯◯◯ Very low[a]
Gentle, 2020 (U.S.)[16] ★★★★★★★	Severe neurodevelopmental impairment • severe cerebral palsy (GMFCS levels 4-5), BSID-III motor or cognitive composite score <70, bilateral blindness, or hearing impairment	76/358	28/158	Adj OR: 0.98 (0.62-1.55)	32 fewer per 10,000 (from 633 fewer to 837 more)	Meta-analyzed (Table 2)
	Hearing impairment • whether infant has any hearing impairment event with amplification	8/364	6/158	Adj OR: 0.84 (0.34-2.08)	60 fewer per 10,000 (from 249 fewer to 394 more)	Meta-analyzed (eTable 6)
Hutcheon, 2020 (Canada)[17] ★★★★★★★	Having special needs based on British Columbia Ministry of Education designation			Adj RR 0.9 (0.6 to 1.4)	N/A	⨁◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
Miyazaki, 2015 (Japan)[19] ★★★★★★½	Neurodevelopmental impairment • Cerebral palsy, visual impairment, severe hearing impairment, or a KSPD quotient < 70	• *HCA*+: 46/194 • *HCA*-: 105/381	• *HCA*+: 37/160 • *HCA*-: 171/683	• *HCA*+; Adj OR: 0.94 (0.54-1.65) • *HCA*-; Adj OR: 0.92 (0.67-1.26)	• 108 fewer per 10,000 (from 915 fewer to 1,005 more) • 153 fewer per 10,000 (from 675 fewer to 458 more)	Meta-analyzed (Table 2)
	Visual impairment • defined as unilateral or bilateral blindness	• *HCA*+: 2/246 • *HCA*-: 9/584	• *HCA*+: 3/192 • *HCA*-: *12*/904	• *HCA*+; Adj OR: 0.46 (0.04-5.18) • *HCA*-; Adj OR: 0.94 (0.34-2.60)	• 84 fewer per 10,000 (from 150 fewer to 604 more) • 8 fewer per 10,000 (from 87 fewer to 205 more	⊕◯◯◯ Very low[a] ⊕◯◯◯ Very low[a]
	Severe hearing impairment • defined as the need for hearing aids	• *HCA*+: 3/247 • *HCA*-: 4/580	• *HCA*+: 2/195 • *HCA*-: 11/914	• *HCA*+; Adj OR: 4.00 (0.30-53.39) • *HCA*-; Adj OR: 0.47 (0.15-1.53)	• 295 more per 10,000 (from 72 fewer to 3,459 more) • 63 fewer per 10,000 (from 102 fewer to 63 more)	Meta-analyzed (eTable 6)

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Cerebral palsy	• *HCA*+: 21/249 • *HCA*-: 50/575	• *HCA*+: 15/194 • *HCA*-: 72/906	• *HCA*+; Adj OR: 0.90 (0.41-1.99) • *HCA*-; Adj OR: 1.07 (0.72-1.59)	• 72 fewer per 10,000 (from 441 fewer to 656 more) • 51 more per 10,000 (from 209 fewer to 412 more)	⨁◯◯◯ Very low[a] ⨁◯◯◯ Very low[a]
	KSPD quotient <70	• *HCA*+: 27/189 • *HCA*-: 62/398	• *HCA*+: 25/161 • *HCA*-: 116/698	• *HCA*+; Adj OR: 0.93 (0.48-1.81) • *HCA*-; Adj OR: 0.74 (0.51-1.08)	• 93 fewer per 10,000 (from 742 fewer to 944 more) • 377 fewer per 10,000 (from 739 fewer to 109 more)	⨁◯◯◯ Very low[a] ⨁◯◯◯ Very low[a]
Basset, 2018 (France)[22] ★★★★★★	Optimal neurodevelopmental outcome at 2 years for ZS HC -3 to -1 • an optimal outcome was considered as: absence of cerebral palsy (or when the clinical examination revealed neurological signs of abnormal muscular tone when walking), Brunet-Lézine test >85, or Ages and Stages questionnaire score >185	425/589	258/346	Adj OR: 1.46 (0.98-2.20)	650 more per 10,000 (from 39 fewer to 1,201 more)	⨁◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Optimal neurodevelopmental outcome at 2 years for ZS HC -1 to +1 • using the same definition for ZS HC -3 to -1	1566/2042	1082/1393	Adj OR: 1.10 (0.92-1.31)	161 more per 10,000 (from 148 fewer to 433 more)	⊕◯◯◯ Very low[a]
	Optimal neurodevelopmental outcome at 2 years for ZS HC +1 to +3 • using the same definition for ZS HC -3 to -1	264/344	182/251	Adj OR: 1.46 (0.98-2.20)	688 more per 10,000 (from 40 fewer to 1,279 more)	⊕◯◯◯ Very low[a]
Young, 2016 (Canada)[26] ★★★★★½	Cognitive measures on BSID-III at 2 years • partial least squares bootstrap ratios for antenatal corticosteroid use			**Adjusted bootstrap ratio: -3.883; p<0.05**	N/A	⊕◯◯◯ Very low[a]
	Cognitive measures at 4 years • three different indices of cognitive ability verbal IQ, performance IQ, and full-scale IQ			**Adjusted Bootstrap ratio: 3.716; p<0.05**	N/A	⊕◯◯◯ Very low[a]
	Behavioural measures at 4 years • as measured by t-scores on the Behavioral Rating Inventory of Executive Functioning–Preschool and Behavior Assessment System for Children Parent Rating Scales			**Adjusted Bootstrap ratio: -2.606; p<0.05**	N/A	⊕◯◯◯ Very low[a]
Ishikawa, 2015 (Japan)[23] ★★★★★½	Neurodevelopmental impairment • cerebral palsy, development quotient <70, or severe hearing impairment or visual impairment	66/285	93/505	Adj OR: 1.03 (0.62-1.70)	45 more per 10,000 (from 614 fewer to 932 more)	⊕◯◯◯ Very low[a,b]
	Visual impairment • unilateral or bilateral blindness	1/275	3/490	Adj OR: 1.03 (0.02-36.15)	2 more per 10,000 (from 60 fewer to 1,760 more)	⊕◯◯◯ Very low[a,b]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
	Cerebral palsy • characterized by abnormal muscle tone in at least one extremity and abnormal control of movement and posture	19/278	25/498	Adj OR: 1.12 (0.41-2.96)	57 more per 10,000 (from 290 fewer to 851 more)	⨁◯◯◯ Very low[a,b]
	KSPD quotient <70	51/271	70/486	Adj OR: 1.08 (0.63-1.85)	98 more per 10,000 (from 482 fewer to 934 more)	⨁◯◯◯ Very low[a,b]
Kallen, 2015 (Sweden)[27] ★★★★½	Any moderate or severe disability • visual or hearing impairment, cerebral palsy, low BSID-III composite cognitive, language or motor score	114/411	10/45	Adj OR: 1.20 (0.50-2.90)	331 more per 10,000 (from 972 fewer to 2,309 more)	Meta-analyzed (Table 2)
	Neurosensory impairment • moderate or severe impairment regarding vision and hearing	31/411	3/45	Adj OR: 1.10 (0.30-4.80)	62 more per 10,000 (from 457 fewer to 1,887 more)	⨁◯◯◯ Very low[a,b]
	Mental developmental delay • cognitive or language BSID-III scale < mean -2 SD	82/411	6/45	Adj OR: 0.70 (0.30-1.90)	361 fewer per 10,000 (from 892 fewer to 929 more)	⨁◯◯◯ Very low[a,b]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
Kiechl-kohlendorfer, 2009 (Austria)[28] ★★★★½	Neurodevelopmental delay • defined as <85 on either the BSID-II PDI or the MDI, cerebral palsy, blindness, or hearing loss requiring hearing aid	• *GA <30w:* 28/81 • *GA 30-32w:* 20/101	• *GA <30w:* 9/15 • *GA 30-32w:* 5/8	• *GA <30w*; **Adj OR: 0.256 (0.07-0.96)** • *GA 30-32w*; **Adj OR: 0.170 (0.04-0.81)**	• **3,225 fewer per 10,000** (from 5,050 fewer to 98 fewer) • **4,042 fewer per 10,000** (from 5,625 fewer to 505 fewer)	Meta-analyzed (Table 2)
Children born at term						
Melamed, 2019 (Canada)[30] ★★★★★★★★	Composite long-term outcome of any of the following: • audiometry testing • visual testing • suspected neurocognitive disorder	3346/5423	302520/523782	**Adj HR: 1.12 (1.08-1.16)**	**415 more per 10,000** (from 281 more to 544 more)	⊕⊕◯◯ Low
	Visual testing • any consultations or assessments from an ophthalmologist or optometrist	2461/5423	227948/523782	**Adj HR: 1.08 (1.04-1.12)**	**252 more per 10,000** (from 128 more to 374 more)	⊕⊕◯◯ Low
	Audiometry testing • physician service claim for this testing outside the routine provincial infant screening programme for hearing deficits	827/5423	66555/523782	**Adj HR: 1.18 (1.11-1.25)**	**211 more per 10,000** (from 130 more to 292 more)	⊕⊕◯◯ Low
	Suspected neurocognitive disorder • any physician service claim with a diagnosis code related to a suspected neurocognitive disorder	1397/5423	113181/523782	**Adj HR: 1.16 (1.10-1.21)**	**299 more per 10,000** (from 189 more to 391 more)	⊕⊕◯◯ Low

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported relative effect (95% CI)**	**Absolute effect (95% CI)**	**GRADE certainty**
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Psychological development disorders	269/6730	17994/634757	**Adj HR: 1.45 (1.28-1.64)**	**125 more per 10,000** (from 78 more to 177 more)	⨁⨁◯◯ Low
	Autism spectrum disorders	28/6730	2684/634757	Adj HR: 1.06 (0.73-1.54)	3 more per 10,000 (from 11 fewer to 23 more)	⨁◯◯◯ Very low[a]
	Attention-deficit/hyperactivity or conduct disorders	84/6730	6448/634757	**Adj HR: 1.33 (1.06-1.65)**	**33 more per 10,000** (from 6 more to 65 more)	⨁⨁◯◯ Low
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	87/6730	6077/634757	**Adj HR: 1.47 (1.36-1.60)**	**45 more per 10,000** (from 34 more to 57 more)	⨁⨁◯◯ Low
	Other behavioral and emotional disorders	115/6730	7583/634757	**Adj HR: 1.42 (1.14-1.76)**	**50 more per 10,000** (from 17 more to 90 more)	⨁⨁◯◯ Low
	Psychotic, mood, neurotic, stress-related, or somatization disorders	24/6730	2143/634757	Adj HR: 1.20 (0.80-1.80)	7 more per 10,000 (from 7 fewer to 27 more)	⨁◯◯◯ Very low[a]
	Eating disorders	4/6730	224/634757	Adj HR: 1.61 (0.60-4.35)	2 more per 10,000 (from 1 fewer to 12 more)	⨁◯◯◯ Very low[a]
	Sleep disorders	41/6730	2082/634757	**Adj HR: 1.79 (1.31-2.44)**	**26 more per 10,000** (from 10 more to 47 more)	⨁⨁◯◯ Low

Study (country) [Risk of bias assessment]	Neurodevelopmental/psychological outcomes (with definitions when available)	Unspecified number of courses of ACS (n/N)	Unexposed group (n/N)	Reported relative effect (95% CI)	Absolute effect (95% CI)	GRADE certainty
	Mild, moderate, unspecified intellectual disability	25/6730	2093/634757	Adj HR: 0.96 (0.64-1.42)	1 fewer per 10,000 (from 12 fewer to 14 more)	⨁◯◯◯ Very low[a]
	Severe, profound intellectual disability	3/6730	197/634757	Adj HR: 1.37 (0.62-3.02)	1 more per 10,000 (from 1 fewer to 6 more)	⨁◯◯◯ Very low[a]

Legend:
ACS – antenatal corticosteroids; CI – confidence interval; SD – standard deviation; diff – difference; adj – adjusted; HR – hazard ratio; OR – odds ratio; KSPD – Kyoto Scale of Psychological Development; BSID – Bayley Scales of Infant and Toddler Development; GMFCS – Gross Motor Function Classification System; ZS – z-score; HC – head circumference; NS – not stated/defined; IQ – intelligence quotient; HCA – histological chorioamnionitis; MDI – mental development index; PDI – psychomotor development index; GA – gestational age

Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded

GRADE Assessment: Low rating indicates no serious concerns in GRADE domains and no other considerations were made; a–serious rating for imprecision due to small sample size/wide 95% CI's; b–serious rating for risk of bias due to low Newcastle-Ottawa scale rating (i.e., <6 stars). For pooled outcomes refer to eTable 6.

