

## **MFM Neo Clinical Trials Workshop Information September 2017**

At the NICHD Young Investigators Meeting, there is a Clinical Trials Workshop. In this activity, we will be discussing and designing a clinical trial. Prior to the workshop there will be a presentation on the topic to set the stage. In addition, the questions below will help you to prepare for the workshop – you will be expected to have reviewed this material and the suggested reading to actively participate in the workshop.

### **Questions to help you prepare for the Clinical Trial Design Workshop: Cord Milking and Delayed Cord Clamping in Infants**

1. What is the quality of evidence for each of the following\*
  - Cord clamping or cord milking reduces neonatal complications
  - Cord clamping or cord milking improves short and long term outcomes

\*Quality of Evidence:

  - I. RCT's
  - II. Controlled Trials / No randomization
    - cohort (case control studies)
    - multiple time series / dramatic effect
  - III. Opinion of experts / descriptive studies, expert committees
  
2. Before doing an RCT on delayed cord clamping and/or cord milking, is there a need for (a) descriptive epidemiology; (b) observational study(ies) to determine if there are associated morbidities and assess the effectiveness and safety of treatment (c) review of current trials? Are these studies possible?
  
3. In development of the study design, what treatment regimens should/can be compared?
  
4. Masking: Should/can the treatment groups be masked or "blinded"? How could this be accomplished?
  
5. Primary outcome:
  - a) Should this be efficacy or safety of the treatment? Which outcome(s) should be included as clinically significant measures? How do you specify the outcome measure(s)?
  - b) Which perinatal outcome(s) are of secondary importance, but worthwhile collecting data on?
  - c) Are there any long-term effects that should be measured in the infants/mothers exposed in this protocol?
  
6. Study population: a) What group of patients would you screen to obtain the study population? b) What would your inclusion and exclusion criteria be?
  
7. What proportion of potential enrollees with the condition would be ineligible by the criteria?

8. Are there any subgroups that should be focused on for analysis (gestational age, birth weight, race, ethnicity, multiple gestation, etc)? What is the effect of subgroup analysis on study design?
9. To what extent would you "standardize" the clinical management of the randomized patients?
10. If a well-designed RCT showed no difference between groups, how would you explain these results?
11. **Sample Size** (will be discussed at the meeting)
  - a) Prevalence of primary outcome: How would you go about estimating the frequency of the primary outcome in this population?
  - b) Effect size: How much more effective should treatment be than non-treatment in terms the primary outcome?
12. **Feasibility** (will be discussed at the meeting)
  - a) Study sample: What proportion of the eligible pool would reasonably consent to be randomized in a RCT?
  - b) How many pregnancies would be required to recruit the required sample?
  - c) Ensuring coverage for 24 hour/7 days a week for the duration of the study?
13. Compliance with protocol and protocol violations: how important is compliance with the protocol? What effect does protocol violations, withdrawals or loss to follow up have on the interpretation of the results? Would you exclude patients with protocol violations or who withdraw?

## **Suggested Reading**

Agarwal S, Jaiswal V, Singh D, Jaiswal P, Garg A, Upadhyay A. Randomised control trial showed that delayed cord clamping and milking resulted in no significant differences in iron stores and physical growth parameters at one year of age. *Acta Paediatr.* 2016 Nov;105(11):e526-e530. doi: 10.1111/apa.13559.

Aladangady N, McHugh S, Aitchison TC, Wardrop CA, Holland BM. Infants' blood volume in a controlled trial of placental transfusion at preterm delivery. *Pediatrics.* 2006; 117(1):93-98.

Al-Wassia H, Shah PS. Efficacy and safety of umbilical cord milking at birth: a systematic review and meta-analysis. *JAMA Pediatr.* 2015 Jan;169(1):18-25. doi: 10.1001/jamapediatrics.2014.1906. Review.

Allan DS, Scrivens N, Lawless T, Mostert K, Oppenheimer L, Walker M, Petraszko T, Elmoazzen H. Delayed clamping of the umbilical cord after delivery and implications for public cord blood banking. *Transfusion.* 2016 Mar;56(3):662-5. doi: 10.1111/trf.13424. Epub 2015 Nov 20.

