WHO Recommendations on Interventions to Improve Preterm Birth Outcomes

World Health Organization

Agenda for today

1. Introduction: by Metin Gülmezoglu

- Welcome and agenda
- Introduction of the guideline and introduction of presenters

2. Presentation of the Recommendations:

A. Maternal component by Femi Oladapo – 15 minutes
B. Newborn component by Rajiv Bahl – 15 minutes

3. Question and Answers from participants

Introduction

Metin Gülmezoglu,
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Preterm birth - a global problem

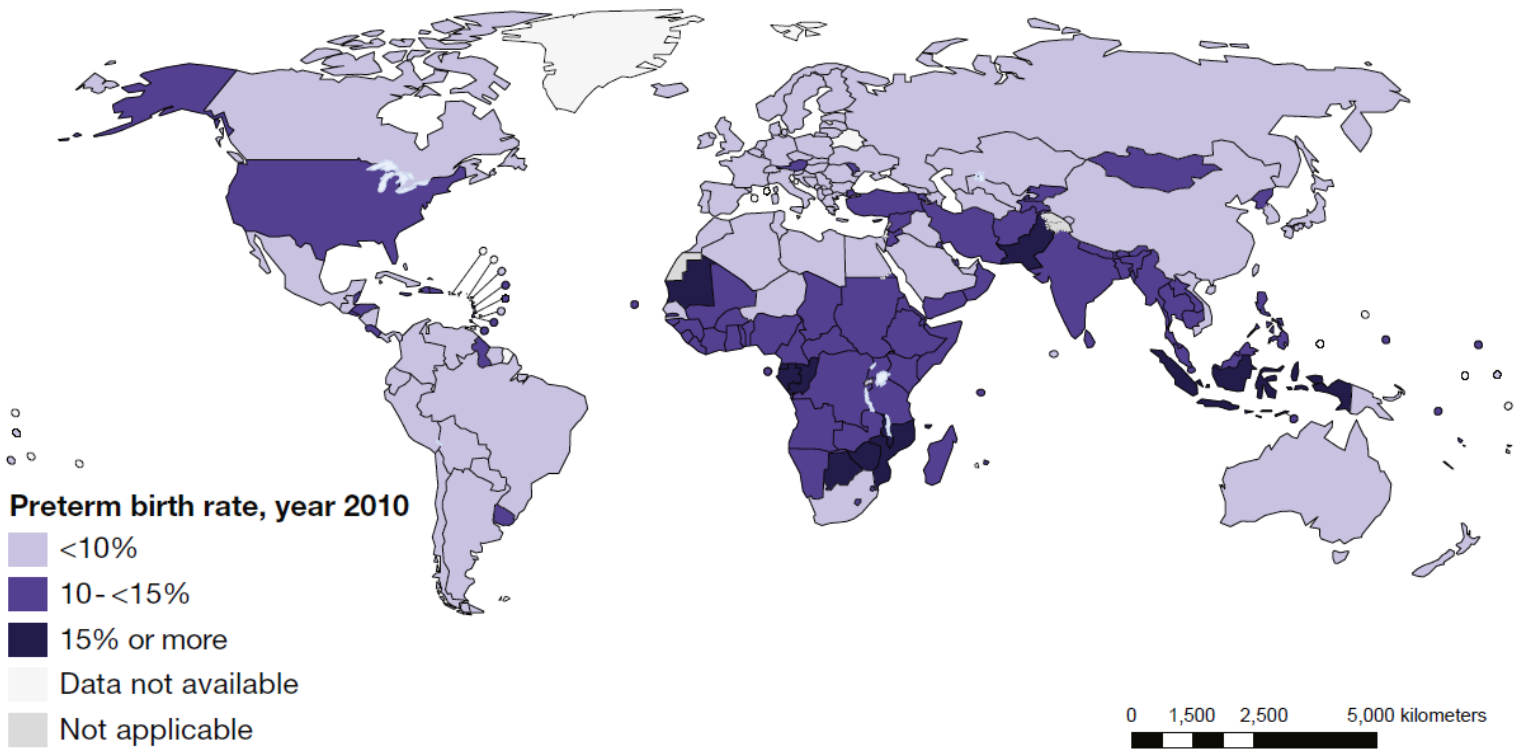
- Preterm birth affected an estimated 11.1% (9.1%–13.4%) of live births globally in 2010