Green font– a statistically sign

Significant beneficial outcome, grey highlighting – not measured/reported, **red font**– a statistically significant harmful outcome

eTable 5. Individual Unadjusted Neurodevelopmental/Psychological Outcomes of Included Studies on an Unspecified Number of Courses of Antenatal Corticosteroids vs. Non-Exposure in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Children born preterm or at term					
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Any mental and behavioral disorder in all children born preterm/term • *all consecutive sibling pairs discordant for treatment-exposure vs concordant for non-exposure* • *younger treatment-exposed and older non-exposed vs both younger and older non-exposed* • *all consecutive sibling pairs with first sibling pair discordant for treatment-exposure for each mother versus first sibling pair concordant for non-exposure for each mother*	1785/14868	42243/655229	**Unadjusted absolute diff: 5.56 (5.04-6.19)** • **Unadjusted absolute diff: 2.40 (1.67-3.21)** • **Unadjusted absolute diff: 1.58 (0.66-2.66)** • **Unadjusted absolute diff: 2.35 (1.51-3.30)**	⊕⊕◯◯ Low
	Psychological development disorders	956/14868	19089/655229	**Unadjusted absolute diff: 3.52 (3.12-3.93)**	⊕⊕◯◯ Low
	Autism spectrum disorders	96/14868	2807/655229	**Unadjusted absolute diff: 1.22 (0.10-0.36)**	⊕⊕◯◯ Low

Study (country) [Risk of bias assessment]	Neurodevelopmental/psychological outcomes (with definitions when available)	Unspecified number of courses of ACS (n/N)	Unexposed group (n/N)	Reported effect measure & size (95% CI)	GRADE certainty
	Attention-deficit/hyperactivity or conduct disorders	216/14868	6773/655229	**Unadjusted absolute diff: 0.42 (0.24-0.64)**	⊕⊕◯◯ Low
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	181/14868	6350/655229	**Unadjusted absolute diff: 0.25 (0.08-0.44)**	⊕⊕◯◯ Low
	Other behavioral and emotional disorders	345/14868	8049/655229	**Unadjusted absolute diff: 1.09 (0.86-1.35)**	⊕⊕◯◯ Low
	Psychotic, mood, neurotic, stress-related, or somatization disorders	71/14868	2241/655229	**Unadjusted absolute diff: 0.14 (0.04-1.26)**	⊕⊕◯◯ Low
	Eating disorders	6/14868	243/655229	Unadjusted absolute diff: 0.02 (-0.01-0.08)	⊕◯◯◯ Very low[a]
	Sleep disorders	79/14868	2110/655229	**Unadjusted absolute diff: 0.21 (0.10-0.34)**	⊕⊕◯◯ Low
	Mild, moderate, unspecified intellectual disability	101/14868	2259/655229	**Unadjusted absolute diff: 0.33 (0.21-0.48)**	⊕⊕◯◯ Low
	Severe, profound intellectual disability	18/14868	219/655229	**Unadjusted absolute diff: 0.09 (0.04-0.16)**	⊕⊕◯◯ Low
Children born preterm					
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Any mental and behavioral disorder	1187/8138	2192/20472	**Unadjusted absolute diff: 3.88 (2.95-4.87)**	⊕⊕◯◯ Low
	Psychological development disorders	687/8138	1095/20472	**Unadjusted absolute diff: 3.09 (2.35-3.91)**	⊕⊕◯◯ Low

Study (country) [Risk of bias assessment]	Neurodevelopmental/psychological outcomes (with definitions when available)	Unspecified number of courses of ACS (n/N)	Unexposed group (n/N)	Reported effect measure & size (95% CI)	GRADE certainty
	Autism spectrum disorders	68/8138	123/20472	**Unadjusted absolute diff: 0.23 (0.02-0.52)**	⊕◯◯◯ Very low[a]
	Attention-deficit/hyperactivity or conduct disorders	132/8138	325/20472	Unadjusted absolute diff: 0.03 (–0.26-0.02)	⊕◯◯◯ Very low[a]
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	94/8138	273/20472	Unadjusted absolute diff: –0.18 (–0.42-0.12)	⊕◯◯◯ Very low[a]
	Other behavioral and emotional disorders	230/8138	466/20472	Unadjusted absolute diff: –0.18 (–0.42-0.12)	⊕◯◯◯ Very low[a]
	Psychotic, mood, neurotic, stress-related, or somatization disorders	47/8138	98/20472	Unadjusted absolute diff: 0.10 (–0.07-0.34)	⊕◯◯◯ Very low[a]
	Eating disorders	5/8138	19/20472	Unadjusted absolute diff: –0.03 (–0.07 - 0.07)	⊕◯◯◯ Very low[a]
	Sleep disorders	38/8138	82/20472	Unadjusted absolute diff: 0.07 (–0.08 - 0.28)	⊕⊕◯◯ Low
	Mild, moderate, unspecified intellectual disability	76/8138	166/20472	Unadjusted absolute diff: 0.12 (–1.10 - 0.41)	⊕⊕◯◯ Low
	Severe, profound intellectual disability	15/8138	22/20472	Unadjusted absolute diff: 0.01 (–0.02 - 0.11)	⊕◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Gentle, 2020 (U.S.)[16] ★★★★★★★	Severe neurodevelopmental impairment • severe cerebral palsy (GMFCS levels 4-5), BSID-III motor or cognitive composite score <70, bilateral blindness, or hearing impairment	76/358	28/158	Unadjusted OR: 1.01 (0.65-1.55)	Meta-analyzed (eTable 6)
	Bilateral blindness • with no useful vision in either eye	1/333	0/252		⊕◯◯◯ Very low[a]
	Hearing impairment • whether infant has any hearing impairment event with amplification	8/364	6/158	Unadjusted OR: 0.84 (0.35-2.02)	⊕◯◯◯ Very low[a]
	Moderate to severe cerebral palsy	35/361	13/159		Meta-analyzed (eTable 6)
	BSID-III motor composite score <70	59/355	22/156		⊕◯◯◯ Very low[a]
	BSID-III cognitive composite score <70	43/355	14/157		⊕◯◯◯ Very low[a]
Bulbul, 2020 (Turkey)[18] ★★★★★★½	BSID-III cognitive score	Mean (SD): 91.4 (12.3), n=51	Mean (SD): 94.3 (10.7), n=45		⊕◯◯◯ Very low[a]
	BSID-III language score	Mean (SD): 89.5 (11.6), n=51	Mean (SD): 96.7 (11.5) n=45		⊕◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Ushida, 2020a (Japan)[20] ★★★★★★½	Visual impairment	303/4906 • *Singletons:* 243/3908 • *Twins:* 60/998	243/4497 • *Singletons:* 189/3547 • *Twins:* 54/950	• *Singletons;* unadjusted OR: 1.18 (0.97-1.43) • *Twins;* unadjusted OR: 1.06 (0.73-1.55)	Meta-analyzed (eTable 6)
	Hearing impairment	25/4008 • *Singletons*: 21/3192 • *Twins*: 4/816	38/3460 • *Singletons*: 31/2737 • *Twins*: 7/723	• *Singletons;* unadjusted OR: 0.58 (0.23-1.01) • *Twins;* unadjusted OR: 0.50 (0.15-1.73)	Meta-analyzed (eTable 6)
	Cerebral palsy	405/5076 • *Singletons*: 313/4042 • *Twins*: 92/1034	437/4683 • *Singletons*: 332/3693 • *Twins*: 105/990	• *Singletons;* **unadjusted OR: 0.85 (0.72-0.99)** • *Twins;* unadjusted OR: 0.82 (0.61-1.11)	Meta-analyzed (eTable 6)

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
	KSPD Development quotient <70	500/3320 • *Singletons*: 391/2687 • *Twins*: 109/633	494/3126 • *Singletons*: 395/2496 • *Twins*: 99/630	• *Singletons;* unadjusted OR: 0.91 (0.78-1.05) • *Twins;* unadjusted OR: 1.12 (0.83-1.50)	⨁◯◯◯ Very low[a]
Ushida, 2020b (Japan)[21] ★★★★★★½	Blindness • with no functional vision in at least one eye or bilateral amblyopia	• *HDP*: 47/942 • *Non-HDP*: 191/3402	• *HDP*: 36/827 • *Non-HDP*: 142/2347	• *HDP*; unadjusted OR: 1.15 (0.74-1.80) • *Non-HDP*; unadjusted OR: 0.92 (0.74-1.16)	⨁◯◯◯ Very low[a]
	Hearing impairment • need for hearing aids	• *HDP*: 4/713 • *Non-HDP*: 42/2725	• *HDP*: 6/631 • *Non-HDP*: 38/1793	• *HDP*; unadjusted OR: 0.61 (0.18-2.04) • *Non-HDP*; unadjusted OR: 0.72 (0.46-1.13)	⨁◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
	Cerebral palsy	• *HDP*: 58/975 • *Non-HDP*: 271/3510	• *HDP*: 46/851 • *Non-HDP*: 259/2458	• *HDP*; unadjusted OR: 1.11 (0.74-1.65) • *Non-HDP*; **unadjusted OR: 0.71 (0.59-0.85)**	⨁◯◯◯ Very low[a]
	KSPD Quotient <70	• *HDP*: 117/743 • *Non-HDP*: 416/2612	• *HDP*: 93/593 • *Non-HDP*: 274/1643	• *HDP*: unadjusted OR: 1.00 (0.75-1.35) • *Non-HDP*; unadjusted OR: 0.95 (0.80-1.12)	⨁◯◯◯ Very low[a]
	KSPD Quotient <85	• *HDP*: 364/743 • *Non-HDP*: 1283/2612	• *HDP*: 268/593 • *Non-HDP*: 874/1643	• *HDP*: unadjusted OR: 1.16 (0.94-1.45) • *Non-HDP*; **unadjusted OR: 0.85 (0.75-0.96)**	⨁◯◯◯ Very low[a]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Li, 2019 (China)[24] ★★★★★½	Neurodevelopmental disability • moderate-to-severe cerebral palsy (GMFCS level 3-5), Gesell Development Scale development quotient <75 (considered as motor and cognition delay), or language delay (does not achieve the level corresponding to age, assessed with Sign-Significant relations)	10/25	37/106		Meta-analyzed (eTable 6)
Ochiai, 2014 (Japan)[25] ★★★★★½	KSPD Development quotient >50 at 3 years of age	NS	NS	Unadjusted OR: 1.37 (0.35-5.34)	⊕◯◯◯ Very low[a,b]
Kallen, 2015 (Sweden)[27] ★★★★½	Any moderate or severe disability • visual or hearing impairment, cerebral palsy, low BSID-III composite cognitive, language or motor score	114/411	10/45	Unadjusted OR: 1.10	Meta-analyzed (eTable 6)
	Neurosensory impairment • moderate or severe impairment regarding vision and hearing	31/411	3/45	Unadjusted OR: 1.00	⊕◯◯◯ Very low[a,b]
	Mental developmental delay • cognitive or language BSID-III scale < mean -2 SD	82/411	6/45	Unadjusted OR: 0.70	⊕◯◯◯ Very low[a,b]
Sun, 2015 (China)[29] ★★★★½	Cerebral palsy	13/214	6/74		Meta-analyzed (eTable 6)
	BSID-II MDI score <70	50/214	24/74	Unadjusted OR: 0.60 (0.30-1.21)	⊕◯◯◯ Very low[a,b]

Study (country) [Risk of bias assessment]	**Neurodevelopmental/psychological outcomes (with definitions when available)**	**Unspecified number of courses of ACS** (n/N)	**Unexposed group** (n/N)	**Reported effect measure & size (95% CI)**	**GRADE certainty**
Children born at term					
Raikkonen, 2020 (Finland)[12] ★★★★★★★½	Any mental or behavioral disorder	598/6730	40051/634757	**Unadjusted absolute diff: 2.58 (1.92-3.29)**	⊕⊕◯◯ Low
	Psychological development disorders	269/6730	17994/634757	**Unadjusted absolute diff: 1.16 (0.72-1.66)**	⊕⊕◯◯ Low
	Autism spectrum disorders	28/6730	2684/634757	Unadjusted absolute diff: –0.01 (–0.14 - 0.18)	⊕◯◯◯ Very low[a]
	Attention-deficit/hyperactivity or conduct disorders	84/6730	6448/634757	Unadjusted absolute diff: 0.23 (–0.01-0.53)	⊕⊕◯◯ Low
	Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders	87/6730	6077/634757	**Unadjusted absolute diff: 2.58 (1.92-3.29)**	⊕⊕◯◯ Low
	Other behavioral and emotional disorders	115/6730	7583/634757	**Unadjusted absolute diff: 0.34 (0.09-0.64)**	⊕⊕◯◯ Low
	Psychotic, mood, neurotic, stress-related, or somatization disorders	24/6730	2143/634757	Unadjusted absolute diff: 0.02 (–0.10 - 0.20)	⊕◯◯◯ Very low[a]
	Eating disorders	4/6730	224/634757	Unadjusted absolute diff: 0.02 (–0.01 - 0.12)	⊕◯◯◯ Very low[a]
	Sleep disorders	41/6730	2082/634757	**Unadjusted absolute diff: 0.29 (0.13-0.51)**	⊕⊕◯◯ Low

Study (country) [Risk of bias assessment]	Neurodevelopmental/psychological outcomes (with definitions when available)	Unspecified number of courses of ACS (n/N)	Unexposed group (n/N)	Reported effect measure & size (95% CI)	GRADE certainty
	Mild, moderate, unspecified intellectual disability	25/6730	2093/634757	Unadjusted absolute diff: 0.04 (–0.08 - 0.22)	⊕◯◯◯ Very low[a]
	Severe, profound intellectual disability	3/6730	197/634757	Unadjusted Absolute diff: 0.08 (–0.01 - 0.25)	⊕◯◯◯ Very low[a]

Legend:
ACS – antenatal corticosteroids; CI – confidence interval; diff – difference; adj – adjusted; HR – hazard ratio; OR – odds ratio; KSPD – Kyoto Scale of Psychological Development; BSID – Bayley Scales of Infant and Toddler Development; SD – standard deviation; GMFCS – Gross Motor Function Classification System; HDP – hypertensive disorders of pregnancy; NS – not stated/defined; MDI – mental development index; PDI – psychomotor development index; GA – gestational age

Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded

GRADE Assessment: Low rating indicates no serious concerns in GRADE domains and no other considerations were made; a–serious rating for imprecision due to small sample size/wide 95% CI's; b–serious rating for risk of bias due to low Newcastle-Ottawa scale rating (i.e., <6 stars). For pooled outcomes refer to eTable 6.