Alan S, Arsan S, Okulu E, Akin IM, Kilic A, Taskin S, Cetinkaya E, Erdeve O, Atasay B. Effects of umbilical cord milking on the need for packed red blood cell transfusions and early neonatal hemodynamic adaptation in preterm infants born  $\leq 1500$  g: a prospective, randomized, controlled trial. *J Pediatr Hematol Oncol.* 2014 Nov;36(8):e493-8. doi: 10.1097/MPH.000000000000143.

Andersson O, Hellström-Westas L, Andersson D, Domellöf M. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. *BMJ.* 2011; 343:d7157.

Andersson O, Hellström-Westas L, Andersson D, Clausen J, Domellöf M. Effects of delayed compared with early umbilical cord clamping on maternal postpartum hemorrhage and cord blood gas sampling: a randomized trial. *Acta Obstet Gynecol Scand.* 2013; 92(5):567-574.

Andersson O, Domellöf M, Andersson D, Hellström-Westas L. Effects of delayed cord clamping on neurodevelopment and infection at four months of age: a randomised trial. *Acta Paediatr.* 2013; 102(5):525-531.

Andersson O, Domellöf M, Andersson D, Hellström-Westas L. Effect of delayed vs early umbilical cord clamping on iron status and neurodevelopment at age 12 months: a randomized clinical trial. *JAMA Pediatr.* 2014 Jun;168(6):547-54. doi: 10.1001/jamapediatrics.2013.4639.

Andersson O, Lindquist B, Lindgren M, Stjernqvist K, Domellöf M, Hellström-Westas L. Effect of Delayed Cord Clamping on Neurodevelopment at 4 Years of Age: A Randomized Clinical Trial. *JAMA Pediatr.* 2015 Jul;169(7):631-8. doi: 10.1001/jamapediatrics.2015.0358.

Andersson O, Hellström-Westas L, Domellöf M. Elective caesarean: does delay in cord clamping for 30 s ensure sufficient iron stores at 4 months of age? A historical cohort control study. *BMJ Open.* 2016 Nov 2;6(11):e012995. doi: 10.1136/bmjopen-2016-012995.

Backes CH, Huang H, Cua CL, Garg V, Smith CV, Yin H, Galantowicz M, Bauer JA, Hoffman TM. Early versus delayed umbilical cord clamping in infants with congenital heart disease: a pilot, randomized, controlled trial. *J Perinatol.* 2015 Oct;35(10):826-31. doi: 10.1038/jp.2015.89. Epub 2015 Jul 30.

Baenziger O, Stolkin F, Keel M, von Siebenthal K, Fauchere JC, Kundu SD, Dietz V, Bucher HU, Wolf M. The influence of the timing of cord clamping on postnatal cerebral oxygenation: a randomized, controlled trial. *Pediatrics.* 2007; 119(3):455-459.

Boere I, Roest AA, Wallace E, Ten Harkel AD, Haak MC, Morley CJ, Hooper SB, te Pas AB. Umbilical blood flow patterns directly after birth before delayed cord clamping. *Arch Dis Child Fetal Neonatal Ed.* 2015 Mar;100(2):F121-5. doi: 10.1136/archdischild-2014-307144. Epub 2014 Nov 11.

Bolstridge J, Bell T, Dean B, Mackley A, Moore G, Swift C, Viscount D, Paul DA, Pearlman SA. A quality improvement initiative for delayed umbilical cord clamping in very low-birthweight infants. *BMC Pediatr.* 2016 Sep 13;16(1):155. doi: 10.1186/s12887-016-0692-9.

Bora R, Akhtar SS, Venkatasubramaniam A, Wolfson J, Rao R. Effect of 40-cm segment umbilical cord milking on hemoglobin and serum ferritin at 6 months of age in full-term infants of anemic and non-anemic mothers. *J Perinatol.* 2015 Oct;35(10):832-6. doi: 10.1038/jp.2015.92. Epub 2015 Jul 30.

