Preterm infant feeding and growth monitoring: Implementation of the INTERGROWTH-21st protocol

Module 1
Background on preterm birth

On successful completion of this module you should be able to:

- Define the different categories of preterm delivery and low birth weight.
- Know the global burden of preterm deliveries and calculate preterm birth rates.
- Identify the risk factors for preterm delivery.
- List the long-term effects of preterm deliveries.
- State the global goals for reduction of preterm deaths and the 2025 Global Nutrition targets.
- Know the different methods for gestational age estimation and their strengths and limitations.
- Assess gestational age from crown-rump length and symphysis-fundal height measurements using the respective INTERGROWTH-21st international standards.
- Conduct an anthropometric assessment of the newborn preterm.
- Use the INTERGROWTH-21st postnatal growth standards for preterm infants and INTERGROWTH-21st Newborn Size Application Tool.
- Know the WHO recommendations on the following interventions for preterm deliveries: Kangaroo mother care, continuous positive airway pressure, surfactant administration, oxygen therapy, antenatal corticosteroids administration, tocolysis for inhibiting preterm labour and magnesium sulfate administration.

Introduction

Preterm delivery is a public health concern of global magnitude with 15 million preterm babies born annually. It is the leading cause of neonatal mortality and second cause of mortality in children below 5 years (Howson CP, 2013; Liu L, 2016).

Premature interruption of maternal transfer of macro and micronutrients coupled with inability to produce the necessary amount of metabolically essential forms of key nutrients such as Docosahexaenoic acid (DHA) and arachidonic acid by the premature infant poses a development challenge. As such, most preterm infants do not achieve a growth trajectory similar to the last intrauterine trimester (Raiten DJ, 2016).

Moreover, while preterm postnatal growth has been portrayed in many growth charts to mimic that of infants who grow to term, assuming a convex curve with late flattening of "growth", the Preterm Postnatal Follow-up Study of the INTERGROWTH-21st Project established that postnatal growth in preterm infants assumes an upward curve instead, up to 42 weeks' gestation (see animation below in the next slide) (Villar J, 2015).

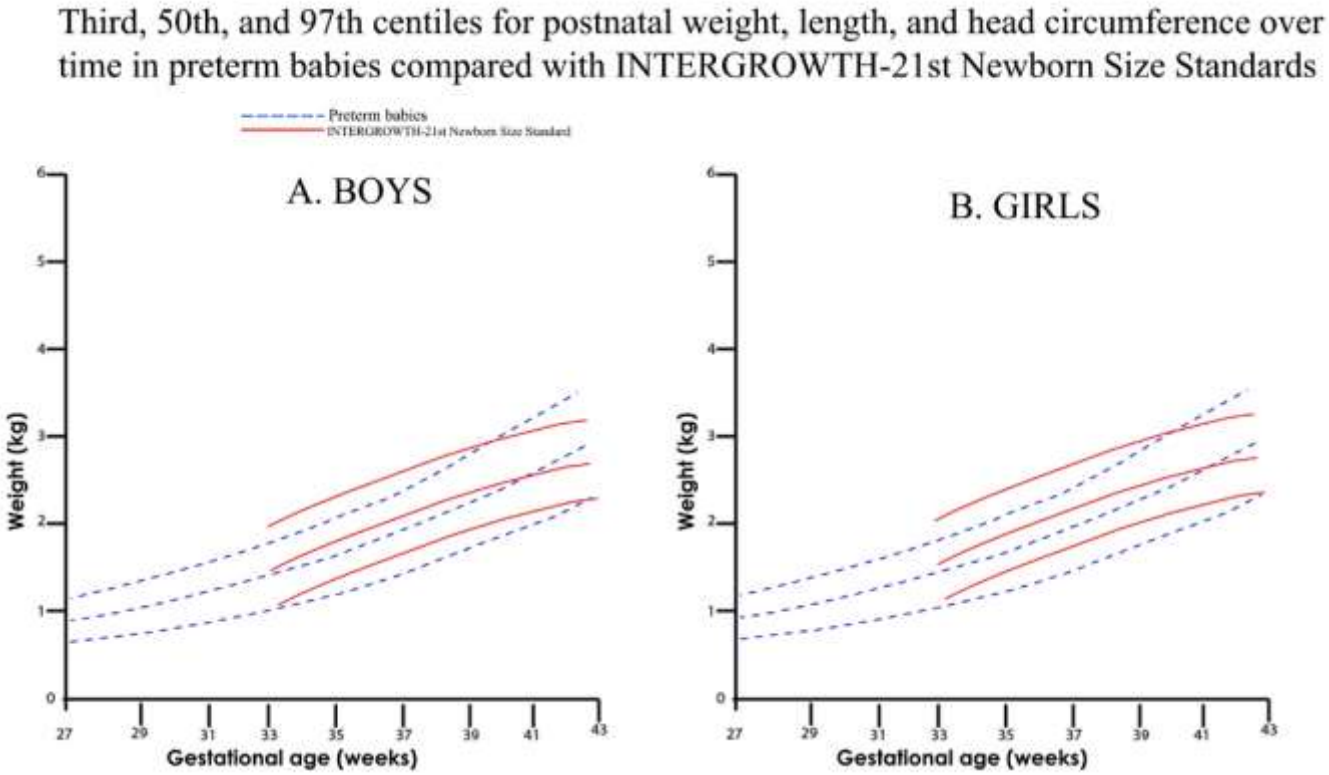
Howson CP, Kinney MV, McDougall L, Lawn JE, Born Too Soon Preterm Birth Action Group. Born too soon: preterm birth matters. Reprod Health. 2013;10 Suppl 1:S1. doi: 10.1186/1742-4755-10-S1-S1

Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet. 2016;388(10063):3027-35. Epub 2016/11/11. doi: 10.1016/S0140-6736(16)31593-8.

Raiten DJ, Steiber AL, Carlson SE, Griffin I, Anderson D, Hay WW, et al. Working group reports: evaluation of the evidence to support practice guidelines for nutritional care of preterm infants-the Pre-B Project. Am J Clin Nutr. 2016;103(2):648S-78S. Epub 2016/01/20. doi: 10.3945/ajcn.115.117309.

Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, et al. Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015;3(11):e681-91. doi: 10.1016/S2214-109X(15)00163-1.

Click to play infographic on how growth trajectories differ between preterm infants **(blue)** and fetuses who grow to term **(red) matched for gestational age**, in both boys and girls.



Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, et al. Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015;3(11):e681-91. doi: 10.1016/S2214-109X(15)00163-1.

Introduction

The difference in growth trajectories noted in the preceding charts between postnatal preterm babies and foetuses growing to term in the Preterm Postnatal Follow-up Study (PPFS) of the INTERGROWTH-21st Project, as compared to previous charts, emanates from the fact that previous studies used in creating preterm postnatal growth standards were noted to have several inconsistencies, which could have compromised the quality.

For example, studies previously used to derive preterm postnatal growth charts were noted to have shortcomings regarding anthropometric assessments, estimation of gestational age, duration of follow-up, reporting of postnatal care and morbidity, assessment of outliers and covariates, and the presentation of charts.

The PPFS, however, used a prescriptive approach, longitudinally following healthy, well nourished preterm infants free from environmental and socioeconomic constraints on growth, in eight centres across the globe. This approach implies that the INTERGROWTH-21st growth standards are generalisable to other populations irrespective of ethnic and geographical differences.

Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, et al. Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015;3(11):e681-91. doi: 10.1016/S2214-109X(15)00163-1.

Introduction

While more interventional studies are needed, current evidence (especially from observational studies) suggests that an accelerated growth between preterm and term-corrected age is beneficial to long-term neurodevelopment, although this also poses a metabolic risk later in life given that most of the catch-up growth is composed of increase in body fat (Ong KK, 2015; Belfort MB, 2013).

Nutritional needs of preterm infants therefore exceed those of healthy term infants in the sense that extra care is needed to optimize growth while at the same time avoiding the risks of undernutrition and overnutrition both in early and later life.

In summary, early postnatal growth in all neonates including preterm babies should be as physiological as possible for optimum survival and long-term outcomes (Villar J 2015).

These three modules focus on preterm birth and on preterm infant feeding modalities to ensure optimum growth based on existing evidence, as well as monitoring of this growth.

Belfort MB, Gillman MW, Buka SL, Casey PH, McCormick MC. Preterm infant linear growth and adiposity gain: trade-offs for later weight status and intelligence quotient. J Pediatr. 2013;163(6):1564-9.e2. Epub 2013/07/30. doi: 10.1016/j.jpeds.2013.06.032.
Ong KK, Kennedy K, Castañeda-Gutiérrez E, Forsyth S, Godfrey KM, Koletzko B, et al. Postnatal growth in preterm infants and later health outcomes: a systematic review. Acta Paediatr. 2015;104(10):974-86. doi: 10.1111/apa.13128.
Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, et al. Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015;3(11):e681-91. doi: 10.1016/S2214-109X(15)00163-1.

Definitions

Consistent definitions to describe the length of gestation and age in neonates are necessary to promote accurate interpretation of data on neurodevelopmental, medical, and **growth** outcomes as well as allowing comparisons, especially for those born preterm or conceived using assisted reproductive technology. To avoid confusion, you will find the following definitions useful:

Term	Definition	Units of time
Gestational age	Time elapsed between the first day of the last menstrual period and the day of delivery. If pregnancy was achieved using assisted reproductive technology, gestational age is calculated by adding 2 weeks to the conceptional age.	Completed weeks
Chronological age	Time elapsed since birth	Days, weeks, months, years
Postmenstrual age	Gestational age + chronological age	Weeks
Corrected age	Chronological age reduced by the number of weeks born before 40 weeks' gestation	Weeks, months

Engle WA, Newborn AAoPCoFa. Age terminology during the perinatal period. Pediatrics. 2004;114(5):1362-4. doi: 10.1542/peds.2004-1915.

Definitions

Preterm delivery is defined as all births (live or still births) before gestational age of **37 weeks or fewer than 259 days** since the first day of a woman's last menstrual period (Goldenberg RL, 2012; Villar J, 2012, March of Dimes, 2012).

Gestational age at birth forms the basis of sub-categories as follows:

- Extremely preterm (<28 weeks)
- Very preterm (28 to <32 weeks)
- Moderate preterm (32 to <37 weeks).
- Moderate preterm birth may be further split to focus on late preterm birth (34 to <37 completed weeks). (March of Dimes, 2012)

Low birth weight is defined as weight at **birth of less than 2,500 grams (5.5 pounds)**. This is based on epidemiological observations that infants weighing less than 2,500 g are approximately 20 times more likely to die than heavier babies. This is further subdivided as follows:

- Very low birthweight is less than 1,500 g (up to and including 1,499 g)
- Extremely low birthweight is less than 1,000 g (up to and including 999 g).

Preterm birth is a risk factor for low birth weight. (March of Dimes, 2012)

Goldenberg RL, Gravett MG, Iams J, Papageorghiou AT, Waller SA, Kramer M, Culhane J, Barros F, Conde-Agudelo A, Bhutta ZA, Knight HE, Villar J. The preterm birth syndrome: issues to consider in creating a classification system. Am J Obstet Gynecol. 2012 Feb;206(2):113-8.
March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.
Villar J, Papageorghiou AT, Knight HE, Gravett MG, Iams J, Waller SA, Kramer M, Culhane JF, Barros FC, Conde-Agudelo A, Bhutta ZA, Goldenberg RL. The preterm birth syndrome: a prototype phenotypic classification. American Journal of Obstetrics & Gynecology. 2012 Feb 1;206(2):119-23.

Global burden of preterm deliveries

- Preterm delivery is a major risk factor for neonatal deaths, responsible for 35% of the world's 3.1 million deaths a year, and the second most common cause of under-5 deaths only surpassed by pneumonia.
- Approximately 55% of all preterm births occur in males; boys have a disproportionately higher risk of dying when compared to girls born at a similar gestation.
- 15 million preterm births occur every year and this figure is rising.
- 1.1 million babies die from preterm birth complications.
- The range of preterm birth rates across 184 countries of the world is 5-18%.
- More than 80% of preterm births occur between 32-37 weeks' gestation and most of these babies can survive with essential newborn care.
- More than 75% of deaths of preterm births can be prevented without intensive care.

