National Institute for Health and Care Excellence

Draft for Consultation

Specialist neonatal respiratory care for babies born preterm

[A] Evidence review for diagnosing respiratory disorders

NICE guideline <TBC at publication>

Evidence review

October 2018

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

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Diagnosing respiratory disorders

This evidence report contains information on 1 review relating to the diagnosis of respiratory disorders:

- Review question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Review question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Introduction

Despite advances in neonatal medicine, bronchopulmonary dysplasia (BPD) is the most frequent adverse outcome for infants born less than 30 weeks' gestation and the most common chronic lung disease in infancy. BPD is responsible for prolonged hospitalisation, and readmissions after discharge, and can have a significant impact on quality of life of both the child and family. BPD is associated with significant healthcare costs.

BPD results from complex interactions of both perinatal and postnatal factors. Awareness of these factors may help to identify preterm babies who are at risk for this complication and its associated respiratory consequences and neurodevelopmental outcomes. Knowledge of the risk factors may also influence the use of preventive measures and approaches to neonatal respiratory care that may reduce the risk (for example, approaches to oxygen supplementation, assisted ventilation and surfactant administration).

This review aims to identify the risk factors for BPD before, during, and after birth in preterm infants.

Summary of the protocol

See Table 1 for a summary of the population, predictors, confounders and outcome characteristics of this review.

Table 1: Summary of the protocol

Population	Preterm babies **Exclusions:** • Preterm babies with any congenital abnormalities except patent ductus arteriosus

Predictive factors	**Risk factors before birth:**
	• Antenatal steroids
	• Chorioamnionitis - defined as:
	  ○ Histological
	  ○ Clinical
	• IUGR – defined as fetal weight <10th or 3rd percentile for gestational age determined through an ultrasound.
	Risk factors at birth:
	• Gestational age:
	  ○ < 26 + 6 weeks
	  ○ 27-31 + 6 weeks
	  ○ 32-36+ 6 weeks
	• Birth weight:
	  ○ <1000 g
	  ○ 1001 g - 1500 g
	  ○ >1501 g
	• Small for gestational age defined as birth weight <10th or 3rd percentile for gestational age
	• Sex

	• Ethnicity
	• Need for resuscitation at birth
	
	Risk factors after birth:
	• Surfactant
	• Invasive ventilation
	  ○ Invasive ventilation (volume targeted ventilation, triggered pressure limited ventilation, synchronised intermittent mandatory ventilation, non-triggered pressure limited ventilation, conventional invasive ventilation)
	• Supplementary oxygen
	• Postnatal steroids
	• Patent ductus arteriosus – defined as requiring treatment:
	  ○ Medical
	  ○ Surgical
	• Sepsis – defined as:
	  ○ Positive culture sepsis
	  ○ Clinical
	• Necrotising enterocolitis (NEC) - defined as NEC Stage 2 or above
	• Thermoregulation – defined as NICU admission temperature of
	  ○ > 36.5 degrees Celsius:
	  ○ 36-36.5 ^{o}C
	  ○ 35.5-35.9 ^{o}C
	  ○ <35.5 ^{o}C
	• Preterm feeding regimen – defined as:
	  ○ Exclusively fed human (mother or donor) milk
	  ○ Exclusively fed formula milk
	  ○ Mixture of human and formula milk

Confounding factors	Analysis should adjust for important confounding factors, as a minimum include: • Gestational age • Sex Unless found to be a non-significant risk factor in the univariate analyses in the study.
Outcomes	**Outcomes:** BPD (oxygen dependency at 36 weeks postmenstrual age) **Comparisons:** • Preterm babies exposed vs unexposed to risk factors **Stratification:** • Babies born at different gestational ages

1 *BPD: Bronchopulmonary dysplasia. IUGR: intra-uterine growth restriction; NEC: Necrotising enterocolitis;*
2 *NICU: Neonatal Intensive Care Unit;*

3 For full details see review protocol in appendix A.

Clinical evidence

Included studies

Nineteen publications of prospective cohort studies were included in this review. 10 were population-based cohort studies (Costeloe 2012; Dargaville 2016; De Waal 2012; Edstedt Bonamy 2017; Hanke 2015; Kamper 2004; Klinger 2009; Ohlin 2014; Reiss 2003; Wyckoff 2012), 8 were multicentre cohort studies (Chawla 2016; Farstad 2011; Figueras-Aloy 2005; Gagliardi 2007; Marshall 1999; Morrow 2017; Spiegler 2016; Viscardi 2004), and 1 was a single-centre cohort study (Patel 2017).

In addition, 5 publications from 2 prospective population-based cohort studies were also included (El Ayoubi 2016 [MOSAIC]; Monier 2017 [EPIPAGE-2]; Torchin 2016 [EPIPAGE-2]; Torchin 2017 [EPIPAGE-2]; Zeitlin 2010 [MOSAIC]).

The studies reported on the following risk factors for BPD: antenatal steroids, chorioamnionitis, intra-uterine growth restriction, gestational age, birthweight, sex, small for gestational age at birth, ethnicity, resuscitation, surfactant use, invasive ventilation, postnatal steroid use, patent ductus arteriosus, sepsis, themoregulation and breastmilk feeding.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies excluded from this review and their reasons for exclusion are listed in appendix K.

Summary of clinical studies included in the evidence review

Table 2 provides a brief summary of the included studies.

Table 2: Summary of included studies

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
Chawla 2016 Prospective multicentre cohort study USA	n=3,219 analysed Extremely low gestational age neonates, gestational age < 26 weeks	Antenatal steroids	BPD defined as need for supplemental oxygen at 36 weeks PMA	GA, sex, race/ethnicity, maternal health insurance, and participating centre	Moderate risk of bias
Costeloe 2012 Prospective national cohort study **(EPICURE studies)** England	n=859 analysed Preterm births 22-26 weeks gestation, or more immature but with a birth weight over 400g.	Gestational age Birthweight Sex Thermoreg-ulation	BPD defined as need for supplemental oxygen at 36 weeks PMA	Multivariate models used to adjust for statistically significant confounders between the 2 cohorts (not clearly reported)	Moderate risk of bias
Dargaville 2016 Prospective population-	n=19,103 analysed Preterm infants born 25-32 completed weeks of gestation.	Invasive ventilation	BPD defined as need for respiratory support and/or supplemental	Gestation, birth weight <10th percentile, sex, mode of delivery, plurality, ANS,	Low risk of bias

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
based cohort study Australia and New Zealand			oxygen at 36 weeks PMA	and 5-min apgar score	
De Waal 2012 Prospective population-based cohort study Netherlands	n=144 analysed Infants born at gestational age of 23^{+0} to 26^{+6} weeks	Gestational age Birthweight	BPD defined as need for supplemental oxygen 36 weeks PMA	GA, birth weight, gender, caesarean section, antenatal steroids, Dutch nationality	Low risk of bias
Edstedt Bonamy 2017 Prospective population-based cohort study **(EPICE)** Europe	n=6,262 analysed Births between 22^{+0} and 31^{+6} weeks of gestation in 19 regions across 11 European countries.	PDA (various treatment regimens)	BPD defined as need for supplemental oxygen at 36 weeks PMA	Presence of preeclampsia, spontaneous onset of labour, PROM, maternal infection as indication for delivery, ANS, mode of delivery, GA, birth weight, infant sex, SGA, and use of invasive ventilation on first day of life	Moderate risk of bias
El Ayoubi 2016 Prospective population-based cohort study **(MOSAIC)** Europe	n= 621 analysed Live births between 24 and 31 weeks	Antenatal detection of FGR	BPD defined as need for supplemental oxygen 36 weeks PMA	First analysis adjusted for GA, sex, type of pregnancy, birthweight ratio, pregnancy complications and regions Second analysis adjusted for corticosteroids and maternity level III in addition to first analysis confounders	Moderate risk of bias
Farstad 2011 Prospective multicentre observational study Norway	n=240 analysed Stillbirths and live births in Norway with a gestational age of 22^{+0} to 27^{+6} with a birth weight of 500-999g	Sex Maternal infection Surfactant Invasive ventilation Treated PDA	BPD defined according to accepted criteria (no timeframe specified)	Multivariate analysis adjusted for confounders, however not clearly stated whether all statistically significant	High risk of bias

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
		Postnatal steroids		confounders are adjusted for in the analysis.	
Figueras-Aloy 2005 Prospective multicentre observation study Spain	n=1,537 analysed All liveborn preterm infants from 23^{+0} weeks to 28^{+6}.	ANS Invasive ventilation >5 day IUGR Resus	Chronic lung disease was defined as need for supplementary oxygen at 36 weeks PMA to maintain oxygen saturations 88-93%	Antibiotics mother, GA, birthweight, IUGR, resus, apgar score, CRIB score, RDS, invasive ventilation >5 days, more than one dose of surfactant, pneumothorax, PDA, IVH, PVL, early sepsis, late sepsis, NEC, and propensity score for ANS	Moderate risk of bias
Gagliardi 2007 Prospective multicentre cohort study Italy	n=1118 analysed Birthweight <1500g, 23-32 GA, admitted to a tertiary-level NICU	ANS Sex Birthweight Late-onset sepsis	BPD defined as the need for supplemental oxygen at 36 weeks PMA	Sex, birthweight, late-onset sepsis **Birthweight used over GA as highly correlated, additionally it has a higher exploratory power*	Moderate risk of bias
Hanke 2015 Prospective population-based observational study Germany	n=3,554 analysed Birth weight <1500g and GA 22^{+0}-32^{+0}	GA (per week) Birth weight (100g steps) ANS Sex SGA	BPD defined as the need for supplemental oxygen at 36 weeks PMA	Sex, Birthweight, GA, ANS, multiple birth, inborn, centre, sex, SGA	Moderate risk of bias
Kamper 2004 Prospective population-based cohort study **(ETFOL)** Denmark	n=269 analysed GA < 28 weeks or with a birthweight <1000g	Invasive ventilation PDA	Chronic lung disease defined as oxygen dependency at 36 weeks PMA	GA, invasive ventilation, treated PDA, CRIB score, location of birth, sex, septicaemia, caesarean section, SGA, ANS, multiparity, surfactant, meningitis, PVL, IVH	Moderate risk of bias

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
Klinger 2010 Prospective population-based cohort study Israel	n=13,539 analysed Very low birthweight infants (<1500g)	Early-onset sepsis	Defined as clinical evidence of BPD together with the requirement of oxygen therapy at 28 days of life.	GA, sex, ethnicity, SGA, multiple pregnancy, ANS, maternal hypertension, premature contractions, PROM, caesarean section, amnionitis, and delivery room resus	High risk of bias
Marshall 1999 Prospective population-based cohort study USA	n=865 analysed Infants with birthweights of 500g to 1500g	Birthweight GA Sex Surfactant Ventilated at 48hrs	Chronic lung disease defined as being invasively ventilated or requiring supplementary oxygen at 36 weeks PMA	Birthweight, GA, sex, inborn, PDA, infection, surfactant, fluid on day 2, ventilated at 48h, fiO2 >42	Moderate risk of bias
Monier 2017 Prospective population-based cohort study **(EPIPAGE-2)** France	n=2,919 analysed Preterm singleton infants born between 24 and 31 completed weeks gestation	SGA	BPD defined as the need for oxygen and/or positive airway pressure and/or invasive ventilator support at 36 weeks PMA	GA, sex, maternity level 3 unit, PROM, vascular disorders, BMI, and smoking	Low risk of bias
Morrow 2017 Prospective multi-centre observational study USA	n=587 analysed Preterm infants who had a GA <34 weeks, birth within the previous 7 days, and a birth weight between 500 and 1,250g	Birthweight Sex Maternal race Maternal ethnicity GA ANS Chorioam-nionitis	BPD was not defined any further, however time frame of 36 weeks PMA used. Diagnosis of BPD split to "no or mild BPD" and "moderate or severe BPD", no elaboration on these definitions and odds ratio's for BPD exclude milder forms of disease	GA, Birthweight, Sex, Ethnicity, ANS, maternal smoking status, multiple gestations, caesarean section, gestational diabetes, preeclampsia, PROM, chorioamnionitis, antepartum haemorrhage	High risk of bias

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
Ohlin 2015 Prospective nation-wide cohort study **(EXPRESS)** Sweden	n=494 analysed Extremely preterm babies, <27 weeks GA	Sepsis Positive blood cultures	Severe BPD defined as 30% oxygen at 36 weeks PMA	GA and sex	Moderate risk of bias
Patel 2017 Prospective single-centre cohort study USA	n=254 analysed Preterm infants with a birthweight <1500g, GA <35 weeks, enteral feeding initiated by day of life 14	Human milk dose as a proportion of enteral feedings	BPD was defined as oxygen requirement >21% or continuous positive airway pressure or invasive ventilation at 36 weeks PMA	GA, gender, NEC, PDA, and SGA	High risk of bias
Reiss 2003 Prospective population-based cohort study Germany	n=1,195 analysed Preterm infants born <32 weeks gestation	SGA GA Sex ANS PDA Surfactant	BPD defined as oxygen requirements or invasive ventilation on day 28 after birth	Birthweight, GA, sex, ANS, PROM, Preterm labour, caesarean section, days on ventilator, probable sepsis, PDA, surfactant therapy, multiple pregnancy	Moderate risk of bias
Spiegler 2016 Prospective multicentre cohort study Germany	n= 1,433 analysed Infants 22^{+0} to 31^{+6} weeks of gestation	Breastmilk feeding	BPD was defined as the need for supplemental oxygen or any respiratory support at 36 weeks PMA including both moderate and severe BPD	Maternal origin, ANS, inborn, sex, multiple birth, GA, birthweight, discharge weight, and completion of enteral feeding	Low risk of bias
Torchin 2016 (See Monier 2017) **(EPIPAGE-2)** France	n=1,506 analysed See Monier 2017	FGR	See Monier 2017	Maternal age, BMI, parity, pre-existing diabetes, smoking during pregnancy, sex, care, level of maternity units, ANS, GA, and birth weight	Low risk of bias
Torchin 2017 (See Monier 2017)	n= 1,480 analysed See Monier 2017	Histologic chorioamnionitis	See Monier 2017	GA, sex, and ANS	Low risk of bias

Study	Population	Risk Factors	Outcome	Adjustment for confounding factors	Quality
(EPIPAGE-2) France					
Viscardi 2004 Prospective multicentre observational study USA	n=262 analysed Infants who had a GA <33 weeks and birth weight <1501g	Clinical and histologic CA	BPD defined as moderate or severe. Moderate BPD need for <30% fraction of inspired oxygen at 36 weeks PMA Severe BPD need for >30% fraction of inspired oxygen or positive pressure support at 36 weeks PMA	GA, birthweight, surfactant, hypotension <96h of age, PDA, IMV, sepsis (sex found to be not statistically significant variable thus not included as confounder)	Moderate risk of bias
Wyckoff 2012 Prognostic population-based cohort study USA	n= 6,654 analysed Infants with birth weight 401-1000 g and estimated GA of 23-30 weeks	Delivery room cardiopulmonary resuscitation	BPD defined as oxygen requirement at 36 weeks PMA	Maternal hypertension, antepartum haemorrhage, ANS, vaginal birth, GA, BW, sex, and ethnicity	Low risk of bias
Zeitlin 2010 (See El Ayoubi 2016) **(MOSAIC)** Europe	n=1,323 analysed See El Ayoubi 2016	SGA	BPD defined as need for supplemental oxygen at 36 weeks PMA	GA, sex, multiple pregnancy, ANS, in utero transfer, birth in level 3 unit, and MOSAIC region	Moderate risk of bias

ANS: antenatal steroids; BMI: body mass index; BPD: bronchopulmonary dysplasia; BW: bodyweight; CA: chorioamnionitis; CRIB: clinical risk index for babies; EPICE: Effective perinatal intensive care in Europe; EPIPAGE-2: Epidemiological study on small gestational ages; ETFOL: Danish National Study in Infants with Extremely low gestational age and birthweight; EXPRESS: Extremely Preterm Infant Study in Sweden; FGR: fetal growth restriction; GA: gestational age; h: hours; IMV: intermittent mandatory ventilation; IVH:ntraventricular haemorrhage; IUGR: Intrauterine Growth Restriction; MOSAIC: Models for OrganiSing Access to Intensive Care for Very Preterm Babies in Europe; NEC: necrotising enterocolitis; NICU: neonatal intensive care unit; PDA: patent ductus arteriosus; PMA: postmenstrual age; PROM: premature rupture of membranes; PVL: Periventricular leukomalacia; RDS: respiratory distress syndrome; SGA: small for gestational age

See appendix D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

The Quality in Prognostic Studies (QUIPS) tool was used to evaluate the risk of bias of each study in the evidence.

Table 3 to Table 18 provide a brief summary of the evidence for each risk factor assessed for BPD before birth, at birth, and after birth.

Table 3: Risk factor before birth: antenatal steroids

Study	Population	Risk factor for BPD	Adjusted Odds Ratio with 95% CI	Quality
Complete ANS vs no ANS				
Chawla 2016	Complete ANS vs no ANS n=3,219 Complete ANS vs partial ANS n=3,840 (22-27 weeks GA)	Complete ANS	Complete ANS vs no ANS 0.93 (0.74, 1.17) Complete ANS vs partial ANS 0.92 (0.78, 1.09)	Moderate risk of bias
Figueras-Aloy 2005	n=1,537 (23-28 weeks GA)	Complete ANS	0.63 (0.45, 0.88)	Moderate risk of bias
Reiss 2003	n=1,365 (<32 weeks GA)	Complete ANS	0.89 (0.72, 1.10)	Moderate risk of bias
Partial ANS vs no ANS				
Chawla 2016	n=1,579 (22-27 weeks GA)	Partial ANS	1.02 (0.79, 1.32)	Moderate risk of bias
Any ANS vs no ANS				
Gagliardi 2007	n=1,118 (23-32 weeks GA)	Any ANS	0.59 (0.36, 0.97)	Moderate risk of bias
Hanke 2015	n=3554 (<32 weeks GA)	Any ANS	1.07 (0.75, 1.53)	Moderate risk of bias
Morrow 2017	n=587 (<34 weeks GA)	Any ANS	0.90 (0.51, 1.59)	High risk of bias

ANS: Antenatal steroids; BPD: bronchopulmonary dysplasia; CI: confidence intervals; GA: gestational age

Table 4: Risk factor before birth: chorioamnionitis (CA)

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Histological CA vs no histological CA				
Torchin 2017	24-26 weeks GA n=452 24-31 weeks GA n=1,231	Histological CA	24-26 weeks GA 0.66 (0.40, 1.10) 24-31 weeks GA 0.59 (0.40, 0.89)	Low risk of bias
Clinical + histological CA vs no clinical + histological CA				
Viscardi 2004	29-32 weeks GA n=177 < 29 weeks GA n=102	Clinical and histological CA	29-32 weeks GA 5.15 (0.61, 43.48) < 29 weeks GA 3.63 (1.20, 10.98)	Moderate risk of bias
Undefined CA vs no undefined CA				
Morrow 2017	n=587 (<34 weeks GA)	Undefined CA	0.87 (0.51, 1.48)	High risk of bias

BPD: bronchopulmonary dysplasia; CA: chorioamnionitis; CI: confidence interval; GA: gestational age

Table 5: Risk factor before birth: intra-uterine growth restriction

Study	Population	Risk factor BPD	Adjusted Odds Ratio and 95% CI	Quality
Intra-uterine growth restriction vs no intra-uterine growth restriction				
El Ayoubi 2016	n=617 (24-31 weeks GA)	Intra-uterine growth restriction	1.20 (0.70, 2.06)	Moderate risk of bias
Torchin 2016	n=1,506 (24-31 weeks GA)	Intra-uterine growth restriction	3.80 (2.00, 7.22)	Low risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval; GA: gestational age

Table 6: Risk factor at birth: gestational age

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Higher GA vs lower GA				
Costeloe 2012	n=859 (22-26 weeks GA)	Higher GA vs lower GA (weekly increments)	0.62 (0.45, 0.85)	Moderate risk of bias
De Waal 2012	n=144 (23-26 weeks GA)	Higher GA vs lower GA (weekly increments)	1.01 (0.37, 2.79)	Low risk of bias
Hanke 2015	n=3,554 (<32 weeks GA)	Higher GA vs lower GA (weekly increments)	0.89 (0.82, 0.97)	Moderate risk of bias
Marshall 1999	n=865 (500g-1500g)	Higher GA vs lower GA (weekly increments)	1.02 (0.90, 1.16)	Moderate risk of bias
Reiss 2003	n=1,195 (<32 weeks GA)	Higher GA vs lower GA (weekly increments)	0.67 (0.60, 0.75)	Moderate risk of bias
Lower GA vs higher GA				
Morrow 2017	n=587 (<34 weeks GA)	Lower GA vs higher GA (weekly increments)	1.89 (1.62, 2.17)	High risk of bias

BPD: bronchopulmonary dysplasia CI: confidence interval; GA: gestational age

Table 7: Risk factor at birth: birthweight

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Higher BW vs lower BW				
Costeloe 2012	n=859 (22-26 weeks GA)	Higher BW vs lower BW (1 SD increments)	0.62 (0.45, 0.85)	Moderate risk of bias
De Waal 2012	n=144 (23-26 weeks GA)	Higher BW vs lower BW (BW categories)	0.44 (0.22, 0.88)	Low risk of bias
Gagliardi 2007	n=1,118 (23-32 weeks GA)	Higher BW vs lower BW (100g increments)	0.63 (0.57, 0.70)	Moderate risk of bias

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Hanke 2015	n=3,554 (<32 weeks GA)	Higher BW vs lower BW (100g increments)	1.00 (0.99, 1.01)	Moderate risk of bias
Marshall 1999	n=865 (500g-1500g)	Higher BW vs lower BW (100g increments)	0.80 (0.71, 0.90)	Moderate risk of bias
Lower BW vs higher BW				
Morrow 2017	n=587 (<34 weeks GA)	Lower BW vs higher BW (1 SD increments)	2.40 (1.66, 3.47)	High risk of bias

BPD: bronchopulmonary dysplasia; BW: birthweight; CI: confidence interval, GA: gestational age; SD: standard deviation

Table 8: Risk factor at birth: sex

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Male vs female				
Costeloe 2012	n=859 (22-26 weeks GA)	Sex	2.08 (1.48, 2.92)	Moderate risk of bias
Gagliardi 2007	n=1,118 (23-26 weeks GA)	Sex	2.08 (1.40, 3.09)	Moderate risk of bias
Marshall 1999	n=865 (500g-1500g)	Sex	1.40 (0.96, 2.04)	Moderate risk of bias
Morrow 2017	n=587 (<34 weeks GA)	Sex	1.37 (0.92, 2.04)	High risk of bias
Female vs male				
Hanke 2015	n=3,554 (<32 weeks GA)	Sex	0.55 (0.45, 0.67)	Moderate risk of bias
Farstad 2011	n=364 (22-27 weeks GA)	Sex	0.50 (0.28, 0.89)	High risk of bias
Reiss 2003	n=1,195 (<32 weeks GA)	Sex	0.63 (0.41, 0.97)	Moderate risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 9: Risk factor at birth: small for gestational age

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Small for gestational age vs no small for gestational age				
Hanke 2015	n=3,554 (<32 weeks GA)	SGA	1.13 (0.79, 1.62)	Moderate risk of bias
Monier 2017	SGA + suspected FGR n=2,505 SGA + no suspected FGR	SGA	SGA + suspected FGR 2.50 (1.60, 3.91) SGA + no suspected FGR	Low risk of bias

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Small for gestational age vs no small for gestational age				
	n=2,199 (24-31 weeks GA)		3.40 (2.20, 5.25)	
Reiss 2003	n=1,195 (<32 weeks GA)	SGA	3.80 (2.11, 6.84)	Moderate risk of bias
Zeitlin 2010	n=1,323 (24-31 weeks GA)	SGA	6.42 (4.51, 9.14)	Moderate risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, FGR: fetal growth restriction; GA: gestational age; SGA: Small for gestational age

Table 10: Risk factor at birth: maternal ethnicity/race

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
White vs non-white				
Morrow 2017	n=587 (<34 weeks GA)	Ethnicity/	White vs non-white 1.85 (1.51, 2.27)	High risk of bias
Hispanic/Latino vs non-hispanic/Latino				
Morrow 2017	Hispanic/Latino n=587 (<34 weeks GA)	Race	Hispanic/Latino vs non-Hispanic/Latino 0.70 (0.42, 1.17)	High risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 11: Risk factor at birth: resuscitation

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Resuscitation at birth vs no resuscitation at birth				
Figueras-Aloy 2005	n=1,537 (23-28 weeks GA)	Resuscitation at birth	1.61 (1.16, 2.23)	Moderate risk of bias
Wyckoff 2012	n=6,654 (23-30 weeks GA)	Resuscitation at birth	1.34 (1.13, 1.59)	Low risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 12: Risk factor at birth: surfactant use

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Any surfactant use vs no surfactant use				
Farstad 2011	n=240 (22-27 weeks GA)	Any surfactant use	2.56 (1.00, 6.55)	High risk of bias
Marshall 1999	n=865 (500g-1500g)	Any surfactant use	2.86 (1.59, 5.14)	Moderate risk of bias
Reiss 2003	n= 1,195 (<32 weeks GA)	Any surfactant use	1.57 (1.01, 2.44)	Moderate risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 13: Risk factor after birth: invasive ventilation

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Invasive ventilation at 24 hours or less of age vs no invasive ventilation at 24 hours or less of age				
Dargaville 2016	25-28 weeks GA n=6,771 29-32 weeks GA n=12,332	Invasive ventilation	25-28 weeks GA 1.30 (1.09, 1.55) 29-32 weeks GA 1.57 (1.23, 2.00)	Low risk of bias
Farstad 2011	n=240 (22-27 weeks GA)	Invasive ventilation	0.86 (0.41, 1.80)	High risk of bias
Invasive ventilation at 48 hours of age vs no invasive ventilation at 48 hours of age				
Marshall 1999	n=865 (500g-1500g)	Invasive ventilation	2.18 (1.29, 3.68)	Moderate risk of bias
Invasive ventilation at 5 days or more of age vs no invasive ventilation at 5 days or more of age				
Figueras-Aloy 2005	n=1,537 (23-28 weeks GA)	Invasive ventilation	4.55 (3.24, 6.39)	Moderate risk of bias
Invasive ventilation at undefined time frame vs no invasive ventilation at undefined time frame				
Kamper 2004	n=269 (<28 weeks GA)	Invasive ventilation	3.68 (1.31, 10.34)	Moderate risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 14: Risk factor after birth: postnatal steroid use

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Postnatal steroid use vs no postnatal steroid use				
Farstad 2011	n=240 (22-27 weeks GA)	Postnatal steroid use	2.50 (1.22, 5.12)	High risk of bias

BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age

Table 15: Risk factor after birth: patent ductus arteriosus

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Pharmacologically treated PDA vs no pharmacologically treated PDA				
Edstedt Bonamy 2017	Low PDA treatment proportion n=2,645 Medium PDA treatment proportion n=3,087 High PDA treatment proportion n=530 (22-31 weeks GA)	PDA	Low PDA treatment proportion 1.41 (1.09, 1.82) Medium PDA treatment proportion 1.63 (1.22, 2.18) High PDA treatment proportion 2.54 (1.48, 4.36)	Moderate risk of bias

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Surgically treated PDA vs no surgically treated PDA				
Edstedt Bonamy 2017	Low PDA treatment proportion n=2,645 Medium PDA treatment proportion n=3,087 High PDA treatment proportion n=530 (22-31 weeks GA)	PDA	Low PDA treatment proportion 1.97 (1.51, 2.57) Medium PDA treatment proportion 2.90 (1.76, 4.78) High PDA treatment proportion 3.79 (1.62, 8.87)	Moderate risk of bias
Pharmacologically and surgically treated PDA vs no pharmacologically and surgically treated PDA				
Edstedt Bonamy 2017	Low PDA treatment proportion n=2,645 Medium PDA treatment proportion n=3,087 High PDA treatment proportion n=530 (22-31 weeks GA)	PDA	Low PDA treatment proportion 1.63 (1.00, 2.66) Medium PDA treatment proportion 2.57 (1.76, 3.75) High PDA treatment proportion 3.73 (1.69, 8.23)	Moderate risk of bias
Any treated PDA vs no treated PDA				
Farstad 2011	n=240 (22-27 weeks GA)	PDA	2.20 (1.05, 4.61)	High risk of bias
Kamper 2004	n=269 (<28 weeks GA)	PDA	2.84 (1.09, 7.40)	Moderate risk of bias

1 *BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age; PDA: patent ductus arteriosus*

2 **Table 16: Risk factor after birth: sepsis**

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Clinical sepsis vs no clinical sepsis				
Ohlin 2014	n=263 (<27 weeks GA)	Clinical sepsis	Clinical sepsis 1.10 (0.60, 2.02)	Moderate risk of bias
Blood culture positive sepsis vs no blood culture positive sepsis				
Ohlin 2014	CoNS without other bacteria n=307 CoNS with other bacteria	Blood culture positive sepsis	CNS without other bacteria 1.60 (0.90, 2.84) CNS with other bacteria	Moderate risk of bias

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
	n=211 Other bacteria n=229 (<27 weeks GA)		1.90 (0.90, 4.01) Other bacteria 1.60 (0.80, 3.20)	
Clinical + blood culture positive sepsis vs clinical + blood culture positive sepsis				
Kamper 2004	n=269 (<28 weeks GA)	Clinical + blood culture sepsis	1.74 (1.24, 2.44)	Moderate risk of bias
Ohlin 2014	n=405 (<27 weeks GA)	Clinical + blood culture sepsis	1.60 (1.00, 2.56)	Moderate risk of bias
Clinical +/- blood culture sepsis vs clinical +/- blood culture sepsis				
Reiss 2003	n=1,195 (<32 weeks GA)	Clinical sepsis +/- blood culture	1.56 (1.02, 2.39)	Moderate risk of bias
Gagliardi 2007	n=1,118 (23-26 weeks GA)	Clinical sepsis +/- Blood Culture	4.26 (2.76, 6.58)	Moderate risk of bias

1 *BPD: bronchopulmonary dysplasia; CI: confidence interval; CoNS: coagulase negative staphylococci; GA:*
2 *gestational age*

3 **Table 17: Risk factor after birth: thermoregulation**

Study	Population	Risk factor for BPD	Adjusted Odds Ratio and 95% CI	Quality
Thermoregulation: 35 degrees Celsius or higher vs less than 35 degrees Celsius				
Costeloe 2012	n=859 (22-26 weeks GA)	Thermoregulation	0.57 (0.33, 0.98)	Moderate risk of bias

4 *BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age*

5 **Table 18: Risk factor after birth: breastmilk feeding**

Study	Population	Risk factor breastmilk feeding	Adjusted Odds Ratio and 95% CI	Quality
Breastmilk feeding vs no breastmilk feeding				
Patel 2017	n=254 (<32 weeks GA)	Human milk as proportion of enteral feeding (10% increase)	1.10 (1.01, 1.21)	High risk of bias
Spiegler 2016	Exclusively formula fed vs exclusively breastmilk fed n=462 Mixed feeding vs exclusively breastmilk fed n=1,194 (<32 weeks GA)	Exclusively formula feeding and mixed breastmilk + formula feeding	Exclusively formula fed vs exclusively breastmilk fed 2.59 (1.33, 5.04) Mixed feeding vs exclusively breastmilk fed 1.61 (1.15, 2.25)	Low risk of bias

6 *BPD: bronchopulmonary dysplasia; CI: confidence interval, GA: gestational age*

E Economic evidence

No economic evidence on risk factors associated with the development of BPD in preterm babies was identified by literature searches of the economic literature undertaken for this review.

F Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

G Clinical evidence statements

R Risk factors before birth

1 A Antenatal steroids (ANS)

- Evidence with moderate to high risk of bias was available from 6 studies (n=11,380) that examined complete, partial or any antenatal steroid therapy (ANS) as risk factors for the development of BPD.

1 C *Complete ANS*

- 2 studies (n=4,584) with a moderate risk of bias showed that there was no association between ANS and BPD in preterm babies with a gestational age of <32 weeks. One study (n=1,537) with a moderate risk of bias showed that preterm babies (23-28 weeks gestational age) of women who received ANS were less likely to develop BPD than those mothers who did not receive ANS. One study (n=3,840) with a moderate risk of bias showed that there was no association between complete ANS and BPD compared to partial ANS and BPD in preterm babies with a gestational age of 22-27 weeks gestational age.

2 P *Partial ANS*

- 1 study (n=1,579) with a moderate risk of bias showed that there was no association between ANS and BPD in preterm babies with a gestational age of 22-27 weeks.

2 A *Any ANS*

- 2 studies (n=4,141) with a moderate to high risk of bias showed that there was no association between ANS and BPD in preterm babies with a gestational age <34 weeks. One study (n=1,118) with a moderate risk of bias showed that preterm babies (23-32 weeks) of women who received ANS were less likely to develop BPD than those mothers who did not receive ANS.

3 2 Chorioamnionitis (CA)

- Evidence with low to high risk of bias was available from 3 studies (n=2,355) that examined histological, clinical and histological, and undefined CA as risk factors for the development of BPD.

3 H *Histological CA*

- 1 study (n=1,432) with a low risk of bias showed mixed results. Preterm babies with a gestational age 24-31 weeks (n=1,231) whose mothers were diagnosed with histological CA were less likely to develop BPD than those who were not diagnosed with histological CA. Whereas there was no association between preterm babies with a gestational age of 24-26 weeks (n=452) whose mothers were diagnosed with histological CA.

Histological with or without clinical CA

- 1 study (n=262) with a moderate risk of bias showed mixed results. Preterm babies with a gestational age <29 weeks (n=102) whose mothers were diagnosed with clinical and histological CA were more likely to develop BPD than those who were not diagnosed with clinical and histological CA. Whereas, there was no association between in preterm babies with a gestational age 29-32 weeks (n=177)whose mothers were diagnosed with clinical and histological CA.

Undefined CA

- 1 study (n=587) with a high risk of bias showed that there was no association between undefined CA and BPD in preterm babies with a gestational age <34 weeks.

Intrauterine growth restriction (IUGR)

- Evidence with a low to moderate risk of bias was available from 2 studies (n=2,123) that examined IUGR as a risk factor for the development of BPD.
- 1 study (n=617) with a moderate risk of bias showed that there was no association between IUGR and BPD in preterm babies with a gestational age 24-31 weeks. Whereas, a larger study (n=1,506) with a low risk of bias in preterm babies with a gestational age of 24-31 weeks showed that babies with IUGR were more likely to develop BPD than those without IUGR.

Risk factors at birth

Gestational age

- Evidence with a low to high risk of bias was available from 6 studies (n=7,204) that examined gestational age as a risk factor for the development of BPD.
- 4 studies (n=6,195) with a moderate to high risk of bias showed that preterm babies (<32 weeks) with a higher gestational age were less likely to develop BPD with each age gain of a week.
- 2 studies (n=1,009) with a low to moderate risk of bias showed that there was no association between gestational age and BPD in preterm babies with a gestational age of 23-26 weeks in one study (n=144) and an undefined age in the other study (n=865).