- Equates to approximately 15 million liveborn preterm babies

- 15% of the estimated 6.3 million under 5 child mortality in 2013 were due to complications of preterm birth (1 million deaths)

- Preterm birth is the leading cause of neonatal death

Global burden of preterm birth



11 countries with preterm birth rates over 15% by rank:

1. Malawi
2. Congo
3. Comoros
4. Zimbabwe
5. Equatorial Guinea
6. Mozambique
7. Gabon
8. Pakistan
9. Indonesia
10. Mauritania
11. Botswana

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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
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Maternal interventions to improve preterm birth outcomes

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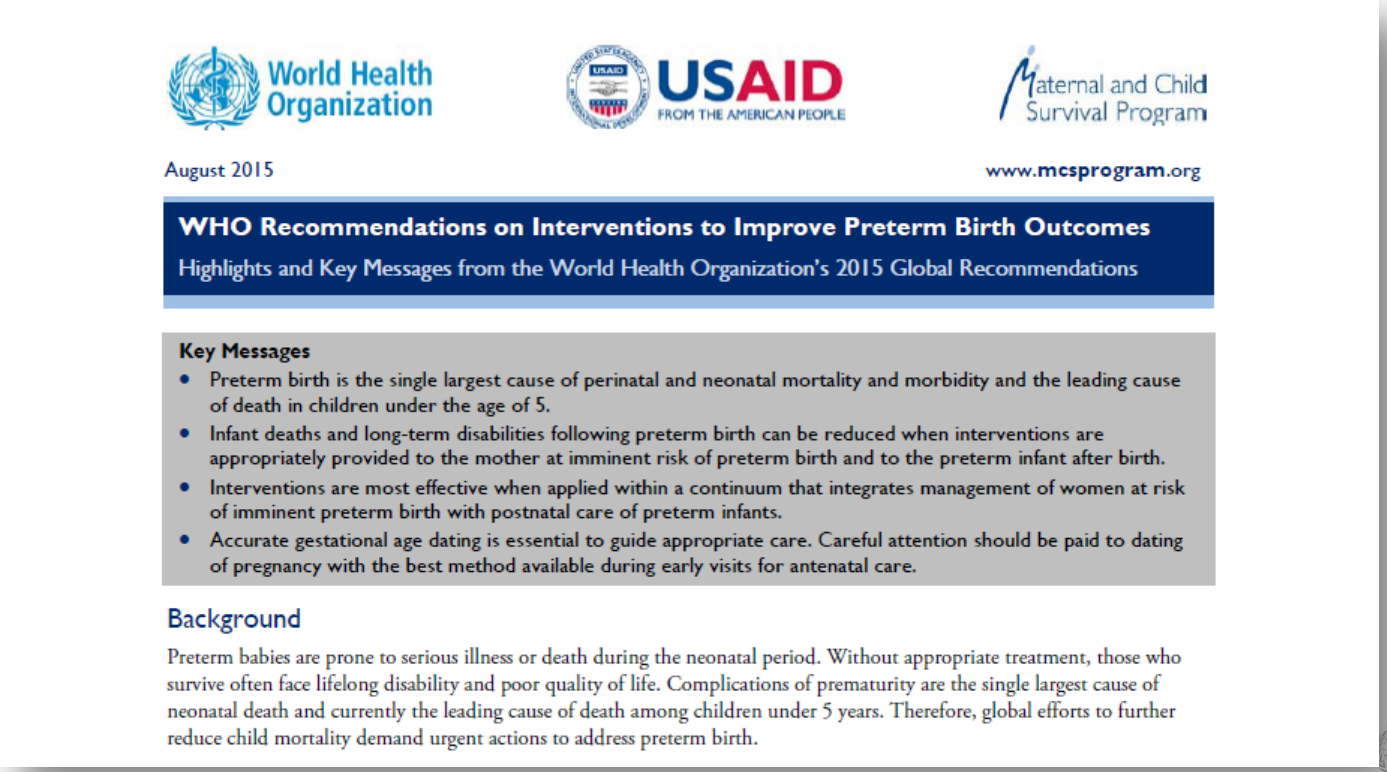
Purpose of the WHO preterm birth guideline - 1

- To provide evidence-based recommendations on interventions during pregnancy, labour and during the newborn period that are aimed at improving outcomes for preterm infants

Purpose of the WHO preterm birth guideline - 2

- To inform the development of protocols and health policies and not intended to provide a comprehensive practical guide for the management of preterm labour and preterm infants



