بسم الله الرحمن الرحيم

PRETERM BIRTH

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INTRODUCTION

15 million babies are born too soon every year.

- **More than 1 in 10 babies are born preterm, affecting families all around the world.**

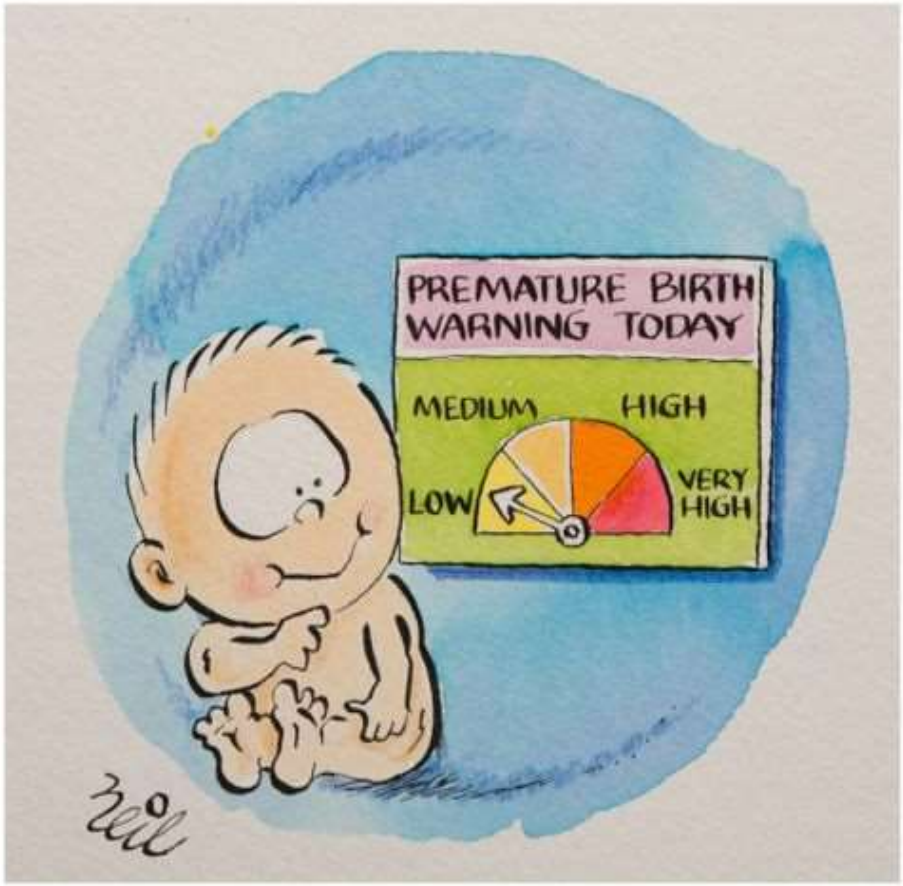
- **Over one million children die each year due to complication of preterm birth. Many survivors face a life-time of disability, including learning disabilities and visual and hearing problems.**

Definition of preterm birth

Babies born alive before 37 weeks of pregnancy are completed.

Sub-categories of preterm birth based on weeks of gestational age:

- **Extremely preterm (< 28 weeks) very preterm 28 to < 32 weeks.**
- **Moderate to late preterm 32 to < 37 weeks.**


PREMATURE BIRTH
WARNING TODAY
MEDIUM
HIGH
LOW
VERY
HIGH

There are two major clinical subtypes of preterm deliveries:

- **1st indicated preterm deliveries for maternal and fetal reasons, it make up 1/3 of preterm birth.**

- **2nd spontaneous preterm and it forms the remaining 2/3 of such birth and it has two subdivisions:**

  - **Spontaneous preterm labour.**

  - **Preterm pre-labour rupture of membranes (P-PROM).**

PRETERM BIRTH BY THE NUMBERS

- **60% of preterm birth occur in sub Saharan Africa and South Asia.**
- **5-18% is the range of preterm birth rates across 184 countries of the world.**
- **The 10 countries with the highest numbers include: Brazil, the united states, India and Nigeria ..demonstrating that preterm birth is truly a global problem.**
- **> 80% of preterm births occurs between 32-37 weeks of gestation.**

- **Most of these babies can survive with essential newborn care.**

- **> 75% of deaths of preterm babies can be prevented without intensive care.**

The present WHO guideline is focused on:

- **Interventions that could be provided during pregnancy, labor and during newborn period with the aim of improving outcomes for preterm infants.**

WHO guideline development methods:

- **The guideline was developed using standard operating procedures. Briefly these include:**

1.Identification of priority questions and critical outcomes.