Green font– a statistically sign

Significant beneficial outcome, grey highlighting – not measured/reported, **red font**– a statistically significant harmful outcome

eTable 6. Summary of Findings Table of Secondary Meta-analyzed Outcomes in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Single course of ACS**	**unexposed to ACS**	**Relative (95% CI)**	**Absolute (95% CI)**	
A single course of ACS versus those unexposed											
Children born preterm											
Cerebral palsy (adjusted)											
Two studies	observational studies	not serious	not serious	not serious	not serious	none	-	-	**OR 0.60 (0.43 to 0.83)**	**1 fewer per 1,000** (from 1 fewer to 0 fewer)	⊕⊕◯◯ Low
Moderate/severe cerebral palsy (adjusted)											
Two studies	observational studies	not serious	not serious	not serious	not serious	none	-	-	OR 0.82 (0.56 to 1.19)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⊕⊕◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Auditory impairment (adjusted)											
Three studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	-	-	OR 0.58 (0.33 to 1.01)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low
Visual impairment (adjusted)											
Three studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	-	-	OR 1.42 (0.57 to 3.54)	1 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Single course of ACS**	**unexposed to ACS**	**Relative (95% CI)**	**Absolute (95% CI)**	
Neurodevelopmental impairment (unadjusted)											
Four studies	observational studies	not serious	not serious	not serious	not serious	none	1049/3452 (30.4%)	253/596 (42.4%)	RR 0.83 (0.65 to 1.05)	72 fewer per 1,000 (from 149 fewer to 21 more)	⨁⨁◯◯ Low
Cerebral palsy (unadjusted)											
Four studies	observational studies	not serious	not serious	not serious	not serious	none	390/3453 (11.3%)	105/597 (17.6%)	**RR 0.73 (0.56 to 0.96)**	**47 fewer per 1,000** (from 77 fewer to 7 fewer)	⨁⨁◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
BSID MDI-II <70 (unadjusted)											
Four studies	observational studies	not serious	not serious	not serious	serious[b]	none	339/1071 (31.7%)	78/194 (40.2%)	RR 0.94 (0.72 to 1.23)	24 fewer per 1,000 (from 113 fewer to 92 more)	⨁◯◯◯ Very low
BSID-III cognitive score <85 (unadjusted)											
Three studies	observational studies	not serious	serious[c]	not serious	serious[b]	none	643/2569 (25.0%)	175/470 (37.2%)	RR 0.56 (0.28 to 1.13)	164 fewer per 1,000 (from 268 fewer to 48 more)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Auditory impairment (unadjusted)											
Four studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	62/3561 (1.7%)	17/616 (2.8%)	RR 0.63 (0.37 to 1.07)	10 fewer per 1,000 (from 17 fewer to 2 more)	⊕◯◯◯ Very low
Visual impairment (unadjusted)											
Four studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	38/3558 (1.1%)	6/615 (1.0%)	RR 1.33 (0.58 to 3.08)	3 more per 1,000 (from 4 fewer to 20 more)	⊕◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Hemiparesis (unadjusted)											
Two studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	5/815 (0.6%)	1/150 (0.7%)	RR 0.83 (0.14 to 5.02)	1 fewer per 1,000 (from 6 fewer to 27 more)	⨁◯◯◯ Very low
Diparesis (unadjusted)											
Two studies	observational studies	serious[a]	not serious	not serious	serious[b]	none	8/815 (1.0%)	5/150 (3.3%)	RR 0.35 (0.06 to 2.18)	22 fewer per 1,000 (from 31 fewer to 39 more)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Body weight (kg) (unadjusted)											
Two studies	observational studies	not serious	serious[c]	not serious	serious[b]	none	2453	424	-	MD 0.29 lower (1.1 lower to 0.51 higher)	⨁◯◯◯ Very low
Head circumference (cm) (unadjusted)											
Two studies	observational studies	not serious	serious[c]	not serious	serious[b]	none	2396	421	-	MD 0.33 lower (1.6 lower to 0.93 higher)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Unspecified number of courses of ACS versus those unexposed											
Children born preterm											
Neurodevelopmental impairment (unadjusted)											
Five studies	observational studies	not serious	not serious	not serious	not serious	none	399/1547 (25.8%)	297/1175 (25.3%)	OR 0.96 (0.61 to 1.50)	8 fewer per 1,000 (from 82 fewer to 84 more)	⊕◯◯◯ Very low
Cerebral palsy (unadjusted)											
Three studies	observational studies	not serious	not serious	not serious	not serious	none	453/5651 (8.0%)	456/4916 (9.3%)	**RR 0.86 (0.76 to 0.98)**	**13 fewer per 1,000** (from 22 fewer to 2 fewer)	⊕⊕◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single course of ACS	unexposed to ACS	Relative (95% CI)	Absolute (95% CI)	
Auditory impairment (unadjusted)											
Two studies	observational studies	not serious	not serious	not serious	serious[b]	none	33/4372 (0.8%)	44/3618 (1.2%)	**RR 0.57 (0.36 to 0.90)**	**5 fewer per 1,000** (from 8 fewer to 1 fewer)	⨁◯◯◯ Very low
Visual impairment (unadjusted)											
Two studies	observational studies	not serious	not serious	not serious	serious[b]	none	304/5239 (5.8%)	243/4749 (5.1%)	RR 1.15 (0.97 to 1.35)	8 more per 1,000 (from 2 fewer to 18 more)	⨁◯◯◯ Very low

Legend:
BSID–Bayley Scales of Infant and Toddler Development; MDI – mental development index; CI– confidence interval; MD– mean difference; OR–odds ratio; RR–risk ratio; bold–statistically significant

GRADE explanations

a. at least one larger study has a high risk of bias rating; b. Small number of total events and wide 95% CI's; c. Significant heterogeneity between studies

eTable 7. Other Long-Term Outcomes of Included Studies in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study (country) [Risk of bias assessment]	Other outcome(s)	Single course of ACS		Unexposed group		Reported effect measure + size (95% CI)	GRADE certainty
		Mean (SD)	No. / Total No.	Mean (SD)	No. / Total No.		
	Children born preterm						
Chawla, 2013 (U.S.)[3] ★★★★★★★★	Body weight at follow-up (kg)	81.2 (4.2)		80.7 (3.7)			Meta-analyzed (eTable 6)
	Length at follow-up (cm)	46.5 (1.6)		47.8 (2.4)			Meta-analyzed (eTable 6)
Gover 2012 (Canada)[2] ★★★★★★★½	Cortisol level at 18 months (ug/dl)	Median: 0.13 (IQR 0.07-0.24)		Median:0.11 (IQR 0.06-1.15)			⊕◯◯◯ Very low[a]
Chawla, 2016 (U.S.)[3] ★★★★★★★	Body weight at follow-up (kg)	10.8 (1.57)		10.76 (1.57)		Adj MD: 0.02 (-0.15-0.19)	Meta-analyzed (eTable 6)
	Head circumference (cm)	46.9 (2)		46.8 (3.2)		Adj MD: -0.05 (-0.28-0.18)	Meta-analyzed (eTable 6)
	Intact survival (defined as the absence of any cerebral palsy, deafness, or blindness and a BSID-III cognitive score of ≥85 at 18-22 months)	1670/2405		233/419		**Adj OR: 1.51 (1.2-1.9)**	⊕⊕◯◯ Low
Tseng, 2016 (Taiwan)[10]	Allergic disease		18/24		3/16	**NS; p<0.0001**	⊕◯◯◯ Very low[a,b]

★★★★½	Asthma		10/24		0/16	**NS; p=0.003**	⊕◯◯◯ Very low[a,b]
	Allergic rhinitis		14/24		3/16	**NS; p=0.013**	⊕◯◯◯ Very low[a,b]
	Atopic dermatitis		6/24		1/16	NS; p=0.126	⊕◯◯◯ Very low[a,b]

Legend:
ACS – antenatal corticosteroids; SD – standard deviation; No. – number; CI – confidence interval; kg – kilograms; Adj – adjusted; MD – mean difference; cm – centimeters; BSID – Bayley Scales of Infant and Toddler Development; OR – odds ratio; NS – not stated; IQR – interquartile ratio;

Newcastle-Ottawa Scale: ★ – point awarded, ½ – half point awarded
*RoB assessments for each outcome for the study resulted in the same domain scores
Green font – a statistically significant beneficial outcome, grey highlighting – not measured/reported, **red font**– a statistically significant harmful outcome

eTable 8. Newcastle-Ottawa Scale Quality Assessment Scores for Non-Randomized Studies Included in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Study, Year (Country)	Total score (max: 9★)	Component scores							
		Representativeness of exposed cohort (max: ★)	Selection of non-exposed cohort (max: ★)	Ascertainment of exposure (max: ★)	Demonstration that outcome of interest was not present at study start (max: ★)	† Comparability of cohorts based on the design or analysis* (max: ★★)	Ascertainment of outcome (max: ★)	Follow-up long enough for outcomes to occur? (max: ★)	Adequacy of cohort follow up (max: ★)
A single course of ACS versus those unexposed									
Children born preterm									
Chawla, 2013 (United States)[1]	8 ★★★★★★★★	★	★	★	★	★☆	★	★	★
Gover, 2012 (Canada)[2]	7.5 ★★★★★★★½	★	★	★	★	★½	☆	★	★
Chawla, 2016 (United States)[3]	7 ★★★★★★★	★	★	★	☆	★☆	★	★	★
Lee, 2008 (United States)[4]	6.5 ★★★★★★½	★	★	★	★	★½	☆	★	☆
Agarwal, 2018 (Singapore)[5]	6 ★★★★★★	★	★	★	★	☆☆	☆	★	★
Kim, 2018 (Korea)[6]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Laughon, 2009 (United States)[7]	5.5 ★★★★★½	★	★	★	☆	½	★	★	☆
McElrath, 2009 (United States)[8]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Lardon, 2017 (Spain)[9]	4.5 ★★★★½	★	★	☆	★	½	☆	★	☆
Tseng, 2016 (Taiwan)[10]	4.5 ★★★★½	★	★	★	☆	½	☆	★	☆
Unspecified number of courses of ACS versus those unexposed									
Children born preterm or at term									

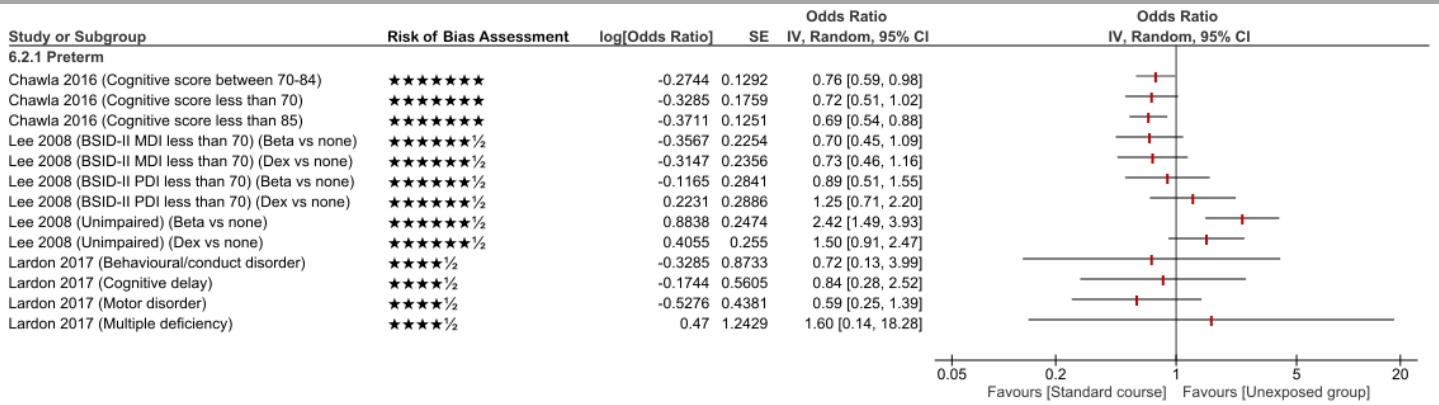
Lamminmaki 2021 (Finland)[11]	7.5 ★★★★★★★½	★	★	★	★	½	★	★	★
Raikkonen, 2020 (Finland)[12]	7.5 ★★★★★★★½	★	★	★	☆	★½	★	★	★
Wolford, 2020 (Finland)[13]	7 ★★★★★★★	★	★	★	☆	★★	★	★	☆
Children born preterm									
Haslam, 2018 (Canada)[14]	8.5 ★★★★★★★★½	★	★	★	★	★½	★	★	★
Aviram, 2021 (Canada)[15]	8 ★★★★★★★★	★	★	★	★	★	★	★	★
Raikkonen, 2020 (Finland)[12]	7.5 ★★★★★★★½	★	★	★	☆	★½	★	★	★
Gentle, 2020 (United States)[16]	7 ★★★★★★★	★	★	★	★	★☆	☆	★	★
Hutcheon, 2020 (Canada)[17]	7 ★★★★★★★	★	★	★	☆	★	★	★	★
Bulbul, 2020 (Turkey)[18]	6.5 ★★★★★★½	★	★	★	★	½	★	★	☆
Miyazaki, 2015 (Japan)[19]	6.5 ★★★★★★½	★	★	★	★	½	★	★	☆
Ushida, 2020a (Japan)[20]	6.5 ★★★★★★½	★	★	★	★	½	★	★	☆
Ushida, 2020b (Japan)[21]	6.5 ★★★★★★½	★	★	★	★	½	☆	★	★
Basset, 2018 (France)[22]	6 ★★★★★★	★	★	☆	★	★☆	☆	★	★
Ishikawa, 2015 (Japan)[23]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Li, 2019 (China)[24]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Ochiai, 2014 (Japan)[25]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Young, 2016 (Canada)[26]	5.5 ★★★★★½	★	★	★	★	½	☆	★	☆
Kallen, 2015 (Sweden)[27]	4.5 ★★★★½	★	★	★	☆	½	☆	★	☆
Kiechl-kohlendorfer, 2009 (Austria)[28]	4.5 ★★★★½	★	★	☆	★	½	☆	★	☆
Sun, 2015 (China)[29]	4.5 ★★★★½	★	★	☆	★	½	☆	★	☆

Children born at term									
Melamed, 2019 (Canada)[30]	8 ★★★★★★★★	★	★	★	★	★☆	★	★	★
Raikkonen, 2020 (Finland)[12]	7.5 ★★★★★★★½	★	★	★	☆	★½	★	★	★

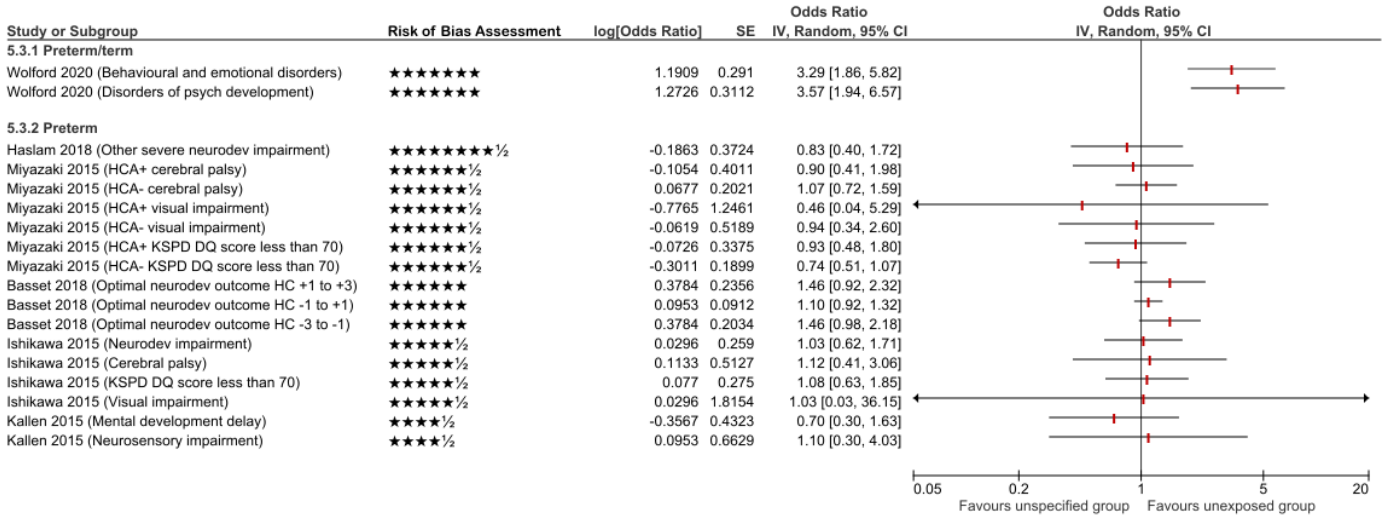
Legend:
★ – point awarded; ½ – half point awarded; ☆ – no point awarded, max – maximum; ACS – antenatal corticosteroids
† If the study addressed any of the following confounding variables (whether through exclusion, stratification, adjustment or matching), we assigned ½ star per factor with a maximum of 2 stars total: postnatal steroids; gestational age at birth; family or maternal history of neurodevelopmental and psychological outcomes (including maternal stress); socioeconomic status; maternal substance use (drugs, alcohol or smoking); and intrauterine growth restriction;

eFigure 1. Visual Representation of Available Individual Adjusted Neurodevelopmental/Psychological Outcomes in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

