Version	Date	Comments / Changes
1.0	APR 2019	Initial Clinical Practice Guideline Released

Please refer to section 5 and 6 for the key recommendations.

1. FOCUS

The focus of this clinical practice guideline (CPG) is to provide evidence-based recommendations to support delayed cord clamping (DCC) as a standard of care in Fraser Health to improve newborn outcomes.

2. BACKGROUND

In utero, the placenta is responsible for respiratory, nutritional, metabolic and excretory function of the fetus. Fetal circulation relies on connection to the low resistance placental vascular bed from where blood is supplied to the right heart. It is subsequently pumped back to systemic circulation through the foramen ovale via the left heart (bypassing the lungs) and via the ductus arteriosus (bypassing both lungs and left heart). Before birth, the lungs are fluid-filled. At birth, effective ventilation through spontaneous breathing or by positive pressure ventilation leads to a rapid rise in hemoglobin oxygen saturation. This rising oxygen saturation leads to vasodilation of the pulmonary vasculature and a decrease in pulmonary vascular resistance. This causes an increase of pulmonary blood flow, ultimately resulting in transition to newborn circulation.

Cord clamping delayed past the onset and establishment of effective respirations results in a smoother cardiovascular transition to extra utero life in a preterm lamb model with improved peripheral SpO_2 and cerebral oxygenation readings, arterial pressure, cerebral blood flow and cerebral oxygenation extraction in comparison to early cord clamping (Polglase et al., 2015). This is due to an ongoing stable placental blood supply to the right heart while avoiding the strain on the left heart from the immediate increase in afterload associated with immediate cord clamping (Hooper et al., 2014).

Similar to unpublished data discussed by Linderkamp (1982), an early study by Yao et al. (1969) of 111 term newborns showed the distribution of blood between the placenta and newborn to be 67%/33%, 80%/20% and 87%/13% at time of delivery, 1 minute and 3 minutes post-delivery respectively; nearly half of the placental transfusion occurs by 1 minute of age with minimal additional transfusion beyond 3 minutes of age. As such, DCC results in placental transfusion which contributes to about 20% of the infant's total blood volume or an additional 24 to 32mls/kg of blood compared to immediate cord clamping (Farrar et al., 2011). Though many factors may affect placental transfusion (Linderkamp, 1982; Philip & Saigal, 2004), infant positioning during DCC has not been shown to significantly affect the volume of placental transfusion in a randomized control trial of 391 term infants born vaginally (Vain et al., 2014). When DCC is indicated, current recommendations suggest placing the infant skin to skin on the abdomen or chest (vaginal) and on the maternal abdomen or legs (cesarean) (ACOG, 2017).

2.1. Standard of Care

Delayed cord clamping is now recommended as a standard of care.

Organization	Duration	Population
World Health Organization (2014)	At least 1 minute	Term and preterm not requiring positive pressure ventilation If practitioner is experienced, ventilation can be initiated before cutting the cord.
NRP (Weiner et al., 2016) Endorsed by CPS and APP	30 to 60 seconds	Most vigorous term and preterm infants

Canadian Paediatric Society (CPS, 2015; Finan et al. 2017)	30 to 180 seconds	Preterm infants not in immediate need of resuscitation
American Academy of Pediatrics (AAP, 2017) Endorsed ACOG	At least 30 to 60 seconds	Vigorous term and preterm infants
National Institute for Health and Care Excellence (NICE, 2015)	Minimum of 60 seconds	Unless concerns about cord integrity or baby's heartbeat (i.e. heartbeat below 60 beats/minute and not getting faster)
American Collage of Nurse-Midwives (2014)	2 to 5 minutes 30 to 60 seconds	Term Preterm
The American College of Obstetricians and Gynecologists (ACOG, 2017a)	At least 30 to 60 seconds	Term and preterm infants (except if maternal or neonatal indications for immediate clamping {e.g. Hemorrhage, resuscitation, placenta circulation not intact})
Society of Obstetricians and Gynecologists (SOGC, 2016)	Minimum of 60 seconds (irrespective of mode of delivery)	Term and preterm not requiring resuscitation
Royal Colleague of Obstetricians and Gynaecologists (RCOG, 2015)	Not defined	Term and preterm. Recommend strategies to initiate resuscitation with cord intact.

