2nd Edition

Beyond survival:

Integrated delivery care practices for long-term maternal and infant nutrition, health and development

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

Beyond survival:

Integrated delivery care practices for long-term maternal and infant nutrition, health and development

2nd Edition

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

PAHO HQ Library Cataloguing-in-Publication Data

****

Pan American Health Organization.
Beyond survival: integrated delivery care practices for long-term maternal and infant nutrition, health and development. 2. ed. Washington, DC : PAHO, 2013.

1. Infant, Newborn. 2. Infant Care. 3. Infant Nutrition. 4. Child Development. 5. Delivery, Obstetric. I. Title.

ISBN 978-92-75-11783-5 (NLM classification: WS 420)

Table of contents

List of boxes, figures and tables

Acknowledgments

This document updates a previously published version written by Camila Chaparro (Consultant) and Chessa Lutter (Pan American Health Organization) in 2007. Camila Chaparro wrote the updated version. We would like to thank the following individuals for their valuable comments on the original and/or updated versions: Wally Carlo (University of Alabama at Birmingham), Dilberth Cordero (Consultant, Pan American Health Organization), Kathryn Dewey (University of California, Davis), Leslie Elder (World Bank), Matthews Mathai (World Health Organization), Goldy Mazia (PATH), Judith Mercer (University of Rhode Island), Juan Pablo Pena Rosas (World Health Organization), Sybrich Tiemersma (University Medical Center Gronigen, Netherlands), Hedwig Van Asten (World Health Organization (retired), Patrick van Rheenen (University Medical Center Gronigen, Netherlands), and Steve Wall (Save the Children). We also wish to thank Dianne Farrar (Bradford Teaching Hospitals NHS Foundation Trust) for providing an original version of Figure 3.

Introduction

It is now well recognized that delivery and the immediate postpartum period is a vulnerable time for both the mother and infant. During the first 24 hours after delivery it is estimated that 25% to 45% of neonatal deaths and 45% of maternal deaths occur (*1, 2*). Thus delivery and postpartum care practices that attend to the most serious and immediate risks for the mother (e.g., postpartum hemorrhage and postpartum infections) and neonate (e.g., asphyxia, low birth weight, prematurity, and severe infections) are the most common conditions addressed by public health interventions. Only in the past decade has the fate of the newborn been directly focused upon, since previous delivery care initiatives mainly addressed the health and safety of the mother at childbirth (*2*) while child survival programs tended to concentrate on conditions affecting survival after the neonatal period (i.e., after the first 28 days of life) (*1*).

Though neonatal mortality is decreasing, in 2008, deaths within the first month of life comprised 41% of overall under-five child mortality (*3*). This quantification provides the opportunity to highlight several simple, inexpensive and evidence-informed delivery care practices that can improve survival of the "newborn" during delivery and the postpartum period (*4, 5*). However, while attention is now being paid more equally to improving survival of both components of the mother-infant dyad during delivery and the post-partum period, a crucial opportunity to implement simple practices that can affect long-term nutrition, health and development outcomes is being overlooked. Delayed umbilical cord clamping, early mother to newborn skin-to-skin contact, and early initiation of exclusive breastfeeding, are three simple practices recommended by WHO (*8, 9*) that, in addition to providing immediate benefit, can have long-term impact on the nutrition and health of both mother and child and possibly affect the development of the child far beyond the newborn period. Therefore, an integrated package of care that includes these three practices, together with maternal care practices already being promoted to prevent maternal morbidity and mortality, such as active management of the third stage of labor, will optimize both short- and long-term infant and maternal outcomes.

Delayed umbilical cord clamping, early mother to newborn skin-to-skin contact, and early initiation of exclusive breastfeeding, are three simple practices that, in addition to providing immediate benefit, can have long-term impact on the nutrition and health of both mother and child.

Objectives

The objective of the present document is twofold. First, the current knowledge of the immediate and long-term nutritional and health benefits of three practices will be reviewed. These include:

1. Delayed umbilical cord clamping;
2. Early and continued mother to newborn skin-to-skin contact;
3. Early initiation of exclusive breastfeeding (within the first hour after birth).

While there are clearly many essential delivery care practices, these three practices have received inadequate attention, deserve renewed emphasis, and have positive effects on nutritional status, which is generally not an outcome encompassed in the discussion of delivery care practices for improved public health outcomes. When appropriate, the immediate and long-term benefits are described separately for pre-term, low birth weight infants and full-term infants.

Secondly, we aim to illustrate that these three practices can be feasibly and safely implemented together for the benefit of both mothers and their infants. We provide a general recommendation for application in normal (vaginal) delivery of a well-newborn, with notes as needed for adaptations and adjustments for cesarean section delivery, low birth weight and/or premature infants. Previous recommendations have implied that several maternal and infant care practices may not be compatible with one another: for example, early cord clamping was until 2007 recommended as a part of active management of the third stage of labor (*6*) (see **Box 1** for additional discussion on active management of the third stage of labor) and one of the reasons suggested for practicing immediate cord clamping was in order to be able to place the infant in contact with the mother as soon as possible after delivery (*7*). Delivery practices have generally been described without simultaneously mentioning both components of the mother-infant dyad (e.g., guidelines on the active management of the third stage of labor generally do not include mention of the infant). We provide an integrated framework of steps, based on current evidence, which should be readily adaptable to a variety of delivery settings.

Box 1. Active management of the third stage of labor for the prevention of postpartum hemorrhage

Postpartum hemorrhage is the leading cause of maternal mortality worldwide, contributing to 25% of all maternal deaths(*8*), and uterine atony is its most common cause. Fourteen million cases of postpartum hemorrhage are estimated to occur annually on a global level (*8*). Active management of the third stage of labor (in its original form, active management included the administration of a prophylactic uterotonic after the delivery of a baby, early cord clamping and cutting, and controlled traction of the umbilical cord) significantly reduced the incidence of postpartum hemorrhage from uterine atony by 60% (*6*), the incidence of postpartum blood loss of 1 liter or more and the need for costly and risky blood transfusions (*9*), and prevented complications related to postpartum hemorrhage. In 2007, the World Health Organization revised its recommendations for active management to include delayed cord clamping rather than early cord clamping in light of increasing evidence on the benefits of delayed cord clamping to the infant, and lack of evidence on the harms to the mother or infant (*9*). In 2012, the guidelines were

(Continued).

Box 1. (Continued).

once again revised to address new evidence regarding the importance of controlled cord traction (*8*), and to review the evidence for each previously recommended component of the active management package. Research published since 2007 indicates that controlled cord traction does not significantly affect the incidence of postpartum hemorrhage, thus the revised guidelines indicate that controlled cord traction is an optional component of the active management strategy (*10*). The guideline development group concluded that the main intervention of the active management strategy is the provision of the uterotonic (*8*).

Below are the current (as of 2012) WHO recommendations for the prevention of postpartum hemorrhage (*8*) with the associated strength of the recommendation based on available evidence:

1. The use of uterotonics for the prevention of postpartum hemorrhage during the third stage of labour is recommended for all births. (Strong recommendation, moderate quality evidence).
2. Oxytocin (10 IU, IV/IM) is the recommended uterotonic drug for the prevention of postpartum hemorrhage. (Strong recommendation, moderate quality evidence).

…*

5. In settings where skilled birth attendants are available, controlled cord traction is recommended for vaginal births if the care provider and the parturient woman regard a small reduction in blood loss and a small reduction in the duration of the third stage of labour as important (Weak recommendation, high quality evidence).
6. In settings where skilled birth attendants are unavailable, controlled cord traction is not recommended. (Strong recommendation, moderate quality evidence).
7. Late cord clamping (performed after 1 to 3 minutes after birth) is recommended for all births while initiating simultaneous essential newborn care. (Strong recommendation, moderate quality evidence).
8. Early cord clamping (<1 minute after birth) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation. (Strong recommendation, moderate quality evidence).
9. Sustained uterine massage is not recommended as an intervention to prevent postpartum hemorrhage in women who have received prophylactic oxytocin. (Weak recommendation, low quality evidence).
10. Postpartum abdominal uterine tonus assessment for early identification of uterine atony is recommended for all women. (Strong recommendation, very low quality evidence).

**Note that additional recommendations on the choice of uterotonic (recommendations 3 and 4) have been omitted above; the full set of recommendations can be found here: http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548502/en/*

Methods

We performed searches of the scientific literature using PubMed to identify research studies relevant to the three main practices of interest using keyword searches.[1] Examples of search terms used are listed below, though supplemental searches on particular outcomes were also performed (e.g., skin-to-skin contact and hypothermia). The "snowball technique" as well as the PubMed "Related Citations in PubMed" function were used to identify additional related references.

Umbilical cord clamping: umbilical cord clamping; umbilical cord milking; umbilical cord clamping AND cesarean section; umbilical cord clamping AND pre-term infants

Skin-to-skin contact: skin to skin contact newborn; skin-to-skin contact AND cesarean section; kangaroo mother care; early skin-to-skin contact AND breastfeeding

Early initiation of breastfeeding: early initiation of breastfeeding; pre-lacteal feeds; early initiation of breastfeeding AND morbidity; early initiation of breastfeeding AND mortality; breastfeeding AND maternal outcomes

We also consulted guidelines and other documents of normative bodies (e.g., WHO, International Confederation of Midwives, International Federation of Gynecologists and Obstetricians, International Liaison Committee for Resuscitation) regarding relevant recommended practices (cord clamping, active management of the third stage of labor and neonatal resuscitation). Results of existing systematic reviews and meta-analyses (e.g., Cochrane Systematic Reviews) of controlled trials were used preferentially for providing an overall measure of effect of each practice on different outcomes. These results were complemented by individual studies that may have not been included in a meta-analysis due to the type of trial (e.g., observational or non-randomized) or that studied particular outcomes that the meta-analysis was inconclusive about due to the few number of trials investigating these outcomes.

Target audience

Our target audience for this document includes health practitioners attending deliveries in health facilities as well as public health decision makers who are responsible for establishing health policy for maternal and newborn care. The intended target audience for this document is intentionally broad in order to increase knowledge regarding the recommended practices among a wide range of individuals who will all be essential in effecting change. While we acknowledge that different individuals involved in maternal and newborn care will need varying levels of knowledge in order to promote and implement the recommended practices, the scientific evidence and practical recommendations included in this document will be useful to the entire audience. For example, practicing obstetricians, pediatricians, midwives and nurses may want more practical information on "how" to implement the practices. For that, the must have skills needed to assess how existing systems and programs can be adapted to accommodate the recommended practices. Thus for all groups, the "why" and "how" behind the recommended practices are essential knowledge, and therefore

[1] Searches most recently performed in March 2013.

this document will be valuable to both practicing clinicians and public health decision makers.

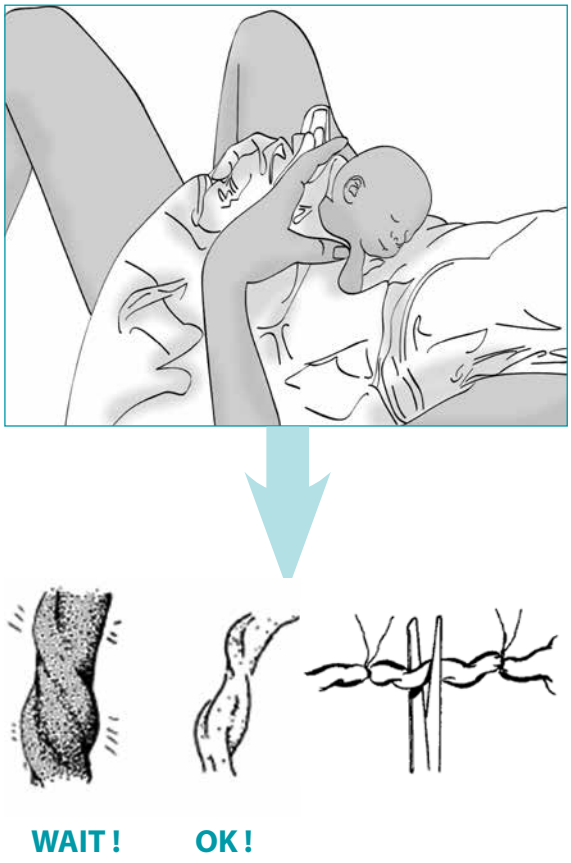
Organization of document

The first three sections of the document address each of the three practices in the following format: a recommendation for practice is presented first followed by a discussion of the evidence indicating short- and long-term benefit for both mother and infant (in most cases, both pre-term, low birth weight and full-term infants). The final section of the document presents an integration of the separate steps into a feasible sequence and addresses what is known regarding current delivery care practices. We conclude with a discussion of what steps may need to be taken to overcome barriers for the adoption and sustained implementation and integration of the essential delivery care practices discussed.

1. Optimal timing of umbilical cord clamping

Recommendation for practice

After delivery[1], dry the infant with a clean, dry cloth, and place the fully reactive infant[2] prone on the lower part of the maternal abdomen where s/he can be covered with a warm dry blanket. The cord should not be clamped earlier than one minute after birth (*8, 9*), and the optimal time to clamp the umbilical cord for all infants regardless of gestational age or fetal weight is when the circulation in the cord has ceased, and the cord is flat and pulseless (approximately 3 minutes or more after birth) (*10*). After the cord is flat,[3] clamp and cut the cord following strict hygienic techniques.



[1] In cesarean deliveries, the infant may be dried, wrapped and placed on the mother's thighs (or a surface level or slightly lower than the placenta) while waiting to clamp the cord. If there is a need to attend to the infant that cannot be addressed while the cord is intact, umbilical cord milking ("stripping" the cord from the placental end towards the infant 5 times) may be employed to allow a partial placental transfusion to occur in a shorter time period.

[2] If the infant is pale, limp, or not breathing, resuscitative measures can be performed while the infant is kept at the level of the perineum to allow optimal blood flow and oxygenation through the unclamped cord if there is experience doing so (see Box 2 for a discussion of neonatal resuscitation measures and the timing of cord clamping). However, many practitioners may not have this experience or may be unable to provide effective resuscitation measures when the cord is still intact (for example, due to the location of needed equipment relative to the mother); therefore, when newly-born term or pre-term babies require positive-pressure ventilation the cord should be clamped and cut to allow effective ventilation to be performed. Newly-born babies who do not breathe spontaneously after thorough drying should be stimulated by rubbing the back 2 to 3 times before clamping the cord and initiating positive-pressure ventilation (*9*). It is important to note that most infants (more than 90%) respond to the initial steps of resuscitation, including drying and stimulation. A smaller percentage, less than 10%, require active resuscitative interventions to establish regular respirations, and approximately half of those infants will respond without further active resuscitative efforts (*11*).

[3] See Figure 1 for an illustration of the changes in cord appearance during the first 15 minutes of life.

Box 2. Neonatal resuscitation and delayed cord clamping

In 2012, WHO released updated guidelines for neonatal resuscitation to provide guidance for resource-limited settings in particular on appropriate resuscitation practices (*9*). Previous resuscitation guidelines put forth by WHO and other normative bodies (e.g., International Liaison Committee on Resuscitation, ILCOR) did not include mention of the timing of umbilical cord clamping relative to neonatal resuscitation procedures. In the most recent guidelines of both groups, cord clamping is recommended to be performed no earlier than one minute after delivery (*9, 101*). Specifically, WHO provides the following recommendations (along with the strength of the recommendation as determined by the guideline development group, and related remarks):

- **In newly-born term or pre-term babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than one minute after birth.**
  (Strong recommendation based on moderate to high quality evidence for benefits in reducing the need for blood transfusion and increasing body iron stores and very low quality evidence for risk of receiving phototherapy for hyperbilirubinaemia.)
  ***Remark**: "Not earlier than one minute" should be understood as the lower limit supported by published evidence. WHO recommendations for the prevention of postpartum haemorrhage recommend that the cord should not be clamped earlier than is necessary for applying cord traction, which the [guideline development group] clarified would normally take around 3 minutes.*
- **When newly-born term or pre-term babies requires positive-pressure ventilation, the cord should be clamped and cut to allow effective ventilation to be performed.**
  (Weak recommendation based on the consensus of the WHO [guideline development group] in the absence of evidence in babies who need positive-pressure ventilation.)
  ***Remark**: If there is experience in providing effective [positive-pressure ventilation] without cutting the cord, ventilation can be initiated before cutting the cord.*

It is important to remember that the majority of infants will not need additional assistance (other than drying and warmth) to begin breathing. Only 1% of infants will require extensive resuscitation efforts. Providing resuscitation measures while the cord is still intact may allow for continued placental circulation if the placenta has not yet separated from the uterus—providing a source of oxygen to the infant—as well as much needed blood volume. There are a few different approaches to combining delayed cord clamping and resuscitation that have been suggested. Van Rheenen describes that bag and mask ventilation can be performed with the infant between the mother's legs (*120*). If more extensive resuscitation efforts are needed, a mobile trolley has recently been developed (named the BASICS or LifeStart trolley), that contains all of the equipment contained on a standard resuscitation table, but because of its mobility, can be moved alongside the delivery bed so that the cord does not need to be clamped and cut and taken to a stationary table away from the mother. For more information on the BASICS/LifeStart trolley see the ***Additional Resources and Websites*** section of this document.

1.1 History of the timing of umbilical cord clamping

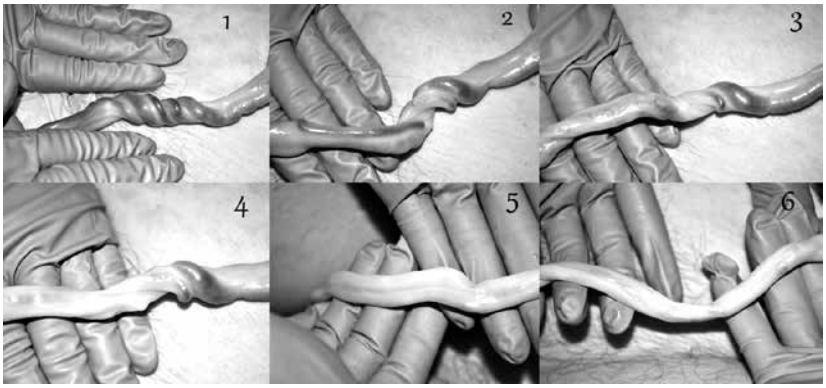
Debate as to the "correct" time to clamp the umbilical cord after delivery has been documented since at least the early 1900s, when obstetric practices began to shift from the "present prevalent practice" of delayed clamping (i.e., 2 to 3 minutes after delivery or at the end of cord pulsations) in 1935 (*12*), towards early umbilical cord clamping (i.e., 10 to 15 seconds after delivery) which appears to be the current and prevalent practice now in many settings. It is not clear why practices changed, but it has been suggested that many different factors played a role, including an overall movement in obstetrics towards more "interventionist" techniques (e.g., where women usually labor in dorsal positions rather than more upright positions, receive more analgesics and intravenous fluids, and where the umbilical cord and placenta are managed more actively). The movement of more births from the home into the hospital setting may also have created a situation where "ligation of the cord makes it possible to get babies and mothers out of the delivery room more rapidly" (*13*). Other reasons that have been suggested for the institution of early clamping include: the fear of increasing hyperbilirubinemia and/or polycythemia in the late clamped infant, the presence of a neonatologist or pediatrician in the delivery room anxious to attend to the infant, the rush to measure cord blood pH and gases, and to place the infant in skin-to-skin contact with the mother as soon as possible (*7*). Regardless of the particular reasons behind the change in practice from delayed clamping to early clamping, it is clear that there was little to no scientific evidence supporting early clamping as the more beneficial practice for the infant, or for the mother.

1.2 Physiological effects of the timing of cord clamping and determinants of the "placental transfusion"

For a period of time after birth there is still circulation between the infant and placenta through the umbilical vein and arteries, and thus the timing of cord clamping will have profound effects on infant blood volume at delivery. By measuring placental residual blood volume after clamping the umbilical vein and/or arteries at various time points, it was shown that blood flows through the umbilical arteries (from the infant to the placenta) during the first 20 to 25 seconds after birth but is negligible by about 40 to 45 seconds (*14*). In contrast, in the umbilical vein, blood flow continues from the placenta to the infant up to at least 3 minutes after delivery, after which blood flow is insignificant. The blood that the infant receives from the placenta during this time period is referred to as the "placental transfusion" (**Figure 1** provides a series of photos that demonstrates the change in appearance of the umbilical cord during the first 15 minutes of life as placental transfusion is occurring and ends). Following on studies in the 1960s and 1970s which attempted to measure the amount of pla-

Regardless of the particular reasons behind the change in practice from delayed clamping to early clamping, it is clear that there was little to no scientific evidence supporting early clamping as the more beneficial practice for the infant, or for the mother.

Figure 1. Demonstration of changes in umbilical cord appearance during the first 15 minutes of life



Note the changes in cord appearance from photo 1, immediately after birth when placental transfusion is occurring, to photos 5 and 6, where the cord is flat, pale and lifeless, indicating that placental transfusion has ended.

