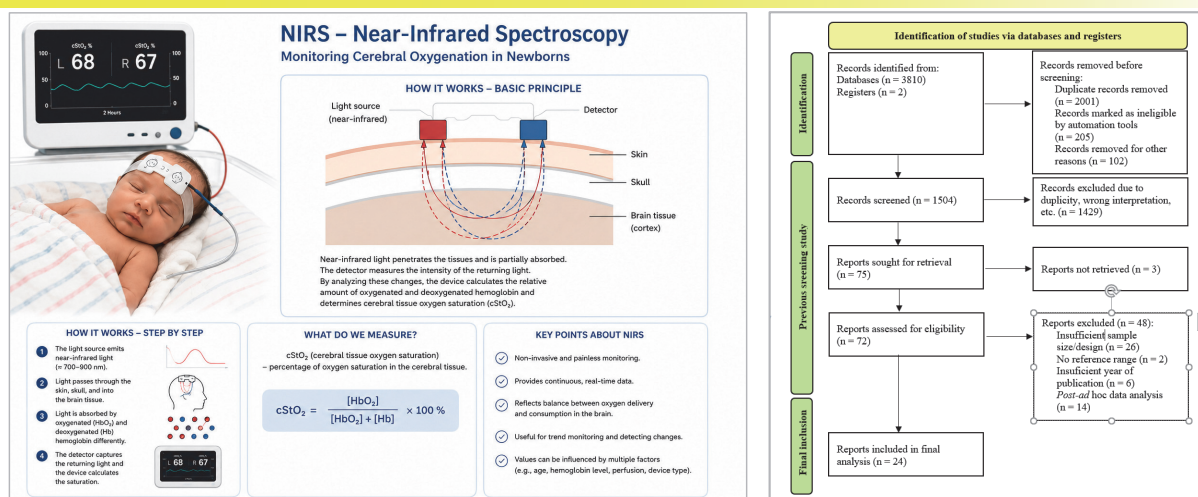


Evolution of near-infrared spectroscopy (NIRS) monitoring of cerebral oxygenation during the first minutes of life: An up-to-date review

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Near-infrared spectroscopy (NIRS) is a technology capable of non-invasive, continuous measurement of regional tissue oxygen saturation ($rStO_2$). No longer limited to the domain of laboratory research, this technology has become a routine bedside monitoring tool in neonatal intensive care units. The neonatal period is a unique stage in human life, during which the infant undergoes profound physiological adjustments essential for the transition from the intrauterine to the extrauterine environment. The temporal dynamics of regional cerebral tissue oxygenation during the first minutes after birth are among the most extensively investigated in contemporary neonatal research. This systematic qualitative review aims to summarize reference ranges defined as normal values or centile charts of cerebral oxygenation ($cStO_2$) and cerebral fractional tissue oxygen extraction ($cFTOE$) during postnatal adaptation for term and preterm neonates. Systematic measurement and statistical evaluation of physiological values are essential for establishing benchmarks, especially for critically ill neonates.

EVOLUTION OF NEAR-INFRARED SPECTROSCOPY (NIRS) MONITORING OF CEREBRAL OXYGENATION DURING THE FIRST MINUTES OF LIFE: AN UP-TO-DATE REVIEW



The review summarizes reference ranges and centile charts of cerebral oxygenation ($cStO_2$) and cerebral fractional tissue oxygen extraction ($cFTOE$) in term and preterm neonates during postnatal adaptation.

Gumulak R. et al., doi: 10.5507/bp.2026.021

Graphical Abstract

Biomedical Papers

<https://biomed.papers.upol.cz>

Key words: cerebral monitoring, cerebral tissue oxygenation, near-infrared spectroscopy, neonate

Received: March 5, 2026; Revised: June 21, 2026; Accepted: July 15, 2026; Available online: August 18, 2026

<https://doi.org/10.5507/bp.2026.021>

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INTRODUCTION

Non-invasive assessment of tissue oxygenation using near-infrared spectroscopy (NIRS) has experienced a significant increase in utilization over recent years. No longer limited to the domain of laboratory research, this

technology has become a routine bedside monitoring tool in neonatal intensive care units (NICUs) (ref.¹). NIRS enables continuous monitoring of regional tissue oxygenation, encompassing not only the cerebral region but also abdominal, muscular, and renal tissues^{2,3}.

