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PATIENT BLOOD MANAGEMENT

TRANSFUSION

Results from a type two hybrid-effectiveness study to implement a preoperative anemia and iron deficiency screening, evaluation, and management pathway

Alana Delaforce[1,2,3] | Shannon Farmer[4,5] | Jed Duff[1,6] | Judy Munday[6,7] | Kristin Miller[2] | Lynne Glover[2] | Chris Corney[2] | Gareth Ansell[2,8] | Naadir Gutta[2,8] | Haitham Tuffaha[9] | Janet Hardy[2,3] | Cameron Hurst[10]

[1]School of Nursing and Midwifery, The University of Newcastle, Callaghan, New South Wales, Australia

[2]Mater Health Services, South Brisbane, Queensland, Australia

[3]Mater Research Institute-UQ, South Brisbane, Queensland, Australia

[4]Department of Haematology, Royal Perth Hospital, Perth, Western Australia, Australia

[5]Discipline of Surgery, Medical School, The University of Western Australia, Perth, Western Australia, Australia

[6]Centre for Healthcare Transformation/ School of Nursing, Queensland University of Technology, Kelvin Grove, Queensland, Australia

[7]Faculty of Health and Nursing Science, The University of Agder, Kristiansand, Norway

[8]School of Clinical Medicine—Mater Clinical Unit, The University of Queensland, St Lucia, Queensland, Australia

[9]Centre for the Business and Economics of Health, The University of Queensland, St Lucia, Queensland, Australia

[10]QIMR Berghoffer Medical Research Institute, Brisbane, Queensland, Australia

Correspondence
Alana Delaforce, School of Nursing and Midwifery, College of Health, Medicine and Wellbeing, University of Newcastle,

Abstract

Background: Implementation of pathways to screen surgical patients for preoperative anemia and iron deficiency remains limited. This study sought to measure the impact of a theoretically informed, bespoke change package on improving the uptake of a Preoperative Anemia and Iron Deficiency Screening, Evaluation, and Management Pathway.

Study Design and Methods: Pre-post interventional study using a type two hybrid-effectiveness design evaluated implementation. Four hundred (400) patient medical record reviews provided the dataset (200 pre- and 200-post implementation). The primary outcome measure was compliance with the pathway. Secondary outcome measures (clinical outcomes) were anemia on day of surgery, exposure to a red blood cell (RBC) transfusion, and hospital length of stay. Validated surveys facilitated data collection of implementation measures. Propensity score-adjusted analyses determined the effect of the intervention on clinical outcomes, and a cost analysis determined the economic impact.

Results: For the primary outcome, compliance improved significantly post-implementation (Odds Ratio 10.6 [95% CI 4.4–25.5] $p < .000$). In secondary outcomes, adjusted analyses point estimates showed clinical outcomes were slightly improved for anemia on day of surgery (Odds Ratio 0.792 [95% CI 0.5–1.3] $p = .32$), RBC transfusion (Odds Ratio 0.86 [95% CI 0.41–1.78] $p = .69$) and hospital length of stay (Hazard Ratio 0.96 [95% CI 0.77–1.18] $p = .67$), although these were not statistically significant. Cost savings of $13,340 per patient were realized. Implementation outcomes were favorable for acceptability, appropriateness, and feasibility.

Conclusion: The change package significantly improved compliance. The absence of a statistically significant change in clinical outcomes may be

University Drive, Callaghan, NSW 2308, Australia.
Email: alana.delaforce@uon.edu.au

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because the study was powered to detect an improvement in compliance only. Further prospective studies with larger samples are needed. Cost savings of $13,340 per patient were achieved and the change package was viewed favorably.

KEYWORDS
blood management, RBC transfusion, transfusion practices (surgical)

1 | INTRODUCTION

On average, about 40% of patients presenting for major surgery are anemic.[1] Preoperative anemia is associated with poorer patient outcomes and increases by about 5-fold the risk of receiving a Red Blood Cell (RBC) transfusion.[1] Substantial blood loss at the time of surgery also results in anemia or exacerbates pre-existing anemia, further increasing the risk of RBC transfusion.[2] Blood transfusions are linked to poor postoperative outcomes, including an increased risk of infection, venous thromboembolism, and longer length of hospital stay.[3–7] Transfusions should only be administered when the benefits outweigh the risks. In the context of perioperative patients, this scenario is usually due to critical bleeding where surgical blood loss has been substantial enough to reduce a patient's hemoglobin level to 7 g/dl or less, or when the loss is such that cardiac and respiratory decompensation symptoms are present—for example, tachycardia, hypotension, dizziness, fainting, and shortness of breath, not responding to volume replacement or other therapies.[4,8] In addition, substantial surgical bleeding results in a loss of recyclable iron, and may deplete iron stores postoperatively and lead to sustained anemia long after discharge.[9,10] Optimization of patients before surgery can help reduce the impact of surgical blood loss and exposure to unnecessary transfusion.[11–13]

