# Blood Transfusion Rates in Non-Syndromic Craniosynostosis: A Proportion Meta-analysis of Open Versus Minimally Invasive Techniques

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## *Abstract*

**Background and Aim:** Premature suture fusion in non-syndromic craniosynostosis often requires surgery to permit normal brain growth. To minimize blood transfusion needs, minimally invasive surgery (MIS) has been proposed. This study will pool the prevalence of blood transfusion requirements in non-syndromic craniosynostosis surgeries, comparing open versus minimally invasive surgeries.

**Methods:** A systematic review and proportion meta-analysis was conducted in accordance with PRISMA guidelines and registered in PROSPERO (CRD42024604632). PubMed, Scilit, Scopus, and Web of Science were searched uto March 7, 2024. Pooled prevalence was calculated using the Freeman-Tukey double arcsine transformation.

**Results:** Nine studies with a total of 619 patients met the inclusion criteria. The pooled prevalence of blood transfusion was 52.0% (95% CI: 32.0–72.0) for open surgery (OS) and 10.0% (95% CI: 1.0–20.0) for minimally invasive surgery (MIS). Within OS, cranial vault remodeling exhibited the highest transfusion prevalence of 58.1% (95%CI: 37.5–78.7). Among those undergoing MIS, strip-assisted surgery had a lower prevalence (3.9%; 95%CI: -0.5–8.2) compared to endoscopic strip craniectomy (13.1%; 95% CI: -0.4–26.6). OS for metopic craniosynostosis yielded a blood transfusion prevalence of 76.2% (95% CI: 62.9–89.5), the highest among affected sutures. Sagittal craniosynostosis repairs showed a prevalence of 22.5% (95%CI: 9.6–35.3) in OS, contrasting with be 2.6% (95%CI: 1.7–11.9) in MIS.

**Conclusion:** The prevalence of blood transfusion in craniosynostosis repair is significantly lower in MIS compared to OS, suggesting its relative safety in terms of transfusion risks.

**Keywords:** Craniosynostosis; Cranial Deformity, Blood Transfusion; Cranial Vault Remodeling; Endoscopic Surgery; Meta-analysis

## Introduction

Craniosynostosis is a congenital cranial deformity resulting from the premature fusion of cranial sutures, producing abnormal head shape and risking complications such as increased intracranial pressure (ICP) and disturbance on respiratory and neurologic systems.[1] The condition is usually non-syndromic, occurring independently from other congenital anomalies.[1,2] Common types include sagittal synostosis, coronal synostosis, metopic synostosis, and lambdoid synostosis.[3]

The primary treatment for craniosynostosis is surgical intervention, aimed at correcting the shape of the skull and allowing for normal brain growth.[4] Open surgery (OS) involves a large incision that provides direct access and clear visualization of the target organs and tissues.[5] Principal OS techniques include cranial vault remodeling (CVR), cranial distraction osteogenesis (CDO), fronto-orbital advancement (FOA), and strip craniectomy (SC). [6] However, the large incisions increases the likelihood of blood transfusion, long hospital stay, and post-surgical complications.[7]

On the other hand, minimally invasive surgery (MIS), especially endoscopic methods, need significantly smaller incisions.[8–10] Its other benefits include minimum trauma to surrounding tissues, shorter procedure time, and earlier recovery with fewer complications. In both OS and MIS, if the blood loss exceeds 100 mL (or ~10% of the patient's blood volume), blood transfusion should be administered intraoperatively.[11]

Measuring the prevalence of blood transfusion is crucial for peri operative planning including blood bank logistics, patient safety, and resource allocation.[11,12] Existing studies are mostly single-center, with limited sample sizes.[12–15] To derive robust estimates regarding the rates of blood transfusion in craniosynostosis surgeries, we conducted this multi-center proportion meta-analysis.[16–19]

## Methods

The study employed a proportional meta-analysis design, as per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol.[20] The research question was, 'What is the prevalence of blood transfusion in OS and MOS for the management of non-syndromic craniosynostosis?' The study was officially recorded in PROSPERO (registration number CRD42024604632, November 01, 2024).

