**Table S1: Literature overview of the antenatal corticosteroids-to-birth interval**

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| Article | Study period, country and design | Patients | Intervention: antenatal corticosteroids | Interval | Outcome | Results | Conclusion | Optimal interval |
| Liggings G,19721 | Dec 1969-Oct 1971New ZealandRCT | - Preterm labour and 24-36 weeksOR- Planned delivery before 37 weeks282 mothers, ? infants | Betamethasone*route:* IM *dose:* 2x6 mg*interval:* 24h Comparison: cortisone*route:* IM *dose:* 2x6 mg*interval:* 24h  | <24h24h-48h2-7d≥7d | RDSclinical signs of grunting respirations and chest retraction during the first 3h and persisting beyond the first 6h after delivery and an Rx pattern of fine generalised granularity of lung fields with air bronchogram | < 24h: 24.1 vs 31.8% (p = ?)24h-48h: 10.0 vs 36.8% (p = ?)2-7d: 3.6 vs 33.3% (p = .03)≥7d: 2.2 vs 9.4% (p = ?) | Sufficient evidence of beneficial effects on lung function, with optimal interval antenatal corticosteroids-to-birth of 2-7d | 2-7 days |
| Schutte M, 198326 | 1) Apr 1974-Apr 19772) Apr 1977-Jan 1980The NetherlandsRCT  | All infants born at 26-33 weeks1) 259 infants2) 223 infantsMultiples: ?  | 1 + 2) Betamethasone disodium phosphate + betamethasone acetate *route:* IM *dose:* 8 + 6 mg*interval:* ? Comparison: 1) placebo or no treatment 2) no treatment  | <12h12h-7d8-21d>21d | RDS retraction score of ≥3, groaning, low PO2 in room air, oxygen need >24h, PCO2 ≥50mmHg, Rx air bronchogram and reticulogranular structure, symptoms worsening on 2nd day of life, or hyaline membrane disease on necropsy | More RDS and deaths of hyaline membrane disease at <12h (RR = ?) or >21d (RR = ?) compared to 12h-7d and 8-21d The relationship between the *admission-to-delivery interval* and RDS was the same in the steroid-treated, placebo-treated and untreated groups | Primarily time factors and only secondarily the methods of treatment influence the occurrence of RDS | >12h-21 days with no difference in RDS between antenatal corticosteroids or not |
| McNamara M, 199827 | 1991-1993United StatesRetrospective | Infants exposed to antenatal corticosteroids, born at 28-32 weeks119 infantsMultiples: no | Betamethasone phosphate, not further specified | 1-7d>7d | RDS physical signs such as nasal flaring and retractions with >24h need for oxygen and typical radiographic ground glass appearance | No difference in RDS between 1-7d and >7d | Findings suggest that the process of pulmonary maturation induced by steroid administration is permanent rather than transient | / |
| Vermillion S, 200128 | Jan 1996-Jan 1999United StatesRetrospective | Infants exposed to single antenatal corticosteroids course, born at 28-34 weeks216 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | 1-2d3-7d8-14d | RDS clinical manifestations and RxIVH grade 3-4, days of ventilator, surfactant, early-onset sepsis | No differences in outcomes between 1-2d, 3-7d and 8-14d | Delivery between 8-14d after a single course of antenatal corticosteroids was not associated with increased perinatal morbidity compared with delivery at shorter intervals | / |
| Smrcek J, 200329 | Jan 1991-Oct 1999GermanyRetrospective | Infants with birthweight ≤ 1,500g106 infants Multiples: yes | Betamethasone*route:* IV *dose:* 2x4 mg*interval:* 24h Additional courses of 4 mg every 7-10 days | ≤7d>7d | Lung maturation duration mechanical ventilation, need supplemental oxygen, surfactant, RDS (respiratory failure requiring mechanical ventilation with supplemental oxygen for ≥48h or exogenous surfactant and/or typical findings on Rx) | No difference in lung maturation between birth within or after 7d interval | The time interval between last corticosteroid treatment and delivery was without influence on RDS | / |
| Sehdev H, 200430 | Jan 1998-Dec 2002United StatesRetrospective  | Infants exposed to antenatal corticosteroids, with birthweight between 500 and 1500g324 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | <24h24-48h2-7d>7d | Neonatal outcomes anthropometry, Apgar, RDS treated with surfactant, IVH grade 3 or 4, NEC, days mechanical ventilation, neonatal death, CLD, other complications | No differences in neonatal outcome between <24h, <24h, 2-7d and >7d | Neonatal mortality and major neonatal complications were similar for babies born within a week of the last dose compared to born ≥ 1 week after exposure | / |
