SYSTEMATIC REVIEW

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# Impact of Skin Pigmentation on Cerebral Regional Saturation of Oxygen Using Near-Infrared Spectroscopy: A Systematic Review

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**OBJECTIVES:** Near-infrared spectroscopy (NIRS) is used in critical care settings to measure regional cerebral tissue oxygenation ($rSo_2$). However, the accuracy of such measurements has been questioned in darker-skinned individuals due to the confounding effects of light absorption by melanin. In this systematic review, we aim to synthesize the available evidence on the effect of skin pigmentation on $rSo_2$ readings.

**DATA SOURCES:** We systematically searched MEDLINE, Cochrane Database of Systematic Reviews, Embase, and Google Scholar from inception to July 1, 2023.

**STUDY SELECTION:** In compliance with our PROSPERO registration (CRD42022347548), we selected articles comparing $rSo_2$ measurements in adults either between racial groups or at different levels of skin pigmentation. Two independent reviewers conducted full-text reviews of all potentially relevant articles.

**DATA EXTRACTION:** We extracted data on self-reported race or level of skin pigmentation and mean $rSo_2$ values.

**DATA SYNTHESIS:** Of the 11,495 unique records screened, two studies ($n$ = 7,549) met our inclusion criteria for systematic review. Sun et al (2015) yielded significantly lower $rSo_2$ values for African Americans compared with Caucasians, whereas Stannard et al (2021) found little difference between self-reported racial groups. This discrepancy is likely because Stannard et al (2021) used a NIRS platform which specifically purports to control for the effects of melanin. Several other studies that did not meet our inclusion criteria corroborated the notion that skin pigmentation results in lower $rSo_2$ readings.

**CONCLUSIONS:** Skin pigmentation likely results in attenuated $rSo_2$ readings. However, the magnitude of this effect may depend on the specific NIRS platform used.

**KEYWORDS:** cerebral oximetry; near-infrared spectroscopy; race; regional cerebral tissue oxygen saturation; skin pigmentation

Cerebral oximetry is a noninvasive technology that uses near-infrared spectroscopy (NIRS) to estimate the regional cerebral tissue oxygenation ($rSo_2$) of blood within brain tissue of the frontal lobe (1). $rSo_2$ is used as an index of tissue oxygenation in critical care settings such as in cardiac anesthesia and neurocritical care units, where the presence of brain hypoxia may be of great concern (1). The baseline principles of NIRS are similar to pulse oximetry, whereby leveraging the spectral properties of hemoglobin, wavelengths of near-infrared light are absorbed differentially between oxyhemoglobin and deoxyhemoglobin (1). Oxygen saturation of hemoglobin in the cerebral vasculature, and thus an associated $rSo_2$ recording, are thought to be



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## KEY POINTS

**Question:** What is the effect of skin pigmentation on regional cerebral tissue oxygenation ($rSo_2$) readings?

**Findings:** This systematic review finds that increased skin pigmentation may effect $rSo_2$ measurements. However, the magnitude of this effect may depend on the near-infrared spectroscopy (NIRS) platform used.

**Meaning:** Clinicians should be aware of the potential racial bias of NIRS devices

principally influenced by cerebral blood flow. However, other factors such as skin pigmentation (2), blood pH (3), serum albumin concentration (3), and even underlying comorbidities such as diabetes (3) may influence these readings. A recent systematic review has shown clear impacts of skin pigmentation on peripheral oxygen saturation readings; however, a thorough review has not been performed on the effect of skin pigmentation on $rSo_2$ in reference to cerebral oximetry readings (4). For this systematic review, we sought to determine the relationship between skin pigmentation and NIRS-derived $rSo_2$ readings in a critical care setting.

## METHODS

We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (5) and this review was registered on the PROSPERO (CRD42022347548).

### Literature Search

We searched for studies investigating the effect of skin pigmentation on cerebral oximetry readings (**Appendix 1**, http://links.lww.com/CCX/B308). We searched electronic databases using Boolean operators that combined text words, controlled vocabulary words, and medical subject headings. Databases including U.S. National Library of Medicine database (MEDLINE), the Cochrane Database of Systematic Reviews, the EMBASE, and Google Scholar were searched from the date of inception to October 1, 2022. Before completion of the review, a repeat search was done from October 1, 2022, to July 1, 2023, to ensure new articles were included. Additionally, reference lists of included studies were manually searched for any additional eligible studies. Language restrictions were not applied in this review.

