# Delayed Cord Clamping in Preterm and Term Infants

**[July 2024 (replaces May 2019)]**

This guideline covers the separate literature for delayed cord clamping and cord milking in both preterm and term infants, with a suggested combined algorithm and checklist.



# Summaries

## Delayed Cord Clamping (DCC)

DCC appears to be safe in the preterm infant and appears to decrease the risk of death, improve one-minute Apgar scores, and decrease the number of infants requiring a transfusion. There is an increased risk of hypothermia (but only by 0.12 degrees.) Maternal adverse events are not increased by DCC.

DCC appears to be safe in the term infant and may decrease the risk of iron deficiency. Maternal adverse events are not increased by DCC, but these have not been studied extensively.

Each delivery is unique and the decision for DCC should be made after discussion between the delivering obstetrician, neonatologist, and resuscitation team. We suggest that before each delivery that the obstetrician discusses the patient's history and whether or not DCC should be attempted. The appropriateness of DCC should take maternal, placental, and fetal/neonatal factors into account. An algorithm is suggested below to help identify cases where DCC should not be attempted.

If DCC is agreed upon and performed, the resuscitation team can help monitor the vigorousness of the infant, suggest additional resuscitation maneuvers before the cord is clamped (see below for cord milking), and prompt earlier cord clamping if clinically indicated. Cord gases can be sent on a segment taken after cord clamping.

## Cord Milking

Cord milking can be performed in non-vigorous neonates who are born at 35 weeks or greater (strong recommendation). Cord milking is also reasonable to consider for preterm babies 28+0-34+6 week preterm

babies who cannot receive DCC (weak recommendation). Cord milking should NOT be performed in GA 27+6 weeks or less (strong recommendation).

# Delayed Cord Clamping:

Delayed cord clamping (DCC) of preterm infants had been historically practiced until the early to mid 1900s, when the standard or care transitioned to immediate cord clamping (ICC). Immediate cord clamping was done particularly in preterm neonates secondary to concerns of harm from delayed resuscitation, as well as hypothermia for increased exposure and jaundice and/or polycythemia from the additional red blood cell mass. Recently, attention has returned to the possible benefits of delayed cord clamping with much research focused on preterm infants. Delayed cord clamping is typically defined as delay in clamping the cord after birth of the neonate by at least 30-60 seconds.

Delayed cord clamping is thought to be associated with increased autotransfusion from the placenta to the neonate, resulting in increased blood volume and aiding time for physiologic transition (ensuring adequate cardiac output, oxygenation, and arterial blood pressure until respiration is established). Secondary to the increased blood volume, infants are thought to benefit from decreased anemia (and its sequelae), and decreased hypoxia.

## Literature Review

### *Preterm Infants*

A systematic review and meta-analysis of delayed cord clamping was published January of 2018 and included the studies up through July 2017, including the results of a large Australian RCT of delayed cord clamping in premature neonates born at less than 30 weeks. (1) This systematic review included RCTs that looked at delayed cord clamping in premature infants where delayed cord clamping was at least 30 seconds. Studies that included cord milking in addition to delayed cord clamping were excluded unless those trials had less than 20% of infants receiving cord milking. The review identified 18 RCTs with a total of 2834 infants. Two studies were ongoing at the time of the meta-analysis. The majority of the infants randomized to DCC had the cord clamped after 60 seconds. Included studies had varying exclusion criteria.

In their study-level meta-analysis, delayed cord clamping reduced the primary outcome of all-cause (hospital) mortality (RR 0.68, 95% CI 0.52-0.90; risk difference -0.03, 95% CI -0.05 - -0.01; for a number needed to benefit of 33, 95% CI 20-100). A similar difference was seen in the analysis of the 3-studies assessment delayed cord clamping in infants born at 28 weeks or less. No differences were seen in mortality by type of delivery, where the infant was held in relation to the introitus/incision, or duration of cord clamping (early was anything less than 30 seconds).

