

**Guidelines on**

# **BASIC NEWBORN RESUSCITATION**

**2012**

*Avec résumé d'orientation en Français*



**World Health  
Organization**

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## ACRONYMS

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CI	Confidence interval
ES	Effect size
GDG	Guidelines Development Group
GRADE	The system for grading the quality of evidence and the strength of recommendations
HIE	Hypoxic ischaemic encephalopathy
HQ	Headquarters
ILCOR	International Liaison Committee on Resuscitation
MAS	Meconium aspiration syndrome
MCA	Department of Maternal, Newborn, Child and Adolescent Health
MD	Mean difference
NGO	Nongovernmental organization
NICU	Neonatal intensive care unit
NMR	Neonatal mortality rate
PICO	Population/Patient group, Intervention, Comparator and Outcome
PPV	Positive-pressure ventilation
RCT	Randomized controlled trial
RR	Relative risk
SpO <sub>2</sub>	Oxygen saturation
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development

## EXECUTIVE SUMMARY

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Globally, about one quarter of all neonatal deaths are caused by birth asphyxia. In this document, birth asphyxia is defined simply as the failure to initiate and sustain breathing at birth. Effective resuscitation at birth can prevent a large proportion of these deaths. The need for clinical guidelines on basic newborn resuscitation, suitable for settings with limited resources, is universally recognized. WHO had responded to this need by developing guidelines for this purpose that are contained in the document *Basic newborn resuscitation: a practical guide*. As this document is over a decade old, a process to update the guidelines on basic newborn resuscitation was initiated in 2009.

The International Liaison Committee on Resuscitation (ILCOR) published *Consensus on science and treatment recommendations for neonatal resuscitation* in 2000, 2005 and 2010. Regional resuscitation councils publish guidelines based on the ILCOR consensus; however, these generally are not designed for resource-limited settings, and require the presence of more than one health provider with extensive training as well as advanced technology. The objective of these updated WHO guidelines is to ensure that newborns in resource-limited settings who require resuscitation are effectively resuscitated. These guidelines will inform WHO training and reference materials, such as *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice*; *Essential newborn care course*; *Managing newborn problems: a guide for doctors, nurses and midwives*; and *Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources*. These guidelines will assist programme managers responsible for implementing maternal and child health programmes to develop or adapt national or local guidelines, standards and training materials on newborn care.

The Guideline Development Group considered evidence related to the 13 highest-priority research questions for development of recommendations. For each question, *mortality* and *severe morbidity* were considered to be critical outcomes. Benefits and harms in critical outcomes formed the basis of the recommendations for each question. Studies from low- and middle- income as well as high-income countries were considered for inclusion in evidence reviews. Studies that did not address any of the pre-defined outcomes, were unpublished or were available only as an abstract were excluded. Animal studies were included only when sufficient evidence from human studies was not available. Efforts were made to identify relevant English and non-English language articles. A standardized form was used to extract relevant information from studies. Systematically extracted data included: study identifiers, setting, design, participants, sample size, intervention or exposure, control or comparison group, outcome measures and results. Quality characteristics were also recorded for all studies: allocation concealment or risk of selection bias (observational studies); blinding of intervention or observers, or risk of measurement bias; loss to follow-up; intention to treat analysis or adjustment for confounding factors; and analysis adjusted for cluster randomization (the latter only for cluster-randomized controlled trials). The GRADE approach was used for assessing the quality of evidence and the recommendations (for details, see Methodology section). For each set of studies reporting results for a given outcome, the quality of studies was graded as high, moderate, low or very low.

The strength of a recommendation reflects the degree of confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects. Decisions on these issues were made by the Guidelines Development Group, which met in June 2011, on

the basis of evidence of benefits and harms; quality of evidence; values and preferences of policy-makers, health care providers and parents; and whether costs are qualitatively justifiable relative to benefits in low- and middle- income countries. Each recommendation was graded as *strong* when there was confidence that the benefits clearly outweigh the harms, or *weak* when the benefits probably outweigh the harms, but there was uncertainty about the trade-offs. The resulting recommendations are shown below.

### 2012 WHO Recommendations on Basic Newborn Resuscitation

No.	Recommendation*	Strength of recommendation	Quality of evidence
<b>IMMEDIATE CARE AFTER BIRTH</b>			
1.	In newly-born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than one minute after birth <sup>1</sup> .  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.	<i>Strong</i>  <i>Weak</i>	<i>High to moderate</i>  <i>Guidelines Development Group (GDG) consensus in absence of published evidence</i>
2.	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.	<i>Weak</i>	<i>GDG consensus in absence of published evidence</i>
3.	In neonates born through clear amniotic fluid who start breathing on their own after birth, suctioning of the mouth and nose should not be performed.  In neonates born through clear amniotic fluid who do not start breathing after thorough drying and rubbing the back 2-3 times, suctioning of the mouth and nose should not be done routinely before initiating positive-pressure ventilation. Suctioning should be done only if the mouth or nose is full of secretions.	<i>Strong</i>  <i>Weak</i>	<i>High</i>  <i>GDG consensus in absence of published evidence</i>
4.	In the presence of meconium-stained amniotic fluid, intrapartum suctioning of the mouth and nose at the delivery of the head is not recommended.	<i>Strong</i>	<i>Low</i>
5.	In neonates born through meconium-stained amniotic fluid who start breathing on their own, tracheal suctioning should not be performed.  In neonates born through meconium-stained amniotic	<i>Strong</i>  <i>Weak</i>	<i>Moderate to low</i>  <i>GDG consensus in absence of</i>

<sup>1</sup> "Not earlier than one minute" should be understood as the lower limit supported by published evidence. WHO *Recommendations for the prevention of postpartum haemorrhage* (Fawole B et al. Geneva, WHO, 2007) state that the cord should not be clamped earlier than is necessary for applying cord traction, which the GDG clarified would normally take around 3 minutes.

	<p>fluid who start breathing on their own, suctioning of the mouth or nose is not recommended.</p> <p>In neonates born through meconium-stained amniotic fluid who <b>do not</b> start breathing on their own, tracheal suctioning should be done before initiating positive-pressure ventilation.</p> <p>In neonates born through meconium-stained amniotic fluid who <b>do not</b> start breathing on their own, suctioning of the mouth and nose should be done before initiating positive-pressure ventilation.</p>	<p><i>Weak</i> (in situations where endotracheal intubation is possible)</p> <p><i>Weak</i></p>	<p><i>published evidence</i></p> <p><i>Very low</i></p> <p><i>GDG consensus in absence of published evidence</i></p>
6.	In settings where mechanical equipment to generate negative pressure for suctioning is not available and a newly-born baby requires suctioning, a bulb syringe (single-use or easy to clean) is preferable to a mucous extractor with a trap in which the provider generates suction by aspiration.	<i>Weak</i>	<i>Very low</i>
<b>POSITIVE-PRESSURE VENTILATION</b>			
7.	In newly-born babies who do not start breathing despite thorough drying and additional stimulation, positive-pressure ventilation should be initiated within one minute after birth.	<i>Strong</i>	<i>Very low</i>
8.	In newly-born term or preterm (>32 weeks gestation) babies requiring positive-pressure ventilation, ventilation should be initiated with air.	<i>Strong</i>	<i>Moderate</i>
9.	In newly-born babies requiring positive-pressure ventilation, ventilation should be provided using a self-inflating bag and mask.	<i>Weak</i>	<i>Very low</i>
10.	In newly-born babies requiring positive-pressure ventilation, ventilation should be initiated using a face-mask interface.	<i>Strong</i>	<i>Based on limited availability and lack of experience with nasal cannulae, despite low quality evidence for benefits</i>
11.	In newly-born babies requiring positive-pressure ventilation, adequacy of ventilation should be assessed by measurement of the heart rate after 60 seconds of ventilation with visible chest movements.	<i>Strong</i>	<i>Very low</i>
12.	In newly-born babies who do not start breathing within one minute after birth, priority should be given to providing adequate ventilation rather than to chest compressions.	<i>Strong</i>	<i>Very low</i>
<b>STOPPING RESUSCITATION</b>			
13.	In newly-born babies with no detectable heart rate	<i>Strong</i>	<i>Low</i>

<p>after 10 minutes of effective ventilation, resuscitation should be stopped.</p> <p>In newly-born babies who continue to have a heart rate below 60/minute and no spontaneous breathing after 20 minutes of resuscitation, resuscitation should be stopped.</p>	<p><i>Weak (relevant to resource-limited settings)</i></p>	<p><i>Very low</i></p>
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## RESUMÉ D'ORIENTATION

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Environ un quart de l'ensemble des décès néonataux dans le monde sont causés par une hypoxie à la naissance. Dans ce document, une hypoxie à la naissance est définie simplement comme l'incapacité de commencer à respirer à la naissance et de continuer à le faire de manière pérenne. Une proportion importante de ces décès peuvent être prévenus par une réanimation efficace à la naissance. Disposer de directives cliniques sur les premiers soins de réanimation du nouveau-né adaptées aux situations de ressources limitées est un besoin universellement reconnu. Pour y répondre, l'OMS a élaboré des lignes directrices qui se trouvent dans le document *Premiers soins de réanimation du nouveau-né : guide pratique*. Ce document datant de plus de dix ans, un processus a été mis en route en 2009 pour mettre à jour ces lignes directrices.

L'International Liaison Committee on Resuscitation (ILCOR) a publié en 2000, 2005 et 2010 un document intitulé *Consensus on science and treatment recommendations for neonatal resuscitation* (Consensus sur les données scientifiques et les recommandations en matière de traitement pour la réanimation néonatale). Des conseils régionaux sur la réanimation publient des lignes directrices en s'appuyant sur ce consensus ILCOR. Cependant, ces lignes directrices ne sont généralement pas conçues pour les situations de ressources limitées et exigent la présence de plus d'un agent de santé formé de manière approfondie et de technologies avancées. L'objectif des lignes directrices actualisées de l'OMS décrites dans le présent document est de s'assurer qu'en situation de ressources limitées, les nouveau-nés qui ont besoin d'une réanimation bénéficient d'une réanimation efficace. Ces lignes directrices serviront de base aux matériels de formation et de référence de l'OMS, notamment aux documents suivants : *Soins liés à la grossesse, à l'accouchement et à la période néonatale : guide de pratiques essentielles* ; *Essential newborn care course* (Cours de formation sur les soins essentiels du nouveau-né) ; *Prise en charge des problèmes du nouveau-né : manuel de la sage-femme, de l'infirmière et du médecin* ; et *Soins hospitaliers pédiatriques : prise en charge des affections courantes dans les petits hôpitaux*. Elles aideront les administrateurs de programme responsables de l'exécution des programmes de santé maternelle et infantile à élaborer ou à adapter des directives, des normes et des matériels de formation à usage national ou local sur les soins du nouveau-né.

Afin d'élaborer des recommandations, le Groupe d'élaboration des lignes directrices a pris en considération les données relatives aux 13 questions de recherche présentant le plus haut niveau de priorité. Pour chaque question, la *mortalité* et la *morbidité sévère* ont été considérées comme des résultats essentiels. Pour chacune des questions, les recommandations ont été basées sur les avantages et les dangers pour les résultats essentiels. Les études menées dans les pays à revenu faible ou moyen et dans les pays à revenu élevé ont été prises en considération pour faire partie de l'examen des données. Les études ne traitant pas des résultats prédéfinis, n'ayant pas fait l'objet d'une publication ou uniquement disponibles sous la forme d'un résumé ont été exclues. Les études menées chez l'animal n'ont été retenues que si l'on ne disposait pas de données suffisantes issues d'études menées chez l'homme. Des mesures ont été prises afin d'identifier les articles pertinents publiés en langue anglaise ou dans une autre langue. Un formulaire normalisé a été utilisé pour extraire des études les informations pertinentes. Les données obtenues de manière systématique étaient les suivantes : identificateur de l'étude, cadre, méthodologie, participants, taille de l'échantillon, intervention ou exposition, groupe témoin ou groupe de comparaison, critères de jugement et résultats. Des caractéristiques relatives à la qualité ont également été enregistrées pour chaque étude : dissimulation de l'affectation des sujets aux groupes d'étude ou risque de biais de sélection (études observationnelles) ; mesures pour garantir l'intervention en aveugle ou le travail des observateurs en aveugle ou risque de biais de mesure ; perdus de vue ; analyse selon l'intention de traiter ou ajustement pour tenir compte des facteurs de confusion ; et analyse avec ajustement pour tenir compte de la randomisation en grappe (cette caractéristique ne s'appliquant qu'aux essais contrôlés randomisés en grappes). L'approche GRADE a été utilisée pour évaluer la qualité des données et des recommandations (des informations supplémentaires se trouvent dans la section Méthodologie). Pour

chaque ensemble d'études disposant de résultats pour un critère de jugement donné, un grade a été attribué à la qualité des études (qualité bonne, moyenne, faible ou très faible).

La force d'une recommandation représente le degré de confiance avec lequel les effets souhaités obtenus en suivant cette recommandation l'emportent sur les effets indésirables. Le Groupe d'élaboration des lignes directrices a tranché sur ces questions lors d'une réunion qui s'est tenue en juin 2011. Les décisions ont été prises en se fondant sur les éléments suivants : données relatives aux avantages et aux dangers ; qualité des données ; valeurs et préférences accordées par les responsables de l'élaboration des politiques, les agents de santé et les parents ; et si les coûts étaient justifiés sur le plan qualitatif par rapport aux avantages dans les pays à revenu faible ou moyen. Chaque recommandation a été classée comme étant *forte* s'il pouvait être affirmé avec confiance que les avantages l'emportaient clairement sur les dangers ou comme étant *faible* lorsque les avantages l'emportaient probablement sur les dangers, mais que l'équilibre ne pouvait pas être déterminé avec certitude. Les recommandations qui en découlent sont présentées ci-dessous.