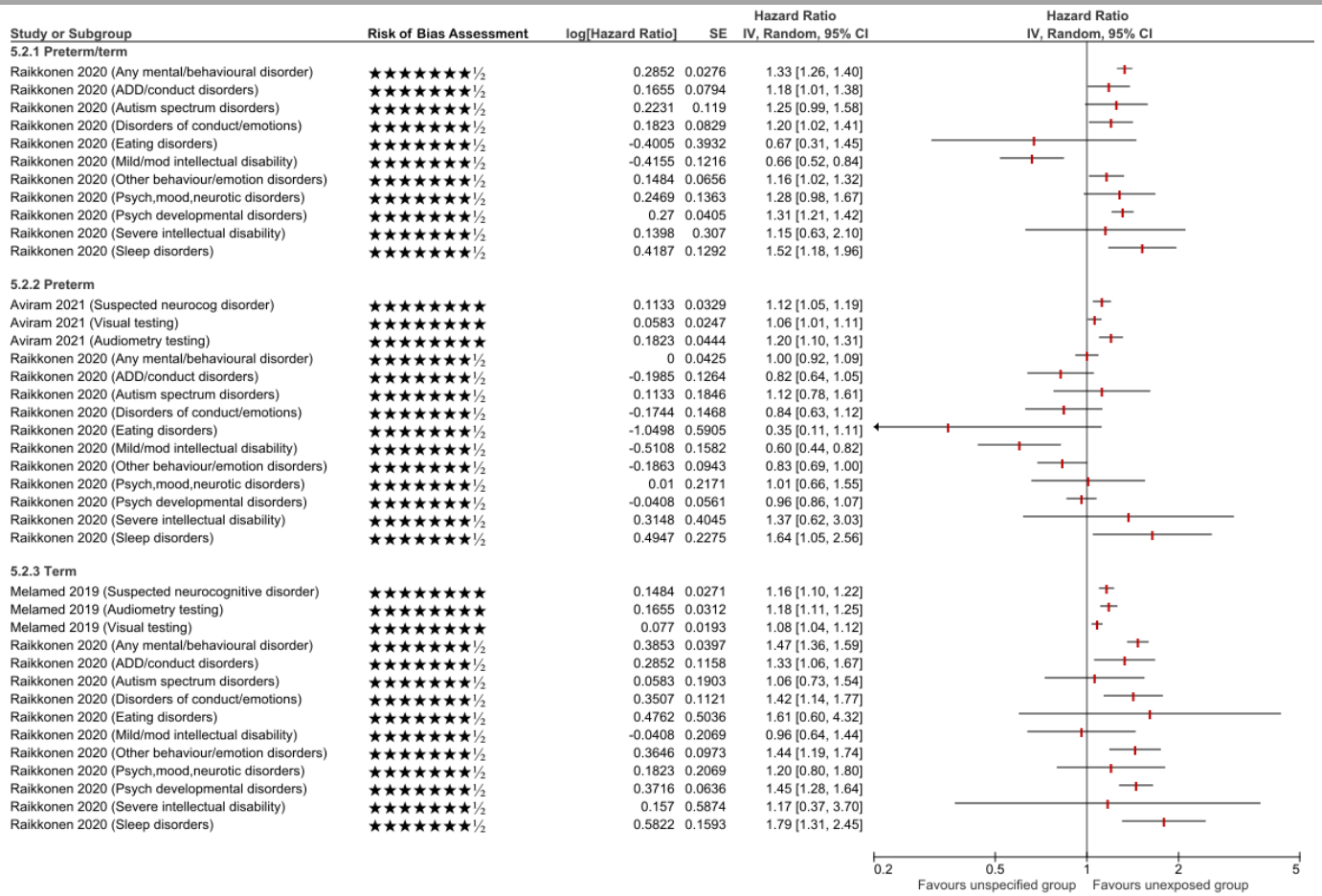
A single (i.e., standard) course of ACS versus those unexposed (adjusted odds ratios)



Unspecified number of courses of ACS versus those unexposed (adjusted odds ratios)



Unspecified number courses of ACS versus those unexposed (adjusted hazard ratios)



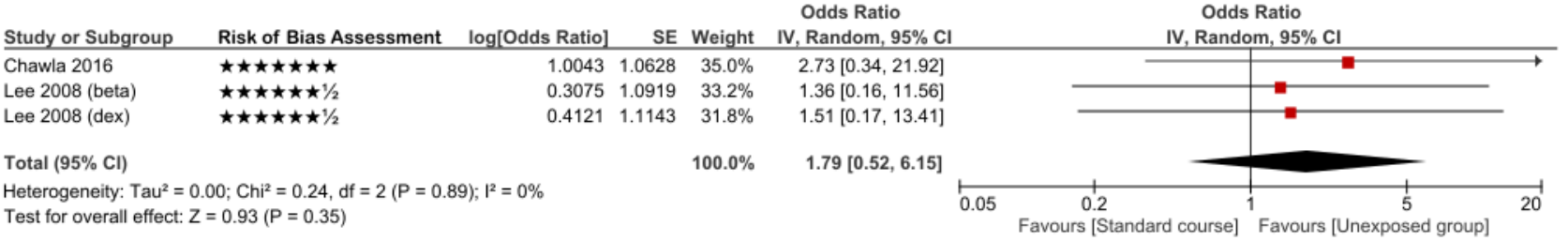
Legend:
ACS – antenatal corticosteroids; SE – standard error; IV – instrumental variable; CI – confidence interval; cognitive score – on BSID-III; neurodev – neurodevelopmental; Beta – betamethasone; vs – versus; Dex – dexamethasone; BSID – Bayley Scales of Infant and Toddler Development; MDI – Mental Development Index; PDI – Psychomotor Development Index; HC – head circumference; KSPD – Kyoto Scale of Psychological Development; DQ – developmental quotient; wk – weeks; GA – gestational age; ADD – attention deficit disorder; mod – moderate; Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded

eFigure 2. Forest Plots of Sensitivity Analyses and Meta-analyzed Unadjusted Neurodevelopmental/Psychological and Other Outcomes in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

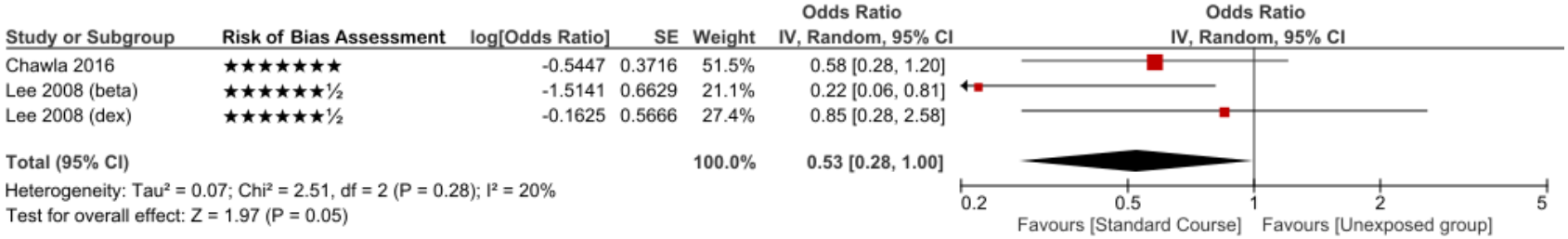
A single (i.e., standard) course of ACS versus those unexposed

Children born preterm

Visual impairment (adjusted data)- sensitivity analysis (removing studies with <6 stars)



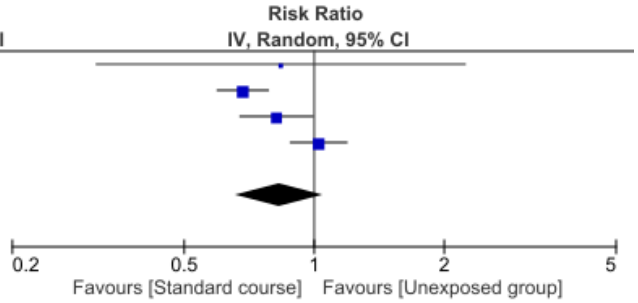
Auditory impairment (adjusted data)- sensitivity analysis (removing studies with <6 stars)



Neurodevelopmental impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	16	51	3	8	5.0%	0.84 [0.31, 2.23]
Chawla 2016	★★★★★★★	651	2405	166	419	33.0%	0.68 [0.60, 0.78]
Lee 2008	★★★★★★½	358	971	69	153	29.7%	0.82 [0.67, 0.99]
Kim 2018	★★★★★½	24	25	15	16	32.2%	1.02 [0.88, 1.19]
Total (95% CI)			**3452**		**596**	**100.0%**	**0.83 [0.65, 1.05]**
Total events		1049		253			

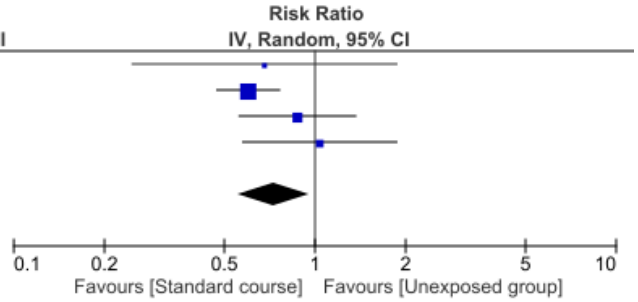
Heterogeneity: Tau² = 0.04; Chi² = 15.46, df = 3 (P = 0.001); I² = 81%
Test for overall effect: Z = 1.55 (P = 0.12)



Cerebral palsy (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	13	51	3	8	6.7%	0.68 [0.25, 1.87]
Chawla 2016	★★★★★★★	252	2404	73	418	50.3%	0.60 [0.47, 0.76]
Lee 2008	★★★★★★½	111	971	20	153	25.9%	0.87 [0.56, 1.36]
Kim 2018	★★★★★½	14	27	9	18	17.1%	1.04 [0.58, 1.87]
Total (95% CI)			**3453**		**597**	**100.0%**	**0.73 [0.56, 0.96]**
Total events		390		105			

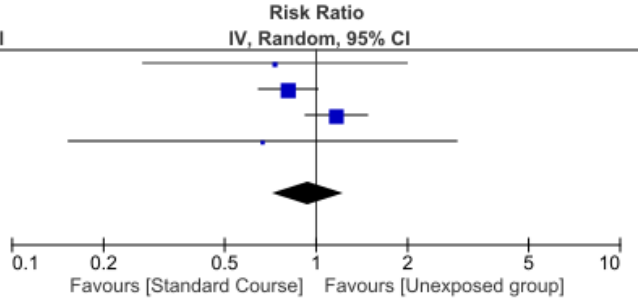
Heterogeneity: Tau² = 0.02; Chi² = 4.24, df = 3 (P = 0.24); I² = 29%
Test for overall effect: Z = 2.23 (P = 0.03)



BSID-II MDI <70 (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	14	51	3	8	6.7%	0.73 [0.27, 1.99]
Lee 2008	★★★★★★½	298	971	58	153	45.7%	0.81 [0.65, 1.01]
Kim 2018	★★★★★½	24	25	14	17	44.4%	1.17 [0.92, 1.47]
Tseng 2016	★★★★½	3	24	3	16	3.3%	0.67 [0.15, 2.90]
Total (95% CI)			**1071**		**194**	**100.0%**	**0.94 [0.72, 1.23]**
Total events		339		78			

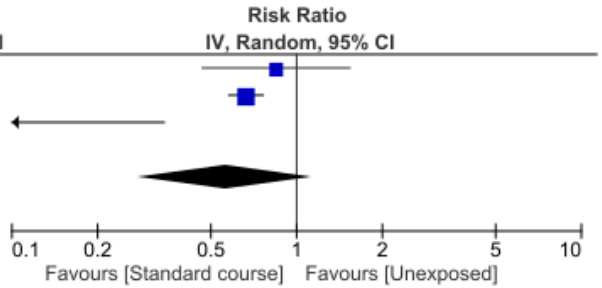
Heterogeneity: Tau² = 0.03; Chi² = 5.38, df = 3 (P = 0.15); I² = 44%
Test for overall effect: Z = 0.45 (P = 0.65)



BSID-III cognitive domain score <85 (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	27	51	5	8	38.4%	0.85 [0.47, 1.54]
Chawla 2016	★★★★★★★	615	2396	162	419	52.0%	0.66 [0.58, 0.76]
Agarwal 2018	★★★★★★	1	122	8	43	9.6%	0.04 [0.01, 0.34]
Total (95% CI)			**2569**		**470**	**100.0%**	**0.56 [0.28, 1.13]**
Total events		643		175			

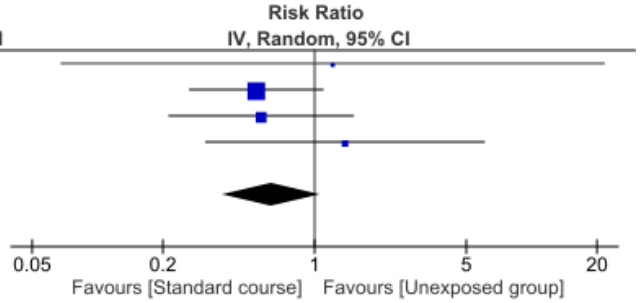
Heterogeneity: Tau² = 0.24; Chi² = 7.37, df = 2 (P = 0.03); I² = 73%
Test for overall effect: Z = 1.61 (P = 0.11)



Auditory impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	3	51	0	8	3.3%	1.21 [0.07, 21.53]
Chawla 2016	★★★★★★★	31	2405	10	418	55.2%	0.54 [0.27, 1.09]
Lee 2008	★★★★★★½	18	971	5	153	28.8%	0.57 [0.21, 1.51]
Lardon 2017	★★★★½	10	134	2	37	12.6%	1.38 [0.32, 6.03]
Total (95% CI)			**3561**		**616**	**100.0%**	**0.63 [0.37, 1.07]**
Total events		62		17			

