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EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES FOR THE FOLLOW-UP OF AT-RISK NEONATES

abridged version

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ABRIDGED VERSION

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Evidence-based Clinical Practice Guidelines for the Follow-Up of At-Risk Neonates. Abridged version

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Introduction

Advances in neonatal care worldwide have helped to reduce the neonatal mortality rate considerably, particularly in Latin America and the Caribbean. This, in turn, has increased survival rates for infants born premature or presenting risk factors that can affect their growth, development, and quality of life. Improved survival rates and the reduced impact of specific risk factors are associated with neonatal care, special care units, and the follow-up of neonates in accordance with these factors.

During their stay in the neonatal intensive care unit (NICU), infants with particular risk factors require specialized care and follow-up based on the conditions of identified biological and social risks. The provision of care should not end after a patient has been discharged from hospital. It is crucial that both newborns and their caregivers are given the proper follow-up so their short-term and long-term progress can be tracked in order to accompany and assist and help decide what actions are appropriate to each situation. At the same time, by understanding this process, we can evaluate the quality of the care provided and set up a system for improvement. There are successful examples of neonatal follow-up programs in countries of the Americas and they are gradually being assessed, although their attributes vary depending on local resources.

The World Health Report 2005, *Make every mother and every child count*, recommends focusing on care during the neonatal period and highlights the importance of actions that ensure the health of neonates at higher risk after they are integrated into their family and society.

For this reason, neonates with particular risk factors require appropriate follow-up, which helps us to assess their growth and cognitive development during the first years of life, or at least until they start school. Some effects linked to perinatal illness can be identified at birth, and some can only be identified when the impaired function presents itself. Some sequelae may therefore appear in the first days, weeks, or months of life, while others may appear much later. For this reason, it is crucial that we understand the factors and potential conditions that are highly likely to occur in this population, so that infants can receive systematic follow-up and any conditions can be detected, treated, and resolved in a timely manner.

Guidelines therefore need to be developed for following up neonates in Latin America and the Caribbean who present risk factors, in order to identify and address these factors early on and to improve the infant's health and quality of life.

Scope and users

Newborns presenting risk factors require adequate follow-up during the neonatal period and infancy. The Pan American Health Organization hopes to provide evidence-based recommendations for proper follow-up. These clinical practice guidelines give evidence-based recommendations for following up at-risk neonates until they reach 2 years of age, which is the first stage of their follow-up. We are fully aware of how important it is to continue providing proper care beyond the first two years of a child's life, and specific recommendations will be prepared for other age groups at a later date. There is a consensus that follow-ups during the first two years of life can allow us to identify many of the abnormalities in neurology, metabolism, and motor function, among other areas, although addressing this two-year period alone is insufficient.

The recommendations in this document are intended for all health workers responsible for the primary care of at-risk neonates: general practitioners, family practitioners, pediatricians, neonatologists, pediatric ophthalmologists, pediatric otolaryngologists, nursing professionals, specialists in other fields, and multidisciplinary staff involved in the care process.

The purpose of these guidelines is to facilitate policy implementation by decision makers and members of governmental entities. They will also be useful for parents, mothers, and caregivers. The main topics covered by this document include: hospital discharge criteria, including screening tests; information and support for parents, mothers, and caregivers; screening at the follow-up visit, and the frequency of follow-ups until the infant is 2 years of age. These guidelines do not address matters related to nursing or comorbidities.

Objectives and target population

These clinical practice guidelines were developed with a view to providing evidence-based recommendations for the follow-up of at-risk neonates from birth until they reach 2 years of age (corrected age for premature babies) so that particular conditions that present early can be detected, and adequate care can be provided..

Specific objectives

- Propose strategies for following up at-risk neonates and detecting conditions early, during the first two years of life (or corrected age for premature babies).
- Create a space where families or caregivers of at-risk neonates can learn to provide the proper care for neonates.
- Refer neonates who present risk factors or who are suspected of having a specific condition, to the relevant specialist.