Birthweight

- Evidence with a low to high risk of bias was available from 6 studies (n=7,127) that examined birthweight as a risk factor for the development of BPD, and which showed mixed results.
- 5 studies (n=3,543) with a low to high risk of bias examined birthweight increments of 100g, 1 standard deviation, and in categories, all showed that preterm babies (<32 weeks and an undefined age range) with a higher birthweight were less likely to develop BPD.
- 1 study (n=3,554) with a moderate risk of bias showed that there was no association between gestational age examined in 100g increments) and BPD in preterm babies with a gestational age <32 weeks.

Sex

- Evidence with a moderate to high risk of bias was available from 7 studies (n=8,542) that examined sex as a risk factor for the development of BPD.
- 5 studies (n=7,090) with a moderate to high risk of bias showed that male preterm babies were more likely to develop BPD than female preterm babies with a gestational age <32 weeks.

- 2 studies (n=1452) with a moderate to high risk of bias showed that there was no association between sex and BPD in preterm babies with a gestational age <34 weeks and an undefined age range.

Small for gestational age (SGA)

- Evidence with a low to moderate risk of bias was available from 4 studies (n=10,776) that examined SGA as a risk factor for the development of BPD.
- 3 studies (n=7,222) with a low to moderate risk of bias showed that preterm babies who were SGA were more likely to develop BPD than those who were not not SGA with a gestational age <33 weeks.
- 1 study of moderate risk of bias (n=3,554) showed that there was no association between SGA and BPD in preterm babies with a gestational age <32 weeks.

Maternal ethnicity/race

- Evidence with a high risk of bais was available from one study (n=587) which examined maternal ethnicity and race as a risk factor for the development of BPD.

Maternal race

- 1 study (n=587) with a high risk of bias showed that preterm babies born to white mothers were more likely to develop BPD than preterm babies born to non-white mothers with a gestational age <34 weeks.

Maternal ethnicity

- 1 study (n=587) with a high risk of bias showed no association between mothers who were Hispanic/Latino and BPD in preterm babies with a gestational age <34 weeks.

Resuscitation at birth

- Evidence with a low to moderate risk of bias was available from 2 studies (n=8,191) which examined resuscitation at birth as a risk factor for the development of BPD.
- Both studies showed that preterm babies who were resuscitated at birth were more likely to develop BPD than preterm babies who were not resuscitated at birth with a gestational age of <30 weeks.

Surfactant use

- Evidence with a moderate to high risk of bias was available from 3 studies (n=2,300) which examined receipt of surfactant at birth as a risk factor for the development of BPD.
- All 3 studies showed that preterm babies who received surfactant at birth were more likely to develop BPD than preterm babies who did not receive surfactant at birth with a gestational age of <32 weeks and an undefined age range.

Risk factors after birth

Invasive ventilation

- Evidence with a low to high risk of bias was available from 5 studies (n=22,014) that examined invasive ventilation as a risk factor for the development of BPD.

Invasive ventilation at <24 hours of age

- 1 study (n=19,103) with a low risk of bias showed that preterm babies who were invasively ventilated at 24 hours or less of age were more likely to develop BPD than preterm babies who were not invasively ventilated with a gestational age <32 weeks.

- 1 study (n=240) with a high risk of bias showed no association between preterm babies that were invasively ventilated at 24 hours or less of age and BPD with a gestational age of 22-27 weeks.

Invasive ventilation at 48 hours of age

- 1 study (n=865) with a moderate risk of bias showed that preterm babies who were invasively ventilated at 48 hours of age were more likely to develop BPD than preterm babies who were not invasively ventilated with an undefined gestational age.

Invasive ventilation at 5 days or more of age

- 1 study (n=1,537) with a moderate risk of bias showed that preterm babies who were invasively ventilated at 5 days of age or older were more likely to develop BPD than preterm babies who were not invasively ventilated with a gestational age of 23-28 weeks.

Invasive ventilation at an undefined time frame

- 1 study (n=269) with a moderate risk of bias showed that preterm babies who were invasively ventilation were more likely to develop BPD than preterm babies who were not invasively ventilation with a gestational age of <28 weeks

Supplemental oxygen

- No evidence was found on this risk factor

Postnatal steroids

- Evidence with a high risk of bias from 1 study (n=240) showed that preterm babies receiving postnatal steroids were more likely to develop BPD than preterm babies not receiving postnatal steroids with a gestational age of 22-27 weeks.

Patent Ductus Arteriosus (PDA)

- Evidence with a moderate to high risk of bias was available from 3 studies (n=6,771) that examined treated PDA as a risk factor for the development of BPD.

Pharmacologically treated PDA

- 1 study (n=6,262) with a moderate risk of bias showed that preterm babies who had a pharmacologically treated PDA were more likely to develop BPD than preterm babies who did not receive pharmacological treatment for PDA in low, medium, and high treatment portions with a gestational age of 22-31 weeks

Surgically treated PDA

- 1 study (n=6,262) with a moderate risk of bias showed that preterm babies who had surgically treated PDA were more likely to develop BPD than preterm babies who did not receive surgical treatment for PDA in low, medium, and high treatment portions with a gestational age of 22-31 weeks

Pharmacologically and surgically treated PDA

- 1 study (n=6,262) with a moderate risk of bias showed that preterm babies who had a pharmacologically and surgically treated PDA were more likely to develop BPD than preterm babies who did not receive pharmacological and surgical treatment for PDA in low, medium, and high treatment portions with a gestational age of 22-31 weeks.

Any treated PDA

- 2 studies (n=509) with a moderate to high risk of bias showed that preterm babies who had a treated PDA were more likely to develop BPD than preterm babies who did not receive any treatment for PDA with a gestational age of <28 weeks.

Sepsis

- Evidence with a moderate risk of bias was available from 4 studies (n=3,997) that examined clinical sepsis, blood culture positive sepsis, clinical and blood culture positive sepsis, and clinical and/or blood culture positive sepsis as a risk factor for the development of BPD.

Clinical sepsis

- 1 study (n=263) with a moderate risk of bias showed no association between clinical sepsis and BPD in preterm babies with a gestational age of <27 weeks.

Blood culture positive sepsis

- 1 study (n=747) with a moderate risk of bias showed no association between blood culture positive sepsis (coagulase negative staphylococci [CoNS] without other bacteria, CoNS with other bacteria, or other bacteria) and BPD in preterm babies with a gestational age of <27 weeks.

Clinical sepsis and blood culture positive sepsis

- 2 studies (n=674) with a moderate risk of bias showed that preterm babies with clinical and blood culture positive sepsis were more likely to develop BPD than preterm babies without clinical and blood culture positive sepsis with a gestational age of <28 weeks.

Clinical sepsis +/- blood culture positive sepsis

- 2 studies (n=2,313) with a moderate risk of bias showed that preterm babies with clinical sepsis +/- blood culture positive sepsis were more likely to develop BPD than preterm babies without clinical sepsis +/- blood culture positive sepsis with a gestational age <32 weeks.

Necrotising enterocolitis

- No evidence was found on this risk factor

Thermoregulation

- Evidence with a moderate risk of bias from 1 study (n=859) showed that preterm babies admitted to the NICU with a body temperature <35 degrees Celsius are more likely to develop BPD than preterm babies with a body temperature of >35 degrees Celsius with a gestational age of 22-26 weeks.

Breastmilk feeding

- Evidence with a moderate to high risk of bias was available from 2 studies (n=1,687) that examined breastmilk feeding as a risk factor for the development of BPD.
- 1 study (n=254) with a high risk of bias showed that preterm babies that had human milk as a proportion of enteral feeding (10% increase increments) were less likely to develop BPD than preterm babies that didn't receive human milk as a proportion of enteral feeding with a gestational age <32 weeks.
- 1 study (n=1,433) with a low risk of bias showed that preterm babies that were exclusively breastmilk fed or mixed breastmilk + formula fed were less likely to develop BPD than preterm babies that were exclusively formula fed with a gestational age <32 weeks.

See appendix E for Forest plots.

Economic evidence statements

- No economic evidence on risk factors associated with the development of BPD in preterm babies was available.

Recommendations

A1.1 Be aware that the risk factors for bronchopulmonary dysplasia (BPD) include those shown in **Error! Reference source not found.**:

Table 19: Identified risk factors for bronchopulmonary dysplasia[a]

In babies born before 32 weeks	• lower gestational age • lower birthweight • small for gestational age • male sex • core body temperature of less than 35°C on admission to neonatal unit • clinical sepsis with or without positive blood cultures • feeding with formula milk (exclusively or in addition to breast milk) • treated with surfactant[b] • treated for patent ductus arteriosus[b]
In babies born before 30 weeks	• cardiopulmonary resuscitation performed at birth
In babies born before 28 weeks	• invasive ventilation begun within 24 hours of birth, especially if it lasts longer than 48 hours

[a] These risk factors have been identified, but other gestational ages and other risk factors not listed here might also be associated with increased risk of bronchopulmonary dysplasia.

[b] Be aware that 'treated with surfactant' and 'treated for a patent ductus arteriosusa (PDA)' may reflect the severity of the baby's condition rather than being a causal link. Surfactant should be used, and a PDA should be treated, where clinically appropriate.

Rationale and impact

Why the committee made the recommendations

There was evidence that lower gestational age, lower birth weight, being small for gestational age, male sex, lower body temperature, sepsis, any formula feeding, surfactant use, treatment for a patent ductus arteriosus (PDA), cardiopulmonary resuscitation and mechanical ventilation, are all independent risk factors for bronchopulmonary dysplasia (BPD) in preterm babies.

There was no evidence of a link between antenatal steroids, chorioamnionitis, intrauterine growth restriction, ethnicity or race, or postnatal steroid use, and BPD. However, the committee did not prioritise these areas for further research.

The committee was concerned that including surfactant use and treatment for PDA as risk factors for BPD could lead to a reduction in surfactant use and PDA treatment. They agreed that there was unlikely to be a causal link – rather, the increased risk of BPD associated with these factors is more likely to reflect the severity of the baby's condition, and that surfactant should be used, and a PDA should be treated, where clinically appropriate.

The committee noted that there was an absence of evidence for certain risk factors for BPD; some evidence was for specific gestational ages at birth from which the committee was unable to extrapolate to other gestational ages, and for some risk factors, the evidence was underpowered to detect an effect. The committee therefore concluded that other gestational ages and other risk factors not listed here might also be associated with increased risk of BPD.

No evidence was found for some of the potential risk factors that had been suggested by the committee (such as necrotising enterocolitis and supplementary oxygen), but these were not prioritised by the committee for further research.

Impact of the recommendations on practice

Knowledge of BPD risk factors means healthcare professionals can identify preterm babies who are more likely to develop BPD, and prioritise treatment regimens accordingly. This may reduce the incidence of BPD, which will lead to long-term savings for the NHS.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee agreed that the risk factors that are most likely to have a clinically significant association with BPD are gestational age, birthweight, sex, small for gestational age, and invasive ventilation. The committee noted that most of these risk factors were non-modifiable, although there were a number of other risk factors that were modifiable.

The quality of the evidence

The committee agreed that there were gaps in the evidence about risk factors, with a lack of eividence for some risk factors of interest (supplementary oxygen and NEC), or for sub-groups of interest (different gestational ages). This may have been partially due to the strict inclusion and exclusion criteria that had been set out in the review protocol to ensure the highest quality evidence was included in the review. The committee discussed that the recommendations they made should include reference to these gaps in the evidence.

The quality of evidence in this review ranged from high to low. Some of the risk factors were identified only in low quality evidence but the committee agreed that they should be included in the recommendations, However, the committee were aware that better quality evidence may add to these risk factors. The quality of evidence was most often downgraded because of the following:

- Lack of information regarding the population of preterm babies under investigation
- High rates of attrition and failing to report the reasons for a lack of follow-up
- Limited description of the risk factors and how they were measured or assessed
- Limited description of the outcome and how it was measured or assessed
- Unclear justification for choice of potential confounders adjusted for in the analyses

The committee also recognised that there was a high level of heterogeneity across studies in relation to:

- Inclusion/exclusion criteria of the preterm babies
- Gestational age of preterm babies
- Criteria or definitions of risk factors
- Criteria or definitions of the outcome
- Severity of the outcome
- Confounders taken into account in the multivariable analyses

In view of the above, the committee agreed that pooling the studies in meta-analyses would be inappropriate and jeopardise the methodological integrity of the review.

Benefits and harms

Knowledge of risk factors for the development of BPD enables healthcare professionals to effectively identify preterm babies who are more likely to develop BPD and prioritise treatment regimens accordingly. The committee agreed that it was important to assess independent risk factors associated with BPD, but they recognised that in clinical practice risk factors may not present independently, and that decisions would be based on many potential combinations of risk factors.

The committee recognised that while there was a large amount of evidence identified by the evidence review, there were several gaps in the evidence. These gaps included risk factors of interest, such as supplementary oxygen and NEC, and stratification by different gestational ages. For example, if the only evidence found was among babies born before 31 weeks' gestation, it does not necessarily mean preterm babies born at later gestational ages would not be at an increased risk of that outcome, but rather that there is uncertainty due to the absence of evidence. Because of these gaps a footnote was added to the risk factor table to make it clear there was no information available for some risk factors.

Risk factors before birth:

Antenatal steroids

The committee discussed that there is a large body of evidence supporting the protective effect of ANS against BPD in comparative randomised controlled trials. However, the committee agreed that the evidence on the association between ANS and BPD was mixed in this review, with 2 studies showing that ANS was protective against BPD and the other 4 studies showing no association. In view of this conflicting evidence, the committee agreed not to write a recommendation on the association between ANS and BPD. It was also agreed not to make a research recommendation as this area was not considered enough of a priority.

Chorioamnionitis

The committee highlighted that there was uncertainty around the association between CA (defined as histological or histological +/- clinical) and BPD. Studies in the review showed a protective effect of CA against BPD or no association in histological CA, increased risk of BPD or no association with histological +/- clinical CA, and no association between CA and BPD in an undefined CA. The committee were aware that there were more prognostic studies assessing the association between CA and BPD, however these were excluded from the review mainly because pre-defined confounders were not accounted for in their analyses, study design was retrospective in nature, samples sizes did not meet our minimum criteria, and studies were single centre. The committee were also aware of a large systematic review (Hartling 2012) on the association of CA and BPD, whose results from a pooled meta-analysis of studies adjusted for confounders suggested that CA increases the risk of BPD. However, it was highlighted that the methods that the authors used to come to this conclusion were through a meta-analysis and were not considered robust due to the high level of heterogeneity across studies and it was therefore excluded. Furthermore, the authors also suggested that there was significant uncertainty in their results. The committee therefore made the decision not to write a recommendation on the association of CA and BPD, or to make a research recommendation as this area was not considered to have enough priority.

Intrauterine Growth Restriction

The committee agreed that there was insufficient evidence to draw conclusions on the association between IUGR and BPD. In this review there were mixed results, with one study showing a positive association between IUGR and BPD and the other study showing no association between IUGR and BPD. The committee discussed the difficulty in accurately diagnosing IUGR by ultrasound and in view of this and the conflicting evidence decided not to prioritise writing a recommendation on IUGR as a risk factor.

Risk factors at birth:

Gestational age

The committee concluded that the majority of the evidence clearly indicated that degree of prematurity was an independent risk factor for BPD. Of the 6 studies assessing gestational age as a risk factor, only 2 studies showed no association and the committee agreed that these 2 papers were of less significance due to a small sample size and being relatively outdated in comparison to the body of evidence in the analyses. All studies looked at the association of BPD between higher and lower gestational ages in weekly increments and specific comparisons between groups of gestational ages could not be made.

Birthweight

The committee discussed that there was likely to be correlation between gestational age and birthweight and their association with BPD, however it was highlighted that gestational age as a confounder was accounted for in the analysis and that birthweight itself was an independent risk factor. There was mixed evidence for this risk factor, with 5 small studies showing an association, and 1 larger study showing no association between lower birthweight and BPD. However, the committee agreed that there was evidence that lower birthweight was likely to be an independent risk factor for BPD..

Sex

The majority of evidence indicated that male sex was an independent risk factor for BPD. Two studies showed no association, but did indicate a trend in the direction of male sex, although the committee placed less weight on these studies as one study had a high risk of bias and the other study was relatively outdated in comparison to the body of evidence. In view of this, the committee concluded that male sex was an independent risk factor for BPD.

Small for gestational age

All but 1 study showed a clear association between being small for gestational age and BPD. The committee discussed that all studies showing an association between SGA and BPD had a large relative effect (RR >2), thus they concluded that being small for gestational age was an independent risk factor for BPD.

Ethnicity/race

The committee agreed that there was insufficient evidence to draw conclusions on the association between ethnicity/race and BPD. Only 1 study with a high risk of bias was available on the association of maternal race and BPD. Although showing that white race was a clear independent risk factor for BPD the committee agreed that due to the sample size, risk of bias, and differences in racial characteristics within the population, there was uncertainty in making inferences that a maternal white race was an independent risk factor for BPD.

Resuscitation

The committee concluded that evidence from two large studies clearly indicated that cardiopulmonary resuscitation at birth was an independent risk factor for BPD for babies with a gestational age of <30 weeks.

Surfactant use

Although the evidence showed that surfactant use was an independent risk factor for BPD, the committee were concerned that a recommendation to this effect may be interpreted incorrectly. The committee were concerned that writing a statement regarding the positive association between surfactant use and BPD might lead to healthcare professionals reducing their surfactant use in preterm babies where surfactant use was indicated. This was of

particular concern for the committee as surfactant use is clearly established with strong evidence to support its use where indicated in preterm babies. The committee discussed that as this was a prognostic review, the association between surfactant use and BPD was likely to be an indication of the severity of the baby's condition and therefore a footnote was included in the recommendations table to clarify this.

Risk factors after birth:

Invasive ventilation

The majority of the evidence clearly showed that invasive ventilation was an independent risk factor for BPD in babies born before 28 weeks. The only study that showed a lack of association had a high risk of bias and a relatively small sample size. In view of this the committee agreed with the majority of the evidence.

Postnatal steroids

The committee agreed that there was insufficient evidence to draw conclusions on the association between postnatal steroids and BPD. Only one study with a high risk of bias was available on the association of postnatal steroids and BPD. Although showing that postnatal steroid use was a clear, independent risk factor for BPD, the committee agreed that due to the sample size and risk of bias that there was uncertainty in making inferences that postnatal steroid use was an independent risk factor for BPD.

Patent ductus arteriosus

The evidence showed that a PDA that had been treated with pharmacological, surgical, a combination of pharmacological and surgical, or any treatment was an independent risk factor for BPD. The committee discussed that this evidence was of direct relevance to the preterm population in the UK setting as the largest study by Edstedt Bonamy 2017 separated the analyses by the proportion of PDAs that were treated (low <15%, medium 15-25%, high >25%) and the low PDA treatment proportion included data from the UK. The committee were concerned that writing a statement regarding the positive association between treated PDA and BPD may lead to healthcare professionals not treating PDA in preterm babies where treatment is indicated. As with the surfactant risk factor, the committee agreed that the association between treated PDA and BPD was likely to be an indication of the severity of the baby's condition and therefore a footnote was includein the the recommendation table to explain this.

Sepsis

The committee concluded that the evidence clearly showed that the combination of clinical + blood culture positive sepsis and clinical +/- blood culture positive sepsis were independent risk factors for BPD.

Thermoregulation

Although there was only one study on the association of thermoregulation and BPD, the committee agreed that reduced core body temperature (body temperature below 35 degrees Celsius on admission to the NICU) was associated with BPD. Although there was only one study this was directly relevant and drawn from the largest UK population-based study, EPICure (Costeloe, 2012). In view of this the committee agreed that a body temperature below 35 degrees on admission to NICU was an independent risk factor for BPD.

Feeding regimen

The committee concluded that the evidence showed that any formula feeding was an independent risk factor for BPD. The committee discussed that breastmilk feeding included mothers own milk or donor milk, however as this review was prognostic in design and not aligned to making specific recommendations regarding breastmilk regimens the committee

agreed that they could not make recommendations on the type of breastmilk. With regards to the evidence on human milk as a proportion of enteral feeding as a protective factor for BPD, the committee agreed that due to the high risk of bias of the study, relatively small sample size, and proximity to the null effect that no association could be firmly established. The committee did not feel this area was enough of a priority to recommend for further research.

Cost effectiveness and resource use

There was no economic evidence on the risk factors associated with the development of BPD in preterm babies.

The committee considered that recognition of the risk factors that would allow prediction of BPD in preterm babies has important resource use implications. Identification of risk factors could potentially lead to the prevention of BPD if appropriate preventative interventions are delivered to preterm babies identified at higher risk. The committee considered the high costs associated with BPD, including the management of long term consequences that require costly support and that treating BPD therefore would have a substantial impact on NHS. The committee noted that any strategy that potentially leads to the prevention (and timely identification) of babies at risk of BPD is likely to present a cost effective use of NHS resources.

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1 Appendices

2 Appendix A – Review protocols

3 Review protocol for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Field (based on PRISMA-P	Content
Review question in scope	What are the risk factors for bronchopulmonary dysplasia?
Review question in guideline	What are the risk factors for bronchopulmonary dysplasia in preterm babies?
Type of review question	Prognostic review
Objective of the review	To determine the risk factors for bronchopulmonary dysplasia in preterm babies and inform care with regards to the type of ventilation required, surfactant requirements, pressure and oxygen use.
Eligibility criteria – population/disease/condition/issue/domain	Preterm babies Exclusions: Preterm babies with congenital abnormalities except patent ductus arteriosus
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	**Risk factors before birth:** Antenatal steroids Chorioamnionitis - defined as: - Histological - Clinical Intra-uterine growth restriction– defined as fetal weight <10th or 3rd percentile for gestational age determined through an ultrasound. **Risk factors at birth:** Gestational age: - < 26 + 6 weeks - 27-31 $^{+6}$ weeks - 32-36^{+6} weeks Birth weight:

Field (based on PRISMA-P	Content
	- <1000 g - 1001 g - 1500 g - >1501 g Small for gestational age defined as birth weight <10th or 3rd percentile for gestational age Sex Ethnicity Need for resuscitation at birth **Risk factors after birth:** Surfactant Invasive ventilation - Invasive ventilation (volume targeted ventilation, triggered pressure limited ventilation, synchronised intermittent mandatory ventilation, non-triggered pressure limited ventilation, conventional invasive ventilation) Supplementary oxygen Postnatal steroids Patent ductus arteriosus – defined as requiring treatment: - Medical - Surgical Sepsis – defined as: - Positive culture sepsis - Clinical Necrotising enterocolitis (NEC) - defined as NEC Stage 2 or above Thermoregulation – defined as NICU admission temperature of less than 36.5 degrees Celsius: - 36-36.5 °C - 35.5-35.9 °C - <35.5 °C Preterm feeding regimen – defined as: - Exclusively fed human (mother or donor) milk

Field (based on PRISMA-P	Content
	- Exclusively fed formula milk - Mixture of human and formula milk
Confounding factors	Analysis should adjust for important confounding factors, as a minimum include: Gestational age Sex Unless found to be a non-significant risk factor in the univariate analyses in the study.
Outcomes and prioritisation	**Outcome** Bronchopulmonary dysplasia (oxygen dependency at 36 weeks postmenstrual age) **Comparisons** Babies born at: - Different gestational ages - Preterm babies unexposed to risk factors
Eligibility criteria – study design	**Include published full text papers:** Systematic reviews/meta-analyses of cohort studies Prospective population-based cohort studies Prospective multicentre cohort studies **Exclude:** Studies with a sample size <100 Conference abstracts Retrospective studies Follow-up of RCTs Single centre studies Studies where multivariate regression analysis was not conducted or important confounders not adjusted for in the multivariate analysis. *Consideration will be given to the above exclusions if the evidence is judged not to be sufficient – in quality or quantity*
Other inclusion exclusion criteria	Inclusion:

Field (based on PRISMA-P	Content
	English-language Developed countries with a neonatal care system similar to the UK (e.g. OECD countries) Studies conducted post 1990
Proposed sensitivity/sub-group analysis, or meta-regression	Gestational age: < 26 $^{+6}$ weeks 27-31 $^{+6}$ weeks 32-36^{+6} weeks
Selection process – duplicate screening/selection/analysis	Sifting, data extraction and appraisal of methodological quality will be performed by the systematic reviewer. Any disputes will be resolved in discussion with the senior systematic reviewer and the Topic Advisor. Quality control will be performed by the senior systematic reviewer. Dual sifting and data extraction will not be undertaken for this question.
Data management (software)	NGA STAR software will be used for study sifting, data extraction, recording quality assessment using checklists and generating bibliographies/citations.
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase Limits (e.g. date, study design): Apply standard animal/non-English language exclusion Dates: from 1990 Studies conducted post 1990 will be considered for this review question, as the GC felt that significant advances have occurred in ante-natal and post-natal respiratory management since this time period and outcomes for preterm babies prior to 1990 are not the same as post 1990.
Identify if an update	Not an update
Author contacts	Developer: NGA
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy	For details please see appendix B

Field (based on PRISMA-P	Content
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for analysis – combining studies and exploring (in)consistency	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • ROBIS for systematic reviews • Quality in prognostic studies (QUIPS) tool
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. Trial registries will be examined to identify missing evidence: Clinical trials.gov, NIHR Clinical Trials Gateway
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – Current management	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by The National Guideline Alliance (NGA) and chaired by Dr Janet Rennie in line with section 3 of Developing NICE guidelines: the manual. Staff from The National Guideline Alliance (NGA) undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter of the full guideline.

Field (based on PRISMA-P	Content
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds The National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England
PROSPERO registration number	Not registered

1

Appendix B – Literature search strategies

Literature search strategies for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Date of search: 29/06/2017

Database: Embase 1980 to 2017 Week 26, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	exp Infant, Newborn/ use ppez
2	newborn/ use emez
3	prematurity/ use emez
4	(infan* or neonat* or newborn* or baby or babies).ti,ab,jw,nw.
5	(preterm or pre-term or prematur* or pre-matur* or pre?mie* or premie*1).tw.
6	exp low birth weight/ use emez
7	(low adj3 birth adj3 weigh*).tw.
8	(LBW or VLBW).tw.
9	exp Intensive Care, Neonatal/ use ppez
10	newborn intensive care/ use emez
11	exp Intensive Care Units, Neonatal/ use ppez
12	neonatal intensive care unit/ use emez
13	(special and care and baby and unit*).tw.
14	((newborn or neonatal) adj ICU*1).tw.
15	(SCBU or NICU).tw.
16	exp Respiratory Distress Syndrome, Newborn/ use ppez
17	neonatal respiratory distress syndrome/ use emez
18	or/1-17
19	exp Respiration, Artificial/ use ppez
20	exp Intubation, Intratracheal/ use ppez
21	exp artificial ventilation/ use emez
22	exp assisted ventilation/ use emez
23	exp Ventilators, Mechanical/ use ppez
24	exp ventilator/ use emez
25	(ventilat* or respirator or respirators or intubat*).tw.
26	((respirat* or breath* or airway* or oxygen*) adj3 (support* or assist* or artificial or control* or oscillat* or pressure)).tw.
27	nasal cannula.tw.
28	or/19-27
29	18 and 28
30	Bronchopulmonary Dysplasia/ use ppez
31	lung dysplasia/ use emez
32	((bronch* or pulmon* or lung*) adj2 dysplasia*).tw.
33	((bronch* or pulmon* or lung*) adj2 hypoplas*).tw.
34	((chronic or long term) adj lung disease).tw.
35	BPD.tw.
36	or/30-35
37	29 and 36
38	Risk Factors/ use ppez
39	risk factor/ use emez
40	exp Risk Assessment/ use ppez
41	risk assessment/ use emez
42	exp Prognosis/ use ppez
43	prognos*.tw.
44	or/38-43
45	risk.tw.
46	exp Steroids/ use ppez
47	exp corticosteroid/ use emez
48	(steroid* or corticosteroid* or glucocortico*).tw.
49	or/46-48
50	Prenatal Exposure Delayed Effects/ use ppez

#	Searches
51	prenatal exposure/ use emez or prenatal drug exposure/ use emez
52	(antenatal or ante-natal or prenatal or pre-natal or f?etus or f?etal).tw.
53	or/50-52
54	49 and 53
55	Chorioamnionitis/ use ppez
56	exp chorioamnionitis/ use emez
57	(chorioamnioniti* or chorio-amnioniti* or amnioniti* or funisiti*).tw.
58	or/55-57
59	Fetal Growth Retardation/ use ppez
60	intrauterine growth retardation/ use emez
61	((f?etus or f?etal or intrauterine or intra-uterine) adj grow* adj (retard* or impair*)).tw.
62	or/59-61
63	Gestational Age/ use ppez
64	gestational age/ use emez
65	((f?etus or f?etal or gestation*) adj (age or matur*)).tw.
66	or/63-65
67	Birth Weight/ use ppez or exp Infant, Low Birth Weight/ use ppez
68	exp birth weight/ use emez
69	(birthweight or ((birth or newborn or neonat* or baby or babies or infant*) adj weight*)).tw.
70	or/67-69
71	Sex Characteristics/ use ppez or Sex Factors/ use ppez
72	sex difference/ use emez
73	(sex or sexes or gender* or male* or female* or boy* or girl*).tw.
74	or/71-73
75	exp Ethnic Groups/ use ppez
76	ethnicity/ use emez or ethnic group/ use emez
77	ethnic.tw.
78	or/75-77
79	exp Resuscitation/ use ppez and exp Parturition/ use ppez
80	resuscitation/ use emez and birth/ use emez
81	(resuscitat* and birth).tw.
82	or/79-81
83	exp Ventilators, Mechanical/ use ppez
84	exp ventilator/ use emez
85	ventilat*.tw.
86	or/83-85
87	exp Steroids/ use ppez and Postnatal Care/ use ppez
88	exp steroid/ use emez and exp postnatal care/ use emez
89	((postnatal or post-natal or postpartum or post-partum or perinatal or peri-natal or after birth) adj2 steroid*).tw.
90	or/87-89
91	Ductus Arteriosus, Patent/ use ppez
92	patent ductus arteriosus/ use emez
93	(paten* ductus arteriosus or PDA).tw.
94	or/91-93
95	exp Oxygen Inhalation Therapy/ use ppez
96	oxygen therapy/ use emez
97	oxygen*.tw.
98	or/95-97
99	exp Vitamin A/ use ppez
100	retinol/ use emez
101	(vitamin a or retinol).tw.
102	or/99-101
103	exp Systemic Inflammatory Response Syndrome/ use ppez
104	exp systemic inflammatory response syndrome/ use emez
105	(sepsis or septic?emia or systemic inflamma* or blood poison* or py?emia).tw.
106	or/103-105
107	exp Body Temperature Regulation/ use ppez
108	thermoregulation/ use emez
109	(thermoregulat* or thermo-regulat* or body temperature regulat* or heat regulat* or heat loss).tw.
110	or/107-109
111	Water-Electrolyte Balance/ use ppez
112	fluid balance/ use emez
113	((fluid* or water or hydrat*) adj2 (overload* or balance)).tw.
114	or/111-113
115	Milk, Human/ use ppez
116	breast milk/ use emez

#	Searches
117	((human or mother* or breast) adj milk).tw.
118	or/115-117
119	45 and (or/54,58,62,66,70,74,78,82,86,90,94,98,102,106,110,114,118)
120	44 or 119
121	37 and 120
122	limit 121 to english language
123	limit 122 to yr="1990 -Current"
124	Letter/ use ppez
125	letter.pt. or letter/ use emez
126	note.pt.
127	editorial.pt.
128	Editorial/ use ppez
129	News/ use ppez
130	exp Historical Article/ use ppez
131	Anecdotes as Topic/ use ppez
132	Comment/ use ppez
133	Case Report/ use ppez
134	case report/ or case study/ use emez
135	(letter or comment*).ti.
136	or/124-135
137	randomized controlled trial/ use ppez
138	randomized controlled trial/ use emez
139	random*.ti,ab.
140	or/137-139
141	136 not 140
142	animals/ not humans/ use ppez
143	animal/ not human/ use emez
144	nonhuman/ use emez
145	exp Animals, Laboratory/ use ppez
146	exp Animal Experimentation/ use ppez
147	exp Animal Experiment/ use emez
148	exp Experimental Animal/ use emez
149	exp Models, Animal/ use ppez
150	animal model/ use emez
151	exp Rodentia/ use ppez
152	exp Rodent/ use emez
153	(rat or rats or mouse or mice).ti.
154	or/141-153
155	123 not 154
156	remove duplicates from 155
149	exp Models, Animal/ use ppez
150	animal model/ use emez
151	exp Rodentia/ use ppez
152	exp Rodent/ use emez
153	(rat or rats or mouse or mice).ti.
154	or/141-153
155	123 not 154

1 Date of search: 29/06/2017

2 Database: The Cochrane Library, issue 6 of 12, June 2017

ID	Search
#1	MeSH descriptor: [Infant, Newborn] explode all trees
#2	(infan* or neonat* or newborn* or new-born* or baby or babies or preterm or pre-term or prematur* or pre-matur* or pre?mie* or premie or premies)
#3	((low adj3 birth near/3 weigh*) or (LBW or VLBW))
#4	MeSH descriptor: [Respiratory Distress Syndrome, Newborn] explode all trees
#5	MeSH descriptor: [Intensive Care, Neonatal] explode all trees
#6	MeSH descriptor: [Intensive Care Units, Neonatal] explode all trees
#7	(special care baby unit* or ((newborn or neonatal) near ICU*1) or (SCBU or NICU))
#8	{or #1-#7}
#9	MeSH descriptor: [Respiration, Artificial] explode all trees
#10	MeSH descriptor: [Intubation, Intratracheal] explode all trees
#11	MeSH descriptor: [Ventilators, Mechanical] explode all trees
#12	(ventilat* or respirator or respirators or intubat*)

ID	Search
#13	((respirat* or breath* or airway* or oxygen*) near/3 (support* or assist* or artificial or control* or oscillat* or pressure))
#14	nasal cannula
#15	{or #9-#14}
#16	#8 and #15
#17	MeSH descriptor: [Bronchopulmonary Dysplasia] explode all trees
#18	((bronch* or pulmon* or lung*) near/2 dysplasia*)
#19	((bronch* or pulmon* or lung*) near/2 hypoplas*)
#20	((chronic or long term) near lung disease)
#21	BPD
#22	{or #17-#21}
#23	#16 and #22
#24	MeSH descriptor: [Risk Factors] explode all trees
#25	MeSH descriptor: [Risk Assessment] explode all trees
#26	risk factor*
#27	{or #24-#26}
#28	#23 and #27

1 **Health economics**

2 Date of search: 29/06/2017

3 Database: Embase 1980 to 2017 Week 26, Ovid MEDLINE(R) Epub Ahead of Print, In-
4 Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)
5 1946 to Present