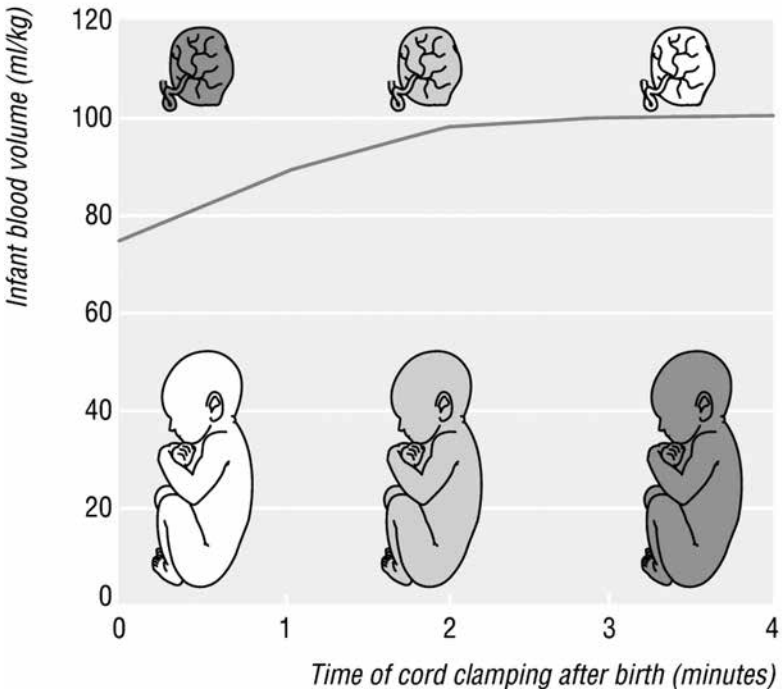
Photo credit: Nurturing Hearts Birth Services (http://www.nurturingheartsbirthservices.com/blog/?p=1542)

cental transfusion, in 1992 Linderkamp and colleagues calculated 35 ml of placental blood per kg of body weight transferred to the infant after a delay in clamping of at least 3 minutes (*15*). Most recently, a study of placental transfusion in 26 term infants (13 delivered vaginally, and 13 delivered by cesarean section) published in 2011 which weighed infants with the cord intact for up to 5 minutes after birth, measured an overall average placental transfusion between 24 and 32 ml/kg body weight (*16*). In this study, for most infants, placental transfusion appeared to be complete by 2 minutes, though in some infants, the transfusion continued through 5 minutes after delivery. Therefore, for a cord clamping delay of at least 2 to 3 minutes in a full-term infant, about 24 to 35 mL blood per kg body weight is provided to the infant from the placental circulation. This represents about one third of the total estimated newborn blood volume (assuming an average of 80 to 90 ml/kg for a newborn).

For pre-term infants, placental transfusion after delivery also occurs, although the amount of transfer is relatively smaller. A delay of 30 to 45 seconds permits an increase in blood volume of approximately 8% to 24% with slightly greater transfusion occurring after vaginal birth (between 2 to 16 ml/kg after cesarean delivery, and 10 to 28 ml/kg after vaginal delivery) (*17, 18*).

Classic studies from the 1960s showed that the rate of placental transfusion is rapid at first and then slows in a stepwise fashion, with approximately 25% of the transfer occurring in the first 15 to 30 seconds after the uterine contraction of birth, 50% to 78% of the transfer by 60 seconds and the remaining transfer by 3 minutes

Figure 2. Stepwise nature of the placental transfusion



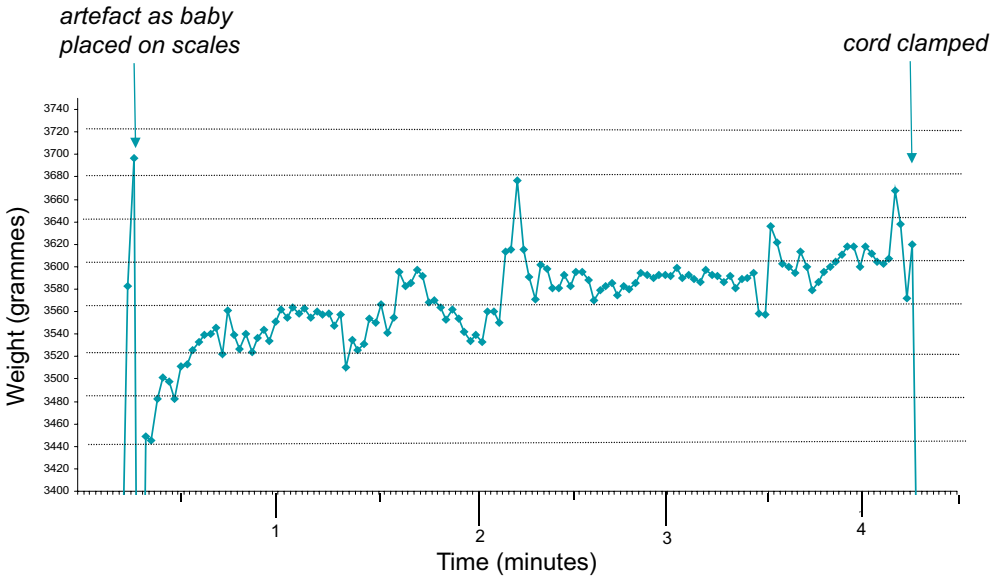
Distribution of blood between infant and placenta depending on time of cord clamping after birth (adapted from Linderkamp (*21*) and Yao (*19*). The term infants are at the level of the introitus, about 10 cm below the placenta.

Reproduced from van Rheenen et al., BMJ 2006;333:954-958 with permission from the BMJ Publishing Group.

(*19*) **(Figure 2)**. Farrar and colleagues (2011) in their recent study measuring placental transfusion by weighing the infant after birth with the cord intact, confirmed the stepwise pattern of placental transfusion, with the greatest increase in weight occurring during the first minute, and a much more gradual increase through 2 to 3 minutes of age and reaching a plateau afterwards (*16*) **(Figure 3)**.

The rate and amount of transfer can be affected by several factors. Uterine contraction is one factor that can accelerate the rate of transfer. The uterine contraction that naturally occurs between 1 and 3 minutes after the birth contraction is thought to be responsible for the last "step" of the placental transfer (*20*). When methylergonovine (a uterotonic drug used to stimulate uterine contractions) was given immediately after birth, placental blood transfer occurred in 1 minute, after a uterine contraction occurred at approximately 45 seconds (*20*). In contrast, though the sample size was small, Farrar and colleagues did not find a significant effect on the amount or rate of placental transfusion of intramuscular oxytocin when it was provided before or after cord clamping (*16*).

Figure 3. Birth weight measurements during placental transfusion (through 5 minutes of age)



This figure demonstrates the change in weight in the first 5 minutes after birth when the cord is not clamped and placental transfusion is allowed to occur. The steep increase during the first minute, followed by a more gradual increase through 3 minutes, and a general plateau between 3 and 5 minutes of age confirms the stepwise nature of placental transfusion illustrated in **Figure 1**.

Reproduced from Farrar et al., Measuring placental transfusion for term births: weighing babies with cord intact. BJOG 2011; 118:70-75 with permission from BJOG.

Gravity can also play a role in the rate and amount of transfer. Studies performed in the 1960's and 1970's showed that if the infant was held significantly below the level of the uterus, gravity seemed to speed the rate of transfer, but did not change the total amount of blood transferred (*21*). If the infant was held sufficiently high enough above the mother's uterus (50 to 60 cm in one study), placental transfusion was prevented by stopping blood flow through the umbilical vein (*14*). Between 10 cm above or below the level of the mother's uterus, the amount and rate of transfer is thought to be approximately similar, however some recent work suggests that placental transfusion in infants placed on the mother's abdomen may take up to 5 minutes to complete (*22*) **(Figure 4)**. Farrar and colleagues, in their study of 26 term infants did not find a significant difference in the amount of placental transfusion when the infant was at the level of

Figure 4. Comparison of clamping time and technique on placental residual blood volume (PRBV) with infants held on the mother's abdomen skin-to-skin after delivery

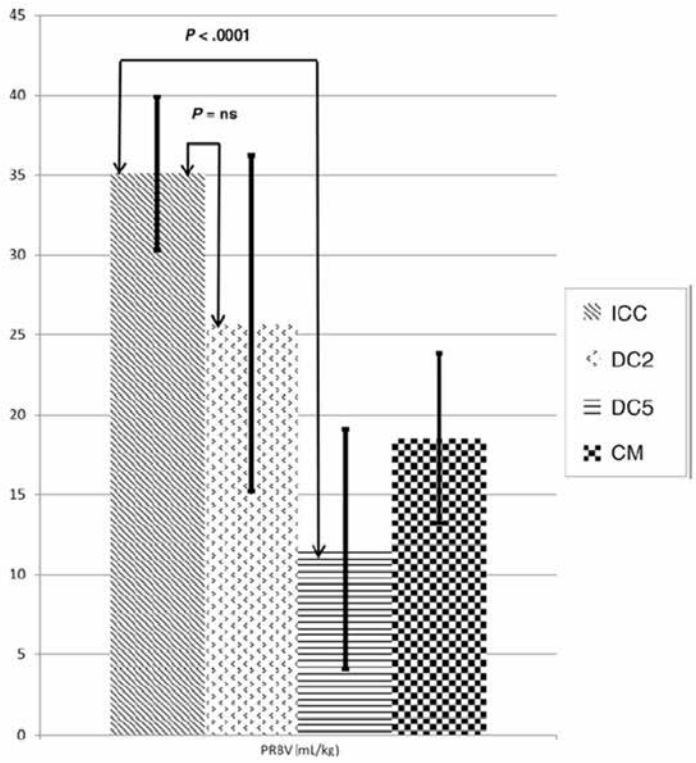


Figure 4 shows how immediate cord clamping (ICC) leaves the greatest amount of blood in the placenta (i.e., provides the smallest placental transfusion). Delayed clamping at 2 minutes (DC2) allows for some placental transfusion, but clamping at 5 minutes (DC5) allows for maximal transfusion when the infant is in skin-to-skin contact with the mother. Cord milking (CM) allows for a placental transfusion between DC2 and DC5 with the infant held in skin-to-skin contact.

Reproduced from Mercer et al., 2012. 26(3):202-217 with permission from the J Perinat Neonat Nurs.

the bed or on the mother's abdomen or thighs (for cesarean section deliveries); however, in this observational study, measurements were taken through 5 minutes after delivery, thus likely allowing a complete transfusion to occur (*16*).

The effect of the mode of delivery (vaginal vs. cesarean) on placental transfusion has also been debated. Some studies have suggested that placental transfusion is reduced or does not occur in cesarean section (*23*) possibly because of uterine atony due to the uterine incision, the anesthesia used for surgery, or the timing of the administration of the uterotonic drug (*16*). In the study performed by Farrar and colleagues published in 2011, there was not a significant difference in the amount of placental transfusion between

vaginal and cesarean deliveries (however there were only 13 infants in each group). The authors suggested that the use of a spinal (regional) anesthetic rather than general anesthesia (which may have been common in older studies) may have prevented uterine atony, allowing placental transfusion to occur (*16*). Ceriani-Cernadas and colleagues included cesarean deliveries in their study on the effects of delayed clamping in full-term infants through 6 months of age, indicating the feasibility of the practices; however subgroup analyses on study outcomes by delivery mode was not done (*24, 25*). Further assessment of placental transfusion in cesarean section deliveries may be useful to better understand the role of different factors in placental transfusion, including gravity (placement of the infant) and uterine contractions.

Another practice that has been used to affect the amount and rate of placental transfer is "cord milking" or "cord stripping", in which the individual attending the delivery "milks" the cord from the placental end towards the infant, forcing blood in the cord towards the infant, usually prior to cord clamping. This practice has been shown to have similar effects on neonatal outcomes—such as hemoglobin or hematocrit—as delayed clamping in both term and pre-term infants, but long-term studies that compare umbilical cord milking to delayed clamping in term or pre-term infants have not been performed. A study published in 2012 examined the effect of umbilical cord milking during cesarean section on neonatal hematocrit and hemoglobin concentrations and found that "milking" the cord five times before clamping resulted in higher hematocrits at 36 to 48 hours as compared to immediately-clamped infants, as well as a smaller volume of blood left in the placenta (*26*). While still recommending delayed clamping as the preferred, and more physiological, approach, the authors concluded that milking the cord could be a good alternative to delayed clamping during cesarean delivery in particular where obstetricians may be hesitant to delay clamping of the cord for several minutes.

1.3 Short- and long-term effects of cord clamping time on pre-term and low birth weight infants

The insufficient circulating blood volume caused by immediate cord clamping can have immediate negative effects in pre-term and low birth weight infants because of their initially smaller fetal-placental blood volume (with a relatively higher percentage contained in the placenta) and slower cardio-respiratory adaptation. A Cochrane systematic review, updated in 2012, included 15 randomized controlled trials, encompassing a total of 738 infants born between 24 and 36 weeks gestation (*27*). As compared to pre-term infants who received immediate cord clamping (i.e., generally within the first 10 seconds after delivery, though clamping time was not always recorded), pre-term infants who received delayed clamping (ranging from a 30 to 180 second delay across studies), had a decreased need for blood transfusions for anemia in the neonatal period, a decreased risk of intraventricular hemorrhage, and a decreased risk of necrotizing enterocolitis. Pre-term infants are more susceptible to intraventricular hemorrhage (i.e., bleeding into the brain's

Table 1. Summary of immediate and long-term effects of delayed umbilical cord clamping for infants (term, pre-term/low birth weight) and mothers

Immediate benefits			Long-term benefits	
Pre-term/low-birth weight infants	Full-term infants	Mothers	Pre-term/Low-birth weight	Full-term
Decreases risk of: – **Intra-ventricular hemorrhage** – **Necrotizing enterocolitis** – **Late-onset sepsis** **Decreases need for:** – **Blood transfusions for anemia or low blood pressure** – **Surfactant** – **Mechanical ventilation** **Increases:** – **Hematocrit** – **Hemoglobin** – **Blood pressure** – **Cerebral oxygenation** – **Red blood cell flow**	**Provides adequate blood volume and birth iron stores** **Increases:** – **Hematocrit** – **Hemoglobin**	**No effect on maternal bleeding or length of the third stage of labor** **Indication from "cord drainage" trials that a less blood filled placenta shortens the third stage of labor and decreases incidence of retained placenta.**	**Increases hemoglobin at 10 weeks of age** **May be a benefit to neurodevelopmental outcomes in male infants**	**Improves hematological status (hemoglobin and hematocrit) at (2 to 4 months of age)** **Improves iron status through 6 months of age**

ventricular system, which especially in severe cases, is a risk to developmental outcomes) than full-term infants, and immediate clamping may increase the risk of intracranial bleeding by causing hypotension, which has been shown to be a risk factor for intraventricular hemorrhage (*28*). Pre-term infants with delayed clamping may also have a decreased need for blood transfusions for low blood pressure, though this outcome did not reach statistical significance in the 2012 Cochrane Review (*27*). This review also found that pre-term infants with delayed clamping had a significantly higher peak bilirubin concentration after birth. Criteria for phototherapy treatment of premature infants are controversial, with no universally accepted treatment guidelines. The peak levels of the studies included in the Cochrane review ranged from 139 to 222 µmol/L for infants ranging from 24 to 36 weeks. One guideline for treatment with phototherapy based on gestational age recommends treatment at 80 µmol/L at 24 weeks gestation, and at 250 µmol/L for infants of 36 weeks gestation (*29*). However, the significant benefits of delayed clamping for pre-term infants of preventing intraventricular hemorrhage, necrotizing enterocolitis, and reducing

The insufficient circulating blood volume caused by immediate cord clamping can have immediate negative effects in pre-term and low birth weight infants because of their initially smaller fetal-placental blood volume.

the need for blood transfusions may outweigh the risk of potentially elevated bilirubin levels in many settings.

Individual studies have shown other immediate benefits of delayed clamping for premature, or very low birth weight infants, which due to the relatively few studies that have examined these outcomes could not in most cases be adequately evaluated in the Cochrane Review. A randomized controlled trial published in 2006 of the effect of a 30 to 45 second delay in clamping as compared to immediate (5 to 10 seconds) umbilical cord clamping in newborns less than 32 weeks gestation showed, in addition to a significantly lower incidence of intraventricular hemorrhage, a significantly lower risk of late-onset sepsis (i.e., sepsis that occurs after the first week of life) in the delayed-clamped infants, with a trend towards greater protection among male infants who received delayed clamping (*30*). The authors proposed that the increased incidence of late-onset sepsis seen in the immediate clamping group (8/33 in the immediate-clamped group versus 1/36 in the delayed-clamped group p = 0.03) could be due to a loss of protective primitive hematopoietic progenitor cells (in which cord blood is very rich) resulting in a compromised immune response. However, a small study published in 2011 of 42 premature infants examined levels of circulating hematopoietic progenitor cells, and did not find significant differences in circulating levels between delayed-clamped and immediate-clamped infants; in fact circulating levels of these cells were lower in the delayed-clamped infants (*31*). The authors speculated that placental transfusion may have also provided greater levels of factors needed for "homing" of these progenitor cells to their target organs, thus reducing circulating levels of these important cells. More research is needed on sepsis and associations with cord clamping time as well as potential mechanisms for such a relationship, particularly since sepsis is estimated to contribute to approximately one quarter (23%) of neonatal deaths (*3*).

Delayed clamping in pre-term and/or low birth weight infants has also been associated with fewer days on oxygen, fewer days on or a decreased need for mechanical ventilation, a decreased need for surfactant, and a decreased need for transfusions for low blood pressure or anemia.

Other outcomes in the neonatal period that may benefit from delayed clamping include hematocrit levels (*32*), oxygen transport (including cerebral oxygenation) (*33*), and red blood cell flow (*34*). Delayed clamping in pre-term and/or low birth weight infants has also been associated with fewer days on oxygen (*35*), fewer days on or a decreased need for mechanical ventilation (*32, 35*), a decreased need for surfactant (*32*), and a decreased need for transfusions for low blood pressure or anemia (*36*). These outcomes may be of particular interest in low resource settings that have limited access to expensive technology. However, due to the low number of studies that have investigated these outcomes, and thus small sample sizes, further research would be useful to confirm these other potential benefits of delayed clamping for preterm and/or low birth weight infants.

There are very few studies that have exam-

ined long-term outcomes in pre-term and/or low birth weight infants. These infants would likely receive significant long-term benefit from delayed clamping because of their increased risk of developing iron deficiency and anemia. Iron reserves at birth are positively related to infant birth size and gestational age, so smaller, premature infants will have smaller iron reserves to begin with. They may also deplete their smaller iron stores more quickly because of their more rapid rate of growth, for which iron is a necessary component. In addition to improved iron status, delayed clamping reduces the risk of intraventricular hemorrhage, and in at least one study, the risk of neonatal sepsis, both conditions that can negatively affect neurodevelopment in premature infants (*37*). Thus, delayed clamping both could potentially affect developmental outcomes in premature infants through positive effects on iron status as well as prevention of intraventricular hemorrhage and sepsis.

The only study to date to examine the effect of clamping time on hematological status of premature infants past the newborn period followed 37 premature infants (gestational age between 34 and 36 weeks) who had been randomly assigned to receive delayed clamping (at 3 minutes after delivery) or early clamping (mean of 13.4 seconds). The delayed-clamped infants showed significantly higher hemoglobin concentrations at both 1 hour and 10 weeks of age (*38*).

Similarly, for the effect of clamping time on developmental outcomes in pre-term/low birth weight infants, there has only been one study published to date (*37*). In this study, 58 infants of mean birth weight of approximately 1160 g and who had received delayed (30 to 45 seconds after delivery) or early clamping (less than 10 seconds after delivery) were assessed at 7 months of age using the Bayley Scales of Infant Development II. The Psychomotor Development Index scores were not significantly different between infants who had received delayed clamping versus early clamping. However, there was a significant interaction effect between gender and cord clamping time on development scores, such that males benefited more than females from delayed clamping in terms of Psychomotor Development Index scores. Male infants with delayed clamping had Psychomotor Development Index scores more than 1 standard deviation greater than male infants with early clamping. The authors hypothesized that hypovolemia caused by early clamping could independently negatively affect motor and mental development in pre-term infants, in addition to the intraventricular hemorrhage and sepsis associated with the practice of early clamping (*37*). Additional research on the long-term effects of cord clamping time on this vulnerable population is needed.

1.4 Short- and long-term effects of cord clamping time on full-term infants

In full-term infants, two meta-analyses, completed in 2007 (*39*) and 2013 (originally published in 2008, and updated in 2013) (*40*), have examined both positive and negative effects of cord clamping time in the neonatal period for term infants. Hutton and Hassan's analysis of 15 controlled trials (8 randomized controlled, 7 controlled, a total of 1912 infants) showed that delayed clamping did not impose an increased risk

Table 2. Worldwide prevalence of anemia in children between 6 and 35 months of age from available Demographic and Health Surveys*

	Prevalence of hemoglobin < 11 g/dL (%) by infant age groups			
	6 to 9 months	10 to 11 months	12 to 23 months	24 to 35 months
Sub-Saharan Africa				
Angola 2006-2007** (MIS)	74	81	66	60
Benin 2006	85	86	86	80
Burkina Faso 2010	94	92	95	91
Burundi 2010	72	65	50	43
Cameroon 2011	78	76	71	57
Congo (Brazzaville) 2005	72	74	69	67
Democratic Republic of Congo 2007	83	90	76	71
Ethiopia 2011	65	70	58	45
Ghana 2008	80	89	85	80
Guinea 2005	82	79	87	82
Lesotho 2009	63	53	60	47
Madagascar 2008-2009	66	69	60	50
Malawi 2010	81	87	73	65
Mali 2006	87	91	90	81
Niger 2006	89	89	93	87
Rwanda 2010	68	71	51	36
Sao Tome and Principe 2008-2009	86	79	79	61
Senegal 2010-2011	83	84	86	81
Sierra Leone 2008	82	80	84	77
Swaziland 2006-2007	66	69	65	43
Tanzania 2010	80	80	70	60
Uganda 2011	70	70	59	50
Zimbabwe 2010-2011	73	75	74	56
Uzbekistan 1996	59	64	62	59
North Africa/West Africa/Europe				
Albania 2008-2009	28	25	30	18
Armenia 2005	74	66	46	33
Azerbaijan 2006	57	51	55	37
Egypt 2005	61	67	57	49
Jordan 2009	50	57	49	28
Republic of Moldova 2005	46	57	44	31
Central Asia				
Kazakhstan 1999	23	42	67	48
Kyrgyz Republic 1997	53	40	61	45
Turkmenistan 2000	38	45	55	38
Uzbekistan 1996	59	64	62	59
South and Southeast Asia				
Cambodia 2010	83	85	77	46
India 2005-2006	80	81	83	75
Nepal 2011	76	75	65	43
Timor-Leste 2009-2010	58	73	49	42
Latin America and the Caribbean				
Bolivia 2008	80	73	79	63
Guyana 2009	57	75	55	36
Haiti 2005-2006	75	75	75	63
Honduras 2005-2006	63	69	53	37
Peru 2007-2008	77	79	65	42

**Source: MEASURE DHS STATcompiler, http://www.statcompiler.com, Accessed January 28, 2013.*

of negative outcomes in the neonatal period, the two most commonly studied being neonatal polycythemia (i.e., venous hematocrit above 70%) and jaundice (i.e., elevated levels of bilirubin) (*41*). Although delayed-clamped infants did have significantly higher hematocrit at 7 hours (2 trials, 236 infants) and between 24 and 48 hours of life (7 trials, 403 infants), no clinical signs of polycythemia were reported in the studies reviewed. Treatment for asymptomatic polycythemia may only be warranted when the venous hematocrit exceeds 70% (*42, 43*), as not all infants with elevated hematocrit will have hyperviscosity (*44, 45*), generally thought to be the cause of clinical symptoms. Even when indicated, there may be negative effects of the most commonly used treatment for polycythemia and/or hyperviscosity, partial exchange transfusion: a systematic review published in 2006 of outcomes associated with partial exchange transfusion, showed no long-term benefit to neurodevelopmental outcomes from the practice, and an increased risk of necrotizing enterocolitis (*46*). McDonald et al's Cochrane Review, which included 15 trials involving a total of 3911 women and infant pairs , also showed that there was not a significant difference in levels of polycythemia between early- and delayed-clamped infants (*40*).

