

Controlling Phlebotomy Volume Diminishes PICU Transfusion: Implementation Processes and Impact

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BACKGROUND AND OBJECTIVES: Phlebotomy excess contributes to anemia in PICU patients and increases the likelihood of red blood cell transfusion, which is associated with risk of adverse outcomes. Excessive phlebotomy reduction (EPR) strategies may reduce the need for transfusion, but have not been evaluated in a PICU population. We hypothesized that EPR strategies, facilitated by implementation science methods, would decrease excess blood drawn and reduce transfusion frequency.

METHODS: Quantitative and qualitative methods were used. Patient and blood draw data were collected with survey and focus group data to evaluate knowledge and attitudes before and after EPR intervention. The Consolidated Framework for Implementation Research was used to interpret qualitative data. Multivariate regression was employed to adjust for potential confounders for blood overdraw volume and transfusion incidence.

RESULTS: Populations were similar pre- and postintervention. EPR strategies decreased blood overdraw volumes 62% from 5.5 mL (interquartile range 1–23) preintervention to 2.1 mL (interquartile range 0–7.9 mL) postintervention ($P < .001$). Fewer patients received red blood cell transfusions postintervention (32.1% preintervention versus 20.7% postintervention, $P = .04$). Regression analyses showed that EPR strategies reduced blood overdraw volume ($P < .001$) and lowered transfusion frequency ($P = .05$). Postintervention surveys reflected a high degree of satisfaction (93%) with EPR strategies, and 97% agreed EPR was a priority postintervention.

CONCLUSIONS: Implementation science methods aided in the selection of EPR strategies and enhanced acceptance which, in this cohort, reduced excessive overdraw volumes and transfusion frequency. Larger trials are needed to determine if this approach can be applied in broader PICU populations.

Anemia in pediatric critical illness is common, with an incidence of 23% to 41%.^{1,2} Causes include bleeding, diminished erythropoietin production, bone marrow suppression, hemolysis, nutritional deficiencies, and blood wastage. Blood wastage can occur as a result of high sampling frequency,

excessive sampling volume, and blood discard practices. Repeated phlebotomy may cause or exacerbate anemia in children with small blood volumes.³ ⁴ For PICU patients, data indicate that 73% of daily blood loss is attributable to phlebotomy,⁵ and phlebotomy volume predicts transfusion likelihood.⁶

abstract



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Dr Steffen contributed to the final qualitative analysis, aided in the statistical analysis, and drafted, reviewed, and revised the manuscript; Dr Doctor made substantial contributions to study conception and design as well as interpretation of data, and he reviewed the manuscript; Ms Hoerr participated in patient recruitment, development of the Pre-Implementation Blood Conservation PICU Staff Survey, development of clinical blood conservation strategies and PICU staff education, and she collected clinical data for the pre- and postintervention periods and reviewed the manuscript; Dr Gill performed the statistical analysis and he contributed to and reviewed the manuscript; Dr Markham organized data for and contributed to the final quantitative analysis and he reviewed the manuscript; Dr Brown served as the primary laboratory medicine liaison for all aspects of this work and reviewed the manuscript; Mr Cohen and Ms Kryzer organized data for and contributed to the initial qualitative analysis and reviewed the manuscript; Ms Hansen played an integral role in leading focus groups and actively led the Patient Blood Management Team in developing and implementing patient blood management strategies, and she reviewed the manuscript; Ms Richards participated in patient recruitment and PICU staff education and she reviewed the manuscript; Ms Small assisted with the selection of an implementation framework,

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Red blood cell (RBC) transfusions are associated with complications including transmission of infection, hemolytic reactions, and transfusion-associated lung injury.^{5,6} Mounting evidence suggests that RBC transfusion in critically ill patients may contribute to longer duration of mechanical ventilation, cardiorespiratory dysfunction, nosocomial infections, thrombosis, multiple organ dysfunction syndrome, and death^{7,8} via mechanisms that alter inflammation, immune function, vasoregulation, and hemostasis.^{9,10} Finally, the cost of transfusion is substantial; a single transfusion incurs ~\$1500 (2016 US dollars) in hospital charges.¹¹

Patient blood management (PBM) strategies to prevent and/or mitigate anemia include optimizing hemostasis, promoting erythropoiesis, lowering transfusion thresholds in physiologically tolerant patients, and blood conservation (including methods to minimize phlebotomy losses). Excessive phlebotomy reduction (EPR) strategies exist, but they have not been widely implemented or studied in the complex PICU environment.^{12–14} With knowledge that our phlebotomy practices led to excessive phlebotomy volumes, we undertook this study to better understand the clinical impact of 4 EPR strategies and to add knowledge about how to bring them into routine practice. Implementation science, or the “study [of] how a specific set of activities and designated strategies are used to successfully integrate an evidence based intervention into practice,”¹⁵ was used to incorporate EPR strategies into care processes. We examined 2 hypotheses: (1) the use of 4 bundled EPR strategies would decrease the amount of blood overdrawn for laboratory testing, and (2) a plan informed by an implementation science framework would enhance uptake, acceptance, and adoption of the EPR strategies.

