# Supplementary table 3: Review outcomes

Table 1-a. Review outcomes

Neonatal outcomes
Neonatal death
Neonatal death within 48 h after birth
Death before discharge home
Apgar score $\leq$ 7 at 5 min after birth
Apgar score < 7 at 5 min after birth
Apgar score < 5 at 1 min after birth
Respiratory distress syndrome (RDS)
Bronchopulmonary dysplasia (BPD)/chronic lung disease (CLD)
Pneumonia
Use of mechanical ventilation
Surfactant use
Oxygen therapy
Oxygen requirement for at least 4 h
Mean duration of mechanical ventilations
Duration of oxygen use
Patent ductus arteriosus (PDA)
Hypotension within 7 postnatal days
Hypotension
Intraventricular hemorrhage (IVH)
Severe IVH

Periventricular leukomalacia (PVL) Major brain lesion damage Necrotizing enterocolitis (NEC) Sepsis Early onset sepsis Systemic inflammatory response syndrome Meningitis Neonatal hypoglycemia Neonatal adrenal insufficiency Intrahepatic cholestasis Retinopathy of prematurity (ROP) Gestational age at birth Birth weight Neonatal intensive care unit (NICU) admission Duration of hospital stay Survival free from disability Death at long-term follow up Death or disability/handicap at 2 years Cerebral palsy Severe hearing impairment Visual impairment

Discharge with respiratory support
Growth < 10% ile in early childhood
Abnormal behavior at long-term follow up at school-age

#### Table 1-b. Outcome definition

Maternal outcomes	Definition
Preeclampsia or eclampsia	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1 <sup>*1</sup> .
Preeclampsia	<u>P4</u>
	Bitar et al. (2020): Identified by the medication administration record, ICD-10 coded, and chart review.
	Cartwright et al. (2019): No data.
	Ishikawa et al. (2015): No data.
	Mitsiakos et al. (2013): Defined as a systolic Blood pressure(BP) >160mmHg and a diastolic BP $\geq$
	90mmHg measured at least twice and proteinuria $\geq 0.3g/24g$ .
Hypertensive disorders	<u>P2</u>
	Kirshembaum et al. (2018): No data.
Pregnancy induced hypertension (PIH)	<u>P4</u>
	Kim et al. (2018): No data.
	Kim YJ et al. (2018): Defined as any maternal diagnoses of preeclampsia, eclampsia or hemolysis,
	elevated liver enzymes, and low platelet count (HELLP) syndrome.
	Feng et al. (2017): No data.
Chorioamnionitis	<u>P4</u>
	Kim et al. (2018): No data.
	Kim YJ et al. (2018): No data.
	Ishikawa et al. (2015): No data.
	Mitsiakos et al. (2013): No data.
	Elimian et al. (1999): No data.
Gestational diabetes mellitus	<u>P2</u>
	de la Hueruga et al. (2019): No data.
	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1 <sup>*1</sup> .

	Bitar et al. (2020): Identified by the medication administration record, ICD-10 coded, and chart review.
	Kim YL et al. (2018): No data
	Ishikawa et al. (2015): No data
Neonatal outcomes	Definition
Neonatal death	Deaths during the first 28 completed days of life.*2
Neonatal death within 48h after birth	<u>P1</u>
	Battarbee et al. (2020): Death within 48h after birth.
Death before discharge home	<u>P3</u>
	Foix-L'Helias et al. (2005): Death before discharge home.
	<u>P4</u>
	Riskin-Mashiah et al. (2016): Death before discharge home.
	Ishikawa et al. (2015): Death before discharge home.
	Foix-L'Helias et al. (2005): Death before discharge home.
	Schaap et al. (2001): Death before discharge home.
	Bernstein et al. (2000): Death before discharge home.
Apgar score $\leq$ 7 at 5 min after birth	<u>P2</u>
	Kishenbaum et al. (2018): Apgar score ≤7 at 5 min after birth.
Apgar score <7 at 5min after birth	<u>P1</u>
	Krispin et al. (2018): Apgar score <7 at 5 min after birth.
	<u>P3</u>
	Elimian et al. (2000): Apgar score <7 at 5 min after birth.
	<u>P4</u>
	Bitar et al. (2020): Apgar score <7 at 5 min after birth.
	Kim et al. (2018): Apgar score <7 at 5min after birth.
	Feng et al. (2017): Apgar score <7 at 5min after birth.
	Elimian et al. (1999): Apgar score <7 at 5min after birth.
Apgar score <5 at 1min after birth	<u>P4</u>
	Kim et al. (2018): Apgar score <5 at 1min after birth.
	Torrance et al. (2007): Apgar score <5 at 1min after birth.
Respiratory distress syndrome (RDS)	<u>P1</u>
	Battarbee et al. (2020): Defined as a clinical diagnosis of respiratory distress syndrome, hyaline