Optimization is achieved by following Preoperative Anemia and Iron Deficiency Screening, Evaluation, and Management Pathways (PAIDSEM-P).[2,11–13] PAIDSEM-P outlines blood tests that should be performed to check if a patient has anemia, iron deficiency, or suboptimal iron stores.[10] PAIDSEM-P tests should be performed on patients who are scheduled to undergo major elective surgery expected to result in blood loss of 500 ml or more.[14] Based on the blood test results, PAIDSEM-P outlines recommended assessments and treatments to address results outside of recommended reference ranges.[14] For example, when a patient has been diagnosed as having iron deficiency anemia and is scheduled for urgent surgery, administration of intravenous iron is recommended to correct anemia and replenish iron stores quickly.[14–17] If patients are not anemic but have a ferritin <100 mcg/L (suboptimal iron stores), blood loss resulting in a postoperative hemoglobin drop of >3 g/dl may deplete iron stores following discharge. In this setting, guidelines suggest considering preoperative iron therapy.[10]

Despite the World Health Organization endorsing the uptake of PAIDSEM-P, there remains high variability in its implementation among health care facilities.[11,18,19] A 2017 survey indicated that only 38% of international facilities had a protocol to address preoperative anemia.[18] Within Australia, a 2020 survey showed that only 56% of hospitals had a preoperative anemia screening pathway in place.[18,20] There are limited data reporting the reasons for low uptake.[21] However, the recent Policy Brief released by the World Health Organization suggests the primary reason is low awareness of PBM among both health care physicians and patients.[11] A 2020 systematic review, which investigated the barriers to patient blood management initiatives more broadly, mirrors this prevailing view and found that the key barriers among the 14 studies included were: access to knowledge and information ($n = 7$), knowledge and beliefs about the intervention ($n = 7$), and tension for change ($n = 6$).[21] An Australian qualitative study also found similar barriers locally (access to knowledge and information, knowledge and beliefs about the intervention, patient needs and resources, available resources, and networks and communication), suggesting that some of the reasons for low uptake are shared among facilities, despite the varied contexts.[22]

Barriers to PAIDSEM-P can be addressed using theoretically informed change packages. Change packages should comprise tailored knowledge tools and interventions supported by appropriate implementation strategies.[23] Knowledge tools include highly synthesized research such as clinical decision aids or pathways (e.g., the National Blood Authority Patient Blood Management Guidelines).[24] Interventions are what assist in delivering the knowledge tool, for example, having a preoperative anemia coordinator.[24–26] Implementation strategies support the implementation of both the knowledge tool and intervention, for example, educating clinicians on how to follow a pathway and why it is important.[27]

Implementation plans should include bespoke change packages that are conceptualized and delivered with the support of implementation theories, models, and frameworks.[28] In this study the Consolidated Framework for Implementation Research (CFIR) was used to identify barriers, which were then classified according to actor (stakeholder) categories and mapped to the Expert Recommendations for Implementing Change (ERIC) framework, explained in detail elsewhere.[23,27,29,30] However, testing of these tools remains limited in the context of patient blood management and, more specifically, PAIDSEM-P.[21,23] This study aimed to test if a theoretically informed change package that leveraged implementation science theory could improve the uptake of PAIDSEM-P.[23] It measures the impact of the change package on provider, facility, patient, and outcomes, as well as implementation outcomes of acceptability, appropriateness, and feasibility.

2 | MATERIALS AND METHODS

2.1 | Aim

To test whether a theoretically informed change package would improve the uptake of a preoperative anemia and iron deficiency pathway.