METHODS

Context

The setting of the current study was a tertiary, university-affiliated, 30-bed PICU with ~2000 annual admissions. Preliminary data indicated phlebotomy overdraw volumes exceeded the actual blood volumes required for laboratory studies; it was hypothesized that this may contribute to the need for blood transfusions in our unit.

EPR Interventions and Implementation

We selected EPR interventions based on previous evidence,^{12–14,16} survey and focus group data (see below), and anticipated utility in decreasing blood volume drawn. The interventions included: (1) the development of a bedside reference guide that included minimal volumes for >50% of the most common laboratory combinations (Supplemental Fig 6); (2) the use of a closed-loop system to minimize blood discarded from central venous catheter blood draws; (3) the use of microtubes when possible; and (4) a standardization of the blood volume for cultures.

We developed an implementation program to improve PBM awareness and provide education about the EPR intervention. Strategies were designed to increase provider acceptance and EPR adoption. The program is based on comprehensive unit-based safety programs,¹⁷ which have been successful in effecting change in other intensive care settings, and included the following: (1) the development of an EPR team, (2) the selection and training of EPR champions, (3) educational training sessions for nurses, and (4) providing audit and feedback to bedside nurses. The EPR team consisted of PICU physicians, nurse practitioners, nursing and laboratory medicine leadership and staff, and phlebotomy educators who met regularly before

and during implementation. EPR champions included PICU nurses and nurse practitioners who were invested in EPR and readily available to support nursing staff. The EPR team educated all PICU nursing staff during education days and individually during bedside teaching sessions by using a defined approach. EPR champions provided audit and feedback to nurses regarding the EPR interventions during the postintervention period.

Study of the EPR Interventions

We performed a prospective, single-center study in the St Louis Children’s Hospital (SLCH) PICU using a pre- and postintervention study design. Preintervention clinical data were collected from April to August 2011. Postintervention clinical data collection occurred from October 2012 to January 2013 after a 1-month run-in period after staff education. First, we assessed existing clinical practice and culture to guide the selection of EPR strategies and an implementation plan (Fig 1). Nursing knowledge of and attitudes about EPR were evaluated. Patient data were collected during the preintervention period. Next, we implemented the EPR bundle via the specific implementation strategy, collected postimplementation patient data, and assessed changes in nursing knowledge and attitudes.

Qualitative and quantitative data were collected for both exploratory and confirmatory purposes¹⁸ to enable a more robust understanding of blood draw practices and attitudes about PBM. We chose the validated Consolidated Framework for Implementation Research (CFIR)¹⁹ as an implementation framework for its ability to assess aspects of implementation in an organized and customizable fashion.²⁰ Preintervention, the CFIR guided the assessment of implementation barriers and facilitators; postintervention, it was

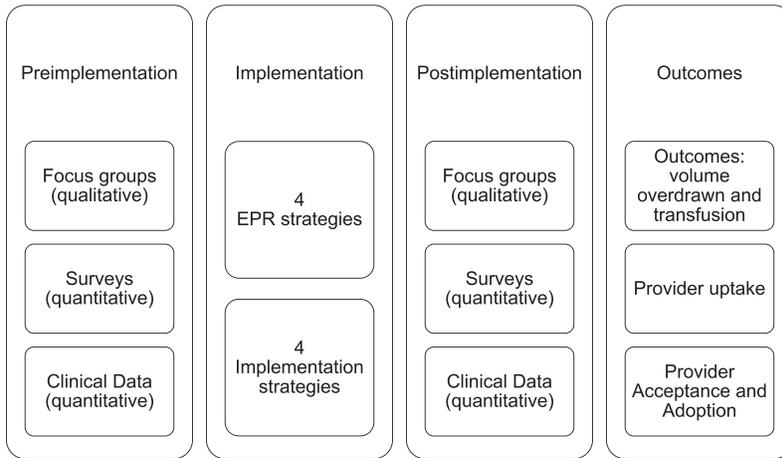


FIGURE 1
Implementation of PBM strategies: study flow.

TABLE 1 Demographic and Clinical Characteristics of Pre- and Postintervention Groups

	Preintervention (n = 112)	Postintervention (n = 111)	P
Age, mo	61 (18–146.5)	39 (8–121)	.09
Male, n (%)	61 (54.5)	68 (61.3)	.34
Wt, kg	20.5 (9–45.2)	17.1 (9.4–39)	.44
Diagnosis category, n (%)			
Respiratory	25 (22.3)	58 (52.3)	.00
Neurologic	29 (25.9)	20 (18.0)	.20
Trauma	13 (11.6)	8 (7.2)	.36
Surgical	14 (12.5)	4 (3.6)	.02
Oncologic	7 (6.3)	4 (3.6)	.54
Gastrointestinal	7 (6.3)	2 (1.8)	.17
Renal	3 (2.7)	4 (3.6)	.72
Infectious disease	5 (4.5)	2 (1.8)	.45
Cardiovascular	2 (1.8)	4 (3.6)	.68
Metabolic	4 (3.6)	1 (0.9)	.37
Hematologic	0 (0)	3 (2.7)	.25
Dermatology	2 (1.8)	1 (0.9)	.99
Anemia risk (diagnosis), n (%)	33 (29.5)	18 (16.2)	.03
PRISM III score	3 (0–6)	3 (0–6)	.39
Death, n (%)	3 (2.7)	5 (4.5)	.5
Total study d	3 (2–6)	3 (2–9)	.35
Admission Hb, g/dL	11.2 (9.6–12.6)	10.9 (9.9–12.5)	.82
Admission Hct, %	33.1 (28.4–37)	33.6 (29.7–37.3)	.35