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012

Global burden of preterm deliveries

Click on the image to find out the 10 countries with the highest burden of preterm births as well as preterm birth rate range of your country.

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Measuring preterm birth

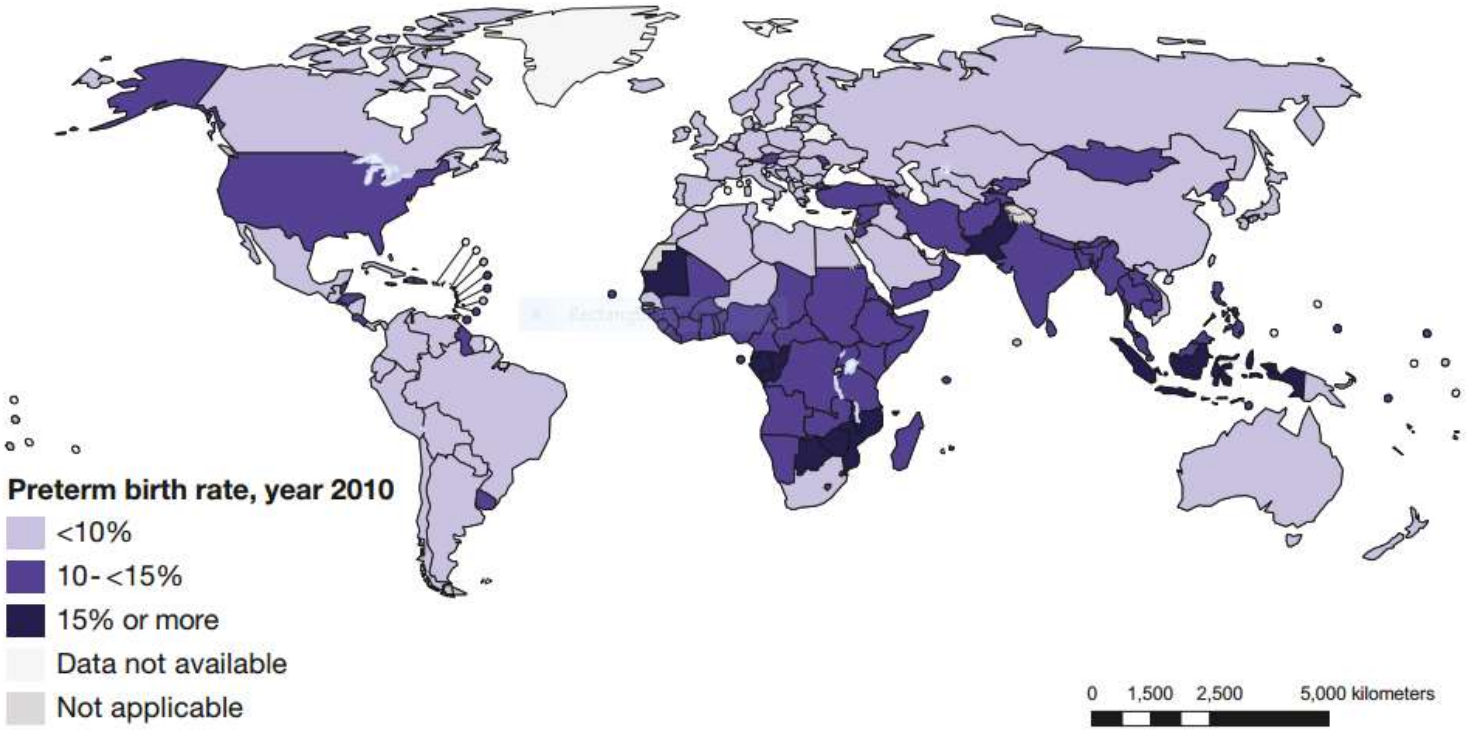
By definition, preterm birth rate is:

$$\frac{\text{All live births before 37 completed weeks (whether singleton or multiple)}}{\text{Per 100 live births.}}$$

Challenges in estimation of preterm birth rates for comparison arise mostly from the numerator because of a) variations in the definition of the term 'preterm'; b) varying methods used to measure gestational age, and c) differences in case ascertainment and registration in different countries (both numerator and denominator).

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

World Health Organization estimates of preterm birth rates



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

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications.
Note: rates by country are available on the accompanying wall chart.
Not applicable= non WHO Members State

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

World Health Organization estimates of preterm birth rates

Statistical modelling has been used to estimate preterm birth rates. For countries with available data based on good vital registration for maternal deaths, using the standard definition for preterm birth, and with data for more than 50% of the years 1990–2010, country-level loess regression to estimate preterm birth rates for all years was used.

In countries with inadequate data, due to regional variations in the quality of data available and the underlying causes and predictors of preterm birth between high-income settings and the rest of the world, two additional models have been employed for “Developed regions” and “Latin America and the Caribbean” (**model I**), and another to estimate the preterm birth rate in all other regions of the world (**model II**).

As a result, distribution of preterm birth according to gestational age subgroup based on meta-analysis may be summarised as follows:

Preterm birth grouping	Gestational age	Proportion of all <37 weeks (%)	Lower 95% uncertainty interval	Higher 95% uncertainty interval (%)
Extremely preterm	<28 weeks	5.2%	5.1%	5.3%
Very preterm	28-<32 weeks	10.4%	10.3%	10.5%
Moderate or Late	32-36 weeks	84.3%	84.1%	84.5%

Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-72. doi: 10.1016/S0140-6736(12)60820-4.

Risk factors for preterm births

Preterm birth can either be **spontaneous** or **provider-initiated**.