### Recommandations 2012 de l'OMS sur les premiers soins de réanimation du nouveau-né

N°	Recommandation	Force de la recommandation	Qualité des données
<b>SOINS IMMÉDIATS APRÈS LA NAISSANCE</b>			
1.	<p>Chez un nouveau-né à terme ou prématuré qui ne nécessite pas de ventilation en pression positive à la naissance, le cordon doit être clampé au plus tôt une minute après la naissance.<sup>1</sup></p> <p>Si un nouveau-né à terme ou prématuré nécessite une ventilation en pression positive à la naissance, le cordon doit être clampé et coupé pour permettre d'effectuer une ventilation efficace.</p>	<i>Forte</i>	<i>Bonne à moyenne</i>
		<i>Faible</i>	<i>Consensus du Groupe d'élaboration des lignes directrices, en l'absence de données publiées</i>
2.	Un nouveau-né qui ne respire pas spontanément à la naissance après avoir été essuyé doit être stimulé en lui frottant le dos à deux ou trois reprises avant de clamper le cordon et de commencer une ventilation en pression positive.	<i>Faible</i>	<i>Consensus du Groupe d'élaboration des lignes directrices, en l'absence de données publiées</i>
3.	<p>Chez un nouveau-né pour qui le liquide amniotique était clair et qui commence à respirer spontanément après la naissance, il ne faut pas effectuer d'aspiration de la bouche et du nez.</p> <p>Chez un nouveau-né pour qui le liquide amniotique était clair et qui ne commence pas à respirer après avoir été essuyé entièrement et stimulé en lui frottant le dos à deux ou trois reprises, une aspiration de la bouche et du nez ne doit pas être effectuée de manière systématique avant de commencer une ventilation en pression positive. Une aspiration ne doit être effectuée que si le nez ou la bouche est rempli de sécrétions.</p>	<i>Forte</i>	<i>Bonne</i>
		<i>Faible</i>	<i>Consensus du Groupe d'élaboration des lignes directrices, en l'absence de données publiées</i>

<sup>1</sup> « Au plus tôt une minute » doit être considéré comme la limite inférieure sur la base des données publiées. Dans le document *WHO Recommendations for the prevention of postpartum haemorrhage* (Fawole B et al. Genève, OMS, 2007), il est stipulé que le cordon ne doit pas être clampé plus tôt que nécessaire pour réaliser une traction du cordon ; le Groupe d'élaboration des lignes directrices a précisé que cela prend habituellement environ trois minutes.

4.	En présence de liquide amniotique teinté de méconium, il n'est pas recommandé d'effectuer une aspiration per-partum de la bouche et du nez après accouchement de la tête.	<i>Forte</i>	<i>Faible</i>
5.	Chez un nouveau-né pour qui le liquide amniotique était teinté de méconium et qui commence à respirer par lui-même, il ne faut pas effectuer d'aspiration trachéale.  Chez un nouveau-né pour qui le liquide amniotique était teinté de méconium et qui commence à respirer par lui-même, il n'est pas recommandé d'effectuer une aspiration de la bouche et du nez.  Chez un nouveau-né pour qui le liquide amniotique était teinté de méconium et qui <b>ne commence pas</b> à respirer par lui-même, une aspiration trachéale doit être effectuée avant de commencer une ventilation en pression positive.  Chez un nouveau-né pour qui le liquide amniotique était teinté de méconium et qui <b>ne commence pas</b> à respirer spontanément, une aspiration de la bouche et du nez doit être effectuée avant de commencer une ventilation en pression positive.	<i>Forte</i>  <i>Faible</i>  <i>Faible</i> (dans les situations où une intubation endotrachéale est possible)  <i>Faible</i>	<i>Moyenne à faible</i>  <i>Consensus du Groupe d'élaboration des lignes directrices, en l'absence de données publiées</i>  <i>Très faible</i>  <i>Consensus du Groupe d'élaboration des lignes directrices, en l'absence de données publiées</i>
6.	Dans les situations où aucun dispositif mécanique pour obtenir la pression négative nécessaire pour effectuer une aspiration n'est disponible et qu'un nouveau-né a besoin d'une aspiration à la naissance, il est préférable d'utiliser une poire (à usage unique ou facile à nettoyer) à un extracteur de mucosités avec réservoir pour lequel l'aspiration est produite par l'agent de santé.	<i>Faible</i>	<i>Très faible</i>
<b>VENTILATION EN PRESSION POSITIVE</b>			
7.	Chez un nouveau-né qui ne commence pas à respirer à la naissance après avoir été essuyé entièrement et avoir reçu des stimulations supplémentaires, une ventilation en pression positive doit être commencée dans la minute qui suit la naissance.	<i>Forte</i>	<i>Très faible</i>
8.	Chez un nouveau-né à terme ou prématuré (> 32 semaines de gestation) qui nécessite une ventilation en pression positive à la naissance, la ventilation doit être commencée en utilisant de l'air.	<i>Forte</i>	<i>Moyenne</i>
9.	Chez un nouveau-né qui nécessite une ventilation en pression positive à la naissance, la ventilation doit être effectuée en utilisant un insufflateur manuel et un masque.	<i>Faible</i>	<i>Très faible</i>
10.	Chez un nouveau-né qui nécessite une ventilation en pression positive à la naissance, la ventilation doit être commencée en utilisant pour interface un masque.	<i>Forte</i>	<i>Fondée sur la disponibilité réduite de la canule nasale et le manque d'expérience dans son utilisation, malgré l'existence de données de faible qualité sur ses avantages</i>

11.	Chez un nouveau-né qui nécessite une ventilation en pression positive à la naissance, l'efficacité de la ventilation doit être évaluée en mesurant la fréquence cardiaque après 60 secondes de ventilation avec des mouvements thoraciques visibles.	<i>Forte</i>	<i>Très faible</i>
12.	Chez un nouveau-né qui ne commence pas à respirer dans la minute qui suit la naissance, il faut effectuer en priorité une ventilation adéquate plutôt que des compressions thoraciques.	<i>Forte</i>	<i>Très faible</i>
<b>ARRÊT DE LA RÉANIMATION</b>			
13.	Chez un nouveau-né à la naissance pour qui aucun battement cardiaque n'est détectable après 10 minutes de ventilation efficace, la réanimation doit être arrêtée.  Chez un nouveau-né à la naissance qui continue d'avoir un rythme cardiaque inférieur à 60 battements par minute et qui ne présente aucune respiration spontanée après 20 minutes de réanimation, la réanimation doit être arrêtée.	<i>Forte</i>  <i>Faible</i> <i>(pertinente pour les situations de ressources limitées)</i>	<i>Faible</i>  <i>Très faible</i>

## INTRODUCTION AND SCOPE

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About one quarter of all neonatal deaths globally are caused by birth asphyxia<sup>1</sup>. In this document, birth asphyxia is defined simply as the failure to initiate and sustain breathing at birth. Effective resuscitation at birth can prevent a large proportion of these deaths. The need for clinical guidelines on basic newborn resuscitation, suitable for settings with limited resources, is universally recognized. WHO had responded to this need by developing guidelines for this purpose that are contained in the document *Basic newborn resuscitation: a practical guide*<sup>2</sup>. As this document is over a decade old, a process to update the guidelines on basic newborn resuscitation was initiated in 2009.

The International Liaison Committee on Resuscitation (ILCOR) published *Consensus on science and treatment recommendations for neonatal resuscitation* in 2000<sup>3</sup>, 2005<sup>4</sup> and 2010<sup>5</sup>. Regional resuscitation councils publish guidelines based on the ILCOR consensus; however, these guidelines generally are not designed for resource-limited settings, and require the presence of more than one health care provider with extensive training, as well as advanced technology.

The objective of these WHO guidelines is to ensure that newborns in resource-limited settings who require resuscitation are effectively resuscitated. These guidelines will inform WHO training and reference materials such as *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice*<sup>6</sup>; *Essential newborn care course*<sup>7</sup>; *Managing newborn problems: a guide for doctors, nurses and midwives*<sup>8</sup>; and *Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources*<sup>9</sup>. These guidelines will assist programme managers responsible for implementing maternal and child health programmes to develop or adapt national or local guidelines, standards and training materials on newborn care.

### **Target audience**

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<sup>1</sup> About 40% of all under five deaths occurred in the neonatal period in 2008; in the same period asphyxia was the cause of 9% of all under five deaths (WHO. *World health statistics*. Geneva, WHO, 2011).

<sup>2</sup> WHO. *Basic newborn resuscitation: a practical guide*. Geneva, WHO, 1998.

<sup>3</sup> 2000 Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care: international consensus on science, Part 11: Neonatal resuscitation. *Circulation*, 2000, 102(Suppl. I):I343–I358.

<sup>4</sup> 2005 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Part 7: Neonatal resuscitation. *Circulation*, 2005, 112:III-91–III-99.

<sup>5</sup> 2010 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Part 11: Neonatal resuscitation: *Circulation*, 2010, 122(Suppl. 2):S516 –S538.

<sup>6</sup> WHO et al. *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice*. Geneva, WHO, 2006;

<sup>7</sup> WHO. *Essential newborn care course*. Geneva, WHO, 2010.

<sup>8</sup> WHO. *Managing newborn problems: a guide for doctors, nurses and midwives*. Geneva, WHO, 2003.

<sup>9</sup> WHO. *Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources*. Geneva, WHO, 2005.

The primary audience for these guidelines is health professionals who are responsible for attending women in childbirth or for care of the newborn baby immediately after birth, primarily in areas where resources are limited. These health professionals include skilled birth attendants, typically but not limited to midwives, nurse-midwives and auxiliary nurse-midwives who conduct births in primary health care facilities and at home. However, the guidelines are also expected to be used by policy-makers and managers of maternal and child health programmes, health facilities and teaching institutions to set up and maintain maternity and newborn care services. The information in these guidelines will be included in job aids and tools for both pre- and in-service training of health professionals and to improve their knowledge, skills and performance in basic newborn resuscitation.

### ***Population of interest***

The guidelines focus on basic resuscitation of newborns born in resource-limited settings in low- and middle-income countries, often with a single skilled birth attendant.

### ***Critical outcomes***

The two critical outcomes were **mortality** and **severe morbidity** (including hypoxic ischaemic encephalopathy [HIE], meconium aspiration syndrome [MAS], pulmonary air leaks including pneumothorax, intraventricular haemorrhage, severe anaemia, admission to neonatal intensive care unit, severe hyperbilirubinaemia and cerebral palsy). Other important outcomes considered included Apgar scores, onset of spontaneous respiration, need for chest compressions, need for endotracheal intubation, oxygen saturation and duration of hospital stay.

### ***Priority questions***

A total of 13 PICO<sup>1</sup> questions were formulated at a technical consultation on neonatal resuscitation in 2009 for evidence collation and synthesis. This consultation was jointly organized by the Department of Child and Adolescent Health and the Department of Making Pregnancy Safer. The two Departments were subsequently merged to form the Department of Maternal, Newborn, Child and Adolescent Health (MCA). The questions were:

1. In normal or depressed<sup>2</sup> newly-born babies (P), does **late cord clamping** (I) compared with **standard management** (C) improve outcome (O)?
2. In neonates not breathing spontaneously after birth (P), does **additional stimulation** (I) compared with **thorough drying alone** (C) reduce the need for positive-pressure ventilation (PPV) (O)?
3. In depressed neonates with clear amniotic fluid (P), does **suctioning of the mouth and nose** (I) before starting PPV versus **no suctioning** (C) improve outcome (O)?
4. In neonates born through meconium-stained amniotic fluid (P), does **intrapartum oropharyngeal and nasopharyngeal suctioning** at the delivery of the head (I) compared with **no intrapartum suctioning** (C) prevent MAS and mortality (O)?

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<sup>1</sup> PICO: Population/Patient Group, Intervention, Comparator, and Outcome. A PICO question is one that is formulated using the PICO framework, wherein the health care providers ask and answer a series of questions meant to elicit information about their patients and their conditions, interventions that have been undertaken or should be taken, any comparisons between the current treatment and possible alternatives, and outcomes to be desired or achieved.

<sup>2</sup> A "depressed" newborn is a baby not breathing or crying at birth who usually has poor muscle tone and heart rate below 100 beats/minute.

5. In neonates born through meconium-stained amniotic fluid (P), does **oropharyngeal and/or endotracheal suction** (I) compared with **no suctioning of either oropharynx or trachea** (C) prevent MAS and mortality (O)?
6. In neonates who require suction to clear their airways (P), what is the safety and efficacy (O) of different types of **suction devices** (I/C)?
7. In neonates who fail to breathe after birth (P), should **PPV** be **initiated within one minute after birth** if the baby has not started breathing after initial steps of resuscitation (I) as compared to a **later time** (C) for preventing HIE and mortality (O)?
8. In newborns who require resuscitation at birth (P), is PPV with **air** (I) more effective than that with **higher concentrations of oxygen** (C) in reducing subsequent mortality and HIE (O)?
9. In neonates who require PPV (P), does ventilation with a **self-inflating bag and mask** (I) compared with **mouth-to-tube and mask (or mouth-to-mask)** ventilation (C) improve outcome (O)?
10. In neonates receiving PPV (P), does the use of **nasal cannulae** (I) versus **face-mask interface** (C) improve outcome (O)?
11. In neonates who require PPV (P), is **measuring heart rate and chest movements** (I) compared with **chest movements alone** (C) better to assess ventilation (O)?
12. In neonates requiring resuscitation after birth (P), is **PPV** alone (I) as effective as **PPV and chest compressions** (C) in reducing mortality (O)?
13. In neonates who continue to have no heart rate or severe bradycardia despite resuscitation (P), should resuscitation efforts be **stopped after 10 minutes** (I) as opposed to **20 minutes or longer** (C)?