Delayed cord clamping was also associated with reduced incidence of low one-minute APGARs. DCC increased the peak hematocrit by 2.37 percentage points (95% CI 1.94-3.52, $p<0.00001$). The proportion of infants receiving a blood transfusion was reduced by 10% (95% CI 6-13%, $p<0.00001$); a similar difference was seen in neonates born at or before 28 weeks. No differences were seen in 5-minute APGARS, need for intubation for resuscitation, admission temperature, mechanical ventilation, intraventricular hemorrhage, brain injury, chronic lung disease, patent ductus arteriosus, necrotizing enterocolitis, late-onset sepsis, or retinopathy of prematurity. The incidence of polycythemia was increased (RR 2.65, 95% CI 1.61-4.37), but there was no impact on the use of partial exchange transfusion for polycythemia. DCC was associated with increased peak bilirubin, but there was no difference in the use of exchange transfusion. In terms of maternal outcomes, there was no difference in the number of women with postpartum hemorrhage or requiring blood transfusion. The study does not report on long-term outcomes.

Of note, the Australian Placental Transfusion Study (APTS), published in December 2017, was the largest RCT included in the meta-analysis, having randomized 1634 premature neonates born at less than 30 weeks

gestation to delayed cord clamping. In this study, DCC was done for at least 60 seconds. (2) The primary outcome chosen for this study was a composite of death and major morbidity (severe brain injury, severe retinopathy, necrotizing enterocolitis, late-onset sepsis, chronic lung disease). In this RCT, there were no differences in the composite primary outcome (37.0% for DCC versus 37.2 for early/immediate cord clamping (RR 1.00, 95% CI 0.88-1.13, P= 0.096). In unadjusted univariate analysis, mortality in the DCC group was decreased (6.4% versus 9.0%, RR 0.69, 95% CI 0.49-0.97). When this outcome was adjusted post-hoc for multiple comparisons, the difference was no longer significant (p=0.39). There was no difference in secondary outcomes. Long-term outcomes were published in a follow up study and showed reduced mortality or neurodevelopmental impairment with DCC (12). When neurodevelopment impairment was assessed alone, the association was not significant, but still suggestive of benefit of DCC.

### Umbilical artery pH

In terms of the effect of DCC on umbilical artery pH, the limited studies that have been conducted show either no change or a small decrease in pH (0.03). It is not known how DCC affects umbilical artery pH in non-vigorous infants.

### Blood banking

DCC is associated with decreased volume and nucleated cell counts in cord blood donations (sufficient collection in 17% of DCC cases compared to 39% of early CC cases.

### Multifetal pregnancy

Some of the studies of DCC have included twin pregnancies. There is still insufficient evidence to recommend or avoid DCC in multiple gestations, especially in monochorionic pregnancies.

### FGR

In a sub-analysis of the FGR/SGA preterm infants at Brown University, DCC in these infants was noted to be safe and associated with a higher admission temperature, lower risk of suspected NEC (but not confirmed NEC). (3) Of note, the parent study was not included in the 2017 meta-analysis as more than 20% of cords were milked. The authors reported that the initial hematocrit, peak bilirubin in the first week, and the outcomes of suspected NEC and bronchopulmonary dysplasia were not different between the groups.

### Resuscitation during DCC

A 2018 Cochrane review identified 1 study (Katheria 2016) that had looked at the provision of respiratory support before cord clamping. (4) 150 infants were randomized to respiratory support by CPAP or PPV versus no respiratory support. Mortality, need for inotropes, receipt of blood transfusion, peak hematocrit, and development of IVH did not different between the two groups. The quality of evidence was rated as low secondary to lack of precision on multiple outcomes. (5)

A newly designed resuscitation table that can be placed between the maternal legs or along her side has been studied for feasibility in the Netherlands. (6) The investigators found that the table could be used (it was feasible) and that heart rates remained stable and SpO2 increased in infants resuscitated with the table. A similar study with a mobile resuscitation trolley showed that the use of the trolley was feasible and was acceptable to parents; providers voiced concerns about access to the neonate for resuscitation. (4)

### Long-*term* outcomes

Long-term data outcomes in preterm infants are lacking.

### Unanswered Questions

How generalizable the meta-analysis is to all groups of premature infants is unclear. There is insufficient data for or against DCC in infants with growth restriction and abnormal umbilical blood flow. The effect of DCC on long-term outcomes is also limited.

### *Term Infants*

A systematic review and meta-analysis of delayed cord clamping in term infants was published in 2013 and included the studies up through February 2013. (1) This systematic review included RCTs that looked at delayed cord clamping in term infants where delayed cord clamping was at least 60 seconds (the exact time comparison groups differed between studies). Breech infants and multifetal gestations were excluded.