Furthermore, Hutton and Hassan's analysis (*41*) showed that delayed clamping did not significantly increase mean serum bilirubin within the first 24 hours of life (2 trials, 163 infants) or at 72 hours of age (2 trials, 91 infants), or the incidence of clinical jaundice at 24 to 48 hours of age (8 trials, 1009 infants) or the number of infants requiring phototherapy (3 trials, 699 infants). In the Cochrane Review, McDonald et al found that significantly more delayed-clamped infants required phototherapy for jaundice than early-clamped infants; however, the criteria for application of phototherapy in the included studies was not provided, nor was it specified or standard across trials measuring this outcome (*40*). Guidelines for cut-offs for implementing phototherapy have also changed over the past few decades. There was no significant difference in the number of infants with clinical jaundice between early- and delayed-clamped infants (*40*).

Delayed clamping does not significantly increase mean serum bilirubin within the first 24 hours of life or at 72 hours of age, or the incidence of clinical jaundice at 24 to 48 hours of age or the number of infants requiring phototherapy.

As previously described, delayed clamping increases the newborn's blood volume, and because 70% of a newborn's body iron is in circulation (as hemoglobin), the amount of iron provided by delayed clamping is significant **(Box 3)**. During the first months after birth, as fetal red blood cells are broken down, the iron contained in hemoglobin is recycled and placed in stores. These iron stores are then used for the next several months for the body's need for growth and blood volume expansion. For full-term normal birth weight infants born to mothers with adequate iron status and whose cords are not clamped immediately, birth iron stores are estimated to be adequate (i.e., maintain hemoglobin levels and provide sufficient iron for growth) until roughly 6 to 8 months of age (*47*) **(Figure 5)**. However, even before factoring in the effect

Box 3. Amount of iron provided in the "placental transfusion" allowed by delayed clamping

Assuming a hemoglobin concentration of 170 g/L at birth, and 3.47 mg of iron (Fe) per gram of hemoglobin (Hb), for a 3.2 kg infant, receiving an "average" placental transfusion (i.e., approximate midpoint of the range of 24 to 35 ml/kg) would receive:

$$3.2\text{kg} \times 30\ \text{ml/kg} = 96\ \text{ml blood}$$

$$96\ \text{ml blood} \times \frac{170\ \text{g Hb}}{1000\ \text{ml blood}} \times \frac{3.47\ \text{mg Fe}}{\text{g Hb}} = 56.6\ \text{mg Fe}$$

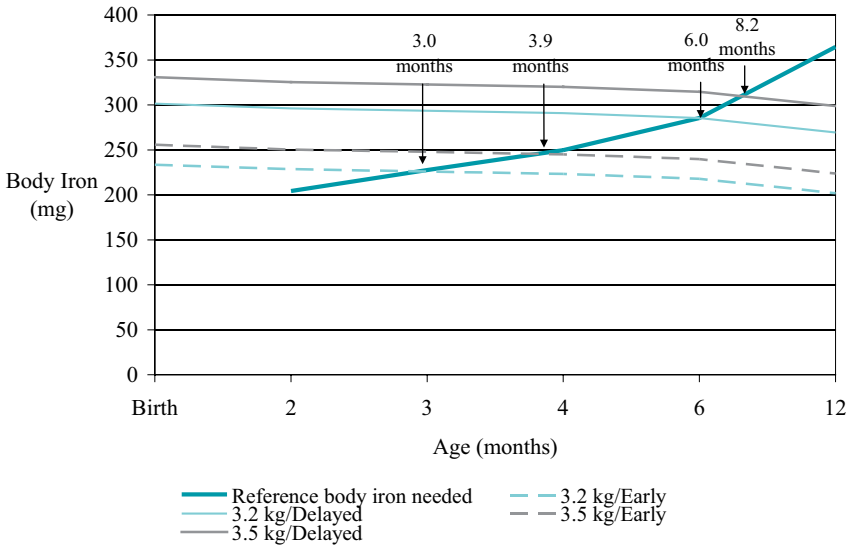
This amount of iron is roughly equivalent to 2.7 months of infant iron requirements for a 6 to 11 month-old infant (0.7 mg/day), (*121*). The range of iron transferred from a placental transfusion of 25 to 35 ml/kg would be 46 to 60 mg, or 1 to 3 months of iron requirements.

of clamping time, birth iron stores of infants in developing countries are already compromised. In these settings, pregnant women frequently are anemic, and pre-term and low-birth-weight births are common. Though not all anemia is due to iron deficiency, the problem of anemia begins well before the end of the first year of life, often in the first 6 months, in almost all world regions as evident in (**Table 2**). Iron deficiency is estimated to be the principal nutritional cause of anemia in young children, contributing to roughly 50% to 60% of anemia cases. However, particularly in settings where the infectious disease burden is high, other non-nutritional causes of anemia (such as malaria, hookworm and other parasites, and general infection or inflammation) as well as other nutritional deficiencies (vitamin A, B12, B6) should be investigated as potential causes in addition to addressing possible iron deficiency. As the peak prevalence of anemia (between 6 and 23 months of age) corresponds to an important and iron-sensitive period of mental and motor development, anemia during infancy is a serious public health problem with long-term health, socioeconomic and social implications. Mechanisms and evidence for the negative and perhaps irreversible effects of iron deficiency on development are discussed in detail in section 1.6.

As the peak prevalence of anemia (between 6 and 23 months of age) corresponds to an important and iron-sensitive period of mental and motor development, anemia during infancy is a serious public health problem with long-term health, socioeconomic and social implications.

Assuming that iron plays a role in at least half of anemia cases during these young ages, focusing attention on birth iron endowment is important. Birth iron endowment is a strong predictor of iron status and anemia later in infancy (*48, 49*) and the high prevalence of anemia already evident at 6 to 9 months of age indicates that in

Figure 5. How long should birth iron stores last? An analysis by birth weight and cord clamping time



The green line indicates the estimated body iron needed to maintain adequate hemoglobin levels and provide for growth (i.e., the "reference" body iron needed). The grey and light green lines (solid and dashed) indicate the levels of body iron available for the first 12 months of life (including the birth iron stores and iron provided through breast milk) for 4 different scenarios of birth weight and cord clamping time (*47*). The intersection of each light green/gray line with the heavy green line indicates the point at which body iron becomes insufficient to support growth and haemoglobin concentrations.

many cases, birth iron endowments are not adequate in many populations. Delayed clamping, through its effect on birth iron endowment, is one strategy to improve iron status and prevent anemia in infancy.

The two systematic reviews previously mentioned (*39, 40*) have included the majority of randomized controlled trials investigating longer-term iron status outcomes as a result of cord clamping time. Hutton and Hassan, from their review of 15 controlled trials, found that a delay in clamping of the umbilical cord for a minimum of 2 minutes was beneficial for infant hematological and iron status through 6 months of age (*39*). The benefits of delayed clamping to hematological and iron status that were identified from this review included improved hematocrit (at 6 hours, 24 to 48 hours, 5 days and 2 months of age), hemoglobin concentration (at 7 days and in one trial at 2 months of age), ferritin concentration (at 2, 3 and 6 months of age), as well as a "clinically important reduction" (15%) in the risk of anemia (at 24 to 48 hours and 2 to 3 months of age). McDonald et al examined both maternal and infant

effects of cord clamping time and included several of the same trials as the review by Hutton and Hassan, unpublished data from the first author and several studies published since 2007 (and not included in Hutton and Hassan's review). 15 randomized controlled trials, including a total of 3911 mother-infant pairs representing countries on 6 continents (North America, South America, Europe, Asia, Africa and Australia) were included. Similar results to those of Hutton and Hassan were shown: delayed clamping improved newborn hemoglobin and improved iron status through 6 months of life (*40*). The trial included in both previously mentioned reviews with the longest follow-up through 6 months of age showed that infants whose cords were clamped at approximately 1.5 minutes after birth had significantly higher iron status at 6 months of age than infants whose umbilical cords were clamped immediately (approximately 17 seconds after birth) (*50*). In this study, at 6 months of age, in comparison to early-clamped infants, body storage iron was greater in delayed-clamped infants by approximately 27 mg of iron (the equivalent of 1.25 months of infant iron requirements). Infants who were at higher risk of developing iron deficiency during infancy—because of smaller birth size (birth weight between 2500 to 3000 grams) or who were born to mothers with iron deficiency—derived a significantly greater benefit from a delay in cord clamping than those born to iron-replete mothers. Furthermore, infants who received delayed clamping also had lower blood lead levels, an effect due in part to improved iron status during infancy (*51*).

One of the most recent studies included in the Cochrane review, was conducted in Sweden and addresses the important question of the effect of cord clamping time on infant iron status in a high-income country, where levels of anemia and iron deficiency are relatively low (*52*). This randomized controlled trial of 400 term infants followed through 4 months of age showed that cord clamping time is important for iron status even in high income settings. Infants with delayed clamping (at 180 seconds or greater after delivery) as compared to infants with early clamping (at 10 or fewer seconds after delivery) had 45% greater ferritin concentrations at 4 months of age, as well as greater hematocrit, and mean corpuscular volume; all other indicators of iron status measured favored greater iron status in the infants with delayed clamping. Infants with delayed clamping were also significantly less likely to have iron deficiency at 4 months of age (0.6% vs. 5.7%) (*52*). Results of the cord clamping intervention on developmental outcomes at 4 months of age (assessed using the Ages and Stages Questionnaire) and infection/morbidity from the same study population were released in early 2013 (*53*). These results represent the only long-term assessment of development outcomes as a function of cord clamping time that exists to date. There were not significant differences in overall development scores, though the delayed-clamped infants did score significantly higher in the problem-solving domain, but significantly lower in the personal-social domain (however, these differences were no longer significant when the data were analyzed on a per-protocol, rather than intention-to-treat, basis). Symptoms of infections and other mor-

bidity were similar between groups through 4 months of age (*53*). The researchers plan to continue to follow this cohort through 12 months of age to continue to examine the effect of cord clamping time on iron status and development.

1.5 Effects of cord clamping time on maternal outcomes

Fewer studies on the timing of cord clamping have included maternal outcomes. Research studies that have investigated the effects of cord clamping time on maternal outcomes were recently reviewed by McDonald et al,, which found that there were no significant differences by cord clamping time for postpartum hemorrhage (>= 500 ml) or severe postpartum hemorrhage (>= 1000 ml), maternal postpartum hemoglobin, need for blood transfusion, need for manual removal of the placenta, or the length of the third stage of labor, though the number of studies was limited for several of these outcomes. (*40*). It has been speculated that a less blood-filled and distended placenta may be actually easier to deliver (*54, 55*), perhaps contributing to fewer complications during the third stage of labor. A less blood-filled placenta could result from delayed clamping or the practice of placental cord drainage, which involves immediately clamping and cutting the umbilical cord, but then immediately unclamping only the maternal side in order to allow the remaining placental blood to drain freely. A Cochrane review published in 2011 of three studies (a total of 1257 women) on the effect of placental drainage on maternal outcomes showed that it significantly reduced the length of the third stage of labor and the average amount of blood loss (*56*).

1.6 Infant iron status and development: an emphasis on prevention

The negative effects of iron deficiency on development have been the subject of investigation for the past several decades in both animal models and humans. Animal models have been developed to more closely mimic the development of iron deficiency in humans, and to model the effects of iron deficiency occurring at different time points in development (e.g., fetal life through weaning), while controlling for environmental factors that frequently complicate the interpretation of results in humans (*57*). There are several different mechanisms that have been elucidated with animal models through which iron deficiency during infancy is hypothesized to negatively affect development including myelination, dendritogenesis, synaptogenesis, and neurotransmission. The poorer development of iron deficient infants may also be explained by a phenomenon known as "functional isolation", which refers to a collection of behaviors displayed by iron deficient and anemic infants (e.g., being more fearful, wary, hesitant, unhappy, and tense, exhibiting less pleasure and tending to be more "attached" to their mothers during play (*58*)) which may contribute to their poorer development.

A Cochrane review published in 2011 on the effect of placental drainage on maternal outcomes showed that it significantly reduced the length of the third stage of labor and the average amount of blood loss.

The interaction between nutritional and environmental factors can make the interpretation of results in human studies difficult, as infants

more commonly affected by iron deficiency and anemia generally are from lower socioeconomic groups which have characteristics that also may contribute to poor development: lack of stimulation in the home, low maternal education and IQ, maternal depression, absent fathers, low birth weight and early weaning, parasitic infections, elevated blood lead levels and general under-nutrition (*58*). However, even after controlling for these differences, it has been generally found that iron deficiency anemia during infancy (between 6 to 24 months of age) is associated with poorer cognitive, motor, and/or social/emotional outcomes (*57*). Of even more concern are the results of studies that show persistent developmental deficiencies in anemic or chronically iron deficient infants who received treatment to correct the deficiency and/or anemia. In some studies, effects remain even more than 10 years after treatment (*59*). A follow-up study published in 2006 of a cohort of Costa Rican adolescents who had been tested for iron deficiency anemia as infants and children, showed that at 19 years of age, middle-socioeconomic status participants who had chronic iron deficiency as infants and received treatment scored on average 9 points lower on cognitive testing than their peers of similar socioeconomic status who had not suffered from iron deficiency anemia (*60*). For low socioeconomic status young adults, the difference in cognitive test scores associated with iron deficiency anemia during infancy was nearly tripled to 25 points, indicating the compounded negative effect of lower-socioeconomic status and iron deficiency on development. The lasting effect of iron deficiency anemia during infancy was such that young adults of middle socioeconomic status with low iron status in infancy had test scores that were not different from the test scores of young adults of low socioeconomic status who had adequate iron status. Thus, preventing iron deficiency anemia during infancy may ensure that all children are able to optimize the education that they are provided.

Similarly, one study of 6-month old infants showed slower conduction times for auditory brainstem responses in infants with iron deficiency anemia, as compared to normal controls, suggesting that myelination may have been altered in the infants suffering from iron deficiency anemia (*61*). Of particular concern was that during the year of follow-up in the original study, and even 4 years later (*62*), the originally anemic infants did not catch up to the control infants even after treatment to correct the anemia.

From these studies it appears that treatment for an already established deficiency of iron may not be sufficient to prevent the negative and long-term effects of iron deficiency anemia on development, thus emphasizing the need for interventions aimed at preventing the development of iron deficiency. In addition, in light of findings over the past decade of potential negative effects of iron supplementation on morbidity and growth in particular subgroups of children (e.g., infants with adequate iron status (*63*)), interventions such as delayed clamping that help to maintain adequate iron status, are of particular importance.

2. Mother and newborn skin-to-skin contact

Recommendation for practice

After delivery[1] and thoroughly drying the infant, place the reactive newborn directly on the mother's abdomen, prone, with the newborn's skin touching the mother's skin (*80*). While the mother's skin will help regulate the infant's temperature, cover the infant's back and the mother's chest with a warm, dry cloth and cover the infant's head with a cap or cloth to prevent heat-loss. After clamping the cord, the infant may be placed on the mother's chest, with the infant's skin touching the mother's skin and still covered with a cloth or blanket to keep the infant warm. As much as possible, keep mother and infant in this position for at least the first hour of life, delaying any routine procedures, and providing frequent supervision to ensure that the infant is breathing well and that there are no complications, particularly for first-time mothers. Skin-to-skin contact does not have to be limited to the delivery room but should be practiced as frequently as possible during the first days of life, if the mother so desires.

[1] *Infants born by cesarean section can also receive early skin-to-skin contact with their mothers, including in the operating room. See* ***Box 4*** *for a more detailed discussion of adjustments that may need to be made to support early initiation of skin-to-skin after cesarean delivery. Low birth weight and premature infants may need to undergo a period of stabilization (of feeding, breathing and temperature) prior to initiation of skin-to-skin as part of "kangaroo mother care" (a discussion of the benefits of kangaroo mother care is provided in* ***Box 5****).*

Skin-to-skin contact between the mother and her infant after delivery (i.e., placing the naked infant, prone, on the mother's bare chest, and covering both with a warm blanket soon after birth) assists in the adaptation of the newborn to life outside of the womb. The practice promotes immediate breastfeeding as it takes advantage of an infant's early alertness and innate behaviors to latch on to the breast within the first hour of life often without particular assistance (*64, 65*). Because of the importance of early exclusive breastfeeding for neonatal survival and later breastfeeding outcomes (which will be discussed in section 3), environments and practices that allow early exclusive breastfeeding to occur are essential. Routine newborn care practices such as bathing and measuring the newborn may negatively affect early contact between mother and infant (*66*) and initiation of breastfeeding (*67*), as continuous uninterrupted skin-to-skin contact has been shown to improve the success of the first

Box 4. Promoting and supporting early skin-to-skin contact and early initiation of exclusive breastfeeding after cesarean delivery

After cesarean delivery it is common for mother and baby to be monitored for several hours in separate rooms, preventing maternal-infant contact and early breastfeeding, as well as increasing the potential for supplementation with formula. In many cases hospital routines and staffing assignments following cesarean section deliveries may need to be adjusted to allow for more immediate skin-to-skin contact and initiation of breastfeeding. Suggestions to promote early skin-to-skin contact and initiation of breastfeeding after cesarean delivery are outlined below:

- **Eliminate routine observation of a well-newborn in a special care nursery after cesarean delivery while mother is in post-operative recovery** (*122*)**.** Mothers who deliver under regional anesthesia should be able to respond to their infants immediately. Frequently there is a perceived need for the infant to be placed under a warmer while the mother is in post-operative recovery, as infants born by cesarean have lower body temperatures than infants born vaginally (*122*). However, as one of the many benefits of skin-to-skin contact is temperature regulation of the infant, concerns about newborn temperature should not prevent skin-to-skin contact between the well-newborn and mother as soon as possible after cesarean delivery.
- **Explore different staffing models, particularly for nurses, which make providing support for skin-to-skin contact in the operating room easier.** In the experience of one large teaching hospital that increased the rate of early skin-to-skin contact in the operating room after cesarean from 20% to 68%, improving breastfeeding initiation rates and decreasing formula use, it was easier for the nursery charge nurse to remain in the operating room with the mother and newborn to provide support for skin-to-skin contact , rather than call the nursery admit nurse (who was responsible for multiple infants, including sick newborns) to provide such support (*123*). Another staffing possibility is that a midwife be present in the operating room to assist with the newborn and provide support for skin-to-skin contact , while the labor and delivery nurse continues to provide care for the mother.
- **Address the spatial set-up in the operating room and identify tasks that that may need to be done to support skin-to-skin contact.** Staff may need to assist the mother by moving the surgical drape to below the mother's breasts, adjusting her gown taking care with the placement of her IV, removing ties from mother's arms, moving equipment to allow more room for skin-to-skin contact support, and positioning the infant to allow easier monitoring by nursing staff (*123*).
- **Delay routine newborn procedures (e.g., bathing and measuring) so that well-newborns can be with their mothers for as much time as possible after birth.** Similar to vaginal deliveries, routine procedures that disrupt initial mother-infant contact should be delayed as much as possible.
- **Develop and implement flexible policies that allow for mothers and infants to be together as much as possible after cesarean delivery.**
- **Establish open and clear communication prior to delivery between the patient and the medical team as to the desire for skin-to-skin contact after cesarean.** Mothers may not know that skin-to-skin contact after delivery is a possibility, and may not be empowered to ask for their infant after delivery if it is routine for the infant to be taken to the nursery immediately. Informing mothers and their partners of the benefits of skin-to-skin contact and the possibility for skin-to-skin contact after cesarean should be done prenatally. Health care staff should discuss with the mother (and her partner) her preference for skin-to-skin contact prior to delivery so that all members of the medical team are aware and can facilitate and support the process as much as possible.

breastfeed (*64*). Cesarean-section delivery can be an impediment to early skin-to-skin contact in many settings (and also a potential barrier to early initiation of breastfeeding); a discussion of ways to promote skin-to-skin contact after cesarean delivery is provided in **Box 4.**

Skin-to-skin contact also provides additional short- and long-term benefits independent of the establishment of breastfeeding. Although skin-to-skin contact originally gained exposure through it's role in temperature regulation of low birth weight infants as part of "Kangaroo mother care"(*68*) (discussed in **Box 5**, as kangaroo mother care is generally not implemented immediately after delivery), skin-to-skin contact is beneficial for term infants as well, because of positive effects on breastfeeding, infant temperature regulation, prevention of morbidity and mortality, and maternal-infant bonding, all essential components of neonatal survival.

Skin-to-skin contact is beneficial because of positive effects on breastfeeding, infant temperature regulation, prevention of morbidity and mortality, and maternal-infant bonding, all essential components of neonatal survival.