membrane disease, or respiratory insufficiency requiring oxygen therapy with FiO2  $\geq 0.40$  started within the first 24 hours after birth and continued for  $\geq 24$  hours or until neonatal demise. Krispin et al. (2018): No data.

## <u>P2</u>

de la Huerga Lopez et al. (2019): Defined ad the presence of clinical signs of respiratory distress with oxygen requirement and chest X-ray with reticulonodular infiltrate.

Kishenbaum et al. (2018): Defined as early respiratory distress that comprised cyanosis, grunting, retraction and tachypnea combined with ground glass appearance and air bronchogram on chest X-ray.

## <u>P3</u>

Ryu et al. (2019): Defined if the chest radiographic findings were consistent with RDS together with an oxygen requirement of >0.4 for the fraction of inspired oxygen.

Ahn et al. (2012): Diagnosed in infants with respiratory distress, an increased oxygen requirement and a radiological finding consistent with RDS.

Been et al. (2009): Diagnosed in a clinical presentation (expiratory grunting, sub- or intercostal or sternal retractions, nasal flaring, tachypnea, cyanosis in room air with or without apnea) and characteristic radiographic appearance according to Giedion et al. \*3

Goldenberg et al. (2006): Defined as the documentation of any of three criteria: (1) oxygen requirement at 6 through 24 hours of life; (2) an abnormal chest radiograph consistent with RDS within the first 24 hours of life; and (3) need for surfactant.

Dempsey et al. (2005): Defined from a combination of three of the following: clinical signs, oxygen need greater than 30% from 12 to 72 hours, need for assisted ventilation (continuous positive airway pressure or mechanical ventilation), and typical chest X-ray appearance.

Foix-L'Helias et al. (2005): No data.

Baud et al. (2000): Diagnosed if any two criteria were present in the first 24 hours of life: clinical symptoms (respiratory failure requiring assisted ventilation and administration of exogenous surfactant), typical radiological feature, and biological evidence of lung immaturity (fetal lung maturity test on tracheal aspirates).

Elimian et al. (2018): Diagnosed clinically by need for mechanical ventilation and oxygen for at least 48 hours, and radiologic chest findings.

## <u>P4</u>

Kim et al. (2018): No data.
Riskin-Mashiah et al. (2018): No data.
Riskin-Mashiah et al. (2016): Diagnosed by a chest radiography consistent with RDS together with supplementary oxygen or mechanical ventilation therapy.
Feng et al. (2017): No data.
Ishikawa et al. (2015): Diagnosed based on the clinical and radiographic finings.
Mitsiakos et al. (2013): Diagnosed based on clinical and radiological criteria and oxygen requirements