There is ongoing research and interest in cord milking in premature infants; however, at present the evidence is not sufficient to provide a definitive recommendation (Al-Wassia et al., 2015; Katheria et al., 2015).

2.2. Benefits of DCC

Infants receiving DCC have an increased hemoglobin level at birth, improved iron stores in the first several months of life and may have improved developmental outcomes (ACOG, 2017; McDonald et al., 2013).

A Cochrane systematic review (five trials, N=1152) found that term infants who received DCC were half as likely to be iron deficient at three to six months of age when compared to infants who received early cord clamping (RR:2.65, 95% CI 10.04-6.73) (McDonald et al., 2013). Iron stores at birth have been shown to correlate with iron stores at six, nine and 12 months of age (Michaelsen et al., 1995). Most newborn iron stores are accumulated in the third trimester of pregnancy. However maternal conditions, such as anemia, maternal hypertension with intrauterine growth restriction, or diabetes during pregnancy, can result in low fetal iron stores in both term and preterm infants (AAP, 2010). Despite the greater percentage of iron absorbed from breastmilk (50-70%) compared to that absorbed from iron fortified formula and cereals (10%), Lonnerdal (2017) estimates that total iron absorption in exclusively breastfed infants is considerably lower than those who are formula fed due to the higher amounts of iron added to artificial supplements. Therefore, delaying cord clamping and increasing red blood cell volume increases iron stores, thereby decreasing the risk of iron deficiency during infancy (Andersson et al., 2011; McDonald et al., 2015) which may be particularly beneficial for those infants who receive breastmilk exclusively.

In preterm infants, DCC encourages improved cardiovascular stability after delivery as evidenced by higher mean blood pressure and decreased need for inotropic support (Rabe et al., 2012). Those that received DCC also had increased red blood cell volume, decreased need for blood transfusion, and a lower incidence of NEC and IVH (ACOG, 2017; Rabe et al., 2012).

A 2012 Cochrane systematic review of 15 studies, including 738 infants born 24-36 weeks gestational age who received DCC (with or without cord milking) for 30 to 180 seconds found less need for anemia-related transfusions, improved circulatory stability, less intraventricular hemorrhage (IVH) all grades, and lower risk of necrotizing enterocolitis (NEC). There was no significant difference in mortality, severe IVH (grade 3 or 4) and periventricular leukomalacia (PVL) between the DCC and ICC groups (Rabe et al., 2012).

Outcome	RR; CI	Inclusion
Transfusion (for anemia)	RR 0.61: 95% CI 0.46-0.81	7 trials, N=392
Need for inotropic support	RR 0.42; 95% CI 0.23-0.77	4 trials, N=158
IVH (all grades)	RR 0.59; 95% CI 0.41-0.85	10 trials, N=539
IVH (grade 3 and 4)	RR 0.68; 95% CI 0.23-1.96	6 trials, N=305
NEC	RR 0.62; 95% CI 0.43-0.90	5 trials, N=241
Death (up to discharge)	RR 0.63; 95% CI 0.31-1.28	13 trials, N=668
PVL	RR 1.02; 95% CI 0.19-5.56	2 trials, N=71

RR, Relative Risk; CI, Confidence Interval; N = sample size

A more recent systematic review of 27 studies (N=2834) found that preterm infants (< 37 weeks GA) that had delayed cord clamping (most often ≥ 60 seconds) had reduced hospital mortality when compared to early cord clamping (Fogarty et al., 2018). The infants who received DCC had higher peak hematocrit and a decreased need for blood transfusions. The DCC group did have an increased incidence of polycythemia and slightly higher peak bilirubin but no significant difference in partial or full exchange transfusions. Similar to the Cochrane review there was no significant difference in incidence of NEC or severe IVH. Contrary to the Cochrane findings, there was no significant difference in IVH – all grades. The following table summarizes the findings of Fogarty et al. (2018).

