The proportions of term or late preterm births after early exposure to antenatal corticosteroids and outcomes: systematic review and meta-analysis of 1.6 million infants

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Infants born at term									
Short-term outcomes:									
Study, Year (Country) Outcome(s)	**Total score (max: 12★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[a] max:5★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Adjusted analyses:									
Diguisto, 2020 (France)[1] Birth length <5th percentile BW <5th percentile	10★★★★★★★★★★	★	★	★	★	★★★☆☆	★	★	★
Diguisto, 2020 (France)[1] HC <5th percentile	9★★★★★★★★★	★	★	★	★	★★★☆☆	★	★	☆
McKinzie, 2021 (U.S.A)[2] All included outcomes	8★★★★★★★★	☆	★	★	★	★★☆☆☆	★	★	★
Rodriguez, 2019 (Finland)[3] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★
Unadjusted analyses:									
Diguisto, 2020 (France)[1] BW <5th percentile Birth length <5th percentile	8★★★★★★★★	★	★	★	★	★☆☆☆☆	★	★	★
Melamed, 2019 (Canada)[4] All included outcomes	8★★★★★★★★	☆	★	★	★	★★☆☆☆	★	★	★
Raikkonen, 2022 (Finland)[5] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★
McKinzie, 2021 (U.S.A)[2] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★
Diguisto, 2020 (France)[1] HC <5th percentile	7★★★★★★★	★	★	★	★	★☆☆☆☆	★	★	☆
Rodriguez, 2019 (Finland)[3] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★

Long-term outcomes:										
Study, Year (Country) Outcome(s)	**Total score (max: 13★)**	**Component scores**								
		Selection				Comparability	Outcome			
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[b] max:6★	Q1 max:1★	Q2 max:1★	Q3 max:1★	
Adjusted analyses:										
Melamed, 2019 (Canada)[4] All included outcomes	10★★★★★★★★★★	☆	★	★	★	★★★★☆☆	★	★	★	
Raikkonen, 2022 (Finland)[5] All included outcomes	9★★★★★★★★★	☆	★	★	★	★★★☆☆☆	★	★	★	
Raikkonen, 2020 (Finland)[6] All included outcomes	9★★★★★★★★★	☆	★	★	★	★★★☆☆☆	★	★	★	
Osteen, 2022 (U.S.A)[7] All included outcomes	8★★★★★★★★	☆	★	★	★	★★☆☆☆☆	★	★	★	
Unadjusted analyses:										
Melamed, 2019 (Canada)[4] All included outcomes	8★★★★★★★★	☆	★	★	★	★★☆☆☆☆	★	★	★	
Raikkonen 2022 (Finland)[5] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆☆	★	★	★	
Raikkonen, 2020 (Finland)[6] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆☆	★	★	★	
Osteen, 2022 (U.S.A)[7] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆☆	★	★	★	
Proportion outcomes:										
Study, Year (Country) Outcome(s)	**Total score (max: 13★)**	**Component scores**								
		Selection				Comparability	Outcome			
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[c] max: 6★	Q1 max:1★	Q2 max:1★	Q3 max:1★	
Raikkonen, 2020 (Finland)[6] Proportion of infants born at term after exposure to ACS	7★★★★★★★	☆	★	★	★	★☆☆☆☆☆	★	★	★	

Infants born late preterm									
Short-term outcomes:									
Study, Year (Country) Outcome(s)	**Total score (max: 12★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[a] max: 5★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Adjusted analyses:									
Malloy, 2012 (U.S.A)[8] All included outcomes	7★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★
Unadjusted analyses:									
Aviram, 2022 (Canada)[9] All included outcomes	8★★★★★★★★	☆	★	★	★	★★☆☆☆	★	★	★
Malloy, 2012 (U.S.A)[8] All included outcomes	6★★★★★★	☆	★	★	★	☆☆☆☆☆	★	★	★
Long-term outcomes:									
Study, Year (Country) Outcome(s)	**Total score (max: 13★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[b] max:6★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Adjusted analyses:									
Aviram, 2022 (Canada)[9] All included outcomes	10★★★★★★★★★★	☆	★	★	★	★★★★☆☆	★	★	★
Unadjusted analyses:									
Aviram, 2022 (Canada)[9] All included outcomes	8 ★★★★★★★★	☆	★	★	★	★★☆☆☆☆	★	★	★

Proportion outcomes:									
Study, Year (Country) Outcome(s)	**Total score (max: 13★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max: 1★	Q4 max: 1★	Q1[c] max:6★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Malloy, 2012 (U.S.A)[8] Proportion of infants born late preterm after exposure to ACS	6 ★★★★★★	☆	★	★	★	☆☆☆☆☆☆	★	★	★
Infants born at term/late preterm (combined)									
Proportion outcomes:									
Study, Year (Country) • **Outcome(s)**	**Total score (max: 13★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[c] max:6★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Razaz, 2015 (Canada)[10] Proportion of infants born at term/late preterm (combined) after exposure to ACS (≥35 weeks GA)	6 ★★★★★★	☆	★	★	★	☆☆☆☆☆☆	★	★	★
Short-term outcomes (post-hoc analyses):									
Study, Year (Country) Outcome(s) & definitions (when available)	**Total score (max: 12★)**	**Component scores**							
		Selection				Comparability	Outcome		
		Q1 max:1★	Q2 max:1★	Q3 max:1★	Q4 max:1★	Q1[a] max:5★	Q1 max:1★	Q2 max:1★	Q3 max:1★
Adjusted analyses (post-hoc analyses):									
Rodriguez, 2019 (Finland)[3] All included outcomes	7 ★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★
Unadjusted analyses (post-hoc analyses):									
Rodriguez, 2019 (Finland)[3] All included outcomes	7 ★★★★★★★	☆	★	★	★	★☆☆☆☆	★	★	★

Legend:

ACS – antenatal corticosteroids; BW – birthweight; GA – gestational age; HC – head circumference; Max – maximum

Newcastle-Ottawa Scale: ★ – point awarded; ☆ – no point awarded; Selection Q1 – Representativeness of exposed cohort; Selection Q2 – Selection of non-exposed cohort; Selection Q3 – Ascertainment of exposure; Selection Q4 – Demonstration that outcome of interest was not present at study start; Comparability Q1: Comparability of cohorts based on the design or analysis; Outcome Q1 – Ascertainment of outcome; Outcome Q2 – Follow-up long enough for outcomes to occur?; Outcome Q3 – Adequacy of cohort follow-up

[a] If the study addressed any of the following **potential confounders** or **co-variates for outcomes** (whether through exclusion, stratification, adjustment, or matching), we assigned 1 star per factor: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **fetal anomalies**; **preterm premature rupture of membranes**.

[b] If the study addressed any of the following **potential confounders** or **co-variates for outcomes** (whether through exclusion, stratification, adjustment or matching), we assigned 1 star per factor: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **preterm premature rupture of membranes; substance use**; **socioeconomic status.**

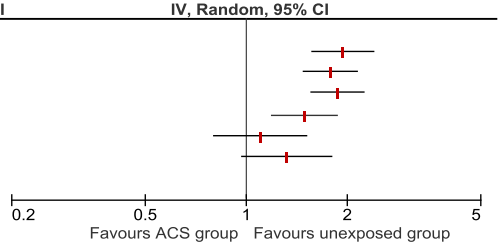
[c] If the study addressed any of the following **potential confounders** or **co-variates for outcomes** (whether through exclusion, stratification, adjustment or matching), we assigned 1 star per factor: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **preterm premature rupture of membranes; fetal anomalies; maternal smoking/substance use**.

eFigure 1: Adjusted and unadjusted analyses of secondary outcomes for infants born at term from population-based studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

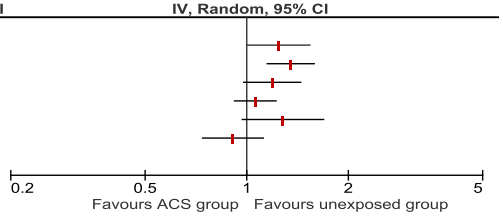
Adjusted data

Study (short-term outcome)

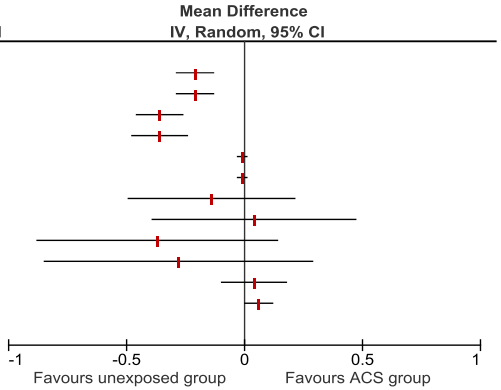
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Odds Ratio]	SE	Odds Ratio IV, Random, 95% CI
Short-term outcomes					
McKinzie 2021 (Admission to NICU w/o EGA)	⨁⨁◯◯	★★★★★★★★	0.6627	0.108	1.94 [1.57, 2.40]
McKinzie 2021 (SGA)	⨁⨁◯◯	★★★★★★★★	0.5766	0.0942	1.78 [1.48, 2.14]
McKinzie 2021 (SGA w/o EGA)	⨁⨁◯◯	★★★★★★★★	0.6259	0.0925	1.87 [1.56, 2.23]
McKinzie 2021 (Admission to NICU)	⨁◯◯◯	★★★★★★★★	0.3988	0.1147	1.49 [1.19, 1.86]
McKinzie 2021 (Diagnosis of TTN)	⨁◯◯◯	★★★★★★★★	0.0953	0.1625	1.10 [0.80, 1.51]
McKinzie 2021 (Diagnosis of TTN w/o EGA)	⨁◯◯◯	★★★★★★★★	0.2776	0.1572	1.32 [0.97, 1.79]



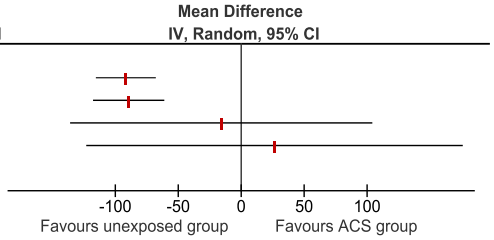
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Risk Ratio]	SE	Risk Ratio IV, Random, 95% CI
Short-term outcomes					
Diguisto 2020 (Birth length less than 5th% UE1)	⨁◯◯◯	★★★★★★★★★★	0.2151	0.1098	1.24 [1.00, 1.54]
Diguisto 2020 (Birth length less than 5th% UE2)	⨁◯◯◯	★★★★★★★★★★	0.3001	0.0818	1.35 [1.15, 1.58]
Diguisto 2020 (Birthweight less than 5th% UE1)	⨁◯◯◯	★★★★★★★★★★	0.174	0.0991	1.19 [0.98, 1.45]
Diguisto 2020 (Birthweight less than 5th% UE2)	⨁◯◯◯	★★★★★★★★★★	0.0583	0.0723	1.06 [0.92, 1.22]
Diguisto 2020 (HC less than 5th% UE1)	⨁◯◯◯	★★★★★★★★★	0.2469	0.1415	1.28 [0.97, 1.69]
Diguisto 2020 (HC less than 5th% UE2)	⨁◯◯◯	★★★★★★★★★	-0.0943	0.1055	0.91 [0.74, 1.13]



Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Head circumference term born)	⨁⨁◯◯	★★★★★★★	-0.21	0.04	-0.21 [-0.29, -0.13]
Rodriguez 2019 (HC term PS cohort)	⨁⨁◯◯	★★★★★★★	-0.21	0.04	-0.21 [-0.29, -0.13]
Rodriguez 2019 (Body length term born)	⨁⨁◯◯	★★★★★★★	-0.36	0.05	-0.36 [-0.46, -0.26]
Rodriguez 2019 (Body length term PS cohort)	⨁⨁◯◯	★★★★★★★	-0.36	0.06	-0.36 [-0.48, -0.24]
Rodriguez 2019 (Ponderal index term born)	⨁⨁◯◯	★★★★★★★	-0.01	0.01	-0.01 [-0.03, 0.01]
Rodriguez 2019 (PI term PS cohort)	⨁⨁◯◯	★★★★★★★	-0.01	0.01	-0.01 [-0.03, 0.01]
Rodriguez 2019 (Head circumference post-term born)	⨁◯◯◯	★★★★★★★	-0.14	0.18	-0.14 [-0.49, 0.21]
Rodriguez 2019 (HC post-term PS cohort)	⨁◯◯◯	★★★★★★★	0.04	0.22	0.04 [-0.39, 0.47]
Rodriguez 2019 (Body length post-term born)	⨁◯◯◯	★★★★★★★	-0.37	0.26	-0.37 [-0.88, 0.14]
Rodriguez 2019 (Body length post-term PS cohort)	⨁◯◯◯	★★★★★★★	-0.28	0.29	-0.28 [-0.85, 0.29]
Rodriguez 2019 (Ponderal index post-term born)	⨁◯◯◯	★★★★★★★	0.04	0.07	0.04 [-0.10, 0.18]
Rodriguez 2019 (PI post-term PS cohort)	⨁◯◯◯	★★★★★★★	0.06	0.03	0.06 [0.00, 0.12]

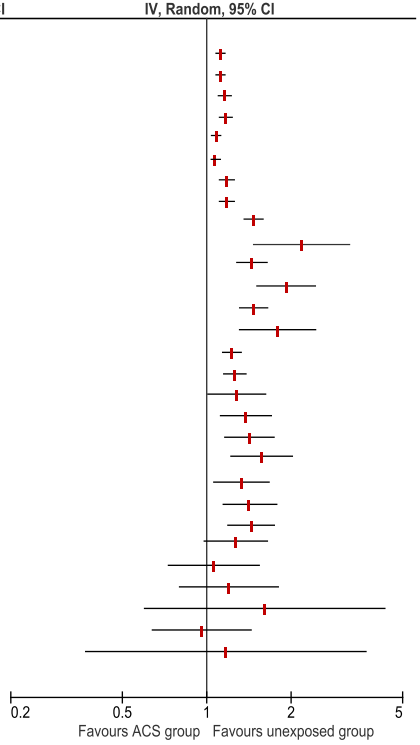


Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Birthweight term born)	⊕⊕◯◯	★★★★★★★	-91.62	11.86	-91.62 [-114.87, -68.37]
Rodriguez 2019 (Birthweight term PS cohort)	⊕⊕◯◯	★★★★★★★	-89.38	14.16	-89.38 [-117.13, -61.63]
Rodriguez 2019 (Birthweight post-term born)	⊕◯◯◯	★★★★★★★	-15.87	60.96	-15.87 [-135.35, 103.61]
Rodriguez 2019 (Birthweight post-term PS cohort)	⊕◯◯◯	★★★★★★★	26.46	76.01	26.46 [-122.52, 175.44]

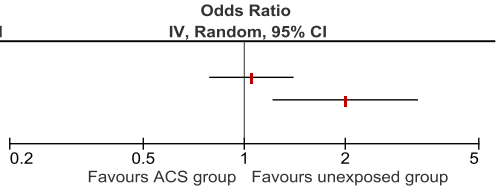


Study (long-term outcome)