	≧30%.
	van Stralen et al. (2009): Based on radiological criteria (poor lung expansion) and clinical criterial (need for supplemental oxygen, sternal retraction, intercostal and subcostal recession, grunting and tachypnea
	Torrance et al. (2007): Defined as clinical signs of RDS with oxygen requirement and typical findings on a chest X-ray.
	Foix-L'Helias et al. (2005): No data.
	Schaap et al. (2001): Defined as tachypnea, chest wall retractions, and oxygen requirement in the presence of a chest X-ray classified as RDS.
	Bernstein et al. (2000): Required both a PaO2 <50mmHg in room air plus central cyanosis in room air of a requirement for supplemental oxygen to maintain a PaO2 >50mmHg.
	Elimian et al. (1999): Diagnosed clinically and by the need for mechanical ventilation and oxygen for a least 48 hors and the presence of radiologic chest findings.
	Ley et al. (1997): No data.
	Spinillo et al. (1995): Diagnosed with physical signs of respiratory distress (grunting, chest retraction, tachypnea) and required ventilatory support for >48hr and radiologic chest findings.
	Di Lenardo et al. (1990): Based on the basis of radiological indications and worsening of the symptoms from a clinical point of view.
Bronchopulmonary dysplasia (BPD)/	<u>P3</u>
Chronic lung disease (CLD)	Ryu et al. (2019): Listed in the online supplementary Table1.*1
	Ahn et al. (2012): Based on National Institute of Child and Human Development criteria.*4
	Been et al. (2009): Diagnosed with a dependency on oxygen supplementation at a postmenstrual age of 36 weeks.
	Goldenberg et al. (2006): Defined as infant oxygen requirement at 28 days or oxygen requirement at 36 weeks of life.
	Foix-L'Helias et al. (2005): No data.
	<u>P4</u>
	Kim YJ et al. (2018): No data.
	Riskin-Mashiah et al. (2018): No data.
	Feng et al. (2017): No data.
	Riskin-Mashiah et al. (2016): Diagnosed according to the criteria of Bancalari et al. <sup>*5</sup> including clinical and radiologic features. Together with the requirement for oxygen supplementation at 36 weeks post menstrual age.
	Ishikawa et al. (2015): Defined when an infant continued to receive supplemental oxygen on the 28 <sup>th</sup> da after birth and at the 36 <sup>th</sup> week based on postmenstrual age.
	Mitsiakos et al. (2013): Based on oxygen supplementation at 36 weeks postmenstrual age.
	van Stralen et al. (2009): No data.

	Torrance et al. (2007): Defined as the need for extra oxygen on day 28 of life with chronic abnormalities on a cheet X-ray and symptoms of respiratory distress
	Foix-L'Helias et al. (2005): No data
	Schaap et al. (2001): Defined as the presence of chronic respiratory distress and oxygen requirement beyond 28 days of life accompanied by a chest radiograph that showed persistent streaks of increased density in both lungs interspersed with normal hyperlucent areas.
Pneumonia	<u>P3</u>
	Dempsey et al. (2005): Defined by a combination of X-ray changes, endotracheal tube aspirates, and positive inflammatory markers.
Use of mechanical ventilation	<u>P3</u>
	Been et al. (2009): No data.
	<u>P4</u>
	Bitar et al. (2020): No data.
	Cartwright et al. (2019): No data.
	Kim et al. (2018): Mechanical ventilation within 48 hours after birth.
	van Stralen et al. (2009): No data.
	Torrance et al. (2007): No data.
	Schaap et al. (2001): No data.
Surfactant use	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
	Been et al. (2009): No data.
	Elimian et al. (2000): No data.
	<u>P4</u>
	Bitar et al. (2020): No data.
	Cartwright et al. (2019): No data.
	Kim YJ et al. (2018):Defined as the administration of any prophylactic or rescue surfactant.
	van Stralen et al. (2009): No data.
	Torrance et al. (2007): No data.
	Elimian et al. (1999): No data.
Oxygen therapy	<u>P4</u>
	Bitar et al. (2020): No data.
	Cartwright et al. (2019): No data.
Oxygen requirement for at least 4 h	<u>P2</u>
	Kishenbaum et al. (2018): Oxygen requirement for at least 4 hours.