### Eligibility Criteria

We selected studies comparing cerebral oximetry in adult patients of various self-reported racial backgrounds to Caucasians or comparing pigmented skin to light skin. Studies evaluating patients in critical care settings were included (including cardiac anesthesia and neurointensive care patients). Trials with pediatric patients or those using NIRS exclusively at noncerebral sites were excluded. As our outcome of interest was cerebral regional saturation of oxygen (i.e., $rSo_2$), studies that did not clearly report this metric were excluded.

### Study Selection

The title and abstract screening of citations retrieved by the electronic search was performed by the lead author (N.A.P.). Two authors (N.A.P., H.S.B.) conducted a full-text review of all potentially relevant studies. Any disagreements were resolved by consensus from all authors after revisiting the full text.

### Risk of Bias Assessment

The Cochrane Risk of Bias Tool was used by two authors (N.A.P., H.S.B.) to assess the methodological quality of the two included trials (**Appendix 2**, http://links.lww.com/CCX/B308) (6). The results from each author were compared and any disagreements between the two were resolved by consensus.

### Outcomes Assessed

The primary outcome assessed in this study was the mean $rSo_2$. In studies where $rSo_2$ was monitored at various time points, the index/initial measurement was used (beginning of surgery, pre-bypass cardiac surgery, initial monitoring in ICU, etc.).

## RESULTS

Our literature search identified a total of 13,901 records. Hand searching through references sourced another four records. After removing duplicates, there

were 11,495 unique records remaining, all of which underwent title and/or abstract screening. This process identified a total of 63 potentially eligible abstracts. Full-text reviews resulted in two studies that met eligibility criteria for inclusion in the systematic review (7, 8). The PRISMA flow diagram can be found in **Figure 1**. We conducted an additional search including studies of pediatric and neonatal patients. The search revealed over 13,000 records; however, no studies meeting criteria were identified.

### Study Characteristics

The two included studies had a total of 7549 study participants, including: 4615 Caucasians, 1570 African Americans, 201 Asians, 204 Hispanics, 80 Indian/South Asians, 39 Pacific Islanders, and 840 from other self-reported racial backgrounds (7, 8). **Table 1** summarizes the included study characteristics. As outlined in Table 1, there were some differences between the study characteristics between the two articles. In the study by Stannard et al (8), the vast majority of study participants were undergoing elective surgery (> 90%). In the study by Sun et al (7), majority of patients were undergoing emergency surgery. Different monitors were used between the Sun et al (7) and Stannard et al (8) articles with the INVOS 5100C (Medtronic, Minneapolis, MN) and ForeSight Elite (Edwards Lifesciences, Irvine, CA) monitors being used, respectively. In addition, Sun et al (7) looked at $rSo_2$ readings pre-induction and at the end of the case in comparison to pre-cardiopulmonary bypass in Stannard et al (8). Finally, Sun et al (7) compared Caucasians and African Americans, whereas Stannard et al (8) evaluated seven different self-reported racial groups.

In the study by Sun et al (7), a multivariate linear regression was performed for other demographic variables and found that in addition to self-reported race, age, male gender, body mass index, smoking status, diabetes, hematocrit, ejection fraction, atrial fibrillation, and serum creatinine contributed to variations in $rSo_2$ readings.

### Racial Differences in Cerebral Oximetry

Sun et al (7) showed a significantly lower pre-induction mean $rSo_2$ reading (± SD) in African Americans (53 ± 12.6) compared with Caucasians (65 ± 11.6) (7). Conversely, Stannard et al (8) found little difference in pre-bypass $rSo_2$ readings between self-reported racial groups with all group means within a 2% range.