Additionally, the consultation identified the following two questions: *"What maternal history factors predict need for newborn resuscitation at birth?"* and *"What are ethically-justified reasons for not initiating resuscitation in newly-born infants affected by conditions associated with high mortality and morbidity?"* The former question could not be addressed because of the time required in the systematic review on this complex question. In addition, the Guideline Development Group (GDG) at its June 2011 meeting agreed that the question was not critical. A birth attendant needs to be prepared for newborn resuscitation at every birth in any case, as a substantial proportion of newborns who need resuscitation do not have any maternal risk factor. For ethically-justified reasons for not initiating resuscitation, the GDG felt that this situation was very context-specific, so that making a general recommendation would not be appropriate.

## METHODOLOGY

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### Guideline Development Group

The GDG that developed the recommendations and decided on their strength was constituted by the following external experts: Peter Gisore (*African Region*); Jose Luis Díaz-Rossello, Susan Niermeyer, Ana Quiroga and Nalini Singhal (*Region of the Americas*); Vinod K Paul (*South-East Asia Region, participated in the GDG meeting by telephone and email*); Ola Didrik Saugstad and Fabio Uxa (*European Region*); María Asunción Silvestre and Takahiro Sugiura (*Western Pacific Region*).

All GDG members completed a WHO Declaration of Interest form. Out of the ten members, four declared a potential conflict of interest in the subject matter of the meeting, as follows:

1. Susan Niermeyer was the consulting editor for the publication of the American Academy of Pediatrics, *Helping Babies Breathe*, from 2008-2011 and received a significant remuneration for this consultancy. She is an author of worksheets used for the 2000, 2005 and 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations of ILCOR.
2. Ola Didrik Saugstad has applied for a patent on metabolic markers for birth asphyxia, applicable in well-resourced settings (not for basic newborn resuscitation) and has received significant grants from public funds (Norwegian Research Council and Oslo University Hospital) and a private company (Laerdal) for research on birth asphyxia. He has not received any personal remuneration for any of the above.
3. Nalini Singhal is the author of worksheets for the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations of ILCOR, serves on the editorial board for the publication of the American Academy of Pediatrics, *Helping Babies Breathe*, and leads the educational evaluation of that training course. She has not received any remuneration for this work.
4. Vinod K Paul has provided technical advice related to the topic of the meeting to the Government of India and academic bodies. He has not received any remuneration for this work.

These largely professional declarations of interest were considered by the WHO Steering Group, who found that they did not pose a major risk of bias in recommendations. None of the above experts were therefore precluded from participation in the GDG meeting to formulate recommendations.

The WHO Steering Group consisted of the following staff members: Maternal, Newborn, Child and Adolescent Health (MCA)<sup>1</sup>: Rajiv Bahl, José Martines, Matthews Mathai, Severin von Xylander and Jelka Zupan; Reproductive Health and Research: Metin Gulmezoglu and Mario Merialdi.

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<sup>1</sup> The Departments of Child and Adolescent Health and Development (CAH) and Making Pregnancy Safer (MPS) were merged in 2010 as the Department for Maternal, Newborn, Child and Adolescent Health.

The following external experts reviewed the research questions and/or draft guidelines: Uwe Ewald, Pavitra Mohan, Yana Richens, Frederik Were and David Woods.

### *EVIDENCE RETRIEVAL AND SYNTHESIS PROCESS*

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Throughout 2010, MCA coordinated efforts to review and synthesize the evidence on the identified priority questions. The availability of reviews related to many of the identified questions conducted by ILCOR was helpful.<sup>1</sup> The WHO process included targeted, systematic reviews of relevant literature, preparation of GRADE<sup>2</sup> profiles, and analysis of the risk-benefits, values and preferences, and costs of implementation.

A literature search of the Cochrane Database and OVID-Medline was conducted in July 2010 to identify high quality, systematic reviews from the previous two years that were relevant to the priority PICO questions. Where data were not available or up-to-date from the two sources, systematic reviews were commissioned to various groups to collate the evidence.

The systematic reviews, meta-analyses and GRADE profiles followed the methodology recommended by the Guidelines Review Committee. Where data were lacking, systematic searches were conducted from various electronic databases, including Medline/PubMed, Embase, CENTRAL, NLM Gateway and WHO regional databases. Applicable ILCOR research strategies were updated with literature available through April 2011.

Studies from low- and middle-income as well as high- income countries were considered for inclusion in evidence reviews. Efforts were made to identify relevant English and non-English language articles. A standardized form was used to extract relevant information from studies. Systematically extracted data included: study identifiers, setting, design, participants, sample size, intervention or exposure, control or comparison group, outcome measures and results. Quality characteristics also were recorded for all studies: allocation concealment or risk of selection bias (observational studies); blinding of intervention or observers, or risk of measurement bias; loss to follow-up; and intention to treat analysis or adjustment for confounding factors. For each question, data on critical and secondary outcomes were extracted and appraised by evaluating the quality, consistency, and external validity of the evidence.

#### ***Grading the quality of evidence***

An adapted GRADE approach for assessing and grading the quality of evidence was used. Quality was defined as the extent to which one could be confident that an estimate of effect or association was correct. The quality of the set of included studies reporting results for an outcome was graded as high, moderate, low or very low. The implications of these categories are detailed in **Table 1**.

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<sup>1</sup> ILCOR. Special Report —Neonatal resuscitation: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations, *Pediatrics*, 2010, 126:e1319-e1344

<sup>2</sup> GRADE refers to the system for grading the quality of evidence and the strength of recommendations.

**Table 1. Categories of evidence**

<b>Level of Evidence</b>	<b>Rationale</b>
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the effect.
Low	Further research is very likely to have an important impact on estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

The assessment of quality of a set of studies (the majority of those included) was based on the following criteria:

- Study design: randomized controlled trials (RCTs) - individual or cluster RCTs; non-randomized experimental studies; or observational studies.
- Limitations in methods: risk of selection bias – allocation concealment in RCTs and comparability of groups in observational studies; risk of measurement bias – blinding or objective outcomes; extent of loss to follow-up; appropriateness of analysis – intention to treat, adjustment for cluster randomization in cluster RCTs, adjustment for confounding in observational studies.
- Consistency: similarity of results across the set of available studies – direction of effect estimates, most studies showing meaningful benefit or unacceptable harm.
- Precision: based on the width of confidence intervals (CIs) of the pooled effects across studies.
- Directness (also called generalizability or external validity): whether the majority of evidence was from studies conducted in low- and middle-income countries, and evaluated interventions relevant to the identified questions.

Additional considerations included the magnitude of the effect, presence or absence of a dose-response gradient and direction of plausible biases. GRADE tables from systematic reviews were cross-checked, and a discussion on benefits and harms, values and preferences and costs was drafted. Recommendations were formulated and drafted in accordance with procedures outlined in the WHO Handbook for Guideline Development<sup>1</sup>, and guided by the quality of evidence using the GRADE methodology.

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<sup>1</sup> WHO. *Handbook for guideline development*. Geneva, WHO, 2010.

## *FORMULATION OF RECOMMENDATIONS*

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In drafting the recommendations, the WHO Steering Group used the summaries of evidence for the critical outcomes, quality of evidence, risks and benefits of implementing the recommendations, values and preferences and costs.

The draft recommendations, evidence summaries, GRADE tables and information on benefits and risks, values and preferences, and costs were presented to the GDG at its meeting held at WHO headquarters in Geneva, Switzerland, in June 2011. The GDG reviewed and discussed this information to finalize the recommendations. Most decisions were based on the evidence from RCTs or observational human studies. Where these were not available, evidence from relevant animal studies was used. Where the GDG determined that there was insufficient evidence, consensus within the group was used as the basis of the recommendation.

The decisions on the final recommendations and their strength were made by consensus or, where necessary, by vote. In deciding on the strength of the recommendations, the GDG was guided by the agreed-upon assessment criteria described in **Table 2** below.

**Table 2. Assessment criteria for the strength of recommendations**

<b>Strength of recommendation</b>	<b>Rationale</b>
Strong	The GDG is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.
Weak	The GDG concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects. However, the recommendation is only applicable to a specific group, population or setting OR where new evidence may result in changing the balance of risk to benefit OR where the benefits may not warrant the cost or resource requirements in all settings.
No recommendation	Further research is required before any recommendation can be made.

When the GDG felt that the benefits of a recommendation outweighed the harms in some situations but not in others, the situation to which the recommendation is relevant was explicitly stated.

The recommendations, their levels of strength and remarks were circulated to the GDG and peer reviewers for comments before finalization.

## *REVIEW AND UPDATE OF THE RECOMMENDATIONS*

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These recommendations will be regularly updated as more evidence is collated and analysed on a continuous basis, with major reviews and updates at least every 5 years. The next major update will be considered in 2015 under the oversight of the WHO Guidelines

Review Committee. These recommendations will form part of a technical series of the evidence behind several guidelines to be produced by MCA over the coming years.

## RECOMMENDATIONS

### IMMEDIATE CARE AFTER BIRTH

#### ■ RECOMMENDATION 1

**In newly-born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than one minute after birth<sup>1</sup>.**

*(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<sup>2</sup> recommend that the cord should not be clamped earlier than is necessary for applying cord traction, which the GDG clarified would normally take around 3 minutes.*

**When newly-born term or preterm 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 GDG in the absence of evidence in babies who need PPV)*

Remark:

*If there is experience in providing effective PPV without cutting the cord, ventilation can be initiated before cutting the cord.*

#### EVIDENCE FOR RECOMMENDATION 1

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<sup>1</sup> "Not earlier than one minute" should be understood as the lower limit supported by published evidence. WHO *Recommendations for the prevention of postpartum haemorrhage* (Fawole B et al. Geneva, WHO, 2007) state that the cord should not be clamped earlier than is necessary for applying cord traction, which the GDG clarified would normally take around 3 minutes.

<sup>2</sup> **FAWOLE B ET AL. WHO RECOMMENDATIONS FOR THE PREVENTION OF POSTPARTUM HAEMORRHAGE: RHL GUIDELINE (LAST REVISED: 1 MAY 2010). THE WHO REPRODUCTIVE HEALTH LIBRARY. GENEVA, WHO, 2010.**

**Question for systematic review:** In normal or depressed<sup>1</sup> newly-born babies (P), does **late cord clamping** (I) compared with **standard management** (C) improve outcome (O)?

### Summary of evidence

Twenty-one RCTs that evaluated the effects of late cord clamping in normal neonates in the delivery room were identified. Of these, 10 included term neonates (Ceriani Cernadas, 2006; Ceriani Cernadas et al., 2010; Chaparro et al., 2006; Emhamed, van Rheenen & Brabin, 2004; Geethanath et al., 1997; McDonald, 1996; Nelson et al., 1980; Oxford Midwives Research Group, 1991; van Rheenen et al., 2007; Venâncio et al., 2008) while 11 trials enrolled predominantly preterm infants (Baenziger et al., 2007; Hofmeyr et al., 1988; Hofmeyr et al., 1993; Kinmond et al., 1993; Kugelman et al., 2007; McDonnell & Henderson-Smart, 1997; Mercer, 2006; Oh et al., 2002; Rabe et al., 2000; Strauss et al., 2008; Ultee et al., 2008). No studies in depressed neonates were identified. There was considerable heterogeneity in the clamping time and positioning of the infant before clamping between the included studies. The clamping time in the "late clamping" group varied from 30 seconds to 5 minutes after birth, or until the cord stopped pulsating.

Eight randomized trials (Baenziger et al., 2007; Hofmeyr et al., 1988; Hofmeyr et al., 1993; Kugelman et al., 2007; McDonnell et al., 1997; Mercer, 2006; Oh et al., 2002; Rabe et al., 2000), mostly from high-income country settings, that evaluated the effect of late cord clamping on mortality during initial hospital stay were identified. All these trials included only preterm neonates. The quality of evidence for this outcome was graded as *low*. Overall, there was no difference in the risk of mortality between the late and early cord clamping groups (RR 0.73, 95% CI 0.30 to 1.81).

Four RCTs (Hofmeyr et al., 1988; Hofmeyr et al., 1993; Kugelman et al., 2007; Mercer, 2006) evaluated the incidence of intraventricular haemorrhage in preterm neonates who underwent late cord clamping. The quality of evidence for this outcome was graded as *low*. No difference was observed in the risk of intraventricular haemorrhage between the late and early cord clamping groups (RR 0.70, 95% CI 0.16 to 2.93).

Three studies (Ceriani Cernadas, 2006; McDonald, 1996; Nelson et al., 1980) that examined the risk of admission in a neonatal intensive care unit (NICU) immediately after birth in term infants were summarized. The quality of evidence for this outcome was graded as *low*. Late cord clamping did not affect the risk of admission in a NICU (RR 0.95, 95% CI 0.51 to 1.78).

A total of six randomized trials (Kinmond et al., 1993; Kugelman et al., 2007; McDonnell & Henderson-Smart, 1997; Mercer, 2006; Rabe et al., 2000; Strauss et al., 2008) have looked at the rates of anaemia requiring transfusion during initial hospital stay in preterm neonates. The quality of evidence for this outcome was graded as *moderate*. On average, there was about 32% reduction in the need for blood transfusion with late cord clamping (RR 0.68, 95% CI 0.51 to 0.92). An observational study (Farrar et al., 2011) that reported the mean change in birth weight following late cord clamping in term infants supports this finding. The mean change in weight was 116 g [95% CI 72 to 160] after a delay in cord clamping of about 2 to 5 minutes after birth. This change approximates to 110 ml (95% CI 69 to 152) of total transfusion volume which is roughly 40% of total blood volume in these infants.

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<sup>1</sup>A "depressed" newborn is a baby not breathing or crying at birth who usually has poor muscle tone and heart rate below 100 beats/minute.