Median (IQR) or n (%).

used to evaluate EPR adoption and acceptance.²¹

Inclusion criteria required patients to be <18 years old, have an anticipated PICU stay of >48 hours, and speak English. Patients were excluded if they were premature neonates (<34 weeks estimated gestational age and <28 days old), wards of the state, pregnant, had impending brain death, had a PICU stay of >72 hours ≤7 days before, required extracorporeal membrane oxygenation support,

were previously enrolled in this study or involved in other transfusion research, or had a personal or family history of RBC transfusion refusal.

Measures

We collected data on Pediatric Risk of Mortality III (PRISM III) scores²² to enable comparison in the pre- and postimplementation phases. The 2 clinical outcomes of interest were volume overdrawn per patient weight per PICU day (milliliter/kilogram

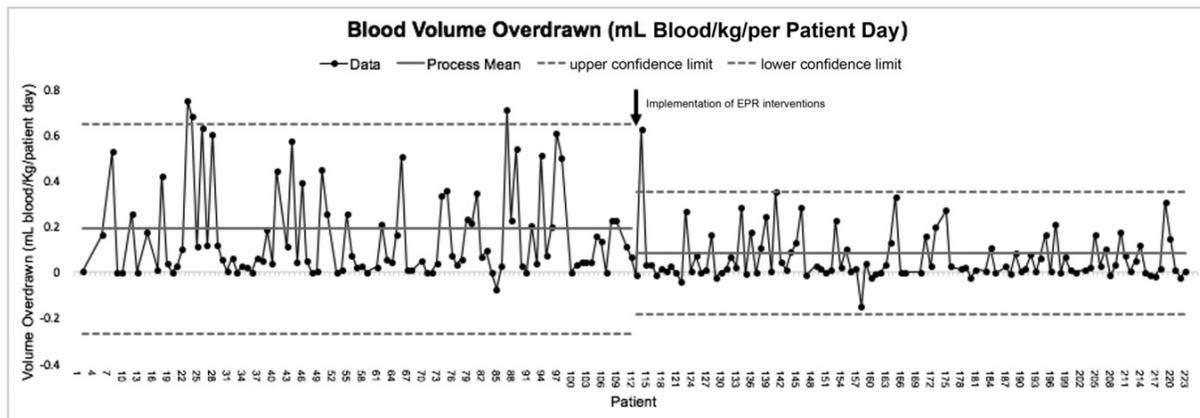
per PICU day) and incidence of RBC transfusion. Blood volume overdrawn was defined as total blood volume removed – minimal volume required by SLCH laboratory devices for the test(s). Volume overdrawn included waste that was not returned to the patient and excess blood not needed for testing.¹⁴ Transfusions administered before enrollment or after the PICU stay were not included.

To evaluate nursing knowledge of and attitudes about PBM, we conducted voluntary nurse surveys and focus groups. All nurses who worked primarily in the PICU were eligible to participate. An anonymous electronic survey was administered to assess understanding of EPR concepts and identify barriers to and facilitators of implementing change in phlebotomy practices (Supplemental Information). Four focus groups expanded on survey data.

We analyzed data from surveys and focus groups within the CFIR framework. Two reviewers (S.S. and K.S.) independently categorized qualitative data into CFIR constructs (Supplemental Information); coding discrepancies were resolved upon further deliberation. A statement such as “there needs to be a better focus on blood conservation” was coded under “relative priority” within the inner setting domain.

Analysis

We calculated sample size estimates separately by using the 2 outcome variables, blood volume overdrawn and transfusion incidence, which required the following: a minimal effect size of 20% lower level of these measures relative to the preintervention period, 2-tailed tests, a conservative Student’s *t* test approximation with small degrees of freedom (10), and 80% power ($\alpha = .05$). The sample size required for both outcomes was 30 and 86, respectively. Our sample size of 111 in the postintervention group



mL, milliliter; Kg, kilogram; EPR, Excessive Phlebotomy Reduction; UCL, upper confidence limit; LCL, lower confidence limit

FIGURE 2

X (individual) moving range chart depicting total blood volume overdrawn (mL blood/kg per patient day) in successive patients. The arrow indicates the transition to the postintervention phase of the study. Notably, mean volume overdrawn is lower with less variation in the postintervention period.