2.2 | Design

The study used a type two hybrid-effectiveness implementation design.[23] Type two hybrid-effectiveness designs evaluate both the effect of an intervention and the implementation strategies which support its delivery.[31] They are appropriate when utilizing interventions that have been proven to be effective but require further investigation regarding the context and implementation strategies that best support delivery.[31] For this reason, compliance was chosen as the primary outcome, with clinical and cost measures as secondary outcomes. A pre- and post-implementation retrospective health record review determined pathway compliance and clinical effectiveness. The pre-period consisted of health records within a six-month time frame before any attempt at improvement (Feb–Aug 2020), and the post period occurred after implementation (Feb–Aug 2021). A cost analysis used hospital-provided patient-level data including the total cost of care provided. A validated survey distributed to healthcare professionals measured implementation outcomes of acceptability, appropriateness, and feasibility.[32]

Setting and population: The PAIDSEM-P was implemented in a large, metropolitan, tertiary referral hospital which provides services for public and privately insured patients across a wide range of specialties. The target population for the screening tool was public patients who underwent major orthopedic, general/colorectal, urology, and gynecological/oncological surgery. The target population of the intervention was health professionals involved in delivering PAIDSEM-P. A Preoperative Anemia Care Coordinator (PACC) delivered the knowledge tool, overseen by an implementation facilitator.

Ethics: Ethical approval was granted by the Mater Misericordiae Ltd Human Research Ethics Committee (HREC) and administrative approval from the University of Newcastle HREC (AM/MML/47826). The screening tests outlined in the PAIDSEM-P occur in the scope of hospital policy and procedure. Any treatment that arose when following the PAIDSEM-P was provided in the setting of fully informed consent.[28,33] A waiver of consent was granted to collect data obtained from retrospective medical chart reviews that were subsequently de-identified. All survey participants were provided with information and consent forms before entering the survey.

2.3 | Change package

2.3.1 | The knowledge tool and intervention

The knowledge tool is a Preoperative Anemia and Iron Deficiency Screening, Evaluation, and Management Pathway (PAIDSEM-P). The intervention is the Preoperative Anemia Care Coordinator (PACC), previously described in our published protocol and displayed in Figure 1.[23]

3 | IMPLEMENTATION STRATEGIES

Theoretically informed implementation strategies supporting the change package delivery are outlined in Table 1.[23] Implementation strategy selection was informed by previously collected data that used semi-structured interviews of relevant stakeholders (including health professionals ($n = 13$) and patients ($n = 2$)).[22] The interviews aimed to understand the barriers to implementation of the PAIDSEM-P. The interview data were coded using the Consolidated Framework for Implementation Research (CFIR),[30] which includes theoretical constructs that