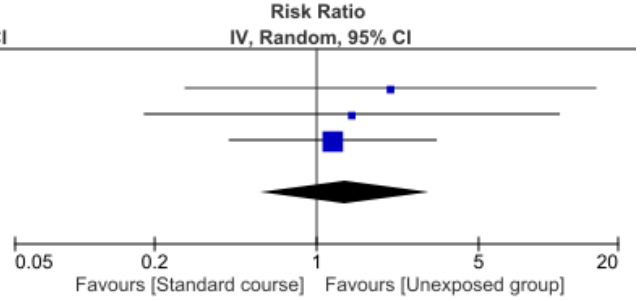
Heterogeneity: Tau² = 0.00; Chi² = 1.52, df = 3 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.71 (P = 0.09)



Visual impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Chawla 2013	★★★★★★★★	0	51	0	8		Not estimable
Chawla 2016	★★★★★★★	12	2402	1	417	16.9%	2.08 [0.27, 15.98]
Lee 2008	★★★★★★½	9	971	1	153	16.5%	1.42 [0.18, 11.11]
Lardon 2017	★★★★½	17	134	4	37	66.6%	1.17 [0.42, 3.28]
Total (95% CI)			**3558**		**615**	**100.0%**	**1.33 [0.58, 3.08]**
Total events		38		6			

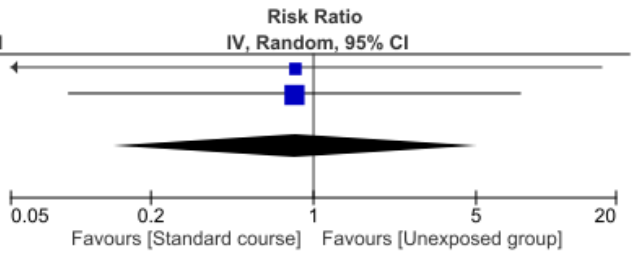
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.67 (P = 0.50)



Hemiparesis (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
McElrath 2009	★★★★★½	2	681	0	113	35.2%	0.84 [0.04, 17.30]
Lardon 2017	★★★★½	3	134	1	37	64.8%	0.83 [0.09, 7.73]
Total (95% CI)			**815**		**150**	**100.0%**	**0.83 [0.14, 5.02]**
Total events		5		1			

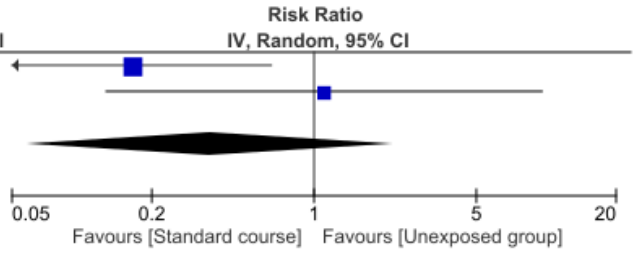
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.20 (P = 0.84)



Diparesis (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
McElrath 2009	★★★★★½	4	681	4	113	60.1%	0.17 [0.04, 0.65]
Lardon 2017	★★★★½	4	134	1	37	39.9%	1.10 [0.13, 9.59]
Total (95% CI)			**815**		**150**	**100.0%**	**0.35 [0.06, 2.18]**
Total events		8		5			

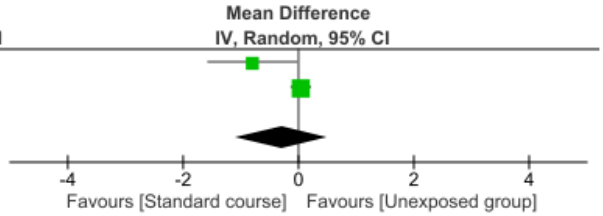
Heterogeneity: Tau² = 0.94; Chi² = 2.11, df = 1 (P = 0.15); I² = 53%
Test for overall effect: Z = 1.12 (P = 0.26)



Body weight (kg) (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard course Mean	Standard course SD	Standard course Total	Unexposed group Mean	Unexposed group SD	Unexposed group Total	Weight	Mean Difference IV, Random, 95% CI
Chawla 2013	★★★★★★★★	10.4	1.2	51	11.2	1	8	39.6%	-0.80 [-1.57, -0.03]
Chawla 2016	★★★★★★★	10.8	1.57	2402	10.76	1.57	416	60.4%	0.04 [-0.12, 0.20]
Total (95% CI)				**2453**			**424**	**100.0%**	**-0.29 [-1.10, 0.51]**

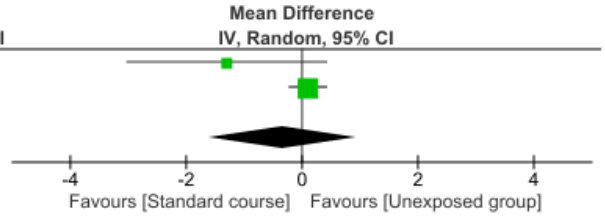
Heterogeneity: Tau² = 0.27; Chi² = 4.40, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.71 (P = 0.48)



Head circumference (cm) (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard course Mean	SD	Total	Unexposed group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chawla 2013	★★★★★★★★	46.5	1.6	51	47.8	2.4	8	31.0%	-1.30 [-3.02, 0.42]
Chawla 2016	★★★★★★★	46.9	2	2345	46.8	3.2	413	69.0%	0.10 [-0.22, 0.42]
Total (95% CI)				**2396**			**421**	**100.0%**	**-0.33 [-1.60, 0.93]**

Heterogeneity: Tau² = 0.58; Chi² = 2.46, df = 1 (P = 0.12); I² = 59%
Test for overall effect: Z = 0.52 (P = 0.61)



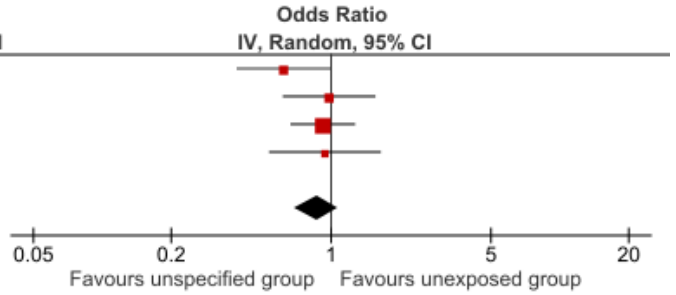
Unspecified number of courses of ACS versus those unexposed

Children born preterm

Neurodevelopmental impairment (adjusted data)- sensitivity analysis (removing studies with <6 stars)

Study or Subgroup	Risk of Bias Assessment	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Haslam 2018	★★★★★★★★½	-0.478	0.2365	20.6%	0.62 [0.39, 0.99]
Gentle 2020	★★★★★★★	-0.0202	0.2336	21.1%	0.98 [0.62, 1.55]
Miyazaki 2015 (HCA-)	★★★★★★½	-0.0834	0.1618	44.0%	0.92 [0.67, 1.26]
Miyazaki 2015 (HCA+)	★★★★★★½	-0.0619	0.2828	14.4%	0.94 [0.54, 1.64]
Total (95% CI)				**100.0%**	**0.86 [0.70, 1.06]**

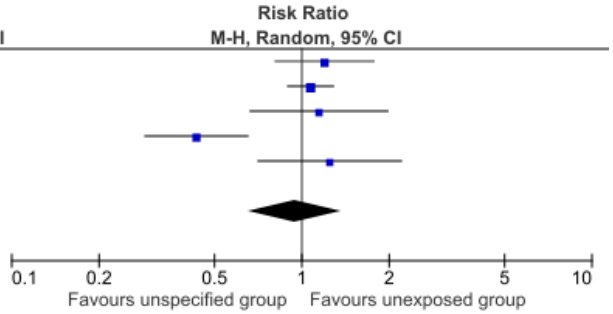
Heterogeneity: Tau² = 0.00; Chi² = 2.50, df = 3 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.38 (P = 0.17)



Neurodevelopmental impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Total	Unexposed Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gentle 2020	★★★★★★★	76	358	28	158	20.8%	1.20 [0.81, 1.77]
Miyazaki 2015	★★★★★★½	151	571	208	843	25.3%	1.07 [0.89, 1.28]
Li 2019	★★★★★½	10	25	37	106	17.1%	1.15 [0.66, 1.98]
Kiechl-Kohlendorfer 2009	★★★★½	48	182	14	23	20.3%	0.43 [0.29, 0.65]
Källén 2015	★★★★½	114	411	10	45	16.6%	1.25 [0.71, 2.20]
Total (95% CI)			**1547**		**1175**	**100.0%**	**0.95 [0.65, 1.38]**
Total events		399		297			

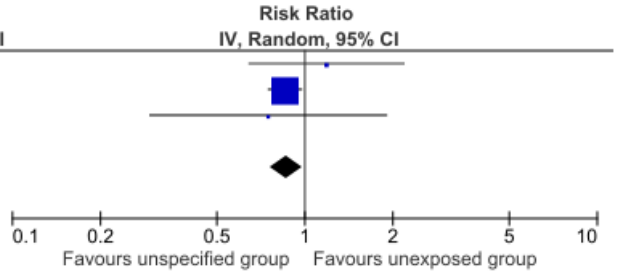
Heterogeneity: Tau² = 0.14; Chi² = 18.96, df = 4 (P = 0.0008); I² = 79%
Test for overall effect: Z = 0.29 (P = 0.77)



Cerebral palsy (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Undefined Courses Events	Undefined Courses Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Gentle 2020	★★★★★★★	35	361	13	159	4.2%	1.19 [0.65, 2.18]
Ushida 2020a	★★★★★★½	405	5076	437	4683	94.0%	0.86 [0.75, 0.97]
Sun 2015	★★★★½	13	214	6	74	1.8%	0.75 [0.30, 1.90]
Total (95% CI)			**5651**		**4916**	**100.0%**	**0.86 [0.76, 0.98]**
Total events		453		456			

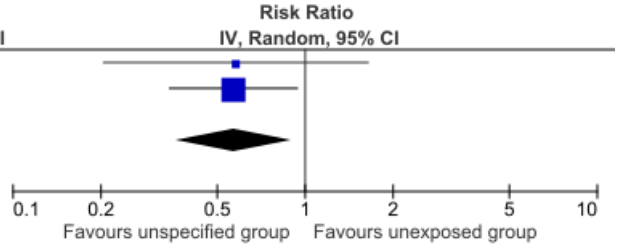
Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.27 (P = 0.02)



Auditory impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Undefined Courses Events	Undefined Courses Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Gentle 2020	★★★★★★★	8	364	6	158	18.9%	0.58 [0.20, 1.64]
Ushida 2020a	★★★★★★½	25	4008	38	3460	81.1%	0.57 [0.34, 0.94]
Total (95% CI)			**4372**		**3618**	**100.0%**	**0.57 [0.36, 0.90]**
Total events		33		44			

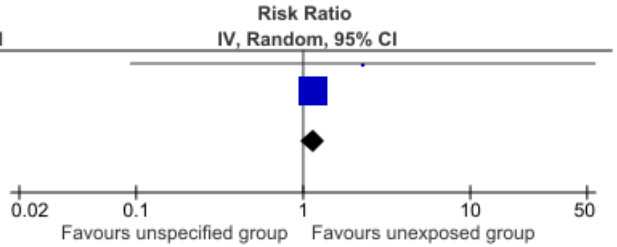
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.43 (P = 0.01)



Visual impairment (unadjusted data)

Study or Subgroup	Risk of Bias Assessment	Undefined Courses Events	Undefined Courses Total	Unexposed Events	Unexposed Total	Weight	Risk Ratio IV, Random, 95% CI
Gentle 2020	★★★★★★★	1	333	0	252	0.3%	2.27 [0.09, 55.55]
Ushida 2020a	★★★★★★½	303	4906	243	4497	99.7%	1.14 [0.97, 1.35]
Total (95% CI)			**5239**		**4749**	**100.0%**	**1.15 [0.97, 1.35]**
Total events		304		243			

Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.62 (P = 0.10)

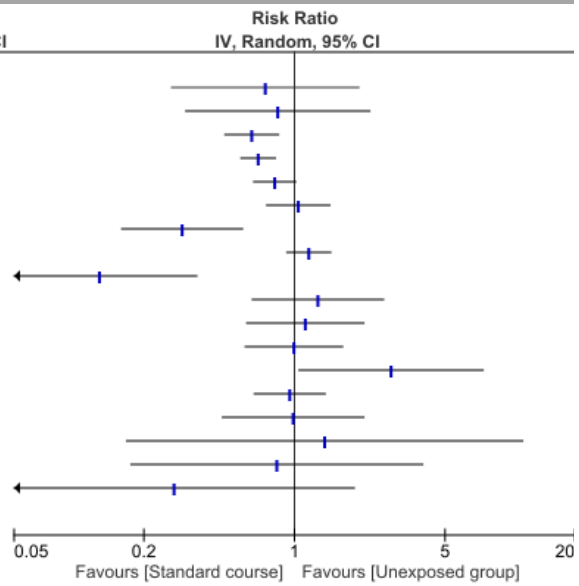


Legend:
ACS – antenatal corticosteroids; IV – instrumental variable; CI – confidence interval; BSID – Bayley Scales of Infant and Toddler Development; MDI – Mental Development Index
Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded

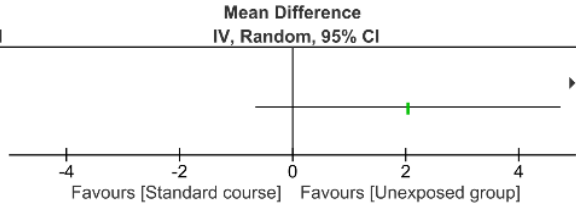
eFigure 3. Visual Representation of Available Individual Unadjusted Neurodevelopmental/Psychological Outcomes in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