The review identified 15 RCTs with a total of 3911 dyads. In their study-level meta-analysis, delayed cord clamping did not reduce the primary outcome of mortality (RR 0.37, 95% CI 0.04-3.41; 2 trials). Mean birth weight was higher in the DCC group (101g difference, 95% CI 45-157g; 12 trials). Need for phototherapy was decreased in the early CC group (RR 0.62, 95% CI 0.41-0.96; 7 trials). Hemoglobin concentrations at 24-48 hours were lower in the early CC group (MD -1.49 g/dL, 95% CI -1.78- 1.21), but did not differ at subsequent assessments. Infants in the early CC group were more likely to be iron deficient at 3-6 months of age (RR 2.65, 95% CI 1.04-6.73; 5 trials). Only one trial reported on longer-term neurodevelopment outcomes and did not show a difference in the Ages and Stages Questionnaire scores.

No studies reported on maternal deaths or severe maternal morbidity. There was no significant difference in severe postpartum hemorrhage (RR 1.04, 95% CI 0.65-1.65; 5 trials) or postpartum hemorrhage (RR 1.17, 95% CI 0.94-1, which can be adapted.44; 5 trials).

### RCTs published since February 2013 –

In 73 infants randomized to DCC of >5 minutes versus ICC of <30 seconds, 48-hour hematocrit was higher in DCC infants (57.6% versus 53.1%, p<0.01), as was hemoglobin; peak bilirubin levels did not differ between groups. (2) 11 infants underwent cord milking instead of DCC. (18)

### CHD infants

A pilot RCT of 30 singleton neonates with congenital heart defects, designed to test safety and feasibility, randomized infants to ECC (<10 sec) versus DCC (>120 sec). (3) There was no difference in safety measures (polycythemia, peak bilirubin, phototherapy, 5-minute Apgar, pre-operative mortality) or surgical parameters between the two arms, nor in neonatal morbidities. Hematocrits were higher within the first 72 hours for infants in the DCC arm, although this difference was not seen later in the hospitalization. The likelihood of needing a blood transfusion was less in the DCC cohort (7% versus 43%, p=0.02), but not during hospitalization.

### LGA infants

Vural et al looked at hematologic parameters in term LGA infants. (4) 51 term LGA infants were randomized in Turkey to ICC (<15 sec) versus DCC (>=60 sec). Apgar scores and cord gas pH did not differ between arms. Neither two-hour hematocrit nor 24-hour bilirubin nor the incidence of polycythemia differed significantly between arms.

### Maternal *outcomes*

De Paco et al looked at the length of the 3rd stage in term vaginal deliveries with DCC. (5) 97 term singleton pregnancies were randomized to ECC (<10c) versus DCC (>2 min). There was no difference in length of second stage, blood indices, or umbilical cord parameters.

### Resuscitation during DCC

Katheria et al randomized 60 vaginally-delivered term infants at risk of resuscitation to 1-minute versus 5-minute DCC. (6) Non-vigorous infants in the 1-minute arm had their cords clamped immediately, while non-vigorous infants in the 5-minute arm were placed on the Life-Start Bed. Infants requiring resuscitation at 5 minutes had CONTINUED delayed cord clamping. The primary endpoint was StO2 (cerebral oxygen saturation). 63% of infants in the 1-minute group required resuscitation versus 43% in the 5-minute group

(p=0.20). StO2 in the 5-minute group was better than the in the 1-minute arm (mean 82 versus 79, p=0.02). Mean blood pressure was also higher in the 5-minute arm (mean 53 versus 47, p = 0.02).

### Long-term outcomes

A few studies have looked at long-term outcomes of infants randomized to DCC. Andersson followed up iron status and neonatal developmental outcomes in 382 infants in Sweden; follow up data was available in 90.8% of participants. (7) Infants had been randomized to ECC (<-10 sec) versus DCC (>-180 seconds). Using the Ages and Stages Questionnaire, scores were 5 points higher in male infants in the DCC arm, but 12 points lower in girls in the same arm. Iron status and hematologic studies did not differ between the arms. At 4 years of age, 263 infants (68.8% of the original cohort) were assessed for neurodevelopment outcomes. (8) No differences were noted in IQ (as measured by WPPSI-II). DCC arm children had higher adjusted mean differences (AMDs) in ASQ in personal-social (2.8; 95%CI, 0.8-4.7) and fine-motor (2.1, 95% CI 0.2-4.0). Fewer children in the DCC arm fell below the cutoff in the ASQ fine motor domain (11.0%vs 3.7%; P = .02) and Movement ABC bicycle trail task (12.9% vs 3.8%; P = .02).. In male children having received DCC had significantly higher AMDs in the WPPSI-III processing-speed quotient (4.2; 95%CI, 0.8-7.6; P = .02). Boys in the DCC arm compared to the ECC arm had higher AMDs in movement ABC bicycle-trail task (0.8; 95%CI, 0.1-1.5; P = .03), and fine-motor (4.7; 95%CI, 1.0-8.4; P = .01) and personal-social (4.9; 95%CI, 1.6-8.3; P = .004) domains of the ASQ.