Mean duration of mechanical ventilations	<u>P2</u>
	de la Huerga Lopez et al. (2019): No data.
	<u>P3</u>
	Ahn et al. (2012): No data.
Duration of oxygen use	<u>P3</u>
	Ahn et al. (2012): No data.
Patent ductus arteriosus (PDA)	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
	Ahn et al. (2012): Diagnosed by echocardiography and medical treatment or surgical ligation were performed when necessary.
	Been et al. (20009): Persistence of the open ductus arteriosus postnatally, as demonstrated by ultrasonographic examination.
	Elimian et al. (2000): Required medical or surgical intervention.
	<u>P4</u>
	Kim YJ et al. (2018): No data.
	Feng et al. (2019): No data.
	Ishikawa et al. (2015): Diagnosed based on both echocardiographic findings and clinical evidence of a volume overload due toa left-to-right shunt.
	Mitsiakos et al. (2013): No data.
	van Stralen et al. (2009): No data.
	Elimian et al. (1999): No data.
Hypotension within 7 postnatal days	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
Hypotension	<u>P4</u>
	van Stralen et al. (2009): Defined as a mean arterial pressure ≤30mmHg requiring treatment with volume
	expanders and/or inotropic support.
Intraventricular hemorrhage (IVH)	<u>P2</u>
	Kishenbaum et al. (2018): No data.
	<u>P3</u>
	Ryu et al. (2019): Defined as grade $\geq 3$ and listed in the online supplementary Table1. <sup>*1</sup>
	Ahn et al. (2012): Defined according to the IVH grading by Papile et al.*6
	Been et al. (2009): Defined according to Volpe. <sup>*7</sup>
	Goldenberg et al. (2006): Defined as grade 3 or 4 by ultrasound criteria.*7
	Dempsey (2005): Graded according to the Papile classification. *6
	Baud et al. (2000): Defined as grade 3 or 4 of Papile classification. *6

	<u>P4</u>
	Kim et al. (2018): Defined as grade 3 or 4.
	Kim YJ et al. (2018): Defined as grade 3 or 4 of Papile classification. *6
	Riskin-Mashiah et al. (2018): Defined as grade 3 or 4 of Papile classification. *6
	Feng et al. (2017): No data.
	Riskin-Mashiah et al. (2016): Diagnosed by ultrasound examination and graded according to Papile et al. *6
	Ishikawa et al. (2015): Defined as Papile grade 1 or more.
	Schaap et al. (2001): Defined as grade 3 or 4.
	Bernstein et al. (2000): Diagnosed according to the criteria by Papile. *6
	Spinillo et al. (1995): Defined as grade 3 or 4 of Papile classification. *6
severe IVH	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
	Ahn et al. (2012): Defined as grade 3 or 4 of Papile classification. *6
	Been et al. (2009): Defined according to Volpe. *7
	Goldenberg et al. (2006): No data.
	Baud et al. (2000): No data.
	<u>P4</u>
	Kim et al. (2018): No data.
	Kim YJ et al. (2018): No data.
	Riskin-Mashiah et al. (2018): Defined as grade 3 or 4 of Papile classification. *6
	Feng et al. (2017): No data.
	Riskin-Mashiah et al. (2016): Diagnosed by ultrasound examination and graded according to Papile et al. $^{*6}$
	Mitsiakos et al. (2013): Defined as grade 3 or 4.
	Schaap et al. (2001): No data.
	Bernstein et al. (2000): Diagnosed according to the criteria by Papile. *6
	Spinillo et al. (1995): Defined as grade 3 or 4 of Papile classification. *6
Periventricular leukomalacia (PVL)	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
	Ahn et al. (2012): Defined according to Volpe. *7
	Been et al. (2009): Defined according to Volpe. *7
	Goldenberg et al. (2006): Defined according to Volpe. *7
	Baud et al. (2000): Diagnosed on cerebral ultrasound scan.