Three studies (Ceriani Cernadas et al., 2010; Chaparro et al., 2006; van Rheenen et al., 2007) evaluated the effect of late cord clamping on the risk of anaemia at 6 months of age in term infants. The quality of evidence for this outcome was graded as *moderate*. No significant difference was found in the rates of anaemia between the late and early clamping groups (RR 0.87, 95% CI 0.69 to 1.10). Four trials from low- and middle-income country settings (Ceriani Cernadas et al., 2010; Chaparro et al., 2006; Geethanath et al., 1997; Venâncio et al., 2008) estimated the serum ferritin concentrations at 3-6 months of age in term neonates. The quality of evidence for this outcome was graded as *high*. The mean difference (MD) in mean serum ferritin concentration was 12.5 mcg/litre higher in infants in the late clamping group (95% CI 5.72 to 19.3).

Three trials (Ceriani Cernadas, 2006; Emhamed, van Rheenan & Brabin, 2004; van Rheenen et al., 2007) reported the effect of timing of cord clamping on the incidence of polycythaemia - haematocrit more than 65% - in term infants. The quality of evidence for this outcome was graded as *low*. There was no difference in the risk of polycythaemia following late cord clamping (RR 2.39, 95% CI 0.72 to 7.93). Seven RCTs (Emhamed, van Rheenan & Brabin, 2004; McDonald, 1996; Nelson et al., 1980; Oxford Midwives Research Group, 1991; Rabe et al., 2000; Strauss et al., 2008; Ultee et al., 2008) examined the risk of receiving phototherapy for hyperbilirubinaemia following late clamping in term and preterm neonates. In a majority of these studies, the criteria used for phototherapy were not strictly defined. On average, there was a 33% increase in the risk of receiving phototherapy for hyperbilirubinaemia. The quality of evidence for this outcome was graded as *very low*.

In conclusion, there is moderate to high quality evidence that late clamping of the umbilical cord is associated with lower risk of anaemia requiring transfusion in preterm infants and with higher serum ferritin levels at follow-up in term neonates. There is low quality evidence that late cord clamping has no effect on mortality and severe morbidity. There is very low quality evidence that the intervention is associated with a higher risk of receiving phototherapy for hyperbilirubinaemia in the immediate neonatal period.

## CONSIDERATIONS IN FORMULATING RECOMMENDATION 1

**Balance of benefits and harms:** The currently available evidence from normal term and preterm infants shows significant benefits of late cord clamping in reducing the need for blood transfusions and increasing body iron stores. These benefits were considered to outweigh the potential harm, i.e. higher risk of receiving phototherapy for hyperbilirubinaemia.

It was not possible to balance benefits and harms in depressed neonates requiring resuscitation at birth because none of the included studies enrolled such neonates. The GDG felt that it may be difficult to initiate resuscitation without clamping and cutting the cord.

**Values and preferences:** Health care providers and policy-makers from both low- and middle-income as well as high-income countries are likely to give a high value to the benefits noted in the reduced need for blood transfusion in preterm infants. Benefits in infant body-iron stores would be valued highly because of the association between iron status and cognitive development. Many health care providers may not feel comfortable providing PPV without clamping and cutting the cord.

**Costs:** Late cord clamping in the delivery room does not have any cost implications, but may reduce the costs for blood transfusions.

▪ **RECOMMENDATION 2**

**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.**

*(Weak recommendation, based on consensus of WHO GDG in the absence of published evidence)*

**EVIDENCE FOR RECOMMENDATION 2**

**Question for systematic review:** In neonates not breathing spontaneously after birth (P), does **additional stimulation** (I) compared with **thorough drying alone** (C) reduce the need for PPV (O)?

**Summary of evidence**

No human studies were identified that compared the effects of additional tactile stimulation with only drying/suctioning in neonates requiring assistance at birth.

Two *animal* studies have looked at the effect of tactile stimulation on spontaneous breathing at around the time of birth in animals. The first study (Faridy, 1983) described the steps of resuscitation employed by maternal rats with their offspring, including increasing levels of stimulation of their newborns. The other study (Scarpelli, Condorelli & Cosmi, 1977) demonstrated that mechanical cutaneous stimulation induces spontaneous breathing in apnoeic fetal lambs.

In conclusion, there is very weak evidence from animal studies that tactile stimulation helps in initiating spontaneous breathing after birth. Thorough drying of the newborn is considered to be a stimulation of the baby, and there is no clear evidence that additional stimulation beyond thorough drying is helpful.

**CONSIDERATIONS IN FORMULATING RECOMMENDATION 2**

**Balance of benefits and harms:** There is a lack of evidence on the relative merits and disadvantages of providing additional tactile stimulation at birth in depressed human neonates. Evidence from animal studies indicates that tactile stimulation might play a role in establishing spontaneous breathing in depressed newborns and avoid the use and possible complications of PPV. On the other hand, providing additional stimulation could delay the initiation of PPV.

**Values and preferences:** Given the lack of evidence for benefits or harms, health care providers are likely to continue with the existing policy of providing additional stimulation at the time of birth in depressed neonates.

**Costs:** Providing additional stimulation at birth does not have any cost implications.

### ■ RECOMMENDATION 3

**In neonates born through clear amniotic fluid who start breathing on their own after birth, suctioning of the mouth and nose should not be performed.**

*(Strong recommendation, based on high quality evidence of lower oxygen saturation and low quality evidence of lower Apgar scores)*

**In neonates born through clear amniotic fluid who do not start breathing after thorough drying and rubbing the back 2-3 times, suctioning of the mouth and nose should not be done routinely before initiating positive-pressure ventilation. Suctioning should be done only if the mouth or nose is full of secretions.**

*(Weak recommendation, based on the consensus of the WHO GDG in the absence of evidence in babies who need PPV and harmful effects of suctioning in healthy neonates)*

### EVIDENCE FOR RECOMMENDATION 3

**Question for systematic review:** In depressed neonates with clear amniotic fluid (P), does **suctioning of the mouth and nose** (I) before starting PPV versus **no suctioning** (C) improve outcome (O)?

#### Summary of evidence

No study was located – observational or interventional – that evaluated the effects of suctioning of the mouth and nose at birth in depressed neonates. Therefore, evidence from studies that examined the effects of oral and nasal suctioning in normal, healthy neonates was summarized.

Three studies (Gungor et al., 2005; Gungor et al., 2006; Waltman et al., 2004) examined the effect of oral and nasal suctioning at birth on oxygen saturation (SpO<sub>2</sub>) levels at 5 minutes of life. The quality of evidence for this outcome was graded as *high*. The pooled MD in oxygen saturation levels was 9.8% lower (95% CI -10.2% to -9.4%) in those who underwent oropharyngeal or nasopharyngeal suctioning. Another study (Carrasco, Martell & Estol, 1997) also looked at the effect of oral/nasal suctioning on SpO<sub>2</sub> levels, but the results of this study could not be included in the pooled effect because of incomplete data. The study also reported significantly lower SpO<sub>2</sub> levels in those who underwent oropharyngeal or nasopharyngeal suctioning at birth than those who did not undergo suctioning.

Three RCTs (Gungor et al., 2005; Gungor et al., 2006; Waltman et al., 2004) evaluated the effect of oropharyngeal suctioning on Apgar scores at 5 minutes of life. The quality of evidence for this outcome was graded as *low*. There was a significant reduction in the proportion of infants with normal Apgar scores in the suctioning group compared to the group with no suctioning (RR 0.54, 95% CI 0.29 to 1.00, p=0.049).

An observational study with no control group (Cordero & Hon, 1971) reported high incidences of cardiac arrhythmias (7/46; 15.2%) and apnoea (5/46; 10.9%) following

suctioning with a nasogastric tube attached to a de Lee trap; however, no such events were observed in infants suctioned with a bulb syringe.

In conclusion, routine oral and nasal suctioning in normal healthy neonates immediately after birth is associated with lower oxygen saturation levels (high quality evidence) and lower Apgar scores (low quality evidence).

### CONSIDERATIONS IN FORMULATING RECOMMENDATION 3

**Balance of benefits and harms:** The available evidence shows that routine oral and nasal suctioning at the time of birth might be associated with potential harms – lower oxygen saturation levels and lower Apgar scores – in normal healthy neonates. It is clear that neonates who begin breathing spontaneously after birth should not be suctioned. No apparent benefits were observed with routine oronasopharyngeal suctioning in any of the included studies. However, there is no evidence of harmful or beneficial effects of suctioning in depressed neonates born through clear amniotic fluid.

**Values and preferences:** Given the lack of benefits and the evidence for potential harms, health care providers and policy-makers from low- and middle-income and high-income country settings are likely to give a low value to the practice of routine oronasopharyngeal suctioning in newly-born infants. However, it is a widely-used practice which has been promoted actively for decades as an important step before PPV. Routine suctioning may delay the start of effective PPV. Whether initiating PPV without suctioning increases complications of air leak or ineffective ventilation has not been studied. Most providers would feel that effective PPV may be hindered if the mouth and nose are full of secretions.

**Costs:** Routine suctioning of mouth and nose requires suction machines, suction catheters or bulb syringes.

### ■ RECOMMENDATION 4

**In the presence of meconium-stained amniotic fluid, intrapartum suctioning of the mouth and nose at the delivery of the head is not recommended.**

*(Strong recommendation, based on low quality evidence for no benefits or harms in clinical outcomes, and the potential risks involved)*

### EVIDENCE FOR RECOMMENDATION 4

**Question for systematic review:** In neonates born through meconium-stained amniotic fluid (P), does **intrapartum oropharyngeal and nasopharyngeal suctioning** at the delivery of the head (I) compared with **no intrapartum suctioning** (C) prevent MAS and mortality (O)?

### Summary of evidence

One RCT (Vain et al., 2004) evaluated the effect of intrapartum suctioning on mortality of neonates born through meconium-stained amniotic fluid. The quality of evidence for this outcome was graded as *low*. There was no significant difference in the risk of mortality between the group of neonates who underwent intrapartum suctioning and the control group of infants (RR 2.22, 95% CI 0.69 to 7.22). Another study that used historical controls (Carson et al., 1976) found no significant difference in the number of deaths due to MAS following implementation of intrapartum suctioning (RR 0.31, 95% CI 0.02 to 5.67).

Four studies (Carson et al., 1976; Falciglia, 1988; Falciglia et al., 1992; Vain et al., 2004) examined the effect of intrapartum suctioning in the presence of meconium on the incidence of MAS. The quality of evidence for this outcome was graded as *low*. There was no significant difference in the incidence of MAS following intrapartum suctioning (RR 1.07, 95% CI 0.80 to 1.44).

Two studies (Falciglia, 1988; Vain et al., 2004) evaluated the effect of intrapartum suctioning on the rates of perinatal asphyxia in infants born through meconium-stained amniotic fluid. The quality of evidence for this outcome was graded as *low*. No significant difference was observed in the proportion of infants with Apgar scores of  $\leq 6$  (RR 0.88, 95% CI 0.63 to 1.23). Another study (Carson et al., 1976) reported mean Apgar scores of 9 and 6.6 respectively in infants who underwent intrapartum suctioning and in those who did not undergo the procedure. The study authors did not elaborate whether the difference was statistically significant.

One RCT (Vain et al., 2004) reported the effect of intrapartum suctioning on the incidence of pulmonary air leaks. The quality of evidence for this outcome was graded as *low*. There was no significant difference in the incidence of pneumothorax between the two groups of infants (RR 0.99, 95% CI 0.20 to 4.90).

The same RCT (Vain et al., 2004) reported the duration of hospital stay of infants with MAS in the intervention and control groups. The quality of evidence for this outcome was graded as *low*. No significant difference was found between the two groups of infants (MD -0.8 days, 95% CI -4.8 to 3.2). Another study (Carson et al., 1976) reported the mean duration of stay in all those who survived until discharge. The mean duration was found to be 8 and 9.7 days respectively in those who underwent suctioning and the control infants. The study authors neither provided the standard deviations nor did they elaborate whether the difference was statistically significant.

In conclusion, there is low quality evidence that routine intrapartum suctioning does not reduce the risk of mortality, MAS or perinatal asphyxia in infants born through meconium-stained amniotic fluid. There is low quality evidence that the procedure does not have harmful effects such as pneumothorax.

#### **CONSIDERATIONS IN FORMULATING RECOMMENDATION 4**

**Balance of benefits and harms:** The evidence available does not show any significant benefits in mortality, MAS, perinatal asphyxia or air leaks following intrapartum suctioning in infants born through meconium. However, the majority of these studies were conducted in settings with low incidence of MAS and/or perinatal asphyxia and availability of endotracheal intubation for depressed infants.

**Values and preferences:** Health care providers and policy-makers from low- and middle-income and high-income country settings are not likely to give a high value to routine

intrapartum suctioning in neonates born through meconium-stained amniotic fluid because of lack of benefits.

**Costs:** Not recommending intrapartum suctioning in neonates born through meconium-stained amniotic fluid would save resources.

## ▪ **RECOMMENDATION 5**

**In neonates born through meconium-stained amniotic fluid who start breathing on their own, tracheal suctioning should not be performed.**

*(Strong recommendation, based on moderate to low quality evidence for no benefits in mortality or MAS in vigorous neonates)*

**In neonates born through meconium-stained amniotic fluid who start breathing on their own, suctioning of the mouth or nose is not recommended.**

*(Weak recommendation, based on consensus of WHO GDG in the absence of published evidence on benefits and harms)*

**In neonates born through meconium-stained amniotic fluid who do not start breathing on their own, tracheal suctioning should be done before initiating positive-pressure ventilation.**

*(Weak situational recommendation, based on very low quality evidence of benefit in reducing MAS, relevant to settings where endotracheal intubation is possible)*

**In neonates born through meconium-stained amniotic fluid who do not start breathing on their own, suctioning of the mouth and nose should be done before initiating positive-pressure ventilation.**

*(Weak recommendation, based on consensus of WHO GDG in the absence of published evidence on benefits and harms)*

## **EVIDENCE FOR RECOMMENDATION 5**

**Question for systematic review:** In neonates born through meconium-stained amniotic fluid (P), does **oropharyngeal and/or endotracheal suctioning** (I) compared with **no suctioning of either oropharynx or trachea** (C) prevent MAS and mortality (O)?