On March 7, 2024, we queried PubMed, Scilit, Scopus, and Web of Science databases using the following search terms: "craniosynostosis" OR "non-syndromic craniosynostosis" OR "cranial suture synostosis" AND ("open surgery" OR "cranial vault remodeling" OR "strip craniectomy" OR "endoscopic surgery" OR "minimally invasive surgery") AND ("blood transfusion" OR "transfusion requirement" OR "perioperative blood loss" OR "intraoperative transfusion"). We used the recommended search syntax and rules specific to each database.[21]

### *Eligibility Criteria*

Inclusion criteria: Studies focusing on patients with non-syndromic craniosynostosis undergoing OS or MIS, including cranial vault remodeling (CVR), endoscopic strip craniectomy (ES), spring-assisted surgery (SAS), strip craniectomy (SC), remodeling with helmet therapy (RH), and posterior vault distraction (PiP). Eligible studies should have reported the prevalence or incidence of blood transfusion as an outcome measure. Accepted study designs included cross-sectional, case-control, and cohort studies that offered primary patient data relevant to surgical outcomes.

Exclusion criteria: Studies with non-comparative or incomplete data, case series without distinct outcome reporting, review articles, commentaries, editorials, and conference abstracts.

### *Study selection and quality assessment.*

Following automatic duplicate removal (using EndNote 19), screening was carried out in two phases: first by evaluating titles and abstracts, and then by reviewing full texts. Two authors independently conducted each stage, resolving disagreements through consensus; if consensus was not reached, a third author was consulted for clarification. The Newcastle-Ottawa Scale (NOS) was employed for the critical appraisal of observational studies, which suggests a maximum score of 9 for cohort studies and 7 for cross-sectional studies.[22,23]

We extracted the following data from each study: first author, year of publication, country, study design, sample size; mean patient age in months, sex distribution; suture type (sagittal, coronal, metopic, lambdoid, or mixed), surgical technique; and blood transfusion rates. Continuous variables were reported as mean ± standard deviation (SD), while other data were converted using standard formulae.[24–26] Data extraction was carried out by one author and verified and confirmed by another author.

### *Statistical analysis*

Meta-analysis was performed using Rstudio version 2024.04.2 (Posit, PBC, Boston, MA, USA). The analysis focused on both open surgeries (such as cranial vault remodeling and strip craniectomy) and minimally invasive procedures (including spring-assisted and spring-endoscope surgeries). The pooled proportion was estimated by Freeman-Tukey double arcsine transformation (FTT) method. Back-transformation was performed based on the inverse of the variance of the pooled FTT proportion. Prevalence was calculated by multiplying 100% with the back-transformed value. Heterogeneity among the studies was evaluated by $I^2$ statistic, with cut-off criteria of 50% and p-Het < 0.1 indicating high heterogeneity. Subgroup analysis compared surgical techniques (CVR, SC, SAS, ES).

## Results

### *Study selection*

A total of 1473 records were retrieved. After removing 904 duplicates, 569 records were screened. Full texts for 102 articles were retrievable; these were scrutinized based on the eligibility criteria. Six were duplicates and 78 studies failed our eligibility criteria due to wrong design (8), missing outcome data (64), ineligible study designs (6), or did not exclude syndromic patients (4).[27–30] Finally, N = 9 studies were identified as eligible to include in our systematic review and meta-analysis [Table 1]. The flow-diagram of the screening and selection process is presented as Figure 1.