The NIRS technology is based on the Beer-Lambert

law, which states that the transmission of light through a solution decreases exponentially with increasing concentration of the absorbing solute⁴. NIRS devices operate at wavelengths within the near-infrared (NIR) spectrum, typically ranging from 650 to 1000 nm for tissue oxygenation monitoring and from 780 to 2500 nm for general material analysis. These wavelengths are selected because they penetrate biological tissues and are differentially absorbed by specific chromophores, such as hemoglobin, thereby enabling non-invasive quantification of tissue oxygenation⁵. Light emitted in the NIR range propagates through biological tissues, where its absorption varies according to the relative concentrations of oxygenated hemoglobin (HbO₂) and deoxygenated hemoglobin (deoxy-Hb) (ref.^{1,6}).

Photons emitted from the light source can follow an arc through the tissue. Specialized detectors detect the fraction of non-absorbed photons. The proximal arc detector captures signals primarily from superficial tissues, whereas the distal arc detector receives signals from both superficial and deeper tissues. By subtracting the proximal signal from the distal signal, the resulting value reflects oxygen saturation at a depth of approximately 1–2 cm within the tissue. This measurement corresponds to the regional oxygen saturation (rStO₂) or tissue oxygenation index (TOI) of the underlying tissue^{6,7}. The rStO₂ is calculated using the following formula: $rStO_2 = [HbO_2 / (HbO_2 + deoxy-Hb)]$. This parameter is regarded as a primary NIRS measurement, representing the mean hemoglobin oxygenation across venous, capillary, and arteriolar compartments, weighted according to ratios estimated by the manufacturer^{8,9}. Fractional tissue oxygen extraction (FTOE) represents the proportion of oxygen extracted by the tissue and reflects the balance between oxygen delivery and consumption in the underlying tissue. Accurate calculation of FTOE requires measurement of arterial oxygen saturation using pulse oximetry (SpO₂). FTOE is calculated using the following formula: $FTOE = [(SpO_2 - rStO_2) / SpO_2]$ (ref.^{7,10}). These fundamental physical principles provide a mathematical description of how the absorption of electromagnetic radiation depends on the material properties. Changes in individual parameters reflect real-time variations in the microcirculation, which may arise from various pathological conditions¹¹. Technological advancements in NIRS devices have facilitated their more widespread use in NICUs, including the incorporation of additional wavelengths by individual instruments. Equally important is the gradual reduction in the cost of both devices and single-use probes for continuous monitoring, which have now become more compact and user-friendly.

The neonatal period is a unique stage in human life, when the infant undergoes profound physiological adjustments essential for the transition from the intrauterine to the extrauterine environment¹². The temporal dynamics of regional cerebral tissue oxygenation during the first minutes after birth are among the most extensively investigated topics in contemporary neonatal research. NIRS is sensitive to all tissues penetrated by the light. In cranial applications, these include the skin, scalp, skull, subarachnoid space, and grey and white matter of the brain².

The establishment of physiological values for tissue oxygenation assessed by near-infrared spectroscopy (NIRS) remains largely dependent on the definition of appropriate reference ranges. In term neonates (defined as infants born at ≥ 37 weeks of gestation), an uncomplicated postnatal transition is typically associated with a standard rooming-in management in neonatal units. In preterm neonates, the definition of physiological tissue oxygen saturation values generally permits the inclusion of a limited degree of respiratory support attributable to prematurity. Hence, the presence of limited respiratory support in otherwise stable preterm infants should not necessarily preclude their inclusion in studies aimed at establishing reference values for this population.

This systematic qualitative review aims to summarize reference ranges defined as normal values or centile charts of cerebral oxygenation (cStO₂) and cerebral fractional tissue oxygen extraction (cFTOE) during postnatal adaptation for term and preterm neonates.

METHODS

A systematic review was performed using major scientific databases (MEDLINE/Pubmed, Embase, and Cochrane) to identify relevant articles on the application of NIRS in neonates. The search was conducted from September 2025 to October 2025. The search strategy incorporated the following terms: brain, cerebral, continuous, infant, neonate, newborn, near-infrared spectroscopy, oxygenation, saturation, monitoring, tissue, term, and preterm. Additional articles were identified through manual screening of reference lists. For term newborns (born $\geq 37^{\text{th}}$ gestation week), we included only studies enrolling infants who required neither medical support nor resuscitation. For preterm newborns, we accepted studies reporting an appropriate medical support, as nearly all very low birth weight (VLBW; < 1.5 kg) infants require some degree of clinical intervention. Studies involving congenital anomalies or requiring surgical and/or cardiological management were excluded. Only original human studies with an adequate sample size of newborns ($n \geq 20$) were accepted. Studies published before 2010, not published in English, and studies with *post-ad hoc* data analysis were excluded. This review followed the guidelines of Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA) (Fig. 1). The quality and applicability of studies were assessed using the Critical appraisal skills programme checklist for Prospective Cohort studies (Fig. 2) (ref.¹³).