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WHO Recommendations on Interventions to Improve Preterm Birth Outcomes

Highlights and Key Messages from the World Health Organization's 2015 Global Recommendations

Key Messages

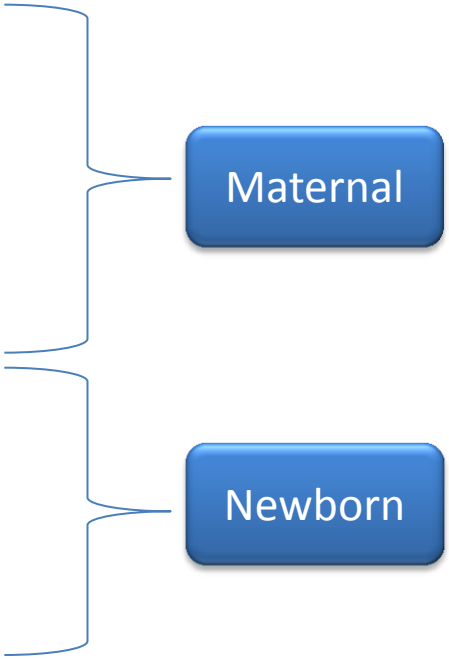
- Preterm birth is the single largest cause of perinatal and neonatal mortality and morbidity and the leading cause of death in children under the age of 5.
- Infant deaths and long-term disabilities following preterm birth can be reduced when interventions are appropriately provided to the mother at imminent risk of preterm birth and to the preterm infant after birth.
- Interventions are most effective when applied within a continuum that integrates management of women at risk of imminent preterm birth with postnatal care of preterm infants.
- Accurate gestational age dating is essential to guide appropriate care. Careful attention should be paid to dating of pregnancy with the best method available during early visits for antenatal care.

Background

Preterm babies are prone to serious illness or death during the neonatal period. Without appropriate treatment, those who survive often face lifelong disability and poor quality of life. Complications of prematurity are the single largest cause of neonatal death and currently the leading cause of death among children under 5 years. Therefore, global efforts to further reduce child mortality demand urgent actions to address preterm birth.

Guideline scope – population and interventions

- Population
  - pregnant women at **imminent risk** of preterm birth (<37 weeks gestation) and preterm babies immediately after birth in all settings
- Interventions
  - Antenatal corticosteroids
  - Tocolytics
  - Magnesium sulfate for fetal neuroprotection
  - Antibiotics for PTL with intact/ruptured membranes
  - Optimal mode of birth
  - Thermal care (KMC, plastic wraps)
  - Continuous Positive Airway Pressure (CPAP)
  - Surfactant
  - Oxygen therapy