Risk factors for spontaneous preterm births include:

- age at pregnancy and pregnancy spacing (e.g. adolescent pregnancy, advanced maternal age, or short interpregnancy interval);
- multiple pregnancy (increased rates of twin and higher order pregnancies with assisted reproduction);
- infections (urinary tract infections, malaria, HIV, syphilis, bacterial vaginosis);
- pre-existing maternal chronic medical conditions (diabetes, hypertension, anaemia, asthma, thyroid disease);
- nutritional (undernutrition, obesity, micronutrient deficiencies);
- lifestyle/ work related (smoking, excess alcohol consumption, recreational drug use, excess physical work/activity);
- maternal psychological health (depression, violence against women);
- genetic and other genetic risks, e.g. family history, cervical incompetence

Risk factors for provider-initiated preterm birth include:

- medical induction
- cesarean birth

Howson CP, Kinney MV, McDougall L, Lawn JE, Born Too Soon Preterm Birth Action Group. Born too soon: preterm birth matters. Reprod Health. 2013;10 Suppl 1:S1. http://dx.doi.org/10.1186/1742-4755-10-S1-S1

Signs and symptoms of preterm labour

It is important for the reader to familiarize themselves with signs and symptoms of preterm labour, especially if labour is spontaneous.

Sudden onset of regular, painful contractions of increasing intensity before 37 completed weeks are probably more likely to represent spontaneous preterm labour than a longer period of irregular contractions.

Other symptoms include menstrual cramps, backache, pelvic pressure, vaginal discharge, urinary frequency, diarrhoea or vaginal bleeding.

The presence of vaginal bleeding increases the risk of preterm birth and this may be suggestive of intrauterine infection. Caesarean section due to abruptio placenta before 37 weeks would definitely result into preterm delivery.

Herbst A, Nilsson C. Diagnosis of early preterm labour. BJOG. 2006;113 Suppl 3:60-7. doi: 10.1111/j.1471-0528.2006.01125.x.

Signs and symptoms of preterm labour

Cervical effacement or dilation is confirmatory of spontaneous preterm labour.

However, digital (using fingers) examination alone may be insufficient in ruling out preterm labour, since with a closed cervix, only the vaginal portion of the cervix is palpable and dilation of the internal cervical os is difficult to detect by palpation.

Herbst A, Nilsson C. Diagnosis of early preterm labour. BJOG. 2006;113 Suppl 3:60-7. doi: 10.1111/j.1471-0528.2006.01125.x.

Signs and symptoms of preterm labour

As such, transvaginal ultrasonographic scanning (TVUSS) assessment of the cervix in spontaneous preterm labour offers additional information where the cervix is closed, as well as providing a more accurate measure of the cervical length.

A short cervix is an independent risk factor for preterm labour. However, a shortened cervical length may be due to funnelling resulting from dilation of the internal os.

A number of studies of cervical length in women with spontaneous preterm labour have been conducted. With 30–32 mm as cutoff, the sensitivity was 81–100% for predicting delivery before 36–37 gestational weeks and 88–100% for preterm birth before 34–35 weeks.

Herbst A, Nilsson C. Diagnosis of early preterm labour. BJOG. 2006;113 Suppl 3:60-7. doi: 10.1111/j.1471-0528.2006.01125.x.

Signs and symptoms of preterm labour

Elevated white blood cell count and serum levels of C-reactive protein (CRP) may reflect infection but also labour, since CRP also rises during labour without signs of infection.

Elevated levels of fetal fibronectin (FFN) in cervico-vaginal secretions, a glycoprotein found in high concentrations in the placenta and amniotic fluid, as well as interleukin 6 (IL-6) in the amniotic fluid and in cervical secretions are also indicative of spontaneous preterm labour.

Herbst A, Nilsson C. Diagnosis of early preterm labour. BJOG. 2006;113 Suppl 3:60-7. doi: 10.1111/j.1471-0528.2006.01125.x.

The 10:90 survival gap

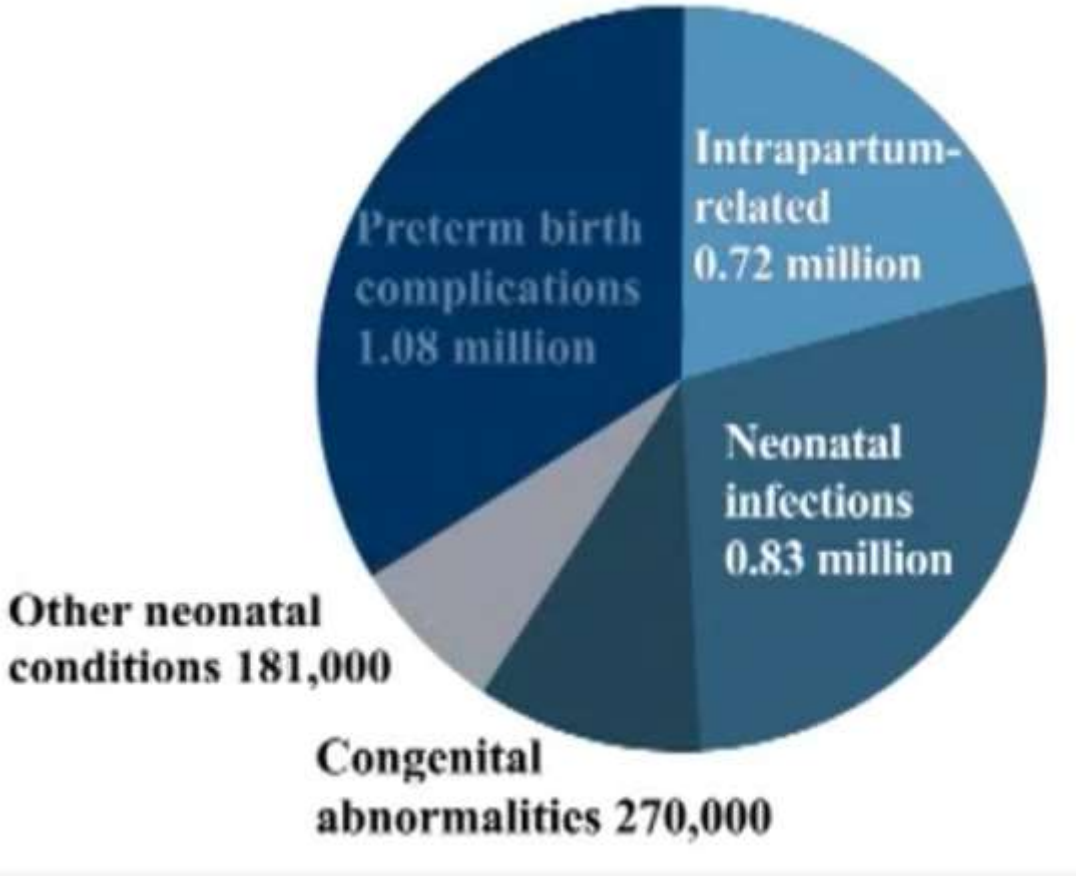
Stark differences in survival of premature babies exist between low- and high-income countries. For example, over 90% of extremely preterm babies (<28 weeks' gestation) born in low-income countries die within the first few days of life; yet less than 10% of babies of this gestation die in high-income settings, a 10:90 survival gap.