### **Summary of evidence:**

*Oropharyngeal suctioning in infants born through meconium-stained amniotic fluid*

No studies were identified that evaluated the effects of oropharyngeal suctioning in either vigorous or depressed neonates born through meconium-stained amniotic fluid.

### *Tracheal suctioning in vigorous neonates*

Two RCTs (Daga et al., 1994; Wiswell et al., 2000) evaluated the effect of endotracheal suctioning on the risk of mortality in *vigorous* neonates born through meconium-stained amniotic fluid. The quality of evidence for this outcome was graded as *low*. There were only a few events in both the studies (total of 1 and 5 deaths respectively). Tracheal suctioning did not reduce the risk of mortality (RR 0.96, 95% CI 0.22 to 4.25).

Two trials (Linder et al., 1988; Wiswell et al., 2000) examined the effect of tracheal suctioning on the risk of MAS in vigorous neonates. The quality of evidence for this outcome was graded as *moderate*. No significant difference was observed in the incidence of MAS (RR 1.33, 95% CI 0.82 to 2.14).

Two trials (Daga et al., 1994; Linder et al., 1988) reported the effect of tracheal suctioning on the incidence of air leaks, such as pneumothorax or pulmonary interstitial emphysema, in infants born through meconium-stained amniotic fluid. The quality of evidence for this outcome was graded as *very low*. Only a few events occurred in either of the groups in both the studies. There was no significant difference in the incidence of air leaks between the two groups (RR 0.87, 95% CI 0.16 to 4.92).

One RCT (Daga et al., 1994) reported the effect of tracheal suctioning on the incidence of HIE. The quality of evidence for this outcome was graded as *very low*. No significant difference was observed in the incidence of HIE between the two groups of infants (RR 2.65, 95% CI 0.30 to 23.8).

### *Tracheal suctioning in depressed neonates*

No RCTs that compared the effects of tracheal suctioning with no suctioning in depressed neonates born through meconium-stained amniotic fluid were found. Three before-and-after studies (Falciglia, 1988; Gregory et al., 1974; Wiswell, Tugell & Turner, 1990) compared the effect of tracheal suctioning on the risk of death and/or MAS in neonates born through meconium. All three studies reported lower risk of either neonatal mortality or deaths attributable to MAS following implementation of routine tracheal suctioning with or without intrapartum suctioning. However, it is unclear whether the reduction in mortality was because of the advances in perinatal care over the years or because of tracheal suctioning. The incidence of MAS was found to be lower in the suctioned infants in only one study (Wiswell, Tugell & Turner, 1990); the other two studies (Falciglia, 1988; Gregory et al., 1974) reported no change in the risk of MAS. Another study (Ting & Brady, 1975) elucidated the risk factors for developing respiratory distress in neonates born through meconium-stained amniotic fluid in a case-control design. This study reported that the only difference between the symptomatic and asymptomatic groups was the history of tracheal suctioning in the delivery room. All these studies included *both* depressed and vigorous neonates born through meconium-stained amniotic fluid.

Four observational studies (Al Takroni et al., 1998; Gupta Bhatia & Mishra, 1996; Peng, Gutcher & Van Dorsten, 1996; Yoder, 1994) evaluated the effect of combined intrapartum oral suctioning and postnatal tracheal suctioning in depressed neonates. These studies did not include any 'control' group, and reported that MAS continued to occur despite tracheal suctioning.

In conclusion, there is moderate to very low quality evidence from randomized trials that tracheal suctioning does not reduce the risk of mortality, MAS or air leaks in vigorous infants born through meconium-stained amniotic fluid. On the other hand, evidence from

retrospective studies indicates that tracheal suctioning might be associated with lower risk of mortality in depressed infants born through meconium-stained amniotic fluid.

#### CONSIDERATIONS IN FORMULATING RECOMMENDATION 5

**Balance of benefits and harms:** Currently available evidence does not show any significant benefits in mortality, MAS, air leaks or HIE with tracheal suctioning in vigorous infants born through meconium-stained amniotic fluid. There is some evidence that tracheal suctioning might reduce the risk of mortality in depressed infants born through meconium-stained amniotic fluid. There is no evidence for either benefits or harms with nasal or oropharyngeal suctioning in newborns born through meconium-stained amniotic fluid.

**Values and preferences:** Given these considerations, health care providers and policy-makers from low- and middle-income country settings are not likely to give a high value to oropharyngeal or tracheal suctioning in vigorous neonates born through meconium-stained amniotic fluid. However, they are likely to value tracheal suctioning for depressed neonates born through meconium-stained amniotic fluid.

**Costs:** Tracheal suctioning requires the availability of skilled personnel capable of performing endotracheal intubation as well as suction catheters, laryngoscopes and suction devices. The observed lack of benefits does not justify the additional costs involved in implementation of this practice in resource-limited settings.

#### ▪ RECOMMENDATION 6

**In settings where mechanical equipment to generate negative pressure for suctioning is not available and a newly-born baby requires suctioning, a bulb syringe (single-use or easy to clean) is preferable to a mucous extractor with a trap in which the provider generates suction by aspiration.**

*(Weak recommendation, based on no evidence of one being better than the other for the neonate, and potential risks for health care providers with use of the mucous extractor)*

#### Remarks:

- *Only single-use bulb syringes or mucous extractors should be used; if this is not possible, use only those devices that can be easily and thoroughly cleaned.*
- *Deep suctioning should never be done.*

#### EVIDENCE FOR RECOMMENDATION 6

**Question for systematic review:** In neonates who require suction to clear their airways (P), what is the safety and efficacy (O) of different types of **suction devices** (I/C)?

#### Summary of evidence

Five studies (Cohen-Addad, Chatterjee & Bautista, 1987; Cordero & Hon, 1971; Dunn et al., 2001; Hageman et al., 1988; Locus, Yeomans & Crosby, 1990) from high-income country settings have compared the effects of oral and/or pharyngeal suctioning by a DeLee mucous

extractor with that by a bulb syringe. None of these studies have, however, described the method used for generating negative pressure while using the DeLee catheter.

Two studies (Cohen-Addad, Chatterjee & Bautista, 1987; Hageman et al., 1988) evaluated the effect of using a mucous extractor or bulb syringe on the risk of mortality due to MAS. Both studies reported no significant difference in the risk of mortality between the two groups.

Four studies (Cohen-Addad, Chatterjee & Bautista, 1987; Dunn et al., 2001; Hageman et al., 1988; Locus, Yeomans & Crosby, 1990) compared the incidence of MAS in infants who underwent suctioning with a DeLee trap with those who underwent suctioning with a bulb syringe. No significant difference in the risk of MAS was observed in any of these studies.

Only one study (Cordero & Hon, 1971) reported the incidence of severe adverse events following nasopharyngeal suctioning with a DeLee catheter or bulb syringe in normal neonates after birth. The study reported that seven infants developed bradyarrhythmias and five developed apnoea following suctioning by a catheter attached to a DeLee trap (n=46); none in the bulb syringe group (n=41) had either arrhythmia or apnoea. The effects for both the outcomes were not statistically significant (arrhythmia: RR 13.4, 95% CI 0.79 to 227.7; apnoea: RR 9.83; 95% CI 0.56 to 172.5).

None of the identified studies compared the effects of suctioning by use of mechanical suctioning devices (wall mounted or foot operated) with that by either bulb syringe or DeLee mucous extractor.

*Animal studies:* One animal study (Gage et al., 1981) compared the effect of suctioning by a catheter with that of suctioning by a bulb syringe on the distribution of meconium in the airways of anaesthetized kittens. The authors used scintigraphy to estimate the distribution of the meconium labelled with technetium-99m. The study reported a significant reduction in radioactivity with catheter suctioning compared with bulb suctioning (43% and 1% decrease respectively;  $P < 0.05$ ).

In conclusion, there is very low quality evidence that suctioning with a mucous extractor does not reduce the risk of mortality, MAS or severe adverse events such as arrhythmias/apnoea when compared with bulb suctioning. Evidence from one animal study suggests that DeLee catheter suctioning might be more effective in removing the meconium from the trachea than suctioning with a bulb syringe.

## **CONSIDERATIONS IN FORMULATING RECOMMENDATION 6**

***Balance of benefits and harms:*** The currently available evidence from clinical studies does not show any significant benefits or harms in the risk of mortality, MAS or severe adverse events with a bulb syringe compared with DeLee catheter suctioning.

A potential harm associated with the use of a DeLee catheter is the risk of inadvertent aspiration of fluids into the resuscitator's mouth. None of the included studies had specified the method used for generating negative pressure - whether by oral suction by health workers or by mechanical devices - while using the DeLee mucous extractor. The modified version of the DeLee mucous extractor has a filter that prevents aspiration of the contents into the mouth of the health worker. Bulb syringes, on the other hand, are difficult to clean; they can easily become a source of cross-infection, if not cleaned properly.

**Values and preferences:** Given these considerations, policy-makers are likely to be equivocal regarding the optimal suctioning device to be used in newly-born infants requiring assistance at birth. Health care providers are likely to prefer a method that does not pose a risk of infection to them.

**Costs:** Both DeLee suction catheters and bulb syringes are relatively inexpensive and available.

## POSITIVE-PRESSURE VENTILATION

### ▪ RECOMMENDATION 7

**In newly-born babies who do not start breathing despite thorough drying and additional stimulation, positive-pressure ventilation should be initiated within one minute after birth.**

*(Strong recommendation, based on very low quality evidence from observational studies)*

### EVIDENCE FOR RECOMMENDATION 7

**Question for systematic review:** In neonates who fail to breathe after birth (P), should **PPV be initiated within one minute after birth** if the baby has not started breathing after initial steps of resuscitation (I) as compared to a **later time** (C) for preventing HIE and mortality (O)?

#### Summary of evidence

Only one very low quality observational study (Berglund et al., 2008) in human neonates related to this question was identified. This was a retrospective chart review of cases of suspected delivery-related malpractice in a high-income country setting. Mortality in neonates in whom PPV was initiated within one minute after birth was not significantly lower than those in whom PPV was initiated at a later time (RR 0.62, 95% CI 0.09 to 4.04). However, there were only seven cases in the comparison group, and many infants who received PPV within one minute after birth were not resuscitated using standard guidelines in the next minutes after birth.

#### *Animal studies*

No controlled trial that compared the effects of early and late initiation of PPV in asphyxiated newborn animals was identified. Observational studies (Hernandez-Andrade et al., 2005; Kaneko, 2003; Thorngren-Jerneck et al., 2001; Yan et al., 2009) showed that after complete occlusion of the cord in animal fetuses, electrocortical activity is reduced on average within about 90 seconds, cerebral blood flow is reduced after about 3 minutes, arterial hypotension sets in by about 7 minutes and cardiac arrest occurs within about 15 minutes.

Two animal studies (Borke et al., 2006; Haney et al., 2005) showed a significant improvement in myocardial function, and another study (Cavus et al., 2006) showed an improvement in cerebral oxygenation following initiation of PPV in asphyxiated animals.

However, none of these studies specifically addressed the issue of timing of initiating PPV in asphyxiated animals.

#### CONSIDERATIONS IN FORMULATING RECOMMENDATION 7

**Balance of benefits and harms:** Currently available evidence from human studies is not helpful in determining the timing of PPV initiation. Evidence from animal studies indicates that important blood pressure and cerebral blood flow reductions occur 7-10 minutes, and cardiac arrest occurs within 15 minutes, after cord occlusion. Initiation of PPV has been found to be associated with a significant improvement in myocardial function and cerebral oxygenation in animals. These two pieces of evidence indicate that the window of opportunity to reverse the consequences of asphyxia is small. Since the period of asphyxia before birth is variable and not precisely known in most cases, the GDG agreed with the currently recommended practice of initiating PPV if the baby does not start breathing within one minute after birth.

**Values and preferences:** Given the considerations of benefits and harms, health care providers and policy-makers are likely to prefer initiating PPV early in asphyxiated neonates.

**Costs:** There is no difference in costs between early and late initiation of PPV.

#### ▪ RECOMMENDATION 8

**In newly-born term or preterm (>32 weeks gestation) babies requiring positive-pressure ventilation, ventilation should be initiated with air.**

*(Strong recommendation, based on moderate quality evidence for benefits in mortality and no evidence for significant harms)*

#### Remarks:

- *For preterm babies born at or before 32 weeks gestation, it is preferable to start ventilation with 30% rather than 100% oxygen. If this is not possible, ventilation should be started with air.*
- *For neonates who continue to have a heart rate of <60/minute after 30 seconds of adequate ventilation with air, progressively higher concentrations of oxygen should be considered. However, if oxygen is not available, ventilation should be continued with air.*
- *Pulse oximetry is desirable to decide on the need for supplemental oxygen and to monitor the needed concentration of oxygen. However, pulse oximetry is not easily available in resource-limited settings, and its use by a single health worker performing basic newborn resuscitation is difficult.*

## EVIDENCE FOR RECOMMENDATION 8

**Question for systematic review:** In newborns who require resuscitation at birth (P), is PPV with air (I) more effective than that with **higher concentrations of oxygen** (C) in reducing subsequent mortality and HIE (O)?