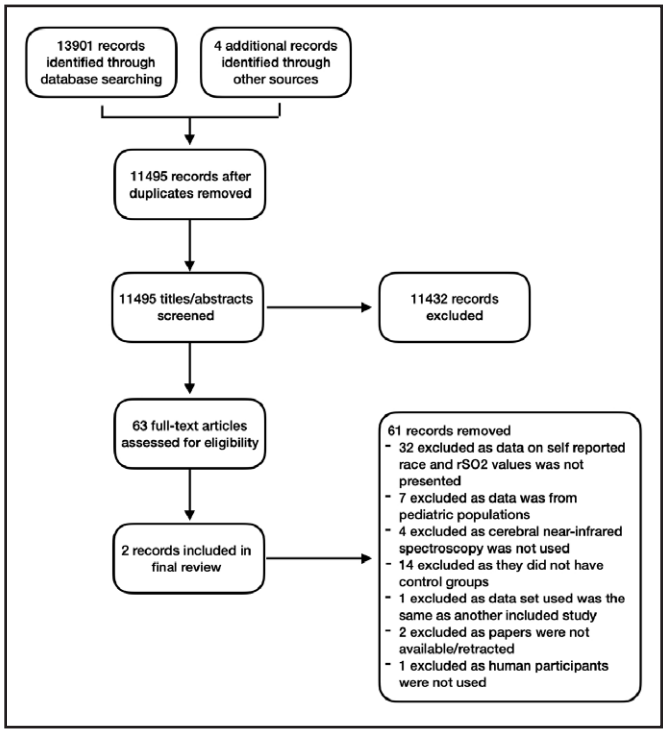


**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram—adult search. $rSo_2$ = regional cerebral tissue oxygenation.

## DISCUSSION

The two studies included in this review suggest that it is still unclear exactly how self-reported race (as an estimator of skin pigmentation and melanin content) impacts NIRS-derived regional saturation of oxygen readings. Although it is quite clear that melanin absorbs light at similar wavelengths as deoxygenated hemoglobin within the near-infrared spectrum, it is unclear how this impacts the final result displayed by the oximeter (9). The difference between the studies by Sun et al (7) and Stannard et al (8) require careful consideration. Whereas the INVOS 5100C Cerebral/Somatic Oximeter used in Sun et al (7) yielded significantly lower $rSo_2$ measurements in African Americans compared with Caucasians, the ForeSight Elite Tissue Oximetry System used in Stannard et al (8) yielded relatively similar $rSo_2$ measurements across self-reported racial groups. Importantly, this platform has an algorithm that may, at least in part, control for the effects of melanin on NIRS through the measurement of absorption spectra at an additional wavelength (9). Therefore, the influence of melanin on the quantification of $rSo_2$

## TABLE 1.
### Study Characteristics

| References | Sun et al (7) | Stannard et al (8) |
|---|---|---|
| Participants, *n* | 3282 | 4267 |
| Study population | Adult African American and Caucasian patients undergoing cardiac surgery | Adult patients undergoing on-pump cardiac surgery |
| Monitor used | INVOS 5100C (Medtronic, Minneapolis, MN) | ForeSight Elite (Edwards Lifesciences, Irvine, CA) |
| Timing of measurement | Pre-induction for cardiac surgery and at skin closure | Pre-bypass for cardiac surgery |
| Included groups (*n*) | Caucasian (2096)<br>African American (1186) | Caucasian (2519)<br>African American (384)<br>Asian (201)<br>Hispanic (204)<br>Indian/South Asian (80)<br>Pacific Islander (39)<br>Other (840) |
| Age, yr (range or SD) | Caucasian: 66 (20–96)<br>African American: 63 (18–92) | Caucasian: 63.8 (13.2)<br>African American: 58.6 (14.4)<br>Asian: 61.6 (13.0)<br>Hispanic: 59.9 (13.6)<br>Indian/South Asian: 59.4 (13.1)<br>Pacific Islander: 61.3 (14.5)<br>Other: 61.2 (13.2) |
| Sex, female, % | Caucasian: 25.5<br>African American: 43.2 | Caucasian: 34.9<br>African American: 43.0<br>Asian: 39.3<br>Hispanic: 43.1<br>Indian/South Asian: 27.5<br>Pacific Islander: 35.9<br>Other: 38.9 |
| Body mass index (SD) | Caucasian: 29.1 (6.4)<br>African American: 30.0 (7.0) | Caucasian: 27.7 (5.4)<br>African American: 29.0 (7.1)<br>Asian: 24.9 (4.3)<br>Hispanic: 28.9 (5.6)<br>Indian/South Asian: 26.0 (5.3)<br>Pacific Islander: 25.4 (5.0)<br>Other: 27.8 (5.8) |
| Elective procedure, % | Caucasian: 34.5<br>African American: 25.7 | Caucasian: 97.3<br>African American: 92.7<br>Asian: 93.0<br>Hispanic: 95.1<br>Indian/South Asian: 98.8<br>Pacific Islander: 100<br>Other: 94.4 |