Outcome	RR/MD; CI	RD; CI & NNB/NNH	Inclusion
Hospital mortality	RR 0.68; 95% CI 0.52-0.90	RD -0.03; 95% CI -0.05 to -0.01 (P=0.005) NNB 33	18 trials, N=2534
IVH (all grades)	RR 0.87; 95% CI 0.75-1.00	RD -0.03; 95% CI -0.06 to -0.00	19 trials, N=2871
IVH (severe IVH)	RR 0.87; 95% CI 0.59-1.27	N/A	11 trials, N=2300
NEC	RR 0.88; 95% CI 0.65-1.18	N/A	12 trials, N=2397
PVL	RR 0.71; 95% CI 0.39-1.27	N/A	8 trials, N=1977
Peak Hematocrit (%)	MD 2.73; 95% CI 1.94-3.52	N/A	2 trials, N=1587
Need of blood transfusion	RR 0.81; 95% CI 0.74-0.87	RD -0.10; 95% CI -0.1 to -0.06 (P=0.00001) NNB 10	13 trials, N=2595
Polycythemia (Hct >65%)	RR 2.65; 95% CI 1.61-4.37	RD 0.03; 95% CI 0.01-0.04, NNH 33	13 trials, N=2529
Partial exchange transfusion	RR 0.14; 95% CI 0.01-2.74	N/A	4 trials, N=1743
Peak bilirubin (umol/L)	MD 4.43; 95% CI 1.15-7.71	N/A	15 trials, N=2358
Exchange transfusion	RR 0.29; 95% CI 0.0.5-1.73	N/A	7 trials, N=2139

RR, Relative risk; CI, Confidence interval; MD, Mean difference; RD, Risk difference; NNB, Number needed to benefit; NNH, Number needed to harm

Emerging theories suggest that DCC may facilitate transfusion of immunoglobulins and stem cells, potentially impacting immediate and long-term health of the infants, though more research is needed in this area (Sanberg et al., 2014).

2.3. Concerns Related to DCC

A number of concerns have been noted in literature and Fraser Health about the safety of DCC. Below is a summary of literature related to commonly-referenced concerns.

Maternal	
Postpartum hemorrhage (PPH)	A Cochrane review of 15 trials (n=3911) found no significant difference in severe PPH when the cord was clamped early (within 60 seconds) or late (greater than one minute of life or when cord pulsation ceased) regardless of mode of birth (McDonald et al., 2015). That being said, some have questioned the impact on maternal blood loss when DCC is performed following caesarean section. In May of 2017 a RCT study protocol was published (Purisch, 2017). This study will examine the impact of DCC at one minute post-delivery following caesarean section on the maternal blood loss during surgery.
Neonatal	
Delay in resuscitation	A small (N=33) RCT of preterm infants (24-28 weeks GA) found no difference in need for resuscitation in those infants who received ICC (within 10 seconds of birth) or DCC (within 30-45 seconds of birth) (Oh et al., 2011). Nevill and Myers (2015) reported similar findings in a pre- (immediate cord clamping) and post- (DCC for 40 seconds with no stimulation) cohort study of preterm infants (GA of 34 weeks or less, N=104). There was no difference between groups in breathing (at birth or during the procedure), Apgar scores (at 1 and 5 minutes), need for positive pressure ventilation or intubation (in the delivery room), and temperature or base deficit on admission. Of those that received DCC, 34 breathed prior to DCC, while 12 did not. Of the 12 who did not breathe, a significant proportion required intubation in the delivery room, had lower one minute Apgar scores, were more likely to be male, had lower day one hemoglobin levels and were more likely to develop chronic lung disease and severe IVH. In a systematic review (Fogarty et al., 2018) of DCC vs early cord clamping in preterm infants (<37 weeks GA), there was a reduced incidence of Apgar scores of less than four at one minute (RR 0.82, CI 0.67-1.00, P=0.5, N=1600) but no significant difference in Apgar scores of less than eight at five minutes (RR 1.03, CI 0.91-1.17, N=1983), cardiorespiratory support (RR 0.89, CI 0.71-1.11, N=748) or need for intubation in the delivery room (RR 0.96, CI 0.82-1.13, N=748). Beyond this, most DCC studies have not included infants requiring resuscitation at birth; therefore, there is paucity of evidence regarding DCC for infants requiring resuscitation and related outcomes (Wyckoff et al., 2015). More recent studies looking at the feasibility and safety of providing initial resuscitation (including ventilation) with an intact cord are promising (Duley et al., 2017). This would minimize delay in resuscitation and allow ventilation to be