#	Searches
1	exp Infant, Newborn/ use ppez
2	newborn/ use emez
3	prematurity/ use emez
4	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw,nw.
5	(preterm or pre-term or prematur$ or pre-matur$ or pre?mie* or premie*1).tw.
6	exp low birth weight/ use emez
7	(low adj3 birth adj3 weigh$).tw.
8	(LBW or VLBW).tw.
9	exp Intensive Care, Neonatal/ use ppez
10	newborn intensive care/ use emez
11	exp Intensive Care Units, Neonatal/ use ppez
12	neonatal intensive care unit/ use emez
13	(special and care and baby and unit*).tw.
14	((newborn or neonatal) adj ICU*1).tw.
15	(SCBU or NICU).tw.
16	exp Respiratory Distress Syndrome, Newborn/ use ppez
17	neonatal respiratory distress syndrome/ use emez
18	or/1-17
19	exp Respiration, Artificial/ use ppez
20	exp Intubation, Intratracheal/ use ppez
21	exp artificial ventilation/ use emez
22	exp assisted ventilation/ use emez
23	exp Ventilators, Mechanical/ use ppez
24	exp ventilator/ use emez
25	(ventilat* or respirator or respirators or intubat*).tw.
26	((respirat* or breath* or airway* or oxygen*) adj3 (support* or assist* or artificial or control* or oscillat* or pressure)).tw.
27	nasal cannula.tw.
28	or/19-27
29	18 and 28
30	Bronchopulmonary Dysplasia/ use ppez
31	lung dysplasia/ use emez
32	((bronch* or pulmon* or lung*) adj2 dysplasia*).tw.
33	((bronch* or pulmon* or lung*) adj2 hypoplas*).tw.
34	((chronic or long term) adj lung disease).tw.
35	BPD.tw.
36	or/30-35
37	29 and 36
38	Risk Factors/ use ppez

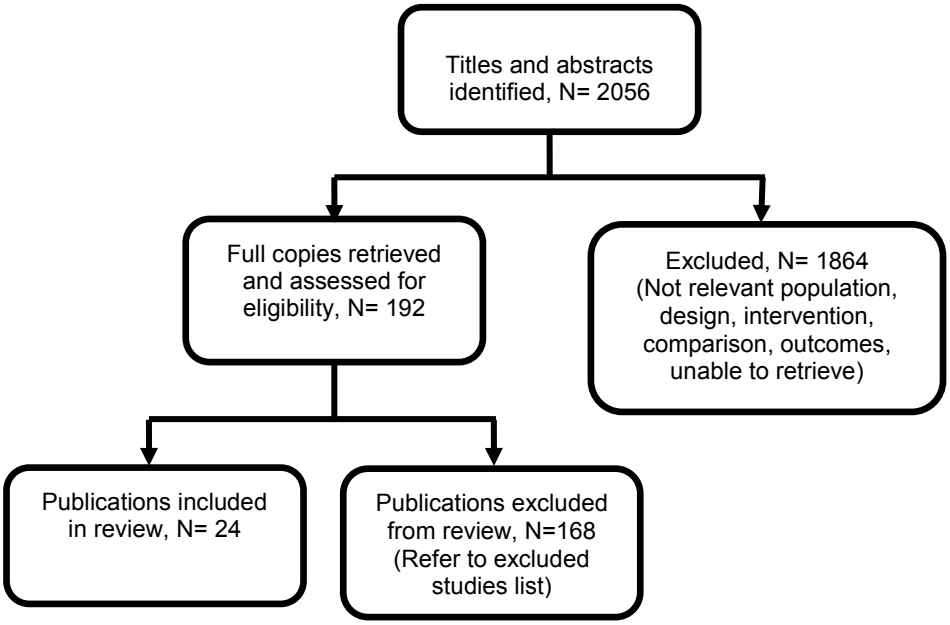
#	Searches
39	risk factor/ use emez
40	exp Risk Assessment/ use ppez
41	risk assessment/ use emez
42	exp Prognosis/ use ppez
43	prognos*.tw.
44	or/38-43
45	risk.tw.
46	exp Steroids/ use ppez
47	exp corticosteroid/ use emez
48	(steroid* or corticosteroid* or glucocortico*).tw.
49	or/46-48
50	Prenatal Exposure Delayed Effects/ use ppez
51	prenatal exposure/ use emez or prenatal drug exposure/ use emez
52	(antenatal or ante-natal or prenatal or pre-natal or f?etus or f?etal).tw.
53	or/50-52
54	49 and 53
55	Chorioamnionitis/ use ppez
56	exp chorioamnionitis/ use emez
57	(chorioamnioniti* or chorio-amnioniti* or amnioniti* or funisiti*).tw.
58	or/55-57
59	Fetal Growth Retardation/ use ppez
60	intrauterine growth retardation/ use emez
61	((f?etus or f?etal or intrauterine or intra-uterine) adj grow* adj (retard* or impair*)).tw.
62	or/59-61
63	Gestational Age/ use ppez
64	gestational age/ use emez
65	((f?etus or f?etal or gestation*) adj (age or matur*)).tw.
66	or/63-65
67	Birth Weight/ use ppez or exp Infant, Low Birth Weight/ use ppez
68	exp birth weight/ use emez
69	(birthweight or ((birth or newborn or neonat* or baby or babies or infant*) adj weight*)).tw.
70	or/67-69
71	Sex Characteristics/ use ppez or Sex Factors/ use ppez
72	sex difference/ use emez
73	(sex or sexes or gender* or male* or female* or boy* or girl*).tw.
74	or/71-73
75	exp Ethnic Groups/ use ppez
76	ethnicity/ use emez or ethnic group/ use emez
77	ethnic.tw.
78	or/75-77
79	exp Resuscitation/ use ppez and exp Parturition/ use ppez
80	resuscitation/ use emez and birth/ use emez
81	(resuscitat* and birth).tw.
82	or/79-81
83	exp Ventilators, Mechanical/ use ppez
84	exp ventilator/ use emez
85	ventilat*.tw.
86	or/83-85
87	exp Steroids/ use ppez and Postnatal Care/ use ppez
88	exp steroid/ use emez and exp postnatal care/ use emez
89	((postnatal or post-natal or postpartum or post-partum or perinatal or peri-natal or after birth) adj2 steroid*).tw.
90	or/87-89
91	Ductus Arteriosus, Patent/ use ppez
92	patent ductus arteriosus/ use emez
93	(paten* ductus arteriosus or PDA).tw.
94	or/91-93
95	exp Oxygen Inhalation Therapy/ use ppez
96	oxygen therapy/ use emez
97	oxygen*.tw.
98	or/95-97
99	exp Vitamin A/ use ppez
100	retinol/ use emez
101	(vitamin a or retinol).tw.
102	or/99-101
103	exp Systemic Inflammatory Response Syndrome/ use ppez
104	exp systemic inflammatory response syndrome/ use emez

#	Searches
105	(sepsis or septic?emia or systemic inflamma* or blood poison* or py?emia).tw.
106	or/103-105
107	exp Body Temperature Regulation/ use ppez
108	thermoregulation/ use emez
109	(thermoregulat* or thermo-regulat* or body temperature regulat* or heat regulat* or heat loss).tw.
110	or/107-109
111	Water-Electrolyte Balance/ use ppez
112	fluid balance/ use emez
113	((fluid* or water or hydrat*) adj2 (overload* or balance)).tw.
114	or/111-113
115	Milk, Human/ use ppez
116	breast milk/ use emez
117	((human or mother* or breast) adj milk).tw.
118	or/115-117
119	45 and (or/54,58,62,66,70,74,78,82,86,90,94,98,102,106,110,114,118)
120	44 or 119
121	37 and 120
122	limit 121 to english language
123	limit 122 to yr="1990 -Current"
124	Economics/
125	Value of life/
126	exp "Costs and Cost Analysis"/
127	exp Economics, Hospital/
128	exp Economics, Medical/
129	Economics, Nursing/
130	Economics, Pharmaceutical/
131	exp "Fees and Charges"/
132	exp Budgets/
133	or/124-132 use ppez
134	health economics/
135	exp economic evaluation/
136	exp health care cost/
137	exp fee/
138	budget/
139	funding/
140	or/134-139 use emez
141	budget*.ti,ab.
142	cost*.ti.
143	(economic* or pharmaco?economic*).ti.
144	(price* or pricing*).ti,ab.
145	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
146	(financ* or fee or fees).ti,ab.
147	(value adj2 (money or monetary)).ti,ab.
148	or/141-146
149	133 or 140 or 148
150	123 and 149

1

Appendix C – Clinical evidence study selection

Clinical evidence study selection for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?



Appendix D – Clinical evidence tables

Clinical evidence tables for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Full citation Chawla, S., Natarajan, G., Shankaran, S., Pappas, A., Stoll, B. J., Carlo, W. A., Saha, S., Das, A., Laptook, A. R., Higgins, R. D., National Institute of Child, Health, Human Development Neonatal Research, Network, Association of Neurodevelopmental Outcomes and Neonatal Morbidities of Extremely Premature Infants With Differential Exposure to Antenatal Steroids, JAMA Pediatrics, 170, 1164-1172, 2016 **Ref Id**	**Sample size** n=4284 neonates with <28 weeks gestational age eligible for follow-up (did not die, weights not greater than 1000g, gestational age not more than 26 weeks, and not outborn) n=3892 follow-up data available (90.8%) and classified into 3 groups: 1) Received no ANS, n=432 2) Received partial ANS course, n=994 3) Received complete ANS course, n=2466 **Characteristics** **<u>Maternal characteristics:</u>** **Race/ethnicity:** White (47.3% to 55%), African American (39.8% to 47.9%), other (4.8% to 5.6%) across the 3 groups	**Limitations** **Other information**	**Factors** Antenatal steroids (ANS) use: No ANS Partial ANS Complete ANS	**Methodology** **Setting** Extremely preterm infants born in 16 centres of the National Institute of Child Health and Human Development Research Network. Neonatal data obtained from the Generic database registry of the research network, outcomes done prospectively. **Definition of risk factor** No ANS; partial ANS (1 dose of betamethasone or less than 4 doses of dexamethasone); complete ANS (2 doses of betamethasone or 4 doses of dexamethasone) **Definition of outcome** Bronchopulmonary dysplasia defined as need	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** <u>Adjusted OR (95% CI)</u> Partial vs no ANS: 1.02 (0.79-1.31) Complete vs no ANS: 0.93 (0.74 to 1.17) Complete vs partial ANS: 0.92 (0.78 to 1.07)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Moderate risk of bias. 90.8% follow-up rate stated in the text and patient flow chart for death and neurodevelopmental outcome data, although for the BPD outcome a different follow-up number is documented (n=4,319) with no further elaboration reported. **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
674754 **Country/ies where the study was carried out** USA **Study type** Prospective multicentre observational study (secondary analysis) **Aim of the study** To compare rates of neonatal morbidities and 18- to 22- month neurodevelopmental outcomes of premature infants <28 weeks gestational age exposed to no antenatal steroids (ANS) or partial or complete courses of ANS. **Study dates**	**Hypertensive disorder of pregnancy**: 17.2% to 22.1% across the 3 groups **Chorioamnionitis:** clinical (12.7% to 22.9%), histologic (47.4% to 56.8%) across the 3 groups **ROP > 18 hours:** 12.5% to 35% across the 3 groups **Cesarean delivery:** 51.9% to 64.8% across the 3 groups **Neonatal characteristics:** **Birth weight, mean (SD), g:** 725 (169) to 760 (173) across the 3 groups **Gestational age, mean (SD), wk:** 24.5 (1.4) 25.1 (1.1) across the 3 groups **Male sex:** 51.4% to 52.4% across the 3 groups **Resus at birth:** 78.8% to 90.1% across the 3 groups **SGA at birth:** 4.6% to 7.6% across the 3 groups **Incidence of BPD:** 54.4% **Inclusion criteria**			for supplemental oxygen at 36 weeks PMA **Statistical methods** Outcome variables were compared among study groups using the X^2 test for categorical variables, analysis of variables for continuous normally distributed variables, and Kruskal-Wallis test for continuous skewed variables. Logistic regression analysis was performed to assess the association between ANS and outcomes, after controlling for GA, sex, race/ethnicity, maternal health insurance, and participating centre. Statistical significance was set at $p<0.05$.		appropriately defined and measured. **Study confounding:** Low risk of bias. Models adjusted for appropriate factors: GA, sex, race/ethnicity, maternal health insurance, and participating centre **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
January 2006 to December 2011. Data were analysed between October 2013 and May 2016 **Source of funding** Eunice Kennedy Shriver NICHHD.	All neonates born with a birth weight of 401 to 1000g and/or a GA of 22 weeks to 27 weeks as determined by early ultrasonography or last menstrual period were included. **Exclusion criteria** Infants who died within 12 hours of birth without aggressive neonatal care were excluded					
Full citation Costeloe,K.L., Hennessy,E.M., Haider,S., Stacey,F., Marlow,N., Draper,E.S., Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies),	**Sample size** Sample recruited n= 666 EPICure admissions to NICU n=1115 EPICure 2 admissions to NICU Sample analysed after exclusions n=266 survivors in EPICure n=593 survivors in EPICure 2 **Characteristics**	**Limitations** **Other information**	**Factors** Gestational age (per week) Birth weight (per SD) Sex Thermoregulation	**Methodology** **Setting** Population based study in 182 maternity units in England **Method of measurement for risk factor** Prospective collection of data on neonatal course and perinatal variables for study participants **Definition of outcome**	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Gestational age (per week): 0.62 (0.45-0.85) Birth weight (per SD): 0.69 (0.52-0.91)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias, all attrition accounted for. **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
BMJ, 345, e7976-, 2012 **Ref Id** 350534 **Country/ies where the study was carried out** England **Study type** Prospective national cohort study **Aim of the study** To determine survival and neonatal morbidity for babies born between 22 and 26 weeks gestation in England during 2006, and to evaluate changes in outcome since 1995 for babies born between 22 and 25 weeks gestation	**Maternal characteristics:** **Race/ethnicity:** White (74% and 65% in EPICure and EPICure 2, respectively), Afro-Caribbean (16% and 19% in EPICure and EPICure 2, respectively), Indian subcontinent (7% and 11% in EPICure and EPICure 2, respectively), other (2% and 3% in EPICure and EPICure 2, respectively) **Pre-eclampsia**: 3% and 5% in EPICure and EPICure 2, respectively **Chorioamnionitis:** clinical 19% and 23% in EPICure and EPICure 2, respectively **ROP > 24 hours:** 24% and 27% in EPICure and EPICure 2, respectively **Cesarean delivery:** 18% and 20% in EPICure and EPICure 2, respectively **Any antenatal steroid:** 68% and 82% in EPICure and EPICure 2, respectively **Neonatal characteristics:** **Birth weight, median (IQR), g:** 695 (620-787)			Bronchopulmonary dysplasia defined as need for supplemental oxygen at 36 weeks PMA **Statistical methods** Logistic, linear, and centile regressions, respectively, to investigate the effect of gestational age (in decimal weeks). For each week of gestation, we report exact 95% binomial confidence intervals of percentages and percentage differences. In the prediction models we used interaction terms to test whether the associations of variables with outcomes were different in the two cohorts. Any unexplained differences between 1995 and 2006 were tested using "cohort" as a variable, thus cohort is included in all the models. We used multivariable logistic regression with a manual forward stepwise	Male vs female: 2.08 (1.48 to 2.91) Admission temperature ≥35 degrees Celsius vs admission temperature <35 degrees Celsius: 0.57 (0.33 to 0.98)	**Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Moderate risk of bias. Multivariate models used to adjust for statistically significant confounders between the 2 cohorts (not clearly reported). Babies born with congenital malformations (unspecified) included in both cohorts, not excluded from review as uncertainty as whether it is PDA or not. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Study dates 1st March 1995 to 31st December for 1995 cohort (EPICure) The whole year of 2006 for the 2006 cohort (EPICure 2) **Source of funding** Medical Research Council (G0401525).	AND 697 (610-779) in EPICure and EPICure 2, respectively **Male sex:** 54% and 52% in EPICure and EPICure 2, respectively **NEC:** 3% and 12% in EPICure and EPICure 2, respectively **Infection:** 8% and 16% in EPICure and EPICure 2, respectively **Congenital malformation:** 2% and 1% in EPICure and EPICure 2, respectively **Surfactant at any time:** 86% and 99% in EPICure and EPICure 2, respectively **Incidence of BPD:** 96.6% **Inclusion criteria** All preterm births reported between 22 and 26 weeks gestation, or more immature but with a birth weight over 400g. **Exclusion criteria**			procedure with replacement Stat statistical software was used for all analyses and Kaplan Meier survival curves. No allowance was made for multiple tests, significance was set at p ≤0.05		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Births to mothers not usually resident in England were excluded					
Full citation Dargaville, P. A., Gerber, A., Johansson, S., De Paoli, A. G., Kamlin, C. O. F., Orsini, F., Davis, P. G., Incidence and outcome of CPAP failure in preterm infants, Pediatrics, 138 (1) (no pagination), 2016 **Ref Id** 653603 **Country/ies where the study was carried out** Australia and New Zealand **Study type**	**Sample size** n=19,103 infants born at 25-32 weeks included in the analysis n= 11,684 infants born at 25-32 weeks managed with CPAP initially (n=1989 and n=9695 for 25-28 weeks and 29-32 weeks, respectively) n= 7,419 infants born at 25-32 weeks intubated (n=4782 and n=2637 for 25-28 weeks and 29-32 weeks, respectively) **Characteristics** Characteristics only given for CPAP cohort and not for intubated cohort Incidence of BPD: characteristics only given for CPAP cohort and not for intubated cohort	**Limitations** **Other information**	**Factors** Invasive ventilation	**Methodology** **Setting** For the calendar years 2007-2013, preterm babies born at 25-32 completed weeks gestation who were born in a tertiary centre or colocated private facility, and were admitted to a level III NICU within 60 min after birth in Australia and New Zealand **Method of measurement for risk factor** Invasive ventilation defined as intubated primarily (either in the delivery room or shortly after arrival at the NICU). CPAP defined as receiving a trial of at least 30 min duration. Infants managed on CPAP were further divided into those	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (99% CI) *25-28 weeks gestational age* Intubation vs CPAP: 1.30 (1.09-1.54) *29-32 weeks gestational age* Intubation vs CPAP: 1.57 (1.23-1.99)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias, all attrition accounted for. **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Multivariate models used to adjust for statistically significant confounders: gestation, birth weight <10th percentile, sex, mode of

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Prospective population-based cohort study **Aim of the study** 1. To examine the incidence and timing of CPAP failure. 2. To compare neonatal outcomes within the CPAP failure group with those infants succeeding on CPAP. 3. To compare resource consumption between the 2 groups **Study dates** 2007-2013 **Source of funding** Supported by grants from the Royal Hobart Hospital Foundation and the Australian National Health and	**Inclusion criteria** Preterm infants born at 25 to 32 completed weeks gestation who were inborn in a tertiary centre or colocated private facility and required respiratory support, and were admitted to a level III NICU within 60 min after birth. **Exclusion criteria** Outborn infants, in whom respiratory management might have been affected or dictated by the needs of safe retrieval, were not included in the study population. Further exclusions were of infants with: 1. A congenital anomaly likely to affect respiratory function or early management			whom CPAP was successfully applied, and those for whom CPAP failed and intubation was required within 72 hours of birth **Definition of outcome** Bronchopulmonary dysplasia defined as need for respiratory support and/or supplemental oxygen at 36 weeks PMA **Statistical methods** Logistic regression models were used to further investigate the impact of CPAP failure on adverse outcomes during hospitalisation, adjusted by demographic and clinical factors, including gestation, birth weight <10th percentile, sex, mode of delivery (vaginal birth or cesarean delivery), plurality (singleton/multiple), antenatal glucocorticoid exposure (incomplete versus complete), and 5-		delivery, plurality, ANSM and 5-min apgar score. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Medical Research Council	2. Prolonged premature rupture of membranes (>14 days) 3. No requirement for respiratory support in the first 24 hours, and 4. Insufficient information regarding early respiratory management			min apgar score. Adjusted odds ratios were derived to describe the association of CPAP failure with adverse outcomes, comparing with both the CPAP-S group, and those intubated primarily. The intubated and CPAP groups were also compared. Given that the dataset is representative of an entire population, we set the probability of a type I error at 0.01.		
Full citation de Waal, C. G., Weisglas-Kuperus, N., van Goudoever, J. B., Walther, F. J., Mortality, neonatal morbidity and two year follow-up of extremely preterm infants born in the Netherlands in 2007, PLoS ONE, 7 (7) (no pagination), 2012	**Sample size** n= 276 preterm infants 23-26 weeks were eligible for follow-up n= 144 follow-up data available (52%, accounted for as deaths in delivery or NICU before discharge) 23 weeks: n=56 24 weeks: n=55 25 weeks: n=104 26 weeks: n=130	**Limitations** **Other information**	**Factors** Gestational age Birth weight	**Methodology** **Setting** The PRospective Evaluation of perinatal management of extremely PREterm infants (Pre-Pre) study is a population-based cohort study in the Netherlands on the outcome of preterm infants with <28 weeks gestational age. All 10 Dutch perinatal centres	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Higher gestational age category vs lower gestational age	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias, all attrition accounted for. **Prognostic factor measurement:** Low risk of bias. Risk factors

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Ref Id 674802 **Country/ies where the study was carried out** Netherlands **Study type** Prospective population-based cohort study **Aim of the study** Evaluate neonatal mortality, morbidity, and long-term disabilities of infants born before 27 weeks of gestation in the Netherlands **Study dates** 2007 **Source of funding**	**Characteristics** **Maternal characteristics:** **ANS:** 0% to 49.2% across the 4 groups **PPROM:** 10.7% to 27.3% across the 4 groups **Cesarean delivery:** 0% to 49.2% across the 4 groups **Neonatal characteristics:** **Birth weight, mean (SD), g:** 545 (156) to 851 (195) across the 4 groups **Female sex:** 38.2% to 51% across the 4 groups **SGA at birth:** 10.6% to 18.2% across the 4 groups **Incidence of BPD:** 24.3% **Inclusion criteria** All infants born at gestational age of 23 0/7 to 26 6/7 weeks in the Netherlands in 2007. Both stillborn and live infants were included. **Exclusion criteria**			collected data on every infants born at 23 to 27 weeks of gestation in 2007. **Method of measurement for risk factor** Gestational age categories: 24, 25, 26, and 27 weeks Birth weight categories: ≤500g, 501-750g, 751-1000g, and >1000g **Definition of outcome** Bronchopulmonary dysplasia defined as need for supplemental oxygen at 36 weeks PMA **Statistical methods** Statistical analyses were performed with SPSS version 17. Odds ratio and 95% CI were calculated by logistic regression analysis included gestational age, birth weight categories, gender, caesarean section, antenatal steroids and Dutch nationality as	category: 1.011 (0.365-2.801) Higher birth weight category vs lower birth weight category (≤500g, 501-750g, 751-1000g, >1000g): 0.437 (0.216-0.883)	appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Multivariate models used to adjust for statistically significant confounders: gestational age, birth weight, gender, cesarean section, antenatal steroids, Dutch nationality. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
None reported	Not specified			independent factors. Groups were compared with x^2 or Mann-Whitney test. P values <0.05 were considered statistically significant.		
Full citation Edstedt Bonamy, A. K., Gudmundsdottir, A., Maier, R. F., Toome, L., Zeitlin, J., Bonet, M., Fenton, A., Hasselager, A. B., Van Heijst, A., Gortner, L., Milligan, D., Van Reempts, P., Boyle, E. M., Norman, M., Patent Ductus Arteriosus Treatment in Very Preterm Infants: A European Population-Based Cohort Study (EPICE) on Variation and Outcomes, Neonatology, 111, 367-375, 2017 **Ref Id**	**Sample size** n= 7,637 infants ≤31 weeks admitted to NICU n=6,896 infants included in analyses (n=232 died <24 hrs, n=431 units with missing info, n=78 infants with missing info) n=6, 262 follow up data available (90.8%) and classified into 3 groups: Low PDA treatment proportion: n=2.645 (UK included) Medium PDA treatment proportion: n=3,087 High PDA treatment proportion: n=530 **Characteristics** **Maternal characteristics:**	**Limitations** **Other information**	**Factors** Patent ductus arteriosus (PDA): 1. Pharmacologically treated PDA 2. PDA surgery after pharmacological treatment 3. PDA surgery without prior pharmacological treatment	**Methodology** **Setting** The Effective Perinatal Intensive Care in Europe (EPICE) cohort study was a population-based study of all births between 22 + 0 and 31 + 6 weeks of gestation in 19 regions across 11 European countries conducted in 2011 and 2012. **Method of measurement for risk factor** PDA treatment was defined as any non-steroidal anti-inflammatory (NSAID) treatment (ibuprofen or indomethacin) or surgery to close the PDA. Surgical treatment was	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted RR (95% CI) *Low PDA treatment proportion* No PDA treatment (ref): 1 Pharma tx only: 1.41 (1.09-1.82) PDA surgery after pharma tx: 1.63 (1.00-2.65) PDA surgery without prior pharmacological treatment: 1.97 (1.51-2.56)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Medium risk of bias, although attrition low, not accounted for **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Generalised linear mixed model

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
674827 **Country/ies where the study was carried out** Europe **Study type** Prospective population-based cohort study **Aim of the study** Study regional variations in patent ductus arteriosus (PDA) treatment in preterm infants (≤31 weeks of gestation), its relation to differences in perinatal characteristics, and associations with BPD and survival without major neonatal morbidity	**ANS:** 89% (No PDA tx); 85.5% (Pharma PDA tx); 85% (Pharma PDA tx + surgery); 82.5% (No pharma tx + surgery) **PPROM:** 25.5% (No PDA tx); 20.1% (Pharma PDA tx); 25.4% (Pharma PDA tx + surgery); 20% (No pharma tx + surgery) **Cesarean delivery:** 67.8% (No PDA tx); 65.8% (Pharma PDA tx); 52.3% (Pharma PDA tx + surgery); 62.5% (No pharma tx + surgery) **Neonatal characteristics:** **Birth weight, mean (SD), g:** 1,285 (1,010-1,555) [No PDA tx]; 930 (750-1,144) [Pharma PDA tx]; 790 (690-950) [Pharma PDA tx + surgery]; 777.5 (650-990) [No pharma tx + surgery] **Gestational age, mean (SD), wk:** 30 (28.4-31.1) [No PDA tx]; 27.4 (25.9-28.9) [Pharma PDA tx]; 26.0 (24.9-27.1) [Pharma PDA tx + surgery];			categorized as either primary surgery or surgery following prior medical treatment. Diagnosis of PDA was based on clinical and/or echographic assessment. **Definition of outcome** Bronchopulmonary dysplasia defined as need for supplemental oxygen at 36 weeks PMA **Statistical methods** Differences between groups were tested using the Krukskal-Wallis test for continuous data, and x^2 test for proportions. Associations between co-variates and risk of PDA treatment were analysed in mixed-effects generalised linear regression models adjusted for GA and with the neonatal unit as the random effect variable and reported as risk ratios (RR) with 95% CI	*Medium PDA treatment proportion* No PDA treatment (ref): 1 Pharma tx only: 1.63 (1.22-2.18) PDA surgery after pharma tx: 2.57 (1.76-3.74) PDA surgery without prior pharmacological treatment: 2.90 (1.76-4.77) *High PDA treatment proportion* No PDA treatment (ref): 1 Pharma tx only: 2.54 (1.48-4.38) PDA surgery after pharma tx: 3.73 (1.69-8.22) PDA surgery without prior pharmacological treatment: 3.79 (1.62-8.89)	adjusted for propensity score for PDA treatment. The propensity score for PDA treatment was estimated from presence of preeclampsia, spontaneous onset of labour, PPROM, maternal infection as indication for delivery, ANS, mode of delivery, gestational age, birth weight, infant sex, SGA, and use of invasive ventilation on first day of life **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Medium **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Study dates 2011-2012 **Source of funding** European Union's Seventh Framework Programme; the Swedish Heart and Lung Foundation; Stockhold county council; and the Department of Neonatal Medicine, Korolinska University Hospital	26.1 (25-28.7) [No pharma tx + surgery] **Male sex:** 53.8% (No PDA tx); 52.9% (Pharma PDA tx); 58% (Pharma PDA tx + surgery); 62.5% (No pharma tx + surgery) **SGA at birth:** 20.8% (No PDA tx); 21.2% (Pharma PDA tx); 17.1% (Pharma PDA tx + surgery); 28.8% (No pharma tx + surgery) Incidence of BPD: 10.8% (No PDA treatment), 31.8% (pharmacological PDA treatment), 64.8% (Pharmacological PDA treatment + PDA surgery), 64.3 (PDA surgery without prior pharmacological treatment) **Inclusion criteria** The Effective Perinatal Intensive Care in Europe (EPICE) cohort study was a population-based study of all births between 22 + 0 and 31 + 6 weeks of gestation in 19 regions			Differences in perinatal characteristics between the regions were explored by calculating a propensity score for PDA treatment for each subject. The propensity score was calculated by fitting a logit model using the pscore command in STATA including the covariates in online supplementary table. Clustering of data was handled using a mixed-effects generalised linear regression model. In supplementary analyses of the association between PDA treatment and BPD in survivors, the results were further adjusted for the total duration of invasive ventilation and number of confirmed septicaemias. All data was analysed in STATA		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	across 11 European countries. Inclusions occurred over 12 months except in France (6 months). Infants who survived ≥24 h after birth were included. **Exclusion criteria** Not reported					
Full citation El Ayoubi, M., Jarreau, P. H., Van Reempts, P., Cuttini, M., Kaminski, M., Zeitlin, J., Does the antenatal detection of fetal growth restriction (FGR) have a prognostic value for mortality and short-term morbidity for very preterm infants? Results from the MOSAIC cohort, Journal of Maternal-Fetal and Neonatal	**Sample size** n=4,585 live births 24-31 weeks GA n=728 preterm babies with FGR detected antenatally eligible for follow-up n=3857 preterm babies with no FGR detected antenatally eligible for follow-up n=133 preterm babies with FGR detected antenatally followed-up for BPD (22.7%) n=484 preterm babies with no FGR detected antenatally followed-up for BPD (14.8%)	**Limitations** **Other information**	**Factors** Antenatal detection of FGR	**Methodology** **Setting** The data came from the MOSAIC study, a European population-based study of preterm infants with gestational age 28-31^{+6} weeks in 10 regions in nine European countries in 2003. Regions included: Hesse in Germany, Flanders in Belgium, the eastern region of Denmark, Ile-de-France, Lazio in Italy, east central Netherlands, the Wielkopolska, and Lubuskie regions in	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Antenatal detection of FGR vs no antenatal detection of FGR: 1.2 (0.7-1.4)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Medium risk of bias, no explanation or flow chart for the attrition between babies eligible for follow-up and those analysed **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Medicine, 29, 596-601, 2016 **Ref Id** 674831 **Country/ies where the study was carried out** European **Study type** Prospective population-based cohort study **Aim of the study** The impact of antenatal diagnosis of fetal growth restriction (FGR) on the risks of mortality and morbidity for preterm infants with gestational age 28-31^{+6} weeks given actual birthweight percentiles	**Characteristics** **Maternal characteristics:** **ANS:** 89% (No PDA tx); 85.5% (Pharma PDA tx); 85% (Pharma PDA tx + surgery); 82.5% (No pharma tx + surgery) **PPROM:** 25.5% (No PDA tx); 20.1% (Pharma PDA tx); 25.4% (Pharma PDA tx + surgery); 20% (No pharma tx + surgery) **Cesarean delivery:** 67.8% (No PDA tx); 65.8% (Pharma PDA tx); 52.3% (Pharma PDA tx + surgery); 62.5% (No pharma tx + surgery) **Neonatal characteristics:** **Birth weight, mean (SD), g:** 1,285 (1,010-1,555) [No PDA tx]; 930 (750-1,144) [Pharma PDA tx]; 790 (690-950) [Pharma PDA tx + surgery]; 777.5 (650-990) [No pharma tx + surgery] **Gestational age, mean (SD), wk:** 30 (28.4-			Poland, the northern region of Portugal and the Northern and Trent regions in the UK. **Method of measurement for risk factor** Antenatal diagnosis or suspicion of FGR mentioned in obstetric medical charts and postnatal birthweight percentile. Suspicion of FGR was noted by investigators when there was a mention of FGR in medical charts. In the MOSAIC regions, monitoring of FGR involves assessment of estimated fetal weight or other biometric measurements and carrying out additional ultrasounds with Doppler measurements to assess growth among fetuses suspected to be FGR. In our study, further details were not available on ultrasounds or Doppler velocimetry.		**Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Adjusted in 2 separate analyses: first analysis adjusted for GA, sex, type of pregnancy, BW ratio, pregnancy complications and regions; second analysis adjusted for corticosteroids and maternity level III additionally. **Statistical analysis and reporting:** Medium risk of bias. Specific details around methods used for the statistical analyses are lacking. **Overall risk of bias:** Medium **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Study dates 2003 **Source of funding** Not reported	31.1) [No PDA tx]; 27.4 (25.9-28.9) [Pharma PDA tx]; 26.0 (24.9-27.1) [Pharma PDA tx + surgery]; 26.1 (25-28.7) [No pharma tx + surgery] **Male sex:** 53.8% (No PDA tx); 52.9% (Pharma PDA tx); 58% (Pharma PDA tx + surgery); 62.5% (No pharma tx + surgery) **SGA at birth:** 20.8% (No PDA tx); 21.2% (Pharma PDA tx); 17.1% (Pharma PDA tx + surgery); 28.8% (No pharma tx + surgery) **Incidence of BPD:** 16% **Inclusion criteria** All live births between 24 and 31 weeks were included. **Exclusion criteria** Infants born at 22 and 23 weeks were excluded because survival before 24 weeks of GA was rare and			**Definition of outcome** Bronchopulmonary dysplasia defined as need for supplemental oxygen at 36 weeks PMA **Statistical methods** We used logistic regression to model the impact of detected FGR on short-term outcome overall and by birthweight percentile on class. We selected covariates for our models because of their hypothesised relationships to suspicion of FGR during pregnancy and outcomes. We ran two multivariable models to assess the relationship of antenatal detection of FGR on each outcome. The first model included GA, sex, type of pregnancy, birthweight ratio, pregnancy complications and region, while the second was further adjusted for antenatal corticosteroids		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	there were differences in practices of active management of these births between MOSAIC regions. We also excluded all births with congenital anomalies, since these are often associated with FGR, and triple of higher order pregnancies, because of specific growth problems in these multi-fetal pregnancies. Stillbirths were not included in our study because our main research question was whether detection of growth restriction had a prognostic value for in hospital mortality and morbidity after live birth.			and level of care at the maternity unit. All analysed were stratified for birthweight percentile class to identify how FGR affected prognosis in infants by SGA status at birth. We used 3 classes (<10th percentile, 10-24th percentile, ≥25th percentile) because babies above the 10th percentile of birthweight curves have been found to be at risk in previous studies. Statistical analyses were carried out using STATA version 11		
Full citation Farstad, T., Bratlid, D., Medbo, S., Markestad, T., Norwegian Extreme Prematurity Study, Group, Bronchopulmonary	**Sample size** n=462 infants admitted to the NICU n=377 infants eligible for follow up (after accounting for deaths and infants with GA >30 weeks): n=53 no BPD	**Limitations** **Other information**	**Factors** Sex Maternal infection Surfactant Invasive ventilation Treated PDA Postnatal steroids	**Methodology** **Setting** National cohort of preterm infants who survived beyond 28 days in Norway admitted to a NICU with a GA of 22-27	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** low risk of bias, flow chart for the

