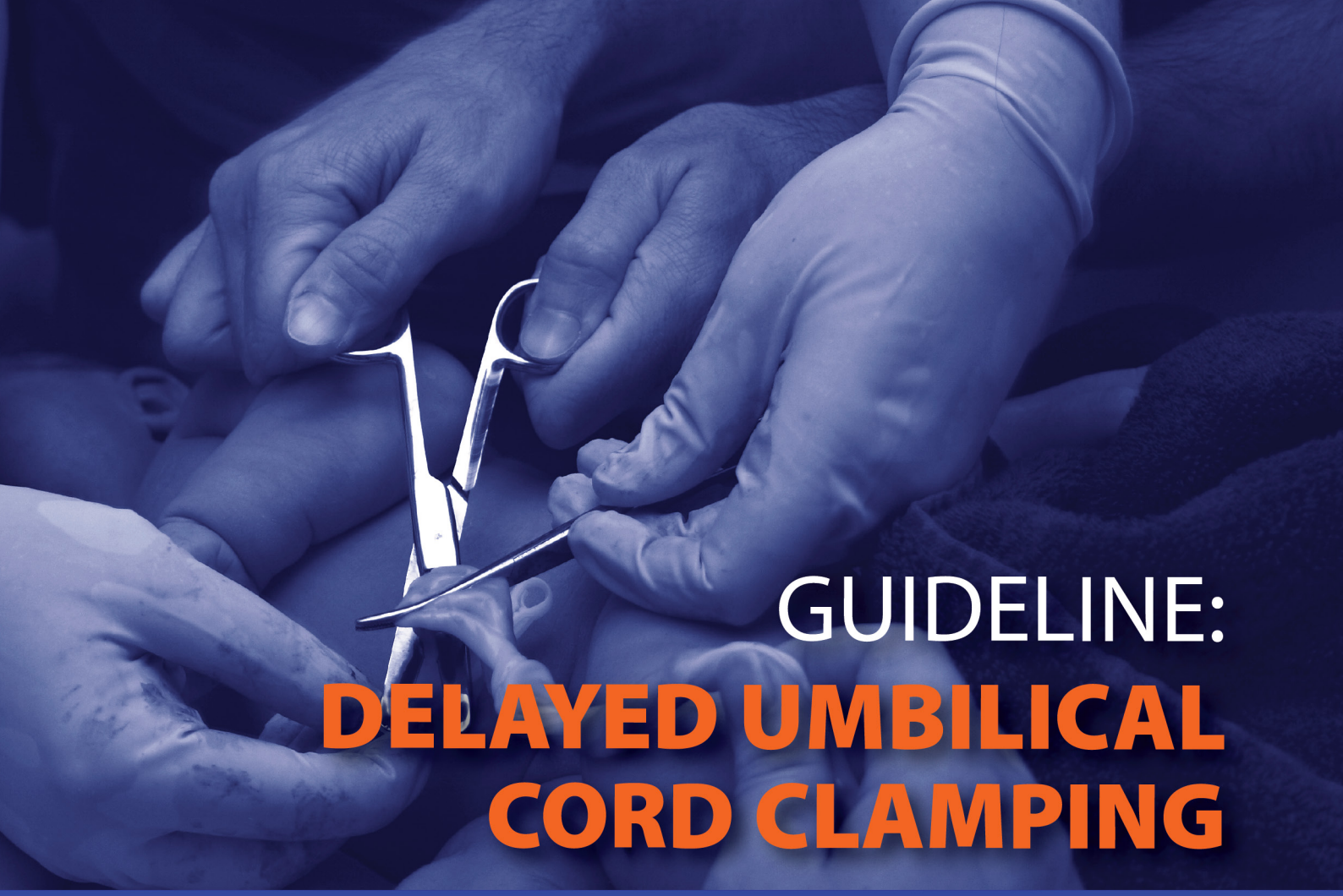

GUIDELINE:
DELAYED UMBILICAL CORD CLAMPING

for improved maternal and infant health and nutrition outcomes

World Health Organization

Guideline:

Delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes

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Contents

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Executive summary

Purpose of the guideline

This guideline[1] is a derivative product from existing World Health Organization (WHO) recommendations on umbilical cord clamping for improving maternal and infant outcomes. The optimal timing of umbilical cord clamping has been debated in the scientific literature for at least a century, and the timing of cord clamping continues to vary according to clinical policy and practice. "Early" cord clamping is generally carried out in the first 60 seconds after birth (most commonly in the first 15–30 seconds), whereas "delayed" (also referred to as "late") cord clamping is generally carried out more than 1 min after the birth or when the umbilical cord pulsation has ceased. For the mother, delayed cord clamping is one of the actions included in a package for reduction of the risk of postpartum haemorrhage.

Member States have requested guidance from WHO on the effects of delayed cord clamping for improving maternal and infant nutrition and health, as a public health strategy in support of their efforts to achieve the Millennium Development Goals, in particular, reduction of child mortality (MDG 4) and improvement of maternal health (MDG 5), as well as the global targets set in the *Comprehensive implementation plan on maternal, infant and young child nutrition*. The guideline is intended for a wide audience, including policy-makers; their expert advisers; technical and programme staff at organizations involved in the design, implementation and scaling-up of nutrition actions for public health; and health staff providing care to mothers and their infants.

Guideline development methodology

WHO developed the present evidence-informed recommendations using the procedures outlined in the *WHO handbook for guideline development*. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) methodology was followed to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

Two guideline development groups were involved in the development of the WHO *Guidelines on basic newborn resuscitation* and *WHO recommendations for the prevention and treatment of postpartum haemorrhage*, in which recommendations for the optimal timing of umbilical cord clamping are provided. A third group, the WHO guideline development group – nutrition actions 2013–2014 evaluated the updated evidence from these recommendations and discussed the research priorities for integration and scaling-up of this intervention in the area of public health and nutrition. The group met in Geneva, Switzerland, on 23–26 June 2014 to discuss issues around research gaps, including implementation research, and the nature of ongoing trials.

[1] This publication is a WHO guideline. A WHO guideline is any document developed by the World Health Organization containing recommendations for clinical practice or public health policy. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

Available evidence

Three Cochrane reviews informed these guidelines: two addressing the timing of cord clamping for term-born infants and preterm infants, and one referring to positioning of the neonate before cord clamping. A recent publication also addresses the importance of the optimal timing of cord clamping for child survival, as part of an integrated package.

Recommendations [1]

From 2012 WHO guidelines on basic newborn resuscitation:

- In newly born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than 1 min after birth (*strong recommendation*).
- When newly born term or preterm babies require positive-pressure ventilation, the cord should be clamped and cut to allow effective ventilation to be performed (*conditional recommendation*).
- Newly born babies who do not breathe spontaneously after thorough drying should be stimulated by rubbing the back 2–3 times before clamping the cord and initiating positive-pressure ventilation (*conditional recommendation*).

From 2012 WHO recommendations for the prevention and treatment of postpartum haemorrhage:

- Late cord clamping (performed approximately 1–3 min after birth) is recommended for all births, while initiating simultaneous essential neonatal care (*strong recommendation*).
- Early umbilical cord clamping (less than 1 min after birth) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation (*strong recommendation*).