### Summary of evidence

Seven RCTs (Bajaj, 2005; Ramji et al., 1993; Ramji et al., 2003; Saugstad, Rootwelt & Aalen, 1998; Vento, 2001a; Vento et al., 2001b; Vento et al., 2003) compared the effect of resuscitation using air with the use of 100% oxygen on mortality in newly-born infants. Some of the data not published in the original papers was extracted from a systematic review which directly received these data from the investigators (Rabi, Rabi & Yee, 2007). Of the seven studies, four are quasi-RCTs (Bajaj, 2005; Ramji et al., 1993; Ramji et al., 2003; Saugstad, Rootwelt & Aalen, 1998) conducted in low- and middle-income country settings. Some of the trials included only term infants, but most of the evidence comes from studies that included 20% to 35% preterm infants. Most preterm infants included were of greater than 32 weeks gestation. Four studies reported the risk of mortality in the first week of life; the other three reported mortality until 28 days or discharge. The quality of evidence for this outcome was graded as *moderate*. The pooled effect was 30% reduction (95% CI 3% to 49%) in the risk of mortality following resuscitation with air compared with 100% oxygen.

A total of four studies (Bajaj, 2005; Ramji et al., 1993; Ramji et al., 2003; Saugstad, Rootwelt & Aalen, 1998) evaluated the effect of room air resuscitation on the risk of HIE (stage 2 or 3) in the neonatal period. The quality of evidence for this outcome was graded as *low*. No significant difference was found in the risk of HIE between the groups of infants resuscitated with air or 100% oxygen (OR 0.89, 95% CI 0.66 to 1.19).

One study (Vento et al., 2003) examined the effect on the time of onset of spontaneous breathing in depressed neonates. The quality of evidence for this outcome was graded as *low*. The mean difference in time of onset to spontaneous breathing was 1.5 minutes less (95% CI -2.02 to -0.98) in those who were resuscitated with air. Two other studies (Bajaj, 2005; Saugstad, Rootwelt & Aalen, 1998) had also reported this outcome, but their results could not be included in the meta-analysis because of incomplete data. While one of these studies reported a significantly shorter time to onset of spontaneous breathing in infants resuscitated with air (Saugstad, Rootwelt & Aalen, 1998), the other did not report any significant difference between the two groups (Bajaj, 2005).

One study (Saugstad, Rootwelt & Aalen, 1998) evaluated the risk of long-term neurodevelopmental outcomes following resuscitation with air. The quality of evidence for this outcome was graded as *very low*. There was no difference between the air and 100% oxygen groups in the risk of cerebral palsy at 18 to 24 months of age (OR 1.38, 95% CI 0.46 to 4.10).

In conclusion, there is moderate quality evidence that resuscitation using air reduces the risk of mortality and the time of onset of spontaneous breathing in neonates born after 32 weeks gestation when compared with resuscitation using 100% oxygen. However, it does not reduce the risk of HIE during the neonatal period or adverse neurodevelopmental outcomes at a later age.

*Studies in preterm infants with  $\leq 32$  weeks gestation*

Two additional RCTs and one observational study were identified comparing resuscitation with air to that using higher oxygen concentrations in only preterm infants  $\leq 32$  weeks gestation. Lundstrom and colleagues (1995) showed that 74% of infants resuscitated with room air were successfully stabilized without the need for supplemental oxygen. Cerebral blood flow at 2 hours after birth was significantly higher in neonates resuscitated with room air compared with those resuscitated with 80% oxygen. Wang and colleagues (2008) showed that resuscitation with room air failed to achieve the arbitrary oxygen saturation target of 70% at 3 minutes and 80% at 5 minutes, and all neonates needed supplemental oxygen. Similar results were reported in an observational study (Dawson et al., 2009).

Two RCTs conducted only in preterm infants  $\leq 28$  weeks gestation compared initiation of resuscitation using 30% oxygen with that using 90% oxygen. Escrig and colleagues (2008) showed that resuscitation in extremely preterm infants can be safely initiated with 30% oxygen which is then adjusted to the infant's needs. Vento and colleagues (2009) reported that initiation of resuscitation with 30% oxygen resulted in better clinical outcomes (days supplemental oxygen required, days of mechanical ventilation, bronchopulmonary dysplasia) than with 90% oxygen.

#### **CONSIDERATIONS IN FORMULATING RECOMMENDATION 8**

**Balance of benefits and harms:** The available evidence shows that using air for resuscitation is associated with significant benefits in short-term mortality but not in long-term developmental outcomes in term and preterm neonates  $>32$  weeks gestation. In most of the studies, 100% oxygen was used as a backup for babies not responding to resuscitation with air after 90 seconds after birth. However, the proportion of non-responders in the group initially randomized to resuscitation with air was *similar* to that in the group allocated to 100% oxygen. No apparent harms have been reported with room air resuscitation in term and preterm babies of  $>32$  weeks gestation in any of the included trials.

Available evidence suggests that the majority of preterm babies  $\leq 32$  weeks gestation may be stabilized with resuscitation using air. However, a substantial proportion of these infants need resuscitation with higher oxygen concentrations. It appears that the outcome is better if resuscitation is initiated with 30% rather than 90% oxygen.

**Values and preferences:** Given the benefits observed in the risk of mortality and lower costs involved in administering it, health care providers and policy-makers from both low- and middle- income and high-income country settings are likely to give a high value to the use of room air for resuscitating newly-born infants.

**Costs:** Use of air requires significantly less resources than 100% oxygen; it can be administered at even the most remote health care facilities. Additional resources are required to provide care to extremely premature infants.

## ■ RECOMMENDATION 9

**In newly-born babies requiring positive-pressure ventilation, ventilation should be provided using a self-inflating bag and mask.**

*(Weak recommendation, based on very low quality evidence for no benefits or harm in clinical outcomes and possible benefits in ease of use)*

### Remark:

*In an emergency situation where a self-inflating bag is not functional, mouth-to-tube and mask or mouth-to-mask can be used for providing PPV.*

## EVIDENCE FOR RECOMMENDATION 9

**Question for systematic review:** In neonates who require PPV (P), does ventilation with a **self-inflating bag and mask (I)** compared with **mouth-to-tube and mask (or mouth-to-mask) ventilation (C)** improve outcome (O)?

### Summary of evidence

Two studies compared the effects of using a self-inflating bag with mouth-to-tube and mask for providing PPV in neonates. One of the studies was a quasi-randomized trial (Massawe et al., 1996), while the other had a before-and-after design (Bang et al., 2005); both were conducted in low- and middle-income country settings, and reported the effect on mortality in the neonatal period. The quality of evidence for this outcome was graded as *very low*. There was no significant difference in the risk of mortality between the group of neonates resuscitated with bag and mask and that resuscitated with mouth-to-tube and mask (Pooled RR 1.01, 95% CI 0.39 to 2.60).

Only one of the studies (Massawe et al., 1996) evaluated the effects on the time to first cry and Apgar scores. The quality of evidence for both these outcomes was graded as *very low*. There was no significant difference in either the proportion of infants who cried within 5 minutes after birth (RR 1.27, 95% CI 0.93 to 1.73) or who had Apgar scores of 4 or more at 5 minutes after birth (RR 0.99, 95% CI 0.86 to 1.14). The study found no significant difference in the risk of convulsions between the two groups (RR 0.92, 95% CI 0.52 to 1.64). The quality of evidence for this outcome was graded as *very low*.

In conclusion, there is very low quality evidence that there is no difference between PPV using a self-inflating bag and using mouth-to-tube and mask in terms of risk of mortality, convulsions, onset of crying and Apgar score in the first 5 minutes after birth.

### *Descriptive studies/surveys/in vitro studies:*

One study published as a report (PATH, 2006) included training a large number of health workers in Indonesia in mouth-to-tube and mask ventilation, and found a lower subsequent mortality rate.

Two surveys (Ariawan et al., 2011; Coffey, Kelly & Tsu, 2007) reported the views of health care providers on the use of bag and mask and tube and mask in neonatal resuscitation. One of these surveys (Coffey, Kelly & Tsu, 2007) reported that bag and mask is much easier to use than tube and mask as the latter requires the user to constantly bend forward and blow for 10 to 15 minutes. The before-and-after study by Bang and colleagues (2005) reported

the same difficulty with tube and mask ventilation. On the other hand, Ariawan and colleagues (2011) found that tube and mask is much easier to clean and more portable, and is therefore preferred by health professionals. One study (Roberts & Day, 1973) described bacterial growth in blood-agar plates after the experimenter exhaled on them through neonatal endotracheal tubes under conditions simulating resuscitation of neonates.

#### CONSIDERATIONS IN FORMULATING RECOMMENDATION 9

**Balance of benefits and harms:** The currently available evidence from clinical studies does not show any significant benefits or harms in mortality, convulsions, or Apgar scores at 5 minutes after birth with the use of bag and mask ventilation when compared with tube and mask ventilation. Other studies and surveys indicate that bag and mask is possibly easier to use and might carry less risk of transmitting infections when compared with mouth-to-tube and mask.

**Values and preferences:** Given these considerations, health providers are likely to prefer a self-inflating bag and mask for PPV in depressed neonates because of ease of use, while policy-makers would probably prefer mouth-to-tube and mask because of lower costs.

**Costs:** Self-inflating bags are more expensive than mouth-to-tube devices.

#### ▪ RECOMMENDATION 10

**In newly-born babies requiring positive-pressure ventilation, ventilation should be initiated using a face-mask interface.**

*(Strong recommendation, based on limited availability and lack of experience with nasal cannula,<sup>1</sup> despite low quality evidence for benefits of nasal cannula in reducing need for chest compressions and endotracheal intubation)*

Remark:

*Currently, there is insufficient evidence to recommend the use of other interfaces.*

#### EVIDENCE FOR RECOMMENDATION 10

**Question for systematic review:** In neonates receiving PPV (P), does the use of *nasal cannula*(I) versus a *face-mask* interface (C) improve outcome (O)?

#### Summary of evidence

A single quasi-RCT (Capasso et al., 2005) from a high-income country setting compared the effects of using a short bi-nasal cannula with that of a face mask interface for providing PPV in neonates. The study used a Rendell-Baker mask which has been shown to be the least

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<sup>1</sup> Nasal cannula is a semi-rigid tube which creates a pressure seal in the nostrils.

effective during neonatal resuscitation and is no longer used in most delivery rooms. There is *very low* quality evidence of no significant difference in the risks of mortality (RR 0.49, 95% CI 0.21 to 1.11), Apgar scores of greater than 7 at 5 minutes of life (RR 1.04, 95% CI 1.0 to 1.08) or pulmonary air leaks (RR 0.66, 0.26 to 1.68). The study reported a significantly lower need for intubation (RR 0.1, 95% CI 0.02 to 0.44) and chest compressions (RR 0.2, 95% CI 0.08 to 0.51) in infants receiving PPV via nasal prongs. The quality of evidence for these outcomes was graded as *low*.

In conclusion, there is low quality evidence that providing PPV via nasal cannula reduces the need for intubation and chest compressions during resuscitation.

#### CONSIDERATIONS IN FORMULATING RECOMMENDATION 10

**Balance of benefits and harms:** Currently available evidence from clinical studies does not show any significant benefits or harms in mortality, air leaks and Apgar scores at 5 minutes of life following PPV delivered via nasal cannula or face mask interface. The use of nasal cannula may reduce the need for endotracheal intubation and chest compressions. This effect was, however, observed in comparison with a mask that is no longer used for providing respiratory support at birth.

**Values and preferences:** Given the limited experience of using nasal cannula as the interface for ventilation, most health care providers are likely to still prefer the face mask interface.

**Costs:** Short bi-nasal cannula is currently more expensive and is not easily available in most delivery rooms in resource-restricted settings.

#### RECOMMENDATION 11

**In newly-born babies requiring positive-pressure ventilation, adequacy of ventilation should be assessed by measurement of the heart rate after 60 seconds of ventilation with visible chest movements.**

*(Strong recommendation, based on very low quality evidence from observational data in newborn humans and animals that heart rate is the first indicator of recovery)*

Remark:

*Where feasible, continuous or repeated monitoring of the heart rate should be carried out during resuscitation.*

#### EVIDENCE FOR RECOMMENDATION 11

**Question for systematic review:** In neonates who require PPV (P), is **measuring heart rate and chest movements** (I) compared with **chest movements alone** (C) better to assess ventilation (O)?

#### Summary of evidence

No study was identified that directly studied the effects of measuring heart rate and chest movements with assessment of chest movements alone after initiation of PPV in newly-born infants requiring assistance at birth. Therefore, observational studies that have evaluated the roles of either heart rate or chest expansion measurement individually in infants requiring PPV at birth were reviewed.

Six studies (Ginott et al., 1980; Palme-Kilander & Tunnell, 1993; Perlman & Risser, 1995; Saugstad et al., 2005; Schubring et al., 1976; Yam et al., 2011) described the effect of resuscitation on heart rates in asphyxiated neonates. All these studies indicated that improvement in heart rate is a sensitive indicator of adequate resuscitation.

Two observational studies (Poulton et al., 2011; Schmölzer et al., 2010) evaluated the role of measurement of chest expansion as an indicator of adequate ventilation in neonates requiring PPV in the delivery room. Both studies correlated visual estimation of tidal volume, as measured by chest expansion, with the measured tidal volume. The studies showed that there is poor agreement between clinical assessment and measured volume. In a majority of the instances, the resuscitators underestimated the delivered tidal volume.

#### *Animal studies:*

One animal study (Dawes, 1968) elucidated the sequence of events following induced asphyxia in fetal monkeys and rabbits by not allowing them to breathe after birth. The animals developed primary apnoea within 30 seconds of birth associated with bradycardia and gasping efforts after about one minute that continued for several minutes. Resuscitation efforts at any point up to or after last gasp, if successful, were associated with a prompt increase in heart rate which was the first sign of recovery. Another animal study (Angell-James & Daly, 1978) showed that artificial lung inflation invariably resulted in tachycardia in anaesthetized dogs with experimentally-induced apnoea and bradycardia.