6-month hematologic indices were investigated by Nesheli et al in Pakistan. (9) They looked at 60 term infants who were delivered vaginally and who had been randomized to ECC (<10 sec) versus DCC (50-60 seconds). Hemoglobin, hematocrit, and transferrin saturation were higher in infants randomized to DCC. MVC and MCH did not differ significantly. No differences were noted in polycythemia, hyperbilirubinemia, tachypnea, or in maternal hemorrhage.

In the follow up of the Mercer study, 44 infants had follow-up at 4 months of age. (10) The DCC cohort infants had higher ferritin levels (96.4 ng/ml versus 65.3, p=0.03) and greater myelin content in the internal capsule and other maturing brain regions. No differences were seen in the Mullen score for neurodevelopment or in hematocrit.

Ashish et al are conducting a long-term follow up study to look at anemia indices and neurodevelopmental scores at 8-24 months. (11)

### Unanswered Questions

How generalizable the meta-analysis and RCTs is to all groups of term is up for debate. DCC times have differed significantly between studies. There is insufficient data for or against DCC in infants with growth restriction and abnormal umbilical blood flow. The effect of DCC on long-term outcomes is also limited, mainly arising from one cohort.

## 2024 Update

A new systematic review and meta-analysis of delayed cord clamping was published December of 2023 and included the studies up through June 2023. The authors assessed outcomes in infants born at <32 weeks and >/=32 weeks. In all infants, DCC was associated with decreased mortality prior to discharge with a number needed to treat of 40. In infants born at less than 32 weeks, DCC was also associated with decreased need for blood transfusion, increased risk of hypothermia (by 0.12 degrees C). These outcomes did not differ in infants born at or after 32 weeks. (19)

# Cord milking in a late preterm/term non-vigorous infant

## Background

Umbilical cord milking (UCM) provides an additional avenue for possible autotransfusion.

## Literature review

In the 2024 systematic review and meta-analysis described above, the authors also looked at umbilical cord milking compared with immediate cord clamping and delayed cord clamping. In this study, there was no clear evidence that cord milking decreased mortality prior to discharge compared to immediate cord clamping, but improvements in hemoglobin and hematocrit were seen. When UCM was compared to DCC, there was also no significant difference in mortality before discharge.

Katheria, et al, performed a cluster randomized controlled trial of umbilical cord milking born between 35-42 weeks' EGA with a primary outcome of NICU admission. In the analysis of 1730 infants for whom the primary outcome was available, UCM did not decrease the risk of NICU admission. UCM, however, was associated with higher hemoglobin, less need for delivery room cardiorespiratory support (OR 0.57, 95% CI 0.33-0.99), lower incidence of moderate or severe HIE (OR 0.48, 95% CI 0. 24-0.98), and less therapeutic hypothermia (OR 0.57, 95% CI 0.33-0.99).

Cord milking should **NOT** be performed in preterm infants born at <28 weeks due to concerns for increased risk of severe IVH (per 2021 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care and 2023 AHA and AAP Focused Update on Neonatal Resuscitation Guidelines).

Katheria et al (Dec 2023) completed a RCT in non-vigorous preterm babies 28-32 weeks GA (n=1019) comparing DCC 60 sec to umbilical cord milking. This trial showed no increase in severe IVH in the cord milking arm compared to the DCC arm (1.4% vs 1.4%). Therefore the 2023 AHA and AAP Focused Update on Neonatal Resuscitation Guidelines considers UCM in the GA range 28-34 to be acceptable when immediate resuscitation is considered necessary and DCC not able to be performed. (22)

| **GA** | **Vigorous Infant** | **Non-Vigorous/ DCC not possible** |
|---|---|---|
| ≤27 6/7 | DCC | Immediate Cord Clamping |
| 28 0/7 -34 6/7 | DCC | Cord Milking may be reasonable |
| ≥35 0/7 | DCC | Cord Milking |