The target population is made up of:

Neonates with risk factors up to 2 years of age (corrected age for premature babies). The term “at-risk neonate” refers to all neonates who present risk factors and require multidisciplinary care after being discharged from the health care provider. This includes premature neonates, neonates with acquired or congenital diseases, and neonates who appear to be healthy but for whom abnormal health outcomes may be detected through timely follow-up.

1. At-risk neonates: newborns in situations that may pose a risk to their health, growth or development, which is identified before hospital discharge.
2. Neonates with risk factors: newborns or infants under 1 year of age whose situation exposes them to risks to their health, growth or development, such as low birth weight, prematurity, sepsis, asphyxia, shock, birth defects, genetic diseases, in addition to neonates requiring assisted ventilation, or neonates who have had pharmacological or surgical interventions.
3. Neonates in adverse socioeconomic situations.

Methodology

These guidelines were developed following the method for rapid adaptation of the GRADE system guidelines (Grading of Recommendations, Assessment, Development and Evaluation) proposed in the second edition of the *WHO Handbook for Guideline Development*.

A multidisciplinary group was formed to develop the guidelines, comprised of subject-matter experts, epidemiologists, and users.

We performed searches of reference databases (MEDLINE, EMBASE, and Cochrane), manual searches, and searches of grey literature. We then created the summary and the evidence profiles based on the GRADE approach and held a virtual panel in three stages with regional experts in order to formulate and adjust the recommendations. The first stage involved a survey which was used to refine the preliminary recommendations, evaluate the degree of agreement, and identify barriers and facilitators. In the second virtual stage, the recommendations we did not agree on were reviewed and the results of the survey were examined. Final approval was obtained in the third stage. The literature was consulted for patient preferences. All members of the panel and those who were part of the development group signed a declaration of interests form which was submitted to the guideline coordination group for review. A detailed explanation of the methodology can be found in the full version of the guidelines.

How to use this guide

For each clinical question, a set of recommendations and good practices provides guidance for the follow-up of at-risk neonates. Each recommendation shows the quality of the evidence based on the GRADE system.

Quality of the evidence	Meaning
High ⊕⊕⊕⊕	Further research is very unlikely to change confidence in the estimate of effect.
Moderate ⊕⊕⊕○	Further research is likely to have a significant impact on confidence in the estimate of effect and may change the estimate.
Low ⊕⊕○○	Further research is very likely to have a significant impact on confidence in the estimate of effect and is likely to change the estimate.
Very low ⊕○○○	Any estimate of effect is very uncertain.

The recommendations also include the strength of the recommendation based on the GRADE system.

Strength of the recommendation	Meaning
Strong for	The desirable effects clearly outweigh the undesirable effects. RECOMMENDED
Conditional for	The desirable effects probably outweigh the undesirable effects. SUGGESTED
Conditional against	The undesirable effects probably outweigh the desirable effects. Further research is likely to change the recommendation not to carry out the recommendation. NOT SUGGESTED
Strong against	The undesirable effects clearly outweigh the undesirable effects. NOT RECOMMENDED

Summary of the recommendations

Question 1. What are the criteria for discharging high-risk neonates from the neonatal intensive care unit?

Strength	N.º	Recommendation
RECOMMENDATIONS FOR PREMATURE INFANTS		
Strong for	1	<p>It is recommended that parents, mothers, or caregivers of neonates who weigh less than 2.5 kg are enrolled into an intermittent or continuous kangaroo mother care program. Alternatively, training in the "skin-to-skin" contact technique is recommended (six hours before the birth if there are no comorbidities contraindicating it) when an infant is discharged from a neonatal intensive care unit in hospitals or countries where it is available. This is in order to increase the neonate's body weight and encourage breastfeeding, and to reduce the risk of death, severe infection or sepsis.</p> <p>Quality of the evidence: moderate ⊕⊕⊕○</p>
Good practice point	✓	<p>The kangaroo mother care program or skin-to-skin technique should be developed by trained teams with the use of protocols and continuous monitoring to ensure that the results of premature neonates can be assessed. In addition, parents should be properly trained on how to care for a newborn at home.</p>
Conditional for	2	<p>Palivizumab prophylaxis is suggested for preventing episodes of bronchiolitis caused by respiratory syncytial virus. Each country should follow the recommendation according to the indication and the target population for which it was approved.</p> <p>Quality of the evidence: very low ⊕○○○</p>
Good practice point	✓	<p>Palivizumab administration is suggested for the most vulnerable neonates. Each country should have local recommendations based on its national epidemiological data. The hexavalent vaccine, as well as the rest of the vaccines, should be administered in accordance with a vaccination schedule adjusted to the neonate's chronological age (while still on the neonatal care unit).</p>