Brocato B, Holliday N, Whitehurst RM Jr, Lewis D, Varner S. Delayed Cord Clamping in Preterm Neonates: A Review of Benefits and Risks. *Obstet Gynecol Surv.* 2016 Jan;71(1):39-42. doi: 10.1097/OGX.0000000000000263. Review.

Ceriani JM. Stem cell transfer in newborn infants through placental transfusion via delayed umbilical cord clamping. *Arch Argent Pediatr.* 2016 Dec 1;114(6):498-499. doi: 10.5546/aap.2016.eng.498. English, Spanish.

Chapman J, Marfurt S, Reid J. Effectiveness of Delayed Cord Clamping in Reducing Postdelivery Complications in Preterm Infants: A Systematic Review. *J Perinat Neonatal Nurs.* 2016 Oct/Dec;30(4):372-378.

Chiruvolu A, Tolia VN, Qin H, Stone GL, Rich D, Conant RJ, Inzer RW. Effect of delayed cord clamping on very preterm infants. *Am J Obstet Gynecol.* 2015 Nov;213(5):676.e1-7. doi: 10.1016/j.ajog.2015.07.016. Epub 2015 Jul 18.

Christensen RD, Baer VL, Gerday E, Sheffield MJ, Richards DS, Shepherd JG, Snow GL, Bennett ST, Frank EL, Oh W. Whole-blood viscosity in the neonate: effects of gestational age, hematocrit, mean corpuscular volume and umbilical cord milking. *J Perinatol.* 2014 Jan;34(1):16-21. doi: 10.1038/jp.2013.112. Epub 2013 Sep 12.

Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. Committee Opinion No.543: Timing of umbilical cord clamping after birth. *Obstet Gynecol.* 2012 Dec;120(6):1522-6. doi: 10.1097/01.AOG.0000423817.47165.48.

Dang D, Zhang C, Shi S, Mu X, Lv X, Wu H. Umbilical cord milking reduces need for red cell transfusions and improves neonatal adaptation in preterm infants: Meta-analysis. *J Obstet Gynaecol Res*. 2015 Jun;41(6):890-5. doi: 10.1111/jog.12657. Epub 2015 Feb 6.

Dash MB, Murali R. Effect of delayed cord clamping on hemoglobin level of newborns. *Indian J Pediatr*. 2014 Oct;81(10):1113-4. doi: 10.1007/s12098-014-1441-4. Epub 2014 May 1.

De Paco C, Herrera J, Garcia C, Corbalán S, Arteaga A, Pertegal M, Checa R, Prieto MT, Nieto A, Delgado JL. Effects of delayed cord clamping on the third stage of labour, maternal haematological parameters and acid-base status in fetuses at term. *Eur J Obstet Gynecol Reprod Biol*. 2016 Dec;207:153-156. doi: 10.1016/j.ejogrb.2016.10.031. Epub 2016 Nov 9.

Dicky O, Ehlinger V, Guyard-Boileau B, Assouline C, Arnaud C, Casper C. Delayed umbilical cord clamping in preterm infants born before 37 weeks of gestation: A prospective observational study. *Arch Pediatr*. 2017 Feb;24(2):118-125. doi: 10.1016/j.arcped.2016.11.006. Epub 2016 Dec 20. French.

Elimian A, Goodman J, Escobedo M, Nightingale L, Knudtson E, Williams M. Immediate compared with delayed cord clamping in the preterm neonate: a randomized controlled trial. *Obstet Gynecol*. 2014 Dec;124(6):1075-9. doi: 10.1097/AOG.0000000000000556.

Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: a randomized controlled trial. *J Perinatol*. 2012; 32(8):580-584.

Ertekin AA, Nihan Ozdemir N, Sahinoglu Z, Gursoy T, Erbil N, Kaya E. Term babies with delayed cord clamping: an approach in preventing anemia. *J Matern Fetal Neonatal Med*. 2016 Sep;29(17):2813-6. doi: 10.3109/14767058.2015.1105951. Epub 2015 Nov 23.

Frändberg S, Waldner B, Konar J, Rydberg L, Fasth A, Holgersson J. High quality cord blood banking is feasible with delayed clamping practices. The eight-year experience and current status of the national Swedish Cord Blood Bank. *Cell Tissue Bank*. 2016 Sep;17(3):439-48. doi: 10.1007/s10561-016-9565-6. Epub 2016 Jun 24.