This is despite the fact that evidence-based interventions exist to reduce mortality from preterm causes. These include feeding, temperature maintenance, hygienic cord and skin care, and early detection and treatment of infections and complications including respiratory distress syndrome.

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

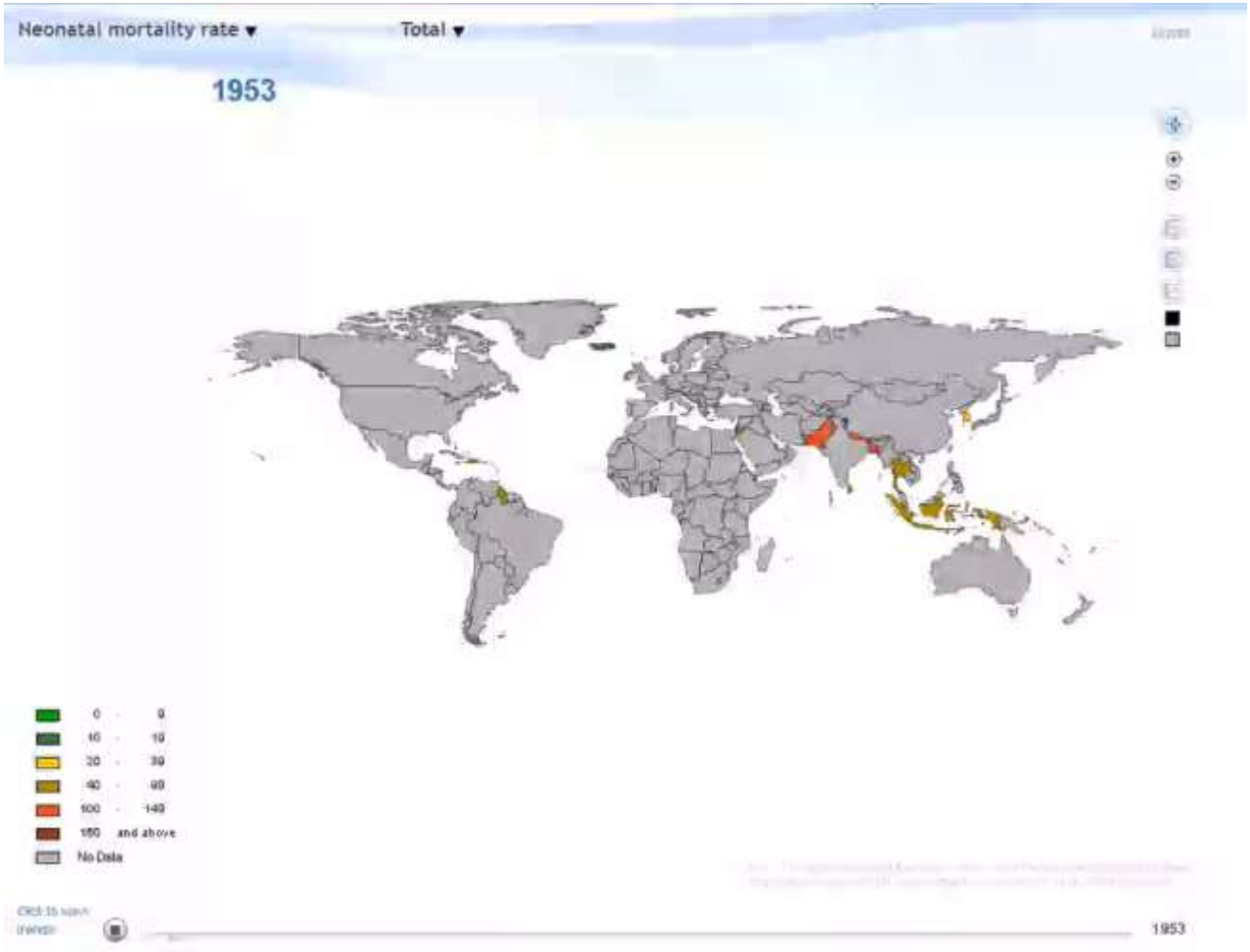
Preterm birth vs other causes of neonatal mortality

The following infographic shows how preterm birth compares with other causes of neonatal mortality. Hover the cursor over the bottom half of the slide and click on the play button to see the infographic.



March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Global trend in neonatal mortality rate 1953-2015



http://www.childmortality.org/index.php?r=site/map

Long term effects of preterm births

Survivors of preterm birth are also at a significant risk of adverse long-term consequences and hence loss of human potential globally. These include:

Visual impairment

- Blindness or high myopia after retinopathy of prematurity
- Increased hypermetropia and myopia

Hearing impairment

- This affects up to 5 to 10% of extremely preterm

Chronic lung disease of prematurity

- From reduced exercise tolerance to requirement for home oxygen

Long-term cardiovascular ill-health and noncommunicable disease

- Hypertension
- Reduced lung function
- Increased rates of asthma
- **Growth failure in infancy**
- **Accelerated weight gain in adolescence**

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Long term effects of preterm births (cont'd)

Neurodevelopmental/ behavioral effects

Disorders of executive functioning

- Specific learning impairments, dyslexia, reduced academic achievement

Moderate to severe global developmental delay

- Moderate/severe cognitive impairment
- Motor impairment
- Cerebral palsy affected by gestational age and quality of care dependent

Psychiatric/ behavioral sequelae

- Attention deficit hyperactivity disorder
- Increased anxiety and depression

Family, economic and societal effects

- Impact on family, the health service and intergenerational effects
- Psychosocial, emotional and economic
- Cost of care – acute and ongoing
- Risk of preterm birth in offspring is common, varying with medical risk factors, disability, socioeconomic factors

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Global goals in the context of preterm feeding and growth monitoring

Greater efforts are needed to minimize preterm delivery and, importantly, maximize the survival chances of those already born too soon.