Strength	N.º	Recommendation
RECOMMENDATIONS FOR PREMATURE INFANTS		
Strong for	3	<p>We suggest ensuring that infants can carry out full oral and enteral feeding (preferably sucking and occasionally with a tube) before being discharged, either through exclusive breastfeeding, mixed feeding, feeding with milk formula or breast milk substitutes, and ensuring that hypoglycemia has been resolved in cases where it has been present.</p> <p>Quality of the evidence: low ⊕⊕○○</p>
Good practice point	✓	<p>Ensure that the indicated volumes of formula are available or that enough breast milk is present, as malnutrition can occur associated with their high level of risk, which would worsen their vital and neurosensory prognosis.</p>
Strong for	4	<p>It is recommended to check the following criteria for discharging high-risk neonates on the neonatal care unit, along with the basic criteria for all neonates:</p> <p>Recommendations for premature neonates</p> <ol style="list-style-type: none"> Ensure that pre-term neonates with gestational ages of 35 weeks or more are clinically stable (temperature of 36.5°C to 37.5°C) for 24 hours. Adequate oral feeding for at-risk neonates. In premature neonates with a gestational age of less than 34 weeks, observing 48 hours of oral feeding is sufficient. Premature babies should have a good latch on the mother's breast and should have established the sucking reflex, swallowing, and breathing. The mother should also be giving enough encouragement to help the baby to suck adequately during feeding. For premature neonates, we recommend confirming that they can regulate their body temperature during skin-to-skin contact. Adequate weight gain, either an established goal of 18 g/kg/d of weight and 0.9 cm/week in head circumference. Alternatively, tolerating the "kangaroo" position for a prolonged period of time, combined with a weight gain of 15 g/kg/day until 37 weeks and 8-11 g/kg/day starting in week 38. In premature neonates, oxygen saturation targets should be between 92% and 94%. <p>Recommendations for all at-risk neonates</p> <ol style="list-style-type: none"> Before being discharged, neonates should be able to maintain a supine position. Check that the neonate does not present with apnea. This should be evaluated in at-risk neonates who tolerate a supine position or premature neonates in the kangaroo care program for 48 hours after oxygen is discontinued. Oxygen saturation targets for neonates with bronchopulmonary dysplasia are 92% to 95%. Vaccination record and the Expanded Program on Immunization for neonates in NICUs in accordance with local schedule and actual age. Social and family risk assessment carried out by the social worker. <p>Quality of the evidence: low ⊕⊕○○</p>

Strength	N.º	Recommendation
RECOMMENDATIONS FOR PREMATURE INFANTS		
Strong for	5	<p>Screening for the following conditions is recommended before discharging neonates, including high-risk neonates, and taking the laws in each country into consideration:</p> <ol style="list-style-type: none"> a. Inborn errors of metabolism and heart diseases. The tests should be carried out with a dried blood spot sample (heel prick), within 24 to 36 hours of birth. The number and type of diseases that should be screened depends on the screening package offered in each country. b. Critical congenital heart disease. This should be tested with pulse oximetry within 24 hours of birth. Neonates requiring supplementary oxygen should be screened after 24 hours of being clinically stable, in ambient air. c. Neurological conditions. Neurological evaluations should be carried out in a comprehensive and systematic manner using the Amiel-Tison neurological examination, the Dubowitz examination or the Prechtl general movements assessment. d. Retinopathy of prematurity. Screening for retinopathy of prematurity (ROP) is recommended for every neonate with a birthweight of less than 2,000 g or a gestational age of 36 weeks of any birthweight, presenting at least one of the situations identified as risk factors for ROP. e. Hearing problems. Assessed by performing auditory evoked potentials (AEPs) and carrying out an otoacoustic emissions (OAE) test before discharge. If the neonate stays in NICU for more than five days, screening should be carried out after the neonate is clinically stable and has reached a gestational age of 32 weeks, and screening should include AEPs. f. Anemia. The following should be checked on discharge: hemoglobin, ferritin, total body iron levels. Depending on these levels, iron may be administered through a multivitamin, supplement or fortified breast milk. The discharge plan should include monitoring for symptoms of premature osteopenia, anemia, tachycardia, poor weight gain, hemoglobin levels, the presence of reticulocytosis and sufficient iron intake in the baby's diet. g. Stable weight gain in at-risk neonates in the last week before discharge. <p>Quality of the evidence: low ⊕⊕○○</p>
Good practice point	✓	<p>The screening results should be recorded in the medical record and on the referral sheet, if they are referred. If the hospital treating the referred patient cannot confirm that the screening has been carried out, it should be performed at the referral hospital before discharging the patient. In general, if a neonate does not reach an oxygen saturation level of more than 95 %, they should be assessed with echocardiography performed by a cardiologist.</p>