In summary:

- Delayed umbilical cord clamping (not earlier than 1 min after birth) is recommended for improved maternal and infant health and nutrition outcomes.

Key remarks

The guideline groups advising WHO on the two guidelines that served as the basis for this compilation discussed several remarks in relation to umbilical cord clamping. Other remarks were made during the revision of this topic by the guideline development group – nutrition actions 2013–2014.

[1] A *strong* recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. Implications of a strong recommendation for patients are that most people in their situation would desire the recommended course of action and only a small proportion would not. Implications for clinicians are that most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care. With regard to policy-makers, a strong recommendation means that it can be adapted as a policy in most situations, and for funding agencies it means the intervention likely represents an appropriate allocation of resources (i.e. large net benefits relative to alternative allocation of resources). A conditional recommendation is one for which the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, although the trade-offs are uncertain. Implications of a conditional recommendation for patients are that while many people in their situation would desire the recommended course of action, a considerable proportion would not. Implications for clinicians are that they should help patients make a decision that is consistent with their values. With regard to policy-makers, a conditional recommendation means that there is a need for substantial debate and involvement from stakeholders before considering the adoption of the recommendation, and for funding agencies it means that the intervention may not represent an appropriate allocation of resources (i.e. alternative uses of resources may produce greater benefits).

- The evidence base for recommendations on the optimal timing of umbilical cord clamping for the prevention of postpartum haemorrhage includes both vaginal and caesarean births. The WHO guideline development group considered this recommendation to be equally important for caesarean sections.
- Delayed umbilical cord clamping should be performed during the provision of essential neonatal care.
- Recommendations for the optimal timing of umbilical cord clamping apply equally to preterm and term births. The guideline development group considered the benefits of delayed cord clamping for preterm infants to be particularly important.
- Some health professionals providing care for an HIV positive pregnant woman and/or working in high HIV prevalent settings have expressed concern regarding delayed cord clamping as part of the management of the third stage of labour. These professionals are concerned that, during placental separation, a partially detached placenta could be exposed to maternal blood and this could lead to a micro-transfusion of maternal blood to the baby. The evidence shows that the benefits of delaying cord clamping for 1-3 minute outweighs the risks of transmission of HIV. HIV testing should be offered intrapartum, if not already done. WHO recommends that all HIV positive pregnant and breastfeeding women and their infants should receive appropriate antiretroviral (ARV) drugs to prevent mother to child transmission of HIV. Thus, the proven benefits of at least a 1–3 minute delay in clamping the cord outweigh the theoretical, and unproven, harms. Delayed cord clamping is recommended even among women living with HIV or women with unknown HIV status. HIV status should be ascertained at birth, if not already known, and HIV positive women and infants should receive the appropriate ARV drugs.
- Delayed umbilical cord clamping should not be confused with milking of the cord. The terms are not necessarily synonymous (milking refers to physically expressing blood from the umbilical cord). There are various recent studies assessing the effect of cord milking, practised at different times after birth, with a variety of "milking" times, associated with early or delayed cord clamping. These studies need further analysis, as cord milking has been proposed as an alternative to delayed cord clamping, especially for preterm infants
- The WHO guideline development group considered that the package of active management of the third stage of labour includes a primary intervention: the use of a uterotonic drug. In the context of oxytocin use, controlled cord traction may add a small benefit, while uterine massage may add no benefit for the prevention of postpartum haemorrhage. Early cord clamping is generally contraindicated.
- Clamping "not earlier than one minute" should be understood as the lower limit period supported by published evidence. *WHO recommendations for the prevention and treatment of postpartum haemorrhage* recommend that the umbilical cord should not be clamped earlier than is necessary for applying cord traction to reduce post-partum haemorrhage and speed expulsion of the placenta, which the guideline development group clarified would normally take around 3 min.
- For basic newborn resuscitation, if there is experience in providing effective positive-pressure ventilation without cutting the umbilical cord, ventilation can be initiated before cutting the cord.

Research priorities

The WHO guideline development group – nutrition actions 2013–2014 identified several research priorities to improve the body of evidence on the benefits or harms of this intervention, at the basic, epidemiological and programmatic levels.

Scope and purpose

This guideline provides global, evidence-informed recommendations on optimal timing of umbilical cord clamping as a public health intervention for the purpose of improving maternal and infant health and nutrition outcomes. It is a derivative product from current WHO recommendations on cord clamping for preventing postpartum haemorrhage in the mother *(1)* and reducing the need for blood transfusions and increasing body iron stores in the infant, as part of the recommendations for basic newborn resuscitation *(2)*. The above-mentioned guidelines followed the procedures for evidence-informed guideline development as described in the *WHO handbook for guideline development (3)*.

This guideline will help Members States and their partners in their efforts to make informed decisions on the appropriate health and nutrition actions to achieve the Millennium Development Goals (MDGs), in particular, reduction of child mortality (MDG 4) and improvement of maternal health (MDG 5). It will also support Member States in their efforts to achieve global targets of the *Comprehensive implementation plan on maternal, infant and young child nutrition (4)*. The guideline is intended for a wide audience, including policy-makers; their expert advisers; technical and programme staff at organizations involved in the design, implementation and scaling-up of nutrition actions for public health; and health staff providing care to mothers and their infants.

This document presents a summary of the key recommendations and their supporting evidence. They are summarized from three existing documents: *WHO Guidelines on basic newborn resuscitation (2)*, *WHO recommendations for the prevention and treatment of postpartum haemorrhage (1)*, and *Beyond survival: integrated delivery care practices for long-term maternal and infant nutrition, health and development (5)*. Further details of the evidence base are provided in documents listed in the reference section.

Background

The optimal timing of umbilical cord clamping has been debated in the scientific literature for over a century. "Early" cord clamping is generally carried out in the first 60 seconds after birth (generally within the first 15–30 seconds), whereas "delayed" umbilical cord clamping is carried out more than 1 min after the birth or when cord pulsation has ceased *(5)*. In the early 19th century, the English physician, Erasmus Darwin mentioned "another thing very injurious to the child is the tying and cutting of the navel string too soon, which should always be left till the child has not only repeatedly breathed but till all pulsation in the cord ceases. As otherwise the child is much weaker" *(6, 7)*. However, the timing of cord clamping continues to vary according to clinical policy and practice, though surveys of cord clamping practices in a variety of settings and countries indicate that early cord clamping is more frequently practised *(8, 9)*.

There is growing evidence that delayed cord clamping is beneficial and can improve the infant's iron status for up to 6 months after birth. For the first few minutes after birth, there is still circulation from the placenta to the infant. Waiting to clamp the umbilical cord for 2–3 min, or until cord pulsations cease, allows a physiological transfer of placental blood to the infant (the process referred to as "placental transfusion"), the majority of which occurs within 3 min. This placental transfusion provides sufficient iron reserves for the first 6–8 months of life, preventing or delaying the development of iron deficiency until other interventions –such as the use of iron-fortified foods– can be implemented.