2.Retrieval of the evidence.

3.Assessment and synthesis of evidence.

4. Planning for dissemination, implementation, impact evaluation, and updating of guideline.

GRADE

- **Each recommendation was synthesized using the GRADE approach (Grading of Recommendation, Assessment, Development, and Evaluation).**

- **In May 2014, the international group of experts established the Guideline Development Group where they formulated and approved the recommendation.**

Recommendation of WHO

The WHO technical consultation led to the adoption of 10 main recommendations covering:

- **Antenatal corticosteroids.**
- **Tocolysis.**
- **Magnesium sulfate.**
- **Antibiotic prophylaxis.**
- **Mode of birth (for the mother).**
- **Kangaroo mother care, plastic wraps.**
- **Continuous positive airway pressure therapy.**
- **Surfactant and oxygen therapy for the newborn.**

For each recommendation, the quality of evidence was graded “very low”, “low”, “moderate” or “high”.

All that is to ensure that each recommendation is correctly understood and applied in practice.

WHO recommendation
On interventions to improve preterm birth outcomes

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	1.0 Antenatal corticosteroids therapy is recommended for women at risk of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met: ▪ Gestational age assessment can be accurately undertaken. ▪ Preterm birth is considered imminent.	**Strong recommendation** Based on moderate quality evidence for newborn outcomes and low quality evidence for maternal outcomes.

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ There is no clinical evidence of maternal infection. ▪ Adequate childbirth care is available (including the capacity to recognize and safely manage preterm labor 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.

Recommendation of 1.0

Evidence is extracted from the Cochrane systematic review of 26 trails (4469 women and 4853 babies)

Quality of the evidence: Moderate (new born) low (mother)

Balance of benefits versus disadvantages: benefits outweigh the disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes.	▪ 1.1 for eligible women, antenatal corticosteroids should be administered when preterm birth is considered imminent within 7 days of starting treatment, including within the first 24 hours.	**Strong recommendation** Based on low quality evidence.

Recommendation of 1.1

- **For eligible women, antenatal corticosteroids should be administrated when preterm birth is considered imminent within 7 days of starting treatment including within the 1st 24 hours.**

Quality of the evidence: LOW	Balance of benefits versus disadvantages: Benefits outweigh the disadvantages	Recommendation directions: In favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes.	▪ 1.2 Antenatal corticosteroids therapy is recommended for women at risk of preterm birth irrespective of whether a single or multiple birth is anticipated.	**Strong recommendation** Based on low quality evidence.

Recommendation of 1.2

- **Antenatal corticosteroid therapy is recommended for women at risk of preterm birth, irrespective of whether a single or multiple birth is expected.**

After evidence was extracted from 12 trails in the same Cochrane review, ONLY 1-2 trials provided data for comparisons related to multiple pregnancies.

Quality of the evidence: "low for both newborn and maternal outcome"

Balance of benefits versus disadvantages: benefits outweigh the disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.3 Antenatal corticosteroids therapy is recommended in women with preterm pre-labor rapture of membranes and no clinical signs of infections.	**Strong recommendation** Based on moderate quality evidence for newborn outcomes and low quality evidence for maternal outcomes.

Recommendation of 1.3

- **Antenatal corticosteroid therapy is recommended in women with preterm pre-labor rupture of membranes and no clinical signs of infection with the same Cochrane review**

Quality of the evidence: Moderate (new born) Low (mother)

Balance of benefits versus disadvantages: benefits outweigh the disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.4 Antenatal corticosteroid therapy is not recommended in women with chorioamnionitis who are likely to delivery preterm.	**Conditional recommendation** Based on very low quality evidence.

Recommendation of 1.4

- **Antenatal corticosteroid therapy is NOT recommended in women with choioaminionitis who are likely to deliver preterm.**

Evidence is extracted from systematic review that included 8 cohort studies involving a total of 1424 mothers expected to deliver at or before 35 weeks of gestation.