TABLE 2 Laboratory Draw and Transfusion Outcomes

	Preintervention (n = 112)	Postintervention (n = 111)	P
Total blood volume drawn, mL	10.5 (2 to 55.4)	7.25 (1.8 to 25.5)	.32
Total blood volume drawn, mL/kg per PICU d	0.22 (0.06 to 0.55)	0.12 (0.04 to 0.34)	.05
No. blood draws per patient	5 (2 to 14.5)	5 (2 to 18)	.47
No. blood draws per patient per d	1.55 (0.72 to 2.85)	1.5 (1 to 3)	.99
No. laboratory tests per patient	10 (2.5 to 35)	9 (3 to 35)	.79
No. laboratory tests per patient per d	3 (1 to 7.58)	2.76 (1.33 to 5.75)	.61
Overdrawn samples, n (%)	1072 (69.5)	1043 (52.6)	<.001
Volume overdrawn per blood draw, mL	1 (0.5 to 2.0)	0.1 (0 to 0.9)	<.001
Volume overdrawn per patient, mL	5.5 (1 to 23)	2.1 (0 to 7.9)	<.001
Volume overdrawn per patient wt per d, mL/kg per d	0.06 (0.02 to 0.23)	0.02 (0 to 0.1)	<.001
Transfused patients, n (%)	36 (32.1)	23 (20.7)	.04
Pretransfusion Hb, g/dL	7 (6.2 to 7.8)	6.9 (6.0 to 7.8)	.67
RBC volume, mL	306 (114 to 350)	264 (180 to 308)	.45
Transfer Hb, g/dL	10 (8.7 to 11.3)	10.1 (8.8 to 11.5)	.60
Hb difference, admission Hb – transfer Hb	1 (–0.4 to 2.1)	0.95 (–0.6 to 2.1)	.85

Median (IQR) or n (%).

exceeded the required size for both models.

Descriptive analyses included determination of median values and interquartile ranges (IQRs), and comparisons were made using Mann–Whitney *U* or Fisher’s exact tests (Stata 12.1, StataCorp LP; College Station, TX). Statistical process control charts evaluated the impact of the EPR intervention on blood volume overdrawn over time. Standard rules to detect special cause variation were used to determine center-line shift after establishing a baseline in the preintervention period.²³ For regression models, analysis was performed in the R

statistical environment (version 3.2.1).²⁴ Missing data (1.67% of variables used in the regression models) were addressed with the multiple imputation by chained equations package.

To understand the factors that affect the total blood volume overdrawn (milliliter/kilogram per PICU day), we fit a multivariate linear regression model with explanatory variables: a dichotomous variable indicating a postintervention versus a preintervention case, admission hemoglobin (Hb) and admission hematocrit (Hct), PRISM III score, number of study days, number of blood draws, total blood volume

removed (mL/kg), and an interaction term that included pre- versus postintervention status and total blood volume removed. Hb was indexed to Hct given that altered RBC volume homeostasis is observed during critical illness,^{25–28} and to adjust for performance differences we observed for Hb and Hct in our models. Fit was assessed with individual Wald statistics as well as the R-squared measure and the F-statistic; there was no evidence of heteroscedasticity. For RBC transfusion, we fit a multivariate logit model with explanatory variables: a dichotomous variable indicating a postintervention versus preintervention case, age of the patient (in months), weight (in kilograms),

TABLE 3 Factors Associated With Total Blood Volume Overdrawn (mL Blood/kg per Patient Day)

	Estimate	SE	P
Intercept	18.6	7.91	.01
Admission Hb and admission Hct	-50.96	23.13	.02
PRISM III	-0.18	0.09	.02
Study d	-0.10	0.07	.06
No. blood draws	0.36	0.02	<.001
Total blood volume removed, mL/kg	-0.15	0.08	.03
Postintervention group	-3.20	0.84	<.001
Interaction term: postintervention group × total blood volume removed, mL/kg	-0.63	0.10	<.001

TABLE 4 Factors Associated With RBC Transfusion

	Estimate	Odds Ratio	95% Confidence Interval	P
Intercept	3.3	27.01	1.39–526.79	.02
Age, mo	0.02	1.02	1.00–1.03	.01
Wt, kg	-0.04	0.96	0.92–1.00	.04
Admission Hb	-0.62	0.54	0.41–0.70	<.001
PRISM III	0.08	1.08	0.97–1.21	.08
Respiratory diagnosis	-0.51	0.60	0.14–2.63	.25
Anemia risk, based on diagnosis	0.9	2.46	0.74–8.21	.07
Study d	-0.08	0.93	0.83–1.03	.08
No. blood draws	0.07	1.08	1.01–1.15	.01
Study total blood volume removed, mL/kg, square root	0.97	2.65	0.99–7.12	.03
Postintervention group	-0.84	0.43	0.15–1.20	.05