Delayed umbilical cord clamping may be particularly relevant for infants living in low-resource settings with less access to iron-rich foods and thus greater risk of anaemia *(10)*. Anaemia, defined as haemoglobin concentration below established cut-off levels *(11)*, is a widespread public health problem with major consequences for human health, affecting and hindering social and economic development. It is estimated that globally 273 million children under 5 years of age were anaemic in 2011, and about 42% of these cases are attributable to iron deficiency *(12)*. Children are particularly vulnerable to iron deficiency anaemia because of their increased iron requirements during periods of rapid growth, especially in the first 2 years of life. Children with iron deficiency are more likely to have delayed psychomotor development, and when they reach school age they are more likely to have impaired performance in tests of language skills, motor skills, and coordination, equivalent to a 5–10-point deficit in intelligence quotient. Both epidemiological and experimental data suggest that when these impairments occur at an early age, they may be irreversible, even after repletion of iron stores, thus reinforcing the importance of approaches (such as delayed cord clamping) that can prevent this condition *(13)*.

The optimal timing of umbilical cord clamping has been previously addressed as part of other perinatal care protocols and guidelines for both the mother and neonate. Postpartum haemorrhage (defined as a blood loss of 500 mL or more within 24 hours after birth) affects approximately 2% of all women who give birth. It is associated with nearly one quarter of all maternal deaths globally, and is also the leading cause of maternal mortality in most low-income countries, as well as a significant contributor to severe maternal morbidity and long-term disability *(1)*. In the past, protocols for the prevention of postpartum haemorrhage (through a package of interventions known as "active management of the third stage of labour") included early cord clamping. It was believed that early cord clamping led to a reduced risk of postpartum haemorrhage and it was thus practised as part of active management of the third stage of labour *(14)*. However, those protocols have since been revised to recommend delayed umbilical cord clamping *(1)*. Thus, analysis of the timing of umbilical cord clamping in relation to postpartum haemorrhage is considered important.

The timing of umbilical cord clamping is also relevant to neonatal resuscitation practices. About one quarter of all neonatal deaths globally are caused by birth asphyxia, defined simply as the failure to initiate and sustain breathing at birth *(15)*. Effective resuscitation at birth can prevent a large proportion of these deaths. The need for clinical guidelines on basic neonatal resuscitation, suitable for settings with limited resources, is universally recognized and WHO has thus published *Guidelines on basic newborn resuscitation (2)*. In many settings, immediate clamping and cutting of the umbilical cord is needed in order to begin resuscitation protocols for the infant, largely due to the location of resuscitation equipment in the delivery room that requires transfer of the neonate. Whether resuscitation with the cord intact is beneficial is an unanswered question, though recent research has shown that it is a feasible practice, at least in some settings *(16)*.

Immediate and long-term benefits of delayed umbilical cord clamping for infants and mothers, based on the results of randomized controlled trials and other type of studies, are summarized in Table 1.

Table 1. Summary of immediate and long-term benefits of delayed umbilical cord clamping for infants (term, preterm/low birth weight) and mothers from individual studies

Immediate benefits			Long-term benefits	
Preterm/low-birth-weight infants	**Full-term infants**	**Mothers**	**Preterm/low-birth-weight infants**	**Full-term infants**
Decreases risk of: • intraventricular haemorrhage • necrotizing enterocolitis • late-onset sepsis	Provides adequate blood volume and birth iron stores	No effect on maternal bleeding or length of the third stage of labour	Increases haemoglobin at 10 weeks of age	Improves haematological status (haemoglobin and haematocrit) at 2–4 months of age
Decreases need for: • blood transfusions for anaemia or low blood pressure • surfactant • mechanical ventilation Increases: • haematocrit • haemoglobin • blood pressure • cerebral oxygenation • red blood cell flow	Increases: • haematocrit • haemoglobin	Indication from "cord drainage" trials that less blood-filled placenta shortens the third stage of labour and decreases the incidence of retained placenta	May be a benefit to neurodevelopmental outcomes in male infants	Improves iron status up to 6 months of age

Source: reference *(5)*.

This guideline compiles current WHO recommendations on umbilical cord clamping for maternal and infant health outcomes, in preterm and term births *(1, 2)*.

Summary of evidence

Three Cochrane systematic reviews informed these guidelines: one analysed maternal outcomes and neonatal outcomes for term infants with early or delayed cord clamping *(17);* another review addressed outcomes in preterm infants as a result of differences in umbilical cord clamping time and other approaches to affect placental transfusion (e.g. positioning of the infant) *(18);* and a third review addressed outcomes related to the positioning of the neonate before cord clamping *(19)*.

Maternal outcomes

The guideline development group – prevention and treatment of postpartum haemorrhage analysed data from a Cochrane review, which included maternal outcomes, specifically postpartum haemorrhage *(20)*. In this recently updated review, five randomized controlled trials (>2000 women) included postpartum haemorrhage as the outcome in relation to umbilical cord clamping time *(17)*. There were no significant differences in the rates of severe postpartum haemorrhage (>1000 mL) or postpartum haemorrhage (>500 mL) between groups with early or delayed umbilical cord clamping. In addition, no significant effect of umbilical cord clamping time was observed in the trials that evaluated the use of manual removal of the placenta (two trials, 1515 women), the need for blood transfusion (two trials, 1345 women), or the length of the third stage of labour (two trials, 1345 women) *(17)*.

Neonatal outcomes (term and preterm infants)

The guideline development group working on the review of the evidence for basic neonatal resuscitation analysed various studies, including many included in the aforementioned Cochrane reviews on preterm and term infants *(17, 18)*. Since additional studies are included in the most recent versions of these Cochrane reviews, a summary of the evidence is provided next. The guideline development group – neonatal resuscitation recommendations on cord clamping *(2)* discussed the evidence from this review.

Fifteen randomized controlled trials (738 infants) have evaluated the effects of umbilical cord clamping time in preterm neonates born predominantly in high-income countries *(18)*. Outcomes studied among preterm infants included risk of mortality, incidence of necrotizing enterocolitis and intraventricular haemorrhage, need for blood transfusions for anaemia or low blood pressure, and hyperbilirubinemia. No studies in neonates with respiratory depression were identified and few studies measured respiratory outcomes. There was considerable heterogeneity between the included studies in the definition of "late" clamping time (from roughly 30 s to 180 s after birth) and positioning of the infant relative to the placenta or uterus before clamping. There was no difference in risk of mortality between preterm infants with delayed or early umbilical cord clamping (13 studies, 668 infants). Preterm infants with delayed umbilical cord clamping had a lower risk of necrotizing enterocolitis (5 trials, 241 infants) and intraventricular haemorrhage (10 trials, 539 infants). Seven randomized trials (392 infants) looked at the need for blood transfusions for anaemia or low blood pressure among preterm infants; on average, there was approximately a 39% reduction in the need for blood transfusion with delayed umbilical cord clamping. Delayed-clamped infants had significantly higher peak bilirubin concentrations as compared to early-clamped infants, in the seven trials (320 infants) reporting this outcome. There was no significant difference in treatment for jaundice between early- and delayed-clamped infants (three trials, 180 infants), though the treatment criteria probably differed between studies and were not always stated.

