

*Topic Expert Group: Medical care and clinical practice*

**Prevention, detection, documentation, and treatment of retinopathy of prematurity (ROP)**

Hellström A, Hellström-Westas L, Zimmermann LJI, Buonocore, G, Hård AL, Stahl A

*Target group*

Preterm infants at risk of severe retinopathy of prematurity (ROP) defined by national guidelines and their parents

*User group*

Healthcare professionals, eye units, neonatal units, hospitals, and health services

*Statement of standard*

Programmes for preventive measures such as control of oxygen supplementation and promotion of optimal nutrition are established as well as screening programmes for detection, documentation, and treatment of sight threatening retinopathy of prematurity (ROP) in all units caring for very preterm infants.

*Rationale*

The goal is to prevent visual impairment and blindness due to retinopathy of prematurity (ROP), which is a major cause of childhood blindness and mainly affects extremely preterm infants. (1,2) Uncontrolled oxygen supplementation and poor neonatal monitoring are important factors contributing to increased ROP risk, even in more mature infants. (3)

Hospitals caring for very preterm infants need programmes promoting adherence to oxygen saturation targets and avoidance of hyperoxia, through implementation of appropriate alarm levels, education of healthcare professionals, oxygen titration guidelines, and sufficient number of skilled attendants. Automated oxygen control can improve SpO<sub>2</sub> targeting and may be an alternative. (4) Prevention and management of ROP require close inter-disciplinary collaboration.

Hospitals caring for very preterm infants should adhere to screening and treatment programmes for ROP, based on existing evidence.

These programmes define:

- screening inclusion criteria,
- timing of eye examination
- choice of dilating drops and information on how to avoid systemic absorption
- pain and stress control at screening examinations (5)
- indication for treatment
- anaesthesia/analgesia during laser treatment (5)
- follow-up of treated infants following appropriate protocols based on the treatment

Currently, most hospitals adhere to the US recommendations for screening (6) and for treatment, the recommendations of the Early Treatment for Retinopathy of Prematurity Group (7) are followed in many countries.

## Benefits

### Short-term benefits

- Reduced occurrence of severe retinopathy of prematurity (ROP) needing treatment (8–10)
- Improved identification of infants needing treatment for ROP (6)
- Increased percentage of infants treated timely (6,11)
- Reduced stress for parents (12)

### Long-term benefits

- Reduced occurrence of visual impairment and blindness caused by ROP (8–10)

### Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
<b>For parents and family</b>		
1. Parents are informed by healthcare professionals about retinopathy of prematurity (ROP), screening, treatment, and outcomes including the importance of provision of mother's own milk for the prevention of ROP (see Care procedures). (12,13)	A (Low quality) B (High quality)	Patient information sheet
<b>For healthcare professionals</b>		
2. Available guidelines on prevention and management of ROP are adhered to by all involved healthcare professionals.	B (High quality)	Guideline
3. Training on oxygen saturation targets is attended by all responsible healthcare professionals. (13)	A (High quality) B (High quality)	Training documentation
<b>For neonatal unit</b>		
4. Unit guidelines on prevention of ROP are available and regularly updated. (6,7,13)	A (High quality) B (High quality)	Guideline
5. Unit guidelines for control of oxygen supplementation and promotion of maternal milk feeding are available and regularly updated. (14,15)	A (Moderate quality) B (High quality)	Audit report, guideline
<b>For eye unit</b>		
6. Guidelines on screening, documentation and management of ROP are available and regularly updated. (2)	A (High quality) B (High quality)	Guideline
<b>For hospital</b>		
7. Training on prevention and management of ROP is ensured.	B (High quality)	Training documentation

8. Availability of expert personnel for fail-safe system of ophthalmological screening and treatment is ensured. (6)	A (Moderate quality) B (High quality)	Audit report
<b>For health service</b>		
9. National guidelines on prevention and management of ROP are available and regularly updated.	B (High quality)	Guideline
10. Rate of blindness and impaired vision due to ROP is monitored nationally.	B (High quality)	Audit report

### *Where to go – further development of care*

<b>Further development</b>	<b>Grading of evidence</b>
For parents and family N/A	
For healthcare professionals N/A	
For neonatal and eye unit	
<ul style="list-style-type: none"> <li>Initiate seamless information transfer systems between clinics and hospitals and measures to improve patient adherence to ophthalmological follow-up during screening and after treatment (see Follow-up &amp; continuing care). (16–18)</li> </ul>	B (Moderate quality)
For hospital N/A	
For health service	
<ul style="list-style-type: none"> <li>Consider telemedicine support for screening for retinopathy of prematurity (ROP). (11,19)</li> <li>Support research into causes and treatment of ROP. (20)</li> </ul>	A (Moderate quality) B (Moderate quality)

### *Getting started*

#### **Initial steps**

##### For parents and family

- Parents are verbally informed by healthcare professionals about retinopathy of prematurity (ROP), screening, treatment and outcomes including the importance of provision of maternal milk for the prevention of ROP.