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
dysplasia - prevalence, severity and predictive factors in a national cohort of extremely premature infants, Acta PaediatricaActa Paediatr, 100, 53-8, 2011 **Ref Id** 674846 **Country/ies where the study was carried out** Norway **Study type** Prospective multicentre observational study **Aim of the study** To study prevalence and predictive factors of BPD in a cohort of preterm infants with a high incidence of	n=154 mild BPD n=95 moderate BPD n=75 severe BPD **Characteristics** **Maternal characteristics:** **ANS:** 86.5% (No BPD); 89% (Mild BPD); 89.1% (Moderate BPD); 89.1% (Severe BPD) **Neonatal characteristics:** **Birth weight, mean (SD), g:** 896 (138) [No BPD]; 904 (175) [Mild BPD]; 829 (150) [Moderate BPD]; 744 (182) [Severe BPD] **Gestational age, mean (SD), wk:** 28.1 (1.2) [No BPD]; 26.4 (1.2) [Mild BPD]; 26.1 (1.5) [Moderate BPD]; 25.7 (1.7) [Severe BPD] **Male sex:** 43.4% (No BPD); 48.1% (Mild BPD); 58.9% (Moderate BPD); 70.7% (Severe BPD) **Surfactant:** 52% (No BPD); 80.6% (Mild BPD); 91%			completed weeks between 1999 and 2000 **Method of measurement for risk factor** Maternal infection was registered in women who had clinical signs of amnionitis, urinary tract infection, other significant infection or CRP elevated at delivery, with or without positive cultures (exclude) Treatment of PDA was defined as treatment with fluid restriction, indomethacin, and/or surgical ligation after echocardiographic diagnosis of PDA Treatment with postnatal steroids was defined as treatment with systemic dexamethasone for lung disease Postnatal infection was defined as a positive blood culture or a diagnosis by the attending physician of clinical sepsis or organ specific infection in infants with relevant	Female vs male: 0.5 (0.28-0.92) Any surfactant treatment vs no surfactant treatment: 2.56 (1.00-6.58) Ventilator at 24 h vs no ventilator at 24 h: 0.86 (0.41-1.82) Treated PDA vs no treated PDA: 2.20 (1.05-4.63) Postnatal steroids vs no postnatal steroids: 2.50 (1.22-5.11)	attrition between babies eligible for follow-up and those analysed **Prognostic factor measurement:** medium risk of bias. Not all risk factors appropriately defined and measured, i.e. surfactant definition not mentioned and unclear whether ventilation included invasive ventilation and CPAP or invasive ventilation alone **Outcome measurement:** medium risk of bias. Timeframe for outcome measures not appropriately defined and measured. **Study confounding:** medium risk of bias. Multivariate analysis adjusted for confounders, however not clearly stated whether all statistically significant confounders are adjusted for in the analysis. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** High

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
prenatal steroid and surfactant treatment **Study dates** 1st of January 1999 - 31st December 2000 **Source of funding** Not reported	(Moderate BPD); 97.3% (Severe BPD) **PDA treated:** 0% (No BPD); 20.8% (Mild BPD); 42.1% (Moderate BPD); 36% (Severe BPD) **Incidence of BPD:** 45.1% **Inclusion criteria** All stillbirths and live births in Norway with a GA of 22 + 0 to 27 + 6 with a birth weight of 500-999g were included. **Exclusion criteria** Not reported			clinical symptoms, elevated CRP, leukopenia, thrombocytopenia, or similar Ventilatory support (invasive ventilation or CPAP) was registered at 24h and at 7 and 14 days of life Surfactant treatment undefined **Definition of outcome** Bronchopulmonary dysplasia defined according to accepted criteria (no timeframe) **Statistical methods** SPSS statistical package version 15 and minitab 15 were used for statistical analysis. Differences between groups were studies by two-tailed analysis. Chi-square test or Fisher exact test was used for categorical data when appropriate. Continuous data were analysed with Student t-		**Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				test. Univariate and multivariate regression analyses were performed to identify statistical associations between potential peri- and neonatal risk factors and the development of BPD. Statistical significance was considered with a p value of <0.05.		
Full citation Figueras-Aloy, J., Serrano, M. M., Rodriguez, J. P., Perez, C. F., Serradilla, V. R., Jimenez, J. Q., Gonzalez, R. J., S. E. N. Spanish Neonatal Network, Antenatal glucocorticoid treatment decreases mortality and chronic lung disease in survivors among 23- to 28-week gestational age preterm infants, American Journal of	**Sample size** n=2448 preterm infants 23-28 wks eligible for follow-up: n=1310 complete AGT n=460 partial AGT n=678 no AGT n=1,537 preterm infants 23-28 weeks analysed (attrition due to mortality or duration of oxygen supplementation unknown): n=968 complete AGT n=264 partial AGT n=305 no AGT **Characteristics** **Maternal characteristics:**	**Limitations** **Other information**	**Factors** Antenatal steroid Invasive ventilation >5 day IUGR Resus	**Methodology** **Setting** Prospective, observational study carried out in 63 neonatal centres that subscribe to the SEN1500 Spanish Neonatal Network. **Method of measurement for risk factor** Antenatal steroid treatment was administered as 2 I.M 12-mg betamethasone doses to the mother 24 hours apart. Partial antenatal steroid treatment defined	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA) in complete course of AGT cohort** Adjusted OR (95% CI) Complete course of AGT vs no course of AGT: 0.63 (0.45-0.89) Invasive ventilation >5 d vs no invasive	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** medium risk of bias, attrition between infants followed up and analysed in the regression model not accounted for **Prognostic factor measurement:** medium risk of bias. Not all risk factors appropriately defined and measured, i.e.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Perinatology, 22, 441-8, 2005 **Ref Id** 674850 **Country/ies where the study was carried out** Spain **Study type** Prospective, multicentre observation study **Aim of the study** To determine if antenatal glucocorticoid treatment reduces the likelihood of mortality and chronic lung disease in survivors **Study dates** 2002-2003	**IUGR:** 14.2% (complete AGT); 10.6% (Partial AGT); 10.2% (No AGT) **PROM >24h:** 37.6% (complete AGT); 15.8% (Partial AGT); 9.6% (No AGT) **Cesarean delivery:** 64.4% (complete AGT); 56.1% (Partial AGT); 53.1% (No AGT) **Neonatal characteristics:** **Birth weight, mean, g:** 964 (complete AGT); 950 (Partial AGT); 946 (No AGT) **Gestational age, mean (SD), wk:** 27.3 (1.11) [complete AGT]; 26.9 (1.31) [Partial AGT]; 26.8 (1.42) [No AGT] **Male sex:** 49.6% (complete AGT); 48.9% (Partial AGT); 53.1% (No AGT) **Incidence of BPD:** 22.9% **Inclusion criteria** All liveborn preterm infants from 23 weeks 0 days to 28			as so if delivery occurred less than 24 hours after the first dose of corticosteroids or more than 1 week after the last dose of corticosteroids. Complete antenatal steroid treatment was defined as so if delivery occurred more than 24 hours and less than 1 week after a dose of corticosteroid. IUGR defined as below the 10th percentile Other risk factors not defined **Definition of outcome** Chronic lung disease was defined as need for supplementary oxygen at 36 weeks PMA to maintain oxygen saturations 88-93% **Statistical methods** Univariate analyses were performed with maternal and neonatal demographics data stratified according to	ventilation at >5 d: 4.55 (3.24-6.39) IUGR vs no IUGR: 2.90 (1.97-4.28) Resus vs no resus: 1.61 (1.16-2.22)	mechanical ventilation and resus **Outcome measurement:** low risk of bias, outcome measures appropriately defined and measured. **Study confounding:** medium risk of bias. Multivariate analysis adjusted for statistically significant confounders: antibiotic mother, GA, birthweight, IUGR, resus, apgar score, CRIB score, RDS, invasive ventilation >5 days, more than one dose of surfactant, pneumothorax, PDA, IVH, PVL, early sepsis, late sepsis, NEC, and propensity score for AGT. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Medium **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Source of funding Not reported	weeks 6 days of gestation who were born or referred and treated in the participating perinatal centres during 2002 and 2003 were enrolled **Exclusion criteria** Not reported			absence, partial, or complete AGT, and presence or absence of death, in the second part of the study, CLD in survivors. Results were expressed as number and percentage. Chi squared test was used to analyse categorical data, and students t test and one-way analysis of variance were used for quantitative variable. AGT was not randomised and it could be conditioned by variable situations (e.g. inborn versus outborn, medical centre). Thereafter, to avoid attributing to AGT what may be due to other variables, we created a propensity score for AGT (administered or not administered). This score was obtained with a logistic regression model that included the demographic variables that in the univariate analysis were associated with AGT at a p value		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				≤0.3 and not considered covariables or confounders. Covariables were the variables probably related to CLD in survivors (<0.1 in univariate analysis), whereas confounders were the variables that at the same time has a p value <0.3 in infants classified by exposure to AGT and by outcomes. However, variables that are in a causal chain between the exposure and outcome were not considered confounders but covariables. Finally, logistic regression analysis was performed with variables selected on the basis of presumed biologic importance, covariables, and potential confounding variables. The forward stepwise method adjusted for confounding factors and the propensity score for AGT was applied to select variables, and the enter		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				method using selected variables was performed to obtain odds ratio		
Full citation Gagliardi,L., Bellu,R., Rusconi,F., Merazzi,D., Mosca,F., Cavazza,A., Brunelli,A., Battaglioli,M., Tandoi,F., Cella,D., Perotti,G.F., Pelti,M., Stucchi,I., Frisone,F., Avanzini,A., Bastrenta,P., Iacono,G., Pontiggia,F., Chirico,G., Cotta-Ramusino,A., Martinelli,S., Strano,F., Fontana,P., Compagnoni,G., Franco,M., Rossi,L., Caccamo,M.L., Agosti,M., Calciolari,G., Citterio,G., Rovelli,R., Poloniato,A., Barera,G.,	**Sample size** n= 1118 preterm infants 23-32 weeks surviving to 36 PMA included in the analyses: n=917 ANS treated n=201 ANS untreated **Characteristics** **Maternal characteristics:** **Cesarean delivery:** 88.2% (ANS treated), 79.2% (untreated) **Neonatal characteristics:** **Birth weight, mean (SD), g:** 1108 (255) [ANS treated], 1114 (266) [untreated] **Gestational age, mean (SD), wk: 2**9.1 (2.1) [ANS treated], 28.8 (2.3) [untreated] **Male sex:** 51.5% (ANS treated), 51.2% (untreated)	**Limitations** **Other information**	**Factors** Antenatal steroids Sex Birthweight Late-onset sepsis	**Methodology** **Setting** National Neonatale Lombardo consisting of 10 tertiary-level neonatal intensive care units in Lombardy, Italy. **Method of measurement for risk factor** ANS treatment defined as administration of corticosteroids I.M or I.V to the mother during pregnancy at any time prior to deliver. Betamethasone was the only steroid used. Late-onset sepsis defined as a clinical deterioration attributed to infection, occurring after 3 days of life, treated with antibiotics and supported by a positive blood culture	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) ANS treatment vs no ANS treatment: 0.59 (0.36-0.97) Male vs female: 2.08 (1.4-3.11) Higher birthweight (per 100g) vs lower birthweight (per 100g): 0.63 (0.57-0.69) Late-onset sepsis vs no late-onset sepsis: 4.26 (2.76-6.58)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias, attrition all accounted for **Prognostic factor measurement:** low risk of bias. All risk factors appropriately defined and measured **Outcome measurement:** low risk of bias, outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Multivariate analysis adjusted for statistically significant confounders: Sex, Birthweight (highly correlated with GA, but used over GA because of

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Gancia,G.P., Rondini,G., Costato,C., Germani,R., Maccabruni,M., Barp,S., Crossignani,R., Santucci,S., Zanini,R., Siliprandi,N., Borroni,C., Ventura,M.L., Abbiati,L., Giardinetti,S., Leva,L., Fusi,M., Bellasio,M., Antenatal steroids and risk of bronchopulmonary dysplasia: A lack of effect or a case of over-adjustment?, Paediatric and Perinatal Epidemiology, 21, 347-353, 2007 **Ref Id** 242504 **Country/ies where the study was carried out**	**Use of invasive ventilation:** 55.6% (ANS treated), 65.2% (untreated) **Use of surfactant:** 43.3% (ANS treated), 50% (untreated) **Late-onset sepsis:** 21.3% (ANS treated), 23.4% (untreated) **PDA:** 25.2% (ANS treated), 34.8% (untreated) **Incidence of BPD:** 15.9% **Inclusion criteria** Birthweight <1500g, 23-32 GA, admitted to a tertiary-level NICU **Exclusion criteria** Neonates <23 weeks GA or <400g birthweight, those with lethal congenital anomalies, and those who died in the delivery room were excluded.			or laboratory signs of infection) **Definition of outcome** Bronchopulmonary dysplasia defined as the need for supplemental oxygen at 36 weeks PMA **Statistical methods** 1. Associations between risk factors known as being intermediate in the causal pathway between ANS and BPD (illness severity, need for invasive ventilation, or presence of PDA) and BPD were assessed by univariable analyses. Results presented as odds ratio and 95% CI 2. Ascertain the association of the		higher exploratory power), late-onset sepsis **Statistical analysis and reporting:** Medium risk of bias, very detailed regarding stepwise process, however lacking in details for statistical techniques used **Overall risk of bias:** Medium **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Italy **Study type** Prospective multicentre cohort study **Aim of the study** To assess the presence and effect of overadjustment for confounding factors by analysing a large data set from a multi-centre network of very low birthweight infants <32 weeks, to see if avoiding the control of factors that are intermediate in the causal pathway between ANS and BPD changed the estimated ANS effect **Study dates** 1999-2002				same risk factors with ANS. Then, before carrying out multivariable regression models, we used propensity score methods to reduce the risk of confounding by indication. 3. Subjects classed into groups on basis of quintiles of the score, and this subclassification was used in subsequent logistic models, that had BPD as an outcome variable, and ANS and other factors (GA, birthweight, race, prenatal care, type of delivery, twin gestation, location of birth) as independent variables. A		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Source of funding Not reported				backward stepwise technique was used. Only significant factors were maintained for the final model. 4. Logistic regression model was created which included ANS as well as intermediate factors associated with ANS and BPD. All logistic regression models were adjusted for centre effect. All analyses were carried out with the statistical package STATA.		
Full citation Hanke, K., Hartz, A., Manz, M., Bendiks,	**Sample size** n=4120 preterm infants eligible for primary analysis (<32 gestational weeks, no	**Limitations**	**Factors** GA (per week) Birth weight (100g steps)	**Methodology** **Setting** Multicentre trial involving 46 neonatal intensive care	**Results** **BPD among survivors (oxygen**	**Limitations** Based on the prognostic study assessment tool QUIPS

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
M., Heitmann, F., Orlikowsky, T., Muller, A., Olbertz, D., Kuhn, T., Siegel, J., von der Wense, A., Wieg, C., Kribs, A., Stein, A., Pagel, J., Herting, E., Gopel, W., Hartel, C., German Neonatal, Network, Preterm prelabor rupture of membranes and outcome of very-low-birth-weight infants in the German Neonatal Network, PLoS ONE [Electronic Resource]PLoS ONE, 10, e0122564, 2015 **Ref Id** 674901 **Country/ies where the study was carried out** Germany **Study type** Prospective population-based observational study	pre-eclampssia, HELLP or placental abruption as cause of preterm birth): n=2559 no PPROM n=1561 PPROM n=4,115 preterm infants analysed in the multivariable logistic regression (99.8%) **Characteristics** **Maternal characteristics:** **ANS:** 91.2% (No PPROM); 92.9% (PPROM) **Elective Cesarean delivery:** 79.6% (No PPROM); 79.3% (PPROM) **Neonatal characteristics:** **Birth weight, mean (SD), g:** 1005 (301) [No PPROM]; 1045 (295) [PPROM] **Gestational age, mean (SD), wk:** 28.1 (2.3) [No PPROM]; 27.7 (2.3) [PPROM] **Male sex:** 51.7% (No PPROM); 54.3% (PPROM) **Surfactant:** 65.2% (No PPROM); 65.2% (PPROM)	**Other information**	ANS Sex SGA	units in Germany - German Neonatal Network **Method of measurement for risk factor** Gestational age was calculated from the best obstetric estimate based on early prenatal ultrasound and obstetric examination. SGA was defined as birth weight less than 10th percentile for GA according to gender specific standards in Germany ANS was defined as maternal treatment with betamethasone or dexamethasone for lung maturity of the feus irrespective of number of doses. **Definition of outcome** Bronchopulmonary dysplasia defined as the need for supplemental oxygen at 36 weeks PMA	**requirement at 36 weeks PMA)** Adjusted OR (95% CI) Higher GA (per week) vs Lower GA (per week): 0.89 (0.82-0.97) Higher birth weight (100g steps) vs lower birth weight (100g steps): 1.00 (0.99-1.00) ANS vs no ANS: 1.07 (0.75-1.54) Female vs Male: 0.55 (0.45-0.68) SGA vs not SGA: 1.13 (0.79-1.61)	**Study participation**: Medium risk of bias, maternal causes of preterm delivery excluded, thus population is homogenous **Study attrition:** Low risk of bias, attrition all accounted for. **Prognostic factor measurement:** low risk of bias. All risk factors appropriately defined and measured. **Outcome measurement:** low risk of bias, outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Multivariate analysis adjusted for statistically significant confounders: Sex, Birthweight, GA, ANS, multiple birth, inborn, centre, sex, SGA **Statistical analysis and reporting:** Low risk of bias **Overall risk of bias:** Medium

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Aim of the study To determine the role of preterm prelabor rupture of membranes as a cause of preterm delivery for infant survival and morbidity in very low birth weight infants (<1500g) <32 gestational weeks enrolled in the German Neonatal Network **Study dates** January 2009 - December 2012 **Source of funding** Grant of the German government (German ministry of education and research)	**Postnatal steroids:** 19.2% (No PPROM); 21% (PPROM) **Incidence of BPD:** 14.1% **Inclusion criteria** Birth weight <1500g and gestational age >22 + 0 and <32 + 0 weeks **Exclusion criteria** Lethal malformations e.g trisomy 18 and trisomy 18, and maternal causes of preterm delivery, e.g. placental abruption, HELLP, and pre-eclampsia			**Statistical methods** Data analysis was performed using the SPSS 20.0 data analysis package. Differences between infants born after PPROM and infants without PPROM were evaluated with Chi-square test, Fishers exact test and Mann-Whitney U test. A p value <0.05 was considered as statistically significant for single tests. To determine the independent impact of PPROM on outcomes, we performed multivariable logistic regression analyses including well-established risk factors for adverse short-term outcomes in the whole cohort of infants <32 + 0 gestational weeks enrolled in GNN		**Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Full citation Kamper, J., Feilberg Jorgensen, N., Jonsbo, F., Pedersen-Bjergaard, L., Pryds, O., Danish, Etfol Study Group, The Danish national study in infants with extremely low gestational age and birthweight (the ETFOL study): respiratory morbidity and outcome, Acta PaediatricaActa Paediatr, 93, 225-32, 2004 **Ref Id** 674960 **Country/ies where the study was carried out** Denmark **Study type**	**Sample size** n=477 preterm infants were eligible for follow-up n=407 preterm infants with perinatal data n=269 preterm infants followed up (n=138 infants died): n=54 (24-25 weeks GA) n=141 (26-27 weeks GA) n=74 (>27 weeks GA) **Characteristics** **Maternal characteristics:** **ANS:** 50% (<24 w), 54% (24 w), 50% (25 w), 55% (26 w), 62% (27 w), 69% (>27 w) **Caesarean section:** 17% (<24 w), 26% (24 w), 45% (25 w), 57% (26 w), 65% (27 w), 87% (>27 w) **Neonatal characteristics:** **Birthweight, mean (SD), g:** 633 (153) [<24 w], 658 (120) [24 w], 812 (143) [25 w], 893 (186) [26 w], 1004 (184) [27 w], 852 (126) [>27 w]	**Limitations** **Other information**	**Factors** Invasive ventilation PDA	**Methodology** **Setting** Gestational age <28 weeks and/or extremely low birthweight infants part of the ETFOL study was planned and organised by the Neonatal committee of the Danish Paediatric Society and included all 18 paediatric departments in the country involved in neonatal and/postnatal care of infants with low GA or birthweight. **Definition of risk factor** PDA defined as treated with indomethacin or surgery No timeframe around invasive ventilation **Definition of outcome** Chronic lung disease defined as oxygen dependency at GA 36 weeks (also separate analyses for 40 weeks but not included in review) **Statistical methods**	**Results** Results **CLD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Invasive ventilation vs no invasive ventilation: 3.68 (1.31-10.37) PDA treatment vs no PDA treatment: 2.84 (1.09-7.42)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Moderate risk of bias. 23% of population retrospectively traced. **Study attrition:** Moderate risk of bias. 17% of attrition not accounted for in the text or a flow chart. **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Moderate risk of bias. Models adjusted for statistically significant confounders: GA, invasive ventilation, treated PDA, CRIB score, location of birth (gender, septicaemia, caesarean section, SGA, ANS,

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Prospective population-based cohort study **Aim of the study** To describe and analyse neonatal care, short and long terms morbidity with special reference to ventilatory support and chronic lung disease **Study dates** 1994-1995 **Source of funding** Not reported	**Male:** 67% (<24 w), 43% (24 w), 63% (25 w), 59% (26 w), 46% (27 w), 45% (>27 w) **SGA:** 0 (<24 w), 26% (24 w), 15% (25 w), 31% (26 w), 33% (27 w), 100% (>27 w) **Surfactant:** 44% (24-25 w), 40% (26-27 w), 19% (>27 w) **Incidence of CLD: 15%** **Inclusion criteria** GA < 28 weeks or with a birthweight <1000g **Exclusion criteria** Not reported			The data were analysed in using the SPSS statistical program. Analyses of categorical variables were performed with the chi-squared test with Yates correction where appropriate and quantitative variables using the non-parametric Mann-Whitney test. Backwards logistic regression was used to identify associations between various demographic, biological and therapeutic factors and oxygen requirement at 36 as well as 40 postmenstrual wk (CLD) and death. Variables analysed included GA, SGA, CRIB status, gender, multiparity, ANS, caesarean section, surfactant treatment, invasive ventilation, symptomatic PDA treated with indomethacin or surgery, septicaemia meningitis, PVL/IVH		multiparity, surfactant, meningitis, PVL, IVH, all tested for associations, but not statistically significant - data not reported with p-values) **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				grade 3-4, and region of birth. He level of statistical significance was <0.05 for all analyses using 2-tailed comparisons.		
Full citation Klinger, G., Levy, I., Sirota, L., Boyko, V., Lerner-Geva, L., Reichman, B., Outcome of early-onset sepsis in a national cohort of very low birth weight infants, Pediatrics, 125, e736-e740, 2010 **Ref Id** 674988 **Country/ies where the study was carried out** Israel **Study type**	**Sample size** n=16,462 infants eligible for follow-up n=15,839 infants followed-up (623 infants died in the delivery room or had lethal congenital malformations): n=383 early-onset sepsis n=15,456 no early-onset sepsis **Characteristics** **Maternal characteristics:** **ANS:** 64.1% (EOS), 65.9% (No EOS) **Caesarean section:** 59% (EOS), 69.1% (No EOS) **Amnionitis:** 33.4% (EOS), 6.8% (No EOS)	**Limitations** **Other information**	**Factors** Early onset sepsis (EOS)	**Methodology** **Setting** Very low birthweight infants in 28 neonatal departments in Israel forming part of the Israel Neonatal Network. **Definition of risk factor** EOS defined clinically and required a positive blood culture obtained within the first 72 hours of life. EOS was not diagnosed if cultures tested positive for organisms considered to be contaminants (corynebacterium spp, or micrococcus spp.). The diagnosis of sepsis caused by coagulase negative staphylococcus was determined according	**Results** **BPD among survivors (oxygen requirement at 28 weeks PMA)** Adjusted OR (95% CI) EOS vs no EOS: 1.74 (1.24-2.43)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition accounted for in the text. **Prognostic factor measurement:** Low risk of bias. Risk factors appropriately defined and measured. **Outcome measurement:** High risk of bias. Outcome measures appropriately defined and measured, however time point taken at 28 days not 36 weeks PMA

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Prospective, population-based cohort study **Aim of the study** To evaluate the mortality and major morbidities among very low birthweight infants with early onset sepsis **Study dates** 1995-2005 **Source of funding** Israel Centre for Disease Control and the Ministry of Health	**Maternal hypertension:** 11.3% (EOS), 20.2% (No EOS) **Neonatal characteristics:** **Gestational age, mean (SD), weeks:** 27.7 (2.6) [EOS], 29.1 (3) [No EOS] **Birthweight, mean (SD), g:** 1005 (287) [EOS], 1102 (283) [No EOS] **Male:** 53.5% (EOS), 50.8% (No EOS) **SGA:** 16.2% (EOS), 31.4% (No EOS) **Incidence of CLD: 85%** **Inclusion criteria** Very low birthweight infants (<1500g) born in Israel from 1995-2005. **Exclusion criteria** Not reported			to the criteria of the Vermont Oxford Network Database and required clinical signs of sepsis, a positive blood culture result, and antibiotic treatment for at least 5 days or until death. **Definition of outcome** Bronchopulmonary dysplasia defined as clinical evidence of BPD together with the requirement of oxygen therapy at 28 days of life. **Statistical methods** The association between EOS and neonatal outcomes was tested by using a chi-squared test for categorical variables and a 2-sample t test for continuous variables. Multivariable analyses were used to identify the independent association of EOS with neonatal outcome variables. The multivariable analyses adjusted for previously		**Study confounding:** Low risk of bias. Models adjusted for statistically significant confounders: GA, sex, ethnicity, SGA, multiple pregnancy, ANS, maternal hypertension, premature contractions, PROM, caesarean section, amnionitis, and delivery room resus **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** High **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				reported perinatal variables, including GA, BW, SGA, sex, multiple pregnancy, ethnicity, PROM, amnionitis, premature contractions, maternal hypertension, ANS, caesarean delivery, and delivery-room resus. Results of the multivariable analyses are presented as adjusted odds ratios with 95% CI. Statistical analyses are performed using SAS.		
Full citation Marshall, D. D., Kotelchuck, M., Young, T. E., Bose, C. L., Kruyer, L., O'Shea, T. M., Risk factors for chronic lung disease in the surfactant era: a North Carolina population-based study of very low birth weight infants. North Carolina Neonatologists	**Sample size** n=1480 preterm infants available for follow up n=1101 preterm infants followed up (not followed up due to death) n=865 preterm infants available for risk factor analysis (reasoning not clear, however comparison was made between infants with missing data and group with full data and no	**Limitations** **Other information**	**Factors** Birthweight GA Male Surfactant Ventilated at 48hrs	**Methodology** **Setting** Very low birthweight infants in 13 nurseries across North Carolina in 1994 **Definition of risk factor** Surfactant nor ventilated at 48hr defined **Definition of outcome** Chronic lung disease defined as being	**Results** **CLD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Higher Birthweight (per 100g) vs lower birthweight (per 100g): 0.80 (0.71-0.90)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Moderate risk of bias. Reason behind lack of follow up data in 3 specific centres not adequately described **Prognostic factor measurement:** Moderate risk of bias. Surfactant use

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Association, Pediatrics, 104, 1345-50, 1999 **Ref Id** 620165 **Country/ies where the study was carried out** USA **Study type** Prospective, population-based cohort study **Aim of the study** Re-examine underlying risk and neonatal interventions associated with CLD, using a large, multicentre, population-based cohort of VLBW infants born after the introduction of surfactant therapy. Specifically were the	statistical difference in characteristics existed) n=224 CLD n=641 No CLD **Characteristics** **Maternal characteristics:** **ANS:** 51% (CLD), 50% (No CLD) **Maternal preeclampsia:** 14% (CLD), 23% (No CLD) **Neonatal characteristics:** **Gestational age, mean (SD), weeks:** 27.3 (2.15) [CLD], 29.46 (2.49) [No CLD] **Birthweight, mean (SD), g:** 926 (2828) [CLD], 1161 (232) [No CLD] **Male:** 54% (CLD), 47% (No CLD) **PDA:** 58% (CLD), 24% (No CLD) **Infection:** 61% (CLD), 24% (No CLD) **Incidence of CLD: 26%**			invasively ventilated or requiring supplementary oxygen at 36 weeks PMA **Statistical methods** Bivariate associations with demographic, prenatal and illness attributes, and postnatal interventions were analysed. To include characteristics of ventilator management, bivariate analyses were reported on the subset of infants who received invasive ventilation at 48 hrs of age. For multivariate analyses, a time-orientated approach was used for stepwise selection of covariates into logistic model. In successive steps, potential risk factors were entered according to their time period of occurrence. For each time period, the variables allowed to compete in the model were those for which	Older GA (per week) vs younger GA (per week): 1.02 (0.90-1.16) Males vs female: 1.40 (0.96-2.06) Surfactant vs no surfactant: 2.86 (1.59-5.14) Ventilated at 48h vs not ventilated at 48h: 2.18 (1.29-3.68)	and ventilation at 48h not adequately defined. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Models adjusted for statistically significant confounders: Birthweight, GA, sex, inborn, PDA, Infection, surfactant, fluid on day 2, ventilated at 48h, fiO2 >42 **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
effects of ANS, nosocomial infection, fluid management, the presence of PDA, and increasing levels of ventilator and oxygen support strategies **Study dates** 1994 **Source of funding** Not reported	**Inclusion criteria** Infants with birthweights of 500g to 1500g and born in North Carolina. Also, included infants born outside North Carolina but were transferred for management to a NICU in North Carolina **Exclusion criteria** Not reported			bivariate analyses yielded significant associations with CLD (P <0.05). Beginning with birthweight and gender, significant variables at each step were carried out through the remaining steps. Bivariate associations were explored using chi-squared analyses or Fischers exact test for dichotomous variables, and the student t test for continuous variables. Results for the multivariable analyses were expressed as odds ratios with a 95% CI. SAS used as statistical software.		
Full citation Monier, I., Ancel, P. Y., Ego, A., Jarreau, P. H., Lebeaux, C., Kaminski, M., Goffinet, F., Zeitlin, J., Fetal and neonatal	**Sample size** n=2919 singleton nonanomalous infants 24-31 weeks GA: n=636 SGA (suspected FGR)	**Limitations** **Other information**	**Factors** SGA	**Methodology** **Setting** EPIPAGE 2 cohort, a national population-based prospective study that includes all live births, stillbirths, and	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)**	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
outcomes of preterm infants born before 32 weeks of gestation according to antenatal vs postnatal assessments of restricted growth, American Journal of Obstetrics and Gynecology, 216, 516, 2017 **Ref Id** 662471 **Country/ies where the study was carried out** France **Study type** Prospective, population-based cohort study **Aim of the study** To investigate fetal and neonatal outcomes based on antenatal vs postnatal	n=330 SGA (no suspected FGR) n=84 not SGA (suspected FGR) n=1869 not SGA (no suspected FGR) **Characteristics** **Maternal characteristics:** **Maternal preeclampsia:** 49.3% (SGA + suspected FGR), 44.9% (SGA + no suspected FGR), 43.9% (not SGA + suspected FGR), 9.6% (not SGA + no suspected FGR) **Neonatal characteristics:** **Gestational age:** **24-25 w:** 9% (SGA + suspected FGR), 13% (SGA + no suspected FGR), 6.5% (not SGA + suspected FGR), 16.1% (not SGA + no suspected FGR) **26-27 w:** 20.5% (SGA + suspected FGR), 17% (SGA + no suspected FGR), 19.9% (not SGA +			terminations of pregnancy between 22 and 31 weeks completed gestation in 25 French regions in 2011. A total of 447 maternity units participated in the study **Definition of risk factor** SGA defined as birthweight <10th percentile for GA and sex Suspected FGR defined as at least one of the following: estimated weight or an abdominal circumference <10th percentile, fetal doppler abnormalities as assessed by the medical team, mention of growth arrest or faltering, or termination of pregnancy for which the reason was growth restriction **Definition of outcome** Bronchopulmonary dysplasia defined as the need for oxygen and/or positive airway pressure	Adjusted OR (95% CI) SGA + suspected FGR vs no SGA + no suspected FGR: 3.4 (2.2-5.3) SGA + no suspected FGR vs no SGA + no suspected FGR: 2.5 (1.6-4.1)	**Study attrition:** Low risk of bias. All attrition accounted for **Prognostic factor measurement:** Low risk of bias. All defined and measured **Outcome measurement:** Low risk of bias. All defined and measured **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA, sex, maternity level 3 unit, PROM, vascular disorders, BMI, and smoking **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
assessments of growth restriction **Study dates** 2011 **Source of funding** None reported	suspected FGR), 21.5% (not SGA + no suspected FGR) **28-29 w:** 27.5% (SGA + suspected FGR), 27.2% (SGA + no suspected FGR), 23.7% (not SGA + suspected FGR), 25.7% (not SGA + no suspected FGR) **30-31 w:** 43% (SGA + suspected FGR), 42.8% (SGA + no suspected FGR), 49.9% (not SGA + suspected FGR), 36.6% (not SGA + no suspected FGR) **Birthweight, mean (range), g:** 830 (634-1040) [SGA + suspected FGR], 950 (700-1140) [SGA + no suspected FGR], 1235 (905-1410) [not SGA + suspected FGR], 1250 (930-1530) [not SGA + no suspected FGR] **Female:** 51.9% (SGA + suspected FGR), 47.9% (SGA + no suspected FGR), 59.8% (not SGA +			and/or invasive ventilator support at 36 weeks PMA **Statistical methods** Poisson regression to estimate risk ratios with robust standard error for fetal and neonatal outcomes for each group, the group of not-SFGR/not-SGA infants as the reference group. Statistical difference between co-efficients were tested with the use of Wald test. For these models we adjusted variables linked to the risk of growth restriction or the detection of growth restriction that independently may impact perinatal outcomes. These variables were GA, sex, ANS, PROM, vascular disorders, BMI, smoking and delivery in a level 3 maternity unit. We carried out a sensitivity analysis to assess the impact of assuming that the time		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	suspected FGR), 44.6% (not SGA + no suspected FGR) **Incidence of BPD:** 47.6% **Inclusion criteria** Preterm singleton infants born between 24 and 31 completed weeks gestation **Exclusion criteria** Multiple pregnancies Congenital abnormalities Births <24 weeks GA			from death to delivery for stillbirth was 2 days because this may be an underestimate if the period is longer or significant weight loss occurs after death. Statistical analyses were performed using STATA		
Full citation Morrow, L. A., Wagner, B. D., Ingram, D. A., Poindexter, B. B., Schibler, K., Cotten, C. M., Dagle, J., Sontag, M. K., Mourani, P. M.,	**Sample size** n=587 preterm infants enrolled: n=345 no or mild BPD n=242 moderate or severe BPD **Characteristics**	**Limitations** **Other information**	**Factors** Birthweight Sex Maternal race Maternal ethnicity GA ANS Chorioamnionitis	**Methodology** **Setting** 5 NICU centres in the USA **Definition of risk factor** Risk factors requiring elaboration not well defined, for example ANS	**Results** **Moderate to severe BPD at 36 weeks PMA** **Adjusted OR (95% CI)** Decreasing birth weight z-score, 1 SD vs increasing	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Moderate risk of bias. No description of participant flow, only