Guideline scope – critical outcomes

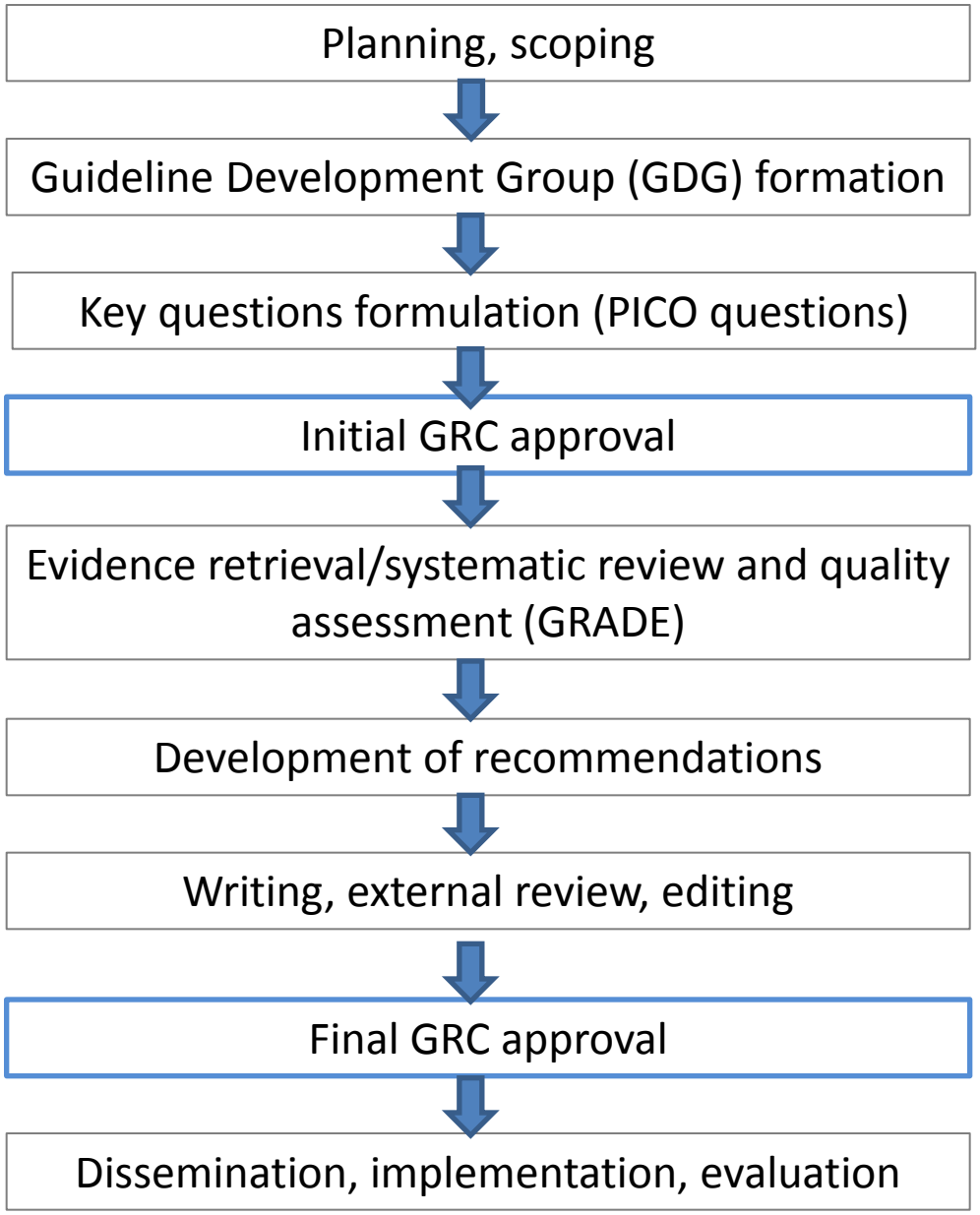
Maternal

- Birth prior to 28, 32, 34 or 37 weeks of gestation
- Pregnancy prolongation (interval between randomization into the study and birth, < 48 hours or < 7 days)
- Severe maternal morbidity or death
- Maternal sepsis (chorioamnionitis, puerperal sepsis)
- Severe adverse effects of treatment

Newborn

- Neonatal death
- Fetal death or stillbirth
- Perinatal death (fetal or early neonatal death)
- Severe neonatal morbidity
- Birth weight (mean; low or very low)
- Infant or child death
- Long-term morbidity

Guideline development methods



Guideline content development

Strength of recommendation

Audience	Strong recommendation	Conditional recommendation
Patients	Most individuals in this situation would want the recommended course of action; only a small proportion would not. Formal decision aides are not likely needed to help individuals make decisions consistent with their values and preferences	Most individuals in this situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the intervention. Adherence to the recommendation could be used as quality criterion or performance indicator.	Different choices will be appropriate for individual patients, who will require assistance in arriving at a management decision consistent with his or her values and preferences. Decision aides may be useful in helping individuals make decisions consistent with their values and preferences
Policy-makers	The recommendation can be adopted as policy in most situations	Policy-making will require substantial debate and involvement of various stakeholders

Source: WHO Handbook for Guideline Development 2014

MATERNAL INTERVENTIONS

Overarching priority questions

- Is antenatal corticosteroid therapy, compared with no antenatal corticosteroid therapy, effective in reducing adverse newborn outcomes?
- Is the use of tocolytic agent(s), compared with no tocolytic agent, effective in delaying preterm birth and reducing adverse newborn outcomes?
- Is magnesium sulfate therapy, compared with no magnesium sulfate therapy, effective in protecting the fetus from neurological complications (i.e. fetal neuroprotection)?
- Among pregnant women at risk of imminent preterm birth with intact/ruptured membranes, is routine antibiotic prophylaxis, compared with no antibiotic prophylaxis, effective in improving maternal and newborn outcomes?
- Is a policy of routine caesarean delivery of preterm infants, compared with planned vaginal birth, effective in reducing adverse newborn outcomes?