In conclusion, there is evidence from observational studies that an increase in heart rate accompanies successful ventilation in depressed neonates. On the other hand, there is evidence from observational studies that visual inspection of chest movements alone is not a reliable indicator of VT.

### **CONSIDERATIONS IN FORMULATING RECOMMENDATION 11**

***Balance of benefits and harms:*** Currently available evidence indicates that an increase in heart rate is a good indicator of response to resuscitation. Observation of chest expansion, as the only sign to assess ventilation, risks underestimating the delivered VTs and therefore inducing lung injury in asphyxiated neonates receiving PPV.

***Values and preferences:*** Given the evidence for potential benefits, health care providers and policy-makers are likely to prefer using heart rate together with chest movements for assessing ventilation.

***Costs:*** Measurement of heart rate during resuscitation by birth attendants requires additional training.

## ■ RECOMMENDATION 12

**In newly-born babies who do not start breathing within one minute after birth, priority should be given to providing adequate ventilation rather than to chest compressions.**

*(Strong recommendation, based on very low quality evidence from observational studies that ventilation is the most effective intervention for asphyxiated neonates)*

### Remark:

*When a second skilled provider is present, and the neonate continues to have a heart rate of less than 60/minute after 1 minute of PPV, consider chest compressions in addition to PPV.*

## EVIDENCE FOR RECOMMENDATION 12

**Question for systematic review:** In neonates requiring resuscitation after birth (P), is **PPV** alone (I) as effective as **PPV and chest compressions** (C) in reducing mortality (O)?

**Summary of evidence:** Only one observational study (Perlman & Risser, 1995) relevant to the research question was identified. This study examined risk factors for failure of bag and mask ventilation, defined as the need for chest compressions and/or epinephrine, during resuscitation. The study reported that in about two thirds of the infants requiring chest compressions, an improvement in heart rate was observed only after institution of proper respiratory management (effective ventilation with higher pressures and/or endotracheal tube placement).

### *Animal studies:*

One animal study (Dannevig et al., 2011) randomized newborn pigs into three groups – ventilation for 30 seconds, 1 minute or 1.5 minutes before initiation of cardiac compressions – and compared the effect on return of spontaneous circulation. The study found no difference between the first two groups; there was, however, a significant delay in the return of spontaneous circulation in the third group (initiation of chest compressions at 1.5 minutes).

Two other studies (Berg et al., 1999; Berg et al., 2000) in a piglet model relevant to cardiac arrest in older children were identified. These interventional studies compared the effect of PPV alone with PPV *plus* chest compressions in 2-3 month-old asphyxiated piglets with cardiac arrest. One study (Berg et al., 2000) showed a significantly reduced incidence of neurologically normal survival at 24 hours in the group resuscitated with PPV alone (RR 0.60, 95% CI 0.36 to 0.99). The other study (Berg et al., 1999) also showed a trend towards reduction in the incidence of intact survival at 24 hours after resuscitation (RR 0.20, 95% CI 0.03 to 1.31).

There is evidence from observational studies that heart rate increases within 30-60 seconds of effective ventilation (see **Recommendation 11**). There is very low quality evidence (summarized above) that failure of increase in heart rate in many cases may be due to ineffective ventilation. However, if the heart rate is absent or very low after 1 minute of adequate PPV, the addition of chest compressions to PPV might be beneficial.

## CONSIDERATIONS IN FORMULATING RECOMMENDATION 12

**Balance of benefits and harms:** Currently available evidence indicates a benefit of adding chest compressions, if the heart rate is absent or very low after 1 minute of adequate ventilation. No harm of this approach has been reported, but a single provider cannot perform effective PPV and chest compressions at the same time.

**Values and preferences:** Given these considerations, most health care providers are likely to give a high value to initiation of chest compressions in asphyxiated neonates whose heart rate does not increase after 1 minute of PPV. However, this intervention is feasible only when more than one skilled provider is available.

**Costs:** Administration of chest compressions requires two skilled providers at every birth, which would have high costs in most resource-limited settings.

## STOPPING RESUSCITATION

### ▪ RECOMMENDATION 13

**In newly-born babies with no detectable heart rate after 10 minutes of effective ventilation, resuscitation should be stopped.**

*(Strong recommendation, based on evidence of unlikely benefits for the baby)*

**In newly-born babies who continue to have a heart rate below 60/minute and no spontaneous breathing after 20 minutes of resuscitation, resuscitation should be stopped.**

*(Weak situational recommendation, based on very low quality evidence for unlikely benefits for the baby in resource-limited settings)*

## EVIDENCE FOR RECOMMENDATION 13

**Question for systematic review:** In neonates who continue to have no heart rate or severe bradycardia despite resuscitation (P), should resuscitation efforts be **stopped after 10 minutes** (I) as opposed to **20 minutes or longer** (C)?

### Summary of evidence

No study was identified, either observational or interventional, that compared the effect of stopping resuscitation efforts at 10 minutes after birth with stopping at a later time in neonates with asystole or severe bradycardia in the delivery room. Therefore, the outcome of neonates who continued to have asystole or severe bradycardia after several minutes of resuscitation was reviewed.

Nine studies, mostly of retrospective cohort or case-series design from high-income country settings (Casalaz, Marlow & Spiedel, 1998; Haddad et al., 2000; Harrington et al., 2007; Jain et al., 1991; Koppe & Kleiverda, 1984; Laptook et al., 2009; Patel & Beeby, 2004; Socol, Garcia & Riter, 1994; Yeo & Tudehope, 1994), reported outcomes of interest in neonates with asystole at 10 minutes after birth. The studies reported a very high risk of mortality, which ranged from 48% to 88% in studies with a sample size of at least 10 infants (Haddad et al., 2000; Jain et al., 1991; Laptook et al., 2009; Patel & Beeby, 2004). The study reporting the lowest mortality risk (Laptook et al., 2009) included neonates who underwent whole-body hypothermia in a multi-centre randomized trial, which may have reduced the risk of mortality in these infants. Most of the survivors had moderate to severe neurological disability. The quality of these studies is *very low*; they do not mention the number of infants with asystole who were *not* resuscitated, do not specify the method of assessing the duration or quality of resuscitation efforts, and have variable developmental assessment of survivors and a significant loss to follow-up.

No studies reporting the outcome of infants with severe bradycardia after 10 minutes of resuscitation were found. However, five studies (Casalaz, Marlow & Spiedel, 1998; Haddad et al., 2000; Laptook et al., 2009; Nelson & Ellenberg, 1981; Nelson et al., 2011) looked at the outcomes of infants with Apgar scores of 1-3 at 10 minutes after birth. None of these studies specifically reported the heart rates of the included infants; it could be assumed that the infants had a detectable heart rate at 10 minutes of life and that the majority of them would have severe bradycardia (heart rate less than 60/minute). The risk of mortality was 19% to 54% in studies with a sample size of at least 10 infants (Haddad et al., 2000; Laptook et al., 2009). Only two studies reported long-term outcomes - disability in 7 of 12 (Laptook et al., 2009) and 2 of 2 survivors (Nelson & Ellenberg, 1981).

### **CONSIDERATIONS IN FORMULATING RECOMMENDATION 13**

***Balance of benefits and harms:*** Currently available evidence from observational studies indicates that neonates with asystole at 10 minutes after birth are at an extremely high risk of mortality or abnormal neurological outcomes. The outcome in neonates with severe bradycardia at 10 minutes is likely to be poor in the majority of cases.

***Values and preferences:*** Given the high rates of adverse outcomes in infants with asystole at 10 minutes, health care providers and policy-makers are likely to give a high value to stopping the resuscitation efforts at 10 minutes after birth in such infants. However, in neonates who have a detectable heart rate, health care providers might want to continue resuscitation efforts if advanced care is available. Where possible, the parents' views on resuscitation should be obtained and supported.

***Costs:*** Cessation of resuscitation efforts in neonates who have asystole at 10 minutes after birth may save health system resources.

The GDG identified the following questions for future research:

- What is the effect of implementation of these basic newborn resuscitation guidelines on practice in low- and middle-income countries?
- What is the effect of different training methodologies for improving skills for basic newborn resuscitation on performance of health workers?
- What is the effect of video recordings of the care provided to a newborn at birth as a teaching and evaluation tool?
- What is the trainability and performance of different categories of health workers in conducting resuscitation?
- What are the feasibility, safety and efficacy of resuscitation done without cutting the umbilical cord in improving newborn outcomes?
- What is 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?
- What is the risk of serious hyperbilirubinaemia associated with late cord clamping?
- What is the efficacy of stimulation in addition to thorough drying for newborns who do not start breathing on their own in avoiding PPV?
- In settings with a risk of asphyxia and MAS, what are the safety and efficacy of intrapartum suctioning in babies with meconium-stained amniotic fluid in improving newborn outcomes?
- In settings with a risk of asphyxia and MAS, what are the safety and efficacy of suctioning before initiating PPV in babies with meconium-stained amniotic fluid who do not start breathing on their own in improving newborn outcomes?
- What are the safety and efficacy of suctioning of the mouth and nose before initiating PPV in babies with clear amniotic fluid who do not start breathing on their own in improving newborn outcomes?
- Which is the best interface for providing PPV (e.g. nasal cannula, nasal mask or nasopharyngeal prongs, compared with a face mask)?
- What are simple and reliable ways to measure heart rate that do not interfere with provision of PPV?

- What are simpler, low-cost ways of administering blended oxygen for preterm babies <32 weeks gestation?
- Does keeping a resuscitated neonate under a warmer improve or worsen outcome?
- How can whole body or head cooling be done safely for babies who have experienced intrapartum hypoxic-ischemic events in low-resource settings?

## IMPLEMENTATION AND EVALUATION

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A strategy for effective uptake of guidelines requires definition of the key messages, the audiences and the actions for them to take. The key messages of these guidelines are the recommendations listed in the Executive Summary (and the text above). By designating some recommendations as “strong”, the GDG is confident that their implementation will yield significant health benefits, outweighing any potential harm. Although for the remaining “weak” recommendations the situation is less clear, the GDG still felt that the recommendations made are the best possible options for resource-limited settings. The implementation of all recommendations on basic resuscitation will be promoted as a package. With regard to monitoring and evaluation of their impact on quality of care, priority will be given to the strong recommendations. The guidelines also highlight areas where evidence is limited, and further research is warranted.

Monitoring and evaluation will be built into implementation, in order to provide important lessons for uptake and continued implementation. An integrated implementation, monitoring and evaluation framework is proposed in **Table 3**.

**Table 3. Implementation, monitoring and evaluation framework for the second edition of the WHO guidelines on basic newborn resuscitation**

Level	Type of activities	Description of activities	Responsibilities	Indicator
<b>GLOBAL</b>				
	Input	Revise all WHO publications (including practice guides, training materials, job aids, quality of care assessment tools) addressing care of the newborn infant at birth	WHO /HQ Secretariat	Number of updated WHO publications
	Input	Seek endorsement of relevant global players in newborn health (e.g. UNICEF, UNFPA, international NGOs)	WHO/HQ Secretariat	Number of international organizations endorsing the guidelines
	Impact	Document reduction in global number of neonatal deaths due to asphyxia	WHO/HQ Secretariat	Estimates of asphyxia-specific, and early (within first week) neonatal mortality (NMR)
<b>REGIONAL</b>				
	Input	Dissemination of and capacity building on the use of tools (e.g. practice guides, training materials, job aids and quality of care assessment tools) containing new basic newborn resuscitation recommendations	WHO Regional Offices	Number of countries adopting tools related to basic newborn resuscitation

NATIONAL				
	Input	Development or revision of national standards and guidelines reflecting WHO recommendations	Ministries of health or delegated authorities	Number of countries with national standards and guidelines reflecting WHO recommendations
	Impact	Reduce national neonatal and early neonatal mortality rates	Member States	NMR, early NMR from nationally representative surveys
SERVICE DELIVERY LEVEL				
	Input	Build and maintain competencies of health workers attending births to perform newborn resuscitation	Ministries of health, facility managers and partners	Proportion of health professionals attending births trained in newborn resuscitation
	Input	Make available and maintain in good working condition equipment and supplies required for basic newborn resuscitation	Ministries of health, facility managers and partners	Proportion of health care facilities with maternity services that have a functional bag and mask
	Outputs	Ensure that every birth is attended by a health worker proficient in and equipped for newborn resuscitation	Ministries of health, facility managers and partners	Proportion of births assisted by a health worker trained in and equipped for newborn resuscitation
	Impact	Reduce early neonatal deaths (within 7 days) of infants weighing 2500 g or more in facilities	Facility managers, health workers and community health workers	Proportion of newborn infants with a birth weight $\geq 2500$ g alive on 7 <sup>th</sup> day of life

In the context of an increasingly complex international health architecture with multiple players in the areas of advocacy and technical assistance to countries in need, it is vital that

messages and approaches to strengthen newborn resuscitation with its benefit of reducing early neonatal mortality are consistent. In this regard, WHO will work with partners such as United Nations agencies, international nongovernmental organizations (NGOs) and bilateral development agencies to achieve consistency of messages. Furthermore, at the implementation level, whether national or sub-national, there needs to be ownership of the recommendations. WHO will support country processes to adopt these guidelines into national policies. Efforts to improve health workers' knowledge and skills need to be well coordinated, especially with respect to training programmes. WHO will support governments in this coordination and will facilitate alignment of partners with national programmes.