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Abman, S. H., Antenatal Determinants of Bronchopulmonary Dysplasia and Late Respiratory Disease in Preterm Infants, American Journal of Respiratory & Critical Care MedicineAm J Respir Crit Care Med, 01, 01, 2017 **Ref Id** 654072 **Country/ies where the study was carried out** USA **Study type** Prospective, multi-centre, observational study **Aim of the study** To identify antenatal risk factors associated with increased risk of	**Maternal characteristics:** **Maternal preeclampsia:** 28.4% (no or mild BPD), 23.1% (moderate or severe BPD) **Chorioamnionitis:** 17.7% (no or mild BPD), 20.2% (moderate or severe BPD) **PROM:** 18.6% (no or mild BPD), 17.8% (moderate or severe BPD) **Maternal smoking:** 10.1% (no or mild BPD), 18.6% (moderate or severe BPD) **Maternal race:** *Asian:* 1.2% (no or mild BPD), 1.2% (moderate or severe BPD) *Black or African American:* 22.3% (no or mild BPD), 17.4% (moderate or severe BPD) *Hawaiian or Pacific Islander:* 0% (no or mild BPD), 0% (moderate or severe BPD) *White:* 75.9% (no or mild BPD), 80.6% (moderate or severe BPD) *Other:* 0% (no or mild BPD), 0.4% (moderate or severe BPD)			and chorioamnionitis was the only definition in the text **Definition of outcome** Bronchopulmonary dysplasia not defined any further, however time frame of 36 weeks PMA used. Diagnosis of BPD split to "no or mild BPD" and "moderate or severe BPD", no elaboration on these definitions and odds ratio's for BPD exclude milder forms of disease **Statistical methods** Chi-square tests, Fishers exact tests, and Wilcoxon signed-rank tests were used to assess associations across BPD and late respiratory outcome status for categorical and continuous variables, respectively. A logistic regression model was fitted using an outcome of moderate or severe BPD at 36 weeks PMA.	birth weight z-score, 1 SD: 2.40 (1.66-3.46) Male vs female: 1.37 (0.92-2.03) Maternal race: white vs maternal race: non-white: 1.85 (1.11-3.08) Maternal ethnicity: Hispanic or latino vs maternal ethnicity: non-hispanic or latino: 0.70 (0.42-1.17) Decreasing GA, wk vs increasing GA, wk: 1.89 (1.65-2.17) ANS vs no ANS: 0,90 (0.51-1.59) Chorioamnionitis vs no chorioamnionitis: 0.87 (0.51-1.48)	infants included in the study and then analysed. **Prognostic factor measurement:** High risk of bias. No risk factors of interest for review defined and measured **Outcome measurement:** Moderate risk of bias. Timing of BPD stated as 36 weeks PMA. No definition of BPD diagnosis, furthermore only moderate and severe BPD used in the analysis, no definition specified here either. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA, Birthweight, Sex, Ethnicity, ANS, maternal smoking status, multiple gestations, caesarean section, gestational diabetes, preeclampsia, PROM, chorioamnionitis, antepartum haemorrhage. **Statistical analysis and reporting:** Low risk of bias.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
BPD and respiratory disease during early childhood after preterm birth. **Study dates** July 2006 - November 2016 **Source of funding** NIH, NHLBI grant R01HL085703	*Unknown:* 0.9% (no or mild BPD), 0% (moderate or severe BPD) **Maternal ethnicity:** *Hispanic or latino:* 21.2% (no or mild BPD), 19% (moderate or severe BPD) *Not hispanic or latino:* 78.6% (no or mild BPD), 81% (moderate or severe BPD) **Caesarean section:** 72.5% (no or mild BPD), 65.3% (moderate or severe BPD) **Neonatal characteristics:** **Gestational age, median (range), weeks:** 27 (26-29) [no or mild BPD], 26 (24-27) [moderate or severe BPD] **Birthweight, median (range), g:** 1000 (855 to 1,125) [no or mild BPD], 800 (680-970) [moderate or severe BPD] **Male:** 47.5% (no or mild BPD), 55.8% (moderate or severe BPD) **ANS:** 83.8% (no or mild BPD), 81.8% (moderate or severe BPD)			Perinatal risk factors and potential confounders were identified a priori on the basis of clinical importance and were restricted to an appropriate number of events. To facilitate clinical interpretation, signs were reversed for birth weight z score, maternal age, and gestational age. A similar logistic regression was fitted modelling the diagnosis of late respiratory disease using a reduced set of the covariates from the prior model. Interactions of maternal smoking with all other covariates were tested. Two logistic regressions were fitted on the diagnosis of late respiratory disease using dichotomised BPD and classification of BPD severity as the only predictors. All analyses		**Overall risk of bias:** High **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Intubated in delivery room: 52.2% (no or mild BPD), 75.6% (moderate or severe BPD) **Intubated in NICU:** 21.4% (no or mild BPD), 19.8% (moderate or severe BPD) **Surfactant:** 69.3% (no or mild BPD), 91.3% (moderate or severe BPD) **PDA medical treatment:** 34.8% (no or mild BPD), 21.9% (moderate or severe BPD) **PDA surgical ligation:** 6.1% (no or mild BPD), 21.9% (moderate or severe BPD) **Incidence of BPD: 77.7%** **Inclusion criteria** Preterm infants who had a gestational age less than or equal to 34 weeks, birth within the previous 7 days, and a birth weight between 500 and 1,250g			were performed using SAS version 9.4 software.		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Exclusion criteria Not reported					
Full citation Ohlin, A., Bjorkman, L., Serenius, F., Schollin, J., Kallen, K., Sepsis as a risk factor for neonatal morbidity in extremely preterm infants, Acta Paediatrica, International Journal of Paediatrics, 104, 1070-1076, 2015 **Ref Id** 654128 **Country/ies where the study was carried out** Sweden **Study type** Prospective, nationwide cohort study	**Sample size** n=707 infants eligible for inclusion n=494 infants survived first year of life and included in analyses: n=171 no sepsis n=40 CoNS with other bacteria n=136 CoNS without other bacteria n=58 Other bacteria n=92 clinical sepsis **Characteristics** **<u>Maternal characteristics:</u>** **Maternal preeclampsia:** 11.7% (no sepsis), 10% (CoNS with other bacteria), 13.2% (CoNS without other bacteria), 10.3% (other bacteria), 7.6% (clinical sepsis)	**Limitations** **Other information**	**Factors** Sepsis and positive blood cultures	**Methodology** **Setting** EXPRESS study, a Swedish prospective multicentre study among preterm infants with <28 weeks gestational age **Definition of risk factor** Definite sepsis defined as one episode with clinical symptoms consistent with sepsis judged by the neonatologist in charge and a positive blood culture Clinical sepsis was defined as one episode with clinical symptoms consistent with sepsis judged by the neonatologist in charge and antibiotic treatment for a minimum of 5 days, but with a negative blood culture	**Results** **Severe BPD at 36 weeks PMA** **<u>Adjusted OR (95% CI)</u>** No sepsis as reference: 1.0 Any sepsis: 1.4 (0.8-2.2) Any definite sepsis: 1.6 (1.0-2.7) Clinical sepsis: 1.1 (0.6-2) CoNS without other bacteria: 1.6 (0.9-2.8) CoNS with other bacteria: 1.9 (0.9-4.2) Other bacteria: 1.6 (0.8-3.2)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition accounted for. **Prognostic factor measurement:** Low risk of bias. All defined and measured **Outcome measurement:** Moderate risk of bias. All defined and measured, however only severe BPD included in analyses. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA and sex **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Moderate

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Aim of the study To evaluate sepsis as a risk factor for neonatal morbidities and investigated the association between specific pathogens and neonatal morbidities **Study dates** 2004-2007 **Source of funding** Swedish research council 2006-3858, Lilla Barnets Fond, the Evy and Gunnar Sandbergs Foundation and the Birgit and Hakan Ohlssons Foundation	**Amnionitis:** 12.9% (no sepsis), 10% (CoNS with other bacteria), 17.6% (CoNS without other bacteria), 24.1% (other bacteria), 17.4% (clinical sepsis) **Neonatal characteristics:** **Gestational age, wk:** **≤22**: 40% (no sepsis), 0% (CoNS with other bacteria), 20% (CoNS without other bacteria), 20% (other bacteria), 20% (clinical sepsis) **23:** 26.4% (no sepsis), 15.1% (CoNS with other bacteria), 26.4% (CoNS without other bacteria), 13.2% (other bacteria), 18.9% (clinical sepsis) **24:** 19.8% (no sepsis), 14.6% (CoNS with other bacteria), 32.3% (CoNS without other bacteria), 12.5% (other bacteria), 20.8% (clinical sepsis) **25:** 34.9% (no sepsis), 4.8% (CoNS with other bacteria), 27.7% (CoNS without other bacteria), 13.9% (other			No sepsis defined as infants without any definite septic episode during the entire hospital stay CoNS without any bacteria defined as one or more definite septic episode caused by CoNS CoNS with other bacteria defined as one or more definite septic episodes where at least one culture was positive for CoNS and at least one culture was positive for another pathogen Other bacteria defined as one definite septic episode or more caused by either fungi or bacteria other than CoNS **Definition of outcome** BPD and severe BPD were defined according to the diagnostic criteria developed by the NIH workshop. Severe BPD defined as 30% oxygen at 26 weeks.		**Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	bacteria), 18.7% (clinical sepsis) **26:** 44.1% (no sepsis), 5.6% (CoNS with other bacteria), 24.9% (CoNS without other bacteria), 8.5% (other bacteria), 16.9% (clinical sepsis) **Birthweight, z scores:** **<-3 SD:** 3.5% (no sepsis), 2.5% (CoNS with other bacteria), 8.1% (CoNS without other bacteria), 10.3% (other bacteria), 8.7% (clinical sepsis) **<-2 SD:** 12.9% (no sepsis), 15% (CoNS with other bacteria), 18.4% (CoNS without other bacteria), 19% (other bacteria), 17.4% (clinical sepsis) **Male:** 49.1% (no sepsis), 42.5% (CoNS with other bacteria), 57.4% (CoNS without other bacteria), 55.2% (other bacteria), 65.2% (clinical sepsis) **Incidence of any BPD:** 95%			**Statistical methods** Neonatal sepsis was evaluated as a risk factor for neonatal morbidity, using multiple logistic linear regression analyses adjusted for sex, and GA entered as a continuous variable. Cases of neonatal sepsis were divided into 6 non disjunctive groups, and separate analyses were conducted for each group, using infants without septic episodes as references. The results were reported as Odds ratios with 95% CI. Tests of homogeneity of the ORs across causative agent strata were based on weighted sums of the squared deviations of the stratum specific log-OR from their weighted means. All statistical analyses were performed using version 6.0 of the GAUSS software package. All testing was two-sided, with p values		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Inclusion criteria All preterm live and stillborn infants <28 weeks gestational age delivered in Sweden from 1 April 2004 to 31 March 2007 **Exclusion criteria** Not reported			of <0.05 considered statistically significant		
Full citation Patel, A. L., Johnson, T. J., Robin, B., Bigger, H. R., Buchanan, A., Christian, E., Nandhan, V., Shroff, A., Schoeny, M., Engstrom, J. L., Meier, P. P., Influence of own mother's milk on bronchopulmonary dysplasia and costs, Archives of Disease in Childhood: Fetal and Neonatal Edition, 102, F256-F261, 2017	**Sample size** n=359 very low birth infants enrolled n=430 completed study (29 excluded for congenital abnormalities, transferred out before day of life 14, met exclusion criteria) n= 254 analysed (exclusions noted in flow chart): n=77 BPD n=177 no BPD **Characteristics** **Maternal characteristics:**	**Limitations** **Other information**	**Factors** Human milk dose as a proportion of enteral feedings	**Methodology** **Setting** Single-centre cohort of infants admitted to the Rush University Medical centre NICU between 2008 and 2012 **Definition of risk factor** All VLBW infants received parenteral nutrition upon admission. Freshly expressed colostrum was administered oropharyngeally once available. Feedings were initiated at 20mL/kg/day, and then advanced daily	**Results** **BPD at 36 weeks PMA** Adjusted OR (95% CI) HM-PCT per 10% increase: 0.905 (0.824 to 0.995) reduction in BPD	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: High risk of bias, single-centre prospective cohort study **Study attrition:** Low risk of bias. All attrition accounted for in a participant flow chart **Prognostic factor measurement:** Low risk of bias. All defined and measured. **Outcome measurement:** Moderate risk of bias. All defined and measured,

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Ref Id 644074 **Country/ies where the study was carried out** USA **Study type** Prospective, single-centre cohort study **Aim of the study** To prospectively study the impact of own mother's milk received in the NICU on the risk of BPD and associated costs. **Study dates** 2008-2012 **Source of funding** None reported	**Chorioamnionitis:** 16% (BPD), 11% (no BPD) **Any ANS:** 91% (BPD), 90% (no BPD) **Completed ANS:** 62% (BPD), 67% (no BPD) **Maternal race:** Black: 51% (BPD), 53% (no BPD) White/other: 31% (BPD), 18% (no BPD) Hispanic: 18% (BPD), 29% (no BPD) **Neonatal characteristics:** **Gestational age, median (SD), weeks:** 26 (1.7) [BPD], 28.7 (2.3) [no BPD] **Birthweight, median (SD), g:** 831 (194) [BPD], 1112 (233) [no BPD] **Male:** 68% (BPD), 46% (no BPD) **SGA:** 23% (BPD), 21% (no BPD) **Surfactant:** 90% (BPD), 61% (no BPD) **PDA:** 77% (BPD), 34% (no BPD) **Early onset sepsis:** 64% (BPD), 39% (no BPD)			by 20mL/kg as tolerated, with PN decreased concomitantly. Initial feedings consisted of unfortified OMM OR 20-calorie preterm formula if OMM was not available. OMM was fortified with powdered bovine human milk fortifier when feeding volume reached 100ml/kg/day; formula was switched to 24-calorie formula at 140ml/kg/day. Freshly expressed OMM was preferentially fed instead of refrigerated or frozen OMM. **Definition of outcome** BPD was defined as oxygen requirement >21% or continuous positive airway pressure or invasive ventilation at 36 weeks PMA **Statistical methods** Data were analysed using x^2 or Fishers exact test as appropriate, the Mann-		however minimum use of 21% oxygen used to define BPD **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA, gender, NEC, PDA, and SGA **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** High **Other information** Only human milk dose as a proportion of enteral feedings extracted as a risk factor, as all other risk factors covered in higher quality studies included in this review

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Late onset sepsis: 12% (BPD), 12% (no BPD) **Incidence of BPD: 30.3%** **Inclusion criteria** Preterm infants with a birthweight <1500g, GA <35 weeks, enteral feeding initiated by day of life 14, absence of major congenital abnormalities or chromosomal disorders and negative maternal drug screen. **Exclusion criteria** Infants dying before NICU discharge or were transferred to another hospital, resulting in incomplete NICU hospitalisation cost data			Whitney U test and t-test. A two step logistic regression analysis was conducted to identify variables associated with BPD. In the first step, BPD was regressed on potential covariates demonstrated in the literature associated with BPD or that were associated with BPD in the current sample. Backward elimination was used to select the final covariates that remained associated with BPD at p<0.1. Then, these final covariates were used to create the propensity score for BPD which was used in the economic analyses. In the second step, HM-PCT was added to the model which included the final covariates to determine the effect of OMM on BPD.		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Full citation Reiss, I., Landmann, E., Heckmann, M., Misselwitz, B., Gortner, L., Increased risk of bronchopulmonary dysplasia and increased mortality in very preterm infants being small for gestational age, Archives of Gynecology and Obstetrics, 269, 40-44, 2003 **Ref Id** 675175 **Country/ies where the study was carried out** Germany **Study type** Prospective, population based cohort study	**Sample size** n=1365 preterm infants analysed: n= 183 SGA n= 1,182 AGA **Characteristics** **Maternal characteristics** **Preeclampsia:** 30% (SGA), 11% (AGA) **ANS:** 57% (SGA), 57% (AGA) **PROM:** 9% (SGA), 24% (AGA) **Caesarean section:** 93% (SGA), 79% (AGA) **Neonatal characteristics:** **Gestational age, median (SD), weeks:** 28.9 (1.7) [SGA], 28.8 (2.1) [AGA] **Birthweight, median (SD), g:** 788.7 (178.7) [SGA], 1,259.5 (348.1) [AGA] **Male:** 59% (SGA), 54% (AGA) **Incidence of BPD:** 15.5%	**Limitations** **Other information**	**Factors** SGA GA Sex ANS PDA Surfactant	**Methodology** **Setting** Infants <32 weeks gestation in the federal state of Hesse, Germany **Definition of risk factor** SGA defined as birth weight <10th percentile A complete course of ANS defined as 2 doses of betamethasone was assumed if the first dose was administered ≤24 hours before birth and less than 1 week from birth. PDA unspecified Probable sepsis defined as presence or characteristics of clinical signs and typical lab data (positive blood culture, abnormal differential blood count, or increased CRP) **Definition of outcome** Bronchopulmonary dysplasia defined as oxygen requirements or	**Results** **BPD at 28 days of age** Adjusted OR (95% CI) SGA vs AGA: 3.80 (2.11-6.84) Higher GA (weeks) vs lower GA (weeks): 0.67 (0.60-0.76) Female vs male: 0.63 (0.41-0.95) ANS vs no ANS: 0.89 (0.72-1.11) Probable sepsis vs no sepsis: 1.56 (1.02-2.38) Surfactant vs no surfactant: 1.57 (1.01-2.43)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Moderate risk of bias. Reasons behind mismatching data not explained further. **Prognostic factor measurement:** Moderate risk of bias. PDA not included in analyses as not defined further, surfactant not defined fully. **Outcome measurement:** Moderate risk of bias. All defined and measured, however timepoint of BPD is at 28 days of age not 36 weeks as defined in the review protocol **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: birthweight, GA, sex, ANS, PROM, Preterm labor, caesarean section, days on ventilator, probable sepsis, PDA,

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Aim of the study Evaluate the impact of being born small for gestational age on neonatal mortality and pulmonary morbidity in preterm infants <32 weeks of gestation **Study dates** 1990-1996 **Source of funding** Not reported	**Inclusion criteria** Preterm infants born <32 weeks gestation **Exclusion criteria** Lethal malformations and chromosomal aberrations were excluded			invasive ventilation on day 28 after birth **Statistical analyses** SPSS stats programme for analyses. To compare differences between groups, t-tests were used for continuous variables when normally distributed: otherwise the Mann-Whitney test was used. Dichotomous variables were analysed by chi-squared test. The level of significance was set at $p<0.05$. The effect of the variables preterm labor, preterm PROM, placental insufficiency, pregnancy induced hypertension, maternal age, and multiple pregnancy, and chorioamnionitis on the risk of delivering an SGA neonate were investigated by multiple logistic regression analyses. The effect of birthweight <10th percentile and other possible risk factors on BPD or death were		surfactant therapy, multiple pregnancy **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				investigated by multiple regression analyses as well. The level of significance was set at p<0.05. Results of the multivariable analyses were expressed as odds ratios with 95% confidence intervals.		
Full citation Spiegler, J., Preuss, M., Gebauer, C., Bendiks, M., Herting, E., Gopel, W., Berghauser, M. A., Bockenholt, K., Bohnhorst, B., Bottger, R., Brune, T., Dawczynski, K., Dordelmann, M., Ehlers, S., Eichhorn, J. G., Felderhoff-Muser, U., Franz, A., Gerleve, H., Gortner, L., Haase, R., Heitmann, F., Hentschel, R., Hepping, N.,	**Sample size** n=1433 very low birth weight infants <32 weeks gestation were eligible for follow-up: n=239 exclusive formula n=223 exclusive breastmilk n=971 mixed breastmilk/formula **Characteristics** **Maternal characteristics** **FGR:** 3% (exclusive formula), 2% (exclusive breastmilk), 3% (mixed) **ANS:** 88% (exclusive formula), 89% (exclusive breastmilk), 93% (mixed)	**Limitations** **Other information**	**Factors** Exclusive breastmilk Mixed breastmilk/formula	**Methodology** **Setting** 48 neonatal centres as part of the German Neonatal Network in Germany in 2013 **Definition of risk factor** Infants who received donor milk in the first days of life and were then switched to mothers own milk and never received formula were included in the exclusively breastmilk-fed group. Infants who received formula and neither donor milk nor their own	**Results** **BPD at 36 weeks PMA** Adjusted OR (95% CI) Exclusive formula fed vs exclusive breastmilk-fed: 2.59 (1.33-5.04) Mixed feeding vs exclusively breastmilk-fed: 1.61 (1.15-2.25)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition explained in the text **Prognostic factor measurement:** Low risk of bias. All factors defined and measured **Outcome measurement:** Low risk of bias. All outcomes defined and measured. **Study confounding:** Low risk of bias. Models

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Hillebrand, G., Hohn, T., Hornig-Franz, I., Hubert, M., Jenke, A., Jensen, R., Kannt, O., Korner, H. T., Kribs, A., Kuster, H., Linnemann, K., Moller, J., Muller, A., Muller, D., Olbertz, D. M., Orlikowsky, T., Reese, J., Roll, C., Rossi, R., Rudiger, M., Schaible, T., Schiffmann, J. H., Schmidkte, S., Seeliger, S., Segerer, H., Siegel, J., Teig, N., Urlichs, F., Wense, A. V. D., Vochem, M., Weller, U., Wieg, C., Wintgens, J., Does Breastmilk Influence the Development of Bronchopulmonary Dysplasia?, Journal of Pediatrics, 169, 76-80e4, 2016 **Ref Id** 675277	**Suspected chorioamnionitis as reason for birth:** 23% (exclusive formula), 22% (exclusive breastmilk), 21% (mixed) **Neonatal characteristics:** **Gestational age, median (range), weeks:** 28.7 (26.6-30.1) [exclusive formula], 29 (26.9-20) [exclusive breastmilk], 28.4 (26.6-30) [mixed] **Birthweight, median (range), g:** 1080 (830-1330) [exclusive formula], 1100 (865-1340) [exclusive breastmilk], 1050 (805-1295) [mixed] **Male:** 53% (exclusive formula), 52% (exclusive breastmilk), 54% (mixed) **Surfactant**: 60% (exclusive formula), 68% (exclusive breastmilk), 64% (mixed) **Incidence of BPD:** 18.4% **Inclusion criteria**			mothers milk were classified as exclusively formula-fed. Infants who received any donor milk or mothers own milk as well as formula, were classified as mixed feedings **Definition of outcome** BPD was defined as the need for supplemental oxygen or any respiratory support at 36 weeks PMA including both moderate and severe BPD **Statistical analyses** The results from continuous and categorical variables are reported using quartiles and absolute and relative frequencies, respectively. Data analysis was performed using SPSS 20.0 data analysis package and statistical environment R. The groups were compared using a Fisher-exact test/ chi-squared test/ 2-sided		adjusted for appropriate confounders: maternal origin, ANS, inborn, sex, multiple birth, GA, SDS of birth weight, SDS of discharge weight, and completion of enteral feeding **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Germany **Study type** Prospective, multicentre cohort study **Aim of the study** To assess whether breastmilk feeding is associated with a reduced risk of BPD **Study dates** 2013 **Source of funding** German Ministry for Education and Research	Infants from 22 + 0 to 31 + 6 weeks of gestation who were discharged alive **Exclusion criteria** Not reported			test. A p value of <0.05 was considered statistically significant. Logistic regression models were estimated for BPD, ROP, and NEC using nutrition as an independent variable with additive coding using formula as reference. Variables reported before in the literature were used as offset so that the lowest events per variable was 27. The firth logistic regression model and Lausso were used for sensitivity analyses. Adjustments for multiple testing were done using BonferrnoHolm. We controlled the model for maternal origin, GA, and sex, inborn vs infants that need external transport to the NICU, prenatal steroids, malformations, single vs multiple births, age at completion of enteral feedings, SDS scores for birth weight,		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				and SDS scores at discharge.		
Full citation Torchin, H., Ancel, P. Y., Goffinet, F., Hascoet, J. M., Truffert, P., Tran, D., Lebeaux, C., Jarreau, P. H., Placental Complications and Bronchopulmonary Dysplasia: EPIPAGE-2 Cohort Study, Pediatrics, 137, 1-10, 2016 **Ref Id** 452670 **Country/ies where the study was carried out** France **Study type** Please see Monier et al 2017, EPIPAGE-2 study	**Sample size** n=2697 preterm infants alive between 22-31 completed weeks gestation n=2638 preterm infants alive between 22-31 completed weeks gestatiob without congenital infections or defects n=2193 preterm infants alive at 36 weeks PMA n=259 moderate to severe BPD n=1852 no or mild BPD **Characteristics** **Maternal characteristics:** **ANS (>1 dose):** 80.8% (moderate to severe BPD), 82.9% (no or mild BPD) **Caesarean section:** 70.5% (moderate to severe BPD), 65.5% (mild or moderate BPD) **Neonatal characteristics:**	**Limitations** **Other information**	**Factors** FGR	**Methodology** **Setting** EPIPAGE 2 cohort, a national population-based prospective study that includes all live births, stillbirths, and terminations of pregnancy between 22 and 31 weeks completed gestation in 25 French regions in 2011. A total of 447 maternity units participated in the study **Definition of risk factor** Fetal disorders only as a risk factor was defined as ante-natal suspected FGR of an estimated fetal weight of <10th percentile (according to the care provider reference curve) with ≥1 of the following: abnormal fetal doppler findings (reduced, absent, or reversed umbilical cord	**Results** **Moderate or severe BPD at 36 weeks PMA** Adjusted OR (95% CI) Fetal disorders vs no fetal disorders (model C): 3.8 (2.0-7.3) Fetal disorders vs no fetal disorders (model D): 4.2 (2.1-8.6) model C: adjusted on maternal age, BMI, parity, pre-existing diabetes, smoking during pregnancy, sex, care level of the maternity units, ANS, GA, and birth weight for GA	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition accounted for. **Prognostic factor measurement:** Low risk of bias. All defined and measured. **Outcome measurement:** Low risk of bias. All defined and measured. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders (documented in results section for different models used) **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Aim of the study To investigate the relationship between placenta-mediated pregnancy complications and BPD in preterm infants with gestational age 28-31^{+6} weeks **Study dates** Please see Monier et al 2017, EPIPAGE-2 study **Source of funding** Please see Monier et al 2017, EPIPAGE-2 study	**Gestational age, median (IQR):** 27.1 (26.1-28.9) [moderate to severe BPD], 30 (28.4-31) [no or mild BPD] **Birthweight, median (IQR):** 840 (710-1040) [moderate to severe BPD], 1240 (1010-1500) [no or mild BPD] **Male:** 50.3% (moderate to severe BPD), 53.2% (no or mild BPD) **PDA:** 75.4% (moderate to severe BPD), 27.3% (no or mild BPD) **Surfactant:** None: 4.3% (moderate to severe BPD), 43.7% (no or mild BPD) 1 dose: 49.7% (moderate to severe BPD), 46.5% (no or mild BPD) >2 doses: 46% (moderate to severe BPD), 9.8% (no or mild BPD) **Postnatal steroids**: 40.9% (moderate to severe BPD), 3.8% (no or mild BPD) **Incidence of BPD:** 12.3%			artery end-diastolic flow; increased middle cerebral redistribution process; reduced, absent, or reversed atrial flow in the ductus venosus), growth arrest, gestational hypertension, or preeclampsia. Growth arrest with abnormal fetal doppler findings was considered suspected FGR regardless of the estimated fetal weight **Definition of outcome** Bronchopulmonary dysplasia categorised as moderate or severe and defined as oxygen requirement for a minimum or 28 days and persistent need for oxygen or ventilatory support at 36 weeks PMA (invasive ventilation or positive pressure) **Statistical methods** Categorical variables were compared by chi-squared tests. Continuous	model D: adjusted on maternal age, BMI, parity, pre-existing diabetes, smoking during pregnancy, sex, care level of the maternity units, ANS, GA, birth weight for GA, PDA, and postnatal bacteraemia	**Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Inclusion criteria Please see Monier et al 2017, EPIPAGE-2 study **Exclusion criteria** Multiple pregnancies Congenital abnormalities			variables are summarised as medians and IQRs and were compared by rank-sum tests. Associations between placenta mediated pregnancy complications and moderately to severe BPD were first analysed by bivariate analyses. Potential confounding factors were identified as characteristics associated with moderate to severe BPD in our sample (p value adjusted on GA ≤0.2) or as relevant factors from the literature. Associations between placenta-mediated pregnancy complications and moderate to severe BPD were then analysed by multivariate logistic regression: model A adjusted for GA because it is the main predictor of BPD, model B additionally adjusted for antenatal potential confounding factors, model C, birth weight z score introduced		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				into the logistic model as a continuous variable to better understand its role in these association, and model D, postnatal events included in the final model. Because most of neonatal respiratory variables are strongly associated with BPD, they were not introduced in multivariable analyses to avoid overadjustment. Results are reported as odds ratios with 95% CI. Significance was set at p<0.05 Statistical analyses involved use of SAS version 9.3 software		
Full citation Torchin, H., Lorthe, E., Goffinet, F., Kayem, G., Subtil, D., Truffert, P., Devisme, L., Benhammou, V., Jarreau, P. H., Ancel, P. Y., Histologic Chorioamnionitis and	**Sample size** n=2601 singleton liveborn neonates at 24 + 0 to 31 +6 weeks of gestation n=2513 singleton liveborn neonates at 24-31 weeks without birth defects/chromosomal abnormalities	**Limitations** **Other information**	**Factors** Histologic chorioamnionitis (with and without funisitis)	**Methodology** **Setting** Please see Monier et al 2017, EPIPAGE-2 study **Definition of risk factor** HCA defined as neutrophil infiltrates in the amnion or	**Results** **Moderate or severe BPD at 36 weeks PMA (whole population)** Adjusted OR (95% CI)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition accounted for.