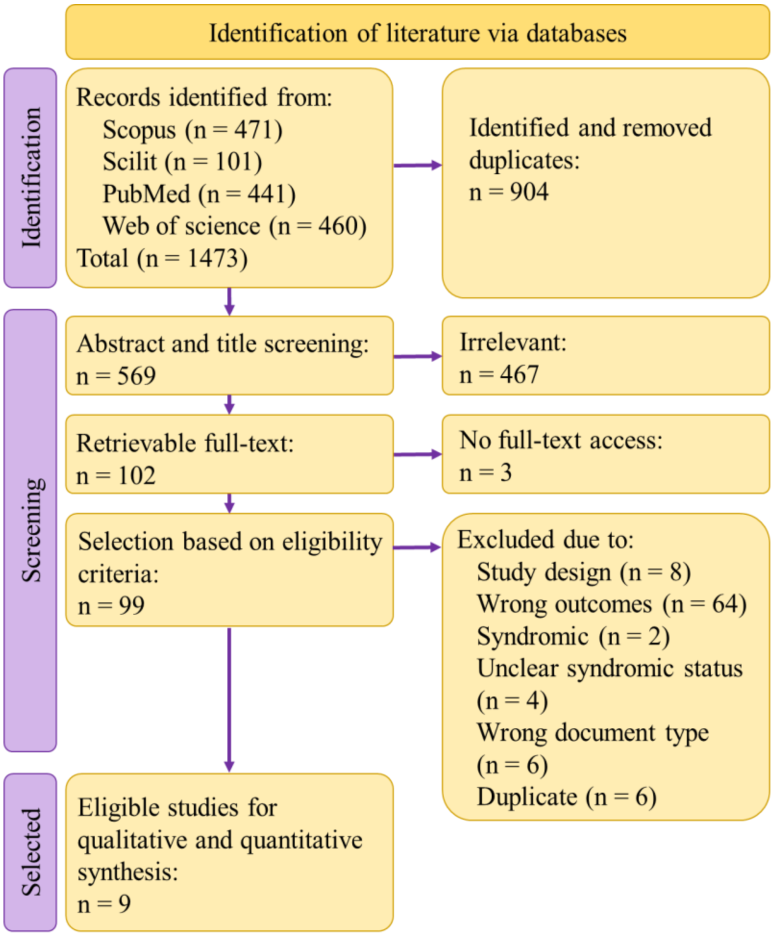



**Figure 1:** Flow-diagram for the screening and selection of studies eligible for the estimation of blood transfusion prevalence in craniosynostosis repairs.

## *Characteristics and quality of studies*

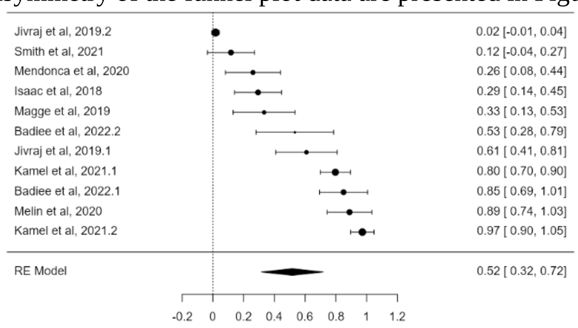
Table 1 summarizes the included nine studies. Seven were from the United States (US), one from the United Kingdom (UK), and one from India. Together they had a total of 619 patients aged 3–19.9 years. The quality of eight studies was assessed as 'good' using Newcastle–Ottawa Scale (NOS). One study (Badiee et al.)[[14]] was assessed 'moderate' due to small sample size (n = 35). Another concern was found in Jivraj et al.[31] because their control group data was sourced from external medical records, thus affecting comparability.[31]

**Table 1:** Characteristics and qualities of studies eligible for the estimation of blood transfusion prevalence in craniosynostosis repairs.