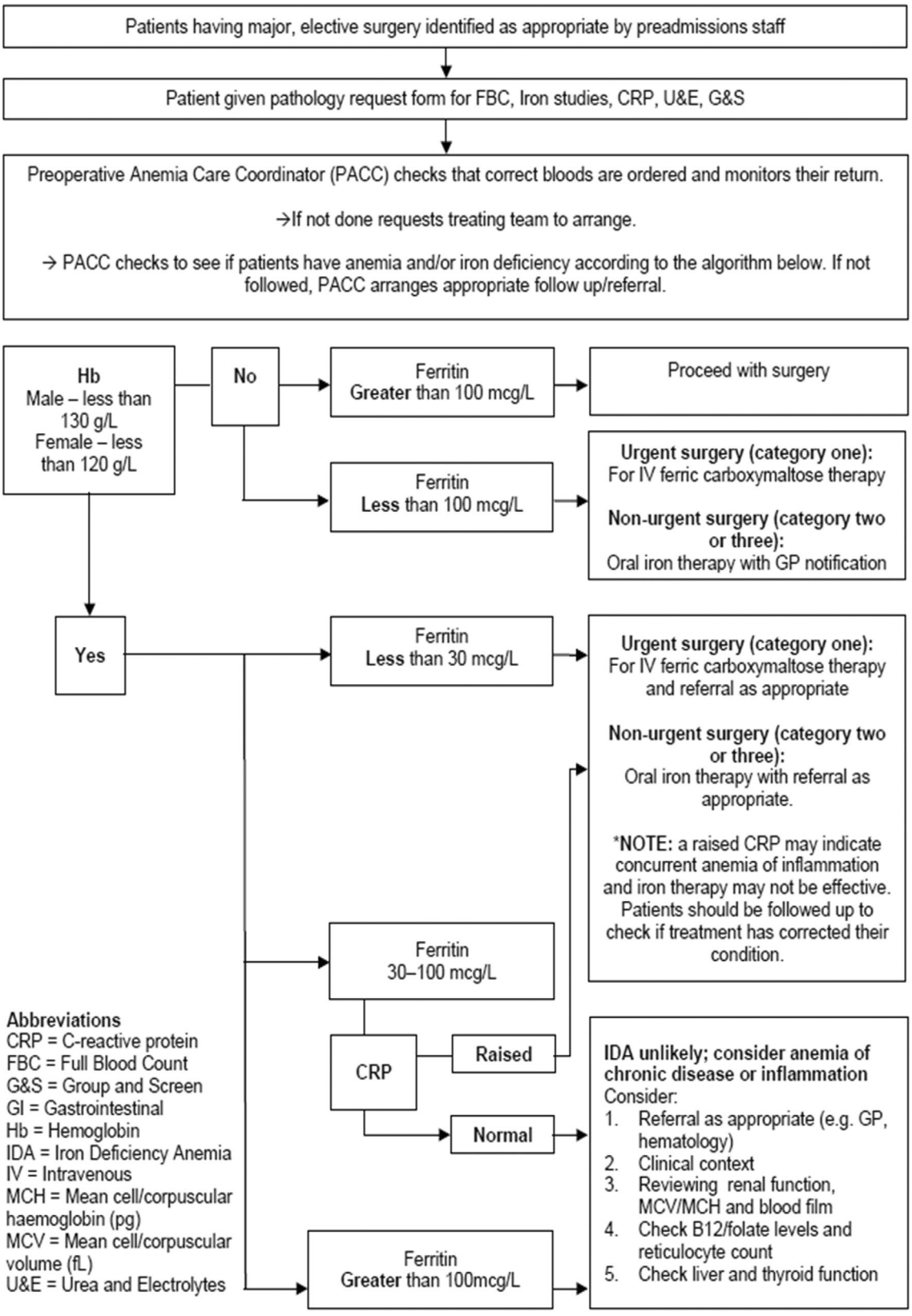

FIGURE 1 PAIDSEM-P change package and flow

influence implementation, for example, knowledge and beliefs about an intervention—if a physician does not know of the intervention, it cannot be expected that it will be used in practice. Barriers identified during coding were mapped to the Expert Recommendations for Implementing Change (ERIC)[27] framework to select appropriate

TABLE 1 Barriers and strategies

Barriers	Implementation strategies	How were these delivered?
Access to knowledge and information	Conduct educational meetings	The implementation facilitator attended specialty group meetings and undertook educational consultations with members of the treating team.
		Education and training were provided to the preadmissions nursing team to ensure adequate preparation to inform patients of the reason for screening and optimization.
	Develop educational materials	A range of key stakeholders were consulted during the development of educational resources.
	***Distribute educational materials**	**The patient information sheet was not delivered as initially anticipated.**
Patient needs and resources	Obtain and use patients'/consumers' family feedback	Patients were consulted during the development of educational resources.
	Involve patients/consumers/family members	Patients were provided with education during their preadmission appointment by nurses as well as by treating consultants where treatment was required.
	Conduct a local needs assessment	Earlier phases of this research project report execution of this strategy.[22]
Knowledge and beliefs about the intervention	Conduct educational meetings	The implementation facilitator ensured all the perioperative medicine team and preoperative admissions team were educated on the intervention during a launch week and, as needed, where compliance issues arose.
Available resources	Access new funding	Funding was obtained for a preoperative anemia care coordinator to ensure the pathway was being followed.
Networks and communications	Promote network weaving	The implementation facilitator ensured ongoing contact and encouraged socialization between groups at appropriate meetings.
	Organize clinician implementation team meetings	A perioperative patient blood management working party was established and met regularly during the pathway's formative stages. They now meet ad-hoc when decisions or consultation is required.

implementation strategies. Some strategies were not delivered as originally intended and are highlighted in bold with an asterisk in Table 1.

3.1 | Outcomes

Outcomes of this study are reported at the provider, patient, and health service levels.

Primary outcome (provider):

- Compliance with the National Blood Authority Patient Blood Management Guidelines, measured by the proportion of patients that receive recommended care, including the performance of appropriate tests and provision of appropriate treatment and/or referral.[14]

Secondary outcomes (patient):

- The proportion who are anemic at the closest point prior to surgery defined by the World Health Organization hemoglobin levels (males <130 g/L, females <120 g/L),[34] and the proportion who received a red blood cell transfusion during the perioperative period.

Secondary outcome (health service):

- Cost analysis estimates the costs of the program to the health system.