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Hazard Ratio]	SE	Hazard Ratio IV, Random, 95% CI
Long-term outcomes					
Melamed 2019 (Composite long-term outcome)	⊕⊕◯◯	★★★★★★★★★★	0.1133	0.0186	1.12 [1.08, 1.16]
Melamed 2019 (Composite long-term w/o NICU/BW)	⊕⊕◯◯	★★★★★★★★★★	0.1133	0.0186	1.12 [1.08, 1.16]
Melamed 2019 (Suspected neurocognitive disorder)	⊕⊕◯◯	★★★★★★★★★★	0.1484	0.0271	1.16 [1.10, 1.21]
Melamed 2019 (Susp. neurocog disorder w/o NICU/BW)	⊕⊕◯◯	★★★★★★★★★★	0.157	0.0269	1.17 [1.11, 1.23]
Melamed 2019 (Visual testing)	⊕⊕◯◯	★★★★★★★★★★	0.077	0.0193	1.08 [1.04, 1.12]
Melamed 2019 (Visual testing w/o NICU/BW)	⊕⊕◯◯	★★★★★★★★★★	0.0296	0.0427	1.03 [1.03, 1.12]
Melamed 2019 (Audiometry testing)	⊕⊕◯◯	★★★★★★★★★★	0.1655	0.0312	1.18 [1.11, 1.25]
Melamed 2019 (Audiometry testing w/o NICU/BW)	⊕⊕◯◯	★★★★★★★★★★	0.1655	0.0312	1.18 [1.11, 1.26]
Raikkonen 2020 (Any mental/behavioural disorder)	⊕⊕◯◯	★★★★★★★★★	0.3853	0.0397	1.47 [1.36, 1.60]
Raikkonen 2022 (Cerebral palsy)	⊕⊕◯◯	★★★★★★★★★	0.7793	0.2011	2.18 [1.47, 3.23]
Raikkonen 2020 (Psych development disorders)	⊕⊕◯◯	★★★★★★★★★	0.3716	0.0636	1.45 [1.28, 1.64]
Raikkonen 2022 (Other psych development disorder)	⊕⊕◯◯	★★★★★★★★★	0.6523	0.1226	1.92 [1.51, 2.43]
Raikkonen 2022 (Speech/language develop disorders)	⊕⊕◯◯	★★★★★★★★★	0.3853	0.0588	1.47 [1.31, 1.66]
Raikkonen 2020 (Sleep disorders)	⊕⊕◯◯	★★★★★★★★★	0.5822	0.1593	1.79 [1.31, 2.44]
Melamed 2019 (Audiometry/susp. neurocog disorder)	⊕◯◯◯	★★★★★★★★★★	0.207	0.0388	1.23 [1.14, 1.34]
Melamed 2019 (Audio/susp. neurocog w/o NICU/BW)	⊕◯◯◯	★★★★★★★★★★	0.2311	0.0466	1.26 [1.15, 1.38]
Raikkonen 2022 (Scholastic skill develop disorder)	⊕◯◯◯	★★★★★★★★★	0.2469	0.1209	1.28 [1.01, 1.63]
Raikkonen 2022 (Motor function develop disorders)	⊕◯◯◯	★★★★★★★★★	0.3221	0.1065	1.38 [1.12, 1.70]
Raikkonen 2022 (Pervasive developmental disorder)	⊕◯◯◯	★★★★★★★★★	0.3507	0.1032	1.42 [1.16, 1.75]
Raikkonen 2022 (Epilepsy)	⊕◯◯◯	★★★★★★★★★	0.4511	0.1287	1.57 [1.22, 2.01]
Raikkonen 2020 (ADD/conduct disorders)	⊕◯◯◯	★★★★★★★★★	0.2852	0.1158	1.33 [1.06, 1.65]
Raikkonen 2020 (Mixed disorders conduct/emotions)	⊕◯◯◯	★★★★★★★★★	0.3507	0.1121	1.42 [1.14, 1.76]
Raikkonen 2020 (Other behaviour/emotion disorders)	⊕◯◯◯	★★★★★★★★★	0.3646	0.0973	1.44 [1.19, 1.73]
Raikkonen 2022 (Vision or hearing loss)	⊕◯◯◯	★★★★★★★★★	0.239	0.1323	1.27 [0.98, 1.64]
Raikkonen 2020 (Autism spectrum disorders)	⊕◯◯◯	★★★★★★★★★	0.0583	0.1903	1.06 [0.73, 1.54]
Raikkonen 2020 (Psych, mood, neurotic disorders)	⊕◯◯◯	★★★★★★★★★	0.1823	0.2069	1.20 [0.80, 1.80]
Raikkonen 2020 (Eating disorders)	⊕◯◯◯	★★★★★★★★★	0.4762	0.5036	1.61 [0.60, 4.35]
Raikkonen 2020 (Mild/mod intellectual disability)	⊕◯◯◯	★★★★★★★★★	-0.0408	0.2069	0.96 [0.64, 1.42]
Raikkonen 2020 (Severe intellectual disability)	⊕◯◯◯	★★★★★★★★★	0.157	0.5874	1.17 [0.37, 3.69]



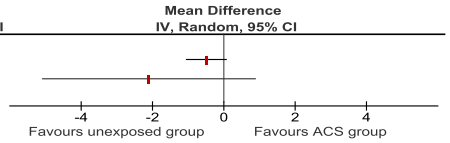
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Odds Ratio]	SE	Odds Ratio IV, Random, 95% CI
Long-term outcomes					
Osteen 2022 (Asthma)	⨁◯◯◯	★★★★★★★★	0.0488	0.1452	1.05 [0.79, 1.39]
Osteen 2022 (Weight less than 10th%)	⨁◯◯◯	★★★★★★★★	0.6931	0.2522	2.00 [1.22, 3.25]



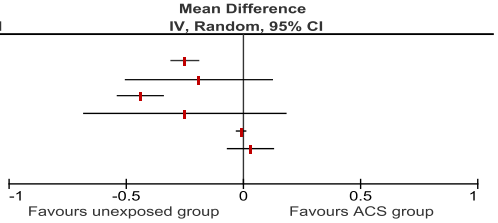
Unadjusted data

Study (short-term outcome)

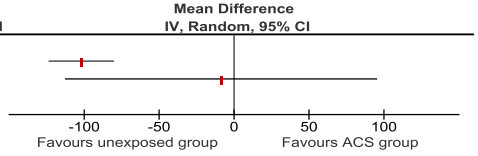
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Mean	ACS group SD	ACS group Total	Unexposed group Mean	Unexposed group SD	Unexposed group Total	Mean Difference IV, Random, 95% CI
Short-term outcomes									
McKinzie 2021 (Head circumference)	⨁◯◯◯	★★★★★★★	33.9	9.1	1459	34.4	9.7	3871	-0.50 [-1.06, 0.06]
McKinzie 2021 (Birth length)	⨁◯◯◯	★★★★★★★	50.5	17.4	1459	52.6	90.3	3871	-2.10 [-5.08, 0.88]



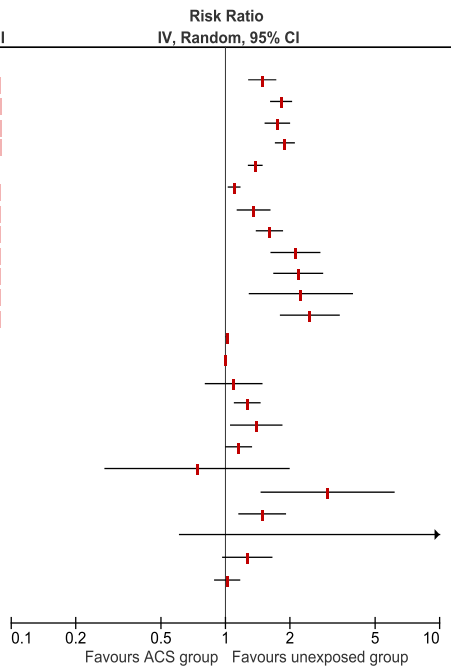
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Head circumference term born)	⨁◯◯◯	★★★★★★★	-0.25	0.03	-0.25 [-0.31, -0.19]
Rodriguez 2019 (Head circumference post-term born)	⨁◯◯◯	★★★★★★★	-0.19	0.16	-0.19 [-0.50, 0.12]
Rodriguez 2019 (Body length term born)	⨁◯◯◯	★★★★★★★	-0.44	0.05	-0.44 [-0.54, -0.34]
Rodriguez 2019 (Body length post-term born)	⨁◯◯◯	★★★★★★★	-0.25	0.22	-0.25 [-0.68, 0.18]
Rodriguez 2019 (Ponderal index term born)	⨁◯◯◯	★★★★★★★	-0.01	0.01	-0.01 [-0.03, 0.01]
Rodriguez 2019 (Ponderal index post-term born)	⨁◯◯◯	★★★★★★★	0.03	0.05	0.03 [-0.07, 0.13]



Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Birthweight term born)	⨁⨁◯◯	★★★★★★★	-101.95	10.89	-101.95 [-123.29, -80.61]
Rodriguez 2019 (Birthweight post-term born)	⨁◯◯◯	★★★★★★★	-8.66	52.02	-8.66 [-110.62, 93.30]

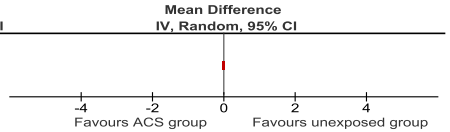


Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Risk Ratio IV, Random, 95% CI
Short-term outcomes							
Digusito 2020 (Birth length less than 5th% UE1)	⨁⨁◯◯	★★★★★★★★	292	3276	411	6848	1.49 [1.29, 1.72]
Diguisto 2020 (Birth length less than 5th% UE2)	⨁⨁◯◯	★★★★★★★★	292	3276	9473	193319	1.82 [1.63, 2.03]
Diguisto 2020 (Birthweight less than 5th% UE1)	⨁⨁◯◯	★★★★★★★★	360	4043	510	10008	1.75 [1.53, 1.99]
Diguisto 2020 (Birthweight less than 5th% UE2)	⨁⨁◯◯	★★★★★★★★	360	4043	12267	261006	1.89 [1.71, 2.09]
Melamed 2019 (BW less than 10th%)	⨁⨁◯◯	★★★★★★★★	656	5423	45989	523782	1.38 [1.28, 1.48]
Melamed 2019 (Resuscitation at birth)	⨁⨁◯◯	★★★★★★★★	856	5423	75305	523782	1.10 [1.03, 1.17]
Diguisto 2020 (HC less than 5th% UE1)	⨁⨁◯◯	★★★★★★★	197	3388	304	7077	1.35 [1.14, 1.61]
McKinzie 2021 (SGA)	⨁⨁◯◯	★★★★★★★	263	1340	436	3565	1.60 [1.40, 1.85]
McKinzie 2021 (Treated hypoglycemia)	⨁⨁◯◯	★★★★★★★	96	1459	120	3871	2.12 [1.63, 2.76]
Rodriguez 2019 (Hospitalization status beyond 7 days)	⨁⨁◯◯	★★★★★★★	77	1344	176	6718	2.19 [1.68, 2.84]
Rodriguez 2019 (Hospital transfer)	⨁⨁◯◯	★★★★★★★	18	1346	40	6730	2.25 [1.29, 3.91]
Rodriguez 2019 (Metabolic disorder screening)	⨁⨁◯◯	★★★★★★★	56	1346	113	6730	2.48 [1.81, 3.40]
Rodriguez 2019 (Hypothyroidism screening)	⨁⨁◯◯	★★★★★★★	1323	1346	6499	6730	1.02 [1.01, 1.03]
Rodriguez 2019 (Vitamin K)	⨁⨁◯◯	★★★★★★★	1337	1346	6674	6730	1.00 [1.00, 1.01]
Melamed 2019 (Apgar score less than 7 at 5 min)	⨁◯◯◯	★★★★★★★★	42	5423	3714	523782	1.09 [0.81, 1.48]
Diguisto 2020 (HC less than 5th% UE2)	⨁◯◯◯	★★★★★★★	197	3388	9129	198462	1.26 [1.10, 1.45]
McKinzie 2021 (Diagnosis of TTN)	⨁◯◯◯	★★★★★★★	74	1459	141	3871	1.39 [1.06, 1.83]
McKinzie 2021 (Hyperbilirubinemia req treatment)	⨁◯◯◯	★★★★★★★	244	1459	562	3871	1.15 [1.00, 1.32]
McKinzie 2021 (Meconium aspiration syndrome)	⨁◯◯◯	★★★★★★★	5	1459	18	3871	0.74 [0.27, 1.98]
Rodriguez 2019 (Respiratory care)	⨁◯◯◯	★★★★★★★	12	1346	20	6730	3.00 [1.47, 6.12]
Rodriguez 2019 (Antibiotic treatment)	⨁◯◯◯	★★★★★★★	76	1346	256	6730	1.48 [1.16, 1.90]
Rodriguez 2019 (Blood transfusion)	⨁◯◯◯	★★★★★★★	1	1346	0	6730	14.99 [0.61, 367.80]
Rodriguez 2019 (Light therapy)	⨁◯◯◯	★★★★★★★	66	1346	261	6730	1.26 [0.97, 1.65]
Rodriguez 2019 (BCG vaccination)	⨁◯◯◯	★★★★★★★	217	1346	1065	6730	1.02 [0.89, 1.16]

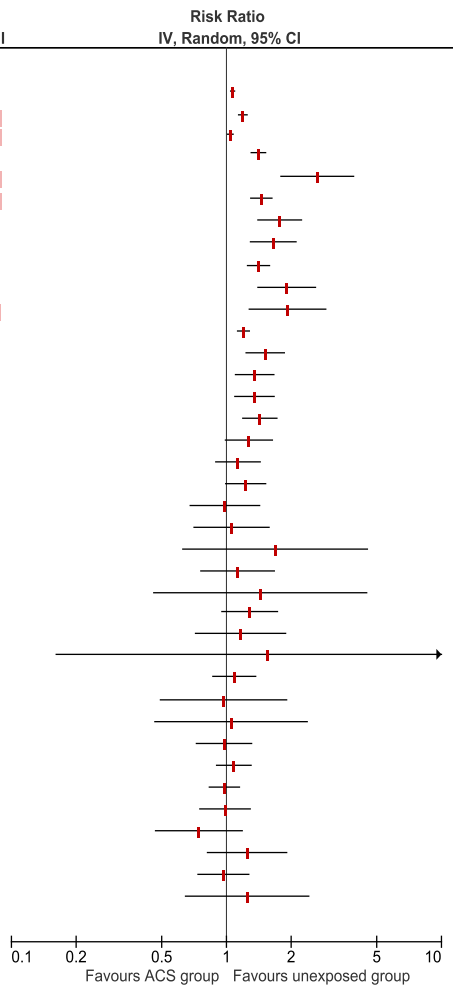


Study (long-term outcome)

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Mean	ACS group SD	ACS group Total	Unexposed group Mean	Unexposed group SD	Unexposed group Total	Mean Difference IV, Random, 95% CI
Long-term outcomes									
Osteen 2022 (Number of childhood hospitalizations)	⨁◯◯◯	★★★★★★★	0.2	0.1	629	0.2	0.1	2927	0.00 [-0.01, 0.01]