2.1 Short- and long-term effects of skin-to-skin contact for mothers and late-pre-term and full-term infants

For near-term and full-term infants, one of the most significant advantages to beginning skin-to-skin contact in the immediate postpartum period is helping to establish breastfeeding. Skin-to-skin contact during the first hour after birth elicits organized "prefeeding behavior" in which the infant first begins spontaneous sucking and rooting movements and then localizes the breast, attaches to the nipple and begins to suckle (*69, 70*). The website www.breastcrawl.org provides a striking video of how a newborn infant finds his mother's breast and initiates breastfeeding soon after birth. A randomized controlled study published in 2007 found that infants who were placed in early skin-to-skin contact with their mother starting in the first minute post-birth and remaining in contact for on average one and a half hours, had significantly more successful breastfeeding scores for the first latch ($p = 0.02$) and a shorter time to begin effective breastfeeding ($p = 0.04$) than infants who had been swaddled in blankets and held by their mother following standard hospital care procedures (*71*). A prospective cohort study published in 2010 that examined close to 22,000 mother-infant pairs found that the odds ratio of exclu-

Table 3. Summary of immediate and long-term effects of early mother to newborn skin-to-skin contact for full-term infants

Immediate effects		Long-term effects	
Full-term infants	Mother	Full-term infants	Mother
Improves effectiveness of first breastfeed and reduces time to effective suckling **Improves cardio-respiratory stability[a]** **May help with thermoregulation of infant**	**May slightly improve maternal affectionate and attachment behaviors** **Decreases maternal breast engorgement pain**	**Positively associated with breastfeeding status at 1 to 4 months postpartum and a longer breastfeeding duration**	**May improve maternal-infant attachment/interaction** **May be associated with decreased risk of postpartum depression**

[a] *Late pre-term infants.*

sively breastfeeding during the maternity stay in the hospital increased in a dose-response fashion with increased time spent in skin-to-skin contact in the first 3 hours of birth (*72*). Since breastmilk production is determined by how frequently the infant suckles and empties the breast, early, frequent and effective nursing is important for both establishing milk production and preventing excess neonatal weight loss (*73*). "Insufficient milk" and newborn weight loss are very common reasons for abandoning breastfeeding or supplementing breastmilk with formula or other liquids. Early supplementation with formula or other liquids reduces the frequency of suckling and thus sets up a potentially vicious cycle where supplementation is continually increased because of decreased breast milk production. Therefore, by improving initial breastfeeding outcomes, early skin-to-skin contact can potentially affect long-term breastfeeding outcomes as well. A Cochrane review updated in 2012 examined the effects of early skin-to-skin contact (i.e., contact initiated between the mother and infant soon after birth) as compared to "standard" contact (infants either swaddled or dressed and held by their mothers, and in several cases separated physically from their mothers) on longer-term breastfeeding outcomes (*74*). This review of 34 randomized controlled trials, including a total of 2177 mother-infant pairs, showed that mother-infant pairs experiencing skin-to-skin contact in the neonatal period were more likely to be breastfeeding at 1 to 4 months of age, and more likely to be exclusively breastfeeding between 3 and 6 months of age (*74*). Whether additional skin-to-skin contact during the newborn period (i.e., during the first days or weeks of life) also affects breastfeeding outcomes remains to be assessed. Other outcomes were more difficult to interpret due to a low number of studies examining the outcome, variability in how the outcome was measured, or variation in practices applied to the intervention and control groups. The authors of the Cochrane review concluded that there appeared to be a small effect of early skin-to-skin on maternal-infant attachment (*65, 74*). Closely linked to maternal-infant interactions and attachment, research published in 2012 found that skin-to-skin contact may positively affect maternal mood during the postpartum period: a quasi-randomized controlled study published in 2012 found that mothers of full-term infants who practiced at least 5 hours of skin-to-skin contact with their infant for the first week of life and at least 2 hours per day for the rest of the first month, had significantly lower depressive symptoms scores at 1 week and 1 month postpartum than mothers who did not practice skin-to-skin contact during this period (*75*). Other benefits identified in the Cochrane review include better cardio-respiratory stability in late pre-term infants and a shorter length of time crying as compared to infants not in skin-to-skin contact with their mothers (*74*).

In individual studies, early skin-to-skin contact has also been shown to provide benefits to both the mother and infant independent of its role in establishing breastfeeding. Thermal control is an essential component of preventing neonatal morbidity (*4*) and skin-to-skin contact provides an inexpensive, safe and effective method for maintaining newborn temperature. Though the Cochrane review found variability in the results across trials, skin-to-skin contact has been shown in individual trials to be as effective as incubator care

for re-warming of hypothermic infants (*76*) and infants placed in skin-to-skin contact with their mother were significantly warmer than infants placed in cots (*77*), likely because of the thermal response of maternal skin temperature (mediated by oxytocin) (*65*) in reaction to skin-to-skin contact with her infant (*78*). Mothers with skin-to-skin contact also reported decreased breast engorgement pain at 3 days postpartum in one trial (*79*).

Box 5. Short- and long-term effects of skin-to-skin contact as part of kangaroo mother care for mothers and pre-term infants

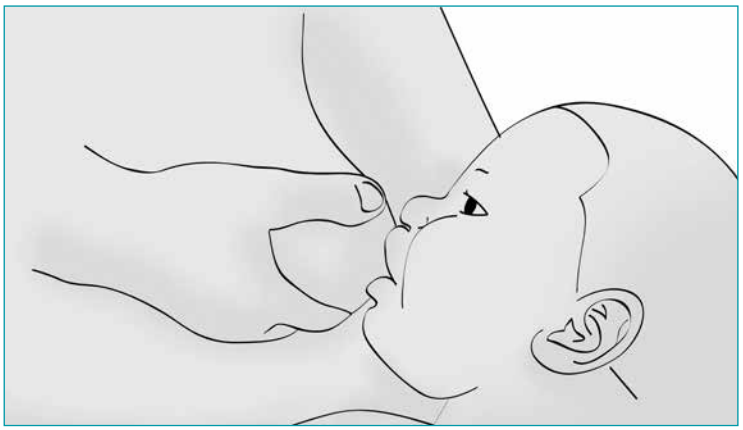
Skin-to-skin contact between a mother and her infant is the main component of "kangaroo mother care", a set of practices first described in Colombia in the late 1970s for the care of low birth weight infants in low-resource settings where incubators and other technology were scarce (*68*). In addition to skin-to-skin contact—generally beginning after a period of stabilization of the low birth weight infant around 24 hours after birth when feeding, respiration, and temperature have been stabilized — kangaroo mother care as it is originally defined also included early and exclusive (or nearly exclusive) breastfeeding, and early discharge from the hospital with strict follow-up (http://fundacioncanguro.co/).[1]

A Cochrane Review updated in 2011 which evaluated the effects of kangaroo mother care on morbidity and mortality in low birth weight infants included 16 randomized controlled trials (a total of 2518 infants) (*124*). The majority of the trials reviewed implemented intermittent kangaroo mother care in stabilized low birth weight infants in low- or middle- income countries, though there was significant variability in the duration and initiation time of the interventions. The review showed that compared to conventional neonatal care, kangaroo mother care was associated with a significant reduction in mortality at hospital discharge, at 40 to 41 weeks postmenstrual age, and at latest follow-up (~50%). Kangaroo mother care was also associated with a significant reduction (at discharge or at 40 to 41 weeks postmenstrual age) in nosocomial infection/sepsis, hypothermia, and length of hospital stay. At latest or 6 months follow up, kangaroo mother care was also associated with a decreased risk of severe infection/sepsis, severe illness and lower respiratory tract infection. Infants receiving kangaroo mother care gained more weight per day, and length and head circumference per week than infants receiving conventional care. Breastfeeding outcomes were also positively influenced by kangaroo mother care: compared to infants receiving conventional care, infants receiving kangaroo mother care were more likely to be breastfeeding (at all) or exclusively breastfeeding at discharge, at 40 to 41 weeks postmenstrual age and at 1 to 3 months follow-up. There was also some evidence in a limited number of studies that kangaroo mother care improved maternal-infant attachment and interaction, improved the home environment and possibly involvement of the father. Overall, the authors concluded that there was sufficient evidence to recommend kangaroo mother care as an alternative for conventional care for stabilized low birth weight infants in low- to middle-income countries (*124*).

1 Different types of kangaroo mother care have evolved which may alter the duration (continuous or intermittent) or timing of initiation of skin-to-skin contact (before or after stabilization) or the mode of feeding (*124*).

3. Early initiation of exclusive breastfeeding

Recommendation for practice



After delivery, routine newborn care procedures that separate mother and baby should be delayed for at least the first hour to allow mother and newborn to be in uninterrupted skin-to-skin contact to encourage and promote initiation of breastfeeding within the first hour (*80*). Trained assistance should be offered to mothers for the first and subsequent breastfeeds if necessary to ensure that the infant is adequately latched to the breast and suckling effectively. Assistance should be provided in a supportive and appropriate manner, being sensitive to the mother's desire for modesty and privacy, and making adjustments for greatest comfort of mothers who have delivered by cesarean. Mothers should be encouraged to breastfeed frequently and should be allowed unrestricted access to their infant through rooming-in in maternity wards. Practices shown to be detrimental to breastfeeding should be avoided (e.g., separation of mother and newborn, use of pre-lacteal feeds or other non breastmilk liquids, and use of bottles or pacifiers).

The importance of breastfeeding for infant nutrition and the prevention of infant morbidity and mortality as well as the prevention of long-term chronic diseases are well established, and thus breastfeeding is an essential component of infant and child survival and health programs. The impact of breastfeeding on neonatal and child survival was quantified in 2003 through an analysis of mortality data from 42 countries which contributed 90% of worldwide child deaths in 2000 (*81*). Of the interventions studied, it was estimated that exclusive breastfeeding for the first 6 months followed with continued breastfeeding from 6 to 11 months of age was the single most effective intervention for preventing child mortality, estimated to prevent 13% of all under-5 deaths **(Table 4).** Therefore, establishing breastfeeding immediately after delivery (i.e., within the first hour after birth) is crucial for survival. Early breastfeeding is also related to long-term breastfeeding behaviors and breastfeeding has been associated with many addi-

Table 4. Under-5 deaths that could be prevented in the 42 countries with 90% of worldwide child deaths in 2000 through achievement of universal coverage with individual interventions

	Estimated under-5 deaths prevented	
	Number of deaths ($\times 10^3$)	Proportion of all deaths
Preventive interventions		
Breastfeeding	1301	13%
Insecticide-treated materials	691	7%
Complementary feeding	587	6%
Zinc	459 (351)*	5% (4%)*
Clean delivery	411	4%
Hib vaccine	403	4%
Water, sanitation, hygiene	326	3%
Antenatal steroids	264	3%
Newborn temperature management	227 (0)*	2% (0%)*
Vitamin A	225 (176)*	2% (2%)*
Tetanus toxoid	161	2%
Nevirapine and replacement feeding	150	2%
Antibiotics for premature rupture of membranes	133 (0)*	1% (0%)*
Measles vaccine	103	1%
Antimalarial intermittent preventive treatment in pregnancy	22	<1%
Treatment interventions		
Oral rehydration therapy	1477	15%
Antibiotics for sepsis	583	6%
Antibiotics for pneumonia	577	6%
Antimalarials	467	5%
Zinc	394	4%
Newborn resuscitation	359 (0)*	4% (0%)*
Antibiotics for dysentery	310	3%
Vitamin A	8	<1%

*Numbers represent effect if both levels 1 (sufficient) and 2 (limited) evidence are included, value number in brackets shows effect if only level-1 evidence is accepted. Interventions for which only one value is cited are all classified as level 1.

Reprinted with permission from Elsevier (Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS, Bellagio Child Survival Study Group. How many child deaths can we prevent this year? The Lancet 2003;362:65- 71.)

tional positive long-term nutrition and health outcomes for both mother and infant (*82*).

3.1 Immediate effects of early and exclusive breastfeeding

Early initiation and exclusivity are two important and related parts of establishing the protective effect of breastfeeding against neonatal morbidity and mortality. Beginning breastfeeding immediately ensures that the newborn receives colostrum, often referred to as the infant's "first immunization", because of its rich content of important immune factors (both secretory and cell-mediated), anti-microbial and anti-inflammatory

Table 5. Summary of immediate and long-term effects of breastfeeding for mother and infant

Immediate effects *		Long-term effects	
Infant	Mother	Infant	Mother
Prevents neonatal and infant morbidity and mortality **Early breastfeeding associated with longer breastfeeding duration during infancy** **Early exclusive breastfeeding associated with exclusive breastfeeding later in infancy**	**Stimulates oxytocin release causing uterine contractions** **Possibly protective of maternal mood**	**Decreases risk of:** – **Acute otitis media** – **Non-specific gastroenteritis** – **Hospitalization for severe lower respiratory-tract infections** – **Atopic dermatitis** – **Obesity** – **Type 1 and 2 diabetes** – **Childhood Leukemia** – **Sudden Infant Death Syndrome** – **Necrotizing entercolitis** **Improved motor development**	**Lactational amenorrhea helps to delay future pregnancies and protects maternal iron status** **Decreases risk of:** – **Type 2 diabetes,** – **Ovarian cancer** – **Breast cancer** **More rapid weight loss**

**Immediate benefits from early initiation of exclusive breastfeeding.*

agents, and Vitamin A, all important for immediate and long-term protection from infections. Human milk as the exclusive and sterile food for the newborn also prevents the introduction of disease-causing pathogens through contaminated liquids (including the water used to make formula as well as the powdered formula itself) or foods. Feeding other liquids or solids not only provides a potential route of entry for pathogens, but also causes gastrointestinal damage, making their entry into the infant's body easier. Contamination of powdered infant formula with *Enterobacter sakazakii* and other bacteria has been associated with reports of neonatal death (due to systemic invasive infections), and is a particular concern for pre-term and low birth weight infants who are more susceptible to the infections caused by these organisms (e.g., necrotizing enterocolitis, septicemia, and meningitis) (*83*). As an example of the impressive impact that exclusive and early breastfeeding can have on neonatal mortality and morbidity, a study from Ghana published in 2006 estimated that early initiation of breastfeeding could reduce all-cause neonatal mortality by 22% and newborns fed breast milk exclusively were four times less likely to die (*84*). In another study from a rural area of The Gambia, use of pre-lacteal feeds was associated with a 3.4 times higher odds of neonatal death (*85*). Finally, exclusive breastfeeding also prevents clinical and sub-clinical gastrointestinal blood loss, caused by mixed feeding (particularly the use of cow's milk), which can negatively impact infant nutritional status, especially iron status. As iron is generally not lost from the body except through bleeding, damage to the intestine from mixed feeding causing blood loss can contribute to poorer nutritional status.

Immediate breastfeeding is also beneficial for

the mother, as early suckling stimulates endogenous oxytocin release (*86*), inducing uterine contraction (*87*), which may reduce maternal bleeding. Uterine atony is the primary cause of postpartum hemorrhage, which in turn is the main cause of maternal mortality worldwide, contributing to 25% of maternal deaths (*88*).

Not breastfeeding, or stopping breastfeeding early also appears to be associated with postpartum depression (*89*), although further research is needed to better establish the temporal nature of this relationship. There is some evidence that breastfeeding may be protective of maternal mood, through its effects on reducing maternal stress and attenuating the inflammatory response, which is hypothesized to be involved in the pathogenesis of depression (*90*). There is also some evidence that women suffering from depression may have lower confidence in their ability to breastfeed (*91*). Although mental health issues have received relatively little attention as public health priorities, particularly in developing countries the relationship between breastfeeding and postpartum depression should not be overlooked as some studies have shown that postpartum depression may have negative effects on infant growth, nutrition and development (*92*). Additional research is needed.

3.2 Long-term effects of breastfeeding

Early breastfeeding behaviors also help to establish longer-term breastfeeding patterns. Early exclusive breastfeeding has been associated with exclusive breastfeeding later in infancy (*93*) and the time of the first breastfeed has been shown to positively relate to the overall duration of breastfeeding (*94-96*). Maintaining exclusive breastfeeding for 6 months followed by continued breastfeeding until the child is two-years-old or beyond as recommended by WHO (*97*), has obvious health and nutritional benefits for the infant for continued prevention of disease, and provision of adequate nutrition. A history of being breastfed has been associated with decreased risk of acute otitis media, non-specific gastroenteritis, hospitalization for severe lower respiratory tract infections, atopic dermatitis, asthma in young children, obesity, type 1 and 2 diabetes, childhood leukemia, sudden infant death syndrome, and necrotizing enterocolitis (*89*).

A longer lifetime duration of breastfeeding has also been associated with long-term maternal health outcomes, including a decreased risk for type 2 diabetes and ovarian and breast cancer.

For the mother, establishment of breastfeeding and continued frequent on-demand nursing of the infant helps to delay future pregnancies through lactational amenorrhea. Lactational amenorrhea can have benefits for the mother's nutritional status, particularly with regard to iron, as it prevents iron loss through menstrual bleeding. A longer lifetime duration of breastfeeding has also been associated with long-term maternal health outcomes, including a decreased risk for type 2 diabetes and ovarian and breast cancer (*89*). Exclusive breastfeeding also accelerates pregnancy weight loss, which with increasing rates of overweight and obesity among women of reproductive age in the developing world, could be a considerable benefit.

4. Integration of essential delivery care practices within maternal and newborn health services

Care during pregnancy, delivery and the postpartum period involves two individuals whose health and nutrition are tightly linked; thus, in making recommendations for delivery care practices, the relative benefit of each practice to both short- and long-term outcomes of both mother and infant should be assessed. On the practical side, recommendations that are primarily directed at the care of one half of the dyad (e.g., active management of the third stage of labor for the mother) should be consistent with practices recommended for the other half (e.g., resuscitation for the newborn) so that there is not a conflict in how to approach the care of both in an integrated manner and to allow feasible implementation. Most importantly, these recommendations should be based on the best level of scientific evidence available. Practices that have become routine or were implemented out of convenience but are not supported by scientific evidence—as is the case with immediate cord clamping—should be identified and discouraged, and replaced with evidence-based practices.

Revised WHO Guidelines for the active management of the third stage of labor for prevention of postpartum hemorrhage include delayed cord clamping.

WHO, since 2007, has adopted a transparent process for guideline development that takes into account current best evidence, revising guidelines as new scientific evidence becomes available (*98*). As an example, between 2007 and 2012, the guidelines for active management of the third stage of labor for prevention of postpartum hemorrhage were revised at least two times to take into account new data. In 2007, in response to the accumulating evidence as to the benefit of delayed clamping for infant outcomes, and a lack of evidence—physiological or clinical—as to the role of early clamping for the prevention of uterine atony, revisions were made to the protocol for active management of the third stage of labor to remove early clamping as part of the recommended package (*99*). In 2012, the guidelines were once again revised in response to additional data on the benefit of controlled cord traction as part of the active management of the third stage of labor package (*8*). Controlled cord traction, which has been found to not significantly impact the incidence of postpartum hemorrhage (*100*), has now become an optional component (see **Box 1** for additional discussion of current active management of the third stage of labor guidelines and their evolution). On the newborn side, as an example of the need to take into account the multiple different activities occurring in the perinatal period, neonatal resuscitation guidelines (both of WHO and other

internationally recognized normative bodies) until 2011 did not mention how clamping of the cord should be addressed if a newborn needs assistance with respiration after delivery. Revised guidelines do allow for delayed clamping, which is consistent with the active management of the third stage of labor recommendations (*101*). (See **Box 2** for a more detailed discussion of neonatal resuscitation and cord clamping.)

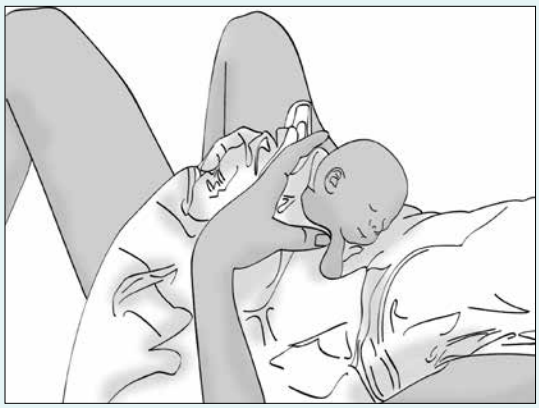
Panel 1 presents a proposed sequence of steps that integrates active management of the third stage of labor, delayed clamping, maternal-newborn skin-to-skin contact and immediate initiation of exclusive breastfeeding, which should be considered for all infants **(Panel 1)**. Adaptations for application in cesarean delivery have been noted, as well as integration with newborn resuscitation. This is a proposed framework of the basic order and integration of steps, but additional adaptations may need to be made according to differences in delivery settings (e.g., position of the mother during delivery) and care providers (e.g., number of personnel assisting with the delivery, skill level of individuals) and prevalent cultural practices. Though we anticipate that these practices can be feasibly integrated in most delivery settings, additional operational research questions arise that will help to refine the implementation of these practices **(Appendix 1)**. In addition, as discussed throughout these documents, it is important to emphasize that these practices are not just limited to vaginally-delivered infants, or just full-term infants. Delayed clamping is recommended for pre-term infants (*8, 9*), and can be practiced after cesarean delivery. Skin-to-skin contact and breastfeeding are essential components of postpartum care, and can also be implemented after cesarean delivery.