A single (i.e., standard) course of ACS versus no ACS exposure

Study or Subgroup	Risk of Bias Assessment	Standard Course Events	Standard Course Total	Unexposed Events	Unexposed Total	Risk Ratio IV, Random, 95% CI
6.1.1 Preterm						
Chawla 2013 (Cognitive score less than 70)	★★★★★★★★	14	51	3	8	0.73 [0.27, 1.99]
Chawla 2013 (Neurodev impairment)	★★★★★★★★	16	51	3	8	0.84 [0.31, 2.23]
Chawla 2016 (Cognitive score less than 70)	★★★★★★★	192	2396	53	419	0.63 [0.48, 0.84]
Chawla 2016 (Cognitive score between 70-84)	★★★★★★★	423	2396	109	419	0.68 [0.57, 0.82]
Lee 2008 (BSID-II MDI less than 70)	★★★★★★½	298	971	58	153	0.81 [0.65, 1.01]
Lee 2008 (BSID-II PDI less than 70)	★★★★★★½	205	971	31	153	1.04 [0.74, 1.46]
Agarwal 2018 (Abnormal language score)	★★★★★★	15	153	14	43	0.30 [0.16, 0.57]
Kim 2018 (Developmental delay)	★★★★★½	24	25	14	17	1.17 [0.92, 1.47]
McElrath 2009 (Quadriparesis)	★★★★★½	6	681	8	113	0.12 [0.04, 0.35]
Laughon 2007 (BSID-II MDI score 55-59)	★★★★★½	65	588	8	93	1.29 [0.64, 2.59]
Laughon 2007 (BSID-II MDI score less than 55)	★★★★★½	71	588	10	93	1.12 [0.60, 2.10]
Laughon 2007 (BSID-II PDI score 55-59)	★★★★★½	88	588	14	93	0.99 [0.59, 1.67]
Laughon 2007 (BSID-II PDI score less than 55)	★★★★★½	71	588	4	93	2.81 [1.05, 7.50]
Lardon 2017 (Cognitive delay)	★★★★½	62	134	18	37	0.95 [0.65, 1.39]
Lardon 2017 (Motor disorder)	★★★★½	25	134	7	37	0.99 [0.46, 2.10]
Lardon 2017 (Multiple deficiency)	★★★★½	5	134	1	37	1.38 [0.17, 11.46]
Lardon 2017 (Behavioural/conduct disorder)	★★★★½	6	134	2	37	0.83 [0.17, 3.94]
Lardon 2017 (Tetraparesis)	★★★★½	2	134	2	37	0.28 [0.04, 1.89]

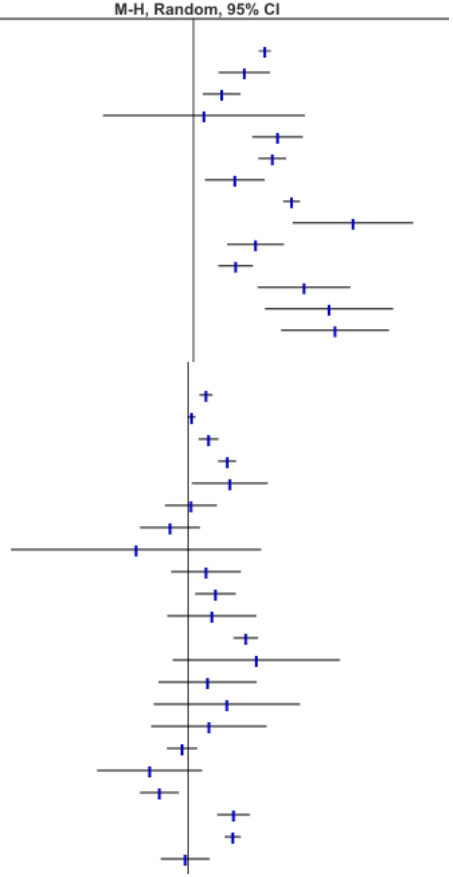


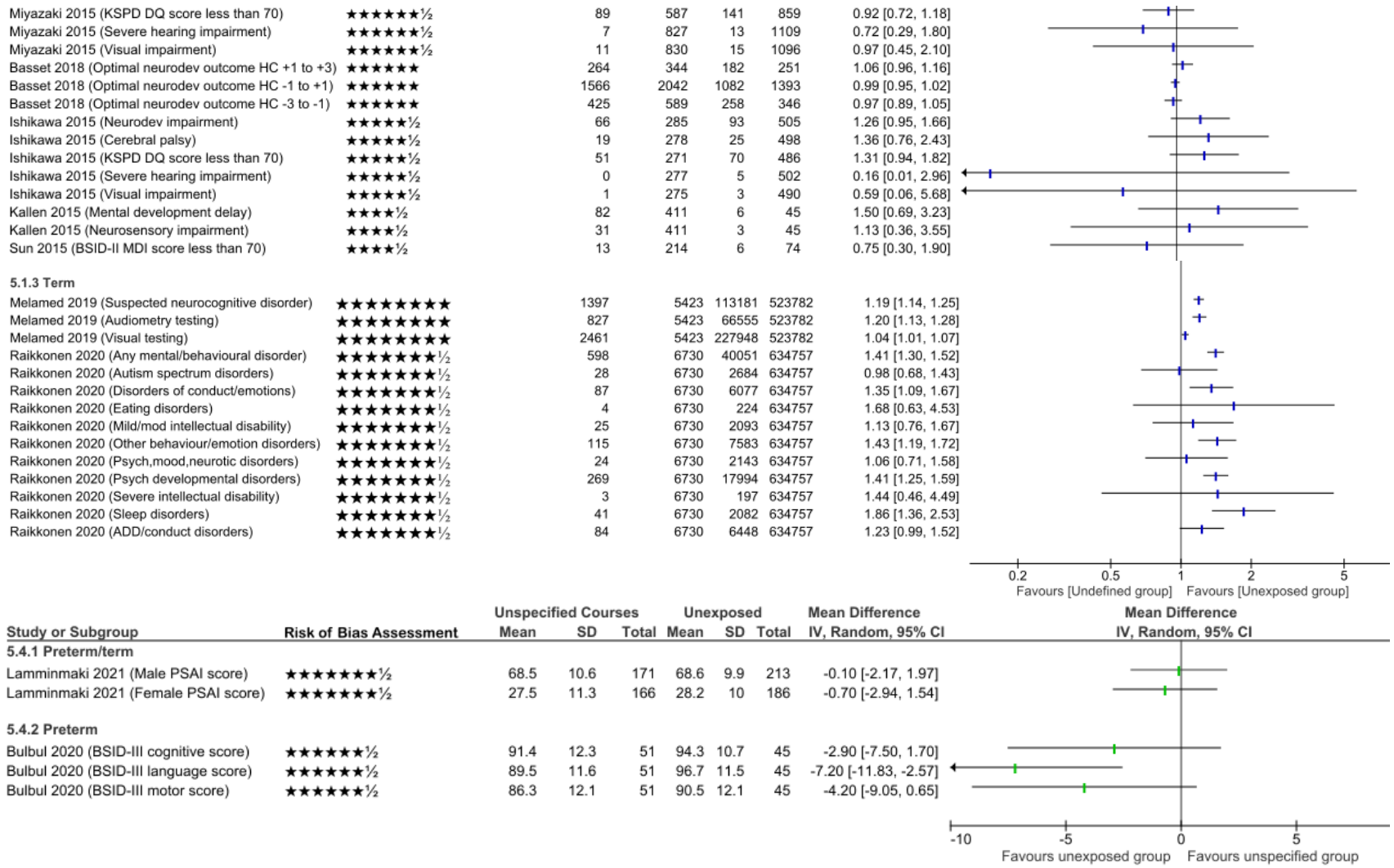
Study or Subgroup	Risk of Bias Assessment	Standard Course Mean	Standard Course SD	Standard Course Total	Unexposed Mean	Unexposed SD	Unexposed Total	Mean Difference IV, Random, 95% CI
6.3.1 Preterm								
Tseng 2016 (BSID-II MDI score)	★★★★★½	90.38	3.31	24	79.94	3.58	16	10.44 [8.24, 12.64]
Tseng 2016 (BSID-II PDI score)	★★★★★½	78.17	3.81	24	76.13	4.51	16	2.04 [-0.64, 4.72]



Unspecified number of courses of ACS versus no ACS exposure

Study or Subgroup	Risk of Bias Assessment	Favours [Undefined group] Events	Total	Unexposed Events	Total	Risk Ratio M-H, Random, 95% CI
5.1.1 Preterm/term						
Raikkonen 2020 (Any mental/behavioural disorder)	★★★★★★★½	1785	14868	44243	655229	1.78 [1.70, 1.86]
Raikkonen 2020 (Autism spectrum disorders)	★★★★★★★½	96	14868	2807	655229	1.51 [1.23, 1.85]
Raikkonen 2020 (Disorders of conduct/emotions)	★★★★★★★½	181	14868	6350	655229	1.26 [1.08, 1.45]
Raikkonen 2020 (Eating disorders)	★★★★★★★½	6	14868	243	655229	1.09 [0.48, 2.45]
Raikkonen 2020 (Mild/mod intellectual disability)	★★★★★★★½	101	14868	2259	655229	1.97 [1.62, 2.40]
Raikkonen 2020 (Other behaviour/emotion disorders)	★★★★★★★½	345	14868	8049	655229	1.89 [1.70, 2.10]
Raikkonen 2020 (Psych,mood,neurotic disorders)	★★★★★★★½	71	14868	2241	655229	1.40 [1.10, 1.77]
Raikkonen 2020 (Psych developmental disorders)	★★★★★★★½	956	14868	19089	655229	2.21 [2.07, 2.35]
Raikkonen 2020 (Severe intellectual disability)	★★★★★★★½	18	14868	219	655229	3.62 [2.24, 5.86]
Raikkonen 2020 (Sleep disorders)	★★★★★★★½	79	14868	2110	655229	1.65 [1.32, 2.06]
Raikkonen 2020 (ADD/conduct disorders)	★★★★★★★½	216	14868	6773	655229	1.41 [1.23, 1.61]
Wolford 2020 (Any mental or behavioural disorder)	★★★★★★★	24	117	386	4591	2.44 [1.69, 3.53]
Wolford 2020 (Behavioural and emotional disorders)	★★★★★★★	14	117	184	4591	2.99 [1.79, 4.98]
Wolford 2020 (Disorders of psych development)	★★★★★★★	19	117	238	4591	3.13 [2.04, 4.81]
5.1.2 Preterm						
Aviram 2021 (Suspected neurocog disorder)	★★★★★★★★	1156	2689	8581	22979	1.15 [1.10, 1.21]
Aviram 2021 (Visual testing)	★★★★★★★★	1860	2689	15483	22979	1.03 [1.00, 1.05]
Aviram 2021 (Audiometry testing)	★★★★★★★★	627	2689	4559	22979	1.18 [1.09, 1.26]
Raikkonen 2020 (Any mental/behavioural disorder)	★★★★★★★½	1187	8138	2192	20472	1.36 [1.28, 1.45]
Raikkonen 2020 (Autism spectrum disorders)	★★★★★★★½	68	8138	123	20472	1.39 [1.04, 1.87]
Raikkonen 2020 (ADD/conduct disorders)	★★★★★★★½	132	8138	325	20472	1.02 [0.84, 1.25]
Raikkonen 2020 (Disorders of conduct/emotions)	★★★★★★★½	94	8138	273	20472	0.87 [0.69, 1.09]
Raikkonen 2020 (Eating disorders)	★★★★★★★½	5	8138	19	20472	0.66 [0.25, 1.77]
Raikkonen 2020 (Mild/mod intellectual disability)	★★★★★★★½	76	8138	166	20472	1.15 [0.88, 1.51]
Raikkonen 2020 (Other behaviour/emotion disorders)	★★★★★★★½	230	8138	466	20472	1.24 [1.06, 1.45]
Raikkonen 2020 (Psych,mood,neurotic disorders)	★★★★★★★½	47	8138	98	20472	1.21 [0.85, 1.71]
Raikkonen 2020 (Psych developmental disorders)	★★★★★★★½	687	8138	1095	20472	1.58 [1.44, 1.73]
Raikkonen 2020 (Severe intellectual disability)	★★★★★★★½	15	8138	22	20472	1.72 [0.89, 3.30]
Raikkonen 2020 (Sleep disorders)	★★★★★★★½	38	8138	82	20472	1.17 [0.79, 1.71]
Gentle 2020 (BSID-III cog score less than 70)	★★★★★★★	43	355	14	157	1.36 [0.77, 2.41]
Gentle 2020 (BSID-III motor score less than 70)	★★★★★★★	59	355	22	156	1.18 [0.75, 1.85]
Ushida 2020a (KSPD DQ score less than 70)	★★★★★★½	500	3320	494	3126	0.95 [0.85, 1.07]
Ushida 2020b (Auditory impairment)	★★★★★★½	46	3438	44	2424	0.74 [0.49, 1.11]
Ushida 2020b (Cerebral palsy)	★★★★★★½	329	4485	305	3309	0.80 [0.69, 0.92]
Ushida 2020b (KSPD DQ score less than 70)	★★★★★★½	533	3355	367	3309	1.43 [1.27, 1.62]
Ushida 2020b (KSPD DQ score less than 85)	★★★★★★½	1647	3355	1142	3309	1.42 [1.34, 1.51]
Ushida 2020b (Visual impairment)	★★★★★★½	238	4344	178	3174	0.98 [0.81, 1.18]

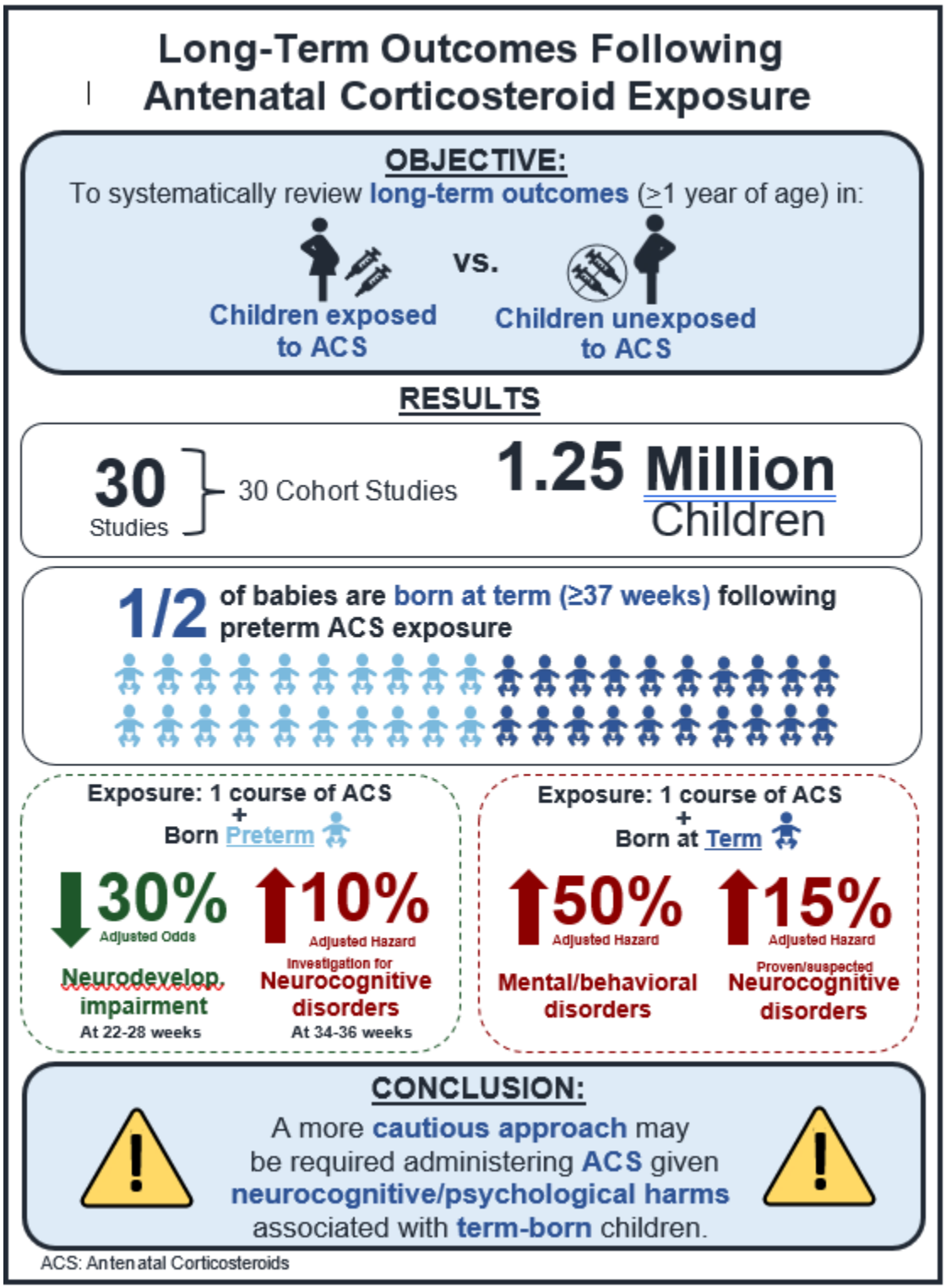




Legend:
ACS – antenatal corticosteroids; IV – instrumental variable; CI – confidence interval; neurocog–neurocognitive; neurodev – neurodevelopmental; BSID – Bayley Scales of Infant and Toddler Development; MDI – mental development index; PDI – psychomotor development index; ECBQ - Early Childhood Behaviour Questionnaire; mod – moderate; ADD – attention deficit disorder; KSPD – Kyoto Scale of Psychological Development; DQ – developmental quotient; HC – head circumference