Implementation outcome:

- Acceptability, appropriateness, and feasibility of the PAIDSEM-P.[27]

3.2 | Data collection and analysis

3.2.1 | Retrospective health record review

A representative sample of health records based on the need to detect a 20% improvement in compliance with the PAIDSEM-P post-implementation was reviewed. Patients aged 18 years or older having major elective surgery with an anticipated blood loss of >500 ml were included in the health record review. The data collection tool was pilot tested and reviewed by all research team members. Demographic data, relevant pathology test values, treatments, and complications were collected. All

categorical variables are described using counts and percentages. Continuous variables are described using means and standard deviations and, for variables likely to be normally distributed, medians and inter-quartile ranges are provided. Three of the outcomes are binary, so binary logistic regression was used to obtain odds ratios for the intervention effect. We used propensity score adjustment based on inverse probability weighting (IPW) to adjust for the potential confounding effects of age, sex, and procedure. For the time-to-event outcome, length of hospital stay, Kaplan Meier plots, and Cox regression were used for the analysis. As time-to-event outcomes cause major difficulties for propensity score analysis, we used standard multivariable adjustment to get adjusted hazard ratios from our Cox proportional hazard regression models. All analysis was conducted using the R statistical package (v4.0.3, R Core Team, 2021), and the R library PSweight (Zhou et al. 2021) was used for propensity score analysis. A significance level of 0.05 was used throughout all inferential analyses.

3.2.2 | Cost analysis evaluation

A cost analysis was undertaken from the health payer perspective. Cost calculations are made based on the care as delivered rather than the intention to treat. Hospital-generated data that provided the total cost (direct and indirect) of each care episode was provided by the facility case-mix team. The total cost data was used to compare the difference in cost of care pre- and post-implementation. Based on care as delivered, the difference in mean cost per patient care episode was calculated. The additional costs in the post-implementation period (total implementation funding $50,000AUD) were deducted from any savings to calculate the cost difference accurately.

3.2.3 | Survey

An electronic survey using REDCap, based on an existing validated tool and pilot tested for content and face validity with research team members, was used. Health professionals involved in the delivery of PAIDSEM-P were recruited through email by members of the research team and provided with copies of the participant information sheet. Upon entry to the survey, the participant information sheet was displayed, and participants were advised that progressing to the next page confirmed consent. Participants were asked to provide a ranking on a Likert scale to answer questions regarding the appropriateness, acceptability, and feasibility of the intervention as delivered by the pathway coordinator, as well as questions that related to previously identified barriers. Answer options ranged from completely disagree to completely agree. Survey item responses were analyzed using descriptive statistical analysis. Because all the data were categorical, counts and percentages are used for reporting.

4 | RESULTS

4.1 | Demographics of included participants

A total of 400 patients (200 pre-implementation and 200 post-implementation) were included in retrospective medical chart audits. Included patients comprised 257 females and 143 males. The mean age of both males and females was 62 years (±14.15). We included surgeries from a range of specialties including orthopedics, gynecology/oncology, general/colorectal, and urology. The sample reflected the proportion of usual surgeries undertaken annually, for example, the majority of major surgery conducted is in orthopedics (see Table 2). Both samples were homogenous in terms of sex ($p = .84$), age ($p = .7$), and procedure ($p = .17$).

4.2 | Primary outcome (compliance)

Among propensity score-adjusted estimates of the intervention (pre/post) effect, which accounted for the case-mix difference between the two study periods, there was a significant difference in compliance with PAIDSEM-P, with the odds of compliance to the pathway post-intervention being over 10 times higher (Odds Ratio 10.6 [95%CI: 4.406, 25.496] $p < .000$).

4.3 | Secondary outcomes (patient and health service)

Despite a high increase in compliance with the pathway, within our sample there was no statistically significant difference in clinical outcomes (anemia on day of surgery, blood transfusion utilization, and hospital length of stay) post-implementation. However, the point estimates favored improvements in anemia on the day of surgery (Odds Ratio 0.79 [95% CI: 0.50, 1.25] $p = .32$), blood transfusion utilization (Odds Ratio 0.86 [95% CI 0.41, 1.78] $p = .69$), and length of hospital stay (Hazard Ratio 0.81 [95% CI 0.59, 1.10] $p = .16$).

TABLE 2 Patient demographics ($n = 400$)