Garabedian C, Rakza T, Drumez E, Poleszczuk M, Ghesquiere L, Wibaut B, Depoortere MH, Vaast P, Storme L, Houfflin-Debarge V. Benefits of Delayed Cord Clamping in Red Blood Cell Alloimmunization. *Pediatrics*. 2016 Mar;137(3):e20153236. doi: 10.1542/peds.2015-3236. Epub 2016 Feb 18.

Hooper SB, Binder-Heschl C, Polglase GR, Gill AW, Kluckow M, Wallace EM, Blank D, Te Pas AB. The timing of umbilical cord clamping at birth: physiological considerations. *Matern Health Neonatol Perinatol*. 2016 Jun 13;2:4. doi: 10.1186/s40748-016-0032-y. eCollection 2016 Jun 13. Review.

Hooper SB, Crossley KJ, Zahra VA, van Vonderen J, Moxham A, Gill AW, Kluckow M, Te Pas AB, Wallace EM, Polglase GR. Effect of body position and ventilation on umbilical artery and venous blood flows during delayed umbilical cord clamping in preterm lambs. *Arch Dis Child Fetal Neonatal Ed.* 2016 Nov 8. pii: fetalneonatal-2016-311159. doi: 10.1136/archdischild-2016-311159.

Hosono S, Mugishima H, Fujita H, Hosono A, Minato M, Okada T, Takahashi S, Harada K. Umbilical cord milking reduces the need for red cell transfusions and improves neonatal adaptation in infants born at less than 29 weeks' gestation: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed.* 2008; 93(1):F14-F19.

Hosono S, Mugishima H, Fujita H, Hosono A, Okada T, Takahashi S, Masaoka N, Yamamoto T. Blood pressure and urine output during the first 120 h of life in infants born at less than 29 weeks' gestation related to umbilical cord milking. *Arch Dis Child Fetal Neonatal Ed.* 2009; 94(5):F328-F331.

Hosono S, Mugishima H, Takahashi S, Takahashi S, Masaoka N, Yamamoto T, Tamura M. One-time umbilical cord milking after cord cutting has same effectiveness as multiple-time umbilical cord milking in infants born at &lt;29 weeks of gestation: a retrospective study. *J Perinatol.* 2015 Aug;35(8):590-4. doi: 10.1038/jp.2015.15. Epub 2015 Mar 12.

Jaiswal P, Upadhyay A, Gothwal S, Chaudhary H, Tandon A. Comparison of Umbilical Cord Milking and Delayed Cord Clamping on Cerebral Blood Flow in Term Neonates. *Indian J Pediatr.* 2015 Oct;82(10):890-5. doi: 10.1007/s12098-015-1734-2. Epub 2015 May 27.

Jelin AC, Zlatnik MG, Kuppermann M, Gregorich SE, Nakagawa S, Clyman R. Clamp late and maintain perfusion (CLAMP) policy: delayed cord clamping in preterm infants. *J Matern Fetal Neonatal Med.* 2016;29(11):1705-9. doi: 10.3109/14767058.2015.1061496. Epub 2015 Aug 12.

Katheria A, Blank D, Rich W, Finer N. Umbilical cord milking improves transition in premature infants at birth. *PLoS One.* 2014 Apr 7;9(4):e94085. doi: 10.1371/journal.pone.0094085. eCollection 2014 Apr 7.

Katheria AC, Leone TA, Woelkers D, Garey DM, Rich W, Finer NN. The effects of umbilical cord milking on hemodynamics and neonatal outcomes in premature neonates. *J Pediatr.* 2014 May;164(5):1045-1050.e1. doi: 10.1016/j.jpeds.2014.01.024. Epub 2014 Feb 20.

Katheria AC, Wozniak M, Harari D, Arnell K, Petruzzelli D, Finer NN. Measuring cardiac changes using electrical impedance during delayed cord clamping: a feasibility trial. *Matern Health Neonatol Perinatol.* 2015 May 22;1:15. doi: 10.1186/s40748-015-0016-3. eCollection 2015 May 22.