RESULTS

A considerable number of studies have defined normal reference values or established percentile charts for cerebral regional oxygen saturation and cerebral fractional tissue oxygen extraction. This represents an important consideration, as devices based on NIRS technology differ in several critical aspects, including the number of

wavelengths employed and the specific technical and computational algorithms implemented by each manufacturer. The primary search identified 3812 abstracts, of which 72 reports were assessed for eligibility. For final inclusion, 24 studies were reviewed (Fig. 1, 2).

Cerebral oxygenation during transition in term neonates

Term infants constituted the most extensively studied group, represented in 17 studies. The majority of studies were designed as formative observational trials using predefined cohorts of healthy infants. Reference ranges for $cStO_2$, $cTOI$ (cerebral tissue oxygenation index), and $cFTOE$ have been published in several studies using different NIRS devices.

Some studies assessed changes and differences in cerebral oxygenation related to the mode of delivery. The study published by Almaazmi et al. used the same NIRS instrument (FORE-SIGHT) within the first 10 minutes after various delivery modes, comparing healthy infants with the previously published VLBW infant cohort. $cStO_2$ in healthy term infants was lower than $cStO_2$ in

VLBW infants during transition. $cStO_2$ values measured with the FORE-SIGHT oximeter were similar to the values measured with the NIRO-300 oximeter. They were lower than values measured by the INVOS 5100 oximeter¹⁴. Similar oxygenation changes from the 2nd minute after birth were detected regardless of the mode of delivery. Another study evaluating the mode of delivery was published by Urlesberger et al. Although oxygen saturation measured by pulse oximetry (SpO_2) and heart rate were significantly lower in cesarean-delivered infants, there were no differences in $cStO_2$ with respect to the mode of delivery¹⁵. Historically, probe positioning has been a topic of considerable debate, with few published studies. In 2011, one prospective study specifically reported regional differences in cerebral oxygenation among three groups of newborns¹⁷. In all newborn subgroups (term and preterm), the $cStO_2$ and $cFTOE$ values in different regions did not differ significantly. Limits of agreement were between ± 14 and $\pm 18\%$ for all subgroups. Left-to-right differences were small across different postnatal and gestational ages. A decrease and subsequent increase over time in