Patient characteristics	Pre intervention group ($n = 200$)	Post intervention group ($n = 200$)	Total
Female % (n)	63.5% (127)	65% (130)	64% (257)
Male % (n)	36.5% (73)	35% (70)	36% (143)
Age—mean (SD)	62 (13.35)	62 (14.12)	63 (14.15)
Anemia on day of surgery % (n)	26.7% (52)	22.4% (44)	25% (99)
Days in hospital mean (SD)	5.80 (5.49)	5.58 (4.82)	6 (4.76)
Average blood loss (L) mean (SD)	447 (293.6)	524 (406.9)	567 (495.7)
Orthopedic—total % (n)	**37% (74)**	**37% (74)**	**37% (148)**
Knee arthroplasty % (n)	19.5% (39)	14% (28)	17% (67)
Hip arthroplasty % (n)	17.5% (35)	21% (42)	19% (77)
Shoulder replacement % (n)	0.0% (0)	2.0% (4)	1% (4)
Urology—total % (n)	**15% (30)**	**15% (30)**	**15% (60)**
Prostatectomy % (n)	8.5% (17)	7.5% (15)	8% (32)
Nephrectomy % (n)	6.5% (13)	6.5% (13)	6.5% (26)
Cystectomy % (n)	0.0% (0)	1.0% (2)	0.5% (2)
Gynecology/oncology—total % (n)	**25% (50)**	**25% (50)**	**25% (100)**
Abdominal hysterectomy % (n)	25% (50)	23.5% (47)	24% (97)
Myomectomy% (n)	0.0% (0)	1.0% (2)	0.5% (2)
Pelvic exenteration % (n)	0.0% (0)	0.5% (1)	0.25% (1)
General/Colorectal—total % (n)	**23% (46)**	**23% (46)**	**23% (92)**
Anterior resection % (n)	7.5% (15)	5.0% (10)	6.3% (25)
Bowel resection % (n)	8.0% (16)	10.5% (21)	9.3% (37)
Gastrectomy % (n)	2.0% (4)	1.0% (2)	1.5% (6)
Liver resection % (n)	2.5% (5)	2.5% (5)	2.5% (10)
Pancreatectomy % (n)	2.5% (5)	1.0% (2)	1.8% (7)
Splenectomy % (n)	0.5% (1)	3.0% (6)	1.8% (7)

4.4 | Cost analysis

The difference in the mean cost per patient care episode was significant between the pre/post periods, with the mean cost being $31,996 post-implementation compared with $45,336 pre-implementation, representing a $13,340 difference ($p < .000$). In the context of the study cohort post implementation ($n = 200$), this represents a total saving of $2,668,000. Given that the coordinator oversaw pathway compliance for patients beyond those included in the study analysis, this saving is likely to be higher in the context of usual care. The exact area in which costs are saved is not known as costing data in aggregate was used. That is, a report containing the total cost of care for all included patients (including items such as pathology, length of stay, operating room cost, prosthesis) was used to compare costs of care before and after the intervention. It is possible that, despite not reaching statistical significance, the absolute reduction in red blood cell transfusion and length of stay may have contributed to the cost reduction. This would be consistent with the findings of other investigators.[35–37]

4.5 | Implementation evaluation

A total of 11 participants completed the online survey including preadmissions nurses ($n = 4$), anesthetists ($n = 3$), a clinical nurse consultant ($n = 1$), medical officer ($n = 1$), surgeon ($n = 1$), and quality manager (anemia pathway coordinator) ($n = 1$). Experience levels varied from less than 1 year ($n = 2$), 1 to 3 years ($n = 3$), 3 to 5 years ($n = 2$), 5 to 10 years ($n = 2$), and over 10 years ($n = 2$).

Ten of eleven participants agreed or completely agreed that the intervention was acceptable and appropriate. All 11 participants agreed or completely agreed that the pathway was feasible. Seven questions were also included to understand if previously determined barriers

had been addressed (see Table 1).[22,23] When asked if patients understood why the pathway was being used, one respondent stated that they disagreed, and four provided a neutral answer. Most respondents agreed that patients are happy to have the required tests ($n = 9$), are not significantly inconvenienced ($n = 9$), and are better off since implementation ($n = 7$).

Most respondents at least agreed that the required infrastructure is in place to support the pathway ($n = 7$) and that the anemia coordinator was helpful ($n = 11$). When asked about sufficient communication between the multidisciplinary team, most provided a neutral response ($n = 7$) or disagreed ($n = 2$). When asked if the pathway is a priority, five respondents at least agreed ($n = 5$), four provided a neutral response, and two disagreed. However, six agreed that they had sufficient resources, and seven agreed that they had sufficient information about the pathway.

5 | DISCUSSION

This study showed that a significant improvement in compliance with the PAIDSEM-P was achieved. Improved compliance was associated with a significant mean cost reduction of $31,996 per patient care episode. The prevalence of anemia on the day of surgery was reduced by 21%, RBC transfusion utilization was decreased by 14%, and hospital length of stay was reduced by 19%. However, none of these reductions were statistically significant (Odds Ratio 0.79 [95% CI: 0.50, 1.25] $p = 0.32$, Odds Ratio 0.86 [95% CI 0.41, 1.78] $p = 0.69$, and Hazard Ratio 0.81 [95% CI 0.59, 1.10] $p = 0.16$ respectively).