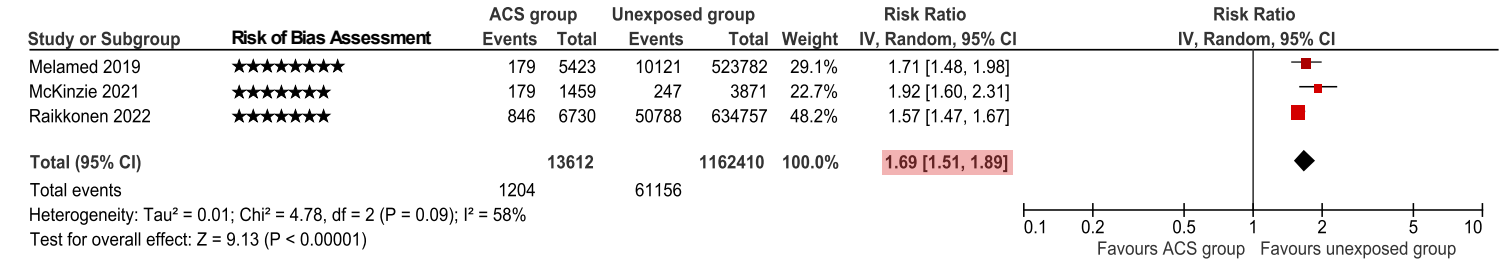
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Risk Ratio IV, Random, 95% CI
Long-term outcomes							
Melamed 2019 (Composite long-term outcome)	⨁⨁◯◯	★★★★★★★★	3346	5423	302520	523782	1.07 [1.05, 1.09]
Melamed 2019 (Suspected neurocognitive disorder)	⨁⨁◯◯	★★★★★★★★	1397	5423	113181	523782	1.19 [1.14, 1.25]
Melamed 2019 (Visual testing)	⨁⨁◯◯	★★★★★★★★	2461	5423	227948	523782	1.04 [1.01, 1.07]
Raikkonen 2020 (Any mental/behavioural disorder)	⨁⨁◯◯	★★★★★★★	598	6730	40051	634757	1.41 [1.30, 1.52]
Raikkonen 2022 (Cerebral palsy)	⨁⨁◯◯	★★★★★★★	26	6730	927	634757	2.65 [1.79, 3.90]
Raikkonen 2022 (Speech/language develop disorders)	⨁⨁◯◯	★★★★★★★	290	6730	18819	634757	1.45 [1.30, 1.63]
Raikkonen 2022 (Other psych development disorder)	⨁⨁◯◯	★★★★★★★	71	6730	3785	634757	1.77 [1.40, 2.23]
Raikkonen 2022 (Epilepsy)	⨁⨁◯◯	★★★★★★★	65	6730	3713	634757	1.65 [1.29, 2.11]
Raikkonen 2020 (Psych development disorders)	⨁⨁◯◯	★★★★★★★	269	6730	17994	634757	1.41 [1.25, 1.59]
Raikkonen 2020 (Sleep disorders)	⨁⨁◯◯	★★★★★★★	41	6730	2028	634757	1.91 [1.40, 2.60]
Osteen 2022 (Weight less than 10th%)	⨁⨁◯◯	★★★★★★★	31	629	75	2927	1.92 [1.28, 2.90]
Melamed 2019 (Audiometry testing)	⨁◯◯◯	★★★★★★★★	827	5423	66555	523782	1.20 [1.13, 1.28]
Raikkonen 2022 (Motor function develop disorders)	⨁◯◯◯	★★★★★★★	92	6730	5727	634757	1.52 [1.23, 1.86]
Raikkonen 2022 (Pervasive developmental disorder)	⨁◯◯◯	★★★★★★★	91	6730	6343	634757	1.35 [1.10, 1.66]
Raikkonen 2020 (Mixed disorders conduct/emotions)	⨁◯◯◯	★★★★★★★	87	6730	6077	634757	1.35 [1.09, 1.67]
Raikkonen 2020 (Other behaviour/emotion disorders)	⨁◯◯◯	★★★★★★★	115	6730	7583	634757	1.43 [1.19, 1.72]
Raikkonen 2022 (Vision or hearing loss)	⨁◯◯◯	★★★★★★★	61	6730	4522	634757	1.27 [0.99, 1.64]
Raikkonen 2022 (Scholastic skill develop disorder)	⨁◯◯◯	★★★★★★★	68	6730	5667	634757	1.13 [0.89, 1.44]
Raikkonen 2020 (ADD/conduct disorders)	⨁◯◯◯	★★★★★★★	84	6730	6448	634757	1.23 [0.99, 1.52]
Raikkonen 2020 (Autism spectrum disorders)	⨁◯◯◯	★★★★★★★	28	6730	2684	634757	0.98 [0.68, 1.43]
Raikkonen 2020 (Psych, mood, neurotic disorders)	⨁◯◯◯	★★★★★★★	24	6730	2143	634757	1.06 [0.71, 1.58]
Raikkonen 2020 (Eating disorders)	⨁◯◯◯	★★★★★★★	4	6730	224	634757	1.68 [0.63, 4.53]
Raikkonen 2020 (Mild/mod intellectual disability)	⨁◯◯◯	★★★★★★★	25	6730	2093	634757	1.13 [0.76, 1.67]
Raikkonen 2020 (Severe intellectual disability)	⨁◯◯◯	★★★★★★★	3	6730	197	634757	1.44 [0.46, 4.49]
Osteen 2022 (Developmental delay)	⨁◯◯◯	★★★★★★★	51	629	185	2927	1.28 [0.95, 1.73]
Osteen 2022 (Attention deficit disorder)	⨁◯◯◯	★★★★★★★	20	629	80	2927	1.16 [0.72, 1.88]
Osteen 2022 (Diabetes)	⨁◯◯◯	★★★★★★★	1	629	3	2927	1.55 [0.16, 14.89]
Osteen 2022 (Asthma)	⨁◯◯◯	★★★★★★★	79	629	338	2927	1.09 [0.86, 1.37]
Osteen 2022 (Hypoxemia)	⨁◯◯◯	★★★★★★★	10	629	48	2927	0.97 [0.49, 1.91]
Osteen 2022 (Tachypnea)	⨁◯◯◯	★★★★★★★	7	629	31	2927	1.05 [0.46, 2.38]
Osteen 2022 (Wheezing)	⨁◯◯◯	★★★★★★★	49	629	234	2927	0.97 [0.73, 1.31]
Osteen 2022 (Bronchiolitis)	⨁◯◯◯	★★★★★★★	114	629	490	2927	1.08 [0.90, 1.30]
Osteen 2022 (Albuterol use)	⨁◯◯◯	★★★★★★★	139	629	661	2927	0.98 [0.83, 1.15]
Osteen 2022 (Weight greater than 90th%)	⨁◯◯◯	★★★★★★★	58	629	274	2927	0.99 [0.75, 1.29]
Osteen 2022 (Height/length greater than 90th%)	⨁◯◯◯	★★★★★★★	20	629	125	2927	0.74 [0.47, 1.18]
Osteen 2022 (Height/length less than 10th%)	⨁◯◯◯	★★★★★★★	26	629	97	2927	1.25 [0.82, 1.91]
Osteen 2022 (BMI greater than 90th%)	⨁◯◯◯	★★★★★★★	57	629	274	2927	0.97 [0.74, 1.27]
Osteen 2022 (BMI less than 10th%)	⨁◯◯◯	★★★★★★★	11	629	41	2927	1.25 [0.65, 2.42]



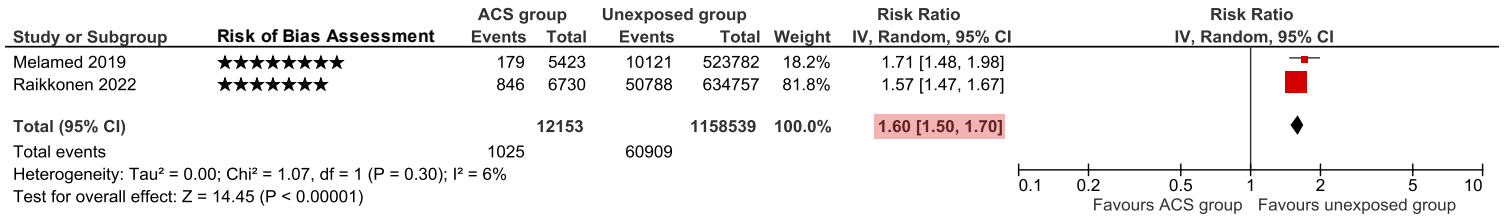
Legend:
ACS – antenatal corticosteroids; ADD – attention deficit disorder; audio – audiometry; BCG – Bacille Calmette-Guérin; BMI – body mass index; BW – birthweight; CI – confidence interval; develop – development/developmental; EGA – estimated gestational age; HC – head circumference; IV – inverse variance; min – minutes; mod – moderate; NICU – neonatal intensive care unit; PI – ponderal index; PS – propensity score; psych – psychological/psychotic; Red highlighting – statistically significant association with adverse outcome; req – requiring; SE – standard error; SGA – small for gestational age; susp. neurocog – suspected neurocognitive; TTN – transient tachypnea of the newborn; UE1 – unexposed group 1 (an episode of threatened preterm labour without corticosteroids); UE2 – unexposed group 2 (neither threatened preterm labor nor corticosteroids); w/o – without

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes, a maximum of 13 points could be awarded when assessing risk of bias for long-term outcomes.
GRADE Assessment: ⊕◯◯◯ – very low certainty; ⊕⊕◯◯ – low certainty

eFigure 2: Pooled secondary outcomes for infants born at <u>term</u> from population-based studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

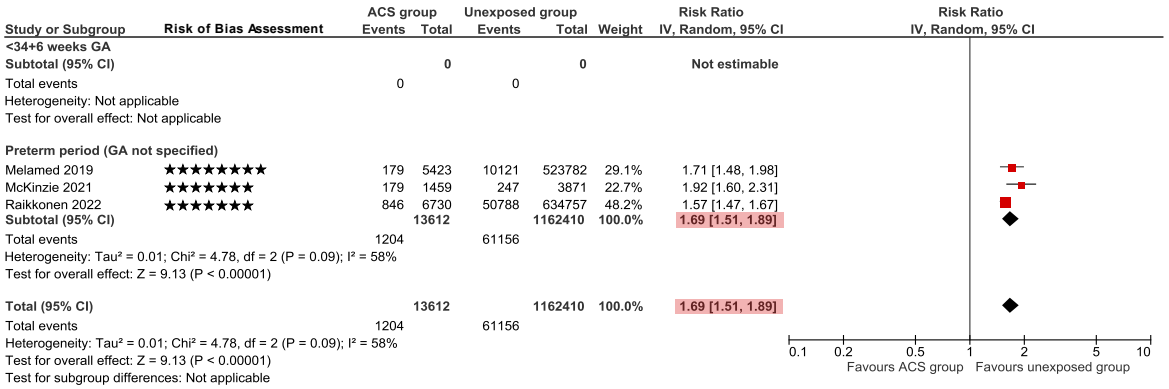
Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]
NICU admission [⊕⊕◯◯]	

<u>Sensitivity analysis</u>: Only studies with all births remain (i.e., removed studies with a sample representative of all births)

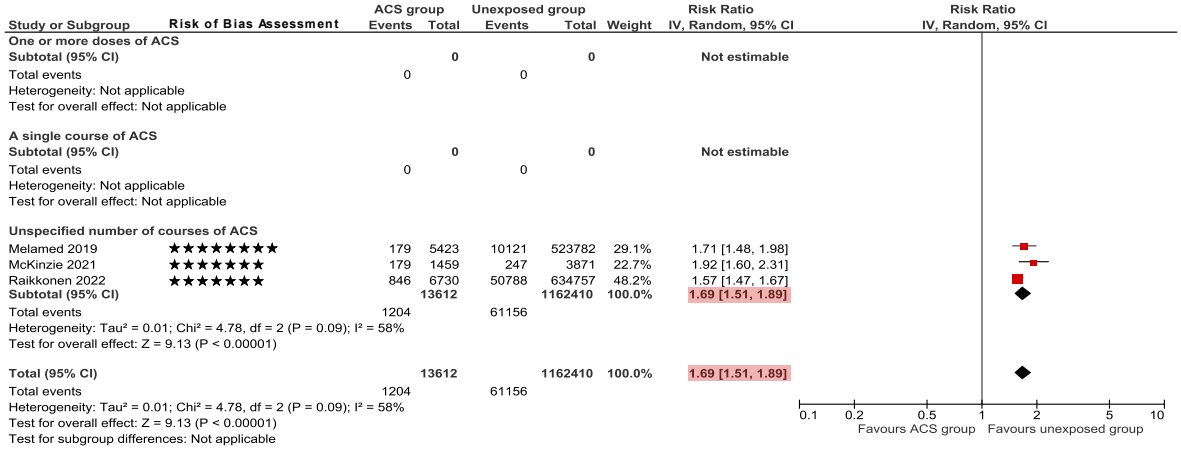


Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]

Subgroup analysis: GA at ACS administration



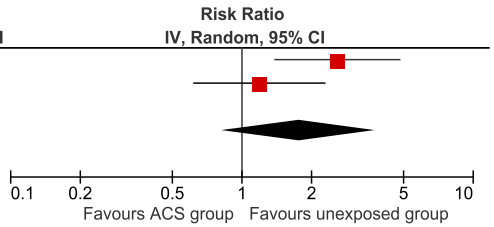
Subgroup analysis: Number of ACS courses*



Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]
Intubation [⊕◯◯◯]	

Study or Subgroup	Risk of Bias Assessment	ACS group Events	Total	Unexposed group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Rodriguez 2019	★★★★★★★	15	1346	29	6730	50.8%	2.59 [1.39, 4.81]
McKinzie 2021	★★★★★★★	13	1459	29	3871	49.2%	1.19 [0.62, 2.28]
Total (95% CI)			**2805**		**10601**	**100.0%**	**1.77 [0.82, 3.78]**
Total events		28		58			

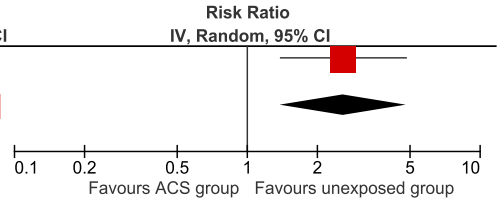
Heterogeneity: Tau² = 0.20; Chi² = 2.86, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 1.46 (P = 0.14)



Sensitivity analysis: Only studies with all births remain (i.e., removed studies with a sample representative of all births)

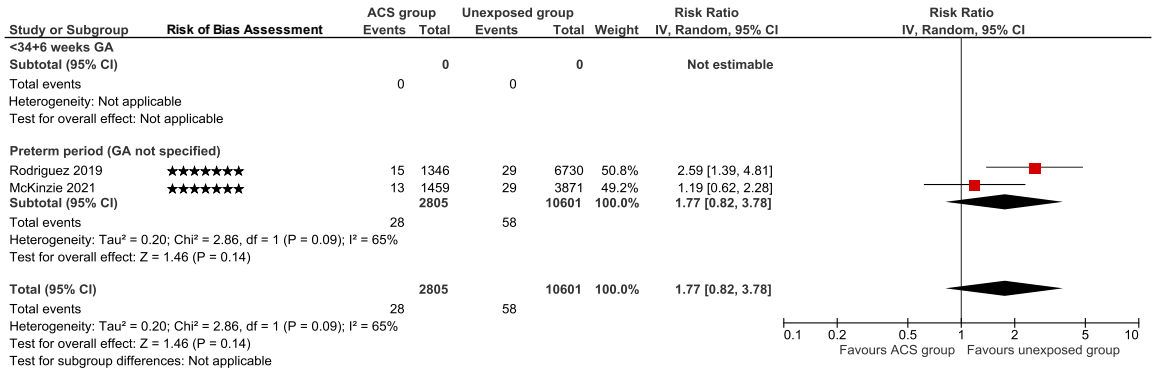
Study or Subgroup	Risk of Bias Assessment	ACS group Events	Total	Unexposed group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Rodriguez 2019	★★★★★★★	15	1346	29	6730	100.0%	2.59 [1.39, 4.81]
Total (95% CI)			**1346**		**6730**	**100.0%**	**2.59 [1.39, 4.81]**
Total events		15		29			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.00 (P = 0.003)

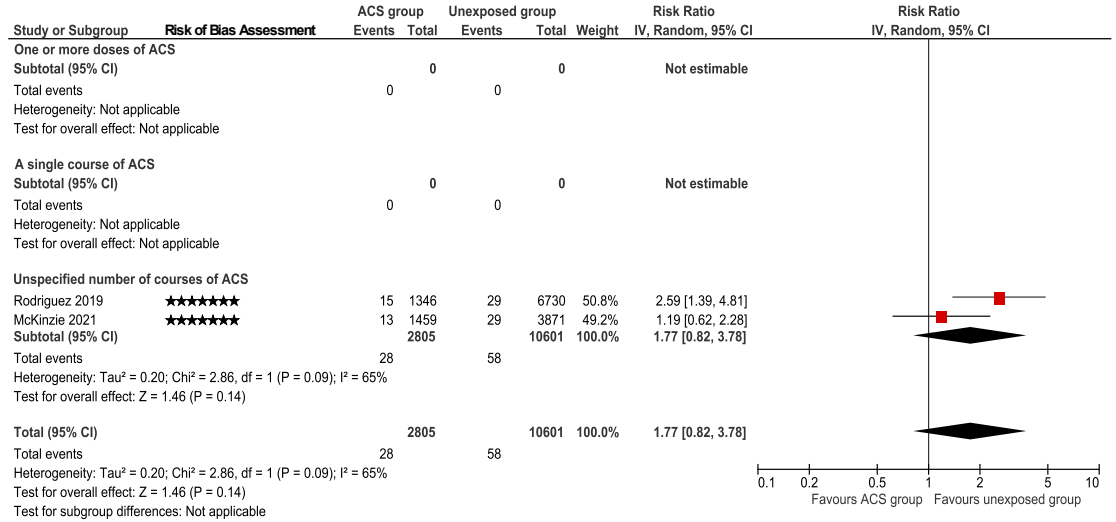


Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]