	established prior to clamping the cord to support the physiologic transition to newborn circulation and cardiac stability (Hopper, 2015).
Hyper-bilirubinemia	A 2012 systematic review (Rabe et al., 2012) found that peak bilirubin levels were higher in preterm infants with DCC, but no significant difference in need for phototherapy. Similarly Forgarty et al. (2018) found a slight increase in peak bilirubin, but not a significant increase in incidence of exchange transfusions in the preterm population. ACOG (2017) recommend that mechanisms be in place to monitor and treat neonatal jaundice as there may be a small increase in the incidence of jaundice requiring phototherapy in term infants undergoing DCC.
Cord Gas Collection	Although studies show that DCC of at least 45 seconds can significantly impact umbilical cord blood gas values, the clinical significance remains questionable. Two studies comparing early and delayed serial, paired umbilical gas samples (Weiberg et al. 2008, n=70; Valero et al., 2012, n=60) demonstrated that DCC resulted in an average decrease in umbilical artery pH of approximately 0.3 and base excess difference of up to 0.16 mmol/L. Alternatively, an RCT (n=158) comparing immediate (<10 sec) versus delayed (two minutes) cord gas samples found no difference in pH or base excess values (Paco et al, 2011). Both Weiberg et al and Paco et al, found significant increases in mean umbilical vein PO_2 that was thought to be explained by neonatal breathing. Andersson et al. (2013) assessed the proportion of valid blood gas samples in low-risk term deliveries (n=382) and found no difference between those drawn earlier than 10 seconds versus 180 seconds of age or more. Samples were taken from unclamped pulsating cords in this study. Di Tommaso et al (2014, n=46) sought to prospectively test reliability of cord gas results drawn from unclamped cords as well as neonatal safety from excessive bleeding. They found no significant difference between cord gas results when samples were drawn from unclamped versus clamped cords within 90 seconds of birth. In addition, no newborns experienced bleeding from puncture sites following unclamped sample collection. Practice points: • DCC may result in slightly lower arterial cord pH and base deficit • Obtaining cord gasses should not preclude DCC • Sample collection from an unclamped cord during DCC appears to be safe for term healthy newborns To accurately interpret values, time of sample collection (in relation to time of birth) **must** be documented.
Cord blood banking	Cord blood banking is feasible with DCC however the volume collected is reduced. The Canadian Blood Services (Allen et al., 2014) found that the proportion of collected units that met the total nucleated cell count (TNC) threshold was reduced to 17 percent (from 39.4%) when DCC occurred at around 60 seconds after birth. A further reduction to six percent was observed when DCC occurred over two minutes of age. Alternatively, Frandbert et al., (2016) assessed the impact of DCC at 60 seconds (compared to immediate clamping) on the volume and TNC counts in cord blood units stored by the Swedish blood bank. They found a significantly-reduced mean difference in volume of 8.1mL in the DCC group yet, unlike Allen et al., no difference in TNC content, with 37 percent of units meeting the same TNC banking threshold. The SOGC (2015) cautions that cord blood collection not interfere with DCC. They stress that while cord blood collection in preterm infants is not contraindicated, DCC is recommended for these newborns. Patients must be made aware of the reduced collection volumes and effect on TNC content.
Multiple	There is insufficient evidence to guide DCC practice following delivery of the first