4.1 Contextual considerations: current health facility and domiciliary delivery care practices

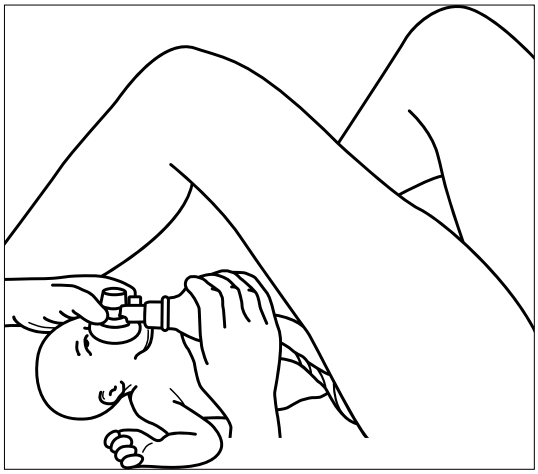
While deliveries occurring in health facilities have the obvious benefit to both the mother and infant of immediate access to skilled care, unfortunately not all current hospital practices are evidence-based, nor of benefit to the mother or infant. As health facility deliveries continue to increase—**Figure 6** provides a global overview of the percentage of deliveries delivered in health facilities from most recent Demographic and Health Survey data (as of March 2013)—it will be imperative to address the particular practices that may be detrimental to maternal and newborn health and identify ways to help institute practices that are evidence informed. For example, there are numerous examples of hospital practices documented as interfering with the establishment of breastfeeding, in particular the hospital practice of giving glucose water or infant formula in a bottle. Separation of the mother and her newborn has also been shown to be detrimental to the establishment of breastfeeding for first time mothers (*102*). In addition, health care providers are frequently not sufficiently trained to support and assist with the establishment of breastfeeding. While the Baby-Friendly Hospital Initiative (BFHI) implemented by WHO and UNICEF in the early 1990s addressed hospital practices detrimental to breastfeeding and helped improve training of health workers in breastfeeding support, there has unfortunately been no monitoring

Panel 1. Integration of essential steps for maternal, neonatal and infant survival, health and nutrition

1. After delivery, immediately dry the infant. Then place the reactive infant, prone, on the mother's lower abdomen. Keep the infant covered with a dry cloth or towel to prevent heat loss



For C-section deliveries: Immediately dry the infant, and place the infant, covered, on the mother's thighs (or a surface level or slightly lower than the placenta) while waiting to clamp the cord. If there is a need to attend to the infant that cannot be addressed while the cord is intact, umbilical cord milking ("stripping" the cord from the placental end towards the infant 5 times) may be employed to allow a partial placental transfusion to occur in a shorter time period.
If the infant is pale, limp, or not breathing and requires resuscitative efforts: steps can be performed while the cord is intact, and the infant is at the level of the perineum to allow optimal blood flow and oxygenation (as shown below).



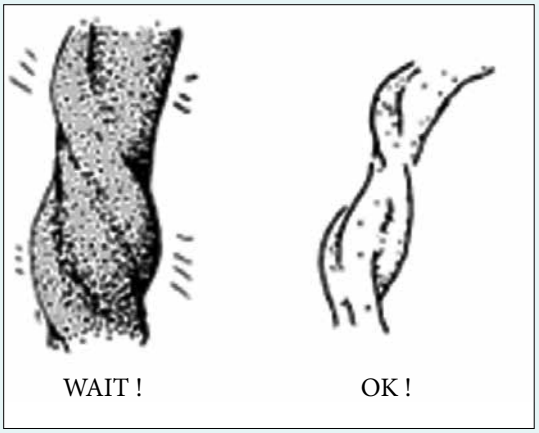
Early cord clamping may be necessary if immediate attention cannot be provided without clamping and cutting the cord, or if the provider is not experienced in performing resuscitation with the cord intact.

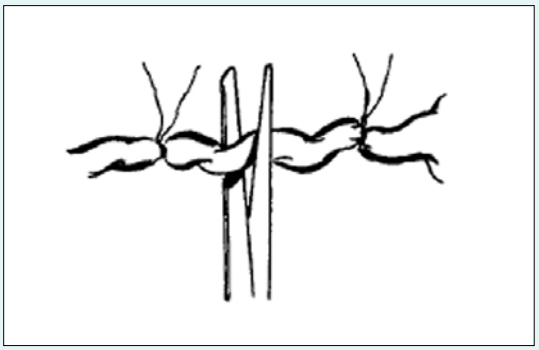
(Continued)

Panel 1. (Continued).

2. Provide 10 IU of oxytocin (intramuscularly or intravenously) soon after delivery.

3. After cord pulsations have ceased and the cord is flat (no earlier than 1 minute, and optimally 3 minutes or more after delivery), clamp and cut the cord following strict hygienic techniques.





For C-section deliveries: Oxytocin is also the recommended uterotonic drug.

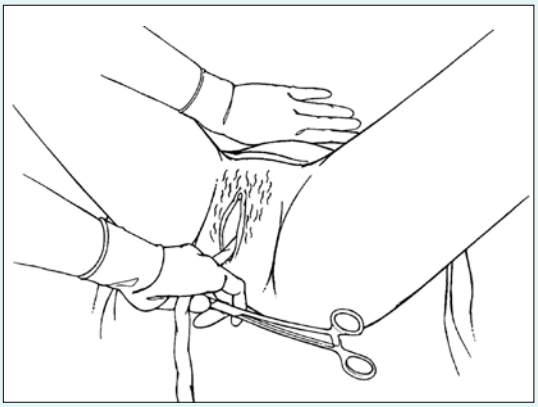
(Continued)

Panel 1. (Continued).

4. Place the infant directly on the mother's chest, prone, with the newborn's skin touching the mother's skin. While the mother's skin will help regulate the infant's temperature, cover both the mother and infant with a dry, warm cloth or towel to prevent heat loss. Cover the baby's head with a cap or cloth.

For C-section deliveries: Adjustments may need to be made to the surgical drape and mother's gown to support initiation of skin-to-skin initiation in the operating room. Additional staffing support may need to be provided.

5. If desired by the mother and care provider, deliver the placenta by controlled cord traction on the umbilical cord and counter-pressure to the uterus. Otherwise, wait for signs of placental separation (e.g., gush of blood, uterine contraction, lengthening of the cord, visualization of the placenta in the vagina) and then encourage the mother to cough or push.



For C-section deliveries: Controlled traction is the recommended method (as opposed to manual removal) for removal of the placenta.

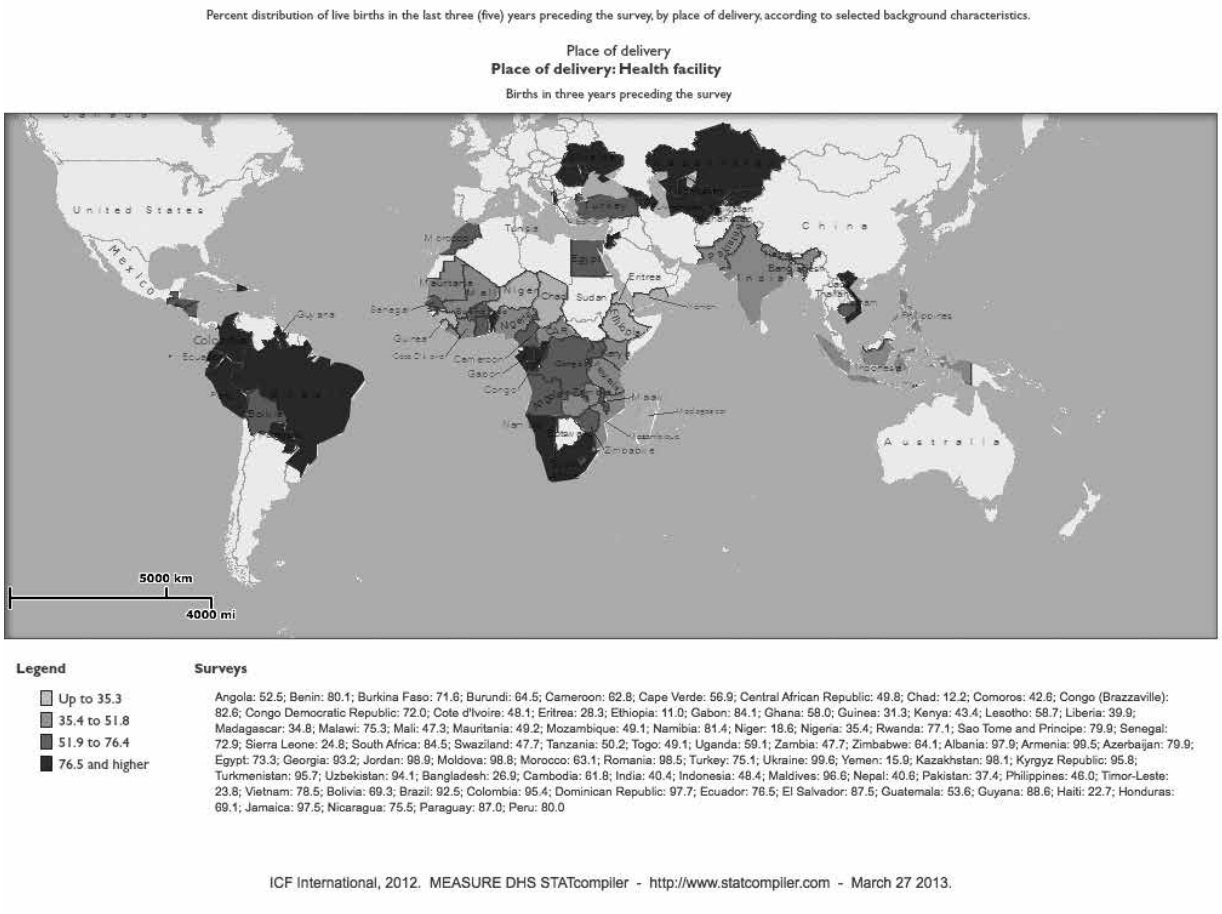
(Continued)

Panel 1. (Continued).

6. During recovery, palpate the uterus through the abdomen every 15 minutes for two hours to make sure it is firm and monitor the amount of vaginal bleeding.

7. Aim to delay routine procedures (e.g. weighing, bathing) for at least the first hour so that mother and baby can be together in uninterrupted skin-to-skin contact and begin breastfeeding. Provide frequent observation by medical staff, and if desired, offer to assist the mother with the first breastfeed, being sensitive to her need for modesty.

Figure 6. Percentage of live births in the last three years delivered in health facilities according to most recent Demographic and Health Survey data

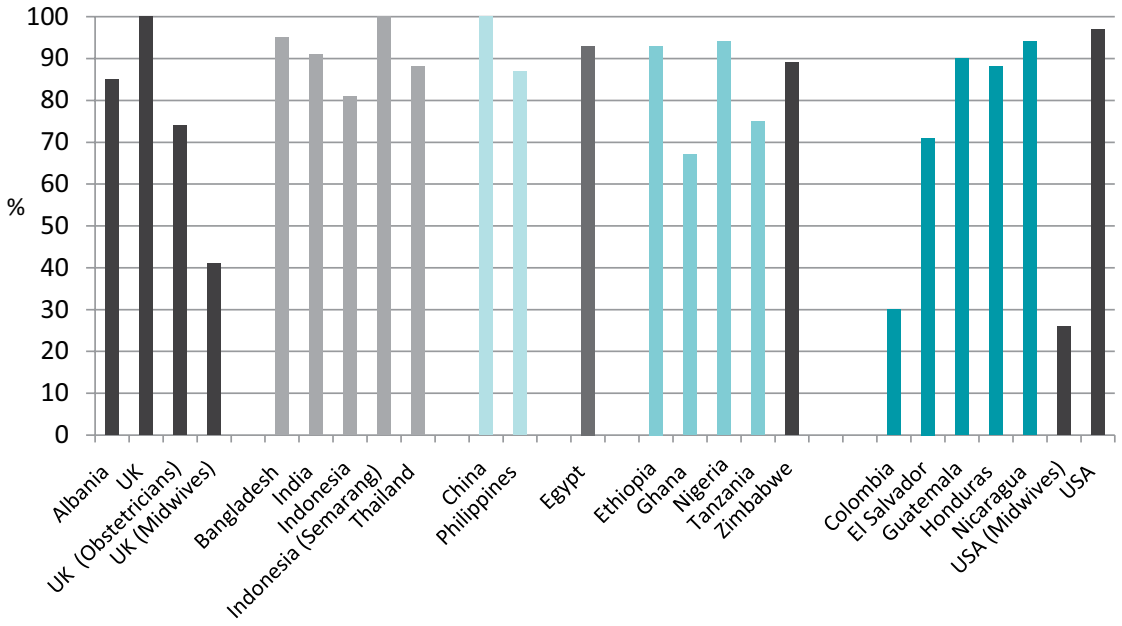


Countries in white do not have data Demographic and Health Survey data available.

of BFHI certification, nor a renewed public health investment in this area (*103*).

As for cord clamping practices, though more recent data are lacking, policies and practices may need to catch up to what current guidelines recommend. A survey of practices employed in third stage management in Europe published in 2007 reported that 68% to 90% of delivery units in Belgium, France, Ireland, Italy, the Netherlands, Portugal, Spain, Switzerland and the United Kingdom had policies of immediate cord clamping (*104*). An earlier study of 15 university-based obstetrical care centers in 10 countries (from North and South America, Africa, Asia, and Europe) found similar variability in practices between and within countries, however on average early clamping was practiced 79% of the time (*105*). A comprehensive overview of surveys of delivery care practices during the third stage of labor in health care facilities conducted between 1999 and 2008 revealed that in both developed and developing countries, early clamping tended to be the standard practice **(Figure 7)**. These surveys—most

Figure 7. Percentage of deliveries from individual surveys in which early cord clamping* is observed or self-reported



**Early cord clamping variably defined as: < 1 minute, < 20 seconds or "immediately"*
Notes on sources:
Albania: Observed data from Tirana (125);
Bangladesh, El Salvador, Ethiopia, Ghana, Guatemala, Honduras, Indonesia, Nicaragua, Tanzania: Observed data from multiple sites in each country (126);
China (Chengdu), Colombia (Bogota), India (Nagpur, Trivandrum, Vellore, New Delhi), Indonesia (Semarang), Philippines (Manila), Thailand (Khon Kaen, Bangkok), UK (Dublin), USA (Philadelphia), Zimbabwe (Harare): Observed data from teaching hospitals in cities identified in each country (105);
Egypt (Cairo): Observed data (127);
UK (obstetricians) and UK (midwives): Self-completed questionnaire on usual practices (114);
USA (midwives): Self-completed questionnaire on usual practices (128).

of which covered multiple sites and facilities—also show that practices, at least before 2008, were not consistent within or between countries, nor even between practitioners in the same country or same facility. Whether there have been significant changes in practices since 2007 when active management guidelines were revised has not yet been evaluated.

Domiciliary births can also include infant care practices that place at risk both the establishment of early and exclusive breastfeeding as well as temperature control of the newborn. Although customs vary by region, detrimental care practices commonly observed in home delivery settings in developing countries include: the use of prelacteal feeds (*106-109*); delaying the initiation of breastfeeding for hours or days (*110*); early bathing of the baby (< 6 h after birth) (*109, 111*) which decreases newborn temperature (*112*) and may remove the vernix, (a cream-like white substance present on the skin of the infant at birth shown to have antimicrobial properties) (*113*); not feeding or discarding colostrum; or placement of the baby on the ground rather than in contact with the mother (often without drying) until the placenta is delivered (*110*). Several studies have shown that mothers delivering at home were more likely to use pre-lacteal feeds for their infants (*106-108*) and less likely to exclusively breastfeed later in infancy (*106*) than mothers delivering in health facilities. There appear to be no published studies on cord clamping practices in home deliveries and while delayed clamping is thought to be practiced more frequently in this setting, this assumption is primarily based on anecdotal reports.

4.2 Steps for achieving universal implementation of an integrated set of delivery care practices

While establishment (and continual update) of normative guidelines and recommendations at a global level is a crucial step towards implementation of evidence-based practices, what occurs in reality (as described above) frequently does not reflect "current best evidence". Practices inconsistent with recommendations may occur for a variety of reasons. Lack of knowledge on the part of practitioners as to the current best evidence, either through an inability to access this knowledge, or to understand and interpret the scientific literature may be one significant barrier. One of the more recent surveys on cord clamping practices, conducted among midwives and obstetricians in the United Kingdom in 2008, showed that the most frequent request for additional evidence to guide third-stage management was in regards to the timing of cord clamping (*114*). Another survey of practitioners found that among those who continued to practice early clamping (in pre-term birth specifically), lack of knowledge of the benefits of delayed clamping was the most frequent justification for their practice (*115*). Thus, one of the most important (and challenging) tasks of evidence-informed guideline development has to be dissemination. When recommendations are updated as a result of new evidence, there also needs to be an effective process for ensuring that global norms are reflected in national policies and norms and ultimately that practices "on the ground" reflect these updates. Ways to support practitioners in obtaining access to guidelines

and scientific literature and how to interpret research results are also needed.

However, knowledge of evidence informed practices is necessary, but not sufficient, to ensure translation into appropriate interventions. As an example, a survey of thermal control practices by health professionals across 7 different countries showed that even though two-thirds to three-quarters of the health professionals surveyed possessed adequate knowledge about thermal regulation, care practices employed were consistently inadequate (*116*). A qualitative study that investigated the reasons that practicing physicians did not always adopt evidence-based perinatal care practices in Latin America identified lack of access to scientific information or an inability to understand the scientific literature, but also lack of time or physical resources, attitudes by health practitioners that resist change as well as conflicting clinical guidelines and policies (*117*). Although this study addressed health care practitioners practicing in hospitals in Latin America, it is likely that similar barriers exist in other regions. Understanding barriers to change beyond insufficient access to evidence informed guidelines will be essential in developing effective and sustainable implementation strategies.

Providing hands-on training as well as hospital- or community- level policies and supervision to support and reinforce these practices are also needed. Strategies to increase the number of deliveries attended to in primary-level health centers by skilled providers, or providing skilled attendance to domiciliary deliveries, will ensure greater coverage of deliveries with "skilled" care, but may not ensure better quality of care nor improved health and nutrition outcomes if providers do not possess and implement the correct and needed skills. Identifying deficiencies and implementing policies and training (in-service and pre-service) to address these deficiencies will help to establish appropriate, integrated and evidence-based care practices such as the ones described in this document as the standard of care, and eliminate practices that have been shown to be detrimental or of no benefit to maternal or infant health.

The process of translating evidence-informed recommendations into practice is challenging. Translating the integrated set of delivery care practices advocated in this document to the standard practice of care can benefit from an assessment and analysis of national and local situations with respect to current practices as well as current barriers to change. Such an assessment should include the review of protocols and guidelines, the observation of actual practices, and qualitative research to identify the most important barriers to change among different delivery care providers. Most countries implement some actions related to active management of third stage labor and breastfeeding promotion. Little information, however, is available on timing of cord clamping though anecdotal reports and limited data suggest it is more likely to be immediate rather than delayed. Also, even when national protocols and/or guidelines for delayed clamping exist, information on the extent to which they are followed is not available. Infor-

mation on the practice of immediate and continued skin-to-skin contact is also scarce. Although many hospitals practice rooming-in, this usually begins later than the critical first hour after birth, after the newborn has been bathed by nursing staff and examined by medical staff. Also, the infant is often dressed and wrapped when finally placed in contact with the mother, thus preventing skin-to-skin contact. Documentation of current practices and barriers together with an analysis outlining the benefits of adopting the new integrated set of care practices is important for the development of a plan to implement the necessary changes in clinical practice and to organize delivery care services to facilitate their application. An implementation plan could benefit from the incorporation of several strategies that address significant barriers to adopting evidence-informed care practices as outlined below.

4.2.1 Increasing access to guidelines and the scientific information supporting evidence-based practices

Knowledge of current guidelines and the evidence base for these practices, as provided in this document, is necessary and should underlie teachings in all medical/nursing school curricula, clinical practice, and public health policy. An effective and coordinated process for ensuring that curricula taught to nursing and medical students are regularly updated to reflect current best evidence and internationally recommended guidelines (e.g., WHO) would be ideal. As part of these curricula updates, providing a basic understanding to students about scientific literature (e.g., standards for judging scientific research, different types of research designs, how to interpret results) and the process for developing evidence informed guidelines (e.g., systematic reviews, strength of recommendations) would be useful. A lack of understanding that guidelines and the practice of medicine are dynamic and should be adjusted as new evidence is gathered has been identified as a barrier to changing medical practices in some settings (*117*). While access to freely available online resources for maternal and infant care practices (such as the sources listed in the **Additional Resources and Websites** section of this document) may always be out of reach to a portion of the population because of financial, language, and other barriers, internet access is becoming increasingly available in many settings. Thus less traditional methods of increasing access to scientific evidence should be explored, for example, e-learning methods which can incorporate more interactive and visual components. Professional societies of midwives, nurses and physicians are also mechanisms for providing up to date evidence-informed information to members. Society meetings and newsletters should be used as conduits for providing new information to "on the ground" practitioners. The Latin American and Caribbean Neonatal Alliance (http://www.alianzaneonatal.org/eng/) is an example of an effective mechanism to disseminate new evidence for implementation.

Knowledge of current guidelines and the evidence-base for these practices is necessary and should underlie teachings in all medical/nursing school curricula, clinical practice, and public health policy.

4.2.2 Addressing the skills needed to implement the recommended practices

A significant barrier to changes in practice that has been documented in other settings is the lack of adequate skills to employ the new practices or techniques. Fortunately, for the practices recommended in this document, the skills required are not "new" (except perhaps for skin-to-skin contact) nor highly technical. However, tightly associated with the process of acquiring new skills, which contributes to resistance to change, is the fear of the unfamiliar, in terms of both performing the new technique and its potential "unknown" outcome. Lacking any previous personal experience with which to guide them, practitioners may fear employing the technique itself, as well as any potential negative outcomes they could see as resulting from the new practice (and the repercussions from supervisors and peers if negative outcomes result from employing "non-standard" practices). Thus appropriate training materials, which address how to deliver each practice, why each practice is important, and answer concerns and questions related to implementation (e.g., risk of neonatal polycythemia with delayed clamping) are essential. Identifying individuals who are respected practitioners and have an interest in improving practices, and can become champions of these practices (both to disseminate the scientific evidence behind them, and to demonstrate and mentor in the "know how" and needed skills to perform them) may help to ease some of the fear associated with learning and implementing new techniques.

4.2.3 Organization of delivery care services

Implementation of the essential delivery care practices can be greatly facilitated by the physical organization of delivery care services, particularly in settings with a high volume of births where delivery rooms need to be turned over quickly and space tends to be scarce. Ideally, a mother would stay in the delivery room in skin-to-skin contact with her newborn infant for at least the first hour after giving birth. (See **Box 4** for a discussion on adjustments to support skin-to-skin contact after cesarean delivery). This room may provide the most privacy as well as prevent disruption during the critical period when the newborn is alert and awake and most likely to initiate breastfeeding with little or no assistance. If this is not possible, skin-to-skin contact should be initiated in the delivery room and the mother and infant covered with a sheet or blanket while they are moved to a recovery room or the general maternity ward. Care should be taken to make this transition as easy as possible for the mother and infant and that, when moved, a bed is immediately available. Staff organization (particularly of nurses) and responsibilities may also need to be adjusted to allow for support to be provided for skin-to-skin contact or initiating breastfeeding initially in the delivery room (or operating room, in the case of cesarean section deliveries). Revitalizing and expanding the Baby Friendly Hospital Initiative and including the

Appropriate training materials, which address how to deliver each practice, why each practice is important, and answer concerns and questions related to implementation are essential.

care practices advocated in this document can serve as a catalyst for their implementation as well as the organization of services to facilitate their achievement.