Strength	N.º	Recommendation
RECOMMENDATIONS FOR PREMATURE INFANTS		
Strong for	6	Booking a first check-up appointment and having a follow-up plan in place is recommended when a neonate is discharged from the neonatal care unit. Quality of the evidence: very low ⊕○○○
Strong for	7	If any abnormalities are detected on screening a premature or at-risk neonate, it is recommended that they be sent for a consultation or to a specialist before being discharged. For congenital heart diseases, we recommend sending the specialist the referral as early as possible depending on severity. Quality of the evidence: very low ⊕○○○

Question 2. What information should be provided to the parents and caregivers of at-risk neonates on discharge?

Strength	N.º	Recommendation
Strong for	8	It is recommended that parents be given information on proper management of the at-risk neonate at home when they are discharged from the neonatal care unit. This includes information on: techniques for drying a newborn after a bath, skin-to-skin contact, eye care, vaccination schedule, thermal protection, exclusive breastfeeding, nutrition requirements, CPR technique, massages, adequate parent-infant interaction, a follow-up plan, proper holding positions, administering medicine, or multivitamins if necessary, warning signs, and where to go in the event of an emergency. Quality of the evidence: low ⊕⊕○○
Good practice point	✓	As well as providing information on discharge, we suggest holding workshops during their stay in hospital. This is to ensure that parents understand all the information and that there are no complications caused by improper management of neonates. Both printed and audiovisual information should be provided so that parents can consult it at home. This information can be conveyed in person, by e-mail, or by text message.
Conditional for	9	It is suggested that parents of at-risk neonates be made aware of the harm caused by smoking, and that they receive information on interventions for stopping smoking, with a view to improving the newborn's quality of life as well as that of the parents. Quality of the evidence: low ⊕⊕○○
Conditional for	10	It is suggested that parents participating in the kangaroo mother care program (in hospitals where it is available) be given the corresponding information on how to continue this for the premature neonate at home. Quality of the evidence: low ⊕⊕○○
Good practice point	✓	Information should be given to parents about the follow-up plan, and the importance of attending all the scheduled visits should be clearly explained.

Question 3. What support do parents and caregivers of at-risk neonates need in order to reduce neonatal morbidity and mortality?

Strength	N.º	Recommendation
Conditional for	11	The development of home visit programs for at-risk neonates is suggested in countries where the health system allows it, with a view to improving general care, parent-child interaction, and anxiety felt by parents and mothers. Quality of the evidence: very low ⊕○○○
Good practice point	✓	The home visit program can begin at the NICU or after discharge. It can also be carried out in institutions providing health services or in community groups.
Conditional for	12	It is suggested that follow-up programs for high-risk neonates have integrated specialist and interdisciplinary services that include specialist points of care. Otherwise, they should have referrals with specialists and social support services. Quality of the evidence: very low ⊕○○○
Good practice point	✓	Neonatal care services should include: 1) a series of evaluations and timely diagnosis, encouraging attendance at follow-up programs for at-risk neonates; 2) psychosocial assessments of parents (by a psychologist and social worker); 3) workshops and educational material on bringing up children, encouraging development, preventing neurosensory complications (early screening), preventing acute respiratory infections (not smoking, keeping vaccinations up to date); and 4) encouraging attendance at follow-up programs in order to perform a series of evaluations and ensure early treatment and diagnosis.