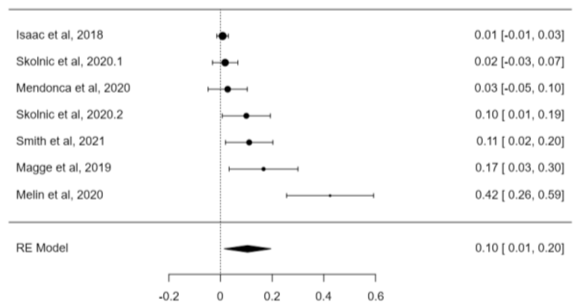
| Study | Location | Study design | Affected suture(s) | Group | | Demographic characteristics | | | Blood transfusion (%) | Quality | Professionals |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Technique | Category | Total n | Age (months) | Sex M/F | | | |
| Badiee et al., 2022[14] | United States | Cross-sectional | Metopic | SC | OS | 15 | 5.5 ± 1.7 | 14/1 | 53.3 | 6 | 1 neurosurgeon |
| | | | | CVR | OS | 20 | 9.8 ± 0.8 | 14/6 | 85.0 | | 4 craniofacial surgeons + 1 neurosurgeon |
| Kamel et al., 2021[31] | United States | Cross-sectional | Coronal | FOA | OS | 64 | 11.6 ± 10.8 | 19/45 | 80.0 | 7 | 2 neurosurgeons + 2 craniofacial surgeons |
| | | | | CDO | OS | 17 | 9 ± 1.6 | 3/14 | 100 | | 1 craniofacial surgeon + 2 neurosurgeons |
| Magge et al., 2019[32] | United States | Cross-sectional | Sagittal | CVR | OS | 21 | 5.1 ± 2.7 | NR | 33.3 | 7 | Multiple surgeons |
| | | | | ES | MIS | 30 | 3.1 ± 1.2 | NR | 16.7 | | Multiple surgeons |
| Jivraj et al., 2019[33] | United Kingdom | Cohort | Unicoronal | FO-CVR | OS | 23 | 18.5 ± 4.2 | 10/13 | 60.9 | 8 | Not applicable |
| | | | | SC | OS | 115 | 3.3 ± 2.0 | 50/65 | 1.7 | | |
| Isaac et al., 2018[34] | United States | Cross-sectional | Coronal | FOA | OS | 34 | 10.4 ± 2.3 | NR | 30.0 | 7 | 1 neurosurgeon + 2 plastic surgeon |
| | | | | ES | MIS | 60 | 3.0 ± 1.1 | NR | 0.0 | | 1 neurosurgeon |
| Melin et al., 2020[7] | United States | Cohort | Mix | CVR | OS | 18 | < 6 | NR | 90.0 | 9 | 1 neurosurgeon + 1 craniofacial plastic surgeon |
| | | | | ES | MIS | 33 | < 6 | NR | 42.0 | | 1 neurosurgeon + 1 craniofacial plastic surgeon |
| Mendonca et al., 2020[15] | India | Cohort | Sagittal | ES | MIS | 17 | 3.8 ± 0.6 | 4/13 | 0.0 | 9 | Not applicable |
| | | | | CVR | OS | 23 | 11.9 ± 2.6 | 10/13 | 27.0 | | |
| Smith et al., 2021[35] | United States | Cohort | Sagittal | SC | OS | 17 | 12.6 ± 3.2 | 14/3 | 11.8 | 9 | 5 neurosurgeons + 1 plastic surgeon |
| | | | | SAS | MIS | 45 | 19.9 ± 3.1 | 33/12 | 11.1 | | 5 neurosurgeons |
| Skolnic et al., 2020[36] | United States | Cross-sectional | Sagittal | SAS | MIS | 27 | 4.5 ± 1.3 | 23/4 | 0.0 | 7 | 1 neurosurgeon |
| | | | | ES-HM | MIS | 40 | 3 ± 0.9 | 29/11 | 11.1 | | NA |

*Note. NR: not reported; SC: strip craniectomy; CVR: cranial vault remodeling; FOA: fronto-orbital advancement; CDO: cranial distraction osteogenesis; ES: endoscopic surgery; FO-CVR: fronto-orbital cranial vault remodeling; SAS: strip-assisted surgery; ES-HM: endoscopic surgery with helmet molding.*