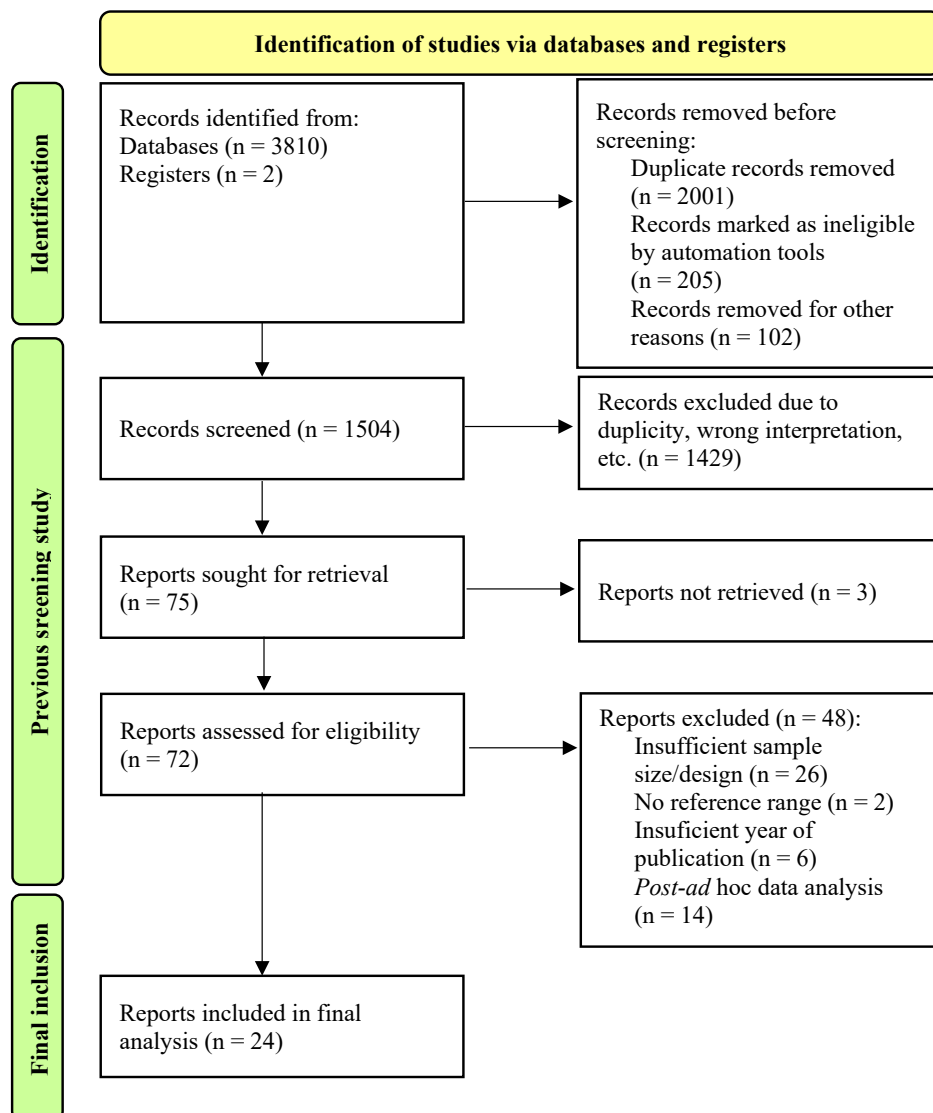


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

	Risk of bias domains						Overall
	D1	D2	D3	D4	D5	D6	
Almaazmi et al. (2013)	+	×	-	+	+	+	+
Baik et al. (2014)	+	+	+	+	+	+	+
Baik-Schneditz et al. (2015)	+	+	-	+	+	+	+
Baik-Schneditz et al. (2021)	+	×	+	+	+	+	+
Baik-Schneditz et al. (2025)	+	+	+	+	+	+	+
Carnicero et al. (2024)	+	×	-	+	+	+	+
Ergon et al. (2024)	+	×	+	+	+	+	+
Fauchere et al. (2010)	+	+	-	-	+	+	+
Fuchs et al. (2012)	+	×	+	-	+	+	+
Katherina et al. (2018)	+	+	+	+	+	+	+
Kato et al. (2020)	+	+	+	-	+	+	+
Kenosi et al. (2015)	+	×	-	+	+	+	+
Leroy et al. (2021)	+	×	-	-	+	+	+
Montaldo et al. (2015)	+	×	+	-	+	+	+
Noori et al. (2012)	+	×	-	-	+	+	+
Ozawa et al. (2020)	+	×	+	-	+	+	+
Pichler et al. (2013) I	+	×	+	+	+	+	+
Pichler et al. (2013) II	+	×	+	+	+	+	+
Swaberger et al. (2015)	+	×	+	+	+	+	+
Tammusino et al. (2016)	+	×	+	+	+	+	+
Urlesberger et al. (2010)	+	×	+	-	+	+	+
Urlesberger et al. (2011)	+	×	+	+	+	+	+
Watanabe et al. (2017)	+	×	+	-	+	+	+
Xue et al. (2020)	+	×	+	-	+	+	+

Fig. 2. Methodological quality criteria of included studies. The table presents the risk of bias in different domains of the Critical Appraisal Skills Programme Checklist¹³.

D1 – clearly defined research question; D2 – suitably chosen study participants; D3 – appropriate sample size with risk of bias ($n = 20 - 50$ moderate risk, $n \geq 50$ low risk); D4 – duration of measurement; D5 – appropriate data analysis; D6 – overall implication of study for practice; Judgment key: Judgment ● high risk of bias domain, ● moderate risk of bias domain, ● low risk of bias domain.

cStO₂ and cFTOE values were detected in all measured brain regions, most pronounced in preterm infants¹⁷.

Cerebral oxygenation in stable preterm and term neonates did not differ for various brain regions during the early neonatal period. However, the variability of measurements was rather high, as indicated by large limits of agreement^{17,18}. These findings may be linked to an observed correlation between cStO₂ and cFTOE values and body positioning. A study by Ergon et al. evaluated

a group of 60 neonates delivered by cesarean section, randomly stabilized in the supine, right-side, left-side, or prone positions. Adaptation parameters were not affected by position, except for lower 1st minute Apgar scores in the prone group and higher perfusion indices in the left lateral position. Authors found no significant differences in cStO₂ values¹⁹.