gestations	fetus. In monochorionic twins, placental vascular connections commonly exist. The MORE^{OB} program suggests that a delay of 60 seconds is unlikely to allow significant twin-to-twin transfusion; however, cord blood sampling or drainage should be delayed until after the birth of the second twin (Salus Global, 2018). Ultimately, the patient and care team must consider the risks and weigh benefits according to zygosity and gestational age primarily (ACOG, 2017).
Hypothermia	No DCC studies have reported temperature in the delivery room as an outcome. A recent systematic review including 11 trials (N=2317, with moderate heterogeneity) reported no significant difference between admission temperature between the early cord clamping and DCC infants (MD -0.02, 95% CI –0.07 to 0.03).

3. DEFINITIONS

The optimal timing of DCC has not been well-established; there is variability in how it has been defined in literature (refer to Appendix A). For premature infants, most studies delay cord clamping for 30 to 180 seconds (Rabe, 2012). For term infants, DCC for more than one minute is studied and recommended most frequently (McDonald, 2013). Using a physiological approach, onset of effective respiration/ventilation as a marker for appropriate timing of cord clamping is recommended (Hooper, 2015). For clarity and practicality in this guideline the following definitions will be used.

Delayed Cord Clamping (DCC): umbilical cord is clamped greater than or equal to 30 seconds after birth.

Early Cord Clamping (ECC): umbilical cord is clamped less than 30 seconds after birth.

Non-Vigorous: apneic (not breathing or crying) and hypotonic/flaccid.

Vigorous: making spontaneous breathing efforts with tone/flexion noted.

Most Responsible Practitioner (MRP): Provider with appropriate credentials and privileges who is accountable and responsible for the admission, ongoing care, transfer of care, consultation and discharge processes for inpatients to and from a Fraser Health acute care facility. The MRP shall be clearly identified in the patient's health care record (refer to Fraser Health Most Responsible Physician - Policy).

4. EXPECTED OUTCOMES

4.1. Increased rate and documentation of DCC when clinically appropriate
4.2. Increased consistency in duration of DCC
4.3. Increased newborn hemoglobin and iron storage levels
4.4. Reduced rate of IVH, NEC, anemia related transfusions and inotrope support for hemodynamic instability in the preterm population

5. ASSESSMENT

5.1. DCC is **contraindicated** with conditions affecting placental circulation, including but not limited to (Weiner et al., 2016):

- placental abruption
- bleeding placenta previa
- bleeding vasa previa
- cord avulsion

5.2. Appropriateness of DCC in the following clinical situations needs to be determined by the delivery MRP or resuscitating physician (if present) **on a case by case basis** (Weiner et al., 2016).

- Fetal intrauterine growth restriction (IUGR)
- Abnormal umbilical artery Doppler measurements
- Abnormal placentation
- Other situations affecting utero-placental perfusion or umbilical cord blood flow
- Multiple gestations

5.3. Recommendations for Cord Clamping - Unless contraindicated or the delivering MRP or resuscitating physician (if present) determines cord clamping is indicated immediately after birth:

- The initial steps of resuscitation (i.e. providing warmth, drying, stimulating and positioning to open airway) should take place while the cord is still attached for both term and preterm infants regardless of the mode of delivery. This may also include ventilation should the infrastructure and team composition allow (Rabe, McDonald, WHO 2014).
- During this time (approximately 20 to 30 seconds) the newborn's tone and breathing effort should be evaluated to determine if the infant is vigorous or non-vigorous (Weiner et al., 2016).
- For all **vigorous** term and preterm infants clamping of the cord should be delayed for at least 60 seconds.
- For infants assessed to be **non-vigorous** after the initial steps of resuscitation (i.e., providing warmth, drying, stimulating and positioning to open airway), the cord may be clamped* and subsequent steps of resuscitation should be initiated per the NRP algorithm.

*subsequent steps of resuscitation (i.e. ventilation) may be provided with the cord intact if the infrastructure and team composition allow.