Evidence-based feeding approaches together with other high impact interventions are therefore crucial. Monitoring of progress should be standardized.

Growth progress at the level of an individual preterm infant should be a continuum from conception through infancy and childhood.

The INTERGROWTH-21st growth standards allow all preterms to benefit from a postnatal growth monitoring strategy that matches the WHO Child Growth standards and provides continuity of care from the first day of postnatal life to life at home.

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Global goals in the context of preterm feeding and growth monitoring

Progress at a global level can only be measured by standardization of practices and working towards set goals. **Born Too Soon** presents a new goal for the reduction of deaths due to complications of preterm birth.

- For countries with a current neonatal mortality rate level of less than 5 per 1,000 live births, the goal is to eliminate remaining preventable preterm deaths, focusing on equitable care for all and quality of care to minimize long-term impairment (March of Dimes, 2012).

Hover the cursor over the bottom half of the slide and click on the play button of the infographic to see if your country falls in this category, its baseline(2010) and 5-year progress (World Bank Group 2016).

Neonatal Mortality/1000 live births

Country	2010	2015	Trend
San Marino	1	1	

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

World Bank Group. Mortality rate, neonatal (per 1,000 live births) Estimates developed by the UN Inter-agency Group for Child Mortality Estimation (UNICEF, WHO, World Bank, UN DESA Population Available from: http://data.worldbank.org/indicator/SH.DYN.NMRT?end=2015&name_desc=true&start=1990

Global goals in the context of preterm feeding and growth monitoring

For countries with a current neonatal mortality rate level of more than or equal to 5 per 1,000 live births, the goal is to reduce the mortality due to preterm birth by 50% between 2010 and 2025. Hover the cursor over the bottom half of the slide and click on the play button to see the infographic.

Neonatal Mortality/1000 live births

Country	2010	2015	Trend
Angola	53	49	

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Global goals in the context of preterm feeding and growth monitoring

Global nutrition targets 2025

A comprehensive implementation plan on maternal, infant and young child nutrition, was endorsed by a resolution of the World Health Assembly, and identified six key areas of focus:

WHO. Global Nutrition Targets 2025: Policy brief series. Geneva: World Health Organization, 2014.

Gestational age assessment

Gestational age (GA) estimation is part of fetal growth monitoring. In estimating the gestational age, the most accurate “gold standard” for assessment is routine early ultrasound assessment using fetal measurements made in the first trimester (March of Dimes, 2012).

This is accomplished in clinical practice by measuring the fetal crown–rump length (CRL) or head circumference at < 14 weeks’ and ≥ 14 weeks’ gestation, respectively. This is because between 9 and 13 weeks’ gestation, linear growth evaluated by CRL is rapid and the standard deviation is rather small, which means that GA can be estimated accurately (Papageorghiou AT, 2014).

As the fetus enters the second and third trimesters, CRL is no longer useful owing to curling of the growing fetus and therefore head circumference is used in later pregnancy. However, variation is greater, which results in less accurate estimation of GA (Papageorghiou, 2014).

In the first trimester access to ultrasound may not be possible in many parts of developing countries due to delay in attending antenatal clinics, lack of skills, unavailability of equipment etc. and hence, there is reliance on other less reliable methods such as last menstrual period (LMP), birth weight, fundal height or newborn examinations (March of Dimes, 2012).

Comparisons between these approaches are elucidated in the next slide.

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Papageorghiou AT, Kennedy SH, Salomon LJ et al. International standards for early fetal size and pregnancy dating based on ultrasound measurement of crown–rump length in the first trimester of pregnancy. Ultrasound Obstet Gynecol. 2014 Dec;44(6):641-8.

Estimating gestational age

Method	Accuracy	Details	Availability/feasibility	Limitations
Early ultrasound scan	+/- 5 days if first trimester +/- 7 days after first trimester	Estimation of fetal crown-rump length +/- biparietal diameter / femur length between gestational age 6 – 18 weeks	Ultrasound not always available in low-income settings and rarely done in first trimester	May be less accurate if fetal malformation, severe growth restriction or maternal obesity
Fundal Height	~ +/- 3 weeks	Distance from symphysis pubis to fundus measured with a tape measure	Feasible and low cost	In some studies similar accuracy to LMP Potential use with other variables to estimate GA when no other information available
Last menstrual period	~ +/- 14 days	Women's recall of the date of the first day of her last menstrual period	Most widely used	Lower accuracy in settings with low literacy. Affected by variation in ovulation and also by breastfeeding. Digit preference
Birthweight as a surrogate of gestational age	More sensitive/specific at lower gestational age e.g. <1500 g most babies are preterm		Birthweight measured for around half of the world's births	Requires scales and skill. Digit preference
Newborn examination	~ +/- 13 days for Dubowitz, higher range for all others	Validated scores using external +/or neurological examination of the newborn e.g. Parkin, Finnstrom, Ballard and Dubowitz scores	Mainly specialist use so far. More accurate with neurological criteria which require considerable skill. Potential wider use for simpler scoring systems	Accuracy dependant on complexity of score and skill of examiner. Training and ongoing quality control required to maintain accuracy
Best obstetric estimate	Around +/- 10 days (between ultrasound and newborn examination)	Uses an algorithm to estimate gestational age based on best information available	Commonly used in high-income settings	Various algorithms in use, not standardized

Adapted from Parker, Lawn and Stanton (unpublished Master's thesis)

March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva, 2012.

Gestational age assessment- The INTERGROWTH-21st International Standards

Crown-Rump Length (CRL)

The INTERGROWTH-21st Project, through the Fetal Growth Longitudinal Study, a multi-center study in eight geographically diverse countries, produced the first prescriptive international standards for early fetal size and ultrasound dating of pregnancy based on CRL measurement.