Katheria AC, Truong G, Cousins L, Oshiro B, Finer NN. Umbilical Cord Milking Versus Delayed Cord Clamping in Preterm Infants. *Pediatrics.* 2015 Jul;136(1):61-9. doi: 10.1542/peds.2015-0368.

Kilicdag H, Gulcan H, Hanta D, Torer B, Gokmen Z, Ozdemir SI, Antmen BA. Is umbilical cord milking always an advantage? *J Matern Fetal Neonatal Med.* 2016;29(4):615-8. doi: 10.3109/14767058.2015.1012067. Epub 2015 Mar 3.

Kinmond S, Aitchison TC, Holland BM, Jones JG, Turner TL, Wardrop CAJ. Umbilical cord clamping and preterm infants: a randomised trial. *Br Med J.* 1993; 306(6871):172-175.

Krueger MS, Eyal FG, Peevy KJ, Hamm CR, Whitehurst RM, Lewis DF. Delayed cord clamping with and without cord stripping: a prospective randomized trial of preterm neonates. *Am J Obstet Gynecol.* 2015 Mar;212(3):394.e1-5. doi: 10.1016/j.ajog.2014.12.017. Epub 2014 Dec 17.

Kugelman A, Borenstein-Levin L, Riskin A, Chistyakov I, Ohel G, Gonen R, Bader D. Immediate versus delayed umbilical cord clamping in premature neonates born <35 weeks: a prospective, randomized controlled trial. *Am J Perinatol.* 2007; 24(5):307-315.

Kumar B, Upadhyay A, Gothwal S, Jaiswal V, Joshi P, Dubey K. Umbilical Cord Milking and Hematological Parameters in Moderate to Late Preterm Neonates: A Randomized Controlled Trial. *Indian Pediatr.* 2015 Sep;52(9):753-7.

Kuo K, Gokhale P, Hackney DN, Ruangkit C, Bhola M, March M. Maternal outcomes following the initiation of an institutional delayed cord clamping protocol: an observational case-control study. *J Matern Fetal Neonatal Med.* 2017 Feb 14:1-5. doi: 10.1080/14767058.2017.1280018.

Lawton C, Acosta S, Watson N, Gonzales-Portillo C, Diamandis T, Tajiri N, Kaneko Y, Sanberg PR, Borlongan CV. Enhancing endogenous stem cells in the newborn via delayed umbilical cord clamping. *Neural Regen Res.* 2015 Sep;10(9):1359-62. doi: 10.4103/1673-5374.165218. Review.

Leslie MS. Perspectives on implementing delayed cord clamping. *Nurs Womens Health.* 2015 Apr-May;19(2):164-76. doi: 10.1111/1751-486X.12188.

Leslie MS, Erickson-Owens D, Cseh M. The Evolution of Individual Maternity Care Providers to Delayed Cord Clamping: Is It the Evidence? *J Midwifery Womens Health.* 2015 Sep-Oct;60(5):561-9. doi: 10.1111/jmwh.12333. Epub 2015 Sep 18.

Mansaray A, Yetman R, Berens P. Effect of Delayed Cord Clamping Above Versus Below the Perineum on Neonatal Hematocrit: A Randomized Controlled Trial. *Breastfeed Med.* 2015 Dec;10(10):464-7. doi: 10.1089/bfm.2015.0109.

March MI, Hacker MR, Parson AW, Modest AM, de Veciana M. The effects of umbilical cord milking in extremely preterm infants: a randomized controlled trial. *J Perinatol.* 2013 Oct;33(10):763-7. doi: 10.1038/jp.2013.70. Epub 2013 Jul 18.

Marotta L. Immediate versus delayed cord clamping. *Am J Obstet Gynecol.* 2015 Jun;212(6):827-8. doi: 10.1016/j.ajog.2015.03.009. Epub 2015 Mar 7.

McAdams RM, Backes CH, Hutchon DJ. Steps for implementing delayed cord clamping in a hospital setting. *Matern Health Neonatol Perinatol.* 2015 Apr 13;1:10. doi: 10.1186/s40748-015-0011-8. eCollection 2015 Apr 13.