Despite the improvement in compliance, there is room to increase this further. The areas needing improvement may have contributed to not seeing a statistically significant impact on clinical outcomes. Test ordering compliance was quite high at almost 80%, but the performance of those tests and subsequent treatment provision (where needed) could be improved further. Often, despite the tests being ordered by the clinician, the patient did not have the required tests performed or was not able to have the recommended treatment before surgery. For example, 78% of patients had iron studies ordered, but only 68% of patients had the test performed. This meant it was not possible to accurately diagnose the type of anemia in a percentage of patients. One possible reason for this is that, during COVID-19 outbreaks, there was a preference for using telephone consultations as opposed to face-to-face preadmission visits. Patients who could travel upstairs after their appointment and have their blood tests done pre-COVID-19 were now posted a form in the mail and able to complete the tests at their leisure. Other facilities have faced similar barriers to achieving full compliance with PAIDSEM-P, including a feasibility study by Jin et al. in 2019, which noted the key problems as being related to a lack of patient engagement/participation in the context of the intervention, and also a high rotation of hospitalists involved with delivering the pathway.[38]

Suboptimal patient engagement could also be because the change package was not delivered as fully intended. During the PAIDSEM-P change package development, a patient information sheet was created but prevented from being used due to major organizational changes at the time. The patient information sheet was developed with patients and clinicians, with the intention that it would be available in hard copy and on the patient information section of the hospital website. Patient education is a known gap within the implementation of PAIDSEM-P and patient blood management more broadly, and efforts have been made to address this. For example, Liao and colleagues conducted a qualitative study to understand how consumers like to receive information about blood transfusions.[39] They found that patients liked a paper-based brochure, and website links should they lose the written information.[39] Had the change package been delivered as intended, information would have been provided to meet this preference. When implementing PBM, hospitals should prioritize education of patients and be mindful of including considering their perspectives when developing resources; otherwise, they may not fully engage with anemia screening and treatment. Local refinement of the intervention that includes co-design from patients may help improve engagement with the PAIDSEM-P.

There are other possible reasons why we did not see a statistically significant result in clinical outcomes. First, the study was powered for detection of changes in compliance, rather than clinical outcomes, and numbers in our study are small with a varied surgical patient population. In addition, as noted earlier, whereas the majority had iron studies ordered to facilitate diagnosis, 32% did not have tests performed. This meant it was not possible to accurately diagnose the type of anemia in those patients, which may have resulted in suboptimal therapy.[17]

Further, our study outcomes focused on the use of intravenous or oral iron to treat identified anemia, iron deficiency anemia, or suboptimal iron stores without anemia. Part of our PAIDSEM-P is based on the Australian PBM Guidelines which includes identifying patients preoperatively with ferritin <100 mcg/L without anemia.[14] This is not referred to as iron deficiency, rather as

suboptimal iron stores for surgery that may reduce the hemoglobin by ≥3 g/dl (the guidelines suggest iron deficiency without anemia should be considered if the ferritin is <30 mcg/L). The rationale for this approach is based on iron physiology. The body needs ~25 mg of iron each day to replace senescent red blood cells.[9] Most of this iron comes from recycled worn-out or damaged red blood cells.[9] Therefore, blood loss results in loss of recyclable iron (1 ml of blood contains 0.5 mg of iron).[9] Each mcg/L of ferritin is equivalent to 8–10 mg of storage iron.[9] It takes ~20 mcg/L of ferritin to reconstitute 1 g/dl hemoglobin in a 70 kg adult.[9] Therefore, a blood loss that reduces a patient's hemoglobin by 4 g/dl would require ~80 mcg/L of ferritin to reconstitute that lost hemoglobin.[9] In this setting, the guidelines suggest considering iron therapy.[14] Post-implementation, 70 of the 200 had a ferritin <100 mcg/L without anemia. Of these, 17% were treated with intravenous iron. Treating suboptimal iron stores in the absence of anemia is not going to impact the proportion of patients with anemia preoperatively, and would not be expected to affect in-hospital RBC transfusion or hospital length of stay (LOS). Its impact is likely to be some time after discharge from hospital. As one large study demonstrated, 41% of patients discharged from hospital anemic are still anemic up to 12 months later.[40] Treating suboptimal iron stores prior to surgery or treating anemia postoperatively, may impact post-discharge iron deficiency, anemia, and outcomes, something our study was not designed to measure.