Newcastle-Ottawa Scale: ★ – point awarded; ½ – half point awarded
Cochrane risk of bias 2.0: +: low bias; −: high bias; ?: some concerns regarding bias; D: bias due to deviations from intended interventions; Me: bias in measurement of the outcome; Mi: bias due to missing outcome data; O: overall risk of bias; R: bias arising from the randomization process; S: bias in selection of reported results

eFigure 4. Infographic Abstract of a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids



eAppendix 1. Electronic Search Strategies for a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Database: OVID Medline (January 1, 2000 – October 29, 2021)		
#	**Searches**	**Results**
1	Premature Birth/	16486
2	exp Infant, Premature/	40544
3	Obstetric Labor, Premature/	7440
4	Prenatal Care/	21468
5	Term Birth/	2651
6	exp Infant, Newborn/	360439
7	exp Pregnancy/	508405
8	pregnan*.mp.	554977
9	((preterm or pre-term or prematur* or term) adj2 (infant* or birth* or child* or deliver* or labour or labor or born)).mp.	101225
10	lbw.mp.	3304
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	825889
12	Glucocorticoids/	53120
13	(antenatal adj4 (cortico* or steroid*)).mp.	2023
14	exp Betamethasone/	4181
15	exp Dexamethasone/	30186
16	betamethasone.mp.	4028
17	celestone.mp.	36
18	dexamethasone.mp.	43199
19	12 or 13 or 14 or 15 or 16 or 17 or 18	89907
20	Prenatal Exposure Delayed Effects/	26737
21	(follow* adj1 up).mp.	1110497
22	(long* adj1 term).mp.	651070
23	(delay* adj2 effect*).mp.	33372
24	exp case control studies/	1144435
25	exp cohort studies/	1909043
26	(observational adj1 stud*).mp.	180880
27	(cohort adj2 (stud* or analys*)).mp.	422052
28	(longitudinal or retrospective or prospective or cross sectional).mp.	2134729
29	exp Randomized Controlled Trials as Topic/	145504
30	Non-Randomized Controlled Trials as Topic/	992
31	RCT.mp.	22108
32	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	807527
33	(quasi adj2 (experiment* or trial)).mp.	12873
34	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 33	3624692
35	(Animals/ or Models, Animal/ or Disease Models, Animal/) not Humans/	2687589
36	11 and 19 and 34	3470
37	36 not 35	2932
38	**limit 37 to ed=20000101-20211029**	**2700**

Database: Embase (January 1, 2000 – October 29, 2021)		
#	Searches	Results
1	Premature Birth/	60139
2	exp Infant, Premature/	111525
3	Obstetric Labor, Premature/	22302
4	Prenatal Care/	43375
5	Term Birth/	3888
6	exp Infant, Newborn/	555990
7	exp Pregnancy/	702036
8	pregnan*.mp.	1002592
9	((preterm or pre-term or prematur* or term) adj2 (infant* or birth* or child* or deliver* or labour or labor or born)).mp.	175491
10	lbw.mp.	6063
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	1517687
12	Glucocorticoids/	75879
13	(antenatal adj4 (cortico* or steroid*)).mp.	3737
14	exp Betamethasone/	17845
15	exp Dexamethasone/	163062
16	betamethasone.mp.	24708
17	celestone.mp.	962
18	dexamethasone.mp.	178533
19	12 or 13 or 14 or 15 or 16 or 17 or 18	262842
20	Prenatal Exposure Delayed Effects/	25066
21	(follow* adj1 up).mp.	2276333
22	(long* adj1 term).mp.	1320222
23	(delay* adj2 effect*).mp.	12567
24	exp case control studies/	197427
25	exp cohort studies/	766607
26	(observational adj1 stud*).mp.	308903
27	(cohort adj2 (stud* or analys*)).mp.	869588
28	(longitudinal or retrospective or prospective or cross sectional).mp.	3414578
29	exp Randomized Controlled Trials as Topic/	213612
30	Non-Randomized Controlled Trials as Topic/	11980
31	RCT.mp.	46393
32	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	1210857
33	(quasi adj2 (experiment* or trial)).mp.	23038
34	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 33	6404169
35	(Animals/ or Models, Animal/ or Disease Models, Animal/) not Humans/	2228988
36	11 and 19 and 34	6602
37	36 not 35	6307
38	**limit 37 to dc=20000101-20211029**	**5807**

Database: APA PsychInfo (January 1, 2000 – October 29, 2021)		
#	**Searches**	**Results**
1	Premature Birth/	5964
2	Prenatal Care/	1986
3	exp Pregnancy/	44598
4	pregnan*.mp.	69875
5	((preterm or pre-term or prematur* or term) adj2 (infant* or birth* or child* or deliver* or labour or labor or born)).mp.	12813
6	lbw.mp.	551
7	1 or 2 or 3 or 4 or 5 or 6	86353
8	Glucocorticoids/	3189
9	Corticosteroids/	1503
10	(antenatal adj4 (cortico* or steroid*)).mp.	75
11	exp Dexamethasone/	1260
12	betamethasone.mp.	84
13	celestone.mp.	3
14	dexamethasone.mp.	4186
15	8 or 9 or 10 or 11 or 12 or 13 or 14	8079
16	Prenatal Exposure/	6685
17	(follow* adj1 up).mp.	135891
18	(long* adj1 term).mp.	153291
19	(delay* adj2 effect*).mp.	2643
20	exp Cohort Analysis/	1555
21	(observational adj1 stud*).mp.	11992
22	(cohort adj2 (stud* or analys*)).mp.	30328
23	(longitudinal or retrospective or prospective or cross sectional).mp.	296016
24	exp Randomized Controlled Trials/	1041
25	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	107917
26	RCT.mp.	5619
27	(quasi adj2 (experiment* or trial)).mp.	14405
28	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27	630630
29	(Animals/ or Models, Animal/ or Disease Models, Animal/) not Humans/	7340
30	7 and 15 and 28	204
31	30 not 29	204
32	**limit 31 to up=20000101-20210601**	**198**

Database: CINAHL (January 1, 2000 – October 29, 2021)		
Numbers	**Search terms**	**Results**
S1	(MH "Childbirth, Premature")	11,712
S2	(MH "Infant, Premature")	24,452
S3	(MH "Infant, High Risk")	598
S4	(MH "Labor, Premature")	3,495
S5	(MH "Term Birth")	1,242
S6	TX ((preterm or pre-term or prematur* or term) N2 (infant* or birth* or child* or deliver* or labour or labor or born))	63,693
S7	(MH "Infant, Newborn+")	146,686
S8	(MH "Pregnancy+")	226,061
S9	TX (pregnan* or lbw)	265,852
S10	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9	389,848
S11	(MH "Glucocorticoids")	9,926
S12	(MH "Betamethasone")	775
S13	(MH "Dexamethasone")	6,087
S14	TX betamethasone	1,131
S15	TX dexamethasone	9,204
S16	TX (Antenatal* N4 (cortico* or steroid*))	1,214
S17	TX celestone	18
S18	S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17	19,579
S19	(MH "Prospective Studies+")	482,102
S20	(MH "Case Control Studies+")	88,410
S21	(MH "Cross Sectional Studies")	216,413
S22	TX (cohort N2 (stud* or analys*)	131,084
S23	TX (observational N1 stud*)	61,572
S24	TX (longitudinal or retrospective or prospective or cross-sectional)	1,085,211
S25	(MH "Randomized Controlled Trials+")	121,365
S26	(MH "Clinical Trials+")	325,783
S27	TX (random* N3 (control* or trial* or allocat* or assign*)	337,007
S28	TX (quasi N2 (experiment* or trial))	20,771
S29	(MH "Quasi-Experimental Studies")	14,206
S30	TX (follow* N1 up)	328,428
S31	TX (long* N1 term)	241,394
S32	TX (delay* N2 effect)	8,066
S33	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S32	1,784,305
S34	**S10 AND S18 AND S33**	**1,387**

Database: Web of Science (January 1, 2000 – October 29, 2021)		
Numbers	**Search terms**	**Results**
# 1	TS=((preterm or pre-term or prematur* or term) NEAR/2 (infant* or birth* or child* or deliver* or labour or labor or born))	150,464
# 2	TS=pregnan*	545,798
# 3	#1 or #2	652,997
# 4	TS=(Antenatal* NEAR/4 (cortico* or steroid*))	2,958
# 5	TS=betamethasone	5,510
# 6	TS=dexamethasone	71,413
# 7	TS=glucocorticoid*	92,135
# 8	TS=celestone	43
# 9	#4 or #5 or #6 or #7 or #8	153,574
# 10	TS=(follow* NEAR/1 up)	1,175,478
# 11	TS=(long* NEAR/1 term)	1,401,676
# 12	TS=(delay* NEAR/2 effect)	19,232
# 13	TS=(case control stud*)	481,093
# 14	TS=(cohort NEAR/2 (stud* or analys*))	320,974
# 15	TS=(observational NEAR/1 stud*)	161,898
# 16	TS=(longitudinal or retrospective or prospective or cross-sectional)	2,090,438
# 17	TS=(random* NEAR/3 (control* or trial* or allocat* or assign*))	809,401
# 18	TS=(quasi NEAR/2 (experiment* or trial))	33,714
# 19	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18	5,096,220
# 20	**#3 and #9 and #19**	**2,819**

Database: clinicaltrials.gov (January 1, 2000 – October 29, 2021)	
Search terms	**Results**
(preterm OR pre-term OR premature OR prenatal or term) AND (glucocorticoids OR antenatal steroids OR corticosteroid OR betamethasone OR dexamethasone) With applied filter: **With Results**	**51**

Database: Google Scholar (January 1, 2000 – June 1, 2021)	
Search terms	**Results**
(preterm OR pre-term OR premature OR prenatal or term) AND (glucocorticoids OR antenatal steroids OR corticosteroid OR betamethasone OR dexamethasone)	**First 400 results**

eAppendix 2. Excluded Key Articles from a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Reference	Reason(s) for exclusion
Asztalos E, Willan A, Murphy K, et al. Association between gestational age at birth, antenatal corticosteroids, and outcomes at 5 years: multiple courses of antenatal corticosteroids for preterm birth study at 5 years of age (MACS-5). *BMC Pregnancy Childbirth*. 2014;14(1):1-8.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Asztalos EV, Murphy KE, Hannah ME, et al. Multiple courses of antenatal corticosteroids for preterm birth study: 2-year outcomes. *Pediatrics*. 2010;126(5):e1045-e1055.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Asztalos EV, Murphy KE, Willan AR, et al. Multiple courses of antenatal corticosteroids for preterm birth study: outcomes in children at 5 years of age (MACS-5). *JAMA Pediatr*. 2013;167(12):1102-1110.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Vanda R. Comparison of the effect of corticosteroid therapy and pre-natal single-period treatment on birth size and neuronal development in preterm infants with one year follow up in Yasuj hospitals in 2015-2017. *Rev Latinoam de Hipertens*. 2018;13(6):567-572.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Kiran PS, Dutta S, Narang A, Bhansali A, Malhi P. Multiple courses of antenatal steroids. *Indian J Pediatr*.2007;74(5):463-469.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Peltoniemi OM, Kari MA, Lano A, et al. Two-year follow-up of a randomised trial with repeated antenatal betamethasone. *Arch Dis Child Fetal Neonatal Ed*. 2009;94(6):F402-F406.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Wapner RJ, Sorokin Y, Mele L, et al. Long-term outcomes after repeat doses of antenatal corticosteroids. *N Engl J Med*. 2007;357(12):1190-1198.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Pesonen A-K, Räikkönen K, Lano A, Peltoniemi O, Hallman M, Kari MA. Antenatal betamethasone and fetal growth in prematurely born children: implications for temperament traits at the age of 2 years. *Pediatrics*. 2009;123(1):e31-e37.	Wrong intervention group (i.e., considers multiple courses of ACS not an unspecified/single course)
Battarbee AN, Ros ST, Esplin MS, et al. Optimal timing of antenatal corticosteroid administration and preterm neonatal and early childhood outcomes. *Am J Obstet Gynecol*. 2020;2(1)100077.	Wrong comparator group (i.e., does not include children who were not exposed to ACS).
Ramos-Navarro C, Sánchez-Luna M, Zeballos-Sarrato S, Pescador-Chamorro I. Antenatal corticosteroids and the influence of sex on morbidity and mortality of preterm infants. *J Matern Fetal Neonatal Med*. 2020:1-8.	Wrong comparator group (i.e., does not include children who were not exposed to ACS).
Supriya, Singh SN, Tripathi S, Kumar M. Outcome of preterm neonates born to women of a developing country at risk of preterm birth exposed to varying doses of antenatal corticosteroid: A prospective observational study. *Clin Epidemiol Glob Health*. 2020;8(2):623-627.	Wrong comparator group (i.e., does not include children who were not exposed to ACS).
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Dessens AB, Haas HS, Koppe JG. Twenty-year follow-up of antenatal corticosteroid treatment. *Pediatrics*. 2000;105(6):E77.	Wrong population (i.e., includes births occurring prior to the year 2000)
Doyle LW, Ford GW, Davis NM, Callanan C. Antenatal corticosteroid therapy and blood pressure at 14 years of age in preterm children. Article. *Clin Sci (Lond)*. 2000;98(2):137-142.	Wrong population (i.e., includes births occurring prior to the year 2000)
Doyle LW, Ford GW, Rickards AL, et al. Antenatal corticosteroids and outcome at 14 years of age in children with birth weight less than 1501 grams. *Pediatrics*. 2000;106(1):E2.	Wrong population (i.e., includes births occurring prior to the year 2000)
Karlsson R, Kallio J, Toppari J, Scheinin M, Kero P. Antenatal and early postnatal dexamethasone treatment decreases cortisol secretion in preterm infants. *Horm Res*. 2000;53(4):170-176.	Wrong population (i.e., includes births occurring prior to the year 2000)
Palta M, Sadeh-Badawi M, Evans M, Weinstein MR, McGuinness G, Newborn Lung P. Functional assessment of a multicenter very low-birth-weight cohort at age 5 years. *Arch Pediatr Adolesc Med*. 2000;154(1):23-30.	Wrong population (i.e., includes births occurring prior to the year 2000)

eAppendix 3. Confounding Factors Addressed in a Systematic Review and Meta-analysis of Long-Term Outcomes Associated with Preterm Exposure to Antenatal Corticosteroids