	<u>P4</u>
	Riskin-Mashiah et al. (2018): No data.
	Riskin-Mashiah et al. (2016): Diagnosed by the presence of multiple periventricular cysts identified by cranial ultrasound examination after 28 days of life.
	Ishikawa et al. (2015): Based on either head ultrasound or cranial MRI scan performed at 2 weeks of age or later.
	Mitsiakos et al. (2013): No data.
Major brain lesion damage	<u>P4</u>
	van Stralen et al. (2009): Defined as the presence of a least one of the following findings: IVH $\geq$ grade3 or ventricular dilatation or cystic PVL.
	Schaap et al. (2001): No data.
	Elimian et al. (1999): Defined as IVH grade 3 and 4, IVH with PVL, and PVL.
	Ley et al. (1997): Defined ad IVH grade 3, IVH grade 4, or PVL.
	Spinillo et al. (1995): No data.
Necrotizing enterocolitis (NEC)	<u>P2</u>
	Kishenbaum et al. (2018): No data.
	<u>P3</u>
	Ryu et al. (2019): NEC stage $\ge 2b$ . *8
	Been et al. (2009): Defined as stage 2 or higher according to Bell et al.*8
	Goldenberg et al. (2006): Defined as stage 2 or higher.
	Dempsey et al. (2005): Classified as the presence of intramural gas on X-ray, perforation or evidence of intestinal necrosis at surgery or autopsy.
	Elimian et al. (2000): Diagnosed clinically and radiologically, and confirmed by surgery or autopsy.
	<u>P4</u>
	Kim et al. (2018): No data.
	Kim YJ et al. (2018): Defined as stage 2b or higher according to Bell et al. <sup>*8</sup>
	Riskin-Mashiah et al. (2018): Defined as stage 2 or higher according to Bell et al.*8
	Feng et al. (2017): No data.
	Riskin-Mashiah et al. (2016): Presence of clinical and radiologic features according to the criteria of Bell et al. *8
	Ishikawa et al. (2015): Defined as stage 2 or higher according to Bell et al.*8
	Mitsiakos et al. (2013): No data.
	Bernstein et al. (2010): No data.
	van Stralen et al. (2009): Defined as stage 2 or higher.
	Elimian et al. (1999): Diagnosed clinically and radiologically and confirmed at surgery or autopsy.

Sepsis	<u>P3</u>
	Ryu et al. (2019): Defined as culture proven sepsis. The presence of clinical symptoms, and signs with proven causative organisms documented from blood cultures.
	Ahn et al. (2012): Defined as a positive blood culture.
	Been et al. (2009): Clinical sepsis or culture-proven sepsis. Clinical sepsis was clinical presentation of sepsis with raised CRP. Culture-proven sepsis was any systemic bacterial infection documented by a positive blood or cerebrospinal fluid culture.
	Goldenberg et al. (2006): No data.
	Dempsey et al. (2005): Defined as a positive blood culture.
	Elimian et al. (2000): Defined as positive blood or cerebrospinal fluid cultures.
	<u>P4</u>
	Kim et al. (2018): Included both suspected infections (with clinical findings suggesting infection) and proven infections.
	Kim YJ et al. (2018): Defined as the presence of clinical symptoms and signs with proven causative organisms documented from blood cultures.
	Feng et al. (2017): No data.
	Ishikawa et al. (2015): No data.
	Mitsiakos et al. (2013): Defined as a positive blood culture and the need for intravenous antibiotics for minimum of 7 days.
	van Stralen (2009): Based on the need for intravenous antibiotics administration for more than 7 days. Schaap et al. (2001): Defined as neonatal septicemia or meningitis confirmed by positive cultures.
	Elimian et al. (1999): Defined as positive blood or cerebrospinal fluid cultures.
Early onset sepsis	P3
•	<b>R</b> yu et al. (2019): Listed in the online supplementary Table $1^{*1}$
	Abn et al. (2012): Defined as a positive blood culture occurring within the first 72 hours.
	Been et al. (2009): Neonatal sensis occurring during the first 72 hours of life
	Dempsey et al. (2005): Defined as a positive blood culture in the first 72 hours.
Systemic inflammatory response syr	ndrome p3
	Goldenberg et al. (2006): Defined as clinically suspected sepsis with negative cerebrospinal fluid and blood cultures or a band: band + polymorphonuclear cell ratio of 0.15 or greater.
Meningitis	P3
Wieningitis	
weiningitis	Dempsey et al. (2005): Defined as a positive cerebrospinal fluid culture.
Neonatal hypoglycemia	Dempsey et al. (2005): Defined as a positive cerebrospinal fluid culture. P1
Neonatal hypoglycemia	Dempsey et al. (2005): Defined as a positive cerebrospinal fluid culture.  P1 Cassimatis et al. (2020): Defined as Blood sugar <40mg/dL within 4 hours of birth.