Additionally, clinical trials of intravenous iron monotherapy to treat all-cause anemia in surgical patients have shown mixed results, with some demonstrating reduced transfusion[16] and others showing no reduction.[41,42] The majority of trials, however, show increased hemoglobin. A 2020 randomized controlled trial found that giving intravenous iron alone to patients with all-cause anemia prior to major abdominal surgery did not reduce transfusion or mortality.[41] However, it did result in significantly increased hemoglobin levels preoperatively and postoperatively at 8 weeks and 6 months. It also resulted in reduced hospital readmissions.[41] Thus, treating anemia without considering its underlying cause and mechanism would not be expected to improve clinical outcomes.[43] The diagnosis and management of preoperative anemia is evolving in the light of increasing understanding of iron physiology, particularly in the presence of inflammation. C-reactive protein (CRP), a marker of inflammation, was the least performed test in our study. In the presence of inflammation, intravenous iron monotherapy may not be sufficient. The anemia of inflammation results in disrupted iron absorption and availability, impaired erythropoietin production, reduced proerythroblast sensitivity, reduced red cell survival, and often other hematinic deficiencies.[44-47] Therefore, the etiology and mechanism of the anemia need to be accurately diagnosed to enable the most appropriate therapy. In the 2022 International Consensus Conference on Anemia Management in Surgical Patients (ICCAMS), only 7 of 77 studies included in the review defined the type of anemia in the inclusion criteria or criteria for anemia.[17] Further research is needed in therapy tailored to the specific patient and the etiology of their anemia.[15,48]

The study showed cost savings of $13,340 per patient care episode, based on a cost analysis that accounted for the total cost of each care episode pre- and post-intervention. These results are unsurprising, as an Australian net cost analysis of a PAIDSEM-P in colorectal surgery by Trentino et al demonstrated a mean net cost saving of $6744 per patient, as well as significantly reduced red cell transfusion and hospital length of stay.[36] In their follow-up study of the cost-effectiveness of a PAIDSEM-P in colorectal surgery, the cost of screening and treatment (nurse, consultant, and registrar time, and laboratory tests, iron, and consumables) was outweighed several-fold by the reduced hospital costs with a mean saving per patient of $3776.[35,36] Beyond the work by Trentino and colleagues, evidence specifically relating to the cost effectiveness of implementing PAIDSEM-P is limited.[35,49] The approaches used in this study and that of Trentino have observational study limitations in assessing cost savings and cost-effectiveness as there are many factors that may have influenced the change in cost of care.[49] Despite these limitations, given the low cost for implementing a PAIDSEM-P overseen by a coordinator, it is reasonable to implement these programs as endorsed by the World Health Organization.[11,49]

In the context of implementation outcomes, the majority of clinician participants found that the PAIDSEM-P was acceptable and appropriate (90%), and there was 100% agreement that it was feasible. However, uptake by both clinicians and patients could have been higher, with 27.5% of patients receiving care that was fully compliant with the PAIDSEM-P. This finding reflects that some work may be needed to improve the intervention and how it is delivered, and further barriers may need addressing. When asked barrier-specific questions, there was evidence that the clinician respondents felt patients were not sufficiently educated preoperatively, and there was a lack of awareness about the level of communication between nursing and medical teams. These issues were initially identified as barriers, indicating that the implementation approach requires adjustments to enhance and strengthen the degree of education provided for both clinicians and patients and to improve the level of communication between treating teams when coordinating and organizing screening and treatment for

patients. So, although the package did significantly improve clinician compliance, there remains room to improve how it is delivered and supported to better address barriers that are not yet mitigated (e.g., knowledge and beliefs, culture, learning climate, complexity, lack of champions, etc.). Li and colleagues report a similar experience from a 2021 study that used CFIR-ERIC to implement a syncope management pathway.[50] They measured both implementation and compliance outcomes and found that, although there was high acceptability at 91.7% (22 of 24 participant responses), the intervention was only performed on 15–40% of patients across providers.[50]

The 2022 ICCAMS recommended "patients should be educated about the impact of anemia" and "patients should be educated about the relationship between anemia and RBC transfusion and the impact of increased RBC transfusion."[17] The WHO PBM Policy Brief lists "patient education and empowerment, informed consent and shared decision-making" as one of the key principles of PBM.[7] Informed patients can be drivers for change in practice.[51] Future improvements to the pathway will focus on ensuring that patients are adequately educated and counseled on the importance of having anemia and iron deficiency screening tests, and trying to embed more automation so that the intervention is not person dependent, that is, the screening and treatment occurs without the need for reminders from an anemia coordinator.[33] Hospitals wishing to implement PBM should consider the lessons learned from this project and