Quality of the evidence: Very low (Newborn critical outcome obtained from observational studies with the some design limitations)

Balance of benefits versus disadvantages: benefits and disadvantages are balanced

Recommendation directions against the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

(because of risk of maternal infection in low and middle income setting)

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.4 Antenatal corticosteroids therapy is NOT recommended for women undergoing planned caesarean section at the late preterm gestations (34–36^{+6} weeks)	**Conditional Recommendation** Based on very low quality evidence.

Recommendation of 1.5

- **Antenatal corticosteroid therapy is NOT recommended in women undergoing planned caesarean section at late preterm gestation (34-36th) weeks.**

Current evidence comes from a single study without major methodological concern. (Non blinded randomized trial in the UK involving 942 mothers and their babies after term elective C/S), comparing betamethazone with usual treatment without corticosteroids

Quality of the evidence: Very low

Balance of benefits versus disadvantages: benefits and disadvantages are balanced

Recommendation directions against the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.6 Antenatal corticosteroid therapy is recommended in women with hypersensitive disorders in pregnancy who are at risk of imminent preterm birth.	**Strong recommendation** Based on moderate quality evidence for newborn outcomes and low quality evidence for maternal outcomes.

Recommendation of 1.6

- **Antenatal corticosteroid therapy is recommended in women with hypertensive disorders in pregnancy who are at risk of imminent preterm birth.**

Cochrane review evaluates the effectiveness of antenatal corticosteroids using subgroup analysis

Quality of the evidence: Moderate (new born), Low (mother)

Balance of benefits versus disadvantages: benefits outweigh disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

STRONG

RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.7 Antenatal corticosteroid therapy is recommended for women at risk of imminent preterm of a growth-restricted fetus.	**Strong recommendation** Based on very low quality evidence.

Recommendation of 1.7

- **Antenatal corticosteroid therapy is recommended for women at risk of imminent preterm birth of growth restricted fetus.**

Evidence is extracted from one systematic review of 9 observational studies (which included 2846 mothers and their infants)

Quality of the evidence: Very low

Balance of benefits versus disadvantages: Benefits outweigh the disadvantages

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.8 Antenatal corticosteroid therapy is recommended for women with pre-gestational and gestational diabetes who are at risk of imminent preterm birth, and this should be accompanied by interventions to optimize maternal blood glucose control.	**Strong recommendation** Based on very low quality evidence.

Recommendation of 1.8

- **Antenatal corticosteroid therapy is recommended for women with pre-gestational and gestational diabetes who are at risk of imminent preterm birth, and this should be accompanied by interventions to optimize maternal blood glucose control.**

One randomized trail was conducted in Brazil, while an observational study was conducted among 30 women in Mexico

Quality of the evidence: Very low (indirect evidence)

Balance of benefits versus disadvantages: Benefits outweigh the disadvantages

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.9 Either intramuscular (IM) dexamethasone or IM betamethasone (total 24 mg in divided doses) is recommended as the antenatal corticosteroid of choice when preterm birth is imminent.	**Strong recommendation** Based on low quality evidence.

Recommendation of 1.9

- **Either intramuscular (IM) Dexamethasone or IM beta methasone total 24 mg in divided doses is recommended as the antenatal corticosteroid of choice when preterm birth is imminent.**

Cochrane systematic review included 12 trails (1557 women and 1661 infants)

Quality of the evidence: Low

Balance of benefits versus disadvantages: Benefits and disadvantages are balanced

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antenatal corticosteroids to improve newborn outcomes	▪ 1.10 single repeat course of antenatal corticosteroid is recommended if preterm birth dose 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** Based on moderate quality evidence for newborn outcomes and low quality evidence for maternal outcomes.

Recommendation of 1.10

- **A single repeat course of antenatal corticosteroids is recommended if preterm birth dose not occur within seven days after the initial dose and a subsequent clinical assessment demonstrates that there is a high risk of preterm birth in the next seven days.**

Data extracted from a Cochrane systematic review of 10 trails (4733 women and 5700 babies included)

Quality of the evidence: Moderate (new born), Low (mother)

Balance of benefits versus disadvantages: Benefits outweigh the disadvantages

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Tocolytics for inhibiting preterm labor	▪ 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** Based on low quality evidence.