4.2.4. Establishment and communication of regional, national and local (hospital and community level) policies and guidelines for implementation of the recommended practices

Establishing the "why" and "how" behind the recommended practices will be an essential step for their implementation, but to ensure that this knowledge is translated into appropriate interventions, it needs to be implemented into national, regional and local policies for delivery care. These policies, in turn, need to be widely and consistently disseminated, monitored, and enforced at a local level with appropriate supervision. While national or regional policies and guidelines will not be sufficient alone to ensure implementation at the individual level, they are an important first step for permitting a new practice that can lead to changing both current and future practices. They provide a basis for the teaching of evidence-informed practices in medical curricula, and also may reduce some of the fear associated with implementation of new techniques felt by practicing physicians. This is particularly important in light of revisions in the WHO Recommendations for the Prevention of Postpartum Hemorrhage and for Newborn Resuscitation (both revised in 2012), which call for delayed clamping (*8, 9*) in contrast to previously established and widely disseminated guidelines for postpartum hemorrhage calling for early clamping. Previously, neonatal resuscitation guidelines did not mention when to clamp the cord with respect to resuscitation steps. These revised WHO recommendations to delay clamping require translation into international and national professional guidelines and policies, academic textbooks and training materials, and the standard of practice for clinical care. As conflicting or unclear clinical policies and norms can be a significant barrier to implementation of change, it is important that revised norms at the regional, national and local level take into account the integrated nature of delivery care practices, so that one practice is not implemented for benefit of the mother at the loss of a beneficial practice for the infant, or vice versa. As evidenced in this document, because of the linked nature of maternal and neonatal health, perinatal care practices frequently affect both parts of the mother-infant dyad. To improve public health indicators of maternal and infant wellbeing, such change needs to occur on a widespread level. In the absence of a well-orchestrated concerted effort at regional, national, and local levels, this can take years, even decades, to occur. At the local or hospital level, it will be important to identify particular individuals—role models or "opinion leaders"—who can motivate and remind current practitioners to continue implementing the recommended practices, and also effectively and consistently communicate hospital policy to any new additions to the maternity service. This will be particularly important in teaching hospital settings, where there is frequent rotation of students, interns and residents, who are learning by

observing the practices of practicing physicians and nurses. However, it has been noted that new practitioners—residents, for example—are more amenable to change and adopting new practices than practitioners who have been practicing for longer periods of time, who may have more ingrained habits and greater resistance to change (*117*). So despite having frequent rotation of staff, teaching hospitals could be more readily amenable to change than other hospitals.

4.2.5 Advocacy and synchronization with other maternal and neonatal care efforts

Advocacy, based on the scientific evidence, to raise awareness and knowledge among important stakeholders is an essential part of the process for implementing change. Continuous advocacy is necessary to engage stakeholders and decision-makers at many levels to initiate and maintain the process of implementation. For the practices outlined in this document, critical initial stakeholders include international, regional, and national professional associations of obstetrics and gynecology, pediatrics, neonatology, midwifery and nursing and leading academic scholars in these fields. Obtaining the support and enthusiasm of these associations and scholars is necessary to initiate the implementation process and to give visibility to the integrated care practices being advocated. These associations and scholars are usually responsible for initiating new and revised protocols and guidelines for clinical practice (or adopting those of other normative bodies), the content of medical journals and the updating medical texts, teaching new professionals, and providing in-service training **(Box 6)**. The Ministry of Health, as the lead normative institution in most countries, also has a key role to play.

Advocacy among pregnant women is also essential. In many settings, pregnant women may have little to no input as to the delivery care practices that are employed in their care, even if those practices are overly aggressive medically, or of no benefit (or even of potential harm) to their own or their infant's health. Increasing women's knowledge of the importance of appropriate care practices for their own health and that of their newborn will help to form a critical mass of beneficiaries that lobby for the institutionalization of these practices during delivery. In addition, providing them with the knowledge of the importance of the correct care practices, ideally beginning in prenatal care, will help to ensure not only a smoother implementation of the new practices (as they will have a better idea of what to expect during delivery) but also create a demand for their implementation.

To increase the impact and coverage of the recommended practices and avoid duplication of efforts, the implementation and advocacy of the practices should be harmonized and coordinated with the efforts of already established global initiatives for improving maternal and neonatal health.

Ideally, to increase the impact and coverage of the recommended practices and avoid duplication of efforts, the implementation and advocacy of the practices outlined in this document should be harmonized and coordinated with the efforts of already established global initiatives for improving maternal and neonatal health (e.g., Saving Newborn Lives,

Box 6. Actions needed to ensure implementation of the essential delivery care practices

- Develop advocacy materials. These materials could include information on the recommended practices and their evidence base, the prevalence of anemia in infants and young children, the relationship between anemia and cognitive development, WHO recommendations, current norms, guidelines, and protocols with respect to timing of cord clamping and proposed changes.
- Develop short teaching videos of both vaginal and caesarean deliveries to document how the three practices are choreographed and integrated.
- Maintain global and regional data bases and copies of norms and policies related to delayed clamping, skin-to-skin contact and earlier initiation of breastfeeding to share with countries considering such policies.
- Identify hospitals that routinely use these practices and that can serve as national and regional "reference and teaching" hospitals which other professionals can visit to learn more about how to implement them.
- Revise and update national and professional protocols.
- Revise and update information in medical, nursing, and midwifery textbooks.
- Conduct in-service training on recommended practices.
- Include sessions on the recommended practices in professional conferences of obstetrics, pediatrics, neonatology, midwifery, and nursing.
- Publish lay articles on the importance of the recommended practices in newspapers and women's magazines.
- Expand implementation of the Baby Friendly Hospital Initiative and reassessment of certified hospitals.

Maternal to Child Health Program, Partnership for Maternal, Newborn and Child Health). As evident by the names of these initiatives, the extent to which each initiative addresses both maternal and neonatal care practices and health outcomes varies. The combination of practices recommended in this document is unique in that it crosses the divide between "maternal" and "neonatal" care, thus truly contributing to the goal of a "continuum of care" for mothers and infants. In addition, the evidence of short- and long-term impact of each of these practices for both mother and infant reinforces the importance of analyzing care practices in the context of the mother-infant dyad, rather than the mother and newborn separately. The combined practices outlined in this document should be integrated among other prenatal, perinatal and postnatal care practices currently being advocated by these initiatives (e.g., prenatal immunizations, prevention of neonatal asphyxia and sepsis and postpartum hemorrhage).

4.2.6 Monitoring and evaluation

The implementation of the recommended practices needs to be monitored and rigorously evaluated in order to determine whether the implementation of practices succeeds and is continued for the long-term. As most facilities already maintain medical records, facilities should consider revising medical record forms and/or delivery room registers to require recording the timing of cord clamping, the timing of initiation of skin-to-skin contact, and if not already done, the timing of the initiation of breastfeeding. These process indicators will allow for regular assessments of how practitioners are doing in terms of the implementation of these practices, and identify areas and skills that need to be improved or require additional training or motivation. Facilities may also want to monitor "impact" outcomes that are affected by cord clamping time or skin-to-skin contact and early initiation of breastfeeding (e.g., hemoglobin concentration during infancy, or rates of exclusive breastfeeding at hospital discharge or at postpartum follow-up visits), but these outcomes may require different monitoring systems that are not already in place. The results from these monitoring systems should be regularly assessed and communicated at the hospital, national and regional level to the appropriate stakeholders. Communicating results at the national or regional level will be important for determining where changes or modifications need to be made in the implementation process, and which practices are more challenging to implement and may need additional support or different strategies. Individual practitioners will want to know whether the effort that they have made in changing their practices is having an effect and thus communication of local and national results will be important.

4.2.7 Scaling up implementation of delayed cord clamping, skin-to-skin contact and early initiation of breastfeeding

Interventions in public health, even when efficacious, like those advocated in this document, are often difficult to bring to scale. An integrated and practical "AIDED" framework of scale-up, likely to be applicable to a wide range of public health interventions in low and middle-income countries was recently developed by a team of researchers from Yale University. This framework can also be usefully applied to delayed cord clamping, skin-to-skin contact and early initiation of breastfeeding (*118*) as it was recently applied for national breastfeeding programs (*119*). It includes five non-linear, interrelated components to *assess* the landscape, *innovate* to fit user receptivity, *develop* support, *engage* user groups, and *devolve* efforts for spreading innovation, as described below.

The *assess* component refers to the assessment of all the factors within a region, country or setting where the scale up is proposed to occur. This assessment can include political, economic, legal/regulatory, technological (if applicable) and social conditions. Thus, for the nutrition delivery care practices it means that national norms have been established and guidelines developed for their implementation.

The *innovate* component is aimed at achieving a "fit" between the innovation—in this case, the recommended practices—and user group.

Thus it involves packaging the innovation to make it acceptable and perceived as advantageous by potential user groups in their specific context or environment. In this case, the user group includes obstetricians, midwives, and other health professionals that assist deliveries as well as pediatricians and other staff who care for the infant. Both pediatricians and obstetricians are sometimes opposed to the practice because of concerns about possible adverse effects in the neonate or mother.

In the *develop* component, enabling relationships, environments, and networks need to be fostered among those who can support and facilitate the spread of the innovation (practices). In the case of the nutrition delivery care interventions, the early adopting by well-respected influential senior health professionals is key to the develop component. It could also involve incorporation of the practices into curricula of medical schools and teaching hospitals.

Engagement is central for introducing the innovation (practices) from outside the user group to inside the user group. It involves translating the innovation so that user groups can assimilate the new information and integrate it into their routine practices, thus making it a normative practice.

The *devolve* component involves the initial groups of users spreading the innovation (practices) among their peers and within their networks, thus ensuring that the process of change is driven by the user groups and their networks rather than by an external stakeholder such as the Ministry of Health.

Thus, as outlined in the AIDED framework, scale-up occurs within a complex adaptive system, which includes interdependent parts, multiple feedback loops and more than one path for achieving intended outcomes. This framework is likely to be useful to bring the evidence-informed practices advocated in this document to scale.

5. Conclusions

As infant mortality declines in the developing world, it becomes increasingly concentrated in the neonatal period. Within the neonatal period, the first 24 hours after delivery can account for up to 45% of all infant and maternal deaths. The essential delivery care practices for maternal and newborn health and nutrition advocated in this document are preventive of neonatal morbidity and mortality and may also be protective of mothers. However, the evidence-base for their benefits goes well beyond survival and demonstrates long-term effects on maternal health and on infant health, nutrition and cognitive development. Unlike many lifesaving and changing interventions, their implementation implies no recurring costs. Once established as the standard practice of care, millions of mothers and newborns will reap their benefits.

Appendix 1. Research questions regarding the implementation and integration of these practices

Does cord clamping time affect neurodevelopmental outcomes in pre-term/low birth weight infants and full-term infants?

As of early 2013, only one study has examined the long-term neurodevelopment as affected by cord clamping time in pre-term and low birth weight infants (*37*). In pre-term and low birth weight infants, delayed cord clamping has been shown to affect hematological status in the short-term, as well as prevent intraventricular hemorrhage and sepsis in pre-term and low birth weight infants. All of these outcomes, along with premature birth itself, have been shown to be associated with long-term development outcomes, and further research should be performed to further elucidate the importance of cord clamping time on development in this vulnerable group.

In full-term infants, there is one published study on developmental outcomes as related to cord clamping time (*53*), which did not show significant differences in development between cord clamping groups, though research has shown significant effects on iron status through 6 months of age in both low-income and higher-income settings which could potentially affect development. Additional research is needed, particularly in low-income settings where the risk of poorer development outcomes is greater.

What are the effects of cord clamping time on small-for-gestational age infants?

While the safety and benefits of delayed cord clamping in adequate-for-gestation age infants [both term (*41, 129*) and pre-term (*27, 36, 130*)] are relatively well established, the short and long-term effects of delayed clamping in small-for-gestational age infants have not been specifically investigated. Small-for-gestational age infants account for approximately 24% of births in developing countries (*131*). There is good evidence that in small-for-gestational age infants, iron status is compromised (*132*) and they have an increased risk of developing anaemia compared to infants born appropriate-for-gestational-age because of their more rapid growth rate. Small-for-gestational age infants may also be at greater risk of polycythemia-hyperviscosity syndrome (due to chronic hypoxemia in utero); however, in developing countries (where maternal anemia is high and cord hemoglobin tends to be low) the baseline risk for polycythemia-hyperviscosity syndrome is likely to be lower among small-for-gestational age infants than in industrialized countries and thus the potential benefits to iron status may outweigh the risks (*133*). It is likely that in already-completed trials of term infants, small-for-gestational age infants have been included, and a potential subgroup analysis could be completed.

(Continued).

Appendix 1. (Continued).

What is the optimal timing of oxytocin administration relative to delayed cord clamping?

Current WHO guidelines revised in 2012 recommend administration of oxytocin to the mother for prevention of postpartum hemorrhage "soon after delivery" (*8*): International Federation of Gynecology and Obstetrics guidelines recommend waiting 1 minute before administration of oxytocin to the mother (*134, 135*). While no negative effects are anticipated, it has not been investigated whether waiting to clamp the cord following administration of oxytocin immediately after the infant's delivery would have effects on the infant. Similarly, whether the timing of oxytocin administration alters its effectiveness on preventing maternal bleeding has not been well examined.

Do depressed infants who are resuscitated with the cord intact demonstrate better outcomes than depressed infants who are resuscitated after clamping and cutting the cord? What are the issues surrounding the feasibility of resuscitation with the cord intact and what interventions are needed to help implement delayed cord clamping and neonatal resuscitation simultaneously?

WHO's guidelines on neonatal resuscitation released in 2012 recommend that the cord be clamped and cut if an infant is found to need positive-pressure ventilation and there is not experience in performing resuscitation while the cord is still intact (*9*). The guideline development group noted that this was a weak recommendation based on the lack of any evidence of the effect of cord clamping time on depressed infants who are resuscitated, and the concern that most care-providers will not be familiar with initiating resuscitation with the cord intact. Early cord clamping in a depressed neonate will cause lower blood volume, and assuming the placenta has not separated, will eliminate a potential source of oxygen to the infant. In many cases, the set-up of the delivery room and the access to neonatal resuscitation equipment may impede this process, and strategies for combining both resuscitation and delayed cord clamping should be investigated (including the use of mobile resuscitation trolleys, such as the BASICS trolley). In addition, assessing whether outcomes are indeed better when resuscitation is performed with the cord intact may also be useful in helping promote the implementation of both practices simultaneously.

What is the effect of delayed cord clamping vs umbilical cord milking during cesarean delivery? Do infants who receive umbilical cord milking following cesarean section have similar long-term outcomes (hematological, iron status and development) to those who receive delayed cord clamping? Which practice is more feasibly performed by physicians?

Few studies have analyzed the effect of delayed cord clamping in cesarean delivery as compared to vaginal deliveries, for either term or pre-term infants. In Latin America, ce-

(Continued).

Appendix 1. (Continued).

searean delivery accounts for as much or more than half of births in some settings. Delayed cord clamping can be practiced in cesarean delivery; a study that showed that placental transfusion did occur with delayed clamping in cesarean deliveries (evident by the increased hemoglobin and hematocrit in the hours after birth as compared to immediate clamping), placed the infants on their mother's laps and clamped the cord at 3 minutes after delivery (*24*). Farrar and colleagues also found no difference in the amount of placental transfusion for infants born vaginally vs. those born by cesarean section (*16*). However, no studies have investigated long-term effects of delayed clamping on iron or hematological status in infants born by cesarean delivery specifically. Another practice to investigate within the context of cesarean delivery, where there may be hesitation to wait 2 to 3 minutes to clamp the cord, is umbilical cord milking. A study published in 2012 showed that milking the cord 5 times before clamping after cesarean delivery was feasible, safe and effective at raising hematocrit and hemoglobin at 36 to 48 hours of age (*26*).Whether this practice has the same long-term effects as delayed clamping remains to be established.

What is the effect of positioning the infant in skin-to-skin contact on the speed of placental transfusion?

While it has been assumed that within 10 cm above or below the level of the placenta, the rate of placental transfusion is not affected, this is the result of work conducted in the 1960s determining how gravity affects placental transfusion, which has not been replicated or further assessed. Recent data indicate that an infant placed in skin-to-skin contact with his/her mother may experience a slightly slower placental transfusion, needing approximately 5 minutes to receive a full transfusion, as opposed to the 2 to 3 minutes usually recommended to allow for a full placental transfusion (*22*). Thus additional work to determine the optimal timing of cord clamping when the infant is placed in skin-to-skin contact is needed.

What are current delivery care practices and norms in facilities and home births? Are updated guidelines for active management of the third stage of labor and newborn resuscitation being followed and regularly practiced?

Since 2007, there have been fairly extensive revisions to international guidelines for active management of the third stage of labor and newborn resuscitation. A review of whether hospital policies and practices reflect these newly recommended practices, as well as an assessment of current practices observed in different delivery settings (both facility and domiciliary, and for different types of care providers) for not only cord clamping time but skin-to-skin contact and breastfeeding initiation is needed.

(Continued).

Appendix 1. (Continued).

What is the feasibility of immediate skin-to-skin contact after cesarean delivery and what are equally-beneficial alternatives?

Immediate skin-to-skin contact after cesarean section for a well-newborn is possible and safe, though cesarean section has been identified as a frequent barrier to implementing early skin-to-skin contact and breastfeeding (*122, 123*). Strategies and multi-faceted interventions to improve the feasibility of implementing skin-to-skin contact (or equally beneficial alternatives) have not been well investigated. In situations where skin-to-skin contact after cesarean is not possible (e.g., mother received general anesthesia or requires significant post-operative care), one study has investigated the benefits of father-to-newborn skin-to-skin contact as a possible alternative after cesarean delivery, showing both decreased crying time, and improved pre-feeding behaviors (*136*). The acceptability of this option in different settings should be evaluated.

What are the barriers to adoption of the recommended practices?

Additional data on the barriers preventing the adoption of evidence based perinatal care practices in specific regions and cultures, particular settings (facilities vs. home births, teaching hospitals vs. public hospitals) and different care providers (obstetricians vs. midwives vs. skilled birth attendants) are necessary in order to develop implementation materials and multifaceted interventions and target advocacy efforts appropriately.

What are effective strategies to implement evidence-based care practices? How can these strategies be implemented at wide levels and sustained?

There are obviously many more essential delivery care practices than those addressed in this document (e.g., clean cord care, neonatal resuscitation, immunizations). Assessing and documenting how best to integrate the combination of practices discussed here with other prenatal and postnatal care practices for both mother and infant will be essential. In addition, identifying appropriate behavior change strategies that can be applied widely to improve uptake of these recommended practices is needed.

Are there special considerations for implementation into domiciliary deliveries?

The limited data available on delivery care practices in domiciliary deliveries, and the special considerations for implementation of the recommended practices in this setting (e.g., training of skilled birth attendants, adaptation of traditional or cultural practices, limited resources) makes this an important area of research.

Appendix 2. Are there exceptions to the recommended practices? Frequently asked questions

There are very few exceptions in which delayed umbilical cord clamping, early skin-to-skin contact and initiation of exclusive breastfeeding should not be practiced. A few common situations in which the application of one or more of the recommended practices may be questioned are discussed below.

Delayed umbilical cord clamping and…

…cesarean section.

Delayed cord clamping can be performed after cesarean delivery. In studies in which infants born by cesarean section were included, infants were dried and wrapped, and placed on a surface level with the placenta (between the mother's legs), or slightly above (on the mothers thighs) while waiting to clamp the cord. There are limited studies on the use of umbilical cord milking as a (faster) alternative to delayed cord clamping in cesarean deliveries, though the limited data on short-term outcomes have shown that umbilical cord milking may be an equally good intervention to provide placental transfusion to the infant.

…the depressed or asphyxiated infant.

If the infant is pale, limp, or not breathing, one can perform resuscitative measures for the infant at the level of the perineum (e.g., with the infant between the mother's legs) to allow optimal blood flow and oxygenation (*120*). Adequate blood volume is necessary for the establishment of respiration, as the pulmonary circulation requires an increase from 8% to 12% of the fetal cardiac output to 40% to 50% of the newborn cardiac output (*137*). Immediately clamping the cord of a depressed neonate deprives the infant of his/her only blood and oxygen source. It is important to note that most infants (more than 90%) respond to the initial steps of resuscitation, including drying and stimulation. A smaller percentage, less than 10%, require active resuscitative interventions to establish regular respirations, and approximately half of those infants will respond without further active resuscitative efforts (*11*). It is possible to conduct "positive-pressure" ventilation with mask and bag, or even a full resuscitation with intubation without severing the infant's umbilical cord (*10*); however most care providers will not be familiar with such a technique and may not have access to the needed equipment (which is usually placed in a separate area of the delivery room) thus necessitating immediate cord clamping. WHO guidelines for newborn resuscitation recom-

(Continued).

Appendix 2. (Continued).

mend that if the care-provider is experienced in providing resuscitation measures with the cord intact, then the care-provider may do so (*9*). However, in cases of severe asphyxia where the cord is flat or pulseless upon delivery (indicating a lack of placental-fetal circulation), immediate cord clamping is indicated so that immediate resuscitative measures can be taken.

…nuchal cord.

The appropriate timing of umbilical cord clamping when the cord is wrapped around the newborn's neck (i.e., nuchal cord) is still controversial. However, increasing evidence indicates that clamping the cord before the infant is delivered may be harmful, increasing the risk of hypovolemia, anemia, cerebral palsy and possibly death (*138*). Nuchal cord combined with the compression of the cord during uterine contractions will compromise fetal blood volume. Cord clamping before delivery may lead to fetal hypovolemia, by preventing the equilibration of placental-fetal circulation after delivery. It is recommended that the integrity of the nuchal cord be maintained as much as possible, by slipping the cord over the infant's head or shoulders (when allowed by the tightness of the cord) or employing the "somersault maneuver" (*139*).