(*Continued*)

**TABLE 1. (*Continued*)**
**Study Characteristics**

| | | |
|---|---|---|
| Carotid stenosis, % (SD) | Caucasian: 0.6<br>African American: 0.8 | Caucasian: 1.7<br>African American: 0.8<br>Asian: 3.0<br>Hispanic: 0.5<br>Indian/South Asian: 0<br>Pacific Islander: 2.6<br>Other: 1.4 |
| Oxygen content | Caucasian: hematocrit 38.7 (5.8)<br>African American: hematocrit 36.1 (5.2) | Caucasian: anemia (0.6%)<br>African American: anemia (1.6%)<br>Asian: anemia (0.5%)<br>Hispanic: anemia (0.5%)<br>Indian/South Asian: anemia (0%)<br>Pacific Islander: anemia (0%)<br>Other: anemia (1.0%) |
| Results group, regional cerebral tissue oxygenation, % (SD) | Caucasian: 65.6 (11.6)<br>African American: 53.3 (12.6) | Caucasian: 72.3 (5.7)<br>African American: 71.7 (6.3)<br>Asian: 70.5 (6.2)<br>Hispanic: 72.4 (6.4)<br>Indian/South Asian: 70.7 (5.6)<br>Pacific Islander: 70.9 (7.1)<br>Other: 71.2 (6.0) |

may vary in magnitude based on the NIRS platform employed.

There were, however, other studies that set out to answer the question of how skin pigmentation affects cerebral oximetry readings that did not meet this review's inclusion criteria. Misra et al (10) examined 94 subjects and measured $rSo_2$ at rest. However, their study populations were differentiated based on light, medium, and dark skin pigmentation rather than self-reported race. Although this study had a small sample size, it did not find any significant differences in $rSo_2$ values as a function of skin pigmentation. Bickler et al (2) evaluated several factors that influence the accuracy of NIRS monitors—including skin pigmentation. Although the raw data for mean $rSo_2$ values was not published for different racial groups or skin-pigmentation groups, the authors did report the bias between the $rSo_2$ reading and the calculated saturation based on blood samples from jugular bulb and arterial catheters. The authors concluded that in patients with dark pigmented skin, increased negative bias was observed, suggesting that NIRS monitors may underestimate true oxygen saturation values. However, it is important to note that Bickler et al (2) studied five different monitors, and only one (ForeSight) showed statistical significance of the negative bias of pigmented skin. In addition, the total sample size was quite low with only 23 study participants, nine of whom had intermediate skin and two who had dark skin.

There were other studies including Redford et al (11), Wong et al (12), Nguyen et al (13), and Kashlan et al (14), which appeared to collect data on race or skin pigmentation as well as cerebral oximetry readings; however, these data was not published nor were we able to obtain this raw data. Potentially, with these data available, a pooled systematic review could be conducted that would provide greater insight into the effect of skin pigmentation/race on cerebral oximetry readings. Finally, Afshari et al (15) conducted a study where a tissue simulating phantom was used to simulate various melanin levels. Two NIRS devices were used,ForeSight Elite and SenSmart X-100 (Nonin, Plymouth, MN), and the authors found that an increase in melanin resulted in a decrease in saturation readings with both devices (15).

In our review, as part of the inclusion criteria, we limited the search to adults to maintain a relatively uniform patient population. Further, the studies we included relied upon self-reported racial groups, which were used as a proxy for estimating the degree of skin pigmentation. We did run the search again looking for studies including neonatal and pediatric patients; however, we did not uncover any articles that met our criteria for the adult portion of the systematic review (**Fig. 2**).

We constricted our review to reflect the impact of skin pigmentation, and hence skin melanin content, on brain oxygenation estimation as the derived $rSo_2$ value is used clinically to trigger interventions such as mean arterial pressure augmentation, RBC transfusion, mild hypercapnia, or is associated with postoperative complications such as delirium and strokes. NIRS has also been used to assess for distal limb perfusion or viability of cutaneous surgical flaps, however, given the clinical indications are different in these cases, we did not include studies using NIRS for non-brain related indications.