Incidence of Transfusion in Pre- and Postintervention Periods

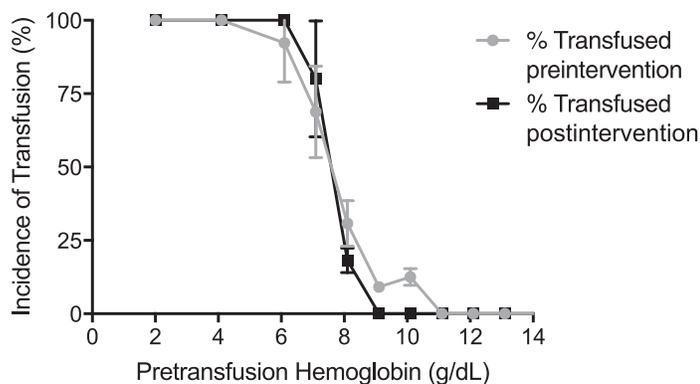


FIGURE 3

Incidence of transfusion in the pre- and postintervention periods based on patient Hb. Overlapping confidence intervals indicate there was not a significant difference in the pre- and postintervention transfusion periods.

Hb at admission, PRISM III score, respiratory diagnosis, anemia risk based on diagnosis (hematologic and/or oncologic, surgical, and trauma), number of study days, number of blood draws, and square root of study total blood volume removed (milliliter/kilogram). The square root of the total blood volume removed was taken to achieve a better fit with the outcome.

Respiratory diagnosis was included because a larger number of patients with respiratory diagnoses were noted in the postintervention group. Fit was assessed with individual Wald statistics, summed deviances, and tests for overdispersion.

Ethics

The study was approved by the Washington University in St Louis

Institutional Review Board; no conflicts of interest were identified.

RESULTS

Preimplementation Focus Group and Survey Data

PICU nurse engagement was robust: 82% participated in focus groups, and 98% completed surveys. Data revealed that nurses felt hospital policies lacked clear guidance about blood draw volumes (CFIR outer setting), and most nurses relied on experience and peer practices to guide the amount of blood drawn (CFIR inner setting) (Supplemental Information). As a concept, EPR was felt to have potential benefits, but challenges related to changing personal practice and lack of prioritization of PBM were seen as barriers (CFIR inner setting).

Clinical Data

Patients from both points in time were similar except for diagnostic category (Table 1), with a larger proportion of preintervention patients admitted with diagnoses that placed them at risk for anemia (hematologic and/or oncologic, trauma, surgical) and a greater proportion with respiratory diagnoses postintervention. PRISM III scores, total study days, admission Hb and Hct, and number of deaths were similar.

Blood Volume Drawn and Transfusion

The EPR intervention reduced the total blood volume drawn by 45.5%, and the number of blood draws and laboratory tests were similar (Table 2). The percentage of overdrawn samples was significantly lower, and the volume overdrawn per blood draw was reduced by 90%. The median volume overdrawn was 62% lower in the postintervention period ($P < .001$). Statistical process control demonstrated lower mean

Number of Patients Transfused by Volume Overdrawn (mL)

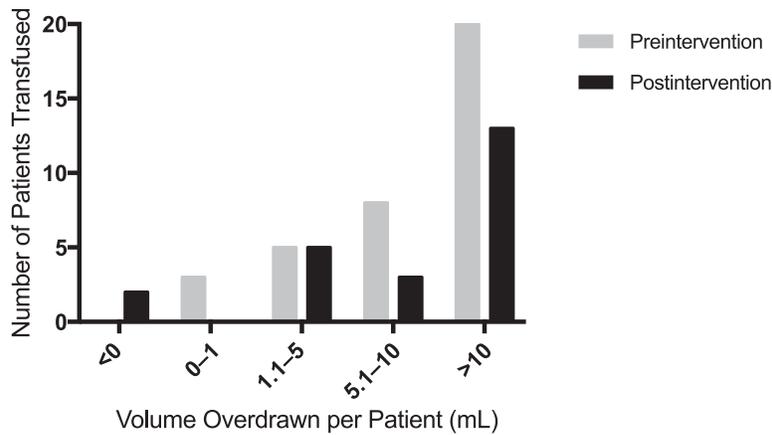


FIGURE 4

Number of patients transfused in pre- and postintervention periods by volume overdrawn per patient (in milliliters). Postintervention reduction in transfusion incidence was most notable with higher overdraw volumes. Implementation was imperfect; 16 transfused patients in the postintervention period had >5 mL overdrawn.

overdraw volumes and decrease in variation of overdraw volume in the postintervention period (Fig 2). Notably, these changes are sustained over time, and less special cause variation is noted in the postintervention period.

Significantly fewer patients received RBC transfusions in the postintervention period ($P = .04$) (Table 2). Transfusion likelihood as a function of pretransfusion Hb did not differ (Fig 3), and there was no difference between time periods with respect to Hb at PICU transfer. The main impact in transfusion reduction during the postimplementation period occurred by reducing the number of patients with higher overdraw volumes (Fig 4).