	<u>P2</u>
	De la Huerga Lopez et al. (2019): No data.
	Kishenbaum et al. (2018): Defined as glucose level ≤45 mg/dl.
	P4
	Bitar et al. (2020): Defined as glucose level <40 mg/dl.
	Kim et al. (2018): Defined as glucose level <40 mg/dl.
Neonatal adrenal insufficiency	P4
	Kim YJ et al. (2018): Defined as the requirement of hydrocortisone treatment.
	Ishikawa et al. (2015): No data.
Intrahepatic cholestasis	<u>P3</u>
	Ahn et al. (2012): Defined when conjugated bilirubin exceed 2.0mg/dl.
Retinopathy of prematurity (ROP)	<u>P3</u>
	Ryu et al. (2019): Defined as requiring treatment.
	<u>P4</u>
	Kim YJ et al. (2018): Defined as requiring treatment.
	Riskin-Mashiah et al. (2018): No data.
	Feng et al (2017): No data.
	Riskin-Mashiah et al. (2016): Defined as grade 3-4 in international standard classification.*9
	Mitsiakos et al. (2013): No data.
Gestational age at birth	<u>P4</u>
	Bitar et al. (2020): Defined as gestational age birth.
	Cartwright et al. (2019): Defined as gestational age at birth.
	Ishikawa et al. (2015): Defined as gestational age at birth.
	Mitsiakos et al. (2013): Defined as gestational age birth.
Birth weight	<u>P4</u>
	Bitar et al. (2020): Defined as birth weight.
	Cartwright et al. (2019): Defined as birth weight.
	Ishikawa et al. (2015): Defined as birth weight.
	Mitsiakos et al. (2013): Defined as birth weight.
Neonatal intensive care unit (NICU)	<u>P1</u>
admission	Krispin et al. (2018): Defined as NICU admission.
	<u>P2</u>
	de la Huerga Lopez et al. (2019): Defined as NICU admission.
	Kishenbaum et al. (2018): Defined as NICU admission.

	<u>P4</u>
	Bitar et al. (2020): Defined as NICU admission.
Duration of hospital stay	<u>P4</u>
	Bitar et al. (2020): No data.
	Mitsiakos et al. (2013): No data.
Survival free from disability	<u>P4</u>
	Cartwright et al. (2019): No data
Death at long-term follow up	<u>P4</u>
	Schaap et al. (2001): No data.
Death or disability/handicap at 2 years	<u>P4</u>
	Schaap et al. (2001): No data.
Cerebral palsy	<u>P4</u>
	Ishikawa et al. (2015): Defined as a non-progressive central nervous system disorder characterized by abnormal muscle tone in at least one extremity and abnormal control of movement and posture.
	Cartwright et al. (2019): Defined as a nonprogressive loss of motor function with disordered muscle tone or tendon reflexes.
Severe hearing impairment	<u>P4</u>
	Ishikawa et al. (2015): Defined as the need for hearing aids.
Visual impairment	<u>P4</u>
	Ishikawa et al. (2015): Defined as unilateral or bilateral blindness diagnosed by an ophthalmologist.
Discharge with respiratory support	<u>P3</u>
	Ryu et al. (2019): Listed in the online supplementary Table1.*1
Growth<10%ile in early childhood	<u>P4</u>
	Schaap et al. (2001): Defined by using standard deviation to adjust for discrepancies in age and sex at school age. <sup>*10</sup>
Abnormal behavior at long-term follow up	<u>P4</u>
at school-age	Schaap et al. (2001): Defined by the DuPaul-score. *11

\*1. www.karger.com/doi/10.1159/000502650.

\*2. Neonatal mortality rate (0 to 27 days) per 1000 live births) (SDG 3.2.2) (who.int).

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\*8. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg. 1978;187(1):1-7. doi:10.1097/00000658-197801000-00001.

\*9. An international classification of retinopathy of prematurity. The Committee for the Classification of Retinopathy of Prematurity. Arch Ophthalmol. 1984;102(8):1130-1134. doi:10.1001/archopht.1984.01040030908011.

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