### **Global Actions**

The first steps in implementation after the final approval of the guidelines will be to revise all WHO publications that deal with newborn resuscitation. These include the clinical guides for maternal, newborn and child health: *Pregnancy, childbirth, postpartum and newborn care*; *Managing complications of pregnancy and childbirth*; *Managing newborn problems*; and *Pocket book on hospital care for children*. The revision will include the development of simple flow charts that can be used as job aids by health workers to perform basic newborn resuscitation. The new guidelines will also serve as a standard for neonatal care on initiation of breathing and resuscitation that can be used to assess the adequacy of programmes and quality of care. The existing training package, *Essential newborn care course*, will also be updated, as well as the related tool for computer-assisted learning. These tools will be made available as printed materials or in electronic format.

WHO will reach out to global partners to obtain their endorsement of the guidelines and tools derived from the guidelines in order to facilitate their dissemination and impact in the global arena. Many organizations active in the area of newborn health have identified newborn resuscitation as a priority intervention; these include, but are not limited to, UNFPA, UNICEF, major bilateral agencies and international NGOs (e.g. Saving Newborn Lives, the American Academy of Pediatrics). At the moment, the clinical guidelines and related training activities on basic newborn resuscitation promoted by these agencies are not consistent, creating a certain level of confusion at country and implementation levels. The above-mentioned advocacy effort will lead to more clarity on basic newborn resuscitation and thus lead to improved performance of health workers and better care for newborn infants. One key collaboration will be that with the *Helping Babies Breathe* programme.

In addition to active promotion of partnerships for implementation, WHO will also initiate a process of harmonized monitoring and evaluation of the coverage of this critical health care intervention and the quality of care that newborns receive around birth. This will include a globally-agreed monitoring and evaluation framework with standard indicators.

### **Regional and Country-level Action**

At country level the main step for implementing the recommendations will be to develop national standards and guidelines on newborn resuscitation that take into account the local context. These should be based on the best evidence available, and the present guideline document provides guidance on this matter. The success of the recommendations will be measured by the extent to which countries follow them. In addition, the competencies of health workers in newborn resuscitation will need to be built, both through pre- and in-

service training; tools related to the guidelines can be used for this purpose. Policy- and decision-makers responsible for health care delivery will need to make the necessary equipment and supplies available. The limited number of supplies required for successful basic newborn resuscitation will facilitate implementation. Ultimately, the impact of the guidelines should be increased coverage of newborn resuscitation for those newborn infants who need it.

Newborn resuscitation is currently a major challenge. Health workers attending births are often not proficient in resuscitation techniques, and equipment may not be available or it may be broken. Also, there is a tendency to over-use resuscitation procedures, if they are available. Therefore, in addition to training of health workers, regular assessments of the quality of care that newborns receive around birth, including appropriate use of resuscitation, are required. The generic tools to assess quality of care derived from these recommendations will be an important element in their implementation.

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ANEX 1: GRADE PROFILE SUMMARIES

**Recommendation 1: Late cord clamping**

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled effect size[ES] (95% CI)
<b>Mortality</b> (during initial hospital stay; only preterm neonates)	8	RCTs	No major limitations	Pooled effect not significant, with wide CI	All 8 studies indicate no effect, but large variation in ES (0.14 to 6.68)	Most of the evidence from studies in high-income country settings	<b>LOW</b>	RR 0.73 (0.30 to 1.81)
<b>Severe intraventricular haemorrhage</b> (only preterm infants)	4	RCTs	No major limitations	Effect not significant, with wide CI	All 4 studies indicate no effect, but ES varies from 0.33 to 2.92	Majority of the evidence from studies in high-income country settings	<b>LOW</b>	RR 0.70 (0.16, 2.93)
<b>Anaemia requiring transfusion</b> (during initial hospital stay; only preterm infants)	6	RCTs	Limitations in measurement	Pooled effect significant but upper limit of CI close to null	ES of all studies in same direction as pooled ES	From high-income country settings	<b>MODERATE</b>	RR 0.68 (0.51, 0.92)
<b>Admission in neonatal intensive care unit</b> (only term neonates)	3	RCTs	Limitations in analysis	Effect not significant, with wide CI	All 3 studies indicate no effect	Most of the evidence from studies in high-income country settings	<b>LOW</b>	RR 0.95 (0.51 to 1.78)
<b>Anaemia at 6 months of age</b> (only term infants)	3	RCTs	No major limitations	Effect not significant, with wide CI	All 3 studies indicate no effect	From low- and middle-income country settings	<b>MODERATE</b>	RR 0.87 (0.69, 1.10)
<b>Serum ferritin levels</b> (at 3 months of age in 2 studies and at 6 months in 2 studies; only term infants)	4	Majority of evidence from RCTs	No major limitations	Pooled effect significant, lower limit of CI meaningful	ES of studies with ≥75% of total evidence in the direction as pooled ES	From low- and middle-income country settings	<b>HIGH</b>	MD 12.5 µg/L (5.72, 19.3)
<b>Polycythemia</b> (haematocrit >65%; only term neonates)	3	RCTs	No major limitations	Effect not significant, with wide CI	All 3 studies indicate no effect, but ES of 2 indicate substantial increase	From low- and middle-income country settings	<b>LOW</b>	RR 2.39 (0.72, 7.93)
<b>Hyperbilirubinaemia receiving phototherapy</b> (in both term and preterm infants)	7	RCTs	Limitations in measurement, follow-up and analysis	Pooled effect significant, lower limit of CI close to null	ES of studies with >75% of total weight in the same direction as pooled effect	Most of the evidence from high-income country settings; outcome not based on objective criteria	<b>VERY LOW</b>	RR 1.33 (1.07, 1.66)

### Recommendation 2: Additional stimulation (beyond drying) after birth

GRADE tables were not generated as none of the studies have compared the effect of 'additional stimulation' with 'no additional stimulation' at the time of birth.

### Recommendation 3: Oral/nasal suctioning in infants born through clear amniotic fluid

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Oxygen saturation levels</b> (at 5 minutes of life)	3	RCTs	No serious limitations	Pooled effect significant, upper limit of CI indicates meaningful effect	Three studies, ES in same direction	From low- and middle-income country settings	<b>HIGH</b>	MD -9.8% (-10.2%, -9.4%)
<b>Normal Apgar scores</b> (≥9 at 5 minutes after birth)	3	RCTs	Limitations in measurement	Pooled effect not significant, with wide CI	ES of studies with <75% weight consistent with no effect	Majority of evidence from studies in developing countries	<b>LOW</b>	RR 0.54 (0.28 to 1.07)

#### Recommendation 4: Intrapartum suctioning in infants born through meconium

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Mortality</b> (during initial hospital stay)	1	RCT	No serious limitations	Effect not significant, with wide CI	Single study	Study from low- or middle-income country setting	<b>LOW</b>	RR 2.22 (0.69 to 7.22)
<b>Meconium aspiration syndrome</b>	4	Majority of evidence from RCT	No serious limitations	Pooled effect not significant, with wide CI	Pooled ES indicates no effect, ES of studies with <75% weight consistent with no effect	Majority of evidence from study in low- or middle-income country setting	<b>LOW</b>	RR 1.07 (0.80, 1.44)
<b>Apgar scores of 6 or less</b> (at 5 minutes after birth)	2	Majority of evidence from RCT	Limitations in measurement	Pooled effect not significant, with wide CI	Only two studies, ES of both in same direction	Majority of evidence from study in low- or middle-income country setting	<b>LOW</b>	RR 0.88 (0.63, 1.23)
<b>Air leaks - pneumothorax/pulmonary interstitial emphysema</b>	1	RCT	No serious limitations	Effect not significant, with wide CI	Single study	Study from low- or middle-income country setting	<b>LOW</b>	RR 2.22 (0.69 to 7.22)
<b>Duration of hospital stay</b>	1	RCT	No serious limitations	Effect not significant, with wide CI	Single study	Study from low- or middle-income country setting	<b>LOW</b>	MD -0.8 days (-4.8 to 3.2)

### Recommendation 5: Oropharyngeal and/or tracheal suctioning in infants born through meconium\*

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Mortality</b> (during initial hospital stay)	2	RCTs	No serious limitations	Pooled effect not significant, with wide CI	Two studies with effects in different directions	Both from low- and middle-income country settings	<b>LOW</b>	RR 0.96 (0.22 to 4.25)
<b>Meconium aspiration syndrome</b>	2	RCTs	No serious limitations	Pooled effect not significant, with wide CI	Two studies; effects of both in same direction as pooled effect	Majority of evidence from study in low- or middle-income country setting	<b>MODERATE</b>	RR 1.33 (0.82, 2.14)
<b>Air leaks</b> (during initial hospital stay)	2	RCTs	Limitations in allocation and measurement	Effect not significant, with wide CI	Two studies with effects in different directions	Majority of evidence from study in low- or middle-income country setting	<b>VERY LOW</b>	RR 0.87 (0.16 to 4.92)
<b>Hypoxic-ischemic encephalopathy and/or convulsions</b> (immediate neonatal period)	1	RCT	Limitations in follow-up and analysis	Effect not significant, with wide CI	Single study	Study from low- or middle-income country setting	<b>VERY LOW</b>	RR 2.65 (0.30 to 23.8)

*\*GRADE profile summary of the effect of tracheal suctioning in neonates who start breathing on their own; no GRADE tables were generated for the effect of tracheal suctioning in infants who do not start breathing on their own (all were observational studies).*

### Recommendation 6: Optimal suctioning device(s) for oropharyngeal suctioning

GRADE tables were not generated as there were no relevant comparative human studies.

### Recommendation 7: Timing of positive-pressure ventilation

GRADE tables were not generated as only one very low quality observational study was identified.

### Recommendation 8: Air versus oxygen during positive-pressure ventilation

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Mortality</b> (in the first week in 4 studies, during neonatal period in 2, and until discharge in 1 study)	7	Majority of evidence from quasi-RCTs	No major limitations	Pooled effect significant, but upper limit of CI close to null	ES of studies with >75% of total evidence in the same direction as pooled effect	Majority of evidence from studies in low- and middle-income country settings	<b>MODERATE</b>	OR 0.70 (0.51 to 0.97)
<b>Hypoxic-ischemic encephalopathy – stage 2 or 3</b>	4	Quasi-RCTs	Limitations in measurement	Pooled effect not significant, with wide CI	All 4 studies indicate no effect	From low- and middle-income country settings	<b>LOW</b>	OR 0.89 (0.66, 1.19)
<b>Onset of spontaneous respiration</b> (in the neonatal period)	1	RCT	Limitations in follow-up and analysis	Effect significant, upper limit of CI meaningful	Single study	From high-income country setting	<b>LOW</b>	MD -1.50 minutes (-2.02, -0.98)
<b>Adverse neurodevelopmental outcome</b> (cerebral palsy at 18-24 months age)	1	Quasi-RCT	Limitations in measurement and follow-up	Effect not significant, with wide CI	Single study	From low- or middle-income country setting	<b>VERY LOW</b>	OR 1.38 (0.46, 4.10)

### Recommendation 9: Optimal method of providing positive-pressure ventilation

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Mortality</b> (during neonatal period in both the studies)	2	One quasi-RCT and one observational study	No serious limitations	Effect not significant, with wide CI	Two studies with effect in different directions	Both studies from low- or middle-income country settings	<b>VERY LOW</b>	RR 1.01 (0.39 to 2.60)
<b>First cry within 5 minutes after birth</b>	1	Quasi-RCT	Limitations in measurement	Effect not significant, with wide CI	Single study	From low- or middle-income country setting	<b>VERY LOW</b>	RR 1.27 (0.93, 1.73)
<b>Apgar score <math>\geq 4</math></b> (at 5 minutes after birth)	1	Quasi-RCT	Limitations in measurement	Effect not significant, with wide CI	Single study	From low- or middle-income country setting	<b>VERY LOW</b>	RR 0.99 (0.86, 1.14)
<b>Convulsions</b> (in the neonatal period)	1	Quasi-RCT	Limitations in measurement	Effect not significant, with wide CI	Single study	From low- or middle-income country setting	<b>VERY LOW</b>	RR 0.92 (0.52, 1.64)

### Recommendation 10: Optimal interface for providing positive-pressure ventilation

Outcome	No. of studies	Design	Limitations in methods	Precision	Consistency	Generalizability / directness	Overall quality of evidence	Pooled ES (95% CI)
<b>Mortality</b>	1	Quasi-RCT	No serious limitations	Effect not significant, with wide CI	Single study	From high-income country setting	<b>VERY LOW</b>	RR 0.49 (0.21, 1.11)
<b>Need for intubation during resuscitation</b>	1	Quasi-RCT	Limitations in measurement	Effect significant; lower limit of CI meaningful	Single study	From high-income country setting	<b>LOW</b>	RR 0.1 (0.02 to 0.44)
<b>Need for chest compressions</b>	1	Quasi-RCT	Limitations in measurement	Effect significant; lower limit of CI meaningful	Single study	From high-income country setting	<b>LOW</b>	RR 0.2 (0.08 to 0.51)
<b>Apgar score <math>\leq 7</math> at 5 minutes of life</b>	1	Quasi-RCT	Limitations in measurement	Effect not significant, with wide CI	Single study	From high-income country setting	<b>VERY LOW</b>	RR 1.04 (1.0, 1.08)
<b>Pulmonary air leaks</b> (in the first 72 hours of life)	1	Quasi-RCT	Limitations in measurement	Effect not significant, with wide CI	Single study	From high-income country setting	<b>VERY LOW</b>	RR 0.66 (0.26, 1.68)

**Recommendation 11: Assessing the response to positive-pressure ventilation**

GRADE tables were not generated as none of the studies compared the effect of measuring heart rate and chest movements with assessment of chest movements alone after initiation of PPV.

**Recommendation 12: Need for providing chest compressions along with positive-pressure ventilation**

GRADE tables were not generated as there were no relevant comparative human studies.

**Recommendation 13: Stopping resuscitation**

GRADE tables were not generated as none of the studies compared the effect of cessation of resuscitation efforts at 10 minutes versus at 20 minutes after birth or later.

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