As a result, GA can be estimated from measurements of CRL between 15mm and 95 mm by the two equations in which CRL is expressed in **mm** and GA in **days**:

GA = 40.9041 + (3.21585 × CRL0.5) + (0.348956 × CRL);
SD of GA = 2.39102 + (0.0193474 × CRL).

Likewise, for GA between 58 and 105 days' gestation, where GA is expressed in **days** and CRL in **mm**:

Mean CRL = –50.6562 + (0.815118 × GA) + (0.00535302 × GA2);
SD of CRL = –2.21626 + (0.0984894 × GA).

These standards complement the existing WHO Child Growth Standards.

Papageorghiou AT, Kennedy SH, Salomon LJ et al. International standards for early fetal size and pregnancy dating based on ultrasound measurement of crown–rump length in the first trimester of pregnancy. Ultrasound Obstet Gynecol. 2014 Dec;44(6):641-8.

Gestational age assessment- The INTERGROWTH-21st International Standards

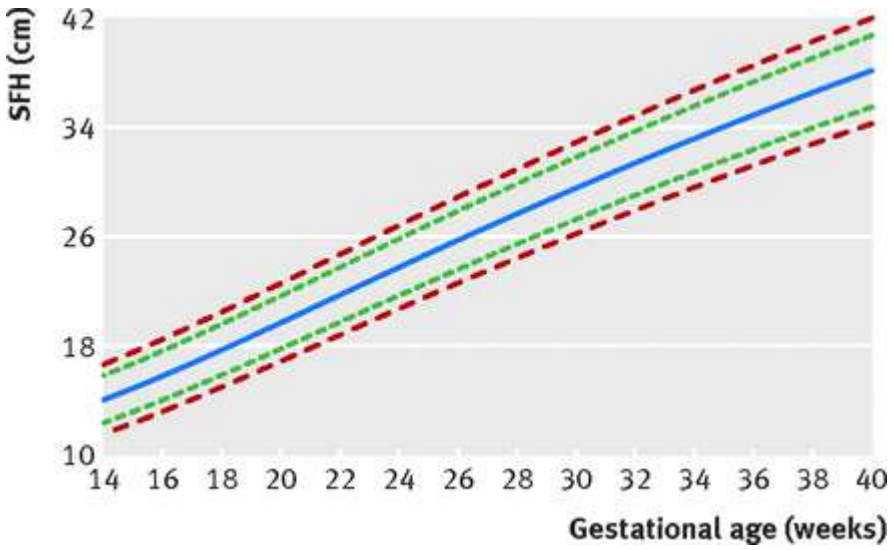
Symphysis-Fundal Height (SFH)

In low and middle income countries, where access to ultrasound machines and trained ultrasonographers is limited, or where women may attend their first antenatal clinic after the first trimester, SFH measurement is applicable as a simple, inexpensive, first level, screening tool.

The Fetal Growth Longitudinal Study has also generated the first prescriptive international standards for measuring symphysis-fundal-height as a first level screening for intrauterine growth disturbances.

Estimation of gestational age from SFH:

GA (exact weeks) = 6.585838 − 2.7072585 × (SFH0.5) + 1.295291 × (SFH)



International symphysis-fundal height (SFH) standards for clinical use. Lines (from bottom to top)=3rd, 10th, 50th, 90th, and 97th centiles. A printable chart is available in the supplementary appendix (can also be found at https://intergrowth21.tghn.org/ under "INTERGROWTH Standards & Tools")

Papageorghiou AT, Ohuma EO, Gravett MG, Hirst J, Silveira MF da, Lambert A, Carvalho M, Jaffer YA, Altman DG, Noble JA, Bertino E, Purwar M, Pang R, Ismail LC, Victora C, Bhutta ZA, Kennedy SH, Villar J. International standards for symphysis-fundal height based on serial measurements from the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project: prospective cohort study in eight countries. BMJ. 2016 Nov 7;355:i5662.

Initial assessment of the preterm infant

Anthropometric assessment

After establishing the gestational age of the preterm infant at birth, head circumference, length and weight are measured.

The equipment and technique used has been described in the module **Assessing newborn size by anthropometry.** The **learner** is encouraged to consult this module. A booklet on anthropometry can also be downloaded from the INTERGROWTH website.

The anthropometric measures are then compared to standards using **INTERGROWTH-21st Postnatal Growth Standards, centiles and z-scores for Preterm Infants.** Charts for head circumference, length, and weight for boys and girls are available here. Likewise, charts for very preterm babies can also be downloaded here.

An online tool, as well as installable Windows and Apple IOS applications available here allow data to be entered manually so that the size of individual newborns can be compared to, and plotted graphically against, the international references.

Initial assessment of the preterm infant

Anthropometric assessment video

Click on the play button to watch.

Intergrowth 21st Video. YouTube; 2016 Sep 27.

Initial assessment of the preterm infant

INTERGROWTH-21st Newborn Size Application Tool

This is an easy-to-use tool for calculating centiles and z-scores for weight, length and head circumference at birth. For example, a very preterm baby boy born at 26 weeks' gestation with a weight of 0.850 kg, 36cm length and 25cm head circumference would compare to standards as shown in the snapshot below. Hover the cursor over the bottom half of the slide and click on the play button to see the demo.

WHO recommendations on interventions to improve preterm birth outcomes

The World Health Organization has developed a set of recommendations designed to improve outcomes for preterm babies. While this module focuses on the newborn interventions, maternal interventions will also be considered, especially where preterm delivery is inevitable.

Newborn interventions

Kangaroo mother care (KMC) is a package that entails early, continuous and prolonged skin-to-skin contact between the mother and the baby, and exclusive breastfeeding (ideally) or feeding with breastmilk. It is recommended for the routine care of newborns weighing 2000 g or less at birth, and should be implemented as follows:

- Initiation in healthcare facilities as soon as the newborns are clinically stable. (Strong recommendation based on moderate-quality evidence)
- Provided as close to continuous as possible. (Strong recommendation based on moderate-quality evidence)
- Provided intermittently, rather than conventional care, if continuous Kangaroo mother care is not possible (Strong recommendation based on moderate-quality evidence)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Newborn interventions (cont'd)

Kangaroo mother care (KMC)

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 not enough evidence in support of routine use of plastic bags/wraps for 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 alternative to prevent hypothermia. (Conditional recommendation based on low-quality evidence)

Continuous positive airway pressure therapy is recommended for the treatment of preterm newborns with respiratory distress syndrome and should be started as soon as the diagnosis is made.