##### For healthcare professionals

- Attend training on prevention and management of ROP.

##### For neonatal unit

- Develop and implement a unit guideline on prevention of ROP.
- Develop formalised programmes for education in oxygen saturation targets.
- Develop formalised programmes for promotion of mother's own milk feeding.

##### For eye unit

- Develop and implement a unit guideline for management of ROP.
- Develop information material on ROP for parents.

- Develop fail-safe systems for the identification of infants at risk of ROP.
- Ensure fail safe systems for referral and continuous cover by ophthalmologist.

#### For hospital

- Support healthcare professionals to participate in training on prevention and management of ROP.
- Identify pathways for infants with progressive ROP to receive expert assessment and treatment.

#### For health service

- Develop and implement a national guideline on prevention and management of ROP.

### *Description*

Despite the success of retinopathy of prematurity (ROP) screening and treatment much is unknown about the progression and response to treatment.

There is controversy over the precise oxygen saturation targets but current evidence suggests that, whereas ROP is less frequent when saturations are targeted at 85-89%, mortality is increased. Thus, most units maintain targets of 91-95%. (21) However, recent European consensus guidelines recommend a target range of 90-94% with alarm limits set at 89% and 95%. (22) It is important to avoid higher saturations and research is ongoing into whether these targets can be refined further. Most importantly better adherence to saturation targets is associated with lower rates of ROP. (14)

Furthermore, early provision of mother's own milk is associated with a reduced risk of ROP. (13,23)

If treated at the appropriate stage, vision of infants with severe ROP can be preserved by laser therapy or anti-VEGF therapy where indicated. (20) The long-term safety of anti-VEGF treatment needs further research. (24) If left untreated, severe ROP may lead to irreversible blindness – often in both eyes. (25) Importantly, even less severe ROP affects vision (26) and infants treated for ROP have an increased risk of retinal detachment, myopia, and other complications throughout life. (27,28)

### *Source*

1. Darlow BA, Gilbert C. Retinopathy of prematurity - A world update. *Semin Perinatol.* 2019 Oct;43(6):315–6.
2. Holmström G, Hellström A, Gränse L, Saric M, Sunnqvist B, Wallin A, et al. New modifications of Swedish ROP guidelines based on 10-year data from the SWEDROP register. *Br J Ophthalmol.* 2020 Jul;104(7):943–9.
3. Blencowe H, Moxon S, Gilbert C. Update on Blindness Due to Retinopathy of Prematurity Globally and in India. *Indian Pediatr.* 2016 Nov 7;53 Suppl 2:S89–92.
4. Dargaville PA, Marshall AP, McLeod L, Salverda HH, Te Pas AB, Gale TJ. Automation of oxygen titration in preterm infants: Current evidence and future challenges. *Early Hum Dev.* 2021 Nov;162:105462.
5. Pirelli A, Savant Levet P, Garetti E, Ancora G, Merazzi D, Bellieni CV, et al. Literature review informs clinical guidelines for pain management during screening and laser photocoagulation for retinopathy of prematurity. *Acta Paediatr Oslo Nor* 1992. 2019 Apr;108(4):593–9.