- McAdams RM. Delayed cord clamping in red blood cell alloimmunization: safe, effective, and free? *Transl Pediatr.* 2016 Apr;5(2):100-3. doi: 10.21037/tp.2016.04.02.
- Mercer JS, McGrath MM, Hensman A, Silver H, Oh W. Immediate and delayed cord clamping in infants born between 24 and 32 weeks: a pilot randomized controlled trial. *J Perinatol.* 2003; 23(6):466-472.
- Mercer JS, Vohr BR, McGrath MM, Padbury JF, Wallach M, Oh W. Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized controlled trial. *Pediatrics.* 2006; 117(4):1235-1242.
- Mercer JS, Vohr BR, Erickson-Owens DA, Padbury JF, Oh W. Seven-month developmental outcomes of very low birth weight infants enrolled in a randomized controlled trial of delayed versus immediate cord clamping. *J Perinatol.* 2010; 30(1):11-16.
- Mercer JS, Erickson-Owens DA, Collins J, Barcelos MO, Parker AB, Padbury JF. Effects of delayed cord clamping on residual placental blood volume, hemoglobin and bilirubin levels in term infants: a randomized controlled trial. *J Perinatol.* 2017 Mar;37(3):260-264. doi: 10.1038/jp.2016.222. Epub 2016 Dec 8.
- Nevill E, Meyer MP. Effect of delayed cord clamping (DCC) on breathing and transition at birth in very preterm infants. *Early Hum Dev.* 2015 Jul;91(7):407-11. doi: 10.1016/j.earlhumdev.2015.04.013. Epub 2015 May 15.
- Oh W, Fanaroff AA, Carlo WA, Donovan EF, McDonald SA, Poole WK; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Effects of delayed cord clamping in very-low-birth-weight infants. *J Perinatol.* 2011 Apr;31 Suppl 1:S68-71.
- Oh W. Cord milking at delivery improves the iron status of term infants at 6 weeks. *Evid Based Med.* 2013 Dec;18(6):e58. doi: 10.1136/eb-2013-101294. Epub 2013 May 4.
- Ononeze ABO, Hutchon DJR. Attitude of obstetricians towards delayed cord clamping: a questionnaire-based study. *J Obstet Gynaecol.* 2009; 29(3):223-224.
- Rabe H, Jewison A, Fernandez Alvarez R, Crook D, Stilton D, Bradley R, Holden D. Milking compared with delayed cord clamping to increase placental transfusion in preterm infants: a randomized controlled trial. *Obstet Gynecol.* 2011; 117(2, pt 1):205-211.
- Patel S, Clark EA, Rodriguez CE, Metz TD, Abbaszadeh M, Yoder BA. Effect of umbilical cord milking on morbidity and survival in extremely low gestational age neonates. *Am J Obstet Gynecol.* 2014 Nov;211(5):519.e1-7. doi: 10.1016/j.ajog.2014.05.037. Epub 2014 May 29.
- Popat H, Robledo KP, Sebastian L, Evans N, Gill A, Kluckow M, Sinhal S, de Waal K, Tarnow-Mordi W, Osborn D. Effect of Delayed Cord Clamping on Systemic Blood Flow: A Randomized Controlled Trial. *J Pediatr.* 2016 Nov;178:81-86.e2. doi: 10.1016/j.jpeds.2016.08.004. Epub 2016 Aug 26.



Rabe H, Diaz-Rossello JL, Duley L, Doswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev.* 2012; Aug 15;8:CD003248.

Rabe H, Sawyer A, Amess P, Ayers S; Brighton Perinatal Study Group. Neurodevelopmental Outcomes at 2 and 3.5 Years for Very Preterm Babies Enrolled in a Randomized Trial of Milking the Umbilical Cord versus Delayed Cord Clamping. *Neonatology.* 2016;109(2):113-9. doi: 10.1159/000441891. Epub 2015 Dec 10.

Raju TN, Singhal N. Optimal timing for clamping the umbilical cord after birth. *Clin Perinatol.* 2012 Dec;39(4):889-900

Raju TN. Timing of umbilical cord clamping after birth for optimizing placental transfusion. *Curr Opin Pediatr.* 2013 Apr;25(2):180-7. doi: 10.1097/MOP.0b013e32835d2a9e.