6. INTERVENTION

Team Briefing	• Patient, MRP and resuscitation team establishes plan for DCC; anticipated length of delay based on contraindications, clinical situation, newborn's condition at delivery (i.e., vigorous/non-vigorous) and maternal preference.
Assign Roles	• Dryer/stimulator, timekeeper (confirm intervals to be announced)
Supplies to facilitate DCC	• Sterile hand towels/large lap sponges (in OR) • <32 weeks; polyethylene bag (sterile in OR) Please refer to clinical protocol: Code Pink for a complete list of supplies required for resuscitation
Time of birth	• Start timing; Apgar timer
Initial steps of resuscitation and positioning	• Place baby: o <32 weeks wet in bag o skin to skin on abdomen/chest (vaginal) o sterile drape on mother's thighs (cesarean) • Do not stretch or pull on the cord • Provide warmth, dry, stimulate, position to open airway • Assess breathing and tone
Announce Delay/Concern	• Announce time at 15 or 20 second intervals • Any team member can verbalize concerns
Clamp Cord	• If baby is noted to be vigorous (breathing effort, tone/flexion present) continue delayed cord clamping for a minimum of 60 seconds • If the baby is noted to be non-vigorous (no/poor breathing effort, hypotonic) o clamp the cord and proceed with the next steps of NRP o initiate ventilation with an intact cord, if the infrastructure and team composition allow • Note time and document (labour birth summary record)

Follow-up care	• Provide routine care (skin to skin)/continue next steps of resuscitation per NRP
Cord Gases	• Document time cord gasses are collected

7. DOCUMENTATION

7.1. Delayed Cord Clamping

Document the:

- interval (in seconds) from birth of the newborn to the time the cord was clamped in the maternal and newborn record.
- reason for early cord clamping if DCC was not offered.
- interval (in seconds) from birth of the newborn to time of first breath/effective ventilation.

Documentation may occur on:

- British Columbia Labor and Birth Summary
- BC Newborn Record: Part 1
- Neonatal Resuscitation Record

7.2. Cord Gases

Document the time of arterial and venous umbilical cord blood gas sampling directly on the specimen collection label.

8. EDUCATION

- Staff education occurs through regular, mandatory NRP courses and new staff orientation with reinforcement through local mock code pink (as appropriate). Refer to the Delayed Cord Clamping (DCC) - Reference Algorithm**.**
- Care practices optimizing newborn transition after birth (including timing of cord clamping) is a standard component of antenatal education.

9. EVALUATION

Potential Data Collection

- % documented early/delayed
- % received DCC (denominator – all births, preterm vs term, NICU admissions, etc.) stratified by time:
  - 30 - <60 seconds
  - 60 - <120 seconds
  - 120 seconds or greater
- Reason for not receiving DCC and the time decision is made (before or after birth)
- % documented time of first breath
- Time of first breath
- % of infants hyperbilirubinemia requiring phototherapy treatment
- % IVH
- % NEC
- % of neonatal transfusions
- % RDS requiring intubation/ventilation
- % RDS requiring surfactant
- % ventilator days
- % Maternal post-partum hemorrhage
- % mortality

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11. APPENDICES

Appendix A: Summary of Duration of Delayed Cord Clamping

APPENDIX A: SUMMARY OF DURATION OF DELAYED CORD CLAMPING

Duration	Study Citing this Duration
At least 30 seconds	Wyllie et al., 2015a
30-60 seconds	ACOG, 2017; AAP, 2017; Finan, 2017
At least 60 seconds	Perlman et al., 2012; Funai & Norwitz, 2018; Rabe et al., 2015; Wyllie et al., 2011, Wyllie et al., 2015b
2-5 minutes	Dulay et al., 2015
≥180 seconds	Andersson et al., 2015; 2014; Kc et al., 2017
1-3 minutes	Ersdal et al, 2014; WHO, 2014
3-4 minutes	Bhatt et al., 2013*
Waiting until the cord has stopped pulsing	Fulton et al., 2016**
181 +/- 31 seconds	Polglase et al., 2015*

*Animal study **Survey study