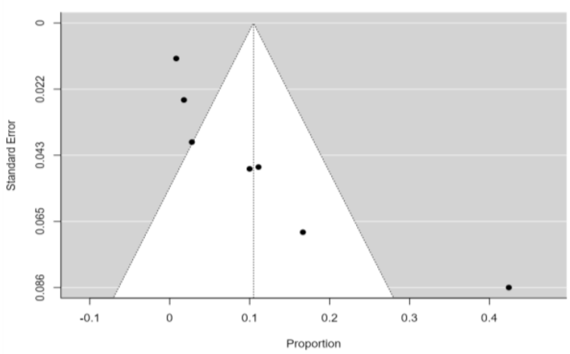
The pooled prevalence of blood transfusion for OS or MIS are presented in Figure 2 (a & b). The prevalence for the OS was 52.0% with 95% CI ranging from 32.0–72.0. As for the MIS, the prevalence was 10.0% (95% CI: 1.0–20.0). Heterogeneities were high in both pooled estimates with $I^2$ values of 92.1% ($p < 0.001$) and 97.5% ($p < 0.001$) for OS and MIS, respectively. Egger's correlation suggested publication bias ($p < 0.001$) in the pooled analysis of blood transfusion prevalence among patients undergoing OS, but negligible for MIS ($p = 0.955$). The symmetry and asymmetry of the funnel plot data are presented in Figure 2 (c & d).



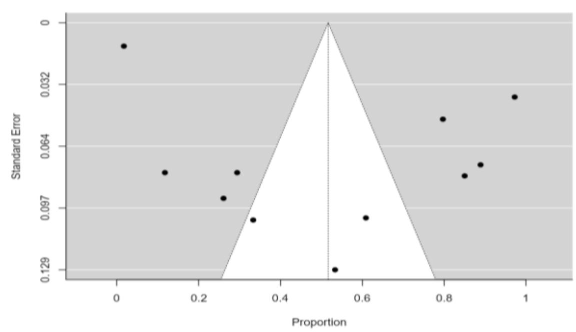

(a)




(b)




(c)




(d)

**Figure 2:** Pooled prevalence of blood transfusion among patients undergoing open (a) and minimally invasive surgeries (b). The funnel plot for publication bias detected in the pooled analysis of the prevalence analysis in open (c) and minimally invasive surgery groups (d).

Results from the pooled estimates based on the surgical techniques and types of sutures are presented in Table 2. The highest blood transfusion prevalence was observed in CDO (100%), though it was only reported in one study. The second highest prevalence was observed in CVR (58.1%; 95% CI: 37.5–78.7), with SC (10.5%; 95% CI: 1.4–19.5) occupied the last position among the OS. The lowest prevalence among MIS was found in SAS (3.9%; 95% CI: -0.5–8.2), followed by ES with a prevalence of 13.1% (95% CI: -0.4–26.6). Among OS, from the highest to the lowest prevalence was observed in metopic (76.2%; 95% CI: 62.9–89.5), coronal (69.2%; 95% CI: 29.8–10.87), sagittal (22.5%; 95%CI: 9.6–35.3), and unicoronal sutures (2.6%; 95% CI: 0.2–4.9). In the case of MIS, we were only able to pool the data for sagittal sutures, where the prevalence was found to be 2.6% (95% CI: 1.7–11.9).

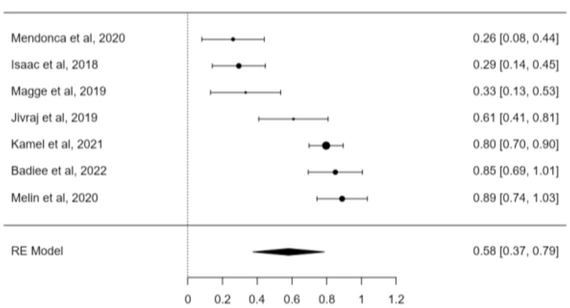
**Table 2:** Subgroup analysis for the pooled estimates of blood transfusion prevalence in craniosynostosis repairs.

| **Variable** | **No of Studies** | **Sample size n** | **Prevalence % (95% CI)** | **$I^2$ (%)** | ***p*-Het** |
|---|---|---|---|---|---|
| **Open surgeries** | | | | | |
| Cranial vault remodeling | 7 | 203 | 58.1 (37.5–78.7) | 92.0 | <0.001* |