| Peaceman A, 200531 | 2002-2004 United StatesRetrospective | Infants exposed to single course antenatal corticosteroids between 24-32 weeks, born at 26-34 weeks 162 women, 197 infantsMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 12h  | 1-7d>7dSubanalysis: 1-7d vs8-14d,15-28d,>28d | Need for respiratory support mechanical ventilation or CPAP ≥24h, surfactant, length of mechanical ventilation, oxygen need at 28d and at 36 weeksNon-respiratory morbiditiesNeonatal mortality | Less mechanical ventilation or CPAP ≥24h in neonates born ≤7d (p<.01), other (non-) respiratory morbidities and mortality not significantly differentsubanalysis: more ventilation/CPAP ≥24h at 15-28d (OR 8.3, 95%CI 2.6,27.2) and >28d (OR 8.3, 95%CI 2.6,26.0) compared to 1-7d | Even if preterm delivery appears imminent after a prolonged interval from antenatal corticosteroids, an empiric rescue course of steroids may not be justified | (1-7d) |
| Ring A, 200732 | Jan 1999-Dec 2004United StatesRetrospective  | Infants exposed to a complete course of antenatal corticosteroids, born at 26-34 weeks357 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 12h  | 2-14d>14d | Need for respiratory support surfactant, ventilator support >24h, days of ventilator support, CLDIVH any gradeComposite outcomePVL, IVH grade 3-4, CLD or death | More mechanical ventilation >24h (OR 1.7, 95%CI 1.1,2.9) and surfactant (OR 1.8, 95%CI 1.1,2.9) in prolonged latency groupNo differences in IVH or composite | There is an association between a prolonged latency period of >14d between antenatal corticosteroids and birth and the severity of neonatal respiratory illness at birth | ≤14d |
| Ferguson S, 200933 | Jan 1989-Dec 2002CanadaRetrospective | Infants exposed to antenatal corticosteroids, from mothers withsevere pregnancy induced hypertension or HELLP, delivered for maternal or fetal concernsbetween 26-34 weeks172 infants | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 12h  | ≤48h>48h | Respiratory outcomesdelay in initiating and maintaining respiration after birth, respiratory depression at birth, surfactant, moderate or severe RDS (need for oxygen, CPAP or ventilated for grunting, retractions and decreased air entry or Rx not explained by any other disease)Perinatal mortalityOther perinatal morbiditiesIVH grade 3-4, NEC, composite, SGA, NICU length of stay Chorioamnionitis | Interval >48h: less delay in initiating and maintaining respiration after birth (RR 0.47, 95%CI 0.23,0.93), less depression at birth (RR 0.59, 95%CI 0.33,0.97), less surfactant (RR 0.55, 95%CI 0.30,0.96), less composite perinatal morbidity and mortality (RR 0.47, 95%CI 0.54,0.98)All other outcomes not significantly different | These data suggest improvement in some perinatal outcomes with an increased interval from steroids to delivery | >48h |
| Waters T, 200834 | Period?United StatesRetrospective | Infants born at 30 and 33+6 weeks524 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 6h  | No antenatal corticosteroids or <48h2-7d>7d | Respiratory outcomesRDS (persistent oxygen requirement >24h) oxygen and ventilator requirements, surfactantIVH, NEC, sepsis, NICU days | Compared to >7d:- at 2-7d: less RDS (56.7 vs 69.5%, p = .04) - no course/< 48h: more surfactant (p<.05)All other outcomes not significantly different | Infants with antenatal corticosteroids exposure >7d prior to delivery had a significantly increased rate of RDS compared to newborns who were exposed within the 48h to 7d window | 2-7d |
| Wilms F, 201135 | 2006The NetherlandsRetrospective | Infants exposed to a single complete course of antenatal corticosteroids, born at 24+5-34 220 mothers, 254 neonatesMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | 0-7d8-14d15-21d22-28d | Severe neonatal respiratory morbidity need for intubation at NICU, need of at least 40% oxygen, RDS (on Rx), CPAP (when 21-40% oxygen need), CLD (need oxygen >28d after birth)Composite outcomeCLD, IVH grade 3-4, NEC, proven sepsis, PVL grade 2-4 | Compared to 0-7d: - Intubation need: increased at 8-14d (OR 2.3, 95%CI 1.1,5.4) and at 15-21d (OR 5.6, 95%CI 1.8,18)- RDS: no difference (8-14d: OR 1.3, 95%CI 0.6,2.8, 15-21d: OR 2.2, 95CI 0.7,6.4) - CPAP: no difference (8-14d: OR 1.0, 95%CI 0.4,2.0, 15-21d: OR 1.6, 95%CI 0.5,4.8)- CLD: no difference at 8-14d (OR 1.4, 95% CI 0.5,41.0), increased at 15-21d (OR 4.0, 95%CI 1.1,15.0)- Composite: no difference at 8-14d (OR 1.4, 95%CI 0.6,3.2), increased at 15-21d (OR 3.2, 95%CI 1.0,9.7) | The effect of antenatal corticosteroids diminishes only in neonates born at a GA of 28-30 weeks, when the time interval becomes >7d | 0-7d |