Fifteen randomized controlled trials have assessed the effects of umbilical cord clamping time in term infants from low-, middle- and high-income countries *(17)*. Outcomes studied among term infants included neonatal mortality, admission to intensive care, haematological and iron status outcomes at birth and through to 6 months of age, polycythaemia, jaundice, and neurodevelopment. In most trials, early clamping occurred within 15 seconds of birth, while delayed clamping varied between 1 and 5 minutes after delivery, or at the end of umbilical cord pulsations. There was no difference in neonatal mortality (two trials, 241 infants), or rate of admission to intensive care (four trials, 1675 infants) between early- and delayed-clamped infants. Four studies (954 infants) looked at the risk of anaemia at 3–6 months of age among term infants and no significant difference was found in the rates of anaemia between the delayed- and early-clamping groups. Five trials of term infants (1152 infants) measured indicators of iron deficiency at 3–6 months of age. Infants with delayed clamping were significantly less likely to have iron deficiency than early-clamped infants, though there was high heterogeneity in this outcome, probably because of different measures/definitions of iron deficiency, as well as the age at which it was assessed. Five trials (1025 infants) reported the effect of timing of umbilical cord clamping on the incidence of polycythaemia among term infants, with no difference between delayed and early umbilical cord clamping. Seven randomized controlled trials (2324 infants) examined the risk of receiving phototherapy for hyperbilirubinaemia following delayed umbilical cord clamping in term neonates. In the majority of the studies, the criteria used for phototherapy were not strictly defined. Delayed-clamped infants were significantly more likely to require phototherapy for jaundice, with a risk difference of <2% between early- and delayed-clamped infants. Only one study (365 infants) evaluated neurodevelopment in term infants, and found no significant effect of umbilical cord clamping time on the measures assessed at 4 months of age.

There were no randomized trials meeting the inclusion criteria set for the Cochrane review assessing alternative positions for the baby immediately at birth before clamping the umbilical cord (e.g. placed on the mother's abdomen versus held at the level of the vagina) (*19*). The criteria were set with the purpose of assessing whether gravity influences placental transfusion at vaginal and caesarean births. Since publication of this review in 2010, a multi-centre randomized controlled trial compared the amount of placental transfusion when the infant was placed on the mother's abdomen versus held at the level of the mother's vagina when delayed umbilical cord clamping occurred *(21)*. The authors of the study reported that the position of the infant did not significantly affect the amount of blood transferred to the infant with delayed clamping.

The International Clinical Trials Registry Platform (ICTRP) *(22)* and Clinical Trials Registry *(23)* were searched (17 September 2014) for any ongoing or planned studies, using the search terms "umbilical cord clamping" and "umbilical cord milking". Details of ongoing trials are presented in Annex 1. Duplicates were removed and completed studies were excluded. Twenty-six ongoing trials on cord clamping were identified. Sixteen of the trials propose to investigate the effect of delayed umbilical cord clamping on preterm infants, the majority of which are being conducted in the United States of America. In seven studies of preterm infants, placental transfusion will be made by milking the umbilical cord; three of these trials will aim to compare milking with delayed cord clamping. One trial of preterm infants aims to determine the combined effects of delayed cord clamping and neonatal resuscitation on placental transfusion. Ten studies on the effects of cord clamping time in term infants are planned or ongoing. One study aims to compare umbilical cord milking to delayed clamping, and two studies aim to look at neurodevelopment outcomes between early- and delayed-clamped infants. Two studies of term infants are investigating the effects of delayed clamping in infants born by caesarean section. The majority of the ongoing trials are expected to be finalized by 2016.

Recommendations[1]

From 2012 WHO guidelines on basic newborn resuscitation:

- In newly born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than 1 min after birth (*strong recommendation*).
- When newly born term or preterm babies require positive-pressure ventilation, the cord should be clamped and cut to allow effective ventilation to be performed (*conditional recommendation*).
- Newly born babies who do not breathe spontaneously after thorough drying should be stimulated by rubbing the back 2–3 times before clamping the cord and initiating positive-pressure ventilation (*conditional recommendation*).

From 2012 WHO recommendations for the prevention and treatment of postpartum haemorrhage:

- Late cord clamping (performed approximately 1–3 min after birth) is recommended for all births, while initiating simultaneous essential neonatal care (*strong recommendation*).
- Early umbilical cord clamping (less than 1 min after birth) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation (*strong recommendation*).

In summary:

- Delayed umbilical cord clamping (not earlier than 1 min after birth) is recommended for improved maternal and infant health and nutrition outcomes.

Remarks

- The evidence base for recommendations on the optimal timing of umbilical cord clamping for the prevention of postpartum haemorrhage includes both vaginal and caesarean births. The WHO guideline development group considered this recommendation to be equally important for caesarean sections.
- Delayed umbilical cord clamping should be performed during the provision of essential neonatal care.
- The recommendations for the optimal timing of umbilical cord clamping apply equally to preterm and term births. The guideline development group considered the benefits of delayed clamping for preterm infants to be particularly important.

[1] A *strong* recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. Implications of a strong recommendation for patients are that most people in their situation would desire the recommended course of action and only a small proportion would not. Implications for clinicians are that most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care. With regard to policy-makers, a strong recommendation means that it can be adapted as a policy in most situations, and for funding agencies it means the intervention likely represents an appropriate allocation of resources (i.e. large net benefits relative to alternative allocation of resources). A conditional recommendation is one for which the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, although the trade-offs are uncertain. Implications of a conditional recommendation for patients are that while many people in their situation would desire the recommended course of action, a considerable proportion would not. Implications for clinicians are that they should help patients make a decision that is consistent with their values. With regard to policy-makers, a conditional recommendation means that there is a need for substantial debate and involvement from stakeholders before considering the adoption of the recommendation, and for funding agencies it means that the intervention may not represent an appropriate allocation of resources (i.e. alternative uses of resources may produce greater benefits).

- Some health professionals providing care for an HIV positive pregnant woman and/or working in high HIV prevalent settings have expressed concern regarding delayed cord clamping as part of the management of the third stage of labour. These professionals are concerned that, during placental separation, a partially detached placenta could be exposed to maternal blood and this could lead to a micro-transfusion of maternal blood to the baby. The evidence shows that the benefits of delaying cord clamping for 1-3 minute outweighs the risks of transmission of HIV. HIV testing should be offered intrapartum, if not already done. WHO recommends that all HIV positive pregnant and breastfeeding women and their infants should receive appropriate antiretroviral (ARV) drugs to prevent mother to child transmission of HIV. Thus, the proven benefits of at least a 1–3 minute delay in clamping the cord outweigh the theoretical, and unproven, harms. Delayed cord clamping is recommended even among women living with HIV or women with unknown HIV status. HIV status should be ascertained at birth, if not already known, and HIV positive women and infants should receive the appropriate ARV drugs *(24)*.
- Delayed umbilical cord clamping should not be confused with milking of the cord. The terms are not necessarily synonymous (milking refers to expression of blood from the umbilical cord). There are various recent studies assessing the effect of cord milking, practised at different times after birth, with a variety of "milking" times, associated with early or delayed cord clamping. These studies need further analysis, as cord milking has been proposed as an alternative to delayed cord clamping, especially for preterm infants *(25–29)*.
- The WHO guideline development group considered that the package of active management of the third stage of labour includes a primary intervention: the use of a uterotonic drug. In the context of oxytocin use, controlled cord traction may add a small benefit, while uterine massage may add no benefit for the prevention of postpartum haemorrhage. Early umbilical cord clamping is generally contraindicated.
- "Not earlier than one minute" should be understood as the lower limit supported by published evidence. *WHO recommendations for the prevention of postpartum haemorrhage (1)* recommend that the umbilical cord should not be clamped earlier than is necessary for applying cord traction, which the guideline development group clarified would normally take around 3 min.
- For basic neonatal resuscitation, if there is experience in providing effective positive-pressure ventilation without cutting the umbilical cord, ventilation can be initiated before cutting the cord.