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Newborn interventions (cont'd)

Surfactant administration

- In health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available, surfactant replacement therapy is recommended for newborns with respiratory distress syndrome. Either animal-derived or protein-containing synthetic surfactants may be used. However, surfactant should not be administered prophylactically before onset of symptoms.
- In intubated preterm newborns with respiratory distress syndrome, surfactant should be administered early (within the first 2 hours after birth) rather than waiting for the symptoms to worsen before giving rescue therapy.

Oxygen therapy

- Preterm babies born at or before 32 weeks' gestation should 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)
- Oxygen concentration should be guided by blood oxygen saturation levels. However, measurement of these saturation levels should not supersede early efforts at resuscitation of the preterm newborn and hence saturation-level monitoring should be initiated 2 minutes after birth. This means that use of cues of hypoxia such as cyanosis should be emphasized.

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions

Antenatal corticosteroids for improving newborn outcomes

- Antenatal corticosteroid therapy is recommended for women at risk of preterm birth from 24 weeks to 34 weeks' gestation when the following conditions are met:

  • gestational age assessment can be accurately undertaken
  • preterm birth is considered imminent
  • there is no clinical evidence of maternal infection
  • adequate childbirth care is available (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).

- For eligible women, antenatal corticosteroid 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)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions (cont'd)

Antenatal corticosteroid 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)
- with hypertensive disorders in pregnancy who are at risk of imminent preterm birth.
- at risk of imminent preterm birth of a growth-restricted fetus. (Strong recommendation based on very low-quality evidence)
- 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)

Antenatal corticosteroid therapy **is not** recommended for women

- undergoing planned caesarean section at late preterm gestations (34–36+6 weeks). (Conditional recommendation based on very low-quality evidence for newborn and maternal outcomes)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions (cont'd)

The use of antenatal corticosteroid therapy in pregnant women with sepsis

- Evidence from systematic review and meta-analysis (Amiya et al., 2016; Been et al., 2011 and Roberts et al., 2017) have shown that the use of antenatal corticosteroid therapy resulted in reductions in neonatal mortality in babies of women with preterm prelabour rupture of membranes and women at risk of imminent preterm birth with chorioamnionitis. The quality of evidence for the Cochrane review was moderate. However, since most evidence were from high-income countries and hospital settings, these benefits may not apply in low-income countries where infection rates are high.
- WHO recommends the use of antenatal corticosteroids among women with preterm prelabour rupture of membranes and no clinical signs of infection. (Strong recommendation based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes)
- WHO does not recommend the use of antenatal corticosteroids in women with chorioamnionitis who are likely to deliver preterm as the balance between the risks and benefits of steroid use may be context-specific. (conditional recommendation, very low-quality evidence)
- Therefore, depending on settings, health care providers should weigh the benefit and harm of the use of antenatal corticosteroid in cases of maternal infections.

Amiya RM, Mlunde LB, Ota E, Swa T, Oladapo OT, Mori R. Antenatal Corticosteroids for Reducing Adverse Maternal and Child Outcomes in Special Populations of Women at Risk of Imminent Preterm Birth: A Systematic Review and Meta-Analysis. PLOS ONE. 2016 Feb 3;11(2):e0147604.
Been JV, Degraeuwe PL, Kramer BW, Zimmermann LJI. Antenatal steroids and neonatal outcome after chorioamnionitis: a meta-analysis. BJOG. 2011 Jan;118(2):113-22.
Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. In: The Cochrane Library. John Wiley & Sons, Ltd; 2017 Mar 21.
WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions (cont'd)

Antenatal corticosteroid therapy

- 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)
- A single repeat course of antenatal corticosteroid 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 based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions (cont'd)

Tocolysis for inhibiting preterm labour and improving newborn outcomes

- 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 very low-quality evidence)

Magnesium sulfate for fetal protection from neurological complications

- The use of magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 weeks' gestation for prevention of cerebral palsy. (Strong recommendation based on moderate-quality evidence)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions (cont'd)

Antibiotics for women in preterm labour (with and without prelabour rupture of membranes)

- Routine antibiotic administration **is not** recommended for women in preterm labour with intact amniotic membranes and no clinical signs of infection. (Strong recommendation based on moderate-quality evidence)
- Antibiotic administration **is** recommended for women with preterm prelabour rupture of membranes. (Strong recommendation based on moderate-quality evidence)
- Erythromycin **is** recommended as the antibiotic of choice for prophylaxis in women with preterm prelabour rupture of membranes (Conditional recommendation based on moderate-quality evidence)

Optimal mode of birth for women in refractory preterm labour

- Routine delivery by caesarean section for the purpose of improving preterm newborn outcomes is not recommended, regardless of cephalic or breech presentation. (Conditional recommendation based very low-quality evidence)

WHO. WHO recommendations on interventions to improve preterm birth outcomes. World Health Organization, 2015.

You have completed the module Background on preterm birth and you should now be able to:

- Define the different categories of preterm delivery and low birth weight.
- Know the global burden of preterm deliveries and calculate preterm birth rates.
- Identify the risk factors for preterm delivery.
- List the long-term effects of preterm deliveries.
- State the global goals for reduction of preterm deaths and the 2025 Global Nutrition targets.
- Know the different methods for gestational age estimation and their strengths and limitations.
- Assess gestational age from crown-rump length and symphysis-fundal height measurements using the respective INTERGROWTH-21st international standards.
- Conduct an anthropometric assessment of the newborn preterm.
- Use the INTERGROWTH-21st postnatal growth standards for preterm infants and INTERGROWTH-21st Newborn Size Application Tool.
- Know the WHO recommendations on the following interventions for preterm deliveries: Kangaroo mother care, continuous positive airway pressure, surfactant administration, oxygen therapy, antenatal corticosteroids administration, tocolysis for inhibiting preterm labour and magnesium sulfate administration.

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