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Bronchopulmonary Dysplasia in Preterm Infants: The Epidemiologic Study on Low Gestational Ages 2 Cohort, Journal of Pediatrics, 187, 98-104.e3, 2017 **Ref Id** 675323 **Country/ies where the study was carried out** France **Study type** Please see Monier et al 2017, EPIPAGE-2 study **Aim of the study** To investigate the association between histologic chorioamnionitis (HCA) and BPD in preterm infants with gestational age 28-	n=1480 infants alive at 36 weeks analysed for BPD (attrition due to death, missing data, placental examination not realised) **Characteristics** **Preterm labor** **Maternal characteristics** **Clinical chorioamnionitis:** 10.2% (HCA), 0.9% (No HCA) **ANS:** 72.3% (HCA), 72.7% (No HCA) **Caesarean section:** 28.3% (HCA), 38.8% (No HCA) **Neonatal characteristics** **Gestational age, median (IQR), wk:** 27.1 (25.7-29.7) [HCA], 29.1 (27.0-30.7) [No HCA] **Birth weight, median (IQR), g:** 1058 (833-1400) [HCA], 1300 (1010-1568) [No HCA] **Male:** 48.2% (HCA), 61.4% (No HCA)			chorion of the membranes of the chorionic plate. Funisitis was defined as neutrophil infiltrates in the fetal chorionic vessels, the umbilical vein, or umbilical arteries. **Definition of outcome** Moderate BPD was defined as oxygen supplementation for at least 28 days and persistent need for oxygen (FiO2 <30%) at 36 weeks PMA. Severe BPD was defined as oxygen supplementation for at least 28 days and persistent need for oxygen (FiO2 >30%) and/or ventilatory support (invasive ventilation or positive pressure) at 36 weeks PMA **Statistical methods** Categorical variables were compared by chi-squared tests. Continuous variables are described	No HCA: Reference (1) HCA alone: 0.6 (0.4-0.9) HCA + funisitis: 0.5 (0.3-0.8) **Moderate or severe BPD at 36 weeks PMA (24-26 weeks gestation)** Adjusted OR (95% CI) No HCA: Reference (1) HCA alone: 0.6 (0.4-1.1)	**Prognostic factor measurement:** Low risk of bias. All defined and measured. **Outcome measurement:** Low risk of bias. All defined and measured. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA, sex, and ANS **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
31^{+6} weeks, both in a general population and for those born after spontaneous preterm labour and after preterm premature rupture of membranes (pPROM) **Study dates** Please see Monier et al 2017, EPIPAGE-2 study **Source of funding** Please see Monier et al 2017, EPIPAGE-2 study	**Early-onset infection:** 2.6% (HCA), 1.2% (No HCA) **Late-onset bacteraemia:** 23.2% (HCA), 20.7% (No HCA) **pPROM** **Maternal characteristics** **Clinical chorioamnionitis:** 11.5% (HCA), 2.8% (No HCA) **ANS:** 90% (HCA), 93.3% (No HCA) **Caesarean section:** 51.2% (HCA), 67.3% (No HCA) **Neonatal characteristics** **Gestational age, median (IQR), wk:** 28 (26.4-30.1) [HCA], 29.4 (27.6-30.9) [No HCA] **Birth weight, median (IQR), g:** 1090 (860-1410) [HCA], 1250 (1020-1569) [No HCA] **Male:** 53.5% (HCA), 54.2% (No HCA) **Early-onset infection:** 6.3% (HCA), 0.9% (No HCA)			with medians and IQR and were compared by rank-sum tests. Percentages, medians and crude ORs were weighted by recruitment period. Significance was set at $p \leq 0.05$. All infants with available data for placental histology were included in the main analysis. The association between HCA and moderate/severe BPD and death or BPD at 36 weeks PMA were studied by bivariate analyses and logistic regression adjusted for GA, sex, and ANS. Adjusting for GA is customary in observational studies when compared groups have different GA compositions, even if GA is probably more an intermediate than a confounder variable. We also accounted for use of ANS because they substantially reduce the		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Late-onset bacteraemia: 21.1% (HCA), 20.8% (No HCA) **Incidence of BPD:** 11.1% **Inclusion criteria** Please see Monier et al 2017, EPIPAGE-2 study **Exclusion criteria** Please see Monier et al 2017, EPIPAGE-2 studyH			mortality of preterm newborns with gestational age 28-31^{+6} weeks. Rates of missing data ranged from 0% to 3.2% for the variables included in multivariate analyses. Missing data for the outcomes and covariates were considered missing at random. Accordingly, we used multiple imputation by fully conditional specification as implemented in the SAS MI procedure; we included the covariates, the outcome, and the variables potentially predictive of missing values. In total, 25 independent imputed datasets were generated with 30 iterations. Each imputed dataset was analysed and the resulting estimates were pooled according to the Rubin rule. We first analysed the impact of HCA in the whole population whatever the context of		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				delivery, then separately for infants delivered after preterm labour and pPROM, which had the highest prevalence of HCA. The first additional analysis was restricted to infants with complete data for placental histology, outcomes and all covariates. We compared the main perinatal characteristics for infants with and without histology, then performed multiple imputation for missing data concerning placental histology.		
Full citation Viscardi,R.M., Muhumuza,C.K., Rodriguez,A., Fairchild,K.D., Sun,C.C., Gross,G.W., Campbell,A.B., Wilson,P.D., Hester,L.,	**Sample size** n=276 infants enrolled n=262 infants analysed (94.9% followed-up, attrition not accounted for): n=151 BPD n=111 no BPD **Characteristics**	**Limitations** **Other information**	**Factors** Clinical and histologic CA	**Methodology** **Setting** Preterm infants admitted to the NICU at the university of Maryland Medical system and Mercy medical centre between June 1999 to 2002	**Results** **BPD at 36 weeks PMA** Adjusted OR (95% CI) Histologic CA vs no Histologic CA: ≤28 wk GA: 3.63 (1.2-11.4)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Moderate risk of bias. Study participants based on small regional cohort

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Hasday,J.D., Inflammatory markers in intrauterine and fetal blood and cerebrospinal fluid compartments are associated with adverse pulmonary and neurologic outcomes in preterm infants, Pediatric Research, 55, 1009-1017, 2004 **Ref Id** 118163 **Country/ies where the study was carried out** USA **Study type** Prospective, multicentre observation study **Aim of the study** To determine whether inflammatory markers	**Maternal characteristics:** **Preeclampsia:** 10% (BPD), 19% (no BPD) **ANS:** 81% (BPD), 86% (mild BPD) **IUGR:** 4% (BPD), 8% (no BPD) **Neonatal characteristics:** **Gestational age, >28 w:** 9% (BPD), 77% (no BPD) **Birthweight, >1000 g:** 23% (BPD), 86% (no BPD) **Female:** 46% (BPD), 50% (no BPD) **PDA:** 75.4% (BPD), 27.3% (no BPD) **Surfactant:** 89% (BPD), 33% (no BPD) **IMV >7 days:** 77% (BPD), 7% (no BPD) **Incidence of BPD:** 57.6% **Inclusion criteria** Inborn infants who had a GA <33 weeks and birth weight <1501 g and were admitted to the NICU at the university of Maryland Medical system and Mercy			**Definition of risk factor** Clinical chorioamnionitis defined as maternal temperature ≥38 degrees celcius and two of the following: uterine tenderness, malodorous vaginal discharge, fetal tachycardia >160 bpm, or maternal white blood cell count 15,000. Histological chorioamnionitis defined as stage 1: neutrophils in the subchorionic plate, stage 2: neutrophils in the chorionic laevae, stage 3: neutrophils in the chorion laevae and adjacent amnion, stage 4: neutrophil karyorrhexis or eosinophilia of basement membrane without amnionic epithelial sloughing, and stage 5: neutrophils plus amniotic sloughing. **Definition of outcome** Mild BPD defined as supplemental oxygen for 28 days but breathing	>28 wk GA: 5.15 (0.61-43.7)	**Study attrition:** Moderate risk of bias. Although low, attrition not accounted for. **Prognostic factor measurement:** Low risk of bias. All defined and measured. **Outcome measurement:** Low risk of bias. All defined and measured. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: GA, birthweight, surfactant, hypotension <96h of age, PDA, IMV, sepsis (sex found to be not statistically significant variable thus not included as confounder) **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Moderate **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
in these compartments are associated with BPD or cranial ultrasound in infants <33 weeks GA and <1501 g birth weight. **Study dates** 1999-2002 **Source of funding** Not reported	medical centre between June 1999 to 2002 **Exclusion criteria** Congenital brain/neural tube defects or confirmed congenital TORCH infection were excluded			room air at 36 weeks PMA. Moderate BPD need for <30% fraction of inspired oxygen at 36 weeks PMA Severe BPD need for ≥30% fraction of inspired oxygen or positive pressure support at 36 weeks PMA **Statistical methods** The t test was used to compare continuous variables and the chi-squared or Fisher exact test was used to compare categorical variables. Univariate ORs and 95% CI were calculated for all variables for outcomes BPD and CUS abnormalities. Because the range of cytokine data expressed as pg/ml were dichotomised using the median of serum and CSF IL 6 concentrations and serum IL-1 Beta concentrations for the whole sample and the lower cutoff of ELISA		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				sensitivity for TNF-alpha concentrations and CSF IL-1 Beta concentrations. Stepwise logistic regressions were performed to identify the clinical variables associated with each inflammatory variable (histologic chorioamnionitis, fetal vasculitis, white blood cell count, absolute neutrophil count, and serum CSF cytokine concentrations). The contribution of each inflammatory variable to risk for BPD and CUS abnormalities was then evaluated in logistic regression models that included the potential confounders identified in the stepwise analyses. All multivariable analyses were performed with and without stratification by GA ≤28 wk and >28 wk. For determining whether there were interactions of postnatal variables with the inflammatory variables		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				for each outcome, interaction terms were generated and included in regression models. All statistical analyses were performed using STATA.		
Full citation Wyckoff, M. H., Salhab, W. A., Heyne, R. J., Kendrick, D. E., Stoll, B. J., Laptook, A. R., Outcome of extremely low birth weight infants who received delivery room cardiopulmonary resuscitation, Journal of Pediatrics, 160, 239-244.e2, 2012 **Ref Id** 348106 **Country/ies where the study was carried out** USA	**Sample size** n=10,476 preterm infants eligible for follow-up n=8685 preterm infants followed up (outborn infants, major congenital abnormalities, not candidates for CPR and invasive ventilation, and missing data excluded): n=1333 received DR-CPR n=7352 did not receive DR-CPR **Characteristics** **Maternal characteristics:** **ANS:** 43% (DR-CPR), 51% (no DR-CPR) **Caesarean section:** 55% (DR-CPR), 59% (no DR-CPR)	**Limitations** **Other information**	**Factors** Delivery room cardiopulmonary resusitation	**Methodology** **Setting** 19 NICU in academic centres as part of the NRN Generic Database 1996-2002 **Definition of risk factor** DR-CPR was defined as chest compressions + drugs **Definition of outcome** Bronchopulmonary dysplasia defined as oxygen requirement at 36 weeks PMA **Statistical methods** Student t-test, chi-squared analysis, and fisher exact test were used to compare the	**Results** **BPD at 36 weeks PMA** Adjusted OR (95% CI) DR-CPR vs no DR-CPR: 1.34 (1.13-1.59)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Low risk of bias. All attrition accounted for. **Prognostic factor measurement:** Low risk of bias. All defined and measured. **Outcome measurement:** Low risk of bias. All defined and measured. **Study confounding:** Low risk of bias. Models adjusted for appropriate confounders: maternal hypertension, antepartum haemorrhage, ANS,

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Study type Prognostic, population-based cohort study **Aim of the study** To determine whether delivery room cardiopulmonary resusitation independently predicts morbidities and neurodevelopmental impairment in extremely low birth weight infants **Study dates** 1996-2002 **Source of funding** NICHD	**Neonatal characteristics:** **Gestational age, mean (SD), wk:** 25.3 (2) [DR-CPR], 26 (2) [No DR-CPR] **Birthweight, mean (SD), g:** 708 (141) [DR-CPR], 764 (146) [No DR-CPR] **Male:** 52% (DR-CPR), 49% (no DR-CPR) **Race/ethnicity:** **% Black, not hispanic:** 46% (DR-CPR), 43% (no DR-CPR) **% White, hispanic:** 39% (DR-CPR), 39% (no DR-CPR) **% Hispanic:** 12% (DR-CPR), 15% (no DR-CPR) **% Other:** 3% (DR-CPR), 3% (no DR-CPR) **Incidence of BPD:** 58% (DR-CPR), 46% (No DR-CPR) **Inclusion criteria** All inborn infants with birth weight 401-1000 g and estimated GA of 23-30 weeks			demographic and outcome variables between infants with or without DR-CPR. Logistic regression models were developed to determine the independent effects of DR-CPR on neonatal morbidities, mortality and neurodevelopmental outcomes. To explore the prognostic implications of DR-CPR, only covariates antecedent to DR-CPR were included in the logistic model: estimated GA, BW, multiple birth, maternal hypertension, maternal haemorrhage, complete course of ANS within 7 days of birth, mode of delivery, sex, race, and centre of birth. The results are expressed as adjusted OR and 95% CI. Infants with and without follow-up were compared for demographic and neonatal morbidities using student t-test and chi-squared analysis. In order		vaginal birth, GA, BW, sex, and ethnicity. **Statistical analysis and reporting:** Low risk of bias. **Overall risk of bias:** Low **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
	Exclusion criteria Congenital abnormalities and not candidates for CPR and invasive ventilation			to assess the potential impact of a longer versus shorter interval of DR-CPR, a similar set of analyses were performed among infants who received DR-CPR comparing infants with an apgar score at 5 minutes of <2 with those >2. A p value of <0.05 was considered significant. All data were analysed by RTI international		
Full citation Zeitlin, J., El Ayoubi, M., Jarreau, P. H., Draper, E. S., Blondel, B., Kunzel, W., Cuttini, M., Kaminski, M., Gortner, L., Van Reempts, P., Kollee, L., Papiernik, E., Impact of fetal growth restriction on mortality and morbidity in a very preterm birth cohort, Journal of	**Sample size** n=4,525 live births 24-31 weeks GA n=462 <10th percentile n=632 10th-24th percentile n=1120 25th-49th percentile n=1166 50th-74th percentile n=679 75th-89th percentile n=466 ≥90th percentile **Characteristics** **Maternal characteristics:** **ANS:** 83.5% (<10th), 79.9 (10th-24th), 78.2 (25th-	**Limitations** **Other information**	**Factors** SGA	**Methodology** **Setting** The data came from the MOSAIC study, a European population-based study of preterm infants with gestational age 28-31^{+6} weeks in 10 regions in nine European countries in 2003. Regions included: Hesse in Germany, Flanders in Belgium, the eastern region of Denmark, Ile-de-France, Lazio in Italy, east	**Results** **BPD among survivors (oxygen requirement at 36 weeks PMA)** Adjusted OR (95% CI) Reference group: 50th-74th percentile SGA: 6.42 (4.51-9.20)	**Limitations** Based on the prognostic study assessment tool QUIPS **Study participation**: Low risk of bias. **Study attrition:** Medium risk of bias, no explanation or flow chart for the attrition between babies eligible for follow-up and those analysed **Prognostic factor measurement:** Low risk of bias. Risk factors

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Pediatrics, 157, 733-739.e1, 2010 **Ref Id** 675410 **Country/ies where the study was carried out** Europe **Study type** Please see El Ayobi et al 2016, MOSAIC study **Aim of the study** To assess the impact of being SGA on very preterm mortality and morbidity rates by using different birthweight percentile thresholds and whether these effects differ by the cause of the preterm birth	49th), 76.7% (50th-74th), 75.3% (75th-89th), 68.9% (≥90th) **Neonatal characteristics: Birth weight, mean (SD), g:** 763 (212) [<10th], 971 (248) [10th-24th], 1122 (287) [25th-49th], 1283 (320) [50th-74th], 1415 (355) [75th-89th], 1593 (421) [≥90th] **Incidence of BPD:** 11.1% **Inclusion criteria** Please see El Ayobi et al 2016, MOSAIC study **Exclusion criteria** Please see El Ayobi et al 2016, MOSAIC study			central Netherlands, the Wielkopolska, and Lubuskie regions in Poland, the northern region of Portugal and the Northern and Trent regions in the UK. **Method of measurement for risk factor** SGA defined as birthweight <10th percentile by gestational age for boys and girls separately **Definition of outcome** Bronchopulmonary dysplasia defined as need for supplemental oxygen at 36 weeks PMA **Statistical methods** Clinical and healthcare characteristics associated with the birthweight percentiles and the percentile distribution for each pregnancy complication. We then tested for the effect of birthweight percentile		appropriately defined and measured. **Outcome measurement:** Low risk of bias. Outcome measures appropriately defined and measured. **Study confounding:** Low risk of bias. Adjusted for appropriate confounders: GA, sex, multiple pregnancy, ANS, in utero transfer, birth in level 3 unit, and MOSAIC region **Statistical analysis and reporting:** Medium risk of bias. Specific details around methods used for the statistical analyses are lacking. **Overall risk of bias:** Medium **Other information**

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
Study dates Please see El Ayobi et al 2016, MOSAIC study **Source of funding** Please see El Ayobi et al 2016, MOSAIC study				group on mortality and morbidity rates with the chi-squared test. We derived unadjusted and adjusted ORs by using a logistic regression model with the fourth group as the reference (50th-74th percentile). Adjusted estimates controlled for clinical and healthcare factors (GA, sex, multiple pregnancy, ANS, in utero transfer, birth in level 3 unit) and region. The variables selected for inclusion in the model were related to the risks of morbidity and mortality in univariable analyses. We ran these adjusted models on our sample excluding twins to assess whether their inclusion impacted on our conclusions. We then stratified our sample in the two groups of pregnancy complications aforementioned and estimated the adjusted model. Analyses were		

Study details	Participants	Risk Factors	Risk factors	Methods	Outcomes and results	Comments
				carried out with STATA software version 10.0 SE.		

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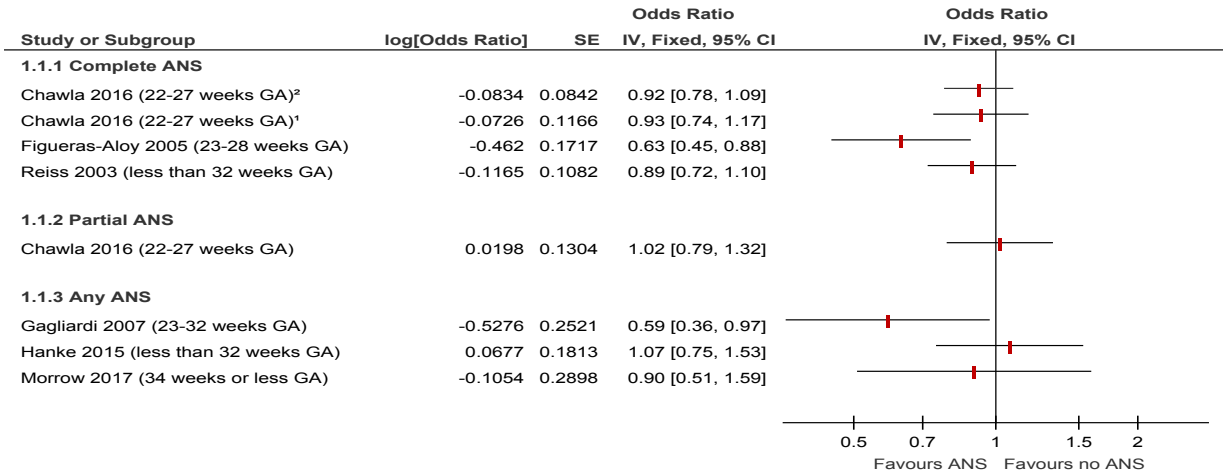
Appendix E – Forest plots

Forest plots for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Risk factors before birth

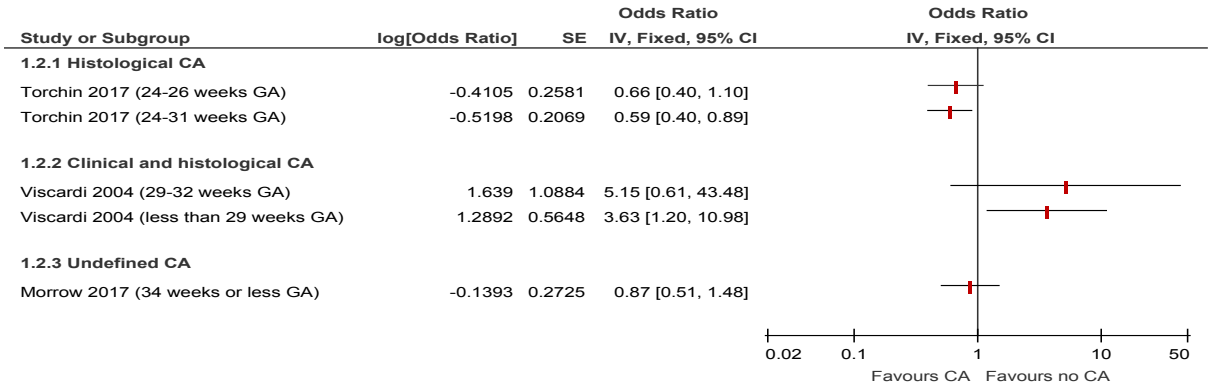
Figure 1: Risk factor: antenatal steroids



ANS: antenatal steroids; CI: confidence interval; GA: gestational age; IV inverse variance

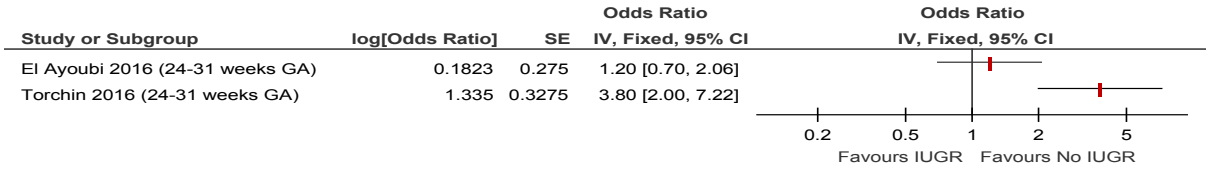
[1]Reference used is No ANS; [2]Reference used is partial ANS

Figure 2: Risk Factor: chorioamnionitis



CA: chorioamnionitis; CI: confidence interval; GA: gestational age; IV: inverse variance

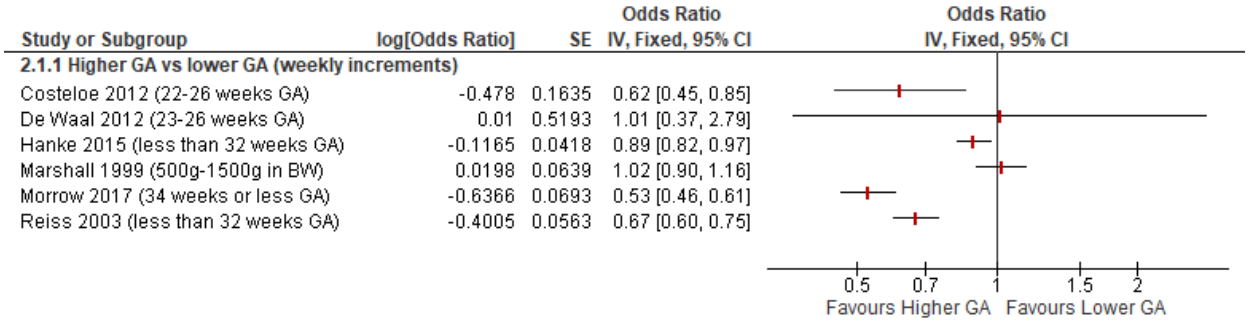
Figure 3: Risk Factor: intrauterine growth restriction



CI: confidence interval; IUGR: Intrauterine growth restriction; GA: gestational age; IV inverse variance

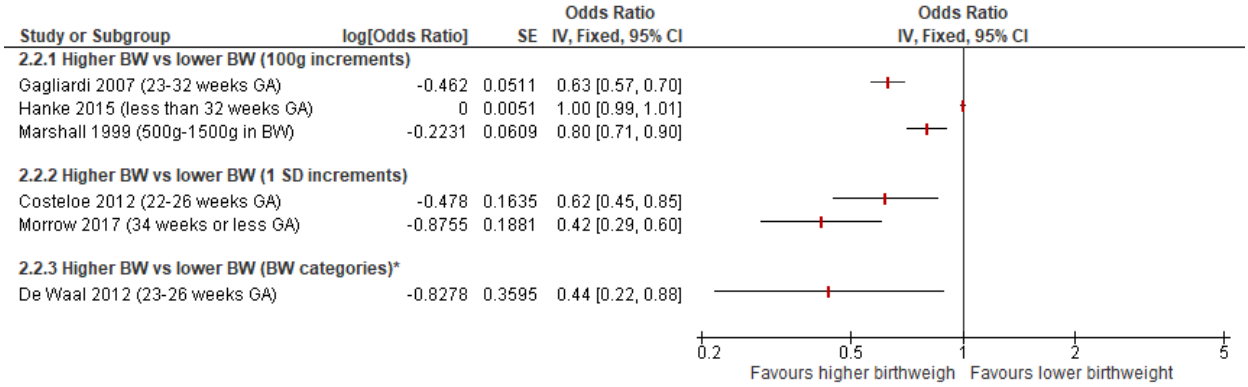
Risk factors at birth

Figure 4: Risk factor: gestational age



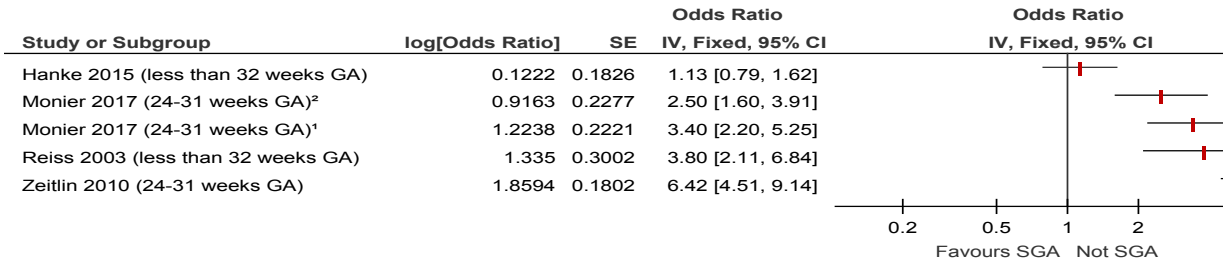
CI: confidence interval; GA: gestational age; IV inverse variance

Figure 5: Risk Factor: birthweight



** Gestational age categories <500g, 501-750g, 751-1000g, >1000g;*

Figure 6: Risk factor: small for gestational age

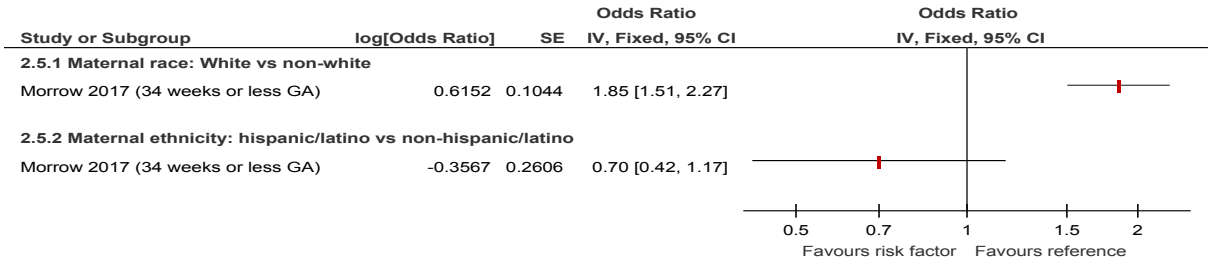


CI: confidence interval; SGA: small for gestational age; GA: gestational age; IV inverse variance

[1]Risk factor defined as small for gestational age + suspected fetal growth restriction

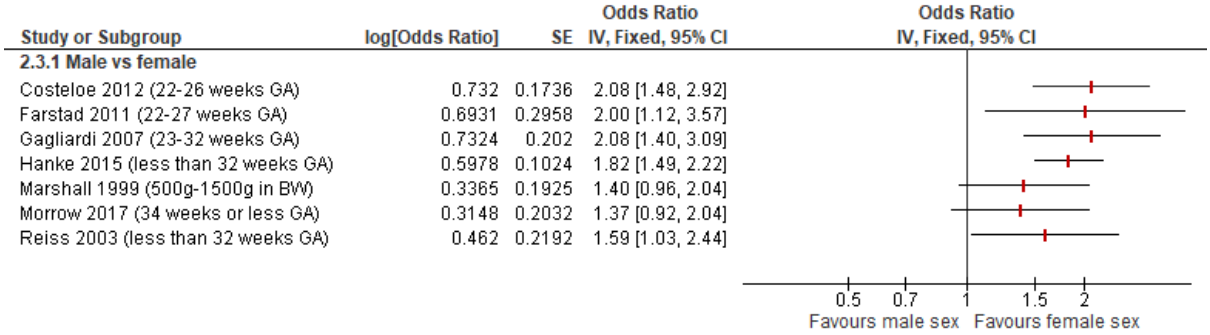
[2]Risk factor defined as small for gestational age + no suspected fetal growth restriction

Figure 7: Risk Factor: ethnicity/race



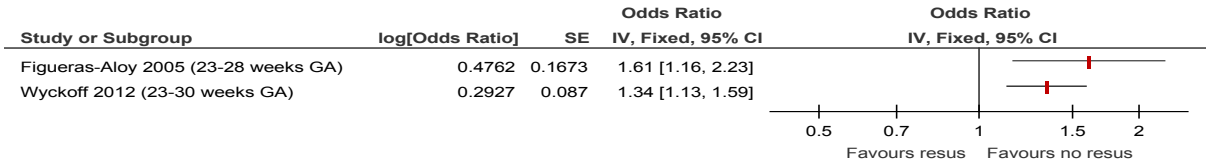
CI: confidence interval; GA: gestational age; IV inverse variance

Figure 8: Risk Factor: gender



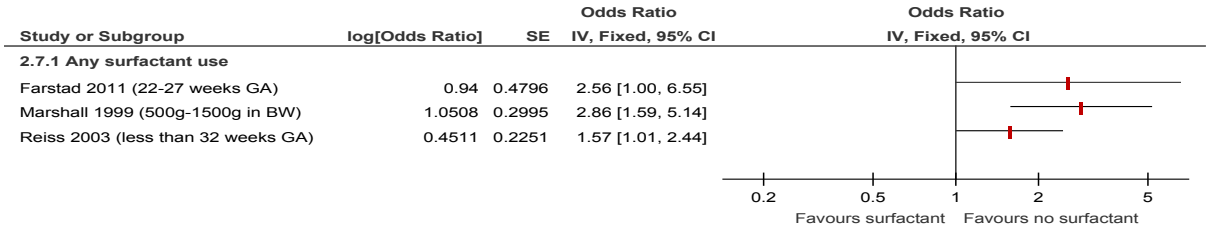
CI: confidence interval; GA: gestational age; IV inverse variance

Figure 9: Risk Factor: resuscitation at birth



CI: confidence interval; GA: gestational age; IV inverse variance

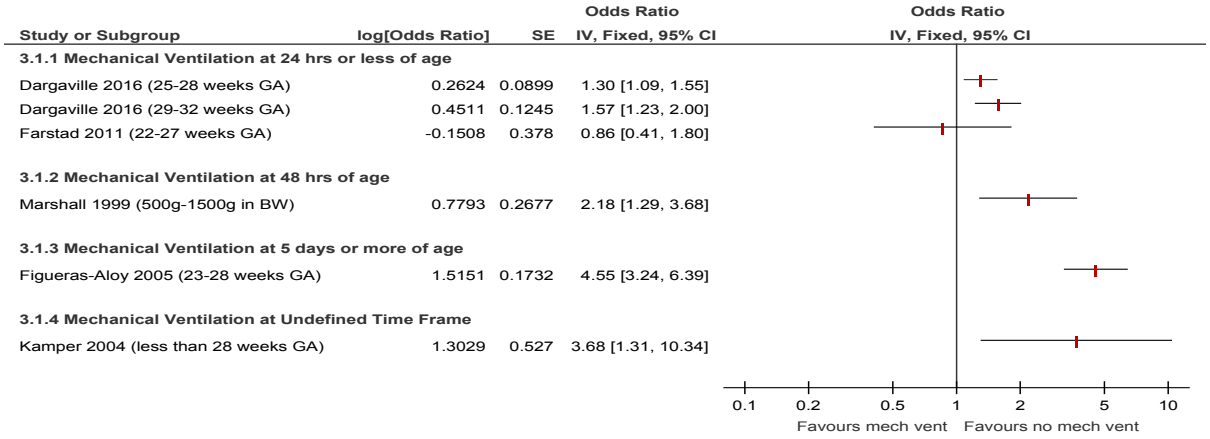
Figure 10: Risk factor: surfactant use



CI: confidence interval; GA: gestational age; IV inverse variance

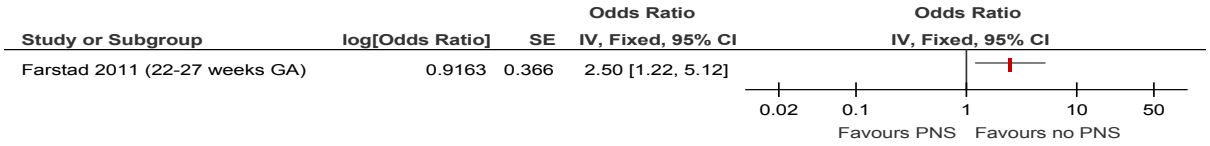
Risk factors after birth

Figure 11: Risk factor: invasive ventilation



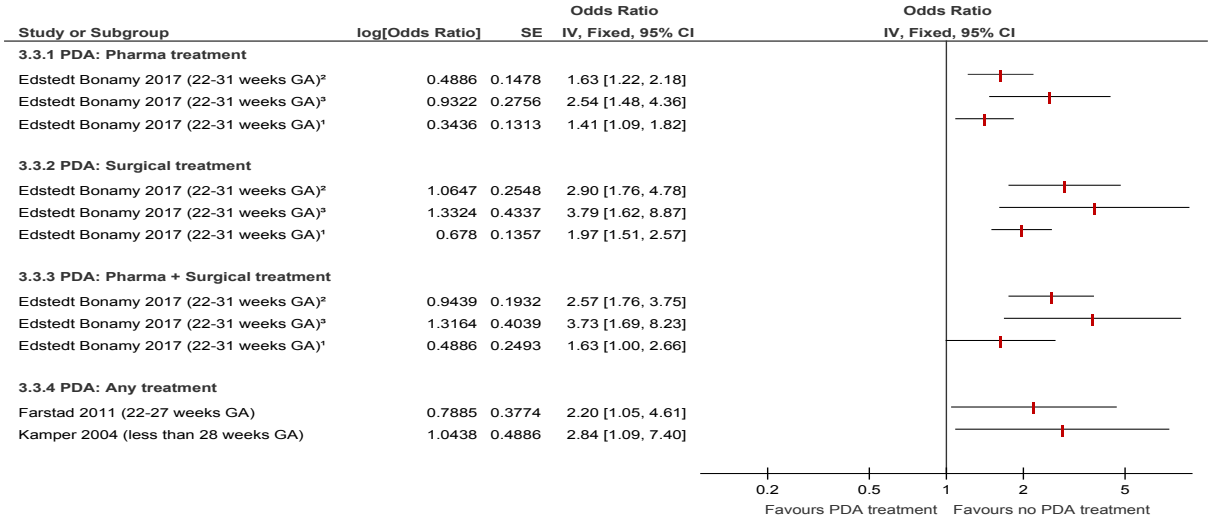
CI: confidence interval; GA: gestational age; IV inverse variance; mech vent: invasive ventilation

Figure 12: Risk factor: postnatal steroids



CI: confidence interval; GA: gestational age; PNS: postnatal steroids

Figure 13: Risk Factor: patent ductus arteriosus (treated)



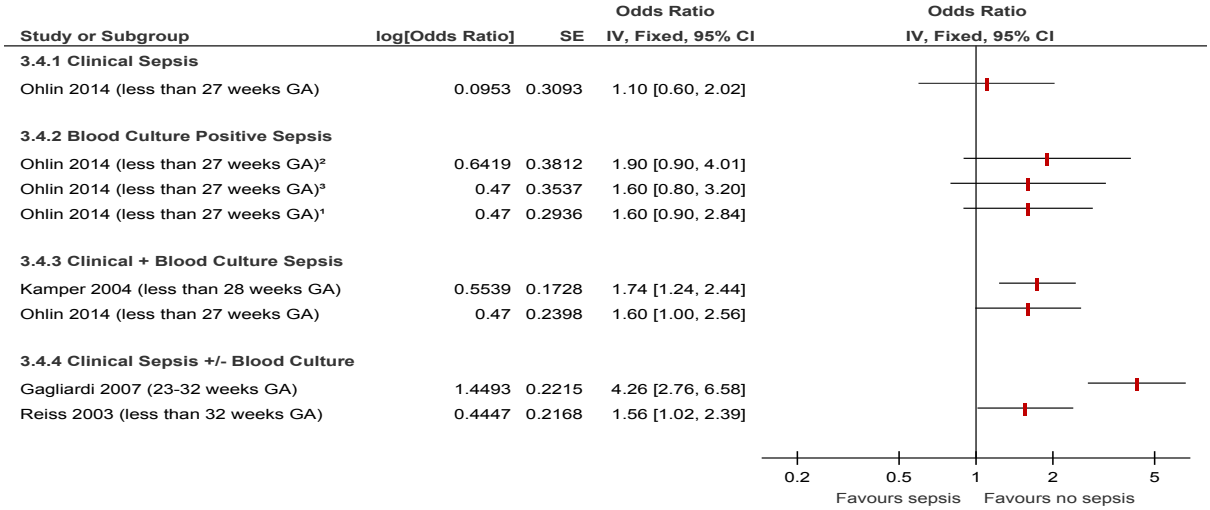
CI: confidence interval; GA: gestational age; IV inverse variance; PDA: patent ductus arteriosus

[1]Risk factor for low patent ductus arteriosus (PDA) treatment proportion

[2]Risk factor for medium patent ductus arteriosus (PDA) treatment proportion

[3]Risk factor for high patent ductus arteriosus (PDA) treatment proportion

Figure 14: Risk factor: sepsis



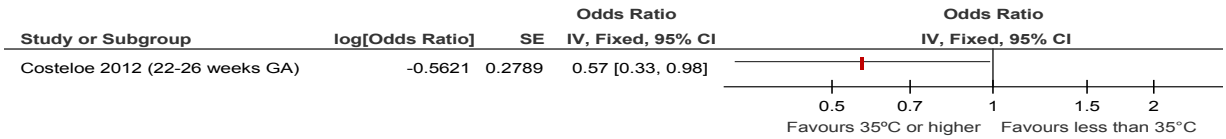
CI: confidence interval; GA: gestational age; IV inverse variance

[1]Risk factor defined as coagulase-negative staphylococci without other bacteria

[2]Risk factor defined as coagulase-negative staphylococci with other bacteria

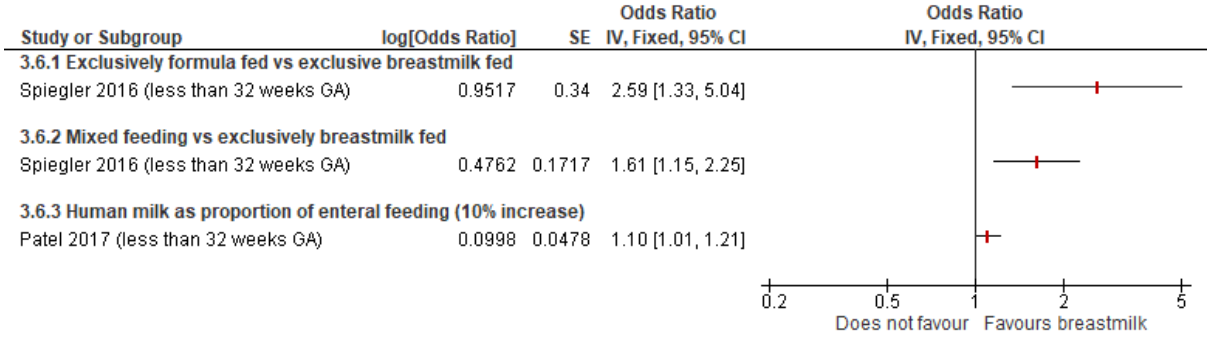
[3]Risk factor defined as other bacteria

Figure 15: Risk factor: thermoregulation



CI: confidence interval; GA: gestational age

Figure 16: Risk Factor: breastmilk feeding



CI: confidence interval; GA: gestational age; IV inverse variance

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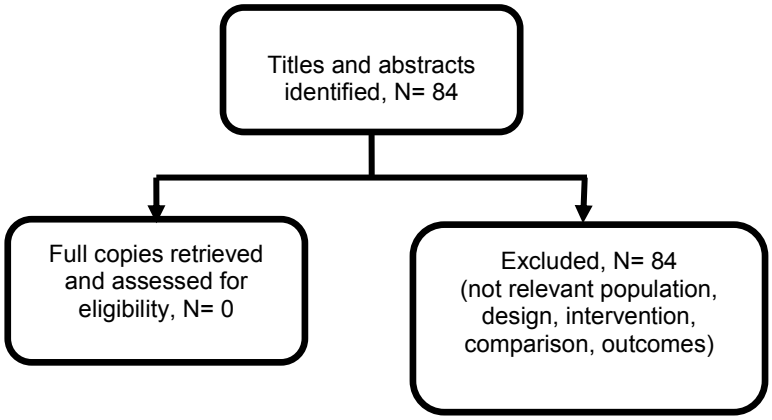
Appendix F – GRADE tables

GRADE tables for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Not applicable to this review.