The impact of cord clamping on changes in cerebral saturation was very limited in the available studies. In

the term neonates, we found no significant difference in the course of cerebral TOI as well as cerebral blood volume, SpO₂, and heart rate during the first 15 minutes after birth in a group of neonates, who received either deferred cord clamping (CC) after the onset of stable regular breathing or standard CC < 1 min. Thus, deferring

CC ≥ 1 min, reflecting a physiologically based approach, offers no benefits to cerebral tissue oxygenation and perfusion after uncomplicated vaginal delivery compared to a time-based CC approach²⁰. Cerebral oxygenation changes also did not differ significantly between male and female neonates²¹. Most prospective studies describe

Table 1. Characteristics of studies including term newborns^{14,15,19-33}.

Author	Year of publishing	Newborns (n)	Used device	Normal values	Additional information	Ref.
Almaazmi et al.	2013	46	FORE-SIGHT	Min. 2 – 42.0 vaginal and caesarean Min. 2 – 36.0 assisted delivery	similar oxygenation changes from min. 2 after birth, regardless of the mode of delivery	14
Baik-Schneditz et al.	2015	140	NIRO-200NX	Min. 2 – 56.0 Min. 5 – 66.0 Min. 10 – 75.0	cFTOE: Min. 2 – 0.24 Min. 5 – 0.2 Min. 10 – 0.21	27
Baik-Schneditz et al.	2021	99	NIRO-200NX	Min. 5 – 63.8 Min. 10 – 73.2	no significant correlation between cardiac output and cTOI	20
Carnicero et al.	2024	44	MASSIMO O3	Min. 10 – 83.0	increase in cerebral oxygenation from 2 to 8 minutes, plateau phase detected	22
Ergon et al.	2024	60	INVOS 5100	(Right frontal): Min. 5 – 72.47 – 77.3 (Left frontal): Min. 5 – 72.87 – 76.40	investigate the effect of body position – no significant differences	19
Fauchère et al.	2010	20	NIRO-300	Min. 5 – 65.0 Min. 10 – 70.0	cFTOE: Min. 5 – 0.24 Min. 10 – 0.25	23
Kato et al.	2020	100	TOCCARE KN-15	Min. 1 – 42.0 Min. 5 – 52.0 Min. 10 – 57.0	values plateau between 8 and 10 minutes	24
Leroy et al.	2021	20	NIRO-200NX		initial increase of the TOI trajectory and plateau phase within the first 5 minutes focus on the dynamics of cortical oxygenation	25
Montaldo et al.	2015	61	EQUANOX-7600	Min.2 – 40.0 Min. 5 – 73.0 Min. 10 – 77.0	measurement of renal regional oxygen saturation	26
Noori et al.	2012	20	INVOS	Min. 1 – 47.0 Min. 5 – 75.0 Min. 10 – 77.0	changes in cFTOE mirrored those in cerebral oxygenation	27
Ozawa et al.	2020	127	TOCCARE KN-15	Min. 1 – 44.6 Min. 5 – 52.4 Min. 10 – 56.2	NIRS sensor frontoparietal left	28
Schwabberger et al.	2015	109	NIRO-200NX	Min. 2 – 57.0 Min. 5 – 64.0 Min. 10 – 73.0	plateau values from the 7th minute	29
Tammusino et al.	2016	59	INVOS	Min. 10 – 67.0 -79.0	study group vs control group, only n = 9 in the study group	30
Urlesberger et al.	2010	59	INVOS 5100	Min.3 – 44.0 Min. 10 – 70.0	cFTOE did not change significantly after 5 minutes	31
Urlesberger et al.	2011	63	INVOS	Min. 5 – 68.0 Min. 10 – 79.0	similar oxygenation changes regardless of the mode of delivery, plateau phase detected	15
Watanabe et. al.	2017	32	TOCCARE KN-15	Min. 5 – 51.0 Min. 10 – 55.0	plateau values from 4 minutes	32
Xue et al.	2020	418	FORE-SIGHT	Min. 2 – 49.0 Min. 5 – 64.5 Min. 10 – 74.0	infants born by CS only NIRS sensor forehead left	33

a gradual, often linear, increase in cStO₂ during early postnatal adaptation in healthy term neonates, reflecting the establishment of cerebral oxygenation homeostasis. Median cStO₂ values at the 5th minute of life range from 65–70%, reaching a stable phase by 10 minutes, with corresponding values for cStO₂ (60–76%), cTOI (68–69%), and cFTOE (0.22–0.25) (ref.^{14,33}). Most studies report the emergence of a plateau phase of varying duration in cStO₂ occurring between 6 and 10 minutes after birth^{15–20,21,33}. Xue et al. published a study with the largest sample of newborns (n = 418) (ref.³³). This study examined the effects of maternal anaesthetic factors on the oxygenation status (mothers received non-oxygen inhaled intrathecal anesthesia). The authors found that cStO₂ of the non-oxygen-inhaled intrathecal anesthesia in neonates without medical support increased from about 49.0% in the 2nd minute. The majority reached cStO₂ relative stabilization at 55.7–81.0% between 7 and 8 minutes after birth. One hour after birth, newborn cStO₂ was maintained at 78.0–87.0%. The low cStO₂ rate among babies born under intrathecal anesthesia with and without maternal oxygen inhalation during cesarean sections was approximately 4.5% and 9.0%, respectively respectively, with no significant difference, and the high cStO₂ rates were approximately 6.1% and 5.5%, respectively, with no significant difference³³. The authors also analyzed the correlation