Regression Analyses

Our 2 models reliably fit explanatory variables associated with volume overdrawn (milliliter/kilogram per PICU day) (Table 3) and RBC transfusion (Table 4). Most importantly, for volume overdrawn, the multivariate linear model revealed a negative and reliable coefficient that indicated the second period had lower total overdraw

volumes ($P < .001$). A higher overdraw volume was more likely in patients with a lower admission Hb-Hct ratio ($P = .02$), a larger number of blood draws ($P < .001$), lower PRISM III scores ($P = .02$), and lower total blood volume removed ($P = .03$). The interaction term revealed that the inverse relationship between total blood volume removed and volume overdrawn was more pronounced in the postintervention period compared with the preintervention period.

Factors Associated With RBC Transfusion

For RBC transfusion, the multivariate logistic model provides a negative and reliable coefficient for postintervention, which indicates that transfusion incidence fell during the second period ($P = .05$). Patients with a lower admission Hb ($P < .001$), larger number of blood draws ($P = .01$), or higher total blood volume removed ($P = .03$) were more likely to receive RBC transfusion. Figure 5 shows the effects of 4 explanatory variables (PRISM III, blood draws, total blood volume removed, and anemia risk) upon transfusion likelihood by

study period. In each case, there is a greater risk of transfusion in the preintervention period. The predicted transfusion probability from this model falls from 0.23 to 0.11 from the pre- to the postintervention period (twofold), with all other explanatory variables set at their mean.

Postimplementation Survey and Focus Group Data

Eighty-nine percent of nurses completed a postintervention survey, and 95% attended a focus group. Given the limited nurse availability and a small degree of staff turnover, not all nurses attended both groups or completed both surveys. Nurses felt the EPR interventions resulted in less blood waste (bedside reference guide, 90.4%; microtubes, 100%; venous safe draw, 89%; minimum blood culture volumes, 97%) and fewer line breaks (CFIR intervention characteristics) (Supplemental Information). Ninety-three percent reported satisfaction with the EPR interventions, most felt they were straightforward and easy to use, and all reported willingness to use them long-term (CFIR intervention characteristics). Nurses reported paying more attention to the amount of blood drawn and wasted postimplementation. Participants did note the venous closed-loop systems did not always work well, particularly with small lines, and only 61.6% of respondents felt satisfied with the education related to the venous closed-loop system (CFIR intervention characteristics). Although 97% “agreed/strongly agreed” that EPR was a priority postintervention (CFIR inner setting), participants commented that physicians were not educated about EPR (CFIR intervention characteristics). As a result, issues related to frequent ordering and a lack of clustering of laboratory studies still existed.

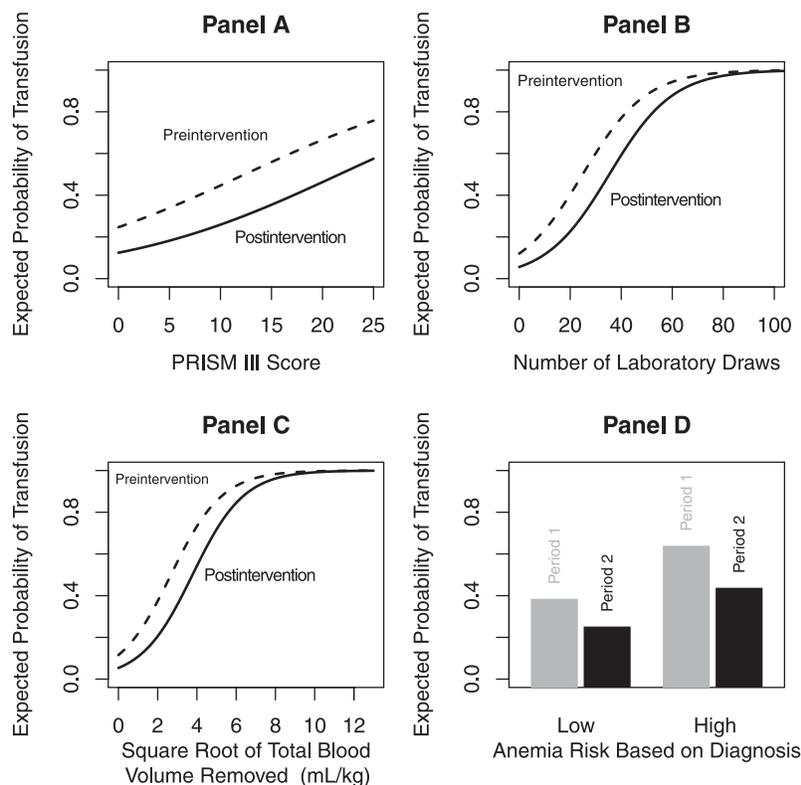


FIGURE 5 Predicted transfusion by explanatory variables. Models derived from regression compare transfusion probability in pre- and postintervention phases relative to the following: A, PRISM III score; B, number of blood draws; C, (square root) total blood volume removed; and D, anemia risk based on diagnosis. Transfusion probability is lower postintervention for each variable.