Maternal factors:

Author, Year	**Family or maternal history of neurodevelopmental and psychological outcomes**	**Socioeconomic status**	**Maternal substance use: drugs, alcohol, smoking**	Chorioamnionitis	Environmental contaminant exposure	Other confounders
A single course of ACS versus those unexposed						
Children born preterm						
Agarwal, 2018[5]						
Kim, 2018[6]						
Lardon, 2017[9]						
Chawla, 2016[3]		**Adj:** health insurance status as surrogate for SES				**Adj:** participating center
Tseng, 2016[10]						
Chawla, 2013[1]		**SU**: Medicaid insurance as surrogate for SES				
McElrath, 2009[8]						
Lee, 2008[4]		**Adj:** education				**Adj:** mother living with the infant at corrected age 18-22 months
Laughon, 2009[7]						
Unspecified number of courses of ACS versus those unexposed						
Children born preterm or at term						
Lamminmaki 2021[11]						**Adj:** age

Author, Year	**Family or maternal history of neurodevelopmental and psychological outcomes**	**Socioeconomic status**	**Maternal substance use: drugs, alcohol, smoking**	Chorioamnionitis	Environmental contaminant exposure	Other confounders
Raikonnen, 2020[12]	**Adj:** lifetime maternal mental disorder diagnosis		**Adj:** maternal smoking during pregnancy			**Adj:** age, parity, pre-pregnancy BMI, GDM, hypertension in pregnancy
Wolford, 2020[13]	**Adj**	**SU, Adj:** education	**Adj**			**Adj:** age, parity, maternal early pregnancy BMI, hypertensive and diabetic disorders in pregnancy and pre-pregnancy, asthma
Children born preterm						
Aviram, 2021[15]		**Adj:** income				**Adj:** Maternal age, parity, chronic hypertension, pregestational diabetes, hypertensive complications, gestational diabetes
Hutcheon, 2020[17]			**Adj:** maternal smoking during pregnancy			**Adj:** maternal age, parity, pre-pregnancy

Author, Year	**Family or maternal history of neurodevelopmental and psychological outcomes**	**Socioeconomic status**	**Maternal substance use: drugs, alcohol, smoking**	Chorioamnionitis	Environmental contaminant exposure	Other confounders
						BMI, hypertension in pregnancy, diabetes,
Gentle, 2020[16]		**Adj:** health insurance status as surrogate for SES				**Adj:** maternal race, study centre
Ushida, 2020[21]				**Adj**		**Adj:** age, parity, diabetes including gestational diabetes **E:** incomplete medical records including maternal characteristics
Li, 2019[24]						
Basset, 2018[22]		**Adj:** SES, and "social security benefits for those with low incomes"		**Adj**		**Adj:** hypertensive disorders, pre-existing disease
Haslam, 2018[14]		**Adj:** employment	**Adj:** substance use			**Adj:** ethnicity
Ishikawa, 2015[23]				**Adj:** histological chorioamnionitis ≥stage 2		**Adj:** age, parity, pre-eclampsia
Kallen, 2015[27]						

Author, Year		**Family or maternal history of neurodevelopmental and psychological outcomes**	**Socioeconomic status**	**Maternal substance use: drugs, alcohol, smoking**	Chorioamnionitis	Environmental contaminant exposure	Other confounders
Miyazaki, 2015[19]					**S** (those with and without histologic chorioamnionitis)		**Adj:** age, parity, diabetes, pre-eclampsia
Sun, 2015[29]							
Ochiai, 2014[25]							
Kiechl-Kohlendorfer, 2009[28]							
Children born at term							
Melamed, 2019[30]			**Adj:** Income				**Adj:** Age, parity, chronic hypertension, pregestational and gestational diabetes, hypertensive complications of pregnancy
Total studies:	**Single course of ACS v unexposed**	**E:** 0; **Adj:** 0 **M:** 0; **S:** 0	**E:** 0; **Adj:** 2 **M:** 0; **S:** 0	**E:** 0; **Adj:** 0 **M:** 0; **S:** 0	**E:** 0; **Adj:** 0 **M:** 0; **S:** 0	**E:** 0; **Adj:** 0 **M:** 0; **S:** 0	
	Unspecified courses of ACS v unexposed	**E:** 0; **Adj:** 2 **M:** 0; **S:** 0	**E:** 0; **Adj:** 6 **M:** 0; **S:** 0	**E:** 0; **Adj:** 4 **M:** 0; **S:** 0	**E:** 0; **Adj:** 3 **M:** 0; **S:** 1	**E:** 0; **Adj:** 0 **M:** 0; **S:** 0	

Legend:
A – adjusted, SU – similar in univariate analysis, E – excluded, S – stratified

Fetal factors:

Author, year	**Postnatal steroid exposure**	**GA at birth**	**IUGR**	Multiple gestation	Chromosomal anomaly	Delivery difficulties/ mode of birth	Neonatal sepsis	Other fetal confounders
A single course of ACS versus those unexposed								
Children born preterm								
Agarwal, 2018[5]								
Kim, 2018[6]		**S**						
Lardon, 2017[9]		**E** (includes preterm infants)			**E**		**Adj**	**Adj:** SGA, PDA
Chawla, 2016[3]		**E** (includes extremely preterm infants), **Adj**						**Adj:** infant sex, race/ ethnicity
Tseng, 2016[10]		**E** (includes infants born <35 weeks, BW <1500g)						
Chawla, 2013[1]		**E:** includes extremely preterm infants only			**E**			**E:** still births, congenital infection, neonates not resuscitated at birth due to extreme prematurity
McElrath, 2009[8]		**E** (includes infants born <28 weeks)						
Lee, 2008[4]	**Adj**	**Adj**		**Adj**	**E**	**Adj:** mode of delivery	**Adj:** early onset or late onset sepsis	**Adj:** infant sex, SGA, severe IVH, PVL, treated PDA, chronic

Author, year	**Postnatal steroid exposure**	**GA at birth**	**IUGR**	Multiple gestation	Chromosomal anomaly	Delivery difficulties/ mode of birth	Neonatal sepsis	Other fetal confounders
								lung disease, race
Laughon, 2009[7]		**E** (includes infants born <28 weeks)						
Unspecified number of courses of ACS versus those unexposed								
Children born preterm or at term								
Lamminmaki 2021[11]		**M**		**Adj**				**Adj:** age, number of brothers, number of sisters, motor, or cognitive impairment
Raikonnen, 2020[12]		**Adj**		**E**		**Adj:** mode of delivery		**Adj:** infant sex, admission to NICU, weight, low 5-min Apgar (maximum at 1 and 5 min)
Wolford, 2020[13]		**Adj**		**E**		**Adj**		**Adj:** infant sex, birth year, birth weight standardized by sex and GA according to Finnish growth charts
Children born preterm								
Aviram, 2021[15]		**Adj, E** (excludes		**E**	**E**	**Adj:** mode of delivery		**Adj:** resuscitation

Author, year	**Postnatal steroid exposure**	**GA at birth**	**IUGR**	Multiple gestation	Chromosomal anomaly	Delivery difficulties/ mode of birth	Neonatal sepsis	Other fetal confounders
		infants born <34 weeks)						at birth, Infant sex, 5 min Apgar, birth weight <10th percentile, NICU admission **E:** deliveries complicated by intrapartum asphyxia,
Hutcheon, 2020[17]		**Adj**				**Adj:** mode of delivery		**Adj:** infant sex, birthweight, 5 min Apgar
Gentle, 2020[16]		**S, Adj**		**SU**	**E**			**Adj:** infant sex, SGA, follow-up window
Ushida, 2020[21]		**E** (excludes infants born <24 weeks), **Adj**		**E**	**E**	**Adj**		**Adj:** out-of-hospital birth, non-reassuring fetal status, SGA, infant sex
Li, 2019[24]		**E** (includes extremely preterm infants)						
Basset, 2018[22]		**Adj**	**Adj**	**Adj**	**E:** genetic abnormalities / malformations			**Adj:** ZS of birth weight and head

Author, year	**Postnatal steroid exposure**	**GA at birth**	**IUGR**	Multiple gestation	Chromosomal anomaly	Delivery difficulties/ mode of birth	Neonatal sepsis	Other fetal confounders
								circumference, sex **S, Adj:** head circumference at birth
Haslam, 2018[14]		**E** (includes preterm infants), **Adj**			**E**		**Adj:** late onset sepsis	**Adj:** male sex, SNAP-II score >20, BPD, brain injury
Ishikawa, 2015[23]		**E** (includes preterm infants), **Adj**		**E**	**E:** major congenital malformation	**Adj:** mode of delivery		**Adj:** infant sex, non-reassuring fetal status, birth weight
Kallen, 2015[27]		**E** (includes infants born <27 weeks), **Adj**						
Miyazaki, 2015[19]		**E** (includes preterm infants), **Adj**		**E**	**E**	**Adj:** mode of delivery		**Adj:** infant sex, non-reassuring fetal status, birth weight, SGA
Sun, 2015[29]		**E** (includes infants <32 weeks)			**E:** genetic or metabolic diseases, congenital anomalies			**E:** pneumothorax
Ochiai, 2014[25]		**E** (includes infants born 22-24 weeks)			**E** (none of the infants had congenital anomalies)			

Author, year		**Postnatal steroid exposure**	**GA at birth**	**IUGR**	Multiple gestation	Chromosomal anomaly	Delivery difficulties/ mode of birth	Neonatal sepsis	Other fetal confounders
Kiechl-Kohlen-dorfer, 2009[28]			**E** (includes infants born 23-32 weeks), **S**: <30 weeks GA, 30-32 weeks						
Children born at term									
Melamed, 2019[30]			**Adj**		**E**	**E:** genetic or major structural abnormalities	**Adj:** mode of delivery, induction of labor		**Adj:** infant sex, birth weight <10th percentile, NICU admission, fetal acidemia (intrapartum asphyxia), need for delivery room CPR, 5 min Apgar <7
Total studies:	**Single course of ACS v unexposed**	**E:** 0 **Adj:** 1 **M:** 0 **S:** 0	**E:** 6 **Adj:** 2 **M:** 0 **S:** 1	**E:** 0 **Adj:** 0 **M:** 0 **S:** 0	**E:** 0 **Adj:** 1 **M:** 0 **S:** 0	**E:** 3 **Adj:** 0 **M:** 0 **S:** 0	**E:** 0 **Adj:** 1 **M:** 0 **S:** 0	**E:** 0 **Adj:** 2 **M:** 0 **S:** 0	
	Unspecified courses of ACS v unexposed	**E:** 0 **Adj:** 0 **M:** 0 **S:** 0	**E:** 10 **Adj:** 12 **M:** 1 **S:** 2	**E:** 0 **Adj:** 1 **M:** 0 **S:** 0	**E:** 7 **Adj:** 2 **M:** 0 **S:** 0	**E:** 10 **Adj:** 0 **M:** 0 **S:** 0	**E:** 0 **Adj:** 8 **M:** 0 **S:** 0	**E:** 0 **Adj:** 1 **M:** 0 **S:** 0	

Legend:
A – adjusted, E – excluded, S – stratified, SU – similar in univariate analysis, M – matched, GA – gestational age, NICU – neonatal intensive care unit, IVH – intraventricular hemorrhage, SGA – small for gestational age, BW – birth weight, PVL – periventricular leukomalacia, BPD – bronchopulmonary dysplasia, PDA – patent ductus arteriosus, **bolded confounders** – prespecified important confounders

Uteroplacental factors:

Author, year	Placental abruption	Other uteroplacental factors
A single course of ACS versus those unexposed		
Children born preterm		
Agarwal, 2018[5]		
Kim, 2018[6]		
Lardon, 2017[9]		
Chawla, 2016[3]		
Tseng, 2016[10]		
Chawla, 2013[1]		
McElrath, 2009[8]		
Lee, 2008[4]		
Laughon, 2009[7]		
Unspecified number of courses of ACS versus those unexposed		
Children born preterm or at term		
Lamminmaki 2021[11]		
Raikonnen, 2020[12]		**Adj:** PPROM
Wolford, 2020[13]		**Adj:** PROM
Children born preterm		
Aviram, 2021[15]		**Adj:** PPROM
Hutcheon, 2020[17]		
Gentle, 2020[16]		
Ushida, 2020[21]		**Adj:** PROM
Li, 2019[24]		
Basset, 2018[22]	**Adj**	**Adj:** PROM
Haslam, 2018[14]		
Ishikawa, 2015[23]		**Adj**: PROM
Kallen, 2015[27]		
Miyazaki, 2015[19]		**Adj**: PROM
Sun, 2015[29]		
Ochiai, 2014[25]		
Kiechl-Kohlendorfer, 2009[28]		

Author, year		Placental abruption	Other uteroplacental factors
Children born at term			
Melamed, 2019[30]			**Adj:** PPROM
Total studies:	**Single course of ACS v unexposed**	**E:** 0; **Adj:** 0; **M:** 0; **S:** 0	
	Unspecified courses of ACS v unexposed	**E:** 0; **Adj:** 1; **M:** 0; **S:** 0	

Legend: A – adjusted, E – excluded, PPROM – preterm premature rupture of membranes, PROM – premature rupture of membrane

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