between oxygen inhalation during intrathecal anesthesia and abnormal cerebral oxygenation in neonates and found weak correlations³³.

The comparison of values between different devices remains a subject of ongoing debate. In studies employing the TOCCARE KN-15 device, the median values were consistently lower across most time points by approximately 12–17% (ref.^{24,28,32}). A prospective study published in 2025 evaluated differences between one of the newest commercially available NIRS devices, the MASIMO O3, and the commonly used NIRO-200NX. A total of 44 neonates were included in the study. The median of cStO₂ values and cFTOE were reported at the 2nd, 5th and 7th minute: 54% (49–54), 71% (64–86), and 79% (73–84), and for cFTOE 0.25 (0.18–0.33), 0.19 (0.15–0.23), and 0.16 (0.12–0.21), respectively, with no significant changes observed thereafter. Data obtained with the MASIMO O3 device were significantly higher than those recorded by the NIRO-200NX (ref.²²).

Cerebral oxygenation during transition in preterm neonates

Preterm-only infants were included in 4 studies. Fuchs et al. measured cStO₂ by NIRS in 51 VLBW infants (mean gestational age 27.8 weeks) during the first 10 min after delivery. A regional cerebral tissue oxygen saturation sig-

Table 2. Characteristics of studies including preterm newborns^{34–37}.

Author	Year of publishing	Newborns (n)	Used device	Normal values	Additional information	Ref.
Baik et al.	2014	24	INVOS	Non-IVH Min. 5 – 40.0 Non - IVH Min. 10 – 67.0 IVH Min. 5 – 32.0 IVH Min. 10 – 47.0	plateau phase at the 7 th minute	36
Fuchs et al.	2012	51	FORE-SIGHT	Min. 1 – 37.0 Min. 5 – 72.0 Min. 10 – 79.0	gestational age 28 (SD 2.6)	34
Katheria et al.	2018	127	FORE-SIGHT	Min. 7–10 threshold – 66.0	gestational age 26.28 (SD 2), infants with severe IVH/ death had lower values at 8–10 minutes	35
Kenosi et al.	2015	47	INVOS	low FiO ₂ Min. 10 – 85.0 high FiO ₂ Min. 10 – 81.0	gestational age 29 (SD 1.6)	37

Table 3. Characteristics of studies including term and preterm newborns^{38,40,41}.

Author	Year of publishing	Newborns (n)	Used device	Normal values	Additional information	Ref.
Baik-Schneditz et al.	2025	122	MASIMO O3 INVOS, NIRO	Min. 2 – 59.0 Min. 10 – 77.0	plateau phase at the 7th minute	41
Pichler et al.	2013	381	INVOS	Graphical interpretation Min. 2 – 43.0 Min. 5 – 79.0 Min. 10 – 79.0	term and preterm neonates have almost the same results plateau phase detected cFTOE measured	38
Pichler et al.	2013	46	INVOS	Min. 5 – 62.0 Min. 10 – 79.0	NIRS and amplitude-integrated EEG	40