Appendix G – Economic evidence study selection

Economic evidence study selection for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?



Appendix H – Economic evidence tables

Economic evidence tables for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

No economic evidence was identified for this review.

1 Appendix I – Economic evidence profiles

2 Economic evidence profiles for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

3 No economic evidence was identified for this review.

Appendix J – Economic analysis

Economic analysis for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

No economic analysis was undertaken for this review.

Appendix K – Excluded studies

Excluded studies for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

Clinical studies

Excluded studies - Observational studies	
Study	**Reason for Exclusion**
Abele-Horn, M., Genzel-Boroviczeny, O., Uhlig, T., Zimmermann, A., Peters, J., Scholz, M., Ureaplasma urealyticum colonization and bronchopulmonary dysplasia: A comparative prospective multicentre study, European Journal of Pediatrics, 157, 1004-1011, 1998	Sample size <100
Abele-Horn, M., Peters, J., Genzel-Boroviczeny, O., Wolff, C., Zimmermann, A., Gottschling, W., Vaginal Ureaplasma urealyticum colonization: influence on pregnancy outcome and neonatal morbidity, Infection, 25, 286-91, 1997	Study design not of interest for review - single centre case control study
Adrouche-Amrani, L., Green, R. S., Gluck, K. M., Lin, J., Failure of a repeat course of cyclooxygenase inhibitor to close a PDA is a risk factor for developing chronic lung disease in ELBW infants, BMC Pediatrics, 12, 10, 2012	Study design not of interest for review - single centre retrospective review
Afjeh, S. A., Sabzehei, M. K., Shariati, M. K., Shamshiri, A. R., Esmaili, F., Evaluation of initial respiratory support strategies in VLBW Neonates with RDS, Archives of Iranian Medicine, 20, 158-164, 2017	Country of study not OECD - Iran
Ahn,H.M., Park,E.A., Cho,S.J., Kim,Y.J., Park,H.S., The association of histological chorioamnionitis and antenatal steroids on neonatal outcome in preterm infants born at less than thirty-four weeks' gestation, Neonatology, 102, 259-264, 2012	Study design not relevant for review - single centre prospective cohort
Ali,Z., Schmidt,P., Dodd,J., Jeppesen,D.L., Predictors of bronchopulmonary dysplasia and pulmonary hypertension in newborn children, Danish Medical Journal, 60, A4688-, 2013	Study design not of interest for review - retrospective regional cohort study
Allen, M. C., Donohue, P. K., Dusman, A. E., The limit of viability--neonatal outcome of infants born at 22 to 25 weeks' gestation, New England Journal of Medicine, 329, 1597-601, 1993	Outside date range for study inclusion - 1988-1991
Aly, H., Massaro, A. N., Patel, K., El-Mohandes, A. A., Is it safer to intubate premature infants in the delivery room?, Pediatrics, 115, 1660-1665, 2005	Study design not of interest for review - single centre retrospective study
Ballard, A. R., Mallett, L. H., Pruszynski, J. E., Cantey, J. B., Chorioamnionitis and subsequent bronchopulmonary dysplasia in very-low-birth weight infants: A 25-year cohort, Journal of Perinatology, 36, 1045-1048, 2016	Study design not of interest for review - single centre prospective review

Excluded studies - Observational studies	
Banks,B.A., Cnaan,A., Morgan,M.A., Parer,J.T., Merrill,J.D., Ballard,P.L., Ballard,R.A., Multiple courses of antenatal corticosteroids and outcome of premature neonates. North American Thyrotropin-Releasing Hormone Study Group, American Journal of Obstetrics and Gynecology, 181, 709-717, 1999	Study design not of interest - multi centre Retrospective study
Bardin,C., Zelkowitz,P., Papageorgiou,A., Outcome of small-for-gestational age and appropriate-for-gestational age infants born before 27 weeks of gestation, Pediatrics, 100, E4-, 1997	Outside date range for study inclusion - 1983-1992
Beeby, P., Chan, D., Henderson-Smart, D., Improved outcomes following the introduction of surfactant to an Australian neonatal unit, Journal of Paediatrics & Child HealthJ Paediatr Child Health, 32, 257-60, 1996	Study design not of interest - retrospective single centre study
Been,J.V., Rours,I.G., Kornelisse,R.F., Jonkers,F., de Krijger,R.R., Zimmermann,L.J., Chorioamnionitis alters the response to surfactant in preterm infants, Journal of Pediatrics, 156, 10-15, 2010	Study design not of interest for review - single centre prospective study
Benitez, A., Schapira, I. T., Aspres, N., Fels, V., Galindo, A., Larguia, M., Distanced evolution of premature neonates born before the twenty-ninth week of gestation: Morbidity, growth and development during the first 2 years of life, Saludarte, 2, 19-31, 2002	Country outside of OECD - Argentina
Berger, J., Mehta, P., Bucholz, E., Dziura, J., Bhandari, V., Impact of early extubation and reintubation on the incidence of bronchopulmonary dysplasia in neonates, American Journal of Perinatology, 31, 1063-72, 2014	Study design not of interest for review - retrospective single centre study
Bhandari, V., Finer, N. N., Ehrenkranz, R. A., Saha, S., Das, A., Walsh, M. C., Engle, W. A., VanMeurs, K. P., Eunice Kennedy Shriver National Institute of Child, Health, Human Development Neonatal Research, Network, Synchronized nasal intermittent positive-pressure ventilation and neonatal outcomes, Pediatrics, 124, 517-26, 2009	Study design not of interest for review - retrospective multicentre study. Study also assesses the difference between 2 non-invasive ventilation techniques, which is not of interest for this review
Bhering, C. A., Mochdece, C. C., Moreira, M. E. L., Rocco, J. R., Sant'Anna, G. M., Bronchopulmonary dysplasia prediction model for 7-day-old infants, Jornal de Pediatria, 83, 163-170, 2007	Study design not of interest for review - retrospective cohort study
Bickle Graz, M., Tolsa, J. F., Fischer Fumeaux, C. J., Being Small for Gestational Age: Does it Matter for the Neurodevelopment of Premature Infants? A Cohort Study, PLoS ONE [Electronic Resource], 10, e0125769, 2015	Study design not of interest for review - single centre prospective study

Excluded studies - Observational studies	
Bose, C., Laughon, M., Allred, E. N., Van Marter, L. J., O'Shea, T. M., Ehrenkranz, R. A., Fichorova, R., Leviton, A., Elgan Study, Investigators, Blood protein concentrations in the first two postnatal weeks that predict bronchopulmonary dysplasia among infants born before the 28th week of gestation, Pediatric Research, 69, 347-53, 2011	Risk factor not of interest for review - blood protein concentrations of pro-inflammatory cytokines
Bose, C., Van Marter, L. J., Laughon, M., O'Shea, T. M., Allred, E. N., Karna, P., Ehrenkranz, R. A., Boggess, K., Leviton, A., Fetal growth restriction and chronic lung disease among infants born before the 28th week of gestation, Pediatrics, 124, e450-8, 2009	Gestational age adjusted for as a confounder, but gender not adjusted for.
Chang, W. C., Jong, H. H., Jae, W. S., Sun, Y. K., Eun, K. L., Sung, S. K., Yun, S. C., Won, S. P., Son, M. S., Decreasing incidence of chronic lung disease despite the gradual reduction of postnatal dexamethasone use in very low birth weight infants, Journal of Korean Medical Science, 19, 514-518, 2004	Study design not of interest for review - single centre study
Chawla, S., Natarajan, G., Rane, S., Thomas, R., Cortez, J., Lua, J., Outcomes of extremely low birth weight infants with varying doses and intervals of antenatal steroid exposure, Journal of Perinatal Medicine, 38, 419-23, 2010	Study design not of interest for review - single centre retrospective study
Check,J., Gotteiner,N., Liu,X., Su,E., Porta,N., Steinhorn,R., Mestan,K.K., Fetal growth restriction and pulmonary hypertension in premature infants with bronchopulmonary dysplasia, Journal of Perinatology, 33, 553-557, 2013	Outcome assessed not of interest for review - pulmonary hypertension at 36 weeks
Choi, C. W., Hwang, J. H., Shim, J. W., Ko, S. Y., Lee, E. K., Kim, S. S., Chang, Y. S., Park, W. S., Shin, S. M., Decreasing incidence of chronic lung disease despite the gradual reduction of postnatal dexamethasone use in very low birth weight infants, Journal of Korean Medical Science, 19, 514-8, 2004	Study design not of interest for review - single centre retrospective review
Choi,C.W., Kim,B.I., Park,J.D., Koh,Y.Y., Choi,J.H., Choi,J.Y., Risk factors for the different types of chronic lung diseases of prematurity according to the preceding respiratory distress syndrome, Pediatrics International, 47, 417-423, 2005	Study design not of interest for review - single centre prospective study
Chong,E., Greenspan,J., Kirkby,S., Culhane,J., Dysart,K., Changing use of surfactant over 6 years and its relationship to chronic lung disease, Pediatrics, 122, e917-e921, 2008	Study design not of interest for review - retrospective study
Chorne, N., Leonard, C., Piecuch, R., Clyman, R. I., Patent ductus arteriosus and its treatment as risk factors for neonatal and	Analyses adjusted for gestational age, but not sex

Excluded studies - Observational studies	
neurodevelopmental morbidity, Pediatrics, 119, 1165-74, 2007	
Clark, R. H., The epidemiology of respiratory failure in neonates born at an estimated gestational age of 34 weeks or more, Journal of Perinatology, 25, 251-257, 2005	Study design not of interest for review - prospective single centre study
Colaizy,T.T., Morris,C.D., Lapidus,J., Sklar,R.S., Pillers,D.A., Detection of ureaplasma DNA in endotracheal samples is associated with bronchopulmonary dysplasia after adjustment for multiple risk factors, Pediatric Research, 61, 578-583, 2007	Risk factor not of interest in review - ureaplasma in endotracheal swabs of preterm babies
Collard,K.J., Godeck,S., Holley,J.E., Quinn,M.W., Pulmonary antioxidant concentrations and oxidative damage in ventilated premature babies, Archives of Disease in Childhood: Fetal and Neonatal Edition, 89, F412-F416, 2004	Risk factor not of interest in review - pulmonary antioxidant concentrations
Corchia, C., Da Fre, M., Di Lallo, D., Gagliardi, L., Macagno, F., Carnielli, V., Miniaci, S., Cuttini, M., Mortality and major morbidities in very preterm infants born from assisted conception or naturally conceived: results of the area-based ACTION study, BMC Pregnancy & ChildbirthBMC Pregnancy Childbirth, 14, 307, 2014	Risk factor not of interest for review - assisted conception
Corchia, C., Spagnolo, A., de Vonderweid, U., Zorzi, C., Chiandotto, V., Chiappe, S., Colarizi, P., Didato, M. A., Paludetto, R., Clinical approach to the analysis of causes of death in the first two years of life of very-low-birthweight infants in a multicentre setting, Paediatric and Perinatal Epidemiology, 11, 44-56, 1997	Study pre-1990
Cordero,L., Ayers,L.W., Davis,K., Neonatal airway colonization with gram-negative bacilli: association with severity of bronchopulmonary dysplasia, Pediatric Infectious Disease Journal, 16, 18-23, 1997	Study design not of interest for review - single centre study
Costakos, D., Allen, D., Krauss, A., Ruiz, N., Fluhr, K., Stouvenel, A., Paxson, C., Surfactant therapy prior to the interhospital transport of preterm infants, American Journal of Perinatology, 13, 309-16, 1996	Study design not of interest for review - single centre retrospective review
Craigo,S.D., Beach,M.L., Harvey-Wilkes,K.B., D'Alton,M.E., Ultrasound predictors of neonatal outcome in intrauterine growth restriction, American Journal of Perinatology, 13, 465-471, 1996	Study design not of interest for review - retrospective single centre study Time period pre-1990
Cunha,G.S., Mezzacappa-Filho,F., Ribeiro,J.D., Risk factors for bronchopulmonary dysplasia in very low birth weight newborns treated with mechanical ventilation in the first week of life, Journal of Tropical Pediatrics, 51, 334-340, 2005	Inappropriate sample size - <100 participants in cohort

Excluded studies - Observational studies	
Dani, C., Poggi, C., Barp, J., Berti, E., Fontanelli, G., Mean platelet volume and risk of bronchopulmonary dysplasia and intraventricular hemorrhage in extremely preterm infants, American Journal of Perinatology, 28, 551-556, 2011	Study design not of interest for review - single centre retrospective review
De Dooy, J., Ieven, M., Stevens, W., De Clerck, L., Mahieu, L., High levels of CXCL8 in tracheal aspirate samples taken at birth are associated with adverse respiratory outcome only in preterm infants younger than 28 weeks gestation, Pediatric Pulmonology, 42, 193-203, 2007	Univariate analysis not adjusting for confounders
De Klerk,A.M., De Klerk,R.K., Nasal continuous positive airway pressure and outcomes of preterm infants, Neonatal Intensive Care, 14, 58-65, 2001	Study design not of interest for review - single centre retrospective study
Del Vecchio, A., Henry, E., D'Amato, G., Cannuscio, A., Corriero, L., Motta, M., Christensen, R. D., Instituting a program to reduce the erythrocyte transfusion rate was accompanied by reductions in the incidence of bronchopulmonary dysplasia, retinopathy of prematurity and necrotizing enterocolitis, Journal of Maternal-Fetal and Neonatal Medicine, 26, 77-79, 2013	Risk factor not of interest for review - erythrocyte transfusion rate
Dessardo, N. S., Mustac, E., Dessardo, S., Banac, S., Peter, B., Finderle, A., Maric, M., Haller, H., Chorioamnionitis and chronic lung disease of prematurity: a path analysis of causality, American Journal of Perinatology, 29, 133-40, 2012	Study design not of interest for review - causal relationship rather than risk assessed
Deulofeut, R., Dudell, G., Sola, A., Treatment-by-gender effect when aiming to avoid hyperoxia in preterm infants in the NICU, Acta PaediatricaActa Paediatr, 96, 990-4, 2007	Analyses not adjusted for confounders
Dorling,J., D'Amore,A., Salt,A., Seward,A., Kaptoge,S., Halliday,S., Ahluwalia,J., Data collection from very low birthweight infants in a geographical region: Methods, costs, and trends in mortality, admission rates, and resource utilisation over a five-year period, Early Human Development, 82, 117-124, 2006	Risk factors not adjusted for confounders
Durrmeyer, X., Kayem, G., Sinico, M., Dassieu, G., Danan, C., Decobert, F., Perinatal risk factors for bronchopulmonary dysplasia in extremely low gestational age infants: a pregnancy disorder-based approach, Journal of Pediatrics, 160, 578-583.e2, 2012	Study design not of interest - single centre retrospective study
Dyke,M.P., Grauaug,A., Kohan,R., Ott,K., Andrews,R., Ureaplasma urealyticum in a neonatal intensive care population, Journal of Paediatrics and Child Health, 29, 295-297, 1993	Study dates pre-1990

Excluded studies - Observational studies	
Egreteau, L., Pauchard, J. Y., Semama, D. S., Matis, J., Liska, A., Romeo, B., Cneude, F., Hamon, I., Truffert, P., Chronic oxygen dependency in infants born at less than 32 weeks' gestation: incidence and risk factors, Pediatrics, 108, E26, 2001	Gestational age adjusted for as a confounder, but gender not adjusted for.
El-Khuffash, A., James, A. T., Corcoran, J. D., Dicker, P., Franklin, O., Elsayed, Y. N., Ting, J. Y., Sehgal, A., Malikiwi, A., Harabor, A., Soraisham, A. S., McNamara, P. J., A Patent Ductus Arteriosus Severity Score Predicts Chronic Lung Disease or Death before Discharge, Journal of Pediatrics, 167, 1354-1361.e2, 2015	Outcome not of interest for review - composite outcome of death/BPD
Eriksson, L., Haglund, B., Ewald, U., Odlind, V., Kieler, H., Short and long-term effects of antenatal corticosteroids assessed in a cohort of 7,827 children born preterm, Acta Obstetricia et Gynecologica Scandinavica, 88, 933-8, 2009	Study commenced pre-1990
Eriksson, L., Haglund, B., Odlind, V., Altman, M., Kieler, H., Prenatal inflammatory risk factors for development of bronchopulmonary dysplasia, Pediatric Pulmonology, 49, 665-72, 2014	Risk factors not of interest for review - prenatal inflammatory risk factors
Eriksson,L., Haglund,B., Odlind,V., Altman,M., Ewald,U., Kieler,H., Perinatal conditions related to growth restriction and inflammation are associated with an increased risk of bronchopulmonary dysplasia, Acta Paediatrica, 104, 259-263, 2015	Analyses accounted for gestational age, but not sex
Express Group, Fellman, V., Hellstrom-Westas, L., Norman, M., Westgren, M., Kallen, K., Lagercrantz, H., Marsal, K., Serenius, F., Wennergren, M., One-year survival of extremely preterm infants after active perinatal care in Sweden, JAMAJama, 301, 2225-33, 2009	Outcome not of interest for review - mortality not BPD
Farstad, T., Bratlid, D., Incidence and prediction of bronchopulmonary dysplasia in a cohort of premature infants, Acta Paediatrica, International Journal of Paediatrics, 83, 19-24, 1994	Study design not of interest for this review - single centre prospective study
Faust, K., Hartel, C., Preus, M., Rabe, H., Roll, C., Emeis, M., Wieg, C., Szabo, M., Herting, E., Gopel, W., Neocirculation, project, the German Neonatal, Network, Short-term outcome of very-low-birthweight infants with arterial hypotension in the first 24 h of life, Archives of Disease in Childhood Fetal & Neonatal EditionArch Dis Child Fetal Neonatal Ed, 100, F388-92, 2015	Study design not of interest for review - retrospective cohort analysis
Flannery, D. D., O'Donnell, E., Kornhauser, M., Dysart, K., Greenspan, J., Aghai, Z. H., Continuous Positive Airway Pressure versus Mechanical Ventilation on the First Day of Life in	Study design not of interest for review - restrospective study

Excluded studies - Observational studies	
Very Low-Birth-Weight Infants, American Journal of Perinatology, 33, 939-944, 2016	
Floros, J., Londono, D., Gordon, D., Silveyra, P., Diangelo, S. L., Viscardi, R. M., Worthen, G. S., Shenberger, J., Wang, G., Lin, Z., Thomas, N. J., IL-18R1 and IL-18RAP SNPs may be associated with bronchopulmonary dysplasia in African-American infants, Pediatric Research, 71, 107-114, 2012	Risk factor not of interest for review - genotype analysis
Fonseca,E., Georgiev,S.G., Gorenflo,M., Loukanov,T.S., Patent ductus arteriosus in preterm infants: Benefits of early surgical closure, Asian Cardiovascular and Thoracic Annals, 22, 391-396, 2014	Study population <100
Friedman, C. A., Menchaca, R. C., Baker, M. C., Rivas, C. K., Laberge, R. N., Rios, E. H., Haider, S. H., Romero, E. J., Eason, E. B., Fraley, J. K., Woldesenbet, M., Bubble nasal CPAP, early surfactant treatment, and rapid extubation are associated with decreased incidence of bronchopulmonary dysplasia in very-low-birth-weight newborns: efficacy and safety considerations, Respiratory Care, 58, 1134-42, 2013	Study design not of interest for this review - single centre retrospective review
Furman,B., Shoham-Vardi,I., Bashiri,A., Erez,O., Mazor,M., Preterm premature rupture of membranes is not an independent risk factor for neonatal morbidity, Journal of Maternal-Fetal Medicine, 10, 107-111, 2001	Study design not of interest for review - single centre study
Gagliardi, L., Rusconi, F., Bellu, R., Zanini, R., Mirri, G., Condo, M., Turoli, D., Vanzati, M., Mosca, F., De Nisi, G., Polacco, P., Villa, E., Barbarini, M., Fasolato, V., Franco, C., Contiero, R., Ellero, S., Cattarossi, L., Abbiati, L., Borroni, C., Prandi, G., Fabris, C., Vielmi, F., Borgione, S., Agosti, M., Tandoi, F., Guidali, R., De Curtis, M., Tozzi, C., Lucchini, R., Battaglioli, M., Lista, G. L., Introvini, P., Ferrari, F., Gallo, C., Bellante, E., Bottura, C., Zeringyte, A., Pasquali, F., Boccacci, S., Latini, G., Giannuzzi, R., Martinelli, S., Brunelli, A., Di Nunzio, M. L., Vendemmiati, A., Carli, G., Bordigato, M. A., Filippone, M., Meneghesso, D., Romeo, N., Mammoliti, P., Mastretta, E., Barberis, L., Farina, D., Gancia, G., Dalmazzo, C., Napolitano, M., Messina, F., Villa Betania, N., Magaldi, R., Rinaldi, M., Litta, R., Lago, P., Zanardo, V., Chiandetti, L., Visentin, S., Presta, G., Cella, D., Poggiani, C., Ferrari, D., Parati, S., Lombardo, F., Grigorio, R., Barera, G., Bove, M., Poloniato, A., Burgio, G., Sala, E., Barberi, I., Tiralongo, V., Arco, A., Mazzeo, D., Dani, C., Pratesi, S., Mignatti, V., Ancora, G., Faldella, G., Grandi, S., Locatelli, C., Stronati, M., Perotti, G., Chirico, G., Migliori, C., De Marini, S., Forleo, V., Paludetto, R.,	Risk factor not of interest for review - focuses on competing risk factors of hypertensive disorders versus chorioamnionitis

Excluded studies - Observational studies	
Capasso, L., Mansi, G., Raimondi, F., Bona, G., Stucchi, I., Savastio, S., Ferrero, F., Parola, A., Padovani, E. M., Viviani, E., Pecoraro, L., Agostino, R., Gizzi, C., Massenzi, L., Messner, H., Staffler, A., Salvia, G., Esposito, L., Forziati, V., Latorre, G., Sandri, F., Alati, S., Demarca, F., Lombardi, O., Costabile, C. D., Scarpelli, G., Cavalli, C., Volante, E., Moretti, S., Ganguzza, O., Spinella, B., Haass, C., Scapillati, E., Consigli, C., Gatta, A., Quitadamo, P., Boldrini, A., Vuerich, M., Sigali, E., Fiorini, P., Petrucci, L., Moroni, M., Meyer, F., Bragetti, P., Casucci, P., Minelli, L., Mezzetti, D., Orfeo, L., De Luca, M. G., Laforgia, N., Grassi, A., Dotta, A., Savignoni, F., Bagnoli, F., De Felice, C., Badii, S., Biasini, A., Belluzzi, A., Stella, M., Romagnoli, C., Zecca, E., Barone, G., Colleselli, P., Vecchiato, L., Nicolussi, S., Giliberti, P., Chello, G., Rojo, S., De Vivo, M., Giovanettoni, C., Colnaghi, C. A., Manfredini, V., Verucci, E., Placidi, G., Belloni, C., Carrera, G., Zambetti, C., Biban, P., Serra, A., Sacco, F., Vetrano, G., Furcolo, G., Pasquariello, B., Falco, L., Ausanio, G., Bernardo, I., Capasso, A., Marchesano, G., Nosari, N., Sarnelli, P., Ciraci, G., Merazzi, D., Gazzolo, D., Temperini, F., Sabatini, M., Colivicchi, M., Del Vecchio, A., Tarantino, M., Gargano, G., Pedori, S., Bellettato, M., Pesavento, R., Cesaro, A., Scollo, M., Mondello, I., Pugliese, A., Iervolino, C., Corsello, G., Giuffre, M., Betta, P., Romeo, M. G., Saporito, A., Leone, M. G., Rodono, A., Franceschi, A., Risso, F. M., Carpentieri, M., Vecchiano, T., Cigliano, M. P., Paolillo, P., Picone, S., Marra, A., Rossetti, G., Testa, T., Del Cuore, F., Crescenzi, F., Poloni, G., Russo, M. C., Nigro, F., Tina, G. L., Brindisino, P., Gurrado, R., Felice, M., Formica, I., Association of maternal hypertension and chorioamnionitis with preterm outcomes, Pediatrics, 134, e154-e161, 2014	
Gagliardi, L., Rusconi, F., Da Fre, M., Mello, G., Carnielli, V., Di Lallo, D., Macagno, F., Miniaci, S., Corchia, C., Cuttini, M., Pregnancy disorders leading to very preterm birth influence neonatal outcomes: Results of the population-based ACTION cohort study, Pediatric Research, 73, 794-801, 2013	Risk factor not of interest for review - disorders of placentation, which is a composite risk factor of hypertension and inter uterine growth restriction
Ghezzi,F., Gomez,R., Romero,R., Yoon,B.H., Edwin,S.S., David,C., Janisse,J., Mazor,M., Elevated interleukin-8 concentrations in amniotic fluid of mothers whose neonates subsequently develop bronchopulmonary dysplasia, European Journal of Obstetrics Gynecology and Reproductive Biology, 78, 5-10, 1998	Risk factors not adjusted for confounders

Excluded studies - Observational studies	
Ghirardello, S., Dusi, E., Cortinovis, I., Villa, S., Fumagalli, M., Agosti, M., Milani, S., Mosca, F., Effects of Red Blood Cell Transfusions on the Risk of Developing Complications or Death: An Observational Study of a Cohort of Very Low Birth Weight Infants, American Journal of Perinatology, 34, 88-95, 2017	Study design not of interest - propspective single centre study
Giapros, V., Drougia, A., Krallis, N., Theocharis, P., Andronikou, S., Morbidity and mortality patterns in small-for-gestational age infants born preterm, Journal of Maternal-Fetal & Neonatal Medicine, 25, 153-7, 2012	Study design not of interest for review - retrospective multicentre cohort study
Gittermann, M. K., Fusch, C., Gittermann, A. R., Regazzoni, B. M., Moessinger, A. C., Early nasal continuous positive airway pressure treatment reduces the need for intubation in very low birth weight infants, European Journal of Pediatrics, 156, 384-8, 1997	Study design not of interest - single centre retrospective study
Goldenberg,R.L., Andrews,W.W., Goepfert,A.R., Faye-Petersen,O., Cliver,S.P., Carlo,W.A., Hauth,J.C., The Alabama Preterm Birth Study: umbilical cord blood Ureaplasma urealyticum and Mycoplasma hominis cultures in very preterm newborn infants, American Journal of Obstetrics and Gynecology, 198, 43-45, 2008	Risk factor not of interest in review - ureaplasma isolated in umbilical cord blood of preterm babies
Gonzalez, A., Sosenko, I. R., Chandar, J., Hummler, H., Claure, N., Bancalari, E., Influence of infection on patent ductus arteriosus and chronic lung disease in premature infants weighing 1000 grams or less, Journal of Pediatrics, 128, 470-8, 1996	Study design not of interest for review - prospective single centre study
Gopel, W., Kribs, A., Hartel, C., Avenarius, S., Teig, N., Groneck, P., Olbertz, D., Roll, C., Vochem, M., Weller, U., von der Wense, A., Wieg, C., Wintgens, J., Preuss, M., Ziegler, A., Roth, B., Herting, E., German Neonatal, Network, Less invasive surfactant administration is associated with improved pulmonary outcomes in spontaneously breathing preterm infants, Acta PaediatricaActa Paediatr, 104, 241-6, 2015	Study assesses the difference between LISA and non-LISA surfactant, which is not of interest for this review
Gortner, L., Misselwitz, B., Milligan, D., Zeitlin, J., Kollee, L., Boerch, K., Agostino, R., Van Reempts, P., Chabernaud, J. L., Breart, G., Papiernik, E., Jarreau, P. H., Carrapato, M., Gadzinowski, J., Draper, E., members of the, Mosaic Research Group, Rates of bronchopulmonary dysplasia in very preterm neonates in Europe: results from the MOSAIC cohort, Neonatology, 99, 112-7, 2011	Comparisons not of interest for review - differences in BPD between regions in MOSAIC study
Gortner,L., Wauer,R.R., Stock,G.J., Reiter,H.L., Reiss,I., Jorch,G., Hentschel,R., Hieronimi,G., Neonatal outcome in small for gestational age	Study design not of interest - RCT

Excluded studies - Observational studies	
infants: do they really better?, Journal of Perinatal Medicine, 27, 484-489, 1999	
Greenough, A., Yuksel, B., Cheeseman, P., Effect of in utero growth retardation on lung function at follow-up of prematurely born infants, European Respiratory Journal, 24, 731-3, 2004	Analyses not adjusted for confounding factors Study design not of interest - single centre study
Grisaru-Granovsky, S., Reichman, B., Lerner-Geva, L., Boyko, V., Hammerman, C., Samueloff, A., Schimmel, M. S., Israel Neonatal, Network, Population-based trends in mortality and neonatal morbidities among singleton, very preterm, very low birth weight infants over 16 years, Early Human Development, 90, 821-7, 2014	Comparisons not of interest for review - differences in BPD between differing time periods
Groves, A. M., Briggs, K. A., Kuschel, C. A., Harding, J. E., Predictors of chronic lung disease in the 'CPAP era', Journal of Paediatrics and Child Health, 40, 290-294, 2004	Study design not of interest for review - retrospective case audit review
Hand, I., Zaghloul, N., Barash, L., Parris, R., Aden, U., Li, H. L., Timing of Caffeine Therapy and Neonatal Outcomes in Preterm Infants: A Retrospective Study, International Journal of Pediatrics, 2016, 9478204, 2016	Study design not of interest for review - single-centre retrospective study
Harkin, P., Marttila, R., Pokka, T., Saarela, T., Hallman, M., Morbidities associated with patent ductus arteriosus in preterm infants. Nationwide cohort study, Journal of Maternal-Fetal & Neonatal MedicineJ Matern Fetal Neonatal Med, 1, 2017	Study design not of interest for review - retrospective multicentre review
Hendson, L., Russell, L., Robertson, C. M. T., Liang, Y., Chen, Y., Abdalla, A., Lacaze-Masmonteil, T., Neonatal and neurodevelopmental outcomes of very low birth weight infants with histologic chorioamnionitis, Journal of Pediatrics, 158, 397-402, 2011	Study design not of interest for review - single centre observational study
Hentschel,J., Berger,T.M., Tschopp,A., Muller,M., Adams,M., Bucher,H.U., Population-based study of bronchopulmonary dysplasia in very low birth weight infants in Switzerland, European Journal of Pediatrics, 164, 292-297, 2005	Outcome not of interest for review - risk factors assessed for two different time periods in a country, rather than BPD
Heuchan,A.M., Hunter,L., Young,D., Outcomes following the surgical ligation of the patent ductus arteriosus in premature infants in Scotland, Archives of Disease in Childhood Fetal and Neonatal Edition, 97, F39-F44, 2012	Study design not of interest for this review - single centre retrospective study
Hintz, S. R., Poole, W. K., Wright, L. L., Fanaroff, A. A., Kendrick, D. E., Laptook, A. R., Goldberg, R., Duara, S., Stoll, B. J., Oh, W., Nichd Neonatal Research Network, Changes in mortality and morbidities among infants born at less than 25 weeks during the post-surfactant era, Archives of Disease in Childhood Fetal &	Outcome not of interest for review - composite outcome of death/major morbidity

Excluded studies - Observational studies	
Neonatal EditionArch Dis Child Fetal Neonatal Ed, 90, F128-33, 2005	
Horowitz, S., Landau, D., Shinwell, E. S., Zmora, E., Dagan, R., Respiratory tract colonization with Ureaplasma urealyticum and bronchopulmonary dysplasia in neonates in southern Israel, Pediatric Infectious Disease Journal, 11, 847-851, 1992	Study design not of interest for review - single centre study
Hossain, S., Shah, P. S., Ye, X. Y., Darlow, B. A., Lee, S. K., Lui, K., Outcome comparison of very preterm infants cared for in the neonatal intensive care units in Australia and New Zealand and in Canada, Journal of Paediatrics and Child Health, 51, 881-888, 2015	Study design not of interest for review - retrospective multicentre study
Hufnagel,M., Liese,C., Loescher,C., Kunze,M., Proempeler,H., Berner,R., Krueger,M., Enterococcal colonization of infants in a neonatal intensive care unit: Associated predictors, risk factors and seasonal patterns, BMC Infectious Diseases, 7 ,;#2007. Article Number, -, 2007	Outcomes are not of interest for this review - colonisation of enterococcus
Ito, M., Tamura, M., Namba, F., Role of sex in morbidity and mortality of very premature neonates, Pediatrics International, 59, 898-905, 2017	Study design not of interest for review - single centre retrospective review
Jacobs, S. E., O'Brien, K., Inwood, S., Kelly, E. N., Whyte, H. E., Outcome of infants 23-26 weeks' gestation pre and post surfactant, Acta Paediatrica, International Journal of Paediatrics, 89, 959-965, 2000	Study design not of interest for review - retrospective cohort study
Jantzen, C., Lodha, A., Lucia, M., Lee, S. K., Ye, X. Y., Sankaran, K., Effects of nosocomial infection trends on neonatal outcomes in preterm infants < 33 weeks of gestational age in Canadian NICUs, Chinese Journal of Contemporary Pediatrics, 17, 1019-1027, 2015	Study design not of interest for review - retrospective study
Jensen, E. A., DeMauro, S. B., Kornhauser, M., Aghai, Z. H., Greenspan, J. S., Dysart, K. C., Effects of multiple ventilation courses and duration of mechanical ventilation on respiratory outcomes in extremely low-birth-weight infants, JAMA PediatricsJama, Pediatr, 169, 1011-1017, 2015	Study design not of interest for review - retrospective study
Jensen, E. A., Dysart, K. C., Gantz, M. G., Carper, B., Higgins, R. D., Stoll, B. J., Walsh, M. C., Caplan, M. S., Polin, R. A., Laptook, A. R., Keszler, M., Hensman, A. M., Basso, K. M., Vieira, E., Little, E., Fanaroff, A. A., Hibbs, A. M., Newman, N. S., Truog, W. E., Kilbride, H. W., Pallotto, E. K., Gauldin, C., Holmes, A., Johnson, K., Knutson, A., Schibler, K., Donovan, E. F., Alexander, B., Grisby, C., Hessling, J., Fischer, E. E., Jackson, L. D., Kirker, K., Muthig, G., Goldberg, R. N., Cotten, C. M., Fisher, K. A.,	Study design not of interest for review - prospectively collected data of retrospective cohort study Prophylactic indomethacin used as opposed to treatment indomethacin