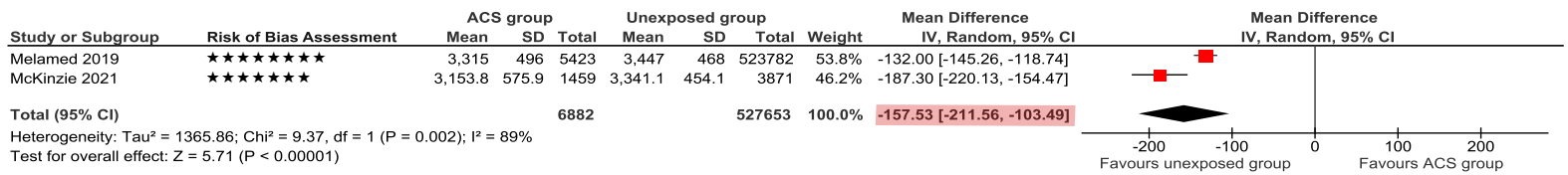
Subgroup analysis: GA at ACS administration



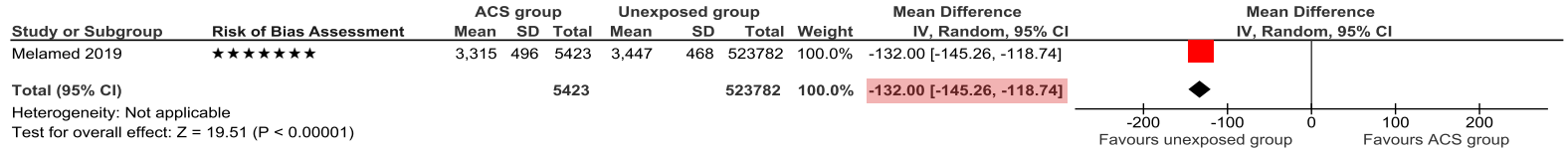
Subgroup analysis: Number of ACS courses*



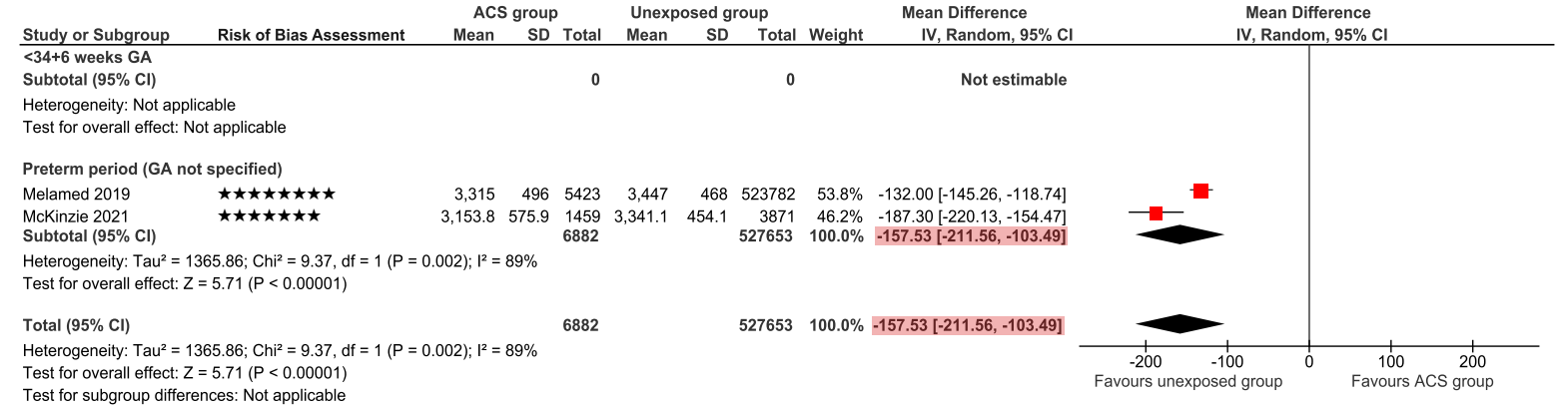
Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]
Birthweight [⊕◯◯◯]	



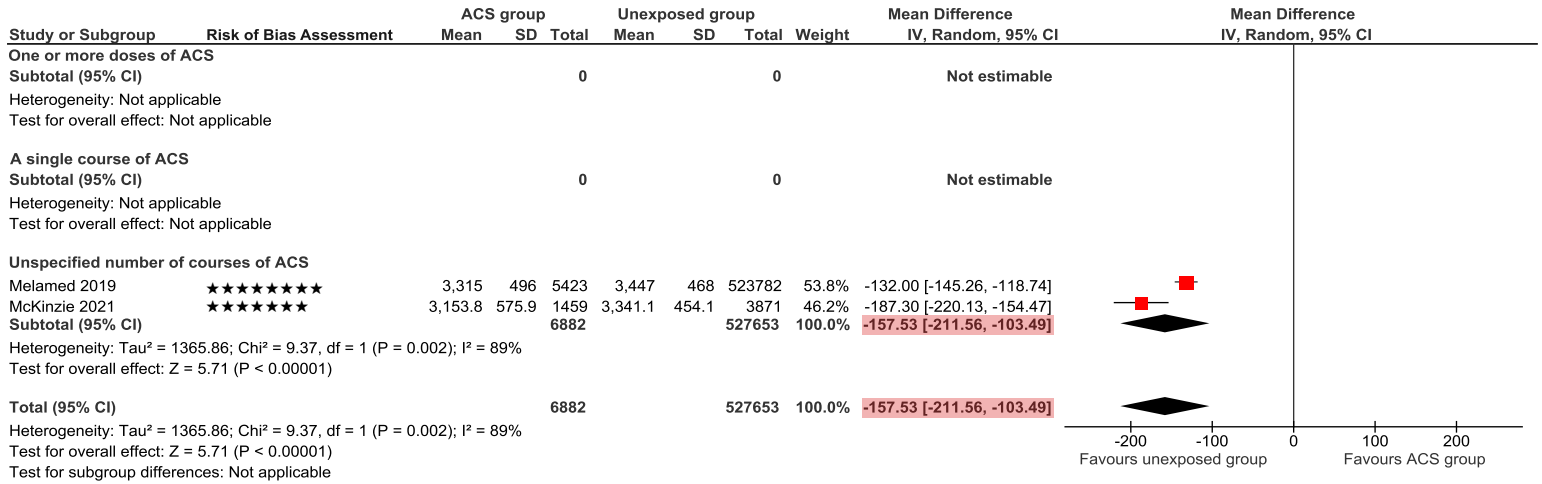
Sensitivity analysis: Only studies with all births remain (i.e., removed studies with a sample representative of all births)



Subgroup analysis: GA at ACS administration



Unadjusted outcome [GRADE assessment]	**Forest plot** [Sensitivity analysis]
	Subgroup analysis: Number of ACS courses*



Legend:

ACS – antenatal corticosteroids; CI – confidence interval; df – degrees of freedom; GA – gestational age; IV – inverse variance; NICU – neonatal intensive care unit; red highlighting – statistically significant association with adverse outcome; SD – standard deviation

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes.
GRADE Assessment: ⊕◯◯◯ – very low certainty; ⊕⊕◯◯ – low certainty

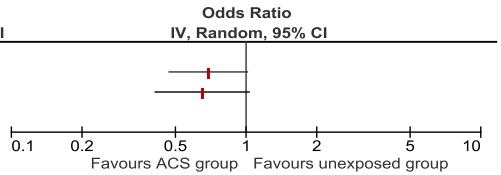
*The subgroup of "unspecified number of courses of ACS" were likely a single course based on clinical guidelines

eFigure 3: Adjusted and unadjusted analyses of secondary outcomes for infants born late preterm from population-based studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Adjusted data

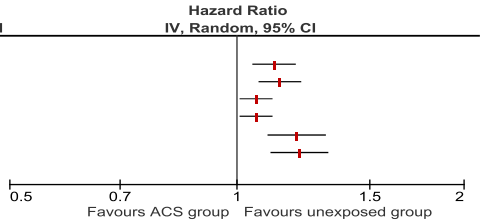
Study (short-term outcome)

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Odds Ratio]	SE	Odds Ratio IV, Random, 95% CI
Short-term outcomes					
Malloy 2012 (Neonatal death)	⨁◯◯◯	★★★★★★★	-0.3711	0.1959	0.69 [0.47, 1.01]
Malloy 2012 (Neonatal death within NICU group)	⨁◯◯◯	★★★★★★★	-0.4308	0.2351	0.65 [0.41, 1.04]



Study (long-term outcome)

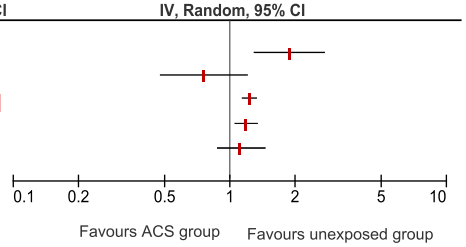
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	log[Hazard Ratio]	SE	Hazard Ratio IV, Random, 95% CI
Long-term outcomes					
Aviram 2022 (Suspected neurocognitive disorder)	⨁⨁◯◯	★★★★★★★★★★	0.1133	0.0329	1.12 [1.05, 1.20]
Aviram 2022 (Susp. neurocog disorder w/o NICU/BW)	⨁⨁◯◯	★★★★★★★★★★	0.131	0.0323	1.14 [1.07, 1.22]
Aviram 2022 (Visual testing)	⨁⨁◯◯	★★★★★★★★★★	0.0583	0.0247	1.06 [1.01, 1.11]
Aviram 2022 (Visual testing w/o NICU/BW)	⨁⨁◯◯	★★★★★★★★★★	0.0583	0.0247	1.06 [1.01, 1.12]
Aviram 2022 (Audiometry testing)	⨁◯◯◯	★★★★★★★★★★	0.1823	0.0444	1.20 [1.10, 1.31]
Aviram 2022 (Audiometry testing w/o NICU/BW)	⨁◯◯◯	★★★★★★★★★★	0.1906	0.044	1.21 [1.11, 1.32]



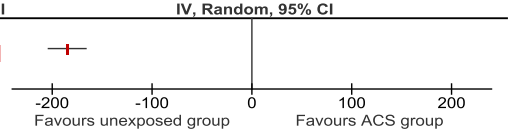
Unadjusted data

Study (short-term outcome)

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Risk Ratio IV, Random, 95% CI
Short-term outcomes							
Malloy 2012 (Neonatal death)	⨁◯◯◯	★★★★★★	29	4456	602	174109	1.88 [1.30, 2.73]
Malloy 2012 (Neonatal death within NICU group)	⨁◯◯◯	★★★★★★	19	2408	337	32409	0.76 [0.48, 1.20]
Aviram 2022 (Resuscitation at birth)	⨁◯◯◯	★★★★★★★★	869	2689	6051	22979	1.23 [1.16, 1.30]
Aviram 2022 (Birthweight less than 10th%)	⨁◯◯◯	★★★★★★★★	296	2689	2086	22979	1.21 [1.08, 1.36]
Aviram 2022 (Apgar score less than 7 at 5 min)	⨁◯◯◯	★★★★★★★★	59	2689	453	22979	1.11 [0.85, 1.46]

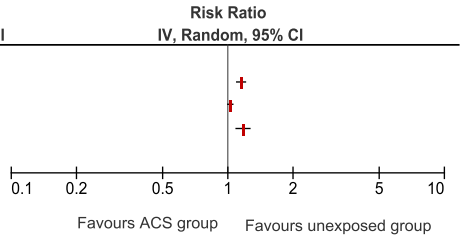


Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Mean	SD	Total	Unexposed group Mean	SD	Total	Mean Difference IV, Random, 95% CI
Short-term outcomes									
Aviram 2022 (Birthweight)	⊕⊕◯◯	★★★★★★★★	2,524	472	2689	2,709	467	22979	-185.00 [-203.83, -166.17]



Study (long-term outcome)

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	Total	Unexposed group Events	Total	Risk Ratio IV, Random, 95% CI
Long-term outcomes							
Aviram 2022 (Suspected neurocognitive disorder)	⊕◯◯◯	★★★★★★★★	1156	2689	8581	22979	1.15 [1.10, 1.21]
Aviram 2022 (Visual testing)	⊕◯◯◯	★★★★★★★★	1860	2689	15483	22979	1.03 [1.00, 1.05]
Aviram 2022 (Audiometry testing)	⊕◯◯◯	★★★★★★★★	627	2689	4559	22979	1.18 [1.09, 1.26]



Legend:

ACS – antenatal corticosteroids; BW – birthweight; CI – confidence interval; IV – inverse variance; min – minutes; NICU – neonatal intensive care unit; red highlighting – statistically significant association with adverse outcome; SE – standard error; susp. neurocog – suspected neurocognitive; w/o – without

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes, a maximum of 13 points could be awarded when assessing risk of bias for long-term outcomes.

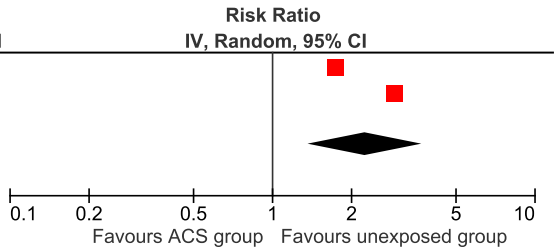
GRADE Assessment: ⊕◯◯◯ – very low certainty; ⊕⊕◯◯ – low certainty

eFigure 4: Pooled secondary outcomes for infants born late preterm from population-based studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Unadjusted outcome [GRADE assessment]	**Forest plot**
NICU admission [⊕◯◯◯]	

Study or Subgroup	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Weight	Risk Ratio IV, Random, 95% CI
Aviram 2022	★★★★★★★★	922	2689	4517	22979	49.9%	1.74 [1.65, 1.85]
Malloy 2012	★★★★★★	2408	4456	32409	174109	50.1%	2.90 [2.82, 2.99]
Total (95% CI)			**7145**		**197088**	**100.0%**	**2.25 [1.37, 3.71]**
Total events		3330		36926			

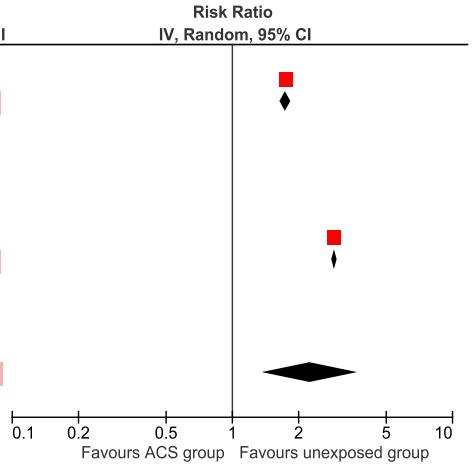
Heterogeneity: Tau² = 0.13; Chi² = 234.53, df = 1 (P < 0.00001); I² = 100%
Test for overall effect: Z = 3.19 (P = 0.001)