ACS for preterm birth – Recommendation 1.0

- ACS therapy is recommended for women at risk of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met:
  - GA assessment can be accurately undertaken;
  - preterm birth is considered imminent;
  - there is no clinical evidence of maternal infection;
  - adequate childbirth care is available (*including the capacity to recognize and safely manage preterm labour and birth*);
  - the preterm newborn can receive adequate care if needed (*including resuscitation, thermal care, feeding support, infection treatment and safe oxygen use*).

Strong recommendation based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes

ACS for preterm birth – guideline panel remarks

- Accurate and standardized GA assessment is essential
- Consideration should be given to local limits of fetal viability when determining the lowest limit of gestational age
- The pre-conditions may not be operationalized in a standard and consistent manner across settings
- Appropriate standard of childbirth care should be available to the mother to recognize and safely manage preterm labour and birth
- Essential and special care for should be available for preterm newborns

ACS for preterm birth – Recommendations 1.1-1.3

- ACS should be administered when preterm birth is considered imminent within 7 days of starting treatment, including within the first 24 hours (*Strong recommendation, low quality of evidence*)
- ACS is recommended for women at risk of preterm birth irrespective of whether a single or multiple birth is anticipated (*Strong recommendation, low quality of evidence*)
- ACS is recommended for women with preterm prelabour rupture of membranes and no clinical signs of infection (*Strong recommendation, moderate-quality evidence for newborn outcomes, low-quality evidence for maternal outcomes*)

ACS for preterm birth – Recommendations 1.4-1.6

- ACS is not recommended for women with chorioamnionitis who are likely to deliver preterm (*Conditional recommendation, very low quality of evidence*)
- ACS is not recommended for women undergoing planned caesarean section at late preterm gestations (34–36+6 weeks) (*Conditional recommendation, very low quality of evidence*)
- ACS therapy is recommended for women with hypertensive disorders in pregnancy who are at risk of imminent preterm birth (*Strong recommendation, moderate-quality evidence for newborn outcomes, low-quality evidence for maternal outcomes*)

ACS for preterm birth – Recommendations 1.7-1.9

- ACS is recommended for women at risk of imminent preterm birth of a growth-restricted fetus (*Strong recommendation, very low quality of evidence*)
- ACS is recommended for women with pre-gestational and gestational diabetes, and this should be accompanied by interventions to optimize maternal blood glucose control (*Strong recommendation, very low quality of evidence*)
- Either IM dexamethasone or IM betamethasone (total 24 mg in divided doses) is recommended when preterm birth is imminent (*Strong recommendation, low-quality evidence*)

ACS for preterm birth – Recommendation 1.10

- Single repeat course of ACS is recommended if preterm birth does not occur within 7 days after the initial dose, and a subsequent clinical assessment demonstrates that there is a high risk of preterm birth in the next 7 days (*Conditional recommendation, moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes*)

Tocolytics for preterm birth – Recommendation 2.0

- Tocolytic treatments (acute and maintenance treatments) are not recommended for women at risk of imminent preterm birth for the purpose of improving newborn outcomes. (*Conditional recommendation, very low quality-evidence*)
  - Acute use to delay birth (up to 48 hours) can be considered for in-utero fetal transfer to appropriate neonatal care setting
  - Nifedipine is the preferred agent in such context
  - Betamimetics have a higher risk of adverse drug reactions and should not be used
  - Further trials needed on whether tocolytics can actually improve substantive perinatal outcomes are a research priority

Magnesium sulfate for neuroprotection – Recommendation 3.0

- Magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 weeks of gestation for prevention of cerebral palsy in the infant and child. (*Strong recommendation, moderate quality-evidence*)
  - Should only be given if preterm birth is likely within the next 24 hours
  - Insufficient evidence to recommend one dosing regimen over the other. Tested regimens include:
    - IV 4 g, then 1 g/hour until delivery or for 24 hours, whichever came first;
    - IV 4 g over 30 minutes or IV 4 g bolus as single dose;
    - IV 6 g over 20-30 minutes, followed by IV maintenance of 2 g/hour.