DISCUSSION

Our findings indicate that the 4 EPR strategies were effective in reducing blood overdraw volume and decreased RBC transfusion incidence. Although the implementation methods cannot be directly linked to the success of these EPR strategies, they likely enhanced the incorporation into clinical care processes. This is impactful because EPR may reduce the need to expose critically ill children to blood products, and it could potentially improve clinical outcomes. Literature highlighting transfusion risk⁵⁻⁷ emphasizes the need to limit blood product administration when possible. EPR practices that limit blood volume drawn may prevent or curtail anemia and transfusion need in many ICU patients.

The 4 EPR strategies tested in this study, in combination, resulted in less volume overdrawn. Lower overdraw volumes were noted in patients with a larger total blood volume removed, which suggests that providers may become more careful about overdrawing as more blood is required for studies. We did observe a significant, direct association between overdraw volume and number of blood draws.

Patients with a lower admission Hb, higher total blood volume removed, or a larger number of blood draws were subject to increased transfusion risk, which suggests a link between anemia, blood draws, and transfusion frequency. The relationship between admission Hb and number of blood draws (Fig 5) suggests that EPR efforts should focus on anemic

patients who are subject to a large amount of testing.

Although a variety of evidence-based EPR techniques have been proposed,^{12-14,16} their impact in a PICU population had not yet been evaluated. By using the CFIR framework, we found that most implementation barriers appeared to be localized to hospital policy (CFIR outer setting) and structural and cultural characteristics of the PICU (CFIR inner setting). Change facilitators included intervention complexity and stakeholder perceptions (CFIR intervention characteristics) as well as tension for change (CFIR inner setting). Identifying barriers and facilitators enabled a targeted approach for implementation plan development. Nursing staff found the EPR strategies straightforward to use and easy to incorporate into their established workflow despite concerns about changing practice. Other EPR strategies or combinations of strategies may have a similar clinical impact. Future studies may focus on evaluating a single EPR strategy, a combination of strategies, or different PBM approaches. Efforts targeted at clustering laboratory studies and reducing unnecessary laboratory orders may further reduce phlebotomy-associated anemia. Finally, sustaining change is essential to perpetuating the benefit of clinical interventions. Audit and feedback likely improved EPR bundle adherence and contributed to lower overdraw volumes; such techniques could be valuable in sustaining change over time. Further study of methods to facilitate education of new and established providers and other methods to maintain consistent use of the EPR strategies is essential. Strengths of this approach include the use of the CFIR model to identify barriers to and facilitators of developing an implementation plan. Focus group data guided EPR strategy selection, which may have

enhanced nurses' investment in the intervention itself. Whereas clinical data demonstrate the impact upon blood volume overdrawn and RBC transfusion, qualitative analyses provide a framework to better understand the challenges and impacts of implementing new care processes. Postintervention qualitative data supported the positive impact of EPR, but we also identified issues with the venous closed-loop system and a lack of physician education about PBM as factors limiting the intervention's impact. These insights would not have been evident with quantitative methods alone.

Limitations of this study include the single-center pre- and postintervention design that does not account for secular trends that could have impacted blood draw and transfusion practices. Despite this, there were no clinical practice or staffing changes that were felt to directly or indirectly impact EPR. Pre- and postintervention populations were similar in terms

of age, severity of illness, and length of PICU stay, with differences found only in primary diagnosis. Patients at both points in time had similar numbers of blood draws, laboratory tests, and incidence of transfusion based on their Hb level (Fig 3), which provides additional evidence for the impact of the EPR strategies upon transfusion. This preliminary study provides evidence to support future studies of EPR methods with more rigorous designs, such as cluster-randomized trials. Larger trials are needed to test the potential impact of these EPR strategies in other PICU settings to confirm our findings.

CONCLUSIONS

An intervention composed of 4 EPR strategies significantly decreased the blood volume overdrawn in PICU patients and reduced the frequency of RBC transfusion. The use of implementation science strategies were integral in developing this EPR intervention and helped assess provider acceptance and adoption of strategies. Implementation science

methods can identify strategies for integrating new clinical practices and assessing their impacts.

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ABBREVIATIONS

CFIR: Consolidated Framework for Implementation Research
EPR: excessive phlebotomy reduction
Hb: hemoglobin
Hct: hematocrit
IQR: interquartile range
PBM: patient blood management
PRISM III: Pediatric Risk of Mortality III
RBC: red blood cell
SLCH: St Louis Children's Hospital

contributed to the final qualitative analysis, and reviewed the manuscript; Dr Valentine provided support with overall study design and reviewed the manuscript; Dr York was fundamental in the initiation, planning, and execution of this work, and she led the research team through the data collection periods, organized both quantitative and qualitative aspects of the study, and reviewed the manuscript; Dr Proctor was a key participant in the overall study design and chief consultant on all implementation aspects of this work, and he reviewed the manuscript; Dr Spinella provided substantial contributions to conception and design as well as data analysis, funding endeavors, and manuscript preparation, and he also reviewed the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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REFERENCES