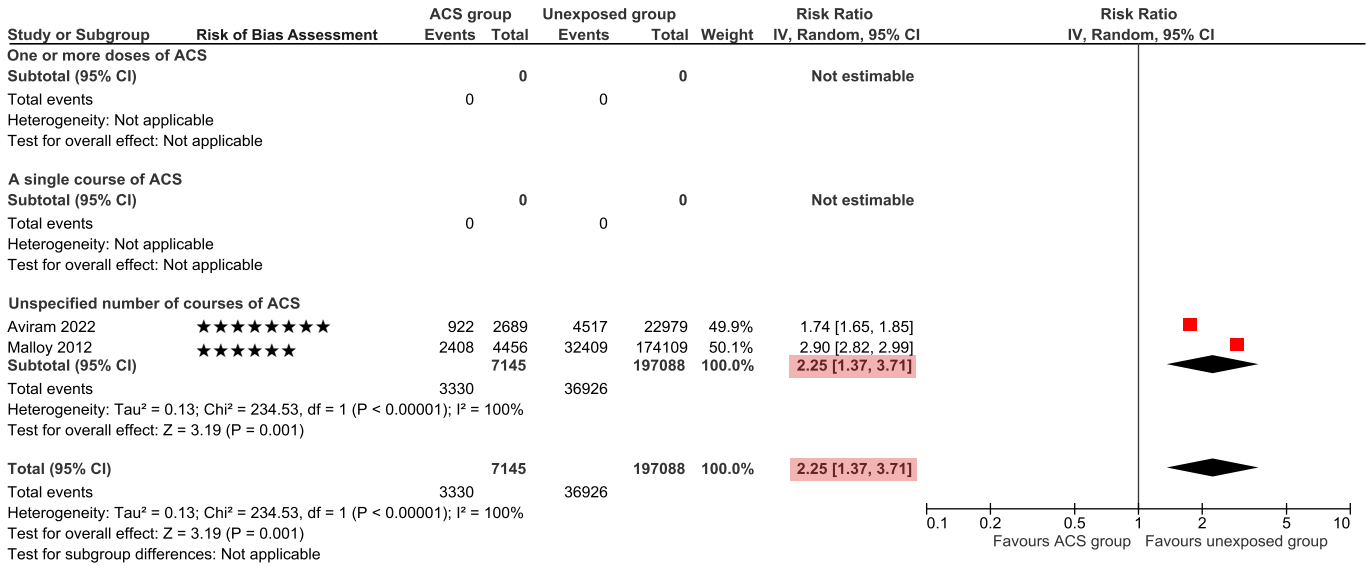
Subgroup analysis: GA at ACS administration

Study or Subgroup	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Weight	Risk Ratio IV, Random, 95% CI
<34 weeks GA							
Aviram 2022	★★★★★★★★	922	2689	4517	22979	49.9%	1.74 [1.65, 1.85]
Subtotal (95% CI)			**2689**		**22979**	**49.9%**	**1.74 [1.65, 1.85]**
Total events		922		4517			
Heterogeneity: Not applicable							
Test for overall effect: Z = 18.64 (P < 0.00001)							
Preterm period (GA not specified)							
Malloy 2012	★★★★★★	2408	4456	32409	174109	50.1%	2.90 [2.82, 2.99]
Subtotal (95% CI)			**4456**		**174109**	**50.1%**	**2.90 [2.82, 2.99]**
Total events		2408		32409			
Heterogeneity: Not applicable							
Test for overall effect: Z = 72.52 (P < 0.00001)							
Total (95% CI)			**7145**		**197088**	**100.0%**	**2.25 [1.37, 3.71]**
Total events		3330		36926			

Heterogeneity: Tau² = 0.13; Chi² = 234.53, df = 1 (P < 0.00001); I² = 100%
Test for overall effect: Z = 3.19 (P = 0.001)
Test for subgroup differences: Chi² = 234.53, df = 1 (P < 0.00001), I² = 99.6%



Unadjusted outcome [GRADE assessment]	**Forest plot**
	<u>Subgroup analysis:</u> Number of ACS courses*



Legend:

ACS – antenatal corticosteroids; CI – confidence interval; df – degrees of freedom; GA – gestational age; IV – inverse variance; NICU – neonatal intensive care unit; Red highlighting – statistically significant association with adverse outcome

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes.
GRADE Assessment: ⊕◯◯◯ – very low certainty

*The subgroup of "unspecified number of courses of ACS" were likely a single course based on clinical guidelines

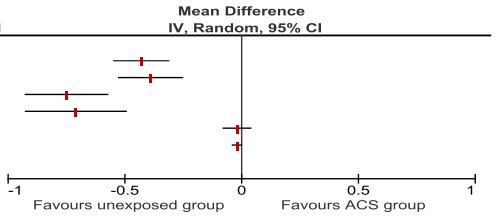
eFigure 5: <u>Adjusted and unadjusted</u> analyses of secondary outcomes for infants born at <u>term/late preterm</u> (combined) from population-based studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids (a post-hoc analysis)

Adjusted data

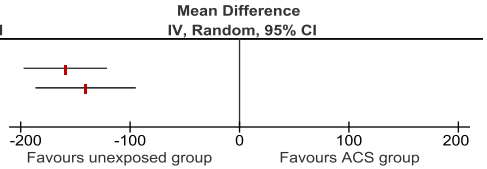
Study (short-term outcome)

35^{+0}- 37^{+6} weeks

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Head circumference)	⊕⊕◯◯	★★★★★★★	-0.43	0.06	-0.43 [-0.55, -0.31]
Rodriguez 2019 (Head circumference PS cohort)	⊕⊕◯◯	★★★★★★★	-0.39	0.07	-0.39 [-0.53, -0.25]
Rodriguez 2019 (Body length)	⊕⊕◯◯	★★★★★★★	-0.75	0.09	-0.75 [-0.93, -0.57]
Rodriguez 2019 (Body length PS cohort)	⊕⊕◯◯	★★★★★★★	-0.71	0.11	-0.71 [-0.93, -0.49]
Rodriguez 2019 (Ponderal index)	⊕◯◯◯	★★★★★★★	-0.02	0.03	-0.02 [-0.08, 0.04]
Rodriguez 2019 (Ponderal index PS cohort)	⊕◯◯◯	★★★★★★★	-0.02	0.01	-0.02 [-0.04, -0.00]



Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Birthweight)	⊕⊕◯◯	★★★★★★★	-159.25	19.14	-159.25 [-196.76, -121.74]
Rodriguez 2019 (Birthweight PS cohort)	⊕⊕◯◯	★★★★★★★	-140.68	23.09	-140.68 [-185.94, -95.42]

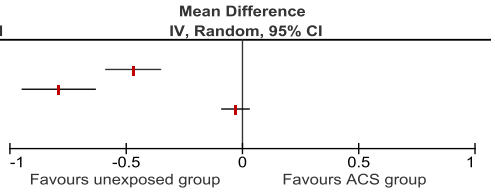


Unadjusted data

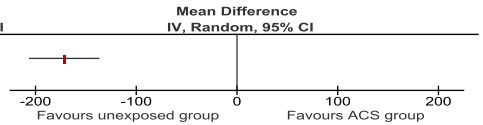
Study (short-term outcome)

35^{+0}- 37^{+6} weeks

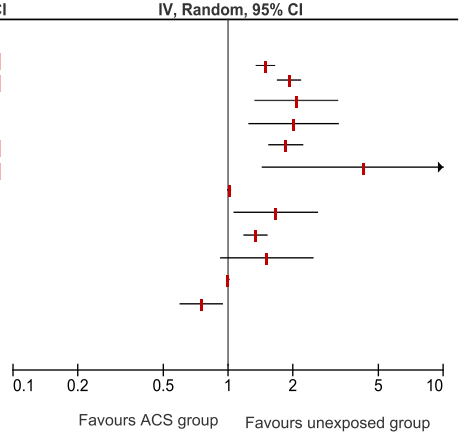
Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Head circumference)	⊕⊕◯◯	★★★★★★★	-0.47	0.06	-0.47 [-0.59, -0.35]
Rodriguez 2019 (Body length)	⊕⊕◯◯	★★★★★★★	-0.79	0.08	-0.79 [-0.95, -0.63]
Rodriguez 2019 (Ponderal index)	⊕⊕◯◯	★★★★★★★	-0.03	0.03	-0.03 [-0.09, 0.03]



Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	Mean Difference	SE	Mean Difference IV, Random, 95% CI
Short-term outcomes					
Rodriguez 2019 (Birthweight)	⊕⊕◯◯	★★★★★★★	-171.5	17.52	-171.50 [-205.84, -137.16]

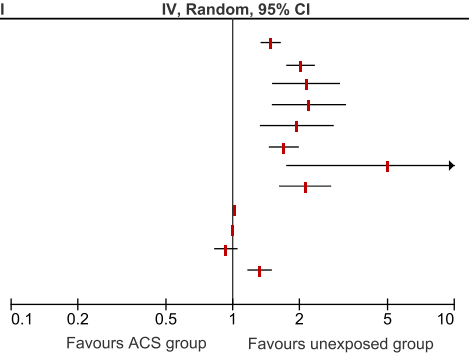


Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Risk Ratio IV, Random, 95% CI
Short-term outcomes							
Rodriguez 2019 (NICU admission)	⊕⊕◯◯	★★★★★★★	288	685	959	3425	1.50 [1.35, 1.66]
Rodriguez 2019 (Hospitalization status beyond 7 days)	⊕⊕◯◯	★★★★★★★	250	685	645	3409	1.93 [1.71, 2.18]
Rodriguez 2019 (Hospital transfer)	⊕⊕◯◯	★★★★★★★	27	685	65	3425	2.08 [1.34, 3.23]
Rodriguez 2019 (Intubation)	⊕⊕◯◯	★★★★★★★	23	685	57	3425	2.02 [1.25, 3.25]
Rodriguez 2019 (Antibiotic treatment)	⊕⊕◯◯	★★★★★★★	134	685	361	3425	1.86 [1.55, 2.22]
Rodriguez 2019 (Blood transfusion)	⊕⊕◯◯	★★★★★★★	6	685	7	3425	4.29 [1.44, 12.71]
Rodriguez 2019 (Hypothyroidism screening)	⊕⊕◯◯	★★★★★★★	664	685	3284	3425	1.01 [1.00, 1.03]
Rodriguez 2019 (Respiratory care)	⊕◯◯◯	★★★★★★★	25	685	75	3425	1.67 [1.07, 2.60]
Rodriguez 2019 (Light therapy)	⊕◯◯◯	★★★★★★★	224	685	835	3425	1.34 [1.19, 1.52]
Rodriguez 2019 (Metabolic disorder screening)	⊕◯◯◯	★★★★★★★	20	685	66	3425	1.52 [0.92, 2.48]
Rodriguez 2019 (Vitamin K)	⊕◯◯◯	★★★★★★★	671	685	3362	3425	1.00 [0.99, 1.01]
Rodriguez 2019 (BCG vaccination)	⊕◯◯◯	★★★★★★★	77	685	513	3425	0.75 [0.60, 0.94]



≥35 weeks

Study or Subgroup	GRADE Assessment	Risk of Bias Assessment	ACS group Events	ACS group Total	Unexposed group Events	Unexposed group Total	Risk Ratio IV, Random, 95% CI
Short term outcomes							
Rodriguez 2019 (NICU admission)	⊕⊕◯◯	★★★★★★★	419	2031	1411	10155	1.48 [1.35, 1.64]
Rodriguez 2019(Hospitalization status beyond 7 days)	⊕⊕◯◯	★★★★★★★	327	2029	821	10127	1.99 [1.76, 2.24]
Rodriguez 2019 (Hospital transfer)	⊕⊕◯◯	★★★★★★★	45	2031	105	10155	2.14 [1.52, 3.03]
Rodriguez 2019 (Intubation)	⊕⊕◯◯	★★★★★★★	38	2031	86	10155	2.21 [1.51, 3.23]
Rodriguez 2019 (Respiratory care)	⊕⊕◯◯	★★★★★★★	37	2031	95	10155	1.95 [1.34, 2.84]
Rodriguez 2019 (Antibiotic treatment)	⊕⊕◯◯	★★★★★★★	210	2031	617	10155	1.70 [1.47, 1.98]
Rodriguez 2019 (Blood transfusion)	⊕⊕◯◯	★★★★★★★	7	2031	7	10155	5.00 [1.76, 14.24]
Rodriguez 2019 (Metabolic disorder screening)	⊕⊕◯◯	★★★★★★★	76	2031	179	10155	2.12 [1.63, 2.76]
Rodriguez 2019 (Hypothyroidism screening)	⊕⊕◯◯	★★★★★★★	1987	2031	9783	10155	1.02 [1.01, 1.02]
Rodriguez 2019 (Vitamin K)	⊕⊕◯◯	★★★★★★★	2008	2031	10036	10155	1.00 [1.00, 1.01]
Rodriguez 2019 (BCG vaccination)	⊕⊕◯◯	★★★★★★★	294	2031	1578	10155	0.93 [0.83, 1.05]
Rodriguez 2019 (Light therapy)	⊕◯◯◯	★★★★★★★	290	2031	1096	10155	1.32 [1.17, 1.49]



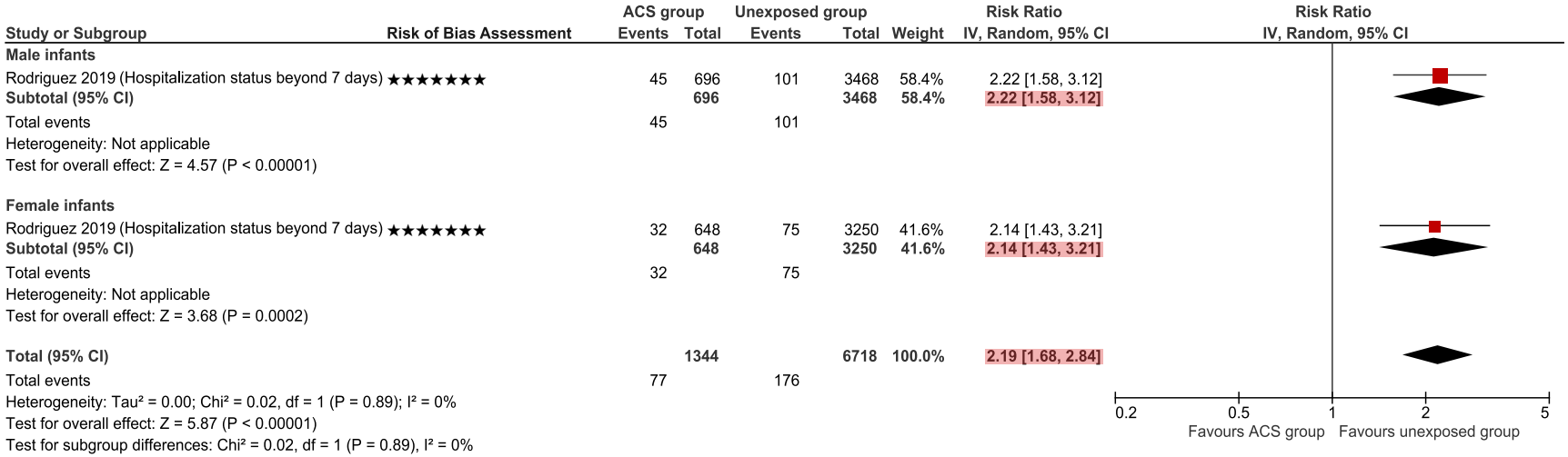
Legend:
ACS – antenatal corticosteroids; BCG – Bacille Calmette-Guérin; CI – confidence interval; green highlighting – statistically significant benefit; IV – inverse variance; NICU – neonatal intensive care unit; PS – propensity score; red highlighting – statistically significant association with adverse outcome; SE – standard error

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes
GRADE Assessment: ⊕◯◯◯ – very low certainty; ⊕⊕◯◯ – low certainty

eFigure 6: Available subgroup data for infant sex in infants born at <u>term,</u> or <u>term/late preterm (combined)</u> from a population-based study in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

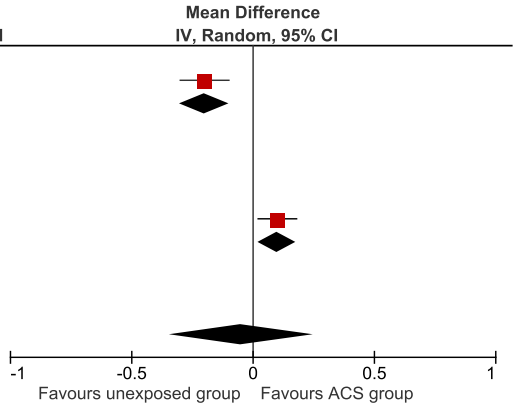
*Infants born at **term/post-term****

Hospitalization beyond the first seven days of life for infants born at term+post-term [⊕⊕◯◯]