Implications for future research

Discussions with the members of the WHO guideline development group – nutrition actions 2013–2014 and the external review group highlighted the limited evidence available, and discussed the following research gaps:

- the optimal time for umbilical cord clamping in the context of physiologic and active management of the third stage of labour;
- the appropriate time to administer oxytocin for the prevention of postpartum haemorrhage, relative to umbilical cord clamping and placental delivery (i.e. before/after cord clamping, before/after placenta delivery);
- the best time to clamp the umbilical cord in term and preterm babies who start breathing on their own within the first minute after birth (1, 2, 3, 4 or 5 minutes, or when the cord becomes flat), after a vaginal delivery or a caesarean section;
- the risk of serious hyperbilirubinaemia associated with delayed umbilical cord clamping.

Additionally, the following areas of research in relation to cord clamping are suggested:

- the magnitude of the benefits from enhanced placental stem cell transfusion by delaying umbilical cord clamping;
- potential conflict of the practice of delayed umbilical cord clamping and collection of cord blood for stem cell banking, including conflicts due to cultural and social factors in certains settings and for some population groups;
- differences in the practice for deliveries in health-care settings and home deliveries;
- analysis of costs related to delayed umbilical cord clamping;
- the feasibility of neonatal resuscitation performed with the umbilical cord intact;
- outcomes of neonatal resuscitation performed with the umbilical cord intact.

Dissemination, adaptation, implementation, monitoring and ethical considerations

Dissemination

The current guideline will be disseminated through electronic media such as slide presentations, CD-ROMs and the World Wide Web, through either the WHO nutrition website *(30)* mailing lists, social media, the or the WHO e-Library of Evidence for Nutrition Actions (eLENA) *(31)*. eLENA compiles and displays WHO guidelines related to nutrition, along with complementary documents such as systematic reviews and other evidence that informed the guidelines; biological and behavioural rationales; and additional resources produced by Member States and global partners. In addition, the guideline will be disseminated through a broad network of international partners, including WHO country and regional offices, ministries of health, WHO collaborating centres, universities, other United Nations agencies and nongovernmental organizations. It will also be published in the WHO Reproductive Health Library *(32)*.

Particular attention will be given to improving access to these guidelines for stakeholders that face more or specific barriers in access to information, for example, rural health workers, such as community midwives or traditional midwives, who provide care at births in many low-income countries or in highly isolated communities where transport barriers may impede equitable access to professional health-care settings. Births occurring in such settings are more likely to involve women and infants at higher risk of iron deficiency and other micronutrient deficiencies; hence, it is important to guarantee that dissemination of these guidelines reaches these population groups and health workers. Opportunities for dissemination through pre- and in-service training should be identified for relevant health care providers at various levels.

Adaptation and implementation

As this is a global guideline, it should be adapted to the context of each Member State. Prior to implementation, a public health programme that includes optimal timing of cord clamping should have well-defined objectives that take into account available resources, existing policies, suitable delivery platforms, communication channels, and potential stakeholders. Ideally, it should be implemented as part of an integrated programme for childbirth and postnatal care. In areas where there is a shortage of health-care workers, task shifting should be considered, whereby the health-care workers are trained and retrained and there is a redistribution of tasks between health-care workers as needed *(33, 34)*. By reorganizing the

existing workforce, task shifting may allow for more effective use of existing human resources. Adaptations should be reflected in facility-based standard operating procedures and available monitoring systems.

To ensure that WHO global guidelines and other evidence-informed recommendations for nutrition interventions are better implemented in low- and middle-income countries, the Department of Nutrition for Health and Development works with the WHO Evidence-Informed Policy Network (EVIPNet) programme *(35)*. EVIPNet promotes partnerships at country level between policy-makers, researchers and civil society, to facilitate policy development and implementation through use of the best available evidence.

Every country has its own particular reproductive health service, so the successful introduction of evidence-informed policies related to delayed cord clamping into national programmes and health care services also depends on the development or revision of existing policy, legal, and monitoring and evaluation frameworks *(1)*. The adaptation of this guideline might be necessary to ensure its applicability to the regional, national or sub-national context, especially in large countries. Identification of areas for advocacy for changes in laws and policies should also be considered.

These guidelines entail certain practices that might be enthusiastically received by health workers, women and families across regions of the world, and population groups in each society. However, they may also challenge long-time assumed beliefs, practices or established authorities in certain communities, which could create resistance to change or to adopting new recommendations. Therefore, any adoption and adaptation of these recommendations at country level and within-country level should bear in mind the following series of key aspects that enhance implementation and scale-up.

Particular attention should be given to the *acceptability* of the recommendation for the target population (health workers at different levels of the system and women/families). Delayed umbilical cord clamping may challenge certain values or practices; hence, information to these stakeholders must be carried out in a manner that makes these recommendations acceptable. In this sense, the *appropriateness* of delayed umbilical cord clamping must be fully explained to the target population (health workers and women/families), emphasizing the relevance and the benefits of the intervention, and it must be done in a fashion that is culturally appropriate and understandable. Sometimes, evidence-informed and proven interventions fail to be adopted by the population because issues of acceptability and appropriateness are not taken into account during implementation.

Moreover, linking the implementation of these recommendations with other intersectoral interventions will benefit the *sustainability* and scale-up of delayed umbilical cord clamping. For instance, the *empowerment* of women in terms of health literacy and self-care for their health will benefit both women themselves and neonates. Information about delayed umbilical cord clamping should be provided to future mothers, as part of comprehensive antenatal care actions.

This is especially important in low- and middle-income settings, where those who are better-off are usually more likely to receive early benefit from health innovations that take time to scale up.

Another element that enhances implementation and scale-up is monitoring and data collection. No actions tackling health inequities can be further sustained without robust, valuable data. Accordingly, monitoring the practice of delayed umbilical cord clamping is key to identifying gaps and barriers hindering scale-up and sustainability. Identifying where delayed cord clamping is practised and where it is not preventing widening of unequal distributions of the benefits of health innovations. Currently, there is not a common framework for monitoring the application of optimally timed cord clamping . Therefore, any monitoring framework put in place as part of a programme should acknowledge and be adapted to the different settings in which women deliver (hospital, health facility, home).