6. Fierson WM, AMERICAN ACADEMY OF PEDIATRICS Section on Ophthalmology, AMERICAN ACADEMY OF OPHTHALMOLOGY, AMERICAN ASSOCIATION FOR PEDIATRIC OPHTHALMOLOGY AND STRABISMUS, AMERICAN ASSOCIATION OF CERTIFIED ORTHOPTISTS. Screening Examination of Premature Infants for Retinopathy of Prematurity. *Pediatrics*. 2018 Dec;142(6):e20183061.
7. Early Treatment For Retinopathy Of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol Chic Ill* 1960. 2003 Dec;121(12):1684–94.
8. Chow LC, Wright KW, Sola A, CSMC Oxygen Administration Study Group. Can changes in clinical practice decrease the incidence of severe retinopathy of prematurity in very low birth weight infants? *Pediatrics*. 2003 Feb;111(2):339–45.
9. Lau YY, Tay YY, Shah VA, Chang P, Loh KT. Maintaining optimal oxygen saturation in premature infants. *Perm J*. 2011;15(1):e108-113.
10. Zepeda-Romero LC, Lundgren P, Gutierrez-Padilla JA, Gomez-Ruiz LM, Quiles Corona M, Orozco-Monroy JV, et al. Oxygen Monitoring Reduces the Risk for Retinopathy of Prematurity in a Mexican Population. *Neonatology*. 2016;110(2):135–40.
11. Antaki F, Bachour K, Kim TN, Qian CX. The Role of Telemedicine to Alleviate an Increasingly Burdened Healthcare System: Retinopathy of Prematurity. *Ophthalmol Ther*. 2020 Sep;9(3):449–64.
12. Davidson J, Aslakson R, Long A, et. al. Guidelines for Family-Centered Care in the Neonatal, Pediatric, and Adult ICU. *Crit Care Med*. 2017;45(1):103–28.
13. Bizzarro MJ, Li FY, Katz K, Shabanova V, Ehrenkranz RA, Bhandari V. Temporal quantification of oxygen saturation ranges: an effort to reduce hyperoxia in the neonatal intensive care unit. *J Perinatol*. 2014 Jan;34(1):33–8.
14. van Zanten HA, Tan RRGB, van den Hoogen A, Lopriore E, te Pas AB. Compliance in oxygen saturation targeting in preterm infants: a systematic review. *Eur J Pediatr*. 2015 Dec;174(12):1561–72.
15. Bharwani SK, Green BF, Pezzullo JC, Bharwani SS, Bharwani SS, Dhanireddy R. Systematic review and meta-analysis of human milk intake and retinopathy of prematurity: a significant update. *J Perinatol*. 2016 Nov;36(11):913–20.
16. Kripalani S, LeFevre F, Phillips CO, Williams MV, Basaviah P, Baker DW. Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. *JAMA*. 2007 Feb 28;297(8):831–41.
17. Nehra V, Pici M, Visintainer P, Kase JS. Indicators of compliance for developmental follow-up of infants discharged from a regional NICU. *J Perinat Med*. 2009;37(6):677–81.
18. Mas C, Gérardin P, Chirpaz E, Carbonnier M, Mussard C, Samperiz S, et al. Follow-up at two years of age and early predictors of non-compliance in a cohort of very preterm infants. *Early Hum Dev*. 2017;108:1–7.
19. Daniel, Quinn, Hildebrand, Eills, GB 3rd H, Jr CA, et al. Validated System for Centralized Grading of Retinopathy of Prematurity: Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study. *JAMA Ophthalmol*. 2015 Jun 1;133(6):675–82.
20. Stahl A, Hellstrom A, Smith LEH. IGF-1 and Anti-VEGF in ROP: Has the time come? *Neonatology*. 2014;106(3):254–60.
21. Stenson BJ. Oxygen Saturation Targets for Extremely Preterm Infants after the NeOProm Trials. *Neonatology*. 2016;109(4):352–8.
22. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, te Pas A, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update. *Neonatology*. 2019;115(4):432–50.



23. Maayan-Metzger A, Avivi S, Schushan-Eisen I, Kuint J. Human milk versus formula feeding among preterm infants: short-term outcomes. *Am J Perinatol*. 2012 Feb;29(2):121–6.
24. Hartnett ME. VEGF ANTAGONIST THERAPY FOR ROP. *Clin Perinatol*. 2014 Dec;41(4):925–43.
25. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter Trial of Cryotherapy for Retinopathy of Prematurity: ophthalmological outcomes at 10 years. *Arch Ophthalmol Chic Ill 1960*. 2001 Aug;119(8):1110–8.
26. Fulton AB, Hansen RM, Moskowitz A, Barnaby AM. Multifocal ERG in subjects with a history of retinopathy of prematurity. *Doc Ophthalmol Adv Ophthalmol*. 2005 Jul;111(1):7–13.
27. Fledelius HC, Jensen H. Late subsequent ocular morbidity in retinopathy of prematurity patients, with emphasis on visual loss caused by insidious “involutive” pathology: an observational series. *Acta Ophthalmol (Copenh)*. 2011 Jun;89(4):316–23.
28. Terasaki H, Hirose T. Late-onset retinal detachment associated with regressed retinopathy of prematurity. *Jpn J Ophthalmol*. 2003 Oct;47(5):492–7.

Second edition, September 2022

*Lifecycle*

3 years/next revision: 2025

*Recommended citation*

EFCNI, Hellström A, Hellström-Westas L et al., European Standards of Care for Newborn Health: Prevention, detection, documentation, and treatment of retinopathy of prematurity (ROP). 2022.