Excluded studies - Observational studies	
Auten, K. J., Foy, K. A., Grimes, S., Finkle, J., Laughon, M. M., Bose, C. L., Bernhardt, J., Bose, G., Carlton, D. P., Hale, E. C., Archer, S. W., Poindexter, B. B., Sokol, G. M., Wilson, L. D., Herron, D. E., Nelin, L. D., Jadcherla, S. R., Luzader, P., Fortney, C. A., Besner, G. E., Parikh, N. A., Das, A., Wallace, D., Auman, J. O., Crawford, M. M., Petrie Huitema, C. M., Zaterka-Baxter, K. M., Van Meurs, K. P., Adams, M. M., Stevenson, D. K., Ball, M. B., Palmquist, A. W., Proud, M. S., Frantz, I. D., Fiascone, J. M., MacKinnon, B. L., Nylen, E., Carlo, W. A., Ambalavanan, N., Collins, M. V., Cosby, S. S., Devaskar, U., Garg, M., Chanlaw, T., Geller, R., Bell, E. F., Ellsbury, D. L., Widness, J. A., Johnson, K. J., Campbell, D. B., Watterberg, K. L., Ohls, R. K., Lacy, C. B., Montman, R. A., Brown, S., Wussow, T., Hartenberger, C., Schmidt, B., Kirpalani, H., DeMauro, S. B., Chaudhary, A. S., Abbasi, S., Mancini, T., Cucinotta, D. M., D'Angio, C. T., Guillet, R., Lakshminrusimha, S., Reynolds, A. M., Reubens, L. J., Jensen, R., Maffett, D., Wadkins, H. I. M., Sacilowski, M. G., Williams, A., Guilford, S., Horihan, C. A., Kennedy, K. A., Tyson, J. E., Burson, K., Harris, B. F., McDavid, G. E., Pierce Tate, P. L., Wright, S. L., Sanchez, P. J., Brion, L. P., Chen, L., Guzman, A., Leps, M. H., Miller, N. A., Morgan, J. S., Vasil, D. M., Torres, L. E., Faix, R. G., Yoder, B. A., Osborne, K. A., Bird, K., Burnett, J., Jensen, J. J., Spencer, C., Weaver-Lewis, K., Zanetti, K., Shankaran, S., Barks, J., Bara, R., Johnson, M., Christensen, M., Wiggins, S., Ehrenkranz, R. A., Jacobs, H., Cervone, P., Konstantino, M., Poulsen, J., Taft, J., Association between Use of Prophylactic Indomethacin and the Risk for Bronchopulmonary Dysplasia in Extremely Preterm Infants, Journal of Pediatrics, 186, 34-40.e2, 2017	
Jhaveri,N., Moon-Grady,A., Clyman,R.I., Early surgical ligation versus a conservative approach for management of patent ductus arteriosus that fails to close after indomethacin treatment, Journal of Pediatrics, 157, 381-387, 387, 2010	Study design not of interest for review - interventional design of early surgical approach vs conservative approach
Jung, E. Y., Park, K. H., Han, B. R., Cho, S. H., Yoo, H. N., Lee, J., Amniotic Fluid Infection, Cytokine Levels, and Mortality and Adverse Pulmonary, Intestinal, and Neurologic Outcomes in Infants at 32 Weeks' Gestation or Less, Journal of Korean Medical Science, 32, 480-487, 2017	Study design not of interest - single centre retrospective study
Jung, E., Choi, C. W., Kim, S. Y., Sung, T. J., Kim, H., Park, K. U., Kim, H. S., Kim, B. I., Choi, J. H., Coexistence of Ureaplasma and	Study design not of interest - single centre retrospective study

Excluded studies - Observational studies	
chorioamnionitis is associated with prolonged mechanical ventilation, Pediatrics International, 59, 34-40, 2017	
Kaempf,J.W., Wu,Y.X., Kaempf,A.J., Kaempf,A.M., Wang,L., Grunkemeier,G., What happens when the patent ductus arteriosus is treated less aggressively in very low birth weight infants?, Journal of Perinatology, 32, 344-348, 2012	Study design not of interest - interventional design conservative vs active treatment of PDA
Kang, S. L., Samsudin, S., Kuruvilla, M., Dhelaria, A., Kent, S., Kelsall, W. A., Outcome of patent ductus arteriosus ligation in premature infants in the East of England: A prospective cohort study, Cardiology in the Young, 23, 711-716, 2013	Analyses did not account for confounders
Kent, A., Dahlstrom, J. E., Chorioamnionitis/funisitis and the development of bronchopulmonary dysplasia, Journal of Paediatrics & Child HealthJ Paediatr Child Health, 40, 356-9, 2004	Study design not of interest for review - single centre prospective study
Kewitz,G., Wudel,S., Hopp,H., Hopfenmuller,W., Vogel,M., Roots,I., Below median birth weight in appropriate-for-gestational-age preterm infants as a risk factor for bronchopulmonary dysplasia, Journal of Perinatal Medicine, 36, 359-364, 2008	Analyses are not adjusted for confounding factors
Khoshnood Shariati, M., Karimi, Z., Rezaienejad, M., Basiri, A., Torkestani, F., Saleh Gargari, S., Perinatal complications associated with preterm deliveries at 24 to 33 weeks and 6 days gestation (2011- 2012): A hospital-based retrospective study, Iranian Journal of Reproductive MedicineIran, 13, 697-702, 2015	Study design not of interest for review - retrospective study Country of study not in OECD - Iran
Kirchner, L., Weninger, M., Unterasinger, L., Birnbacher, R., Hayde, M., Krepler, R., Pollak, A., Is the use of early nasal CPAP associated with lower rates of chronic lung disease and retinopathy of prematurity? Nine years of experience with the Vermont Oxford Neonatal Network, Journal of Perinatal Medicine, 33, 60-6, 2005	Study design not of interest for review - single centre study Analyses not adjusted for confounders
Klinger, G., Sokolover, N., Boyko, V., Sirota, L., Lerner-Geva, L., Reichman, B., Perinatal risk factors for bronchopulmonary dysplasia in a national cohort of very-low-birthweight infants, American Journal of Obstetrics and Gynecology, 208, 115.e1-115.e9, 2013	Single risk factor not correlated with BPD, but rather a composite intervention score
Kobaly,K., Schluchter,M., Minich,N., Friedman,H., Taylor,H.G., Wilson-Costello,D., Hack,M., Outcomes of extremely low birth weight (<1 kg) and extremely low gestational age (<28 weeks) infants with bronchopulmonary dysplasia: effects of practice changes in 2000 to 2003, Pediatrics, 121, 73-81, 2008	Study design not of interest - single centre study

Excluded studies - Observational studies	
Kollee, L. A., Cuttini, M., Delmas, D., Papiernik, E., den Ouden, A. L., Agostino, R., Boerch, K., Breart, G., Chabernaud, J. L., Draper, E. S., Gortner, L., Kunzel, W., Maier, R. F., Mazela, J., Milligan, D., Van Reempts, P., Weber, T., Zeitlin, J., Mosaic Research group, Obstetric interventions for babies born before 28 weeks of gestation in Europe: results of the MOSAIC study, BJOG: An International Journal of Obstetrics & GynaecologyBjog, 116, 1481-91, 2009	Single risk factor not correlated to BPD - composite intervention score used as risk factor
Korhonen, P., Tammela, O., Koivisto, A. M., Laippala, P., Ikonen, S., Frequency and risk factors in bronchopulmonary dysplasia in a cohort of very low birth weight infants, Early Human Development, 54, 245-58, 1999	Study design not of interest for review - single centre retrospective study design
Lahra,M.M., Beeby,P.J., Jeffery,H.E., Intrauterine inflammation, neonatal sepsis, and chronic lung disease: A 13-year hospital cohort study, Pediatrics, 123, 1314-1319, 2009	Study design not of interest - single centre prospective study
Lal, M. K., Manktelow, B. N., Draper, E. S., Field, D. J., Population-based, study, Chronic lung disease of prematurity and intrauterine growth retardation: a population-based study, Pediatrics, 111, 483-7, 2003	Analyses adjusted for gestational age, but not sex
Lardon-Fernandez, M., Uberos, J., Molina-Oya, M., Narbona-Lopez, E., Epidemiological factors involved in the development of bronchopulmonary dysplasia in very low birth-weight preterm infants, Minerva Pediatrica, 69, 42-49, 2017	Study design not of interest for review - single centre retrospective study
Laughon,M., Bose,C., Clark,R., Treatment strategies to prevent or close a patent ductus arteriosus in preterm infants and outcomes, Journal of Perinatology, 27, 164-170, 2007	Study design not of interest - interventional design assessing treatment of PDA
Lee, H. J., Kim, E. K., Kim, H. S., Choi, C. W., Kim, B. I. I., Choi, J. H., Chorioamnionitis, respiratory distress syndrome and bronchopulmonary dysplasia in extremely low birth weight infants, Journal of Perinatology, 31, 166-170, 2011	Study design not of interest for review - single centre retrospective design
Lemons,J.A., Bauer,C.R., Oh,W., Korones,S.B., Papile,L.A., Stoll,B.J., Verter,J., Temprosa,M., Wright,L.L., Ehrenkranz,R.A., Fanaroff,A.A., Stark,A., Carlo,W., Tyson,J.E., Donovan,E.F., Shankaran,S., Stevenson,D.K., Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network, Pediatrics, 107, E1-, 2001	Outcome not of interest for review - mortality not BPD
Leviton, A., Dammann, O., Engelke, S., Allred, E., Kuban, K. C., O'Shea, T. M., Paneth, N.,	No risk factors of interest for review - clustering risk factors

Excluded studies - Observational studies	
Elgan study investigators, The clustering of disorders in infants born before the 28th week of gestation, Acta PaediatricaActa Paediatr, 99, 1795-800, 2010	
Lopez, E. S., Rodriguez, E. M., Navarro, C. R., Sanchez-Luna, M., Initial respiratory management in preterm infants and bronchopulmonary dysplasia, Clinics (Sao Paulo, Brazil)Clinics, 66, 823-7, 2011	Inappropriate study design - single centre prospective observational study
Louis, J. M., Ehrenberg, H. M., Collin, M. F., Mercer, B. M., Perinatal intervention and neonatal outcomes near the limit of viability, American Journal of Obstetrics & Gynecology, 191, 1398-402, 2004	Study design not of interest - retrospective study
Lyu, Y., Shah, P. S., Ye, X. Y., Warre, R., Piedboeuf, B., Deshpandey, A., Lee, S. K., Harrison, A., Synnes, A., Sokoran, T., Yee, W., Aziz, K., Kalapesi, Z., Sankaran, K., Seshia, M., Alvaro, R., Shivananda, S., Da Silva, O., Nwaesei, C., Lee, K. S., Dunn, M., Rouvinez-Bouali, N., Dow, K., Pelausa, E., Barrington, K., Drolet, C., Riley, P., Bertelle, V., Canning, R., Bulleid, B., Ojah, C., Monterrosa, L., Afifi, J., Kajetanowicz, A., Association between admission temperature and mortality and major morbidity in preterm infants born at fewer than 33weeks' gestation, JAMA Pediatrics, 169, 2015	Study design not of interest for review - retrospective multicentre study
Makhoul,I.R., Sujov,P., Smolkin,T., Lusky,A., Reichman,B., Epidemiological, clinical, and microbiological characteristics of late-onset sepsis among very low birth weight infants in Israel: a national survey, Pediatrics, 109, 34-39, 2002	Outcome assessed not of interest for review - late onset sepis
Manktelow,B.N., Lal,M.K., Field,D.J., Sinha,S.K., Antenatal corticosteroids and neonatal outcomes according to gestational age: a cohort study, Archives of Disease in Childhood Fetal and Neonatal Edition, 95, F95-F98, 2010	Analyses not adjusted for confounders
Mansson, J., Fellman, V., Stjernqvist, K., Express Study Group, Extremely preterm birth affects boys more and socio-economic and neonatal variables pose sex-specific risks, Acta PaediatricaActa Paediatr, 104, 514-21, 2015	Outcome not of interest for review - neurodevelopmental outcome
Manuck, T. A., Rice, M. M., Bailit, J. L., Grobman, W. A., Reddy, U. M., Wapner, R. J., Thorp, J. M., Caritis, S. N., Prasad, M., Tita, A. T., Saade, G. R., Sorokin, Y., Rouse, D. J., Blackwell, S. C., Tolosa, J. E., Eunice Kennedy Shriver National Institute of Child, Health, Human Development Maternal-Fetal Medicine Units, Network, Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort, American Journal of Obstetrics &	Confounding factors not adjusted for in the analysis

Excluded studies - Observational studies	
GynecologyAm J Obstet Gynecol, 215, 103.e1-103.e14, 2016	
Marret, S., Ancel, P. Y., Marpeau, L., Marchand, L., Pierrat, V., Larroque, B., Foix-L'Helias, L., Thiriez, G., Fresson, J., Alberge, C., Roze, J. C., Matis, J., Breart, G., Kaminski, M., Epipage Study, Group, Neonatal and 5-year outcomes after birth at 30-34 weeks of gestation, Obstetrics & Gynecology, 110, 72-80, 2007	Outcome not of interest for review - neurodevelopmental outcome at 5 years of age
Melamed, N., Shah, J., Soraisham, A., Yoon, E. W., Lee, S. K., Shah, P. S., Murphy, K. E., Association Between Antenatal Corticosteroid Administration-to-Birth Interval and Outcomes of Preterm Neonates, Obstetrics & GynecologyObstet Gynecol, 125, 1377-84, 2015	Study design not of interest - retrospective study
Mercer, B. M., Goldenberg, R. L., Das, A., Moawad, A. H., Iams, J. D., Meis, P. J., Copper, R. L., Johnson, F., Thom, E., McNellis, D., Miodovnik, M., Menard, M. K., Caritis, S. N., Thurnau, G. R., Bottoms, S. F., Roberts, J., The preterm prediction study: a clinical risk assessment system, American Journal of Obstetrics & Gynecology, 174, 1885-93; discussion 1893-5, 1996	Outcome not of interest for review - spontaneous preterm delivery
Metcalfe, A., Lisonkova, S., Sabr, Y., Stritzke, A., Joseph, K. S., Neonatal respiratory morbidity following exposure to chorioamnionitis, BMC Pediatrics, 17 (1) (no pagination), 2017	Study design not of interest - retrospective multicentre cohort study
Miyazaki, K., Furuhashi, M., Ishikawa, K., Tamakoshi, K., Hayashi, K., Kai, A., Ishikawa, H., Murabayashi, N., Ikeda, T., Kono, Y., Kusuda, S., Fujimura, M., Long-term outcomes of antenatal corticosteroids treatment in very preterm infants after chorioamnionitis, Archives of Gynecology & Obstetrics, 292, 1239-46, 2015	Study design not of interest for review - retrospective study
Miyazaki, K., Furuhashi, M., Ishikawa, K., Tamakoshi, K., Hayashi, K., Kai, A., Ishikawa, H., Murabayashi, N., Ikeda, T., Kono, Y., Kusuda, S., Fujimura, M., Impact of chorioamnionitis on short- and long-term outcomes in very low birth weight preterm infants: the Neonatal Research Network Japan, Journal of Maternal-Fetal & Neonatal Medicine, 29, 331-7, 2016	Study design not of interest for review - retrospective study
Miyazaki,K., Furuhashi,M., Matsuo,K., Minami,K., Yoshida,K., Kuno,N., Ishikawa,K., Impact of subclinical chorioamnionitis on maternal and neonatal outcomes, Acta Obstetricia et Gynecologica Scandinavica, 86, 191-197, 2007	Study design not of interest for review - single centre study
Moreira, A., Caskey, M., Fonseca, R., Malloy, M., Geary, C., Impact of providing vitamin A to the routine pulmonary care of extremely low birth weight infants, Journal of Maternal-Fetal &	Study design not of interest for review - retrospective study

Excluded studies - Observational studies	
Neonatal MedicineJ Matern Fetal Neonatal Med, 25, 84-8, 2012	
Morgillo, D., Morgillo-Mitchell, J., Fontanta, M., Steurer, M., Schmitt-Mechelke, T., Bauder, F., Berger, T. M., Outcome of extremely low gestational age newborns (ELGANs) following a pro-active treatment approach: a Swiss single centre experience over 10 years, Swiss Medical Weekly, 144, w14014, 2014	Analyses did not adjust for confounders
Nasef,N., Shabaan,A.E., Schurr,P., Iaboni,D., Choudhury,J., Church,P., Dunn,M.S., Effect of clinical and histological chorioamnionitis on the outcome of preterm infants, American Journal of Perinatology, 30, 59-68, 2013	Study design not of interest in review - single centre retrospective review
Nobile, S., Marchionni, P., Carnielli, V. P., Neonatal outcome of small for gestational age preterm infants, European Journal of Pediatrics, 176, 1083-1088, 2017	Study design not of interest - single centre retrospectively collected prospective study
O'Dwyer,V., Burke,G., Unterscheider,J., Daly,S., Geary,M.P., Kennelly,M.M., McAuliffe,F.M., O'Donoghue,K., Hunter,A., Morrison,J.J., Dicker,P., Tully,E.C., Malone,F.D., Defining the residual risk of adverse perinatal outcome in growth-restricted fetuses with normal umbilical artery blood flow, American Journal of Obstetrics and Gynecology, 211, 420-425, 2014	Risk factor not of interest for review - umbilical artery Doppler assessment
Ogunyemi,D., Murillo,M., Jackson,U., Hunter,N., Alperson,B., The relationship between placental histopathology findings and perinatal outcome in preterm infants, Journal of Maternal-Fetal and Neonatal Medicine, 13, 102-109, 2003	Study design not of interest for review - retrospective study
Oh, W., Poindexter, B. B., Perritt, R., Lemons, J. A., Bauer, C. R., Ehrenkranz, R. A., Stoll, B. J., Poole, K., Wright, L. L., Association between fluid intake and weight loss during the first ten days of life and risk of bronchopulmonary dysplasia in extremely low birth weight infants, Journal of Pediatrics, 147, 786-790, 2005	Study design not of interest for review - retrospective analysis of RCT
Ohyama, M., Itani, Y., Yamanaka, M., Goto, A., Kato, K., Ijiri, R., Tanaka, Y., Re-evaluation of chorioamnionitis and funisitis with a special reference to subacute chorioamnionitis, Human Pathology, 33, 183-90, 2002	Study design not of interest for review - retrospective study
Ohyama,M., Itani,Y., Yamanaka,M., Goto,A., Kato,K., Ijiri,R., Tanaka,Y., Maternal, Neonatal, and Placental Features Associated with Diffuse Chorioamniotic Hemosiderosis, with Special Reference to Neonatal Morbidity and Mortality, Pediatrics, 113, 800-805, 2004	Study design not of interest for review - retrospective study
Paananen,R., Husa,A.K., Vuolteenaho,R., Herva,R., Kaukola,T., Hallman,M., Blood cytokines during the perinatal period in very preterm infants: relationship of inflammatory	Study design not of interest for review - single centre study

Excluded studies - Observational studies	
response and bronchopulmonary dysplasia, Journal of Pediatrics, 154, 39-43, 2009	
Palta, M., Weinstein, M. R., McGuinness, G., Gabbert, D., Brady, W., Peters, M. E., A population study. Mortality and morbidity after availability of surfactant therapy. Newborn Lung Project, Archives of Pediatrics & Adolescent MedicineArch Pediatr Adolesc Med, 148, 1295-301, 1994	Outside date range for study inclusion - 1988-1991
Paul,D.A., Zook,K., Mackley,A., Locke,R.G., Reduced mortality and increased BPD with histological chorioamnionitis and leukocytosis in very-low-birth-weight infants, Journal of Perinatology, 30, 58-62, 2010	Study design not of interest in review - single centre retrospective review
Payne, N. R., LaCorte, M., Karna, P., Chen, S., Finkelstein, M., Goldsmith, J. P., Carpenter, J. H., Reduction of bronchopulmonary dysplasia after participation in the Breathsavers Group of the Vermont Oxford Network Neonatal Intensive Care Quality Improvement Collaborative, Pediatrics, 118, S73-S77, 2006	single risk factors for BPD are not accounted for in the analysis, study compares practice changes in 2001 vs 2003
Redline,R.W., Wilson-Costello,D., Hack,M., Placental and other perinatal risk factors for chronic lung disease in very low birth weight infants, Pediatric Research, 52, 713-719, 2002	Study design not of interest for review - single centre retrospective cohort study Analyses adjust for gestational age, but not sex
Rieger-Fackeldey, E., Schulze, A., Pohlandt, F., Schwarze, R., Dinger, J., Lindner, W., Short-term outcome in infants with a birthweight less than 501 grams, Acta PaediatricaActa Paediatr, 94, 211-6, 2005	Analyses did not adjust for confounders
Rojas,M.A., Gonzalez,A., Bancalari,E., Claure,N., Poole,C., Silva-Neto,G., Changing trends in the epidemiology and pathogenesis of neonatal chronic lung disease, Journal of Pediatrics, 126, 605-610, 1995	Study design not of interest for review - single centre study commenced pre-1990
Rubaltelli, F. F., Dani, C., Reali, M. F., Bertini, G., Wiechmann, L., Tangucci, M., Spagnolo, A., Acute neonatal respiratory distress in Italy: a one-year prospective study. Italian Group of Neonatal Pneumology, Acta PaediatricaActa Paediatr, 87, 1261-8, 1998	Analyses did not adjust for confounders
Santin,R., Brodsky,N., Bhandari,V., A prospective observational pilot study of synchronized nasal intermittent positive pressure ventilation (SNIPPV) as a primary mode of ventilation in infants ≥ 28 weeks with respiratory distress syndrome (RDS), Journal of Perinatology, 24, 487-493, 2004	Outcomes not of interest for review - BPD not an outcome reported
Sasaki, Y., Ikeda, T., Nishimura, K., Katsuragi, S., Sengoku, K., Kusuda, S., Fujimura, M., Association of antenatal corticosteroids and the mode of delivery with the mortality and morbidity	Study design not of interest for review - retrospective study

Excluded studies - Observational studies	
of infants weighing less than 1,500 g at birth in Japan, Neonatology, 106, 81-86, 2015	
Sasi, A., Abraham, V., Davies-Tuck, M., Polglase, G. R., Jenkin, G., Miller, S. L., Malhotra, A., Impact of intrauterine growth restriction on preterm lung disease, Acta Paediatrica, International Journal of Paediatrics, 104, e552-e556, 2015	Study design not of interest for review - single centre retrospective study
Schaaf, J. M., Mol, B. W., Abu-Hanna, A., Ravelli, A. C., Ethnic disparities in the risk of adverse neonatal outcome after spontaneous preterm birth, Acta Obstetricia et Gynecologica Scandinavica, 91, 1402-8, 2012	Outcome in study is not BPD - a composite outcome of BPD, IVH, RDS, Sepsis, or neonatal mortality is assessed
Seabolt,J.P., Ribes,J.A., Perinatal complications in infants with Mycoplasma and Ureaplasma spp. infection, Laboratory Medicine, 34, 589-591, 2003	Study design not of interest for review - single centre study
Seliga-Siwecka,J.P., Kornacka,M.K., Neonatal outcome of preterm infants born to mothers with abnormal genital tract colonisation and chorioamnionitis: A cohort study, Early Human Development, 89, 271-275, 2013	Study design not of interest for review - single centre study
Serenius, F., Ewald, U., Farooqi, A., Holmgren, P. A., Hakansson, S., Sedin, G., Short-term outcome-after active perinatal management at 23-25 weeks of gestation. A study from two Swedish perinatal centres. Part 3: Neonatal morbidity, Acta Paediatrica, International Journal of Paediatrics, 93, 1090-1097, 2004	Study design not of interest for review - retrospective study
Shah, P. S., Sankaran, K., Aziz, K., Allen, A. C., Seshia, M., Ohlsson, A., Lee, S. K., Canadian Neonatal, Network, Outcomes of preterm infants <29 weeks gestation over 10-year period in Canada: a cause for concern?, Journal of Perinatology, 32, 132-8, 2012	Single risk factors for BPD are not accounted for in the analysis, study compares practice changes in 1996-97 vs 2006-7
Shah, P. S., Shah, P., Tai, K. F. Y., Chest compression and/or epinephrine at birth for preterm infants <32 weeks gestational age: Matched cohort study of neonatal outcomes, Journal of Perinatology, 29, 693-697, 2009	Outcome not relevant for review - composite outcome of death, severe neurological injury, retinopathy of prematurity, or BPD assessed
Shariati, M. K., Karimi, Z., Rezaienejad, M., Basiri, A., Torkestani, F., Gargari, S. S., Perinatal complications associated with preterm deliveries at 24 to 33 weeks and 6 days gestation (2011-2012): A hospital-based retrospective study, International Journal of Reproductive BioMedicine, 13, 697-702, 2015	Study design not of interest for review - retrospective study
Sharma, P., McKay, K., Rosenkrantz, T. S., Hussain, N., Comparisons of mortality and pre-discharge respiratory outcomes in small-for-gestational-age and appropriate-for-gestational-age premature infants, BMC Pediatrics, 4, 9, 2004	Study design not of interest for review - single centre retrospective cohort study

Excluded studies - Observational studies	
Shima, Y., Kumasaka, S., Migita, M., Perinatal risk factors for adverse long-term pulmonary outcome in premature infants: Comparison of different definitions of bronchopulmonary dysplasia/chronic lung disease, Pediatrics International, 55, 578-581, 2013	Study design not of interest for review - single centre retrospective cohort study
Smith, L. M., Qureshi, N., Chao, C. R., Effects of single and multiple courses of antenatal glucocorticoids in preterm newborns less than 30 weeks' gestation, Journal of Maternal-Fetal MedicineJ Matern Fetal Med, 9, 131-5, 2000	Study design not of interest for review - retrospective study
Soraisham, A. S., Lodha, A. K., Singhal, N., Aziz, K., Yang, J., Lee, S. K., Shah, P. S., Kajetanowicz, A., Synnes, A., Rouvinez-Bouali, N., Pied-boeuf, B., Bertelle, V., Bulleid, B., Yee, W., Shivananda, S., Lee, K. S., Seshia, M., Barrington, K., Lefebvre, F., McMillan, D., Andrews, W., Kovacs, L., Dow, K., Da Silva, O., Riley, P., Peliowski, A., Cieslak, Z., Kalapesi, Z., Sankaran, K., Faucher, D., Alvaro, R., Canning, R., Ojah, C., Dunn, M., Sorokan, T., Harrison, A., Nwaesei, C., Adie, M., Neonatal outcomes following extensive cardiopulmonary resuscitation in the delivery room for infants born at less than 33 weeks gestational age, Resuscitation, 85, 238-243, 2014	Study design not of interest for review - multicentre retrospective study
Soraisham, A. S., Singhal, N., McMillan, D. D., Sauve, R. S., Lee, S. K., A multicenter study on the clinical outcome of chorioamnionitis in preterm infants, American Journal of Obstetrics and Gynecology, 200, 372.e1-372.e6, 2009	Study design not of interest for review - multicentre retrospective study
Stoll, B. J., Hansen, N. I., Bell, E. F., Shankaran, S., Laptook, A. R., Walsh, M. C., Hale, E. C., Newman, N. S., Schibler, K., Carlo, W. A., Kennedy, K. A., Poindexter, B. B., Finer, N. N., Ehrenkranz, R. A., Duara, S., Sanchez, P. J., O'Shea, T. M., Goldberg, R. N., Van Meurs, K. P., Faix, R. G., Phelps, D. L., Frantz, I. D., 3rd, Watterberg, K. L., Saha, S., Das, A., Higgins, R. D., Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network, Pediatrics, 126, 443-56, 2010	Adjusted analyses not accounted for BPD, only mortality
Stoll,B.J., Gordon,T., Korones,S.B., Shankaran,S., Tyson,J.E., Bauer,C.R., Fanaroff,A.A., Lemons,J.A., Donovan,E.F., Oh,W., Stevenson,D.K., Ehrenkranz,R.A., Papile,L.A., Verter,J., Wright,L.L., Late-onset sepsis in very low birth weight neonates: A report from the national institute of child health and human development neonatal research network, Journal of Pediatrics, 129, 63-71, 1996	Outcome not of interest for study - not BPD
Valcamonico, A., Accorsi, P., Sanzeni, C., Martelli, P., La Boria, P., Cavazza, A., Frusca, T., Mid- and long-term outcome of extremely low	Study design not of interest for review - single centre study

Excluded studies - Observational studies	
birth weight (ELBW) infants: an analysis of prognostic factors, Journal of Maternal-Fetal & Neonatal MedicineJ Matern Fetal Neonatal Med, 20, 465-71, 2007	
Van Marter, L. J., Allred, E. N., Pagano, M., Sanocka, U., Parad, R., Moore, M., Susser, M., Paneth, N., Leviton, A., Do clinical markers of barotrauma and oxygen toxicity explain interhospital variation in rates of chronic lung disease? The Neonatology Committee for the Developmental Network, Pediatrics, 105, 1194-201, 2000	Study design not of interest - retrospective case-control study
Van Marter, L. J., Dammann, O., Allred, E. N., Leviton, A., Pagano, M., Moore, M., Martin, C., Developmental Epidemiology Network, Investigators, Chorioamnionitis, mechanical ventilation, and postnatal sepsis as modulators of chronic lung disease in preterm infants, Journal of Pediatrics, 140, 171-6, 2002	Analyses adjusted for GA, but not sex (statistically significant between 2 cohorts)
Van Marter, L. J., Leviton, A., Kuban, K. C., Pagano, M., Allred, E. N., Maternal glucocorticoid therapy and reduced risk of bronchopulmonary dysplasia, Pediatrics, 86, 331-6, 1990	Study dates pre-1990
Vendettuoli, V., Bellu, R., Zanini, R., Mosca, F., Gagliardi, L., Changes in ventilator strategies and outcomes in preterm infants, Archives of Disease in Childhood: Fetal and Neonatal Edition, 99, F321-F324, 2014	Comparison not of interest for review - compares different time periods and neonatal outcomes
Wai, K. C., Kohn, M. A., Ballard, R. A., Truog, W. E., Black, D. M., Asselin, J. M., Ballard, P. L., Rogers, E. E., Keller, R. L., Trial of Late Surfactant Study, Group, Early Cumulative Supplemental Oxygen Predicts Bronchopulmonary Dysplasia in High Risk Extremely Low Gestational Age Newborns, Journal of pediatrics, 177, 97-102.e2, 2016	Study design not of interest for review - follow up of RCT
Walsh, M. C., Bell, E. F., Kandefer, S., Saha, S., Carlo, W. A., D'Angio C, T., Laptook, A. R., Sanchez, P. J., Stoll, B. J., Shankaran, S., Van Meurs, K. P., Cook, N., Higgins, R. D., Das, A., Newman, N. S., Schibler, K., Schmidt, B., Cotten, C. M., Poindexter, B. B., Watterberg, K. L., Truog, W. E., Neonatal outcomes of moderately preterm infants compared to extremely preterm infants, Pediatric Research, 24, 24, 2017	Analyses not adjusted for confounders
Watterberg, K. L., Demers, L. M., Scott, S. M., Murphy, S., Chorioamnionitis and early lung inflammation in infants in whom bronchopulmonary dysplasia develops, Pediatrics, 97, 210-215, 1996	Study population <100
Weber,C., Weninger,M., Klebermass,K., Reiter,G., Wiesinger-Eidenberger,G.,	Study design not of interest - retrospective study

Excluded studies - Observational studies	
Brandauer,M., Kraschl,R., Lingitz,K., Grassl-Jurek,R., Sterniste,W., Balluch,B., Kolmer,M., Bruckner,R., Schweintzger,G., Salzer,H., Rath,I., Kubitsch,P., Zissler,W., Muller,W., Urlesberger,B., Mortality and morbidity in extremely preterm infants (22 to 26 weeks of gestation): Austria 1999-2001, Wiener Klinische Wochenschrift, 117, 740-746, 2005	
Yamakawa, T., Itabashi, K., Kusuda, S., Mortality and morbidity risks vary with birth weight standard deviation score in growth restricted extremely preterm infants, Early Human Development, 92, 7-11, 2016	Study design not of interest for review - multicentre retrospective study
Yoder, B. A., Harrison, M., Clark, R. H., Time-related changes in steroid use and bronchopulmonary dysplasia in preterm infants, Pediatrics, 124, 673-679, 2009	Study design not of interest for review - retrospective study
Zanardo,V., Vedovato,S., Cosmi,E., Litta,P., Cavallin,F., Trevisanuto,D., Chiarelli,S., Preterm premature rupture of membranes, chorioamnion inflammatory scores and neonatal respiratory outcome, BJOG: An International Journal of Obstetrics and Gynaecology, 117, 94-98, 2010	Study design not of interest for review - single centre prospective cohort study
Zanardo,V., Vedovato,S., Trevisanuto,D.D., Suppiej,A., Cosmi,E., Fais,G.F., Chiarelli,S., Histological chorioamnionitis and neonatal leukemoid reaction in low-birth-weight infants, Human Pathology, 37, 87-91, 2006	Study design not of interest for review - single centre review
Zaw, W., Gagnon, R., da Silva, O., The risks of adverse neonatal outcome among preterm small for gestational age infants according to neonatal versus fetal growth standards, Pediatrics, 111, 1273-7, 2003	Study design not of interest for review - single centre review

Economic studies

All economic studies were excluded at the initial title and abstract screening stage.

Appendix L – Research recommendations

Research recommendations for question 2.1 What are the risk factors for bronchopulmonary dysplasia in preterm babies?

No research recommendations were made for this review.