…diabetic mothers.

Infants of diabetic mothers may be at increased risk of developing polycythemia because of compromised oxygen delivery during gestation resulting in a higher hematocrit at birth. However, the beneficial effects of delayed clamping for birth iron stores (which have been shown to be frequently compromised in newborns of diabetic mothers (*140*)) and thus long-term iron status (*141*) may outweigh any potential negative effects of an increased neonatal hematocrit.

… Rhesus-sensitization of the mother.

While feto-maternal transfusion may occur during labor and delivery, there is also evidence that microchimerism (both maternal and fetal) occurs during gestation (as early as the first trimester) (*142-144*). It is unlikely that the timing of cord clamping would affect the transfer of fetal cells to the mother or maternal cells to the infant. It has been suggested that delayed cord clamping, by decreasing the volume of placental blood "trapped" in the placenta may actually decrease the possibility of feto-maternal transfusion. A study that compared the effect of different methods for managing delivery of the placenta on feto-maternal transfusion showed that clamping at the end of the cord pulsations followed by placental drainage, caused the lowest degree of feto-maternal transfusion in comparison to early clamping or early clamping followed by placental drainage (*145*).

(Continued).

Appendix 2. (Continued).

…mother-to-child transmission of HIV.

Whether the practice of delayed cord clamping increases the risk of mother-to-child HIV transmission is not known. However, there is no biological evidence that allowing an equilibration of placental blood (i.e., blood that has been in circulation between the placenta and fetus during gestation) between the placenta and the infant by waiting to clamp the umbilical cord would increase the transfer of a blood-borne virus (either HIV or other viruses) to the newborn. When the placenta separates, the integrity of the syncytiotrophoblast and the fetal endothelium may become compromised allowing transfer of the virus; however, placental separation would not likely occur before the recommended time of cord clamping (approximately 3 minutes after delivery). However, to reduce the possibility of HIV transmission at delivery, it is essential that contact between maternal blood (e.g., blood from maternal tearing or lacerations) and the newborn be avoided.

…obtaining cord blood gas measurements.

Blood gas analysis from umbilical cord vessels is used to ascertain intrapartum fetal physiology, and exclude the possibility of fetal hypoxia or asphyxia during the birth process. The standards for blood gas analysis are relative to immediate cord clamping, and the recommended technique is to double clamp the cord immediately after delivery and obtain a sample from the umbilical artery (and vein) from the clamped segment. Few studies have measured blood gas measurements after delayed clamping, and the results are somewhat mixed as to whether delayed cord clamping has an effect on blood gas analysis that would affect its interpretation (*146*). Andersson and colleagues however proposed a modified technique that allows for sampling from the umbilical artery immediately after birth from an unclamped cord to also allow for placental transfusion (*146*).

The proportion of valid paired arterial-venous samples obtained in the delayed-clamped group was similar to the proportion in the early-clamped group, and the blood gas parameters were not significantly different between groups with the exception of PaO2 (which was higher in the delayed-clamped infants, possibly due to continued placental circulation in the these infants when the samples were drawn)(*146*).

…obtaining cord blood for banking.

Delayed cord clamping will result in a smaller placental residual blood volume, on the order of approximately 30 to 45 ml for a newborn of roughly 3 kg, as compared to roughly

(Continued).

Appendix 2. (Continued).

100 ml for the same infant if the cord is clamped immediately. According to one cord blood bank's collection guidelines, approximately 45 ml of cord blood is the minimum needed (*147*). Thus delayed clamping and cord blood collection in most cases will not be compatible practices. Pediatrics and obstetrics organizations (e.g., American Academy of Pediatrics, and the International Federation of Gynecologists and Obstetricians) have policy statements that advise against altering the timing of cord clamping for the benefit of cord blood collection, particularly in settings where the risk of anemia is high (*148, 149*).

Breastfeeding and…

…the HIV-positive mother.

In settings where national authorities have decided that the maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV-infected the greatest chance of HIV-free survival, it is recommended that mothers known to be HIV-infected (and whose infants are HIV-uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided (*150*).

Skin-to-skin contact and…

… the HIV-positive mother.

If a HIV-positive mother has decided not to breastfeed, skin-to-skin contact should still be encouraged for its beneficial effects apart from helping to establish early breastfeeding. Contact between maternal blood and the newborn should be avoided.

…cesarean section.

Skin-to-skin contact after cesarean delivery is feasible and safe for most mothers and well-newborns. For a discussion on how to promote and support skin-to-skin contact after a cesarean delivery, see **Box 4**.

…early sudden unexpected death in infancy.

In the past several years, there have been case reports of "early sudden unexpected death in infancy", (also knows as early neonatal sudden death, or early sudden infant death syn-

(Continued).

Appendix 2. (Continued).

drome) which is generally defined as sudden, unexplained death usually during the first 2 to 4 hours of birth after uneventful pregnancies/deliveries. A review published in 2013 identified 132 cases published in the scientific literature from 1985 to 2012; in most cases, a cause of death was not identified, though upper airway obstruction was hypothesized in several (*151*). Six of the 15 publications describing these cases identified skin-to-skin contact as an apparent risk factor. Other risk factors included infants in the prone position (5 of 15 publications), primiparous mothers (5 of 15 publications) and lack of observation by trained medical staff of the mother and infant (3 of 15 publications). The authors concluded that because skin-to-skin contact has benefits to the mother and infant, that the practice should not be reconsidered due to the rare association with these events; rather, "safe skin-to-skin" practices, which include regular observation and support for skin-to-skin and initiation of breastfeeding by trained staff, particularly for first time mothers during the immediate post-partum, should be recommended (*151*).

References

1. Lawn JE, Cousens S, Zupan K, Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: When? Where? Why? The Lancet. 2005;365(9462):891-900.
2. World Health Organization (WHO). Health and the Milennium Development Goals. Geneva: World Health Organization, 2005.
3. Lawn JE, Kerber K, Enweronu-Laryea C, Cousens S. 3.6 million neonatal deaths--what is progressing and what is not? Seminars in Perinatology. 2010;34(6):371-86.
4. Bhutta ZA, Darmstadt GL, Hasan BS, Haws RA. Community-based interventions for improving perinatal and neonatal health outcomes in developing countries: A review of the evidence. Pediatrics. 2005;115:519-617.
5. Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, de Bernis L. Evidence-based, cost-effective interventions: how many newborn babies can we save? The Lancet. 2005;365:977-88.
6. Prendiville WJ, Harding JE, Elbourne DR, Stirrat GM. The Bristol third stage trial: active versus physiological management of the third stage of labour. British Medical Journal. 1988;297:1295-300.
7. Philip AGS, Saigal S. When should we clamp the umbilical cord? NeoReviews. 2004;5:142-54.
8. World Health Organization (WHO). WHO recommendations for the prevention and treatment of postpartum haemorrhage. Geneva: World Health Organization, 2012.
9. World Health Organization (WHO). Guidelines on basic newborn resuscitation. Geneva: World Health Organization, 2012.
10. van Rheenen P, Brabin BJ. A practical approach to timing cord clamping in resource poor settings. British Medical Journal. 2007;333:954-8.
11. Kattwinkel J, Niermeyer S, Nadkarni V, Tibballs J, Phillips B, Zideman D, et al. ILCOR Advisory Statement: Resuscitation of the Newly Born Infant An advisory statement from the pediatric working group of the International Liason Committee on Resuscitation. Pediatrics. 1999;103(4):e56.
12. Book N. Icterus neonatorum. The Canadian Medical Association Journal. 1935:269-72.
13. Montgomery T. The umbilical cord. In: Montgomery T, editor. Fetal physiology and distress. Clinical Obstetrics and Gynecology. 3 (4): Paul B. Hoeber, Inc.; 1960. p. 900-10.
14. Yao AJ, Lind J. Blood flow in the umbilical vessels during the third stage of labor. Biology of the Neonate. 1974;25:186-93.
15. Linderkamp O, Nelle M, Kraus M, Zilow EP. The effect of early and late cord-clamping on blood viscosity and other hemorheological parameters in full-term neonates. Acta Paediatrica. 1992;81:745-50.
16. Farrar D, Airey R, Law G, Tuffnell D, Cattle B, Duley L. Measuring placental transfusion for term births: weighing babies with cord intact. BJOG. 2011;118:70-5.

17. Aladangady N, McHugh S, Aitchison TC, Wardrop CAJ, Holland BM. Infants' blood volume in a controlled trial of placental transfusion at preterm delivery. Pediatrics. 2006;117(1):93-8.
18. Narenda A, Beckett CAT, Kyle E, al. e. Is it possible to promote placental transfusion at preterm delivery? Pediatric Research. 1998;44:453.
19. Yao AJ, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. The Lancet. 1969 October 24. 1969:871-3.
20. Yao AJ, Hirvensalo M, Lind J. Placental transfusion-rate and uterine contraction. The Lancet. 1968 February 24, 1968:380-3.
21. Linderkamp O. Placental transfusion: Determinants and effects. Clinics in Perinatology. 1982 October;9(3):559-92.
22. Mercer JS, Erickson-Owens DA. Rethinking placental transfusion and cord clamping issues. J Perinat Neonat Nurs. 2012;26(3):202-17.
23. Kleinberg F, Dong L, Phibbs RH. Cesarean section prevents placenta-to-infant transfusion despite delayed cord clamping. American Journal of Obstetrics and Gynecology. 1975;121(1):66-70.
24. Ceriana Cernadas JM, Carroli G, Pellegrini L, Otano L, Ferreira M, Ricci C, et al. The effect of timing of cord clamping on neonatal venous hematocrit values and clinical outcome at term: A randomized, controlled trial. Pediatrics. 2006;117(4):e779-e86.
25. Ceriani-Cernadas JM, Carroli G, Pellegrini L, Ferreira M, Ricci C, Casas O, et al. The effect of early and delayed umbilical cord clamping on ferritin levels in term infants at six months of life: a randomized controlled trial. Arch Argent Pediatr. 2010;108:201-8.
26. Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: a randomized controlled trial. Journal of Perinatology. 2012;32:580-4.
27. Rabe H, Diaz-Rossello J, Duley L, Dowswell 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 of Systematic Reviews. 2012;Issue 8.:Art. No.: CD003248.
28. Watkins AM, West CR, Cooke RW. Blood pressure and cerebral haemorrhage and ischaemia in very low birthweight infants. Early Human Development. 1989;19(2):103-10.
29. Maisels MJ, Watchki JF. Treatment of jaundice in low birthweight infants. Archives of Disease in Childhood Fetal and neonatal edition. 2003;88:F459-F63.
30. 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;117:1235-42.
31. Gokmen Z, Ozkiraz S, Tarcan A, Kozanoglu I, Ozcimen EE, Ozbek N. Effects of delayed umbilical cord clamping on peripheral blood hematopoietic stem cells in premature neonates. Journal of Perinatal Medicine. 2011;39:323-9.

32. Kugelman A, Borenstein-Levin L, Riskin A, Chistyakov I, Ohel G, Gonene R, et al. Immediate versus delayed umbilical cord clamping in premature neonates born < 35 weeks: a prospective, randomized, controlled study. American Journal of Perinatology. 2007;24(5):307-15.
33. Baenziger O, Stolkin F, Keel M, von Siebenthal K, Fauchere JC, Das Kundu S, et al. The influence of the timing of cord clamping on postnatal cerebral oxygenation in preterm neonates: a randomized controlled trial. Pediatrics. 2007;119(3):455-9.
34. Nelle M, Fischer S, Conze S, Beedgen B, Brischke EM, Linderkamp O. Effects of later cord clamping on circulation in prematures [abstract]. Pediatric Research. 1998;44(420).
35. Kinmond S, Aitchison TC, Holland BM, Jones JG, Turner TL, Wardrop CAJ. Umbilical cord clamping and preterm infants: a randomised trial. BMJ. 1993 January 16;306:172-5.
36. Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. Cochrane Database Systematic Reviews. 2004;Issue 4. Art. No.: CD003248. DOI: 10.1002/14651858. CD003248.pub2.
37. 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. Journal of Perinatology. 2010;30:11-6.
38. Ultee K, Swart J, van der Deure H, Lasham C, van Baar A. Delayed cord clamping in preterm infants delivered at 34 to 36 weeks gestation: A randomized controlled trial. Archives of Disease in Childhood Fetal and neonatal edition. 2007;[Epub ahead of print].
39. Hutton EK, Hassan ES. Late vs. early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. JAMA. 2007;297:1241-52.
40. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilcal cord clamping of term infants on maternal and neonatal outcomes. Cochrane Database of Systematic Reviews. 2013;Issue 7.
41. Hutton EK, Hassan ES. Late vs. early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. JAMA. 2007;297(11):1241-52.
42. Werner EJ. Neonatal polycythemia and hyperviscosity. Clinics in Perinatology. 1995 September;22(3):693-710.
43. Oh W. Neonatal polycythemia and hyperviscosity. Pediatric Clinics of North America. 1986 June;33(3):523-32.
44. Drew J, Guaran R, Grauer S. Cord whole blood hyperviscosity: Measurement, definition, incidence and clinical features. Journal of Paediatrics and Child Health. 1991;27:363-5.
45. Ramamurthy RS, Brans YW. Neonatal polycythemia: I. Criteria for diagnosis and treatment. Pediatrics. 1981 August;68(2):168-74.
46. Dempsey EM, Barrington K. Short and long term outcomes following partial exchange

transfusion in the polycythaemic newborn: a systematic review. Archives of disease in childhood Fetal and neonatal edition. 2006;91:2-6.

47. Dewey KG, Chaparro CM. Session 4: Mineral metabolism and body composition Iron status of breast-fed infants. Proceedings of the Nutrition Society. 2007;66(3):412-22.
48. Miller MF, Stoltzfus RJ, Mbuya NV, Malaba LC, Iliff PJ, Humphrey JH, et al. Total body iron in HIV-positive and HIV-negative Zimbabwean newborns strongly predicts anemia throughout infancy and is predicted by maternal hemoglobin concentration. Journal of Nutrition. 2003;133:3461-8.
49. Hay G, Refsum H, Whitelaw A, Lind Melbye E, Haug E, Borch-Iohensen B. Predictors of serum ferritin and serum soluble transferrin receptor in newborns and their associations with iron status during the first 2 y of life. American Journal of Clinical Nutrition. 2007;86:64-73.
50. Chaparro CM, Neufeld LM, Tena Alavez G, Eguia-Liz Cedillo R, Dewey KG. Effect of timing of umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. The Lancet. 2006 June 17 2006;367:1997-2004.
51. Chaparro CM, Fornes RM, Neufeld LM, Tena-Alavez G, Eguia-Liz Cedillo R, Dewey KG. Early umbilical cord clamping contributes to elevated blood lead levels among infants with higher lead exposure. J Pediatr. 2007;151:506-12.
52. Andersson O, Hellstrom-Westas L, Andersson D, Domellof M. Effect of delayed versus early umbilical cord clamping on neonatal outomes and iron status at 4 months: a randomised controlled trial. BMJ. 2011;343.
53. Andersson O, Domellof M, Andersson D, Hellstrom-Westas L. Effects of delayed cord clamping on neurodevelopment and infection at four months of age: a randomised trial. Acta Paediatrica. May 2013;102(5):525-31.
54. Dunn PM. Controversies in neonatal resuscitation. Emirates Medical Journal. 1993;1 (Supplement):5-8.
55. Soltani H, Dickinson F, Symonds I. Placental cord drainage after spontaneous vaginal delivery as part of the management of the third stage of labour. Cochrane Database of Systematic Reviews. 2005;Issue 4. Art. No.: CD004665. DOI: 10.1002/14651858. CD004665.pub2.
56. Soltani H, Poulose TA, Hutchon DJ. Placental cord drainage after vaginal deliver as part of the management of the third stage of labour. Cochrane Database of Systematic Reviews. 2011;Issue 9:Art. No.: CD004665.
57. Lozoff B, Georgieff MK. Iron deficiency and brain development. Seminars in Pediatric Neurology. 2006;13:158-65.
58. Grantham-McGregor S, Ani C. A review of the studies of iron deficiency on cognitive development in children. Journal of Nutrition. 2001;131:649S-68S.
59. Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. Pediatrics. 2000 April;105(4): E51.

60. Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. Archives of Pediatric Adolescent Medicine. 2006;160(11):1108-13.
61. Rocangliolo M, Garrido M, Peirano P, Walter T, Lozoff B. Delayed maturation of auditory brainstem responses in iron-deficient anemic infants. American Journal of Clinical Nutrition. 1998;68(3):683-90.
62. Algarin C, Peirano P, Garrido M, Pizarro F, Lozoff B. Iron deficiency anemia in infancy: Long-lasting effects on auditory and visual system functioning. Pediatric Research. 2003;53(2):217-23.
63. Dewey KG, Domellöf MD, Cohen RJ, Rivera LL, Hernell O, Lönnerdal B. Iron supplementation affects growth and morbidity of breast-fed infants: Results of a randomized trial in Sweden and Honduras. Journal of Nutrition. 2002;132:3249-55.
64. Righard L, Alade MO. Effect of delivery room routines on success of first breastfeed. The Lancet. 1990;336:1105-7.
65. Moore ER, Anderson GC, Bergman N. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database of Systematic Reviews. 2007;Issue 3.:Art.No.: CD003519.
66. Awi DD, Alikor EA. The influence of pre- and post-partum factors on the time of contact between mother and her newborn after vaginal delivery. Nigerian Journal of Medicine. 2004;13(3):272-5.
67. Awi DD, Alikor EA. Barriers to timely initiation of breastfeeding among mothers of healthy full-term babies who deliver at the University of Port Harcourt Teaching Hospital. Nigerian Journal of Clinical Practice. 2006;8(1):57-64.
68. Rey M. Manejo racional del niño prematuro [Rational management of the premature infant]. I Curso de Medicina Fetal y Neonatal. Bogotá, Colombia1983. p. 137-51.
69. Varendi H, Porter RH, Winberg J. Does the newborn baby find the nipple by smell? The Lancet. 1994;344(8928):989-90.
70. Widstrom A, Ransjö-Arvidson AB, Christensson K, Matthiesen AS, Winberg J, Uvnäs-Moberg K. Gastric suction in healthy newborn infants. Effects on circulation and developing feeding behaviour. Acta Paediatrica Scandinavica. 1987;76(4):566-72.
71. Moore E, Cranston Anderson G. Randomized controlled trial of very early mother-infant skin-to-skin contact and breastfeeding status. Journal of Midwifery and Women's Health. 2007;52(2):116-25.
72. Bramson L, Lee JW, Moore E, Montgomery S, Neish C, Bahjri K, et al. Effect of early skin-to-skin mother-infant contact during the first 3 hours following birth on exclusive breastfeeding during the maternity hospital stay. Journal of Human Lactation. 2010;26:130-7.
73. Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. Pediatrics. 2003;112(3 Pt 1):607-19.

74. Moore ER, Anderson GC, Bergman N, Dowswell T. Early skin-to-skin contact for mothers and their healthy newborn infants Cochrane Database of Systematic Reviews. 2012;Issue 5:Art. No.: CD003519.
75. Bigelow A, Power M, MacLellan-Peters J, Alex M, McDonald C. Effect of mother/infant skin-to-skin contact on postpartum depressive symptoms and maternal physiological stress. JOGNN. 2012;41:369-82.
76. Christensson K, Bhat GJ, Amadi BC, Erikkson B, Hojer B. Randomised study of skin-to-skin versus incubator care for rewarming low-risk hypothermic neonates. The Lancet. 1998;352:1115.
77. Christensson K, Siles C, Moreno L, Belaustequi A, De La Fuente P, Lagercrantz H, et al. Temperature, metabolic adaptation and crying in health full-term newborns cared for skin-to-skin or in a cot. Acta Paediatrica. 1992;81(607):488-93.
78. Bergström A, Okong P, Ransjö-Arvidson AB. Immediate maternal thermal response to skin-to-skin care of newborn. Acta Paediatrica. 2007;96:655-8.
79. Shiau S-H. Randomized controlled trial of kangaroo care with full-term infants: effects of maternal anxiety, breast milk maturation, breast engorgement, and breastfeeding status (Dissertation). Cleveland, OH: Case Western Reserve University; 1997.
80. World Health Organization (WHO) Baby Friendly Hospital Initiative. Geneva: World Health Organization, 2009.
81. Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS, Bellagio Child Survival Study Group. How many child deaths can we prevent this year? The Lancet. 2003;362:65-71.
82. Horta BL, Bahl R, Martines JC, Victora CG. Evidence on the long-term effects of breastfeeding: Systematic reviews and meta-analyses. Geneva: World Health Organization, 2007.
83. Drudy D, Mullane NR, Quinn T, Wall PG, Fanning S. Enterobacter sakazakii: An emerging pathogen in powdered infant formula. Clinical Infectious Diseases. 2006;42:996-1002.
84. Edmond KM, Zandoh C, Quigley MA, Amenga-Etego S, Owusu-Agyei S, Kirkwood BR. Delayed breastfeeding initiation increases risk of neonatal mortality. Pediatrics. 2006;117:380-6.
85. Leach A, McArdle TF, Banya WA, Krubally O, Greenwood AM, Rands C, et al. Neonatal mortality in a rural area of The Gambia. Annals of Tropical Medicine. 1999;19(1):33-43.
86. Matthiesen AS, Ransjö-Arvidson AB, Nissen E, Uvnäs-Moberg K. Postpartum maternal oxytocin release by newborns: effects of infant hand massage and sucking. Birth. 2001;28(1):13-9.
87. Chua S, Arulkumaran S, Lim I, Selamat N, Ratnam SS. Influence of breastfeeding and nipple stimulation on postpartum uterine activity. British Journal of Obstetrics and Gynecology. 1994;101(9):804-5.
88. World Health Organization (WHO) Department of Reproductive Health and Research. Maternal mortality in 2000: Estimates developed by WHO, UNICEF, and UNFPA. Geneva: 2004.