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## SOCIETY SUPPORT

In January 2017 (prior to the meta-analysis and the APTS), ACOG recommended a delay in umbilical cord clamping in vigorous term and preterm infants for at least 30-60 sections after birth. Secondary to the small increase in the incidence of jaundice requiring phototherapy in term infants undergoing DCC, ACOG recommends ensuring that mechanisms are in place to monitor/treat neonatal jaundice. The American Association of Pediatricians endorses the 2017 ACOG guidelines. The 2021 Neonatal Resuscitation Program (NRP) also recommends DCC of 30-60 seconds in vigorous preterm infants.

The World Health Organization recommends DCC for at least 60 sections in term and preterm infants who do not require positive pressure ventilation. The Royal College of Obstetricians and Gynecologist recommend DCC of at least 120 seconds in healthy preterm and term infants. The American College of Nurse-Midwives recommends DCC for 2-5 minutes in term and preterm neonates. The 2021 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care guidelines support at least 60 seconds of duration in newborns at 34 weeks or greater and at least 30 seconds in neonates born before 34 weeks.

## PROCEDURE

*How is DCC performed?*

DCC should not delay warming, drying, and stimulating of the neonate. Immediate skin-to-skin contact can be done and the neonate can be cleaned with clean/warm blankets. In a cesarean section, the infant can be held close to the wound. Secretions can be cleared if they are copious or if there is obstruction.

How is UCM performed?

UCM can be performed by consistently and slowly milking the cord 4 times with each swipe performed over 2 seconds. After each swipe, the end of cord is released. This method was used in the MINVI trial (Katheria et al, 2023), as well as the UK trial (Rabe, et al), and Japanese trial (Hosono, et al).

A video demonstrating UCM is available at https://bcmedu-my.sharepoint.com/:v:/g/personal/barbour_bcm_edu/EYyhuv4Q6FNJmnimHZgn0MEBB_rwkhRCrDf_8DFdu6PLeA?nav=eyJyZWZlcnJhbEluZm8iOnsicmVmZXJyYWxBcHAiOiJPbmVEcml2ZUZvckJ1c2luZXNzIiwicmVmZXJyYWxBcHBQbGF0Zm9ybSI6IldlYiIsInJlZmVycmFsTW9kZSI6InZpZXciLCJyZWZlcnJhbFZpZXciOiJNeUZpbGVzTGlua0NvcHkifX0&e=FH8ffN.

If cord banking is planned, this can still be done, but the family should be counseled that inadequate total volume and nucleated cells are likely to be encountered.

*What about the 3rd stage of labor?*

Active management of the third stage of labor can continue, including the use of oxytocin and other uterotonics.

**DCC ALGORITHM**

Discussion with Neonatology/Pediatrics to decide if Delayed Cord Clamping should be done

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## Contraindictions to Delayed Cord Clamping

- **Maternal Contraindications** (hemorrhage, hemodynamic instability)
- **Placental Contraindications** (placental abruption, abnormal placentation, umbilical cord avulsion)
- **Fetal/Neonatal Contraindications** (need for immediate resuscitation, FGR with abnormal cord Doppler evaluation, complicated monochorionic pregnancy)

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**If NO to all:**

**Proceed with delayed cord clamping x 30-60 seconds (or greater if vaginal delivery)**

If YES to 1: proceed with immediate cord clamping; consider UCM

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If infant is born at 35+0 or greater and is non-vigorous, proceed with UCM

**DCC checklist**

⇒ **Discussion with neonatology regarding plans for DCC**
⇒ Decide on amount of planned DCC time
⇒ Ensure room temperature is set to 75F
⇒ Once the infant is delivered, place infant skin-to-skin on the maternal abdomen (or on the surgical drapes near the surgical incision
⇒ Initiate warming, drying, and stimulating
⇒ Bulb suction of the airway as needed
⇒ Continuous assessment by Neonatology and Obstetrics regarding infant status and need for UCM and/or earlier cord clamping
⇒ Cord clamp at goal DCC time or earlier if clinically indicated; consider UCM.

**UCM checklist**

⇒ Ensure EGA of 35+0 or greater (can consider from 28+0 – 34+6)
⇒ Discussion with neonatology regarding possibility of UCM