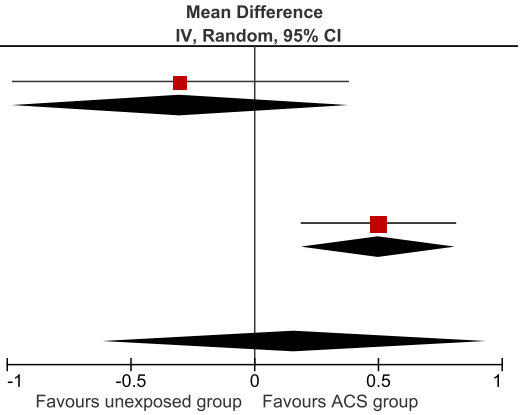
5 minute Apgar score for infants born at term [⊕◯◯◯]

Study or Subgroup	Risk of Bias Assesssment	ACS group Mean	SD	Total	Unexposed group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Male infants									
Rodriguez 2019 (5 min Apgar score)	★★★★★★★	8.9	1.11	510	9.1	0.76	2937	49.5%	-0.20 [-0.30, -0.10]
Subtotal (95% CI)				**510**			**2937**	**49.5%**	**-0.20 [-0.30, -0.10]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.91 (P < 0.0001)									
Female infants									
Rodriguez 2019 (5 min Apgar score)		9.2	0.79	453	9.1	0.84	2763	50.5%	0.10 [0.02, 0.18]
Subtotal (95% CI)	★★★★★★★			**453**			**2763**	**50.5%**	**0.10 [0.02, 0.18]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.47 (P = 0.01)									
Total (95% CI)				**963**			**5700**	**100.0%**	**-0.05 [-0.34, 0.25]**
Heterogeneity: Tau² = 0.04; Chi² = 21.20, df = 1 (P < 0.00001); I² = 95%									
Test for overall effect: Z = 0.32 (P = 0.75)									
Test for subgroup differences: Chi² = 21.20, df = 1 (P < 0.00001), I² = 95.3%									



5 minute Apgar score for infants born post-term [⊕◯◯◯]

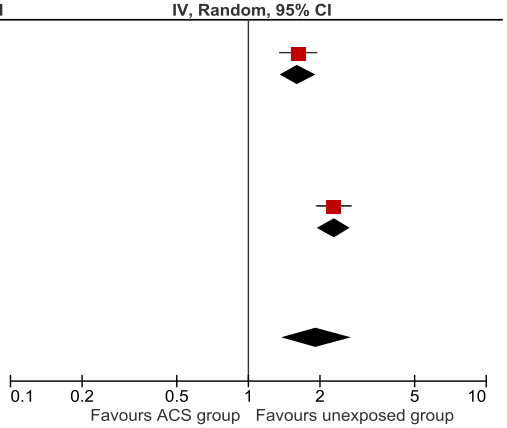
Study or Subgroup	Risk of Bias Assessment	ACS group Mean	SD	Total	Unexposed group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Male infants									
Rodriguez 2019 (5 min Apgar score)	★★★★★★★	8.8	1.21	13	9.1	0.8	92	42.6%	-0.30 [-0.98, 0.38]
Subtotal (95% CI)				**13**			**92**	**42.6%**	**-0.30 [-0.98, 0.38]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.87 (P = 0.39)									
Female infants									
Rodriguez 2019 (5 min Apgar score)	★★★★★★★	9.5	0.52	13	9	0.67	102	57.4%	0.50 [0.19, 0.81]
Subtotal (95% CI)				**13**			**102**	**57.4%**	**0.50 [0.19, 0.81]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.15 (P = 0.002)									
Total (95% CI)				**26**			**194**	**100.0%**	**0.16 [-0.62, 0.93]**
Heterogeneity: Tau² = 0.25; Chi² = 4.42, df = 1 (P = 0.04); I² = 77%									
Test for overall effect: Z = 0.40 (P = 0.69)									
Test for subgroup differences: Chi² = 4.42, df = 1 (P = 0.04), I² = 77.4%									



*Infants born at **term/late preterm (35^{+0}-37^{+6} weeks)****

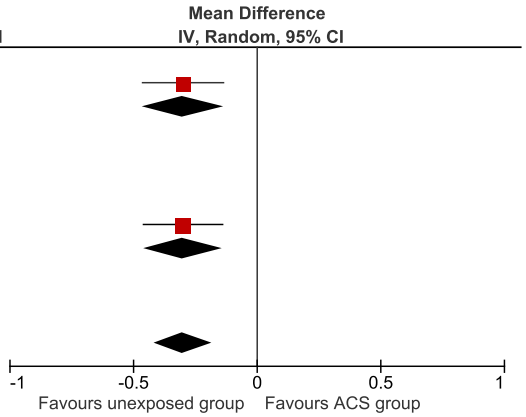
Hospitalization beyond the first seven days of life [⊕◯◯◯]

Study or Subgroup	Risk of Bias Assessment	ACS group Events	Total	Unexposed group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Male infants							
Rodriguez 2019 (Hospitalization status beyond 7 days)	★★★★★★★	113	353	346	1751	49.5%	1.62 [1.35, 1.94]
Subtotal (95% CI)			**353**		**1751**	**49.5%**	**1.62 [1.35, 1.94]**
Total events		113		346			
Heterogeneity: Not applicable							
Test for overall effect: Z = 5.28 (P < 0.00001)							
Female infants							
Rodriguez 2019 (Hospitalization status beyond 7 days)	★★★★★★★	137	332	299	1658	50.5%	2.29 [1.94, 2.70]
Subtotal (95% CI)			**332**		**1658**	**50.5%**	**2.29 [1.94, 2.70]**
Total events		137		299			
Heterogeneity: Not applicable							
Test for overall effect: Z = 9.87 (P < 0.00001)							
Total (95% CI)			**685**		**3409**	**100.0%**	**1.93 [1.38, 2.71]**
Total events		250		645			
Heterogeneity: Tau² = 0.05; Chi² = 7.76, df = 1 (P = 0.005); I² = 87%							
Test for overall effect: Z = 3.81 (P = 0.0001)							
Test for subgroup differences: Chi² = 7.76, df = 1 (P = 0.005), I² = 87.1%							



5 minute Apgar score [⊕⊕◯◯]

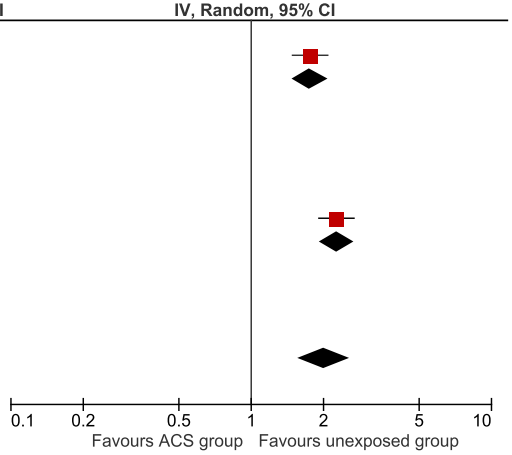
Study or Subgroup	Risk of Bias Assessment	ACS group Mean	SD	Total	Unexposed group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Male infants									
Rodriguez 2019 (5 min Apgar score)	★★★★★★★	8.5	1.3	278	8.8	1.18	1536	48.9%	-0.30 [-0.46, -0.14]
Subtotal (95% CI)				**278**			**1536**	**48.9%**	**-0.30 [-0.46, -0.14]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.59 (P = 0.0003)									
Female infants									
Rodriguez 2019 (5 min Apgar score)	★★★★★★★	8.6	1.23	258	8.9	1.1	1486	51.1%	-0.30 [-0.46, -0.14]
Subtotal (95% CI)				**258**			**1486**	**51.1%**	**-0.30 [-0.46, -0.14]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.67 (P = 0.0002)									
Total (95% CI)				**536**			**3022**	**100.0%**	**-0.30 [-0.41, -0.19]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%									
Test for overall effect: Z = 5.13 (P < 0.00001)									
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 1.00), I² = 0%									



*Infants born at **term/late preterm (≥35 weeks)****

Hospitalization beyond the first seven days of life [⊕◯◯◯]

Study or Subgroup	Risk of Bias Assessment	ACS group Events	Total	Unexposed group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Male infants							
Rodriguez 2019 (Hospitalization status beyond 7 days)	★★★★★★★	158	1049	447	5219	50.0%	1.76 [1.49, 2.08]
Subtotal (95% CI)			**1049**		**5219**	**50.0%**	**1.76 [1.49, 2.08]**
Total events		158		447			
Heterogeneity: Not applicable							
Test for overall effect: Z = 6.55 (P < 0.00001)							
Female infants							
Rodriguez 2019 (Hospitalization status beyond 7 days)	★★★★★★★	169	980	374	4908	50.0%	2.26 [1.91, 2.68]
Subtotal (95% CI)			**980**		**4908**	**50.0%**	**2.26 [1.91, 2.68]**
Total events		169		374			
Heterogeneity: Not applicable							
Test for overall effect: Z = 9.52 (P < 0.00001)							
Total (95% CI)			**2029**		**10127**	**100.0%**	**2.00 [1.56, 2.55]**
Total events		327		821			
Heterogeneity: Tau² = 0.02; Chi² = 4.30, df = 1 (P = 0.04); I² = 77%							
Test for overall effect: Z = 5.48 (P < 0.00001)							
Test for subgroup differences: Chi² = 4.30, df = 1 (P = 0.04), I² = 76.8%							



Legend:

ACS – antenatal corticosteroids; CI – confidence interval; IV – inverse variance; min – minute; red highlighting – statistically significant association with adverse outcome; SE – standard error

Newcastle-Ottawa Scale: ★ – point awarded; a maximum of 12 points could be awarded when assessing risk of bias for short-term outcomes

GRADE Assessment: ⊕◯◯◯ – very low certainty; ⊕⊕◯◯ – low certainty

*Data from the propensity matched cohort (Rodriguez 2019)

eAppendix 1: Electronic search strategies for a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Database: OVID Medline (January 1, 2000 – February 01, 2023)		
#	**Search terms**	**Results**
1	Premature Birth/	18918
2	exp Infant, Premature/	62683
3	Obstetric Labor, Premature/	13700
4	Term Birth/	3203
5	exp Infant, Newborn/	657608
6	exp Pregnancy/	975501
7	Pregnant Women/	12643
8	pregnan*.mp.	1094400
9	((preterm or pre-term or prematur* or term) adj3 (infant* or birth* or child* or deliver* or newborn or labour or labor or born or neonate*)).mp.	181769
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	1597569
11	Glucocorticoids/	69384
12	(antenatal adj4 (cortico* or steroid*)).mp.	2564
13	Betamethasone/	6232
14	Dexamethasone/	54484
15	betamethasone.mp.	8284
16	celestone.mp.	76
17	dexamethasone.mp.	78042
18	11 or 12 or 13 or 14 or 15 or 16 or 17	141818
19	exp Randomized Controlled Trial/	575763
20	clinical trial/	535788
21	Random Allocation/	106866
22	Multicenter study/	324291
23	Placebos/	35918
24	RCT.mp.	30761
25	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	1060587
26	(clinical adj2 trial:).mp.	1133569

27	((single or double or triple) adj (blind* or mask*)).mp.	260363
28	(clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	1136655
29	(populat* adj2 (base* or analys* or cohort*)).mp.	187991
30	((multicentr* or nation* or provinc* or state*) adj2 (stud* or analys* or cohort)).mp.	100926
31	(health* adj2 database*).mp.	11998
32	(discharge* adj2 record*).mp.	3748
33	(birth* adj2 registr*).mp.	3274
34	exp cohort studies/	2379262
35	Epidemiologic studies/	9151
36	(observational adj1 stud*).mp.	229429
37	(cohort adj3 (stud* or analys*)).mp.	532427
38	(follow up adj3 stud*).mp.	728407
39	(longitudinal or retrospective or prospective).mp.	2358784
40	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39	4692684
41	(Animals/ or Models, Animal/ or Disease Models, Animal/) not Humans/	5000299
42	10 and 18 and 40	3680
43	42 not 41	3504
44	**limit 43 to yr="2000 -Current"**	**2940**

Database: Embase (January 1, 2000 – February 01, 2023)		
#	**Search terms**	**Results**
1	exp prematurity/	117547
2	exp premature labor/	52454
3	term birth/	4149
4	newborn/	575507
5	exp pregnancy/ or exp high risk pregnancy/	738765
6	pregnant woman/	100010
7	pregnan*.mp.	1046407
8	((preterm or pre-term or prematur* or term) adj3 (infant* or birth* or child* or deliver* or newborn or labour or labor or born or neonate*)).mp.	215355
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	1582088
10	glucocorticoid/	96084
11	(antenatal adj4 (cortico* or steroid*)).mp.	3970
12	betamethasone/	18597
13	dexamethasone/	173099
14	betamethasone.mp.	25747
15	celestone.mp.	974
16	dexamethasone.mp.	189245
17	10 or 11 or 12 or 13 or 14 or 15 or 16	292140
18	randomized controlled trial/	720622
19	exp randomization/	94840
20	clinical trial/	1040041
21	placebo/	383339
22	controlled clinical trial/	466633
23	multicenter study/	331435
24	RCT.mp.	50769
25	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	1281379
26	(clinical adj2 trial*).mp.	1923754
27	((single or double or triple) adj (blind* or mask*)).mp.	343038
28	(populat* adj2 (base* or analys* or cohort*)).mp.	262244

29	((multicentr* or nation* or provinc* or state*) adj2 (stud* or analys* or cohort)).mp.	143292
30	(health* adj2 database*).mp.	18984
31	(discharge* adj2 record*).mp.	5571
32	(birth* adj2 registr*).mp.	4153
33	exp cohort analysis/ or exp birth cohort/	874913
34	(observational adj1 stud*).mp.	346199
35	(cohort adj3 (stud* or analys*)).mp.	998684
36	(follow up adj3 stud*).mp.	114090
37	(longitudinal or retrospective or prospective).mp.	3104862
38	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37	6138350
39	(animal/ or animal model/) not Human/	2359478
40	9 and 17 and 38	6911
41	40 not 39	6773
42	**limit 41 to yr="2000 -Current"**	**6449**

Database: APA PsychInfo (January 1, 2000 – February 01, 2023)		
#	**Search terms**	**Results**
1	Premature Birth/	6215
2	Birth/	8061
3	exp Pregnancy/	46417
4	pregnan*.mp.	72141
5	((preterm or pre-term or prematur* or term) adj3 (infant* or birth* or child* or deliver* or newborn or labour or labor or born or neonate*)).mp.	17011
6	1 or 2 or 3 or 4 or 5	91845
7	Glucocorticoids/	3318
8	(antenatal adj4 (cortico* or steroid*)).mp.	75
9	Corticosteroids/	1538
10	Dexamethasone/	1269
11	betamethasone.mp.	85
12	celestone.mp.	3

13	dexamethasone.mp.	4211
14	7 or 8 or 9 or 10 or 11 or 12 or 13	8255
15	exp Randomized Controlled Trials/	1241
16	exp Clinical Trials/	13293
17	Placebo/	6290
18	RCT.mp.	6078
19	(random* adj3 (control* or trial* or allocat* or assign*)).mp.	124281
20	(clinical adj2 trial*).mp.	51805
21	((single or double or triple) adj (blind* or mask*)).mp.	36046
22	(populat* adj2 (base* or analys* or cohort*)).mp.	28124
23	((multicentr* or nation* or provinc* or state*) adj2 (stud* or analys* or cohort)).mp.	31976
24	(health* adj2 database*).mp.	15273
25	(discharge* adj2 record*).mp.	478
26	(birth* adj2 registr*).mp.	262
27	(observational adj1 stud*).mp.	12883
28	(cohort adj3 (stud* or analys*)).mp.	52826
29	(follow up adj3 stud*).mp.	61155
30	(longitudinal or retrospective or prospective).mp.	269486
31	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30	546682
32	6 and 14 and 31	121
33	**limit 32 to yr="2000 -Current"**	**120**