Question 4. What screening tests should at-risk neonates receive during the 2 years follow-up period?

Strength	N.º	Recommendation
Strong for	13	Screening for ROP is recommended for every neonate with a birthweight of less than 2,000 g or a gestational age of 36 weeks or less of any birthweight, presenting at least one of the situations identified as risk factors for ROP. Quality of the evidence: very low: ⊕○○○
Conditional against	14	Testing with brain MRI or ultrasound is not suggested for screening for neurological disorders in high-risk infants. These tests should only be performed in cases where it is justified. Quality of the evidence: very low ⊕○○○

Strength	N.º	Recommendation
Strong for	15	Neurological evaluations should be carried out using the Dubowitz examination at the term-equivalent age and the Amiel-Tison examination, Bayley III (or higher) scale, or the test that is approved in each country, with a view to screening for neurological disorders in high-risk infants. Quality of the evidence: moderate ⊕⊕⊕○
Strong for	16	During the at-risk neonate's normal clinical assessment, changes in head circumference should be monitored in order to check for hydrocephalus using the scoring system recommended by the World Health Organization. Available at: https://www.who.int/toolkits/child-growth-standards/standards/head-circumference-for-age Quality of the evidence: very low ⊕⊕○○
Good practice point	✓	The same scale should be used at each follow-up visit for at-risk infants.
Strong for	17	Screening for hearing impairment is recommended for all high-risk infants, using transient evoked otoacoustic emission (TEOAE) test or automated auditory brainstem responses (AABR). Calidad de la evidencia: muy baja ⊕○○○
Condiciona a favor	18	We suggest that follow-up screening be carried out by a multidisciplinary team composed of specialized professionals who are trained in the field, depending on complexity and availability, and led by the pediatrician monitoring the infant. Quality of the evidence: very low ⊕○○○
Strong for	19	If any abnormalities are detected when screening at-risk infants, we recommend referring them to a specialist within 72 hours. Quality of the evidence: very low ⊕○○○
Strong against	20	Screening for autism (M-CHAT) is not recommended for at-risk infants.

Question 5. What is the optimal follow-up for at-risk infants under 2 years of age?

Strength	N.º	Recommendation
Strong for	21	It is recommended that at-risk infants be monitored using the follow-up program below until they are 2 years of age. Quality of the evidence: very low ⊕○○○ (experts' opinion)

Activity	1 w* PD	2 w PD	4 w PD	1 m† CA	2 m CA	3 m CA	4 m CA	5 m CA	6 m CA	8 m CA	9 m CA	10 m CA	12 m CA	14 m CA	15 m CA	16 m CA	18 m CA	20 m CA	22 m CA	24 m CA
Clinical check-ups: First check-up between 3 and 5 days after discharge. - Bi-weekly check-up if weight gain is normal. - If not, check-up at 3 days or readmission if there is weight loss.	●	●	●	●		●	●				●		●				●			●
Detailed neurological evaluation				●		●			●		●		●				●			●
Cranial ultrasound		●																		
Neurodevelopmental evaluation - Completed at 24 months					●		●		●				●		●					●
Hearing assessment																				
- Auditory evoked potentials				●		●			●				●		●					
- Otoacoustic emissions			●						●											●
Eye examination																				
- Retinopathy of prematurity	**	**				●			●				●							
Screening for anemia (before 12 months), if the pediatrician deems it necessary									●											
Immunoprophylaxis				Análogo al del recién nacido a término, teniendo en cuenta el plan de cada país.																
- Blood pressure						●														
- Echocardiography (last check-up after discontinuing oxygen)					●			●					●							

* w: week(s); m: month(s); PD: post-discharge; CA: corrected age; ●: activity; ●: detailed and complete review.