Box 1 presents some examples of successful introduction of changes to cord-clamping practice.

Box 1. Stories of success

A study was carried out to investigate the effect of a two-component intervention, consisting of a 3-day workshop and a hospital directive on changing hospital practice from early to delayed umbilical cord clamping, at Hospital Iquitos "Cesar Garayar Garcia" in the Peruvian Amazon *(36)*. The researchers approached and enrolled mothers arriving at the hospital in labour during a 2-week period before and after the intervention. The authors calculated the sample size of mother–infant pairs, to measure the effect of a change in practice on infant anaemia at 4 months of age. Pre- and post-intervention groups were comparable on all characteristics except gestational age and the proportion with a nuchal cord (when the cord is wrapped around the neonate's neck) at birth. The percentage of preterm deliveries was not significantly different between pre- and post-intervention groups. The proportion of births in which the umbilical cord clamping timing was ≥1 min increased from 39.3% pre-intervention to 85.7% post-intervention, showing a change in behaviour among staff. The authors acknowledged that one limitation of their study was the presence of the research team in the delivery room, which could have affected the practice of the staff. The follow-up of the mother–infant pairs showed no effect of time of umbilical cord clamping on infant anaemia status at 4 and 8 months of age in univariate analysis. Multivariate analyses, however, demonstrated a clinically and statistically significant interaction of maternal anaemia, time of umbilical cord clamping and infant anaemia. The adjusted odds of developing anaemia among infants born to anaemic mothers was 40% lower at 4 months of age and 60% lower at 8 months of age for each minute that clamping was delayed *(37)*.

Monitoring and evaluation of guideline implementation

A plan for monitoring and evaluation with appropriate indicators is encouraged at all stages. The impact of this guideline can be evaluated within countries (i.e. monitoring and evaluation of the programmes implemented at national or regional scale) and across countries (i.e. adoption and adaptation of the guideline globally). Monitoring is also essential for improving equity in access to these interventions and for scale-up. Identification of barriers and implementation bottlenecks are two of the multiple benefits of appropriate monitoring.

For evaluation at the global level, the WHO Department of Nutrition for Health and Development has developed a centralized platform for sharing information on nutrition actions in public health practice implemented around the world. By sharing programmatic details, specific country adaptations and lessons learnt, this platform will provide examples of how guidelines are being translated into actions. The Global database on the Implementation of Nutrition Actions (GINA) *(38)* provides valuable information on the implementation of numerous nutrition policies and interventions. The use of GINA has grown steadily since its launch in November 2012.

Ethical considerations

Ethics refers to "standards of right and wrong that prescribe what humans ought to do, usually in terms of rights, obligations, benefits to society [and] fairness", and to "the study and development of ethical standards" *(39)*. Therefore, being ethical in difficult situations is challenging across professions, work fields and countries. Despite this difficulty, ethics is central to science, research, policy-making and implementation. Every field of human action is subject to facing ethical challenges.

Ethics is not the same as rights. This distinction is of massive importance. Rights are ethically informed and based, and they can be claimed via the different legal instruments set out to contain and develop the various rights frameworks. Ethical standards are not legal instruments, but a set of principles that serve as guidance on what is right and wrong, and on how to act for the benefit of oneself and others. Four principles constitute the most widely accepted framework for ethics in

medicine, and are used in other health-related professional fields *(40)*: (i) respect for autonomy; (ii) beneficence; (iii) non-maleficence; and (iv) justice.[1]

Legislation or regulations specifying the rights, entitlements and responsibilities of patients, health professionals and health-care institutions should be taken into account in the practice of delayed umbilical cord clamping. In this context, Member States should specifically consider: (i) patients' right to be fully informed before any medical intervention; (ii) patients' right to be fully informed about the potential risks and benefits of this intervention (e.g. jaundice), as well as alternatives to the proposed intervention, including the effect of non-treatment; and (iii) patients' right to self-determination, including the right to refuse or to halt the intervention *(41, 42)*. Social rights in health care relate to the government's and other national public bodies' obligation to undertake or enforce provision of health care for the whole population. In this particular case, patients have the right to benefit from health services and interventions, without discrimination and according to the national financial, human and material resources available *(41)*.

As with any guideline, the recommendations herein should be the basis for interventions targeted at specific population groups, which in this case is pregnant women about to give birth and neonates. The progressive implementation of delayed umbilical cord clamping (as the optimal time of umbilical cord clamping) may entail ethical considerations that need to be properly addressed by health-care workers and decision-makers. By using the appropriate ethical framework (see the four principles above), the potential ethical challenges that may arise during the implementation of this recommendation are more likely to be appropriately handled.

Ethically challenging situations are frequently specific and contextual, but some situations that may arise include, for example, doubts or conflicts arising as a result of the increasing practice of collecting cord blood. Although delayed umbilical cord clamping should not alter or interfere with collection of cord blood *(47)*, misinformation or doubts on the part of the mother or the parents, or of delivery health workers, could lead to believing the opposite or believing that a choice should be made. Moreover, the recruitment of pregnant women for for-profit umbilical cord blood banking should not imply a disregard for delayed cord clamping for the neonate and mother whose cord blood will be collected. Health-care professionals should disclose this situation during the consent procedure and at all times. Furthermore, in some cases, donations of cord blood from population groups that are traditionally discriminated against are less represented in public cord blood banks; this is the case for some ethnic and aboriginal populations *(48)*, whose chances of receiving donations are much lower compared to those of population groups that are usually better-off *(49)*. Traditional practices or long-standing beliefs regarding cord clamping and collection of cord blood that are misinformed, or prevent health benefits for the neonate and the mother (e.g. iron deficiency), must be discussed and averted. Moreover, certain risks, although minimal, may arise from the increased blood transfusion to the neonate (e.g. jaundice). Health services adopting delayed umbilical cord clamping should have in place strategies to identify neonatal jaundice and treat it (e.g. phototherapy). Other ethically challenging situations may arise, owing to doubts about whether delayed umbilical cord clamping and other recommended practices are compatible in situations such as caesarean section, nuchal cord, depressed or asphyxiated infants, or mothers with diabetes or HIV. WHO and PAHO/WHO have addressed these issues and provided guidance *(5)* for health workers and managers to consult, and to inform their decision-making.

If ethical guidance is needed, it is advisable to contact the corresponding body in charge of medical ethics. Health-care institutions, and thus their health-care staff, are usually overseen by an ethics board or committee, whose guidance should be sought.