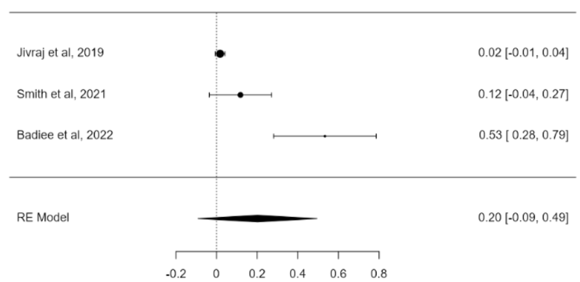
| | | | | | |
|---|---|---|---|---|---|
| Strip craniectomy | 3 | 147 | 10.5 (1.4–19.5) | 92.1 | <0.001* |
| Osteogenesis | 1 | 17 | 100 (not applicable) | Not applicable | Not applicable |
| **Minimally invasive surgeries** | | | | | |
| Spring-assisted | 2 | 72 | 3.9 (-0.5–8.2) | 67.6 | 0.079 |
| Spring-endoscope | 5 | 180 | 13.1 (-0.4–26.6) | 93.1 | 0.057 |
| **Suture** | | | | | |
| Open surgeries | | | | | |
| Coronal | 3 | 115 | 69.2 (29.8–10.9) | 97.7 | <0.001* |
| Sagittal | 3 | 61 | 22.5 (9.6–35.3) | 37.1 | 0.210 |
| Metopic | 2 | 35 | 76.2 (62.9–89.5) | 77.1 | 0.037* |
| Unicoronal | 2 | 138 | 2.6 (0.2–4.9) | 97.0 | <0.001* |
| Minimally invasive | | | | | |
| Sagittal | 5 | 159 | 2.6 (1.7–11.9) | 48.2 | 0.103 |

*Significant

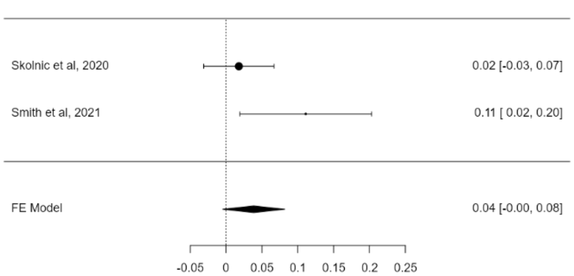
Figure 3 presents the forest plots for the pooled prevalence of blood transfusion in various craniosynostosis repair techniques. The prevalence varied according to the surgical technique. Open cranial vault remodeling demonstrated the highest prevalence at 58.1% (95% CI: 37.5%–78.7%), while strip craniectomy, spring-assisted surgery, and endoscopic-assisted surgery had significantly lower rates (4%– 20%).



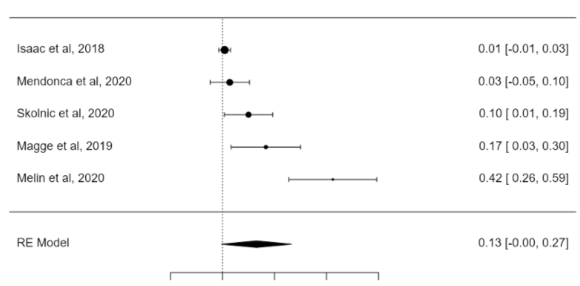

(a)




(b)




(c)




(d)

**Figure 3:** Forest plots for the pooled prevalence of blood transfusion in various craniosynostosis repair techniques such as open cranial vault remodeling (a), strip craniectomy (b), spring-assisted surgery (c), and endoscope-assisted surgery (d)

Among open techniques, cranial vault remodeling (CVR) demonstrated the highest transfusion prevalence, with pooled rates approaching 58% (95% CI: 37%–79%) [Figure 3a]. Strip craniectomy (SC) showed a lower transfusion prevalence of 20% (95% CI: -9%–49%) [Figure 3b]. Spring-assisted surgery (SAS) had the lowest transfusion prevalence at only 4% (95% CI: 0%–8%), suggesting minimal transfusion requirements [Figure 3c]. Endoscopic-assisted surgery (ES) showed a slightly higher pooled prevalence of 13% (95% CI: 0%–27%), but still substantially lower than traditional open techniques [Figure 3d].