Lessons from pulse oximetry can provide important insights into how NIRS-derived $rSo_2$ may be altered by the melanin content of skin, however, mechanistic differences deserve discussion. In the setting of pulse oximetry, the signal is derived by estimating the ratio of light emitted at 600 nm (red light) and 940 nm (infrared light) (16). Oxygenated hemoglobin absorbs light at ~900 nm and thus in the presence of saturated arterial blood, pulse oximetry will record values in the greater than 90% range. However, melanin absorbs infrared light at ~900 nm as well, thereby providing a spuriously high pulse oximetry value than is truly reflected in arterial blood by oxygenated hemoglobin. Conversely, NIRS emits infrared light at 900 nm and then records the return of the signal at a receiver on the same NIRS sensor. Because melanin absorbs infrared light at ~900 nm, the receiver on the NIRS sensor would then receive a spuriously low value, suggesting low cerebral blood flow and reduced brain oxygenation.

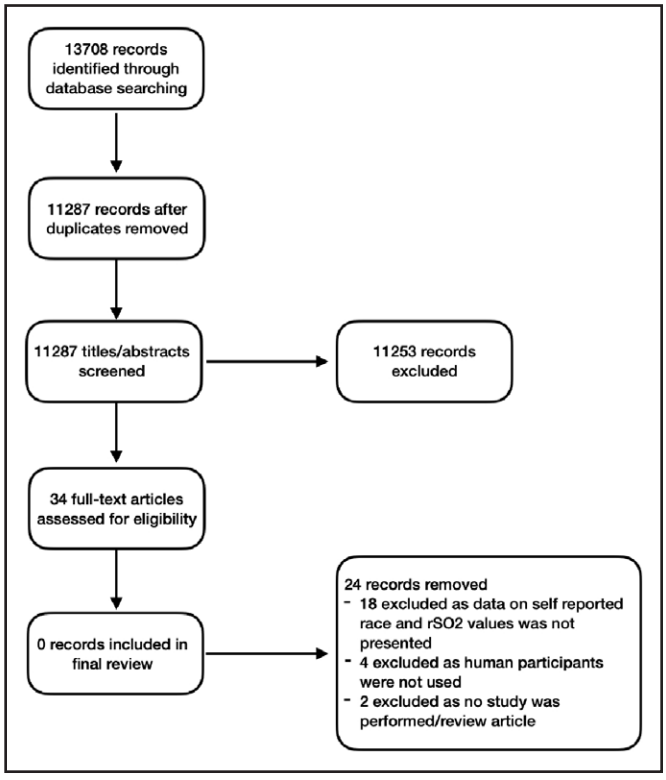


**Figure 2.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram—pediatric/neonate search. $rSo_2$ = regional cerebral tissue oxygenation.

It is clear that further robust research is required in this field to definitively ascertain whether the NIRS-derived $rSo_2$ signal is affected by the content of melanin in skin and thus, the degree of skin pigmentation. Our systematic review has uncovered two similar articles which are retrospective in nature and rely upon self-reported racial designation as a proxy for the degree of skin pigmentation. Both methodologic considerations have inherent weaknesses that limit the strengths of conclusions that can be drawn from their findings. To provide rigorous study to this issue, further research for this issue must incorporate three principles. First, the design of studies should be prospective and investigators should be blinded as to the participants' degree of skin pigmentation to minimize biases (17). Second, the degree of skin pigmentation (and therefore, melanin content) should be quantified according to validated scoring scales (18–21). Such a numerical variable would enable researchers to draw associations between the numerical value of $rSo_2$ vs. the degree of skin pigmentation. Third, assessing the change in $rSo_2$ in subjects with clinical interventions (e.g., blood pressure manipulation, mild hypocapnia, or mild hypercapnia) would provide insights into the change of $rSo_2$ in subjects with varying degrees of skin pigmentation. Such physiologic and clinical data would enable generalization to real-world clinical scenarios where the $rSo_2$ value is often used in clinical decision making.

## CONCLUSIONS

This systematic review has identified conflicting evidence with regard to the impact of skin pigmentation on $rSo_2$ readings. It may be possible that the $rSo_2$

values could be impacted by skin pigmentation; however, further studies are needed. In particular, studies with prospective designs, blinded, incorporating the use of skin pigmentation scoring scales, and using clinical interventions to assess the change of $rSo_2$ across racial groups will be required to provide greater insight.

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