- Armano R, Gauvin F, Ducruet T, Lacroix J. Determinants of red blood cell transfusions in a pediatric critical care unit: a prospective, descriptive epidemiological study. *Crit Care Med*. 2005;33(11):2637–2644
- Bateman ST, Lacroix J, Boven K, et al; Pediatric Acute Lung Injury and Sepsis Investigators Network. Anemia, blood loss, and blood transfusions in North American children in the intensive care unit. *Am J Respir Crit Care Med*. 2008;178(1):26–33
- Doctor A, Spinella P. Effect of processing and storage on red blood cell function in vivo. *Semin Perinatol*. 2012;36(4):248–259
- Linderkamp O, Versmold HT, Riegel KP, Betke K. Estimation and prediction of blood volume in infants and children. *Eur J Pediatr*. 1977;125(4):227–234
- Napolitano LM, Corwin HL. Efficacy of red blood cell transfusion in the critically ill. *Crit Care Clin*. 2004;20(2):255–268
- Spinella PC, Sparrow RL, Hess JR, Norris PJ. Properties of stored red blood cells: understanding immune and vascular reactivity. *Transfusion*. 2011;51(4):894–900
- Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Crit Care Med*. 2008;36(9):2667–2674
- Typpo KV, Petersen NJ, Hallman DM, Markovitz BP, Mariscalco MM. Day 1 multiple organ dysfunction syndrome is associated with poor functional outcome and mortality in the pediatric intensive care unit. *Pediatr Crit Care Med*. 2009;10(5):562–570
- Said A, Rogers S, Doctor A. Red cell physiology and signaling relevant to the critical care setting. *Curr Opin Pediatr*. 2015;27(3):267–276
- Spinella PC, Doctor A. Role of transfused red blood cells for shock and coagulopathy within remote damage control resuscitation. *Shock*. 2014;41(suppl 1):30–34
- Shander A, Hofmann A, Gombotz H, Theusinger OM, Spahn DR. Estimating the cost of blood: past, present, and future directions. *Best Pract Res Clin Anaesthesiol*. 2007;21(2):271–289
- Fowler RA, Berenson M. Blood conservation in the intensive care unit. *Crit Care Med*. 2003;31(suppl 12):S715–S720
- Mahdy S, Khan EI, Attia M, O'Brien BP, Seigne P. Evaluation of a blood conservation strategy in the intensive care unit: a prospective, randomised study. *Middle East J Anaesthesiol*. 2009;20(2):219–223
- Valentine SL, Bateman ST. Identifying factors to minimize phlebotomy-induced blood loss in the pediatric intensive care unit. *Pediatr Crit Care Med*. 2012;13(1):22–27
- United States Department of Health and Human Services. Improving public health practice through translational research. Available at: <http://grants.nih.gov/grants/guide/rfa-files/rfa-cd-07-005.html>. Accessed February 20, 2017
- Hassan NE, Winters J, Winterhalter K, Reischman D, El-Borai Y. Effects of blood conservation on the incidence of anemia and transfusions in pediatric parapneumonic effusion: a hospitalist perspective. *J Hosp Med*. 2010;5(7):410–413
- Pronovost PM, Weast B, Rosenstein B, et al. Implementing and validating a comprehensive unit-based safety program. *J Patient Saf*. 2005;1(1):33–40
- Palinkas LA, Aarons GA, Horwitz S, Chamberlain P, Hurlburt M, Landsverk J. Mixed method designs in implementation research. *Adm Policy Ment Health*. 2011;38(1):44–53
- Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4(1):50
- Atkins D. Connecting research and patient care: lessons from the VA's Quality Enhancement Research Initiative. *J Gen Intern Med*. 2010;25(suppl 1):1–2
- Powell BJ, Proctor EK, Glass JE. A systematic review of strategies for implementing empirically supported mental health interventions. *Res Soc Work Pract*. 2014;24(2):192–212
- Pollack MM, Ruttimann UE, Getson PR. Pediatric risk of mortality (PRISM) score. *Crit Care Med*. 1988;16(11):1110–1116
- Benneyan JC, Lloyd RC, Plsek PE. Statistical process control as a tool for research and healthcare improvement. *Qual Saf Health Care*. 2003;12(6):458–464
- R Development Core Team. *A Language and Environment for Statistical Computing* [computer program]. Vienna, Austria: Foundation for Statistical Computing; 2013
- Glogowska E, Gallagher PG. Disorders of erythrocyte volume homeostasis. *Int J Lab Hematol*. 2015;37(suppl 1):85–91
- Hunziker S, Celi LA, Lee J, Howell MD. Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients. *Crit Care*. 2012;16(3):R89
- Loveday S, Sinclair L, Badrick T. Does the addition of RDW improve current ICU scoring systems? *Clin Biochem*. 2015;48(9):569–574
- Said AS, Spinella PC, Hartman ME, et al. RBC distribution width: biomarker for red cell dysfunction and critical illness outcome? *Pediatr Crit Care Med*. 2017;18(2):134–142

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