Database: Web of Science (January 1, 2000 – February 01, 2023)		
#	**Search terms**	**Results**
#1	TS=(((preterm or pre-term or prematur* or term) NEAR/3 (infant* or birth* or child* or deliver* or newborn or labour or labor or born or neonate*)))	182513
#2	TS=(pregnan*)	567749
#3	#1 OR #2	701877
#4	TS=(((antenatal*) NEAR/4 (cortico* or steroid*)))	3105
#5	TS=(glucocorticoid*	95354

#6	TS=(betamethasone)	5691
#7	TS=(celestone)	42
#8	TS=(dexamethasone)	74068
#9	#4 OR #5 OR #6 OR #7 OR #8	159294
#10	TS=(((random*) NEAR/3 (control* or trial* or allocat* or assign*)))	849793
#11	TS=(RCT)	31534
#12	TS=(((clinical) NEAR/2 (trial*)))	508128
#13	TS=(((single or double or triple) NEXT (blind* or mask*)))	4667
#14	TS=(((populat*) NEAR/2 (base* or analys* or cohort*)))	256729
#15	TS=(((multicentr* or nation* or provinc* or state*) NEAR/2 (stud* or analys* or cohort)))	281065
#16	TS=(((health) NEAR/2 (database*)))	19667
#17	TS=(((discharge*) NEAR/2 (record*)))	5316
#18	TS=(((birth*) NEAR/2 (registr*)))	3278
#19	TS=(((cohort) NEAR/3 (stud* or analys*)))	376828
#20	TS=(((follow up) NEAR/3 (stud*)))	97150
#21	TS=((longitudinal or retrospective or prospective))	1790093
#22	#21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10	3415982
#23	**#22 AND #9 AND #3** **Timespan: 2000-01-01 to 2023-02-1 (Publication date)**	**2245**

Database: Cochrane CENTRAL (January 1, 2000 – February 01, 2023)		
#	**Search terms**	**Results**
#1	MeSH descriptor: [Premature Birth] this term only	1771
#2	MeSH descriptor: [Infant, Premature] explode all trees	4247
#3	MeSH descriptor: [Obstetric Labor, Premature] this term only	837
#4	MeSH descriptor: [Term Birth] this term only	177
#5	MeSH descriptor: [Pregnancy] explode all trees	24735
#6	(pregnan*):ti,ab,kw (Word variations have been searched)	74794
#7	(((preterm or pre-term or prematur* or term) NEAR/2 (infant* or birth* or child* or deliver* or newborn or labour or labor or born))):ti,ab,kw (Word variations have been searched)	25202
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7	92362
#9	MeSH descriptor: [Glucocorticoids] this term only	4805
#10	((antenatal NEAR/4 (cortico* or steroid*))) (Word variations have been searched)	614
#11	MeSH descriptor: [Betamethasone] this term only	1149
#12	MeSH descriptor: [Dexamethasone] this term only	5050
#13	(betamethasone):ti,ab,kw (Word variations have been searched)	2624
#14	(celestone):ti,ab,kw (Word variations have been searched)	59
#15	(dexamethasone):ti,ab,kw (Word variations have been searched)	13706
#16	#9 or #10 or #11 or #12 or #13 or #14 or #15	20238
#17	**#8 and #16 with Publication Year from 2000 to 2023, in Trials**	**1204**

Database: CINAHL (January 2000- February 01, 2023)		
#	**Search terms**	**Results**
S38	**S10 AND S18 AND S37 Limiters - Published Date: 20000101-20230201**	**1,500**
S37	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 S33 OR S34 OR S35 OR S36	2,596,943
S36	TX (longitudinal or retrospective or prospective)	934,856
S35	TX ((follow up) N3 (stud*))	28,136
S34	TX ((cohort) N3 (stud* or analys*))	151,787
S33	TX ((observational N1 (stud*))	67,553
S32	(MH “Prospective Studies")	505,247
S31	TX (birth* N2 registr*)	1,328
S30	TX (discharge* N2 record*)	1,596
S29	TX (health* N2 database*)	20,751
S28	TX ((multicentr* or nation* or provinc* or state*) N2 (stud* or analys* or cohort))	75,420
S27	TX ((populat*) N2 (base* or analys* or cohort*))	74,038
S26	TX ((single or double or triple) N1 (blind* or mask*))	1,232,314
S25	TX ((random*) N3 (control* or trial* or allocat* or assign*))	356,396
S24	TX RCT	27,748
S23	(MH "Placebos")	13,390
S22	(MH "Multicenter Studies")	344,583
S21	(MH "Random Assignment")	74,831
S20	(MH “Clinical Trials+”)	339,921
S19	(MH “Randomized Controlled Trials+”)	130,760
S18	S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17	20,729
S17	TX (Antenatal* N4 (cortico* or steroid*))	1,302

S16	TX dexamethasone	9,811
S15	TX celestone	19
S14	TX betamethasone	1,174
S13	(MH "Dexamethasone")	6,423
S12	(MH "Betamethasone")	806
S11	(MH "Glucocorticoids")	10,400
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	411,760
S9	TX pregnan*	278,584
S8	TX ((preterm or pre-term or prematur* or term) N3 (infant* or birth* or child* or deliver* or newborn or labour or labor or born or neonate*))	73,586
S7	(MH "Labor, Premature")	3,572
S6	(MH "Pregnancy+")	237,463
S5	(MH "Infant, Newborn+")	153,178
S4	(MH "Term Birth")	1,333
S3	(MH "Infant, High Risk")	607
S2	(MH "Infant, Premature")	25,810
S1	(MH "Childbirth, Premature")	12,637

Database: clinicaltrials.gov (Sept 2008- February 01, 2023)	
Search terms	**Results**
(preterm OR pre-term OR premature OR Prenatal or term) AND (glucocorticoids OR antenatal steroids OR corticosteroids OR betamethasone OR dexamethasone) With applied filter: **With Results**	**53**

Database: Google Scholar (January 1, 2000 – February 01, 2023)	
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 275 results**

eAppendix 2: Excluded studies from a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Reference[a]	Reason(s) for exclusion
Battarbee AN, Sandoval G, Grobman WA, et al. Antenatal Corticosteroids and Preterm Neonatal Morbidity and Mortality among Women with and without Diabetes in Pregnancy. *Am J Perinatol*. 2022;39(1):67-74.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Chen X, Lu T, Gould J, et al. Active Treatment of Infants Born at 22-25 Weeks of Gestation in California, 2011-2018. *J Pediatr*. 2022;15:15.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Darlow BA, Harris SL, Horwood LJ. Little evidence for long-term harm from antenatal corticosteroids in a population-based very low birthweight young adult cohort. *Paediatr Perinat Epidemiol*. 2022;16:16.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Fortmann I, Mertens L, Boeckel H, et al. A Timely Administration of Antenatal Steroids Is Highly Protective Against Intraventricular Hemorrhage: An Observational Multicenter Cohort Study of Very Low Birth Weight Infants. *Front Pediatr*. 2022;10:721355.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Kochukhova O, Fredriksson Kaul Y, Johansson M, et al. Antenatal steroids and neurodevelopment in 12-year-old children born extremely preterm. *Acta Paediatr*. 2022;111(2):314-322.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Mwita S, Kamala BA, Konje E, et al. Association between antenatal corticosteroids use and perinatal mortality among preterm singletons and twins in Mwanza, Tanzania: an observational study. *BMJ Open*. 2022;12(4):e059030.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Norman M, Nilsson D, Trygg J, Hakansson S. Perinatal risk factors for mortality in very preterm infants-A nationwide, population-based discriminant analysis. *Acta Paediatr*. 2022;111(8):1526-1535.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Razem K, Tul N, Blickstein I, Trojner Bregar A. The effect of antenatal corticosteroids on small-for-gestational age preterm neonates. *J Matern Fetal Neonatal Med*. 2022;35(2):362-365.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Shipley L, Hyliger G, Sharkey D. Temporal trends of in utero and early postnatal transfer of extremely preterm infants between 2011 and 2016: a UK population study. *Arch Dis Child Fetal Neonatal Ed*. 2022;107(2):201-205.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)

Verhaeghe C, Marchand-Martin L, Kaminski M, et al. Neurodevelopment at 5 years of age for preterm-born children according to mode of conception: a cohort study. *Am J Obstet Gynecol*. 2022;06:06.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Yang J, Epton MJ, Harris SL, et al. Reduced Exercise Capacity in Adults Born at Very Low Birth Weight: A Population-based Cohort Study. *Am J Respir Crit Care Med*. 2022;205(1):88-98.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Yum SK, Lee JH. Dose completion of antenatal corticosteroids and neonatal outcomes in non-small-for-gestational age or small-for-gestational age very-low-birthweight infants: A Korean population-based cohort study. *Pediatr Neonatol*. 2022;63(2):165-171.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Jing J, Dai Y, Li Y, Zhou P, Li X, Mei J, et al. Single-course antenatal corticosteroids is related to faster growth in very-low-birth-weight infant. *BMC Pregnancy Childbirth*. 2021;21(1):50.	Wrong population of interest (i.e., does not include all infants born late preterm and/or at term in an entire area or a representative sample)
Konzett K, Riedl D, Stark C, Simma B. Chorioamnionitis and neurodevelopmental outcome in very preterm infants from 2007 to 2017-a population-based study. *Acta Paediatr*. 2021;110(4):1201-1208.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Kusuda S, Bennett M, Gould J, Neonatal Research Network of J, the California Perinatal Quality Care C. Outcomes of Infants with Very Low Birth Weight Associated with Birthplace Difference: A Retrospective Cohort Study of Births in Japan and California. *J Pediatr*. 2021;229:182-190.e6.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Melamed N, Murphy K, Barrett J, et al. Benefit of antenatal corticosteroids by year of birth among preterm infants in Canada during 2003-2017: a population-based cohort study. *BJOG*. 2021;128(3):521-531.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Mwita S, Konje E, Kamala B, et al. Association between antenatal corticosteroid use and perinatal mortality among preterm births in hospitals in Tanzania. *PLoS ONE*. 2021;16(7):e0254916.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Nabwera HM, Wang D, Tongo OO, et al. Burden of disease and risk factors for mortality amongst hospitalized newborns in Nigeria and Kenya. *PLoS One*. 2021;16:e0244109.	Wrong population of interest (i.e., does not include all infants born late preterm and/or at term in an entire area or a representative sample)

Pan S, Jiang S, Lin S, Lee SK, Cao Y, Lin Z. Outcome of very preterm infants delivered outside tertiary perinatal centers in China: a multi-center cohort study. *Transl Pediatr*. 2021;10(2):306-314.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
Rossi RM, Defranco EA, Hall ES. Association of Antenatal Corticosteroid Exposure and Infant Survival at 22 and 23 Weeks. *Am J Perinatol*. 2021.	Wrong population of interest (i.e., does not include infants born late preterm and/or at term)
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Battarbee AN, Glover AV, Vladutiu CJ, et al. Risk factors associated with prolonged neonatal intensive care unit stay after threatened late preterm birth. *J Matern Fetal Neonatal Med*. 2021;34(7):1042-1047.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
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Hofer OJ, McKinlay CJD, Tran T, Crowther CA. Antenatal corticosteroids, maternal body mass index and infant morbidity within the ASTEROID trial. *Aust N Z J Obstet Gynaecol*. 2021;61(3):380-5.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Robbins LS, Blanchard CT, Sinkey RG, Harris SL, Tita AT, Harper LM. Prenatal Tobacco Exposure and Childhood Neurodevelopment among Infants Born Prematurely. *Am J Perinatol*. 2021;38(3):218-223.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Son SL, Allshouse AA, Heinrichs GA, et al. Is Exposure to Intrapartum Prostaglandins for Labor Induction Associated with a Lower Incidence of Neonatal Respiratory Distress Syndrome? *Am J Perinatol*. 2021;38(10):993-998.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Zafarmand MH, Goossens S, Tajik P, Bossuyt PMM, Asztalos EV, Gardener GJ, et al. Planned Cesarean or planned vaginal delivery for twins: secondary analysis of randomized controlled trial. *Ultrasound Obstet Gynecol*. 2021;57(4):582-91.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Battarbee AN, Anderson SB, Tita ATN, Harper LM. Methods of Glycemic Control and Neonatal Outcomes after Antenatal Corticosteroid Administration among Women with Pregestational Diabetes. *Am J Perinatol*. 2020;37(13):1351-1356.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
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 MFM*. 2020;2(1):100077.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)

Bicocca MJ, Blackwell SC, Sibai BM. Does Prepregnancy Weight or Maternal BMI at Betamethasone Administration Impact Late Preterm Respiratory Morbidity? *Am J Perinatol*. 2020;37(4):365-369.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Fishel Bartal M, Chen HY, Blackwell SC, Chauhan SP, Sibai BM. Factors Associated with Formula Feeding among Late Preterm Neonates. *Am J Perinatol*. 2020;37(14):1393-1399.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Harris C, Lunt A, Bisquera A, Peacock J, Greenough A. Lung function and exercise capacity in prematurely born young people. *Pediatr Pulmonol*. 2020;55(9):2289-2295.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Andrikopoulou M, Overton EE, Seaman SJ, Stern-Ascher CN, Bannerman CG. 335: Does race affect late preterm neonatal respiratory morbidity? *Am J Obstet Gynecol*. 2019;220(1 Supplement):S233-S234.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Battarbee AN, Glover AV, Vladutiu CJ, et al. Sex-Specific Differences in Late Preterm Neonatal Outcomes. *Am J Perinatol*. 2019;36(12):1223-1228.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Cartwright RD, Crowther CA, Anderson PJ, Harding JE, Doyle LW, McKinlay CJD. Association of Fetal Growth Restriction With Neurocognitive Function After Repeated Antenatal Betamethasone Treatment vs Placebo: Secondary Analysis of the ACTORDS Randomized Clinical Trial. *JAMA Network Open*. 2019;2(2):e187636.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Gyamfi-Bannerman C, Zupancic JAF, Sandoval G, Grobman WA, Blackwell SC, Tita ATN, et al. Cost-effectiveness of Antenatal Corticosteroid Therapy vs No Therapy in Women at Risk of Late Preterm Delivery: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Pediatr*. 2019;173(5):462-8.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Werner EF, Romano ME, Rouse DJ, et al. Association of Gestational Diabetes Mellitus With Neonatal Respiratory Morbidity. *Obstet Gynecol*. 2019;133(2):349-353.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Cartwright RD, Harding JE, Crowther CA, Cutfield WS, Battin MR, Dalziel SR, et al. Repeat Antenatal Betamethasone and Cardiometabolic Outcomes. *Pediatrics*. 2018;142(1):07.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Glover AV, Battarbee AN, Gyamfi-Bannerman C, Boggess KA, Manuck TA. True vs. false spontaneous preterm labor in the late preterm period: Predicting late preterm birth. *Am J Obstet Gynecol*. 2018;218(1 Supplement 1):S403.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)