## Discussion

Variables such as patient age, blood volume dynamics, and surgical complexity influence transfusion risk in craniosynostosis repair. Although infants under 24 months are reported to have lower infection rates and shorter hospital stays, limited physiological reserve increases their susceptibility to intraoperative blood loss. Consequently, the overall need for blood transfusion does not significantly differ across age groups.[32–34] However, younger patients may require prolonged hospitalization due to closer postoperative monitoring needs.[35] Importantly, only a minority of transfusion-free hospitalizations have been documented after craniofacial reconstruction. [33] The timing of surgery also significantly influences blood loss and transfusion rates. Optimal intervention within the first year of life, particularly in syndromic cases, reduces complications and supports neurodevelopmental outcomes, whereas delayed intervention is associated with higher perioperative risks. [36] Though Blood loss is generally proportional to duration of surgery[37], reported transfusion rates vary widely (20%–100%).[38] In severe cases, rapid hemorrhage may necessitate massive transfusion requirements.[38,39]

Transfusion management in craniosynostosis requires a patient-specific strategy that considers surgical technique, intraoperative hemodynamics, and transfusion thresholds. Open surgeries often necessitate early transfusion, while minimally invasive procedures typically require less. Guidelines recommend transfusion when hemoglobin falls below 8 g/dL in stable patients or 10 g/dL in unstable patients, with special considerations for infants with congenital conditions.[40] Effective management must balance evidence-based thresholds with patient physiology and intraoperative judgment to minimize complications. Open procedures usually involve extensive tissue manipulation and larger incisions.[37,39] This indicates that surgical approach and suture involvement, rather than age alone, are key determinants of transfusion needs. Our meta-analysis demonstrated that MIS techniques substantially reduce transfusion requirements, supporting their prioritization in patients at higher risk of transfusion-related complications or in settings with limited blood supply.[33] Furthermore, transfusion prevalence data can inform perioperative planning and optimize resource allocation. Of note, OS in the included studies were performed mainly by neurosurgeons and craniofacial plastic surgeons, whereas only neurosurgeons performed MIS. Age distribution also differed, with OS typically performed in older infants (~9–17 months) and MIS in younger infants (~3–5 months).

While guidelines recommend transfusion initiation below 10 g/dL in stable pediatric patients, emerging evidence suggests that restrictive transfusion strategies may even reduce mortality in non-craniosynostosis surgeries.[38] Such findings underscore the importance of tailoring transfusion practices to patient-specific and procedural factors. Prioritizing procedures with lower transfusion requirements also facilitate cost and resource savings.[36] The choice of surgical technique, however, extends beyond transfusion risk. A prior survey indicated that selection often depends on skull maturation.[32] For infants older than 12 months, more invasive approaches such as CVR and CDO have been preferred, as extensive exposure allows more complete correction of cranial deformities. [33] Neurodevelopmental implications also warrant consideration in surgical planning. 34,36.

Taken together, these findings support broader implementation of MIS techniques where feasible, especially in resource-limited hospitals or in patients at high transfusion risk. Improved training opportunities and allocation of resources for MIS are recommended.

The main limitation of this study is the high heterogeneity across prevalence estimates. However, this variability highlights the need for tailored transfusion strategies in craniosynostosis repair. Caution should be applied when generalizing these findings, as institutional protocols and local resources may strongly influence transfusion practices. Large-scale, multicenter studies are needed in the future to compare long-term outcomes of OS versus MIS, not only regarding transfusion but also recurrence rates, neurodevelopment, and patient quality of life.

Standardized study designs will be essential to refine surgical guidelines and optimize perioperative blood management.

## Conclusion

There are significant differences in blood transfusion requirements between OS and MIS for craniosynostosis repair. The pooled prevalence of blood transfusion is notably higher in OS (52.0%) than in MIS (10.0%). Procedures such as CVR and metopic suture repairs are associated with particularly high transfusion rates. Our findings suggest that MIS techniques may minimize transfusion requirements, and better patient safety and outcome. Targeted blood management strategies are recommended for high-risk OS cases.

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