Recommendation of 2.0

- **Tocolytic treatments (acute and maintenance treatments) are not recommended for women at risk of imminent preterm birth for the purpose of improving neonatal outcomes.**

8 trails compared Tocolytic agent versus Placebo. 12 trails compared betaminetic with placebo.

2 trails (123) women compared calcium channel blocker (Nifidipine with placebo)

4 trails compared magnesium Sulphate verses placebo

Quality of the evidence: very low

Balance of benefits versus disadvantages: Benefits outweigh the disadvantages

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Magnesium sulfate for fetal protection against neurological complications	▪ 3.0 the use of magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 week of gestation for prevention of cerebral palsy in the infant and child.	**Strong recommendation** Based on moderate quality evidence.

Recommendation of 3.0

- **The use of magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 weeks gestation for prevention of cerebral palsy in the infant child.**

Use of magnesium sulfate for neuroprotection in preterm infants was extracted from Cochrane systematic review (5 studies including 6145 infants)

Quality of the evidence: Moderate

Balance of benefits versus disadvantages: Benefits outweigh the disadvantages

Recommendation directions in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antibiotics for preterm labor	▪ 4.0 Routine antibiotics administration is NOT recommended for women in preterm labor with intact amniotic membranes and no clinical signs of infection.	**Strong recommendation** Based on moderate quality evidence.

Recommendation of 4.0

- **Routine antibiotic administration is NOT recommended for women in preterm labor with intact amniotic membranes and no clinical signs of infection**

Evidence extracted from Cochrane systematic review of 14 trails (RCT's) involving 7800 woman

Quality of the evidence: Moderate

Balance of benefits versus disadvantages: Disadvantages outweigh benefits

Recommendation directions: Against the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Antibiotics for preterm labor	▪ 5.0 antibiotic administration is recommended for women with preterm pre-labor rupture of membranes. ▪ 5.1 Erythromycin is recommended as the antibiotic of choice for prophylaxis is women with preterm pre-labor rupture of membranes. ▪ 5.2 the use of a combination of amoxicillin and clavulanic acid ("co-amoxiclav") is not recommended for women with preterm pre-labor rupture of membranes.	▪ **Strong recommendation** Based on moderate quality evidence. ▪ **Conditional recommendation** based on moderate-quality evidence. ▪ **Strong recommendation** Based on moderate quality evidence.

Recommendation of 5.0

- **Antibiotic administration is recommended for women with preterm prelabor rupture of membranes.**

Evidence extracted from Cochrane review included 22 RCT's and a total for more than 7000 women

Quality of the evidence: Moderate for both (mothers and newborns)

Balance of benefits versus disadvantages: Benefits outweigh disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Recommendation of 5.1

- **Erythromycin is recommended as the antibiotics of choice for prophylaxis in women with preterm pre-labor rupture of membranes.**

The choice of Erythromycin was based on the findings (of the ORACLE study) with over 2000 women.

Quality of the evidence: Moderate

Balance of benefits versus disadvantages: Benefits outweigh disadvantages

Recommendation directions: in favor of the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

Recommendation of 5.2

- **The use of a combination of amoxicillin and clavulanic acid ("co-amoxiclav") is NOT recommended for women with preterm pre labor rupture of membranes**

ORACLE trial

Quality of the evidence: Moderate

Balance of benefits versus disadvantages: Benefits outweigh disadvantages

Recommendation directions: against the intervention

Overall strength of the Recommendation:

STRONG RECOMMENDATION

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence
Optimal mode of delivery	▪ 6.0 routine delivery by caesareans section for the purpose of improving preterm newborn outcomes is NOT recommended, regardless of cephalic or breech presentation.	**Conditional recommendation** Based on very low quality evidence.

Recommendation of 6.0

- **Routine delivery by caesarean section for the purpose of improving preterm newborn outcomes is NOT recommend, regardless cephalic or breech presentation**

Evidence on the optimal mode of delivery for preterm infant was extracted from one Cochrane systematic review of 4 trails of a total 116 women.