nal was available after a median (interquartile range) age of 52 (44 to 68) seconds. In three infants, the signal was obtained after 10 min of age. After delivery, cerebral tissue oxygen saturation rose continuously from 37 (31 to 49)% at the 1st minute of age and reached a plateau-phase in the range of 61% to 84% around the 7th minute after birth³⁴. Katheria et al. reported that early measurement of cStO₂ and amplitude-integrated electroencephalography (aEEG) can predict infants at risk of intraventricular hemorrhage (IVH) within the first 72 hours of life³⁵. aEEG alone was not predictive of IVH or death in the delivery room or in the neonatal intensive care unit. Infants who developed severe IVH or death had significantly lower cStO₂ from the 8th to the 10th minute of life. There were no differences in either cStO₂ or aEEG in the infants with low-grade IVH (ref.³⁵). Baik et al. found that mean cStO₂ values between the 6th and 15th minute of life were significantly lower in the IVH group than in the non-IVH group, with a median of 40% in the 5th minute and a plateau phase from the 7th minute³⁶. Another noteworthy study was a single-center prospective observational study including 47 infants born before 32 weeks of gestation. All preterm infants initially received an inspired oxygen fraction (FiO₂) of 0.3 and were subsequently divided into two groups based on their further oxygen requirements (FiO₂ ≤ 0.3 vs. FiO₂ > 0.3). Infants requiring FiO₂ > 0.3 had a higher incidence of cerebral hypoxia than those requiring FiO₂ ≤ 0.3. However, no differences were observed in the degree of cerebral hyperoxia, either in the delivery room or in the neonatal intensive care unit. The authors mentioned a mean cStO₂ at the 10th minute of 85% (low FiO₂) and 81% (high FiO₂) (ref.³⁷).

Cerebral oxygenation during transition in mixed studies

Term and preterm infants were included in three studies that met our inclusion criteria. Among the most frequently cited studies are those by Pichler et al. In a study published in 2013, a total of 381 neonates were included: 82 term neonates after vaginal delivery, 272 term neonates after cesarean delivery, and 27 preterm neonates after cesarean delivery³⁸. In all neonates, median (10th–90th percentiles) cStO₂ was 41% (23–64) at 2 minutes, 68% (45–85) at 5 minutes, 79% (65–90) at 10 minutes, and 77% (63–89) at 15 minutes of age. In all neonates, median (10th–90th percentiles) cFTOE was 33% (11–70) at 2 minutes, 21% (6–45) at 5 minutes, 15% (5–31) at 10 minutes, and 18% (7–34) at 15 minutes of age³⁸. The results were further analyzed in the COSGOD III trial³⁹, currently the largest trial investigating cerebral oxygen saturation levels in neonates in the delivery room. In this randomized controlled trial, 607 preterm infants with gestational age less than 32 weeks were assigned to either an NIRS-visible group or a control group. Cerebral oxygenation values were used to guide adjustments of inspired oxygen fraction and escalation of respiratory support. The results demonstrated that decreasing the burden of cerebral hypoxia during the immediate postnatal transition and resuscitation is feasible using cStO₂ monitoring to guide respiratory and supplemental oxygen therapy³⁹. Another interesting study was also carried out by Pichler et al. in

which authors compared the results of 146 neonates (with ≥34 weeks of gestation born via cesarean section) (ref.⁴⁰). They were divided into two groups: uncompromised (31 neonates) and compromised (16 neonates) with need of ventilation support. Uncompromised neonates showed higher values for minimal amplitude in the 3rd minute and higher values for maximal amplitude in the 3rd and 4th minute compared to the 10th minute post-partum. In uncompromised neonates cStO₂ values during the first 6 min after birth were lower compared to 10th minute. Neonates requiring respiratory support exhibited lower cStO₂ values during the first 8 minutes after birth compared with the 10th minute⁴⁰. During transition, compromised neonates requiring resuscitation showed a different cerebral activity pattern compared to uncompromised individuals⁴⁰. A more recent study published in 2025 by Baik-Schneditz et al. incorporated comparative analyses of commercially available NIRS devices, benchmarking them against one of the most recently introduced systems – MASIMO O3. All three – MASIMO O3, INVOS, and NIRO showed correlation with a flattened linear increase in cerebral oxygenation during postnatal adaptation. Compared to the established percentiles, the overall MASIMO O3 values were lower than those of INVOS. Only when the absolute cerebral oxygen saturation was <60%, the MASIMO O3 recordings were higher. Compared with NIRO, MASIMO O3 values showed a similar course, but MASIMO O3 values tend to be slightly higher. However, the study did not provide data comparing individual neonatal subgroups by gestational age (n = 122 neonates: 14 preterm and 108 term neonates). When presenting the percentile charts side by side, the differences between the devices became evident, especially in the lower cerebral oxygen saturation range⁴¹.

