**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 1971  New Zealand  RCT | - Preterm labour and 24-36 weeks  OR  - Planned delivery before 37 weeks  282 mothers,  ? infants | Betamethasone  *route:* IM  *dose:* 2x6 mg  *interval:* 24h  Comparison:  cortisone  *route:* IM  *dose:* 2x6 mg  *interval:* 24h | <24h  24h-48h  2-7d  ≥7d | RDS  clinical 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 1977  2) Apr 1977-Jan 1980  The Netherlands  RCT | All infants born at 26-33 weeks  1) 259 infants  2) 223 infants  Multiples: ? | 1 + 2) Betamethasone disodium phosphate + betamethasone acetate  *route:* IM  *dose:* 8 + 6 mg  *interval:* ?  Comparison:  1) placebo or no treatment  2) no treatment | <12h  12h-7d  8-21d  >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 | 1991-1993  United States  Retrospective | Infants exposed to antenatal corticosteroids, born at 28-32 weeks  119 infants  Multiples: 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 1999  United States  Retrospective | Infants exposed to single antenatal corticosteroids course, born at 28-34 weeks  216 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | 1-2d  3-7d  8-14d | RDS  clinical manifestations and Rx  IVH 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 1999  Germany  Retrospective | Infants with birthweight ≤ 1,500g  106 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 2002  United States  Retrospective | Infants exposed to antenatal corticosteroids, with birthweight between 500 and 1500g  324 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | <24h  24-48h  2-7d  >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 States  Retrospective | Infants exposed to single course antenatal corticosteroids between 24-32 weeks, born at 26-34 weeks  162 women, 197 infants  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* IM  *dose:* 4x6 mg  *interval:* 12h | 1-7d  >7d  Subanalysis:  1-7d vs  8-14d,  15-28d,  >28d | Need for respiratory support mechanical ventilation or CPAP ≥24h, surfactant, length of mechanical ventilation, oxygen need at 28d and at 36 weeks  Non-respiratory morbidities  Neonatal mortality | Less mechanical ventilation or CPAP ≥24h in neonates born ≤7d (p<.01), other (non-) respiratory morbidities and mortality not significantly different  subanalysis: 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 2004  United States  Retrospective | Infants exposed to a complete course of antenatal corticosteroids, born at 26-34 weeks  357 infants  Multiples: 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, CLD  IVH  any grade  Composite outcome  PVL, 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 group  No 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 2002  Canada  Retrospective | Infants exposed to antenatal corticosteroids, from mothers with  severe pregnancy induced hypertension or HELLP, delivered for maternal or fetal concerns  between 26-34 weeks  172 infants | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* IM  *dose:* 4x6 mg  *interval:* 12h | ≤48h  >48h | Respiratory outcomes  delay 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 mortality  Other perinatal morbidities  IVH 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 States  Retrospective | Infants born at 30 and 33+6 weeks  524 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* IM  *dose:* 4x6 mg  *interval:* 6h | No antenatal corticosteroids or <48h  2-7d  >7d | Respiratory outcomes  RDS (persistent oxygen requirement >24h) oxygen and ventilator requirements, surfactant  IVH, 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 | 2006  The Netherlands  Retrospective | Infants exposed to a single complete course of antenatal corticosteroids, born at 24+5-34  220 mothers, 254 neonates  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | 0-7d  8-14d  15-21d  22-28d | 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 outcome  CLD, 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 2011  Korea  Retrospective | Twins born at 24-34 weeks  234 twin pregnancies | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* IM  *dose:* 4x6 mg  *interval:* 6h | No antenatal corticosteroids  <2d  2-7d  >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 2012  Canada  Retrospective | Infants born at 24-33+6 weeks  6,870 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* IM  *dose:* 4x6 mg  *interval:* 6h | No antenatal corticosteroids  <24h  1-7d  >7d | Composite outcome  mortality, BPD, IVH grade 3-4, PVL, ROP grade ≥3  Individual 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 | 2006-2014  Poland  Retrospective | 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 2015  United States  Retrospective (prospective review of cranial ultrasound images) | Infants born at ≤27+6 weeks  392 infants  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | <10d  ≥10d | IVH grade 3-4, ventilation at 24h, death, BPD or death, NEC or death  Subanalysis: ≤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 2013  United States  Retrospective | Infants born at 23-33+6 weeks  548 infants  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | No antenatal corticosteroids  1-23h  24-47h  2-7d  >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 | 2005-2008  Japan  Retrospective | Infants exposed to a single complete course of antenatal corticosteroids, born at 24-33+6w  117 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | 2-7d  7-14d  >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 | 2011-2012  Europe  Prospective | Infants born at 24-31 weeks  4,597 infants  Multiples: no | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h  Dexamethasone  *route:* ?  *dose:* ?  *interval:* ? | Continuous variable | Mortality  Composite outcome  Mortality or severe neonatal morbidity (IVH grade 3-4, PVL, ROP stage 3-5, NEC)  Severe neonatal brain injury  IVH 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 2007  Sweden  Prospective | Infants born at 22-26 weeks  707 infants  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 24h | No antenatal corticosteroids  <24h  24-47h  2-7d  >7d  Unknown timing | Neonatal and infant survival  Infant 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 2015  Singapore  Retrospective | Infants born at 23+5-35+6 weeks  301 women, 325 infants  Multiples: yes | Dexamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* 12h | No antenatal corticosteroids  <48h  2-7d  >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 2016  Sweden  Retrospective | Infants born at 23-33+6 weeks  431 women, 498 infants  Multiples: yes | Betamethasone  *route:* IM  *dose:* 2x12 mg  *interval:* ≤24h | No antenatal corticosteroids  <24h  1-7d  >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