[1] Respect for autonomy refers to the obligation to respect the autonomy of others in so far as such respect is compatible with equal respect for the autonomy of all those potentially affected. Beneficence refers to the obligation to produce benefit to the person, user or patient, with minimal harm. Non-maleficence refers to producing net benefit over harm (it is important to define whose benefit and whose harm are likely to result from any intervention or action). Beneficence and respect for autonomy interact to enhance empowerment. Non-maleficence refers to those circumstances where there is no moral obligation (or possibility) to produce a benefit, so there is an obligation not to produce any harm. Finally, justice refers to the obligation to act on the basis of fair adjudication between competing claims, such as *(43)* fair distribution of scarce resources (distributive justice), respect for people's rights (rights-based justice) and respect for morally acceptable laws (legal justice). In relation to this principle, the concepts of equality and equity are also important and it should be noted that equality is not the same as justice. In this view, equals must be treated equally, but those who are unequal can be treated unequally. Equity goes far beyond equality and refers to the need to avoid preventable inequalities *(44, 45)*; therefore equity refers to social justice *(46)*.

Guideline development process

This guideline was developed in accordance with the WHO evidence-informed guideline development procedures, as outlined in the *WHO handbook for guideline development (3)*.

Advisory groups

Two technical groups have worked on the development of the *WHO Recommendations for the prevention and treatment of postpartum haemorrhage (1)*: a small operative group composed of staff from the WHO Departments of Reproductive Health and Research, and Maternal, Newborn, Child and Adolescent Health, as well as two external experts, and a larger group with international stakeholders including midwives, obstetricians, neonatologists, researchers, experts in research synthesis, experts in health-care programmes and consumer representatives (the guideline development group).

The guideline development group that developed the WHO *Guidelines on basic newborn resuscitation (2)* consisted of external experts representing the different WHO regions. All guideline development group members completed a WHO declaration of interest form. Out of 10 members, four declared a potential conflict of interest in the subject matter of the meeting; these professional declarations of interest were considered by the WHO Steering Group, which found that they did not pose a major risk of bias in the recommendations. None of the experts were therefore precluded from participation in the guideline development group meeting convened to formulate recommendations.

The guideline development group – nutrition actions was established for 2013–2014 (see Annex 3). Its role was to advise WHO on the choice of important outcomes for decision-making and on interpretation of the evidence. The WHO guideline development group – nutrition actions includes experts from various WHO expert advisory panels *(50)* and those identified through open calls for specialists, taking into consideration a balanced gender mix, multiple disciplinary areas of expertise, and representation from all WHO regions. Efforts were made to include content experts, methodologists, representatives of potential stakeholders (such as managers and other health professionals involved in the health-care process), and technical staff from WHO and ministries of health from Member States. Representatives of commercial organizations cannot be members of a WHO guideline group.

An external review group peer-reviewed the draft guideline. The WHO Nutrition and SCN mailing lists, which together include over 5500 subscribers, and the WHO nutrition web site *(30)* were used to identify members of the external review group. Additionally, five content experts peer-reviewed the draft guideline and provided technical input.

Scope of the guideline, evidence appraisal and decision-making

The WHO *Guidelines on basic newborn resuscitation (2)* focused on basic resuscitation of neonates born in resource-limited settings in low- and middle-income countries, often with a single skilled birth attendant. The two critical outcomes were mortality and severe morbidity, including hypoxic ischaemic encephalopathy, meconium aspiration syndrome, pulmonary air leaks, intraventricular haemorrhage, severe anaemia, admission to a neonatal intensive care unit, severe hyperbilirubinaemia, and cerebral palsy. A total of 13 population, intervention, control, outcomes (PICO) questions were formulated.

The *WHO recommendations for the prevention and treatment of postpartum haemorrhage (1)* is an update of the *WHO recommendations for the prevention of postpartum haemorrhage* published in 2007 *(51)* and the *WHO guidelines for the management of postpartum haemorrhage and retained placenta* published in 2009 *(50)*. The guideline steering group prepared a list of potential additional questions related to the prevention and

treatment of postpartum haemorrhage, and the guideline development group reviewed and prioritized the draft questions, with the final list including questions from the earlier versions of the guideline, as well as new ones. The guideline steering group also adopted the outcomes used in the 2007 *(51)* and 2009 *(52)* guideline documents; the outcomes were rated on a scale from 1 to 9, with critical outcomes defined as those with an average score of 7 or more.

WHO staff, in collaboration with researchers from other institutions, summarized and appraised the evidence, using the Cochrane methodology for randomized controlled trials *(53, 54)*.[1] For the recommendations on postpartum haemorrhage, evidence summaries were prepared according to the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) approach to assess the overall quality of the evidence *(55, 56)*. GRADE considers: the study design; the limitations of the studies in terms of their conduct and analysis; the consistency of the results across the available studies; the directness (or applicability and external validity) of the evidence with respect to the populations, interventions and settings where the proposed intervention may be used; and the precision of the summary estimate of the effect. Balance worksheets were used during the technical consultation to summarize the values, preferences and judgements made about the strength of the new and revised recommendations.

For the WHO *Guidelines on basic newborn resuscitation (2)*, the Maternal, Newborn, Child and Adolescent Health Department coordinated the efforts to review and synthesize the evidence on the identified priority questions. The analysis of reviews related to many of the identified questions was conducted by the International Liaison Committee on Resuscitation. The WHO process included targeted, systematic reviews of relevant literature, preparation of GRADE profiles, and analysis of the risk–benefits, values and preferences, and costs of implementation.

For this guideline on *Delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes*, the WHO guideline development group – nutrition actions 2013–2014 discussed the evidence and the implementation challenges, as well as the research gaps. The search for ongoing trials was also summarized to ascertain the expected magnitude of the ongoing body of evidence (see Annex 1). The systematic reviews and the GRADE evidence profiles for each of the critical outcomes were presented during the first consultation held on 18–21 February 2013 in Geneva, Switzerland. The research gaps and implementation needs were discussed at a second consultation with the WHO guideline development group – nutrition actions, held on 23–26 June 2014 in Geneva, Switzerland. The procedures for decision-making were established at the beginning of the meeting, including a minimal set of rules for agreement and decision-making documentation. The guideline development group members discussed the research gaps and provided additional comments, using a form designed for this purpose, which also included a section for documenting their views on (i) the desirable and undesirable effects of the intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings. The process was improved with the availability of a predefined link to an online form prepared using a survey software.

Two co-chairs with expertise in managing group processes and interpreting evidence were nominated at the opening of the consultation, and the nomination was approved by the guideline development group. Members of the WHO Secretariat were available at all times to help guide the overall meeting process, but did not vote and did not have veto power.

[1] As part of the Cochrane pre-publication editorial process, reviews are commented on by external peers (an editor and two referees external to the editorial team) and the group's statistical adviser (http://www.cochrane.org/cochrane-reviews) *(53)*. The *Cochrane handbook for systematic reviews of interventions (54)* describes in detail the process of preparing and maintaining Cochrane systematic reviews on the effects of health-care interventions.

Five content experts peer-reviewed the draft guideline. Additionally, a public call for comments on the final draft guideline was released in August 2014 and closed in November 2014. All interested stakeholders were included as part of an external review group and were allowed to comment on the draft guideline only after submitting a signed declaration of interests form. Feedback was received from three stakeholders: Professor Leila Alouane (National Institute of Nutrition and Food Technology, Tunisia), Ms Heather Ferguson (Department of Health, Australia) and Ms Ali MacLean (Micronutrient Initiative; Ottowa, Canada). WHO staff then finalized the guideline and submitted it for clearance by WHO before publication.