Jordan BK, Schilling D, McEvoy CT. The window of improved neonatal respiratory compliance after rescue antenatal steroids. *J Perinatol*. 2018;38(7):828-33.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Althabe F, Thorsten V, Klein K, McClure EM, Hibberd PL, Goldenberg RL, et al. The Antenatal Corticosteroids Trial (ACT)'s explanations for neonatal mortality - a secondary analysis. *Reproductive Health*. 2016;13(1):62.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Goldenberg RL, Thorsten VR, Althabe F, Saleem S, Garces A, Carlo WA, et al. The global network antenatal corticosteroids trial: impact on stillbirth. *Reproductive Health*. 2016;13(1):68.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Klein K, McClure EM, Colaci D, Thorsten V, Hibberd PL, Esamai F, et al. The Antenatal Corticosteroids Trial (ACT): a secondary analysis to explore site differences in a multi-country trial. *Reproductive Health*. 2016;13(1):64.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Viteri OA, Blackwell SC, Chauhan SP, Refuerzo JS, Pedroza C, Salazar XC, Sibai BM. Antenatal corticosteroids for the prevention of respiratory distress syndrome in premature twins. *Obstet Gynecol*. 2016;128(3):583-91.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Brookfield KF, El-Sayed YY, Chao L, Berger V, Naqvi M, Butwick AJ. Antenatal corticosteroids for preterm premature rupture of membranes: single or repeat course? Am J Perinatol. 2015;32(6):537-44.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Wilms FF, van Baaren GJ, Vis JY, Oudijk MA, Kwee A, Porath MM, et al. Prescribing patterns of antenatal corticosteroids in women with threatened preterm labor. *Eur J Obstet Gynecol Reprod Biol*. 2015;192:47-53.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Asztalos E, Willan A, Murphy K, Matthews S, Ohlsson A, Saigal S, 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;14:272.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Gyamfi-Bannerman C, Son M. Preterm premature rupture of membranes and the rate of neonatal sepsis after two courses of antenatal corticosteroids. *Obstet Gynecol*. 2014;124(5):999-1003.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Murphy KE, Willan AR, Hannah ME, Ohlsson A, Kelly EN, Matthews SG, et al. Effect of antenatal corticosteroids on fetal growth and gestational age at birth. *Obstet Gynecol*. 2012;119(5):917-23.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)

Schmidt B, Seshia M, Shankaran S, et al. Effects of prophylactic indomethacin in extremely low-birth-weight infants with and without adequate exposure to antenatal corticosteroids. *Arch Pediatr Adolesc Med*. 2011;165(7):642-6.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Hashima JN, Lai Y, Wapner RJ, Sorokin Y, Dudley DJ, Peaceman A, et al. The effect of maternal body mass index on neonatal outcome in women receiving a single course of antenatal corticosteroids. *Am J Obstet Gynecol*. 2010;202(3):263.e1-5.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)
Lee MJ, Davies J, Guinn D, Sullivan L, Atkinson MW, McGregor S, et al. Single versus weekly courses of antenatal corticosteroids in preterm premature rupture of membranes. *Obstet Gynecol*. 2004;103(2):274-81.	Wrong study design (i.e., secondary analysis of a randomized controlled trial including a subgroup of data)

Legend:
ACS – antenatal corticosteroids

[a] References are listed for studies excluded due to the wrong intervention group, wrong population, and studies with the wrong study design (secondary analyses of randomized controlled trials). Other studies were excluded due to the following reasons: 1) only abstracts were available; 2) other studies with wrong study design (e.g., single-centred cohort studies); or 3) no outcomes of interest for included infants born at term and/or late preterm

eAppendix 3: List of pre-specified outcomes in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Type of outcome		Pre-specified outcomes
Proportion data	Primary outcome	Proportion of infants born at term after exposure to ACS
	Secondary proportion outcomes	Proportion of infants born late preterm after exposure to ACS
		Proportion of infants born at term/late preterm (combined) after exposure to ACS
Other outcomes	Secondary short-term outcomes	Perinatal death (stillbirth or neonatal death)
		Stillbirth (intrauterine/fetal demise)
		Neonatal death (≤28 days after birth or before discharge)
		Severe RDS in survivors (as defined by study authors)
		Moderate/severe RDS (as defined by study authors)
		Intraventricular haemorrhage (grade III or IV)
		Intraventricular haemorrhage (any grade)
		Surfactant use
		Chronic lung disease (infant's need for continuous supplemental oxygen at 28 weeks postnatal age or 36 weeks postmenstrual age)
		Need for MV/ CPAP
		Mean duration of MV/CPAP (days)
		Duration of oxygen supplementation
		Systemic infection in first 48 hours of life
		Proven infection in the NICU
		cPVL (as defined by study authors)
		Admission to NICU
		5 min APGAR score <7
		Small for gestational age (as defined by study authors)
		Length of hospital stay (days)
		Birthweight (g)
		Head circumference (cm)
		Body length at birth (cm)
		Hypoglycemia (infant's need for oral or intravenous glucose or glucagon administration within 7 days)
		Other reported short-term outcomes (as defined by study authors)

	Secondary long-term outcomes	Neurodevelopmental impairment (as defined by study authors)
		Cerebral palsy (as defined by study authors)
		Auditory impairment (as defined by study authors)
		Visual impairment (as defined by study authors)
		Others long-term outcomes (as defined by study authors)
	Secondary maternal outcomes	Maternal death (death up to 90 days after birth)
		Chorioamnionitis (as defined by study authors)
		Endometritis (as defined by study authors)
		Postpartum depression (as defined by study authors)

Legend:
ACS – antenatal corticosteroids; cm – centimetres; CPAP – continuous positive airway pressure; cPVL – cystic periventricular leukomalacia; g – grams; MV – mechanical ventilation; NICU – neonatal intensive care unit; RDS – respiratory distress syndrome

eAppendix 4: <u>Confounders/co-variates</u> for adjusted and proportion analyses addressed within included population-based studies and randomized studies in a systematic review and meta-analysis on term, late preterm, and term/late preterm births after early exposure to antenatal corticosteroids

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	Fetal anomalies	IUGR	PPROM	Other factors
Short-term outcomes[a]							
Population-based studies – Infants born at term							
Diguisto, 2020 (France)[1]	• Head circumference <5th percentile • Birth length <5th percentile • Birthweight <5th percentile	**Adj**	**Adj**	**E**			**Adj:** Maternal age (20-34 y vs < 20 y vs ≥ 35 y), BMI (18.5-24.9 vs < 18.5 vs ≥ 25), smoking during pregnancy, pregnancy-related disorder, parity, family situation (living with partner: yes/no), geographic origin (France vs South of Europe vs North Africa, vs others countries), parity (nulliparous vs multiparous)
McKinzie, 2021 (U.S.A)[2]	• Admission to NICU • Diagnosis of TTN • SGA	**E**	**Adj**				**Adj:** Maternal age, race, insurance, maternal diabetes mellitus, maternal asthma, and EGA at delivery
	• Treated hypoglycemia • Hyperbilirubinemia requiring treatment • Meconium aspiration syndrome						**Adj:** for multiple comparisons for the 4 secondary outcomes (intubation, hyperbilirubinemia requiring treatment, treated hypoglycemia, meconium aspiration syndrome)

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	Fetal anomalies	IUGR	PPROM	Other factors
Rodriguez, 2019 (Finland)[3]	• Head circumference at birth (cm) • Birthweight (g) • Body length at birth (cm) • Ponderal index	**E**					**M/Adj:** Social economic status, maternal age (years), cohabitation, maternal height (cm), prepregnancy weight (kg), prepregnancy BMI, number of previous pregnancies, number of miscarriages, number of induced abortions, number of ectopic pregnancies, ovum donation, insemination, glucose test performed, glucose test pathological, insulin treatment, self-reported smoking, hospitalization due to high BP, infant sex
Total studies:		**E:** 2; **Adj:** 1	**Adj:** 2	**E:** 1	None	None	
Population-based studies – Infants born late preterm							
Malloy, 2012 (U.S.A)[8]	• Neonatal death • Neonatal death within NICU admission group	**Adj**					**Adj:** Maternal age, education, gravidity, race, mode of delivery, infant sex, birthweight, NICU admission, surfactant administration, assisted ventilation
Total studies		**Adj:** 1	None	None	None	None	

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	Fetal anomalies	IUGR	PPROM	Other factors
Population-based studies – Infants born at term/late preterm (combined)							
Rodriguez, 2019 (Finland)[3]	• Head circumference at birth (cm) • Birthweight (g) • Body length at birth (cm) • Ponderal index	**E**					**M/Adj:** Social economic status, maternal age (years), cohabitation, maternal height (cm), prepregnancy weight (kg), prepregnancy BMI, number of previous pregnancies, number of miscarriages, number of induced abortions, number of ectopic pregnancies, ovum donation, insemination, glucose test performed, glucose test pathological, insulin treatment, self-reported smoking, hospitalization due to high BP, infant sex
Total studies		**E:** 1	None	None	None	None	

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Maternal substance abuse	Socioeconomic status	Other factors
Long-term outcomes[b]								
Population-based studies – Children born at term								
Melamed, 2019 (Canada)[4]	• Composite long-term outcome of any of the following: audiometry testing, visual testing, suspected neurocognitive disorder • Suspected neurocognitive disorder • Audiometry testing AND suspected neurocognitive disorder • Visual testing • Audiometry testing	**E**	**Adj:** chronic hypertension		**Adj**		**Adj:** Income	**Adj:** maternal age (as a continuous variable), week of gestation, parity, pregestational diabetes, hypertensive complications, gestational diabetes, induction of labour, mode of delivery, infant sex, birthweight <10th percentile, 5 min Apgar score <7, resuscitation at birth, admission to NICU
Osteen, 2022 (U.S.A)[7]	• Asthma • Weight <10th percentile	**E**	**Adj:** Maternal hypertensive disorders					**Adj:** Maternal age, maternal diabetes, SGA, EGA at delivery

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Maternal substance abuse	Socioeconomic status	Other factors
Raikkonen, 2020 (Finland)[6]	• Any mental and behavioural disorder • Psychological development disorders • Autism spectrum disorders • Attention-deficit/ hyperactivity or conduct disorders • Mixed disorders of conduct and emotions; emotional, social functioning, or tic disorders • Other behavioural and emotional disorders • Psychotic, mood, neurotic, stress-related, or somatization disorders • Eating disorders • Sleep disorders • Mild, moderate, unspecified intellectual disability	**E**	**Adj**		**Adj**			**Adj:** Maternal age at delivery, parity, mode of delivery, maternal smoking during pregnancy, prepregnancy body mass index, gestational diabetes, any lifetime mental disorder diagnosis, child sex, Apgar score (maximum of 1 and 5 minutes), admission to NICU, weight, GA at birth

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Maternal substance abuse	Socioeconomic status	Other factors
	• Severe, profound intellectual disability							
Raikkonen, 2022 (Finland)[5]	• Cerebral palsy • Vision or hearing loss • Specific developmental disorders of speech and language • Specific developmental disorders of scholastic skill • Specific developmental disorder of motor function • Pervasive developmental disorder • Other or unspecified disorder of psychological development • Epilepsy	**E**	**Adj**		**Adj**			**Adj:** Maternal age at delivery, parity, mode of delivery, maternal smoking during pregnancy, prepregnancy body mass index, gestational diabetes, child sex, Apgar score (maximum of 1 and 5 minutes), admission to NICU, weight, GA at birth For child psychological developmental disorders, **adj:** maternal mental and behavioral disorder diagnoses (ICD-10 codes F00-F99)

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Maternal substance abuse	Socioeconomic status	Other factors
								For child vision and hearing disorders, **adj:** maternal eye, adnexa, ear, and mastoid disorder diagnoses (ICD-10 codes H00-H95) For child epilepsy and cerebral palsy, **adj:** maternal nervous system disorder diagnoses (ICD-10 codes G00-G99)
Total studies:		**E:** 4	**Adj:** 4	None	**Adj:** 3	None	**Adj:** 1	
Population-based studies – Children born late preterm								
Aviram, 2022 (Canada)[9]	• Suspected neurocognitive disorder • Auditory testing • Visual testing	**E**	**Adj:** chronic hypertension		**Adj**		**Adj:** Household income (based on neighbourhood level and divided into quintiles)	**E:** Fetal anomalies, deliveries complicated by intrapartum asphyxia

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Maternal substance abuse	Socioeconomic status	Other factors
								Adj: Maternal age (as a continuous variable), week of gestation at birth, parity, pregestational diabetes, hypertensive complications, gestational diabetes, mode of delivery, induction of labour infant sex, birthweight <10th percentile, 5 min Apgar score <7, need for resuscitation at birth, admission to NICU
Total studies:		**E: 1**	**Adj: 1**	None	**Adj: 1**	None	**Adj:** 1	

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Fetal anomalies	Maternal smoking/ substance abuse	Other factors
Proportion outcomes [c]								
Population-based studies – Infants born at term								
Raikkonen, 2020 (Finland)[6]	• Proportion of infants born at term after exposure to ACS	**E**						
Total studies:		**E: 1**	None	None	None	None	None	
Population-based studies – Infants born late preterm								
Malloy, 2012 (USA)[8]	• Proportion of infants born late preterm after exposure to ACS							
Total studies:		None	None	None	None	None	None	
Population-based studies – Infants born at term/late preterm (combined)								
Razaz, 2015 (Canada)[10]	• Proportion of infants born at term/late preterm (combined) after exposure to ACS • (≥35 weeks GA)							
Total studies:		None	None	None	None	None	None	

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Fetal anomalies	Maternal smoking/ substance abuse	Other factors
RCTs – Infants born at term								
Schmitz, 2022 (France)[11]	• Proportion of infants born at term after exposure to ACS	**E**				**E**		
WHO ACTION Trial Collaborators, 2020 (International)[12]	• Proportion of infants born at term after exposure to ACS					**E:** Major congenital fetal anomalies		
Crowther, 2006 (Australia and New Zealand)[13]	• Proportion of infants born at term after exposure to ACS							**E:** Chorioamnionitis needing urgent delivery
Danesh, 2012 (Iran)[14]	• Proportion of infants born at term after exposure to ACS	**E**				**E**		**E:** Placenta previa, placental abruption, fetal distress
Total studies:		**E: 2**	None	None	None	**E: 3**	None	
RCTs – Infants born late preterm								
Schmitz, 2022 (France)[11]	• Proportion of infants born late preterm after exposure to ACS	**E**				**E**		

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Fetal anomalies	Maternal smoking/ substance abuse	Other factors
Crowther, 2006 (Australia and New Zealand)[13]	• Proportion of infants born late preterm after exposure to ACS							**E:** Chorioamnionitis needing urgent delivery
Peltoniemi, 2007 (Finland)[15]	• Proportion of infants born late preterm after exposure to ACS							**E:** Clinical chorioamnionitis, lethal disease of the fetus
Total studies:		**E: 1**	None	None	None	**E: 1**	None	
RCTs – Infants born at term/late preterm (combined)								
Schmitz, 2022 (France)[11]	• Proportion of infants born at term/late preterm (combined) after exposure to ACS	**E**				**E**		
McEvoy, 2010 (U.S.A)[16]	• Proportion of infants born at term/late preterm (combined) after exposure to ACS	**E:** > twins				**E**		**E:** Clinical chorioamnionitis
Garite, 2009 (U.S.A)[17]	• Proportion of infants born at term/late preterm (combined) after exposure to ACS				**E**	**E**		

Study, Year (Country)	Outcomes	Multiple gestation	Preeclampsia/ severe hypertension	IUGR	PPROM	Fetal anomalies	Maternal smoking/ substance abuse	Other factors
Crowther, 2006 (Australia and New Zealand)[13]	• Proportion of infants born at term/late preterm (combined) after exposure to ACS							**E:** Chorioamnionitis needing urgent delivery
Total studies:		**E: 2**	None	None	**E: 1**	**E: 3**	None	

Legend:
Adj – adjusted; BMI – body mass index; BP – blood pressure; cm – centimetres; E – excluded; EGA – estimated gestational age; g – grams; GA – gestational age; ICD – International Classification of Diseases; IUGR – intrauterine growth restriction; kg – kilograms; M – matched; min – minutes; NICU – neonatal intensive care unit; PPROM – preterm premature rupture of membrane; RCT – randomized controlled trial; SGA – small for gestational age; TTN – transient tachypnea of the newborn

[a] The important **confounders** or **co-variates identified *a priori* for short-term outcomes** are: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **fetal anomalies**; **preterm premature rupture of membranes**.

[b] The important **confounders** or **co-variates identified *a priori* for long-term outcomes** are: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **preterm premature rupture of membranes; maternal substance use**; **socioeconomic status.**

[c] The important **confounders** or **co-variates identified *a priori* for proportion outcomes** are: **multiple gestation**; **preeclampsia/hypertension**; **intrauterine growth restriction**; **preterm premature rupture of membranes; fetal anomalies; maternal smoking/substance use**.

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