| Kuk J-Y, 201336 | Nov 1995-May 2011KoreaRetrospective | Twins born at 24-34 weeks234 twin pregnancies | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 6h | No antenatal corticosteroids<2d2-7d>7d | RDS Rx plus ≥ 1 clinical signs; grunting, retracting, increased oxygen requirement or surfactant | Compared to no course: at 2-7d: less RDS (aOR 0.42, 95%CI 0.18,0.97) | Significantly reduced incidence of RDS after a single complete course of antenatal corticosteroids in preterm twins born between 24 and 34 weeks when the time interval was 2-7d | 2-7d |
| Melamed N, 201537 | Jan 2010-Dec 2012CanadaRetrospective | Infants born at 24-33+6 weeks6,870 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 6h | No antenatal corticosteroids<24h1-7d>7d | Composite outcome mortality, BPD, IVH grade 3-4, PVL, ROP grade ≥3Individual components, NEC | Compared to 1-7d: - not exposed: more composite (aOR 2.12, 95%CI 1.69,2.65), mortality (aOR 2.56 95%CI 1.83,3.59), BPD (aOR 1.45, 95%CI 1.10,1.91), severe IVH (aOR 2.67, 95%CI 2.01,3.54)- <24h: more composite (aOR 1.48, 95%CI 1.22,1.80), mortality (aOR 1.59, 95%CI 1.16,2.18), BPD (aOR 1.26, 95%CI 1.00,1.59), severe IVH (aOR 1.74, 95%CI 1.35,2.25)>7d: more composite (aOR 1.46; 95%CI 1.20,1.77), mortality (aOR 1.40, 95%CI 1.00,1.97), BPD (aOR 1.39, 95%CI 1.11,1.75) | The effectiveness of antenatal corticosteroids is lower when administered at 24h or >7d before birth compared to 1-7d. Administration outside the 1-7d window may still provide benefits compared with not administering antenatal corticosteroids  | 1-7d |
| Kosinska-Kaczynska K, 201638 | 2006-2014PolandRetrospective | Twins exposed to a complete course of antenatal corticosteroids, born at 26-33+6 weeks 106 twin pregnancies | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* IM *dose:* 4x6 mg*interval:* 6h | <7d≥7d | Perinatal mortality, respiratory complications, infections requiring IV antibiotics, IVH grade 3-4, NEC | Significantly less respiratory complications at <7d (p = .003)All other outcomes not significantly different | A single antenatal corticosteroids course should be administered with caution in order to allow for the completion of treatment without exceeding an interval of 7d to delivery | <7d |
| Liebowitz M, 201639 | Jan 1998-Dec 2015United StatesRetrospective (prospective review of cranial ultrasound images) | Infants born at ≤27+6 weeks392 infantsMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | <10d≥10d | IVH grade 3-4, ventilation at 24h, death, BPD or death, NEC or deathSubanalysis: ≤6h, 7-23h, ≥24h | Compared to <10d: increased risk at ≥10d of severe IVH (aOR 4.16, 95%CI 1.59,10.87 and ventilation at 24h (aOR 3.23, 95%CI 1.59,6.57)Subanalysis: compared to ≤6h: increased risk at ≥24h of severe IVH (aOR 0.13, 95%CI 0.07,0.27), ventilation at 24h (aOR 0.47, 95%CI 0.23,0.98) and death (aOR 0.25, 95%CI 0.13,0.47)All other outcomes not significantly different | In infants delivering before 28w exposure to a two-dose course of antenatal corticosteroids was associated with a decreased incidence of severe IVH, need for respiratory support and death | ≥24h<10d |
| Fuller K, 201740 | Jan 2009-Aug 2013United StatesRetrospective | Infants born at 23-33+6 weeks548 infantsMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | No antenatal corticosteroids1-23h24-47h2-7d>7d | RDS, IVH, NEC, surfactant, intubation, culture proven sepsis, ROP, NICU length of stay, death, composite of the above | Compared to no exposure:24-47h: less composite (OR 0.28, 95%CI 0.11,0.74), RDS (OR 0.31, 95%CI 0.12,0.80), surfactant (OR 0.26, 95%CI 0.09,0.75) and intubation (OR 0.27, 95%CI 0.10,0.73) >7d: less composite (OR 0.49, 95%CI 0.26,0.95), RDS (OR 0.49, 95%CI 0.26,0.92), surfactant (OR 0.39, 95%CI 0.21,0.73) and intubation (OR 0.39, 95%CI 0.21,0.71), less IVH (OR 0.29, 95%CI 0.21,0.71) | Neonatal outcomes are improved in less than 48 hours after antenatal corticosteroids compared to no antenatal corticosteroids | 24-47h>7d |