Management of competing interests

According to the rules in the WHO *Basic documents (57)*, all experts participating in WHO meetings must declare any interest relevant to the meeting, prior to their participation. The conflicts of interest statements for all guideline group members were reviewed by the responsible technical officer and the relevant departments, before finalization of the group composition and invitation to attend a guideline group meeting. All guideline group members and participants of the guideline development meetings submitted a declaration of interests form, along with their curriculum vitae, before each meeting. In addition, they verbally declared their interests at the beginning of each meeting. The procedures for management of conflicts of interests strictly followed the WHO *Guidelines for declaration of interests (WHO experts) (58)*. It was considered that there were no real or perceived conflicts of interest relevant to this guideline. The potential conflicts of interest declared by the members of the guideline group are summarized below.[1] External experts did not participate in the decision-making process for any of the guidelines.

Dr Luz Maria De-Regil declared that her present employer is an international nongovernmental organization devoted to the improvement of micronutrient status among infants, children and women. These activities are primarily financed by the government of Canada.

Professor Heba El Laithy declared that in 2013 she received compensation from the World Food Programme and the International Food Policy Research Institute (amount: US$ 5000) for work as a data analyst. The data were based on household income surveys where the nutritional status of all household members in terms of food access, food intake, food diversity and related health outcomes were assessed.

Dr Rukhsana Haider is the Chairperson of the Training and Assistance for Health and Nutrition (TAHN) foundation in Dhaka, Bangladesh. She has published articles on peer counselling for exclusive breastfeeding, and is a member of the World Alliance for Breastfeeding Action (WABA) and the Technical Advisory Group for Helen Keller International's Assessment and Research on Child Feeding (ARCH) Project.

Plans for updating the guideline

This guideline will be reviewed in 2024. The Department of Nutrition for Health and Development at the WHO headquarters in Geneva, along with its internal partners, will be responsible for coordinating the guideline update, following the formal procedures of the *WHO handbook for guideline development (3)*. WHO welcomes suggestions regarding additional questions for evaluation of the guideline when it is due for review.

[1] A conflict of interest analysis must be performed whenever WHO relies on the independent advice of an expert in order to take a decision or to provide recommendations to Member States or other stakeholders. The term "conflict of interest" means any interest declared by an expert that may affect or be reasonably perceived to affect the expert's objectivity and independence in providing advice to WHO. WHO's conflict of interest rules are designed to avoid potentially compromising situations that could undermine or otherwise affect the work of the expert, the committee or the activity in which the expert is involved, or WHO as a whole. Consequently, the scope of the inquiry is any interest that could reasonably be perceived to affect the functions that the expert is performing.

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Annex 1. Ongoing trials

Principal investigator and registration date, year	Study title	Status	Country	URL *(last accessed 12 November 2014)*
Preterm infants				
Bienstock J, 2011	Milking the umbilical cord versus immediate clamping in pre-term infants <33 weeks: a randomized controlled trial.	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT01819532
Carbonell M, 2014	Timing of umbilical cord occlusion in premature babies <33 weeks	Not yet recruiting	Spain	http://clinicaltrials.gov/show/NCT02187874
El-Naggar W, 2011	The effect of umbilical cord milking on hemodynamic status of preterm infantsa	Recruiting	Canada	http://clinicaltrials.gov/show/NCT01487187
Frankel R, 2013	Cord milking and activity of the immune system in preterm infants	Not yet recruiting	Israel	http://clinicaltrials.gov/show/NCT02043249
Josephsen J, 2012	Milking the umbilical cord for extreme preterm infants	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT01666847
Katheria A, 2014	Neonatal resuscitation with intact cord (NRIC)	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT02231411
Katheria A, 2013	The PREMOD trial: a randomized controlled trial of umbilical cord milking vs. delayed cord clamping in premature infants	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT01866982
Martin J, 2013	Optimal timing of cord clamping in preterm pregnancy following vaginal or cesarean delivery (CordClamp)	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT01766908
Mercer J, 2009	Protective effects of delayed cord clamping in very low birth weight (VLBW) infants	Active, not recruiting	United States of America	http://clinicaltrials.gov/show/NCT00818220
Murphy KE, 2007	Delayed umbilical cord clamping in infants less than 32 weeks (DUC)	Unknown	United States of America	http://clinicaltrials.gov/show/NCT00562536
Sebastian L, 2010	The Australian Placental Transfusion Study (APTS): should very pre term babies receive a placental blood transfusion at birth via deferring cord clamping versus standard cord clamping procedures? APTS	Recruiting	Australia	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12610000633088
Sebastian L, 2009	Australian Placental Transfusion Pilot Study: investigating standard cord clamping procedures versus three methods of autologous placental blood transfusion in pre-term infants. APTS	Recruiting	Australia	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12609000248268
Smith K, 2014	Delayed clamping and milking the umbilical cord in preterm infants	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT02092103

Principal investigator and registration date, year	Study title	Status	Country	URL *(last accessed 12 November 2014)*
Preterm infants				
Underwood M, 2009	Delayed cord clamping in premature infants	Unknown	United States of America	http://clinicaltrials.gov/show/NCT01018576
Venkataseshan S, 2014	Delayed cord clamping in preterm neonates 30 to 33 weeks: a randomized controlled trial	Recruiting	India	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2014/02/004414
Term infants				
Andersson O, 2014	Effect of timing of umbilical cord clamping on anaemia at 8 and 12 months and later neurodevelopment	Not yet recruiting	Sweden	http://clinicaltrials.gov/show/NCT02222805
Chantry C, 2014	Delayed umbilical cord clamping – C-section pilot	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT02229162
Dawson J, 2014	Cord clamping study: early versus delayed cord clamping and its effects on infant heart rate and oxygen saturation in the first minutes after birth	Not yet recruiting	Australia	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12614000253606
Goonewardene M, 2013	Effects of early versus delayed umbilical cord clamping during ante-partum lower segment caesarean section on placental delivery and post operative blood loss: a randomized controlled trial	Recruiting	Sri Lanka	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=SLCTR/2013/003
Katheria A, 2014	Changes in cardiac output during delayed umbilical cord clamping	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT02195037
Mercer J, 2012	Infant brain study (IBS)	Recruiting	United States of America	http://clinicaltrials.gov/show/NCT01620008
Morris, P, 2012	Effect of delayed cord clamping on the haemoglobin levels of term newborn Aboriginal infants from remote Aboriginal communities: a pilot randomized controlled trial. ACDC	Not yet recruiting	Australia	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12612000071820
Ping HS, 2009	Immediate vs delayed cord clamping on newborns (no)	Unknown	China	http://clinicaltrials.gov/show/NCT01029496
Sharkey D, 2013	Physiological effects of deferred cord clamping DoppCord	Recruiting	United Kingdom of Great Britain and Northern Ireland	http://clinicaltrials.gov/show/NCT01864421
Upadhyay A, 2013	To compare the effect of umbilical cord milking and delayed cord clamping on haematological parameters in term neonates	Recruiting	India	http://apps.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2013/01/003323

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