Antibiotics for women with PTL and intact amniotic membranes – Recommendation 4.0

- Routine antibiotic administration is not recommended for women in preterm labour with intact amniotic membranes and no clinical signs of infection. (*Strong recommendation, moderate quality-evidence*)
  - Any diagnostic or clinical signs of infection are treated accordingly with antibiotics.
  - High emphasis on the potential risk of harm to the baby and less value on the minimal benefit to mothers

Antibiotics for women with PPROM – Recommendations 5.0-5.1

- Antibiotic administration is recommended for women with PPROM (*Strong recommendation, moderate quality-evidence*)
  - No antibiotic without confirming the diagnosis of PPROM.
  - Monitor women for signs of clinical chorioamnionitis
- Erythromycin is recommended as the antibiotic of choice for prophylaxis in women with PPROM (*Conditional recommendation, moderate quality-evidence*)
  - Oral erythromycin 250 mg four times a day for 10 days (or until delivery)

Antibiotics for women in preterm labour and ruptured amniotic membranes – Recommendation 5.2

- Combination of amoxicillin and clavulanic acid ("co-amoxiclav") is not recommended for women with PPROM (*Strong recommendation, moderate quality-evidence*)
  - Increased risk of NEC when compared with placebo and with erythromycin
  - Where organisms are sensitive to other antibiotics, it would seem sensible to avoid using co-amoxiclav during pregnancy
  - Where erythromycin is not available, penicillin (such as amoxicillin) can be used

Optimal mode of birth for women in preterm labour – Recommendation 6.0

- Routine delivery by caesarean section for the purpose of improving preterm newborn outcomes is not recommended, regardless of cephalic or breech presentation. (*Conditional recommendation, very low quality-evidence*)
  - Insufficient evidence to support the routine delivery of preterm infants by caesarean section instead of vaginal delivery
  - CS should only be performed for obstetric indications

Newborn interventions to improve preterm birth outcomes

By
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Three key elements of preterm care

- Warmth
- Feeding
- Respiratory support

Kangaroo Mother Care

- Kangaroo mother care is recommended for the routine care of newborns weighing 2000 g or less at birth, and should be initiated in healthcare facilities as soon as the newborns are clinically stable. *(Strong recommendation based on moderate-quality evidence)*

- as close to continuous KMC as possible

- Intermittent Kangaroo mother care if continuous KMC is not possible.

Thermal care: when KMC is not possible

- Unstable newborns weighing 2000 g or less at birth, or stable newborns weighing less than 2000 g who cannot be given Kangaroo mother care, should be cared for in a thermo-neutral environment either under radiant warmers or in incubators. *(Strong recommendation based on very low-quality evidence)*

- There is insufficient evidence on the effectiveness of plastic bags/wraps in providing thermal care for preterm newborns immediately after birth. However, during stabilization and transfer of preterm newborns to specialized neonatal care wards, wrapping in plastic bags/wraps may be considered as an option to prevent hypothermia.*(Conditional recommendation based on low-quality evidence)*

Respiratory support

The GDG felt strongly that the technological context of care, including the **ability to monitor oxygen saturation** and cardiorespiratory status, must be considered prior to instituting any respiratory intervention (supplemental oxygen, CPAP, ventilator support and surfactant) to critically ill neonates in less-developed medical settings, as these interventions have the potential to lead to more harm than benefit.

Respiratory support: CPAP, Surfactant

- Continuous positive airway pressure therapy is recommended for the treatment of preterm newborns with respiratory distress syndrome. *(Strong recommendation based on low-quality evidence)*
  - should be started as soon as the diagnosis is made.

- Surfactant replacement therapy is recommended for intubated and ventilated newborns with respiratory distress syndrome. *(Conditional recommendation only in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available, based on moderate-quality evidence)*
  - Either animal-derived or protein-containing synthetic surfactants can be used
  - Surfactant should be administered early after diagnosis.
  - Prophylactic administration is not recommended.

Respiratory support: Oxygen

- During ventilation of preterm babies born at or before 32 weeks of gestation, it is recommended to start oxygen therapy with 30% oxygen or air (if blended oxygen is not available), rather than with 100% oxygen. *(Strong recommendation based on very low-quality evidence)*

- The use of progressively higher concentrations of oxygen should only be considered for newborns undergoing oxygen therapy if their heart rate is less than 60 beats per minute after 30 seconds of adequate ventilation with 30% oxygen or air. *(Strong recommendation based on very low-quality evidence)*
  - Starting 2 minutes after birth, the adjustment of the concentration of oxygen levels should be by 10% (FiO2=0.1) per 30 seconds and must be guided by oxygen saturation levels reached.

THANK YOU