** Clinical Practice Guidelines for the Management of Retinopathy of Prematurity

	Stage	Zone 1	Zone II	Zone III	
WITHOUT PLUS	Immature	Yellow	Green	Green	<div style="background-color: #90EE90; padding: 2px;">Examination in two weeks</div> <div style="background-color: #FFFF00; padding: 2px;">Examination in one week</div> <div style="background-color: #FFA500; padding: 2px;">Type 2, examination in 3 or 4 days</div> <div style="background-color: #FF0000; padding: 2px;">Type 1, treatment in less than 48 hrs</div>
	I	Yellow	Yellow	Green	
	II	Orange	Yellow	Green	
	III	Red	Orange	Yellow	
WITH PLUS	I	Red	Yellow	Yellow	
	II	Red	Red	Orange	
	III	Red	Red	Red	

Strength		Recommendation
Good practice point	✓	At-risk infants should continue in follow-up beyond 2 years of age.
Good practice point	✓	Infants should have follow-up appointments with their pediatrician or the lead neonatologist, with monitoring by an expert in high-risk cases.

Related PAHO and WHO documents

Clinical Practice Guidelines for the Management of Retinopathy of Prematurity

https://iris.paho.org/bitstream/handle/10665.2/51089/PAHOFPL19001_eng.pdf?sequence=1&isAllowed=y

WHO Recommendations on newborn health

<https://apps.who.int/iris/bitstream/handle/10665/259269/WHO-MCA-17.07-eng.pdf?sequence=1&isAllowed=y>

WHO Protecting, promoting and supporting breastfeeding in facilities providing maternity and newborn services

<https://www.who.int/nutrition/publications/guidelines/breastfeeding-facilities-maternity-newborn/en/>

Infant feeding in areas of Zika virus transmission

https://www.who.int/nutrition/publications/guidelines/infantfeeding_zikavirus_transmission/en/

Daily iron supplementation in infants and children

https://www.who.int/nutrition/publications/micronutrients/guidelines/daily_iron_supp_childrens/en/

Paediatric emergency triage, assessment and treatment: care of critically-ill children

https://www.who.int/maternal_child_adolescent/documents/paediatric-emergency-triage-update/en/

WHO Recommendations on interventions to improve preterm birth outcomes

https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/preterm-birth-guideline/en/

WHO Recommendations on health promotion interventions for maternal and newborn health 2015

https://www.who.int/maternal_child_adolescent/documents/health-promotion-interventions/en/

Managing possible serious bacterial infection in young infants when referral is not feasible
Guidelines and WHO/UNICEF recommendations for implementation

https://www.who.int/maternal_child_adolescent/documents/bacterial-infection-infants/en/

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

https://www.who.int/nutrition/publications/guidelines/cord_clamping/en/

Every Newborn Action Plan

https://www.who.int/maternal_child_adolescent/newborns/every-newborn/en/

WHO Recommendations on home-based records for maternal, newborn and child health

https://www.who.int/maternal_child_adolescent/documents/home-based-records-guidelines/en/

Assessing and managing children at primary health-care facilities to prevent overweight and obesity in the context of the double burden of malnutrition

<https://www.who.int/nutrition/publications/guidelines/children-primaryhealthcare-obesity-dbm/en/>

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In this abridged version of the *Evidence-based Clinical Practice Guidelines for Follow-Up of At-Risk Neonates*, we provide recommendations for the care of newborns up to 2 years of age, corresponding to the first phase of their follow-up.

The recommendations are intended for all health sector staff responsible for the primary care of these neonates: general practitioners, family practitioners, pediatricians, neonatologists, pediatric ophthalmologists, pediatric otolaryngologists, nursing professionals, specialists in other fields, and multidisciplinary staff involved in the care process.

The purpose of these guidelines is to facilitate policy implementation processes carried out by decision makers and members of government bodies, and will also be useful for parents, mothers and caregivers.

The main topics covered by this document include: the hospital discharge criteria, including screening tests; information and support for parents, mothers, and caregivers; screening at the follow-up visit and the frequency of follow-ups until the infant is 2 years of age. These guidelines do not address matters related to nursing or comorbidities.

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