Quality of the evidence: very low

Balance of benefits versus disadvantages: Benefits and disadvantages are balanced

Recommendation directions: against the intervention

Overall strength of the Recommendation:

CONDITIONAL RECOMMENDATION

RCOG Green-top Guideline
July 2022

- **A course of antenatal corticosteroids given within the seven days prior to preterm birth reduces perinatal and neonatal death and respiratory distress syndrome. (Grade A).**

- **For women undergoing planned caesarean birth between 37^{+0} and 38^{+6} weeks an informed discussion should take place with the woman about the potential risks and benefits of a course of antenatal corticosteroids. Although antenatal corticosteroids may reduce admission to the neonatal unit for respiratory morbidity, it is uncertain if there is any reduction in respiratory distress syndrome, transient tachypnea of the newborn or neonatal unit admission overall, and antenatal corticosteroids may result in harm to the neonate which includes hypoglycemia and potential developmental delay. (Grade B).**

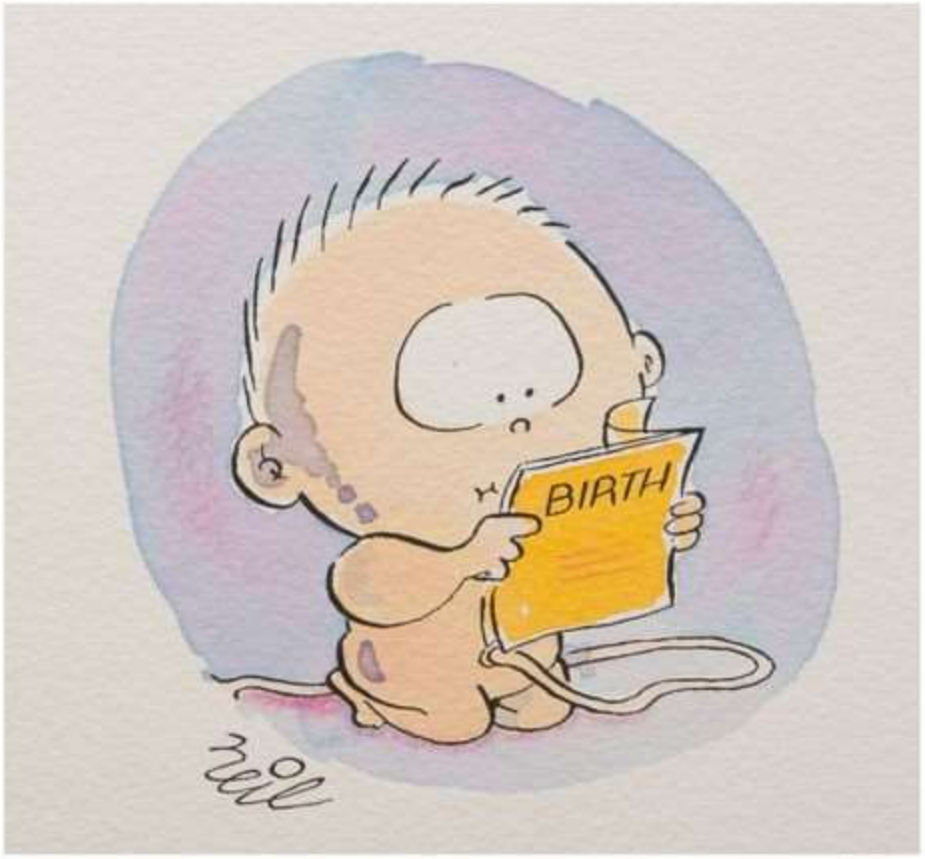
- **Corticosteroids should be offered to women between 24^{+0} and 34^{+6} weeks' gestation in whom imminent preterm birth is anticipated (either due to established preterm labour, preterm prelabour rupture of membranes (PPROM) or planned preterm birth). (Grade A).**
- **Women with twins and triplets should be offered targeted antenatal corticosteroids for early birth in line with recommendations for singletons. (Grade GPP).**

- **Birth should not be delayed for antenatal corticosteroids if the indication for birth is impacting the health of the woman or her baby. (Grade GPP).**

- **Antenatal corticosteroids should be offered to women with PPROM, who are at increased risk of preterm birth. (Grade A).**

- **Antenatal corticosteroids use reduces neonatal death when the first dose is given within the 48 hours prior to birth. (Grade D).**

- **Benefits are also seen when the first dose is given within 24 hours of birth and antenatal corticosteroids should still be given if birth is expected within this time. (Grade D).**



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