89. Ip S, Chung M, Raman G, Chew P, Magula N, DeVine D, et al. Breastfeeding and maternal and infant health outcomes in developed countries. Evidence Report/Technology Assessment. 2007; (153):1-186.
90. Kendall-Tackett K. A new paradigm for depression in new mothers: the central role of inflammation and how breastfeeding and anti-inflammatory treatments protect maternal mental health. International Breastfeeding Journal. 2007;2:6.
91. Zubaran C, Foresti K. The correlation between breastfeeding self-efficacy and maternal postpartum depression in southern Brazil. Sexual and Reproductive Healthcare. 2013;4:9-15.
92. Prince M, Patel V, Shekhar S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. The Lancet. 2007;370:859-77.
93. Chandrashekhar TS, Joshi HS, Binu V, Shankar PR, Rana MS, Ramachandran U. Breast-feeding initiation and determinants of exclusive breast-feeding: A questionnaire survey in an urban population of western Nepal. Public Health Nutrition. 2007;10(2):192-7.
94. Lawson K, Tulloch MI. Breastfeeding duration: prenatal intentions and postnatal practices. Journal of Advanced Nursing. 1995;22(5):841-9.
95. Ekstrom A, Widstrom A, Nissen E. Duration of breastfeeding in Swedish primiparous and multiparous women. Journal of Human Lactation. 2003;19(2):172-8.
96. Rautishauser IH, Carlin JB. Body mass index and duration of breastfeeding: a survival analysis during the first six months of life. Journal of Epidemiology and Community Health. 1992;46:559-65.
97. World Health Organization (WHO). Infant and young child nutrition, (18 May 2001).
98. World Health Organization (WHO). WHO Handbook for Guideline Development. Geneva: World Health Organization; 2012.
99. World Health Organization (WHO). WHO Recommendations for the Prevention of Postpartum Haemorrhage. Geneva: World Health Organization: Department of Making Pregnancy Safer, 2007.
100. Deneux-Tharaux C, Sentilhes L, Maillard F, Closset E, Vardon D, Lepercq J, et al. Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). BMJ. 2013;346.
101. Perlman JM, Wyllie J, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP, et al. Part 11: Neonatal resuscitation: 2010 International consensus on cardiopulmonary resuscitation and emergenc cardiovascular care science with treatment recommendations. Circulation. 2010;122:S516-S38.
102. Perez-Escamilla R, Pollitt E, Lönnerdal B, Dewey KG. Infant feeding policies in maternity wards and their effect on breast-feeding success: An analytical overview. American Journal of Public Health. 1994;84(1):89-97.
103. Lutter CK, Chaparro CM, Grummer-Strawn LM, Victora CG. Backsliding on a key health investment in Latin America and the Caribbena: the case of breastfeeding pro-

motion. American Journal of Public Health. 2011;101(11):2130-6.

104. Winter C, Macfarlane A, Deneux-Tharaux C, Zhang W-H, Alexander S, Brocklehurst P, et al. Variations in policies for management of the third stage of labour and the immediate management of postpartum haemorrhage in Europe. British Journal of Obstetrics and Gynecology. 2007;114:845-54.
105. Festin MR, Lumbiganon P, Tolosa JE, Finney KA, Ba-Thike K, Chipato T, et al. International survey on variation in practice of the management of the third stage of labour. Bulletin of the World Health Organization. 2003;81(4):286-91.
106. Duong DV, Binns CW, Lee AH. Breast-feeding initiation and exclusive breast-feeding in rural Vietnam. Public Health Nutrition. 2004;7(6):795-9.
107. Afzal M, Quddusi AI, Iqbal M, Sultan M. Breastfeeding patterns in a military hospital. Journal of the College of Physicians and Surgeons Pakistan. 2006;16(2):128-31.
108. Chhabra P, Grover VL, Aggarwal OP, Dubey KK. Breast feeding patterns in an urban resettlement colony of Delhi. Indian Journal of Pediatrics. 1998;65(6):867-72.
109. Osrin D, Tumbahangphe KM, Shrestha D, Mesko N, Shrestha BP, Manandhar MK, et al. Cross sectional, community based study of care of newborn infants in Nepal. British Medical Journal. 2002;325:1063-7.
110. Darmstadt GL, Syed U, Patel Z, Kabir N. Review of domiciliary newborn-care practices in Bangladesh. Journal of Health and Population Nutrition. 2006;24(4):380-93.
111. Fikree FF, Ali TS, Durocher JM, Rahbar MH. Newborn care practices in low socioeconomic settlements of Karachi, Pakistan. Social Science and Medicine. 2005;60(2005):911-21.
112. Bergström A, Byaruhanga R, Okong P. The impact of newborn bathing on the prevalence of neonatal hypothermia in Uganda: A randomized, controlled trial. Acta Paediatrica. 2005;94:1462-7.
113. Marchini G, Lindow S, Brismar H, Stabi B, Berggren V, Ulfgren AK, et al. The newborn infant is protected by an innate antimicrobial barrier: peptide antibiotics are present in the skin and vernix caseosa. British Journal of Dermatology. 2002;147(6):1127-34.
114. Farrar D, Tuffnell D, Airey R, Duley L. Care during the third stage of labour: A postal survey of UK midwives and obstetricians. BMC Pregnancy and Childbirth. 2010;10:23. doi:1186/1471-2393-10-13.
115. Ononeze AB, Hutchon DJ. Attitude of obstetricians towards delayed cord clamping: a questionnaire-based study. J Obstet Gynaecol. 2009;29:223-4.
116. Dragovich D, Tamburlini G, Alisjahbana A, Kambarami RA, Karagulova J, Lincetto O, et al. Thermal control of the newborn: knowledge and practice of health professional in seven countries. Acta Paediatrica. 1997;86(6):645-50.
117. Belizan M, Meier A, Althabe F, Codazzi A, Colomar M, Buekens P, et al. Facilitators and barriers to adoption of evidence-based perinatal care in Latin American hospitals: a qualitative study. Health Education Research. 2007;22:839-53.

118. Bradley EH, Curry LA, Pallas S, Talbert-Slagle K, Yuan C, Minhas D, et al. A model for scale up of family health innovations in low- and middle-income settings: A mixed methods study. BMJ Open. 2012;2(4):1-12.
119. Perez-Escamilla R, Curry LA, Minhas D, Taylor L, Bradley EH. Scaling up of breastfeeding promotion programs in low- and middle-income countries: the "breastfeeding gear" model. Advances in Nutrition. 2012;3:790-800.
120. van Rheenen P. Delayed cord clamping and improved infant outcomes: enough evidence exists to encourage a routine change in practice. BMJ. 2011;343:d7127. doi:10.1136/bmj.d7127.
121. Institute of Medicine. Iron. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, D.C.: National Academy Press; 2001.
122. Rowe-Murray HJ, Fisher JRW. Baby friendly hospital practices: Cesarean section is a persistent barrier to early initiation of breastfeeding. Birth. 2002;29(2):124-31.
123. Hung KJ, Berg O. Early skin-to-skin after cesarean to improve breastfeeding. MCN The American journal of maternal child nursing. 2011;36(5):318-24.
124. Conde-Agudelo A, Belizan JM, Diaz-Rossello J. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database of Systematic Reviews. 2011;Issue 3:Art. No.: CD002771 10.1002/14651858.CD002771.pub2.
125. Bimbashi A, Ndoni E, Dokle A, Duley L. Care during the third stage of labour: obstetricians views and practice in an Albanian maternity hospital. BMC Pregnancy and Childbirth. 2010;10:4. doi:10.1186/1471-2393-10-4.
126. POPPHI/PATH. Technical briefs/newsletters: Global AMTSL Surveys Reports 2006.
127. Cherine M, Khalil K, Hassanein N, Sholkamy H, Breebaart M, Elnoury A. Management of the third stage of labor in an Egyptian teaching hospital. Int J Gynaecol Obstet. 2004;87:54-8.
128. Mercer JS, Nelson CC, Skovgaard RL. Umbilical cord clamping: beliefs of American nurse midwives. J Midwifery Womens Health. 2000;45:58-66.
129. van Rheenen P, Brabin BJ. Late umbilical cord-clamping as an intervention for reducing iron deficiency anaemia in term infants in developing and industrialised countries: a systematic review. Annals of Tropical Paediatrics. 2004 March 2004;24:3-16.
130. Rabe H, Reynolds G, Diaz-Rossello J. A systematic review and meta-analysis of a brief delay in clamping the umbilical cord of preterm infants. Neonatology. 2007;93:138-44.
131. de Onis M, Blossner M, Villar J. Levels and patterns of intrauterine growth retardation in developing countries. European Journal of Clinical Nutrition. 1998;52 Suppl 1:S5-S15.
132. Siimes MA. Iron nutrition in low-birthweight infants. In: Stekel A, editor. Iron nutrition in infancy and childhood (Nestle Nutriton Workshop Series 4). New York: Raven Press; 1984. p. 75-94.

133. van Rheenen P, Gruschke S, Brabin BJ. Delayed umbilical cord clamping for reducing anaemia in LBW infants--implications for developing countries. Annals of Tropical Paediatrics. 2006;26:157-67.
134. FIGO/ICM. Prevention and Treatment of Post-partum Haemorrhage: New Advances for Low Resource Settings Joint Statement 2006.
135. FIGO Safe Mothergood and Newborn Health (SMNH) Committee. FIGO Guidelines: Prevention and treatment of postpartum hemorrhage in low-resource settings. International Journal of Gynecology and Obstetrics. 2012;117:108-18.
136. Erlandsson K, Dsilna A, Fagerberg I, Christensson K. Skin-to-skin care with the father after cesarean birth and its effect on newborn crying and prefeeding behavior. Birth. 2007;34(2):105-14.
137. Mercer JS. Neonatal transitional physiology: A new paradigm. Journal of Perinatology and Neonatal Nursing. 2001 March;15(4):56-75.
138. Mercer JS, Skovgaard RL, Peareara-Eaves J, Bowman TA. Nuchal cord management and nurse-midwifery practice. Journal of Midwifery and Women's Health. 2005;50:373-9.
139. Schorn M, Blanco J. Management of the nuchal cord. Journal of Nurse Midwifery. 1991;36:131-2.
140. Georgieff MK, Landon MB, Mills MM, Hedlund BE, Faassen AE, Schmidt RL, et al. Abnormal iron distribution in infants of diabetic mother: spectrum and maternal antecedents. The Journal of Pediatrics. 1990;117(3):455-61.
141. Georgieff MK, Wewerka SW, Nelson CA, deRegnier R-A. Iron status at 9 months of infants with low iron stores at birth. The Journal of Pediatrics. 2002;141:405-9.
142. Lo ES, Lo YM, Hjelm NM, Thilaganathan B. Transfer of nucleated maternal cells into fetal circulation during the second trimester of pregnancy. British Journal of Haematology. 1998;100(3):605-6.
143. Bianchi DW. Prenatal diagnosis by analysis of fetal cells in maternal blood. The Journal of Pediatrics. 1995;127(6):857-6.
144. Petit T, Dommergues M, Socie G, Dumez Y, Gluckman E, Brison O. Detection of maternal cells in human fetal blood during the third trimester of pregnancy using allele-specific PCR amplification. British Journal of Haematology. 1997;98(3):767-71.
145. Ladipo OA. Management of third stage of labour, with particular reference to reduction of feto-maternal transfusion. British Medical Journal. 1972;1:721-3.
146. Andersson O, Hellstrom-Westas L, Andersson D, Clausen J, Domellof 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):567-74..
147. Cryo-Cell International Inc. Cord blood collection instructions [updated March 28 2013March 28 2013]. Available from: http://www.cryo-cell.com/resources/collection_procedure.

148. American Academy of Pediatrics Section on Hematology/Oncology and Section on Allergy/Immunology. Policy Statement: Cord blood banking for potential future transplantation. Pediatrics. 2007;119(1):165-70.
149. FIGO Committee for the Ethical Aspects of Human Reproduction and Women's Health. Ethical guidelines on cord blood banking. International Journal of Gynecology and Obstetrics. 2013;120:208-9.
150. World Health Organization (WHO). Guidelines on HIV and infant feeding. Geneva: World Health Organization, 2010.
151. Gnigler M, Ralser E, Karall D, Reiter G, Kiechl-Kohlendorfer U. Early sudden unexpected death in infancy (ESUDI)--three case reports and review of the literature. Acta Paediatrica. 2013;[Epub ahead of print]. Epub Jan 17.

Additional resources and websites

In addition to the references listed above, the following websites may provide additional information on the topics discussed in this document. All websites are current as of March 2013.

Prevention and treatment of postpartum hemorrhage

WHO recommendations for the prevention and treatment of postpartum hemorrhage (2012)
http://www.who.int/maternal_child_adolescent/documents/postpartum_haemorrge/en/

International Federation of Gynecology and Obstetrics (FIGO) guidelines for the prevention of postpartum haemorrhage in low-resource settings (2012)
http://www.figo.org/publications/PPH_Guidelines

The Postpartum Hemorrhage Prevention and Treatment Website
http://www.pphprevention.org/index.php

The Postpartum Hemorrhage Prevention and Treatment Website provides a forum for joint information sharing and learning between organizations and individuals working on the prevention and treatment of postpartum hemorrhage in developing countries. The website contains resources posted under the USAID-funded Prevention of Postpartum Hemorrhage Initiative (POPPHI) and includes information and links to a range of organizations working on postpartum hemorrhage issues. Website contents include policy documents, technical briefs, posters and a toolkit for the steps of active management of the third stage of labor which includes an animated demonstration. Resources available in English, Spanish and French.

Neonatal resuscitation

WHO Guidelines on basic newborn resuscitation (2012)
http://www.who.int/maternal_child_adolescent/documents/basic_newborn_resuscitation/en/index.html

International Liaison Committee on Resuscitation (ILCOR) 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations, Part 11: Neonatal Resuscitation
http://circ.ahajournals.org/content/122/16_suppl_2/S516.full

Bedside Assessment, Stabilization and Initial Cardiorespiratory Support (BASICS) Trolley

http://www.lw.nhs.uk/Library/news_centre/Life_Saving_Trolley_Basics_Case_Study.pdf

Developed by Dr Andrew Weeks, Peter Watt, Dr Andrew Gallagher, and Dr David Hutchon from the UK, the BASICS trolley (also known as the LifeStart trolley) is a "novel redesign" of a newborn resuscitation trolley, that contains all the basic elements of the existing resuscitation trolley (warmer, suction and oxygen), but can be placed alongside the mother's bed. The trolley can provide a platform for neonatal resuscitation and care for the first few minutes of life without having to separate the infant from the mother (i.e., can allow for resuscitation with the cord intact).

Maternal, newborn and child survival

Saving Newborn Lives, Save the Children

http://www.savethechildren.org/programs/health/saving-newborn-lives/

Saving Newborn Lives program, supported by the Bill & Melinda Gates Foundation, works in partnership with countries to reduce newborn mortality and improve newborn health.

Healthy Newborn Network

http://www.healthynewbornnetwork.org/

An initiative of Save the Children's Saving Newborn Lives program launched in 2010, the Healthy Newborn Network (HNN) is a partnership of organizations and individual members committed to improving newborn health around the world. HNN connects advocates around the world and provides a platform for discussions and interactions on a vast range of newborn and maternal health topics. In addition, the HNN boasts a common library of newborn health resources, featuring the latest in newborn health research, news, resources, events, articles, success stories and more from HNN Partners around the world.

Maternal and Child Health Integrated Program (MCHIP)

http://sites.path.org/mchn/our-projects/

Funded by USAID, MCHIP aims to speed up reduction of maternal, newborn, and child mortality in the 30 USAID priority countries that have the highest disease burden. The project's partners, including PATH, are working together to implement and bring to scale high-impact, effective interventions, based on the country context and using global and local data.

Partnership for Maternal, Newborn and Child Health (PMNCH)

http://www.pmnch.org

A WHO-led partnership joining the reproductive, maternal, newborn and child health communities into an alliance of more than 450 members to ensure that all women, infants and children not only remain healthy, but also thrive. PMNCH's mission is to "[support] Partners to align their strategic directions and catalyse collective action to achieve universal access to comprehensive, high-quality reproductive, maternal, newborn and child health care."

Latin American and Caribbean Neonatal Alliance

http://www.alianzaneonatal.org/eng/

The Newborn Alliance is "an interagency group which promotes newborn health within a Reproductive, Maternal and Child Health continuum. The group promotes evidence-based policy and programmatic interventions at the facility and community levels and supports countries in the LAC region in their efforts to reduce newborn mortality and morbidity." The "Resources and Tools" section of the website provides checklists and reference manuals for essential newborn care practices.

Iron deficiency and anemia and other micronutrient deficiencies

WHO Department of Nutrition for Health and Development

http://www.who.int/nutrition/en/index.html

WHO e-Library for Evidence of Nutrition Actions (eLENA)

http://www.who.int/elena/en/index.html

eLENA is an online library of the latest evidence-informed guidelines for nutrition interventions. The goal of eLENA is to help countries successfully implement and scale-up nutrition interventions by informing as well as guiding policy development and program design. Content on umbilical cord clamping can be found here: http://www.who.int/elena/titles/cord_clamping/en/index.html

WHO Vitamin and Mineral Nutrition Information System (VMNIS)

http://www.who.int/vmnis/

The database includes data by country on prevalence of anemia and other indicators of vitamin and mineral nutrition along with tools for surveillance

Iron Deficiency Project Advisory Service (IDPAS)

http://www.idpas.org/

"IDPAS Iron World" includes an outline of webpages with a diverse set of documentation related to micronutrient nutrition with emphasis on preventing and controlling iron deficiency anemia.

Micronutrient Initiative (MI)

http://www.micronutrient.org/

MI, an independent non-profit organization, has as its mission "to be a global leader in advancing integrated, innovative and sustainable solutions to reduce vitamin and mineral deficiencies through advocacy, technical and programmatic support, in collaboration with others." MI works in partnership with governments, the private sector and civil society organizations.

A2Z Project, The USAID Micronutrient and Child Blindness Project

http://www.a2zproject.org/

The A2Z Project, which ended in 2011, had as its goal to increase the use of key micronutrient and blindness interventions to improve child and maternal health. One of the technical focus areas of the project was anemia reduction in pregnant women and children. A2Z publications on anemia can be found here: http://www.a2zproject.org/~a2zorg/node/44

Importance of nutrition for health and development and achievement of the Millennium Development Goals

"Repositioning Nutrition as Central to Development: A strategy for large-scale action", The World Bank, 2006

Download text:

http://siteresources.worldbank.org/NUTRITION/Resources/281846-1131636806329/NutritionStrategy.pdf

Video presentation and PowerPoint:

http://www1.worldbank.org/hdnetwork/external/he/mshekar.htm

Text excerpt: *"Malnutrition remains the world's most serious health problem and the single biggest contributor to child mortality. Nearly one-third of children in the developing world are either underweight or stunted, and more than 30 percent of the developing world's population suffers from micronutrient deficiencies… It has long been known that malnutrition undermines economic growth and perpetuates poverty. Yet the international community and most governments in developing countries have failed to tackle malnutrition over the past decades, even though well-tested approaches for doing so exist. The consequences of this failure to act are now evident in the world's inadequate progress toward the Millennium Development Goals (MDGs) and toward poverty reduction more generally. Persistent malnutrition is contributing not only to widespread failure to meet the first MDG—to halve poverty and hunger—but to meet other goals in maternal and child health, HIV/AIDS, education, and gender equity…"*

Pan American Health Organization's Regional Strategy and Plan of Action on Nutrition in Health and Development

http://www.paho.org/english/gov/cd/CD47-18-e.pdf

Lancet Series on Maternal and Child Undernutrition

http://www.thelancet.com/series/maternal-and-child-nutrition

Maternal and child undernutrition was the subject of a Series of papers in The Lancet in 2008. Five years after the initial series, the Lancet re-evaluated the problems of maternal and child undernutrition and also examined the growing problems of overweight and obesity for women and children, and their consequences in low-income and middle-income countries. The Lancet series from 2013 also assessed national progress in nutrition programs and international efforts toward previous recommendations.

Breastfeeding resources

The Baby-Friendly Hospital Initiative, (BFHI)

http://www.who.int/nutrition/topics/bfhi/en/
http://www.unicef.org/nutrition/index_24806.html

WHO publications on infant and young child feeding

http://www.who.int/nutrition/publications/infantfeeding/en/index.html

PAHO publications on infant and young child feeding

http://www.paho.org/alimentacioninfantil

Includes information on recommended infant feeding indicators; updated materials (January 2006) for Baby-Friendly Hospital Initiative implementation (training of health workers and policy-makers, with additional sections for settings with high HIV prevalence); the International Code of Marketing of Breast Milk Substitutes; and publications on breastfeeding and complementary feeding.

PAHO publications on infant and young child feeding

http://www.paho.org/alimentacioninfantil

Includes technical and practical information on infant and young child feeding and nutrition in Spanish.

Alive and Thrive

http://www.aliveandthrive.org/

A Bill and Melinda Gates Foundation 6-year project (2009-2014) to improve infant and young child nutrition by increasing rates of exclusive breastfeeding and improving complementary feeding. It seeks to reach 16 million children less than 2 years of age in Bangladesh, Ethiopia, and Vietnam.

Linkages

http://www.linkagesproject.org/

USAID funded the 10-year LINKAGES Project (1996–2006) to provide technical information, assistance, and training to organizations on breastfeeding, related complementary feeding and maternal dietary practices, and the lactational amenorrhea method. Website includes assessment, training, counseling and monitoring and evaluation tools for infant and young child feeding.

Breastfeeding and mother-to-child HIV transmission guidelines

http://www.who.int/maternal_child_adolescent/documents/9789241599535/en/

Breastcrawl (UNICEF India)

http://www.breastcrawl.org

Provides a video as well as resources for promotion of "breastcrawl" as a method of immediately initiating breastfeeding after delivery.

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

525 Twenty-third St. N.W.,
Washington, D.C. 20037

Tel: 202.974.3000
Fax: 202.974.3724

www.paho.org/alimentacioninfantil

9 789275 117835