CONCLUSION

The frequency of NIRS device use for routine non-invasive bedside monitoring of neonatal cerebral oxygenation has increased. During the immediate neonatal transition, major changes in oxygenation occur; for this reason, the reported differences in lower cerebral oxygen saturation ranges are vital when using near-infrared spectroscopy for monitoring during this phase of life. Defining the exact threshold values suitable for direct clinical use remains very challenging, largely owing to ethical considerations. Current evidence from piglet model studies shows irreversible mitochondrial damage and total energy disruption at cStO₂ values ranging from 33% to 45%, persisting for 30 – 120 minutes^{42,43}. Measurements of cerebral oxygen saturation, as well as overall tissue oxygenation using NIRS, share a common challenge: the wide variability in mathematical methods used to calculate individual indices and this complicates across study comparison^{3,44}. Newer, more advanced devices employ multiple wavelengths and multiple sensors simultaneously, providing more accurate measurements. Systematic measurement and statistical evaluation of physiological values are essential for establishing benchmarks, especially necessary for critically ill

neonates^{1,2}. All reviewed studies showed an increase in cStO₂ during postnatal adaptation. Most reported a plateau phase at a certain point of postnatal adaptation. An interesting finding is that cerebral oxygenation values are nearly identical in term infants compared with preterm neonates. These results indicate consistency in the development of cerebral oxygenation despite prematurity. The issue of physiological reference values in neonates appears to have been largely addressed, as suggested by numerous studies published over the past decade^{1,2}.

The most extensively studied clinical application of cerebral NIRS is the monitoring of neonates with hypoxic-ischemic encephalopathy (HIE) undergoing therapeutic hypothermia. A meta-analysis published in 2023 demonstrated that differences in cerebral oxygenation parameters between neonates with favorable and unfavorable outcomes become more pronounced after the first 48 hours of life, supporting the potential prognostic utility of NIRS monitoring.^{45,46}

Cerebral NIRS may provide an opportunity for early identification of infants at increased risk of brain injury before structural abnormalities become evident on cranial ultrasound. However, current evidence is mainly derived from observational studies, and randomized trials demonstrating that NIRS-guided interventions can prevent IVH or improve neurodevelopmental outcomes are still lacking⁴⁷. In the delivery room, cerebral NIRS has also been proposed as a tool for guiding oxygen supplementation during neonatal resuscitation. Reference ranges of cerebral oxygen saturation during the transitional period may help clinicians assess whether cerebral oxygen delivery is appropriate and avoid both insufficient oxygenation and excessive oxygen exposure. Nevertheless, although increasing evidence supports the feasibility of NIRS-guided oxygen titration, optimal target ranges and intervention thresholds have not yet been universally established. Therefore, cerebral NIRS should currently be considered primarily as a physiological monitoring and risk-stratification tool, while its role as a direct guide for clinical interventions requires further validation^{30,39,47}.

The findings and overall conclusions of this manuscript are in agreement with currently available meta-analytical evidence, including both comprehensive meta-analyses and analyses addressing specific aspects of NIRS implementation, such as the establishment of physiological reference values during postnatal transition and the evaluation of the clinical utility of NIRS technology in neonatal intensive care settings^{47,48}.

Despite numerous challenges, the number of studies evaluating this technology is increasing exponentially, highlighting its promising potential and the likelihood of a bright future in neonatal care.

Search strategy and selection criteria

The search strategy and selection criteria are described in detail in the Methods section. The review systematically searched major databases using predefined keywords. Studies were independently screened by two reviewers to ensure a consistent and unbiased selection process.

ABBREVIATIONS

aEEG, Amplitude-integrated electroencephalography; CC, Cord clamping; cFTOE, Cerebral fractional tissue oxygen extraction; cStO₂, Regional cerebral oxygen saturation; cTOI, Cerebral tissue oxygenation index; deoxy-Hb, Deoxygenated hemoglobin; FiO₂, Inspired oxygen fraction; FTOE, Fractional tissue oxygen extraction; IVH, Intraventricular hemorrhage; HbO₂, Oxygenated hemoglobin; HIE, Hypoxic-ischemic encephalopathy; MRI, Magnetic resonance imaging; NICUs, Neonatal intensive care units; NIR, Near-infrared; NIRS, Near-infrared spectroscopy; nm, Nanometer; PRISMA, Preferred reporting of items for systematic reviews and meta-analyses; rStO₂, Regional tissue oxygen saturation; SD, Standard deviation; SpO₂, Arterial oxygen saturation measured by pulse oximetry; TOI, Tissue oxygenation index; VLBW, Very low birth weight

Author contributions: RG, SJ: literature search and manuscript writing; RG, SJ, SK: literature search and critical reading; all authors: manuscript revision; MZ, KM: final approval.

Conflict of interest statement: The authors state no conflict of interest regarding the publication of this article.

Declaration of generative AI and AI-assisted technologies: Use of artificial intelligence tools – Evolution of near-infrared spectroscopy (NIRS) monitoring of cerebral oxygenation during the first minutes of life: An up-to-date review - During the preparation of this work, AI tools were used to improve the readability and language of the manuscript, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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