Rana A, Agarwal K. Safety of Delayed Umbilical Cord Clamping in Preterm Neonates Less than 34 weeks Gestation. *Indian J Pediatr.* 2017 Jan 23. doi: 10.1007/s12098-016-2289-6.

Ranjit T, Nesargi S, Rao PN, Sahoo JP, Ashok C, Chandrakala BS, Bhat S. Effect of early versus delayed cord clamping on hematological status of preterm infants at 6 wk of age. *Indian J Pediatr.* 2015 Jan;82(1):29-34. doi: 10.1007/s12098-013-1329-8. Epub 2014 Feb 6.

Ruangkit C, Moroney V, Viswanathan S, Bholia M. Safety and efficacy of delayed umbilical cord clamping in multiple and singleton premature infants - A quality improvement study. *J Neonatal Perinatal Med.* 2015;8(4):393-402. doi: 10.3233/NPM-15915043.

Safarulla A. A review of benefits of cord milking over delayed cord clamping in the preterm infant and future directions of research. *J Matern Fetal Neonatal Med.* 2017 Jan 12:1-11. doi: 10.1080/14767058.2016.1269319.

Sanberg PR, Divers R, Mehindru A, Mehindru A, Borlongan CV. Delayed Umbilical Cord Blood Clamping: First Line of Defense Against Neonatal and Age-Related Disorders. *Wulfenia.* 2014 Jun 1;21(6):243-249.

Smit M, Dawson JA, Ganzeboom A, Hooper SB, van Roosmalen J, te Pas AB. Pulse oximetry in newborns with delayed cord clamping and immediate skin-to-skin contact. *Arch Dis Child Fetal Neonatal Ed.* 2014 Jul;99(4):F309-14. Epub 2014 Mar 31.

Sorin G, Tosello B. Focus on placental transfusion for preterm neonates: Delayed cord clamping and/or milking? *Gynecol Obstet Fertil.* 2016 Nov;44(11):641-646. doi: 10.1016/j.gyobfe.2016.08.002. Epub 2016 Sep 13. French.

Strauss RG, Mock DM, Johnson KJ, Cress GA, Burmeister LF, Zimmerman MB, Bell EF, Rijhsinghani A. A randomized clinical trial comparing immediate versus delayed clamping of the umbilical cord in preterm infants: short-term clinical and laboratory endpoints. *Transfusion.* 2008; 48(4):658-665.

Takami T, Suganami Y, Sunohara D, Kondo A, Mizukaki N, Fujioka T, Hoshika A, Akutagawa O, Isaka K. Umbilical cord milking stabilizes cerebral oxygenation and perfusion in infants born before 29 weeks gestation. *J Pediatr*. 2012; 161(4):742-747.

Upadhyay A, Gothwal S, Parihar R, Garg A, Gupta A, Chawla D, Gulati IK. Effect of umbilical cord milking in term and near term infants: randomized control trial. *Am J Obstet Gynecol*. 2013 Feb;208(2):120.e1-6. doi: 10.1016/j.ajog.2012.10.884. Epub 2012 Oct 31.

Vatansever B, Demirel G, Ciler Eren E, Erel O, Neselioglu S, Karavar HN, Gundogdu S, Ulfer G, Bahadir S, Tastekin A. Is early cord clamping, delayed cord clamping or cord milking best? *J Matern Fetal Neonatal Med*. 2017 Mar 20:1-4. doi: 10.1080/14767058.2017.1300647.

Winter J, Kattwinkel J, Chisholm C, Blackman A, Wilson S, Fairchild K. Ventilation of Preterm Infants during Delayed Cord Clamping (VentFirst): A Pilot Study of Feasibility and Safety. *Am J Perinatol*. 2017 Jan;34(2):111-116. doi: 10.1055/s-0036-1584521. Epub 2016 Jun 15.

Wright J. Delayed cord clamping? *Am J Obstet Gynecol*. 2015 Jun;212(6):827. doi: 10.1016/j.ajog.2015.03.012. Epub 2015 Mar 7.