| Yasuhi I, 201741 | 2005-2008JapanRetrospective | Infants exposed to a single complete course of antenatal corticosteroids, born at 24-33+6w117 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | 2-7d7-14d>14d | RDS early onset tachypnea, retractions, need for oxygen >24h or mechanical ventilation, Rx | At <30w: less RDS at 2-7d compared to 7-14 (p<.05) and >14d (p<.05) | Singleton pregnant women who delivered preterm between 24-33 weeks, exposed to a single course of antenatal corticosteroids were significantly associated with an increased incidence of neonatal RDS in comparison with deliveries within 7d after antenatal corticosteroids | 2-7d |
| Norman M, 201742 | 2011-2012EuropeProspective | Infants born at 24-31 weeks4,597 infantsMultiples: no | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h Dexamethasone*route:* ? *dose:* ?*interval:* ?  | Continuous variable | MortalityComposite outcomeMortality or severe neonatal morbidity (IVH grade 3-4, PVL, ROP stage 3-5, NEC)Severe neonatal brain injuryIVH grade 3-4, PVL | For all outcomes, the risk reduction associated with antenatal corticosteroids was transient, with increasing mortality and risk of severe neonatal brain injury associated with antenatal corticosteroids -to-birth intervals of 5 to 7d or more | Significant health-promoting effects of antenatal corticosteroids begin just hours before delivery. A large proportion remains at risk for very preterm birth >7d after antenatal corticosteroids and their infants have increased morbidity and mortality | <7d |
| Norberg H, 201743 | Apr 2004-March 2007SwedenProspective | Infants born at 22-26 weeks707 infantsMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* 24h  | No antenatal corticosteroids<24h24-47h2-7d>7dUnknown timing | Neonatal and infant survivalInfant survival without major neonatal morbidity IVH grade ≥3, ROP stage ≥3, PVL, NEC, severe BPD | Compared to 2-7d:- lowest hazard ratios for neonatal and infant survival among infants unexposed to antenatal corticosteroids (hazard ratio 0.26, 95%CI 0.15,0.43)- lower hazard ratios for survival at <24h (hazard ratio 0.53, 95%CI 0.33,0.87) and >7d (hazard ratio 0.56, 95%CI 0.32,0.97) | Shorter or longer administration-to-birth intervals than 24h to 7d were associated with a doubled risk for infant mortality | 2-7d |
| Lau H, 201744 | Nov 2014-Jan 2015SingaporeRetrospective | Infants born at 23+5-35+6 weeks301 women, 325 infantsMultiples: yes | Dexamethasone*route:* IM *dose:* 2x12 mg*interval:* 12h | No antenatal corticosteroids<48h2-7d>7d | RDS respiratory rate >60/min, respiratory distress (grunting, sternal/subcostal/intercostal retraction), occurring within 4-6h of delivery, oxygen requirement to prevent cyanosis and Rx changes | Compared to no course: less RDS at <48h (aOR<0.001, 95%CI <0.001,0.139), 2-7d (aOR <0.001, 95%CI <0.001,0.211), >7d (aOR 0.003, 95%CI <0.001,0.446)Compared to 2-7d: more RDS at >7d (aOR 7.02, 95%CI 1.54,32.07) | There was a benefit of administrating antenatal corticosteroids within 7d of delivery as infants with antenatal corticosteroids exposure beyond 7d are 7 times more likely to have RDS | 2-7d |
| Frändberg J, 201845 | Jan 2013-Dec 2016SwedenRetrospective | Infants born at 23-33+6 weeks431 women, 498 infantsMultiples: yes | Betamethasone*route:* IM *dose:* 2x12 mg*interval:* ≤24h  | No antenatal corticosteroids<24h1-7d>7d | NICU length stay, RDS, BPD, NEC, IVH grade 3-4, ROP stage ≥3, neonatal mortality | Compared to 1-7d: - <24h: more RDS (OR 2.16, 95%CI 1.11,4.22)- >7d: more RDS (OR 2.00, 95%CI 1.05,3.79) and more BPD (OR 2.78, 95%CI 1.45,5.33)All other outcomes not significantly different | An antenatal corticosteroids delivery interval more than 7d was associated with an increased risk of neonatal respiratory morbidity | 1-7d |

**Abbreviations:** RCT = Randomised Controlled Trial, IM = intramuscular, RDS = respiratory distress syndrome, RR = relative risk, IVH = intraventricular hemorrhage, IV = intravenous, NEC = necrotizing enterocolitis, CLD = chronic lung disease, CPAP = continuous positive airway pressure, SGA = small for gestational age, OR = odds ratio, CI = confidence interval, NICU = neonatal intensive care unit, PVL = periventricular leukomalacia, aOR = adjusted odds ratio, BPD = bronchopulmonar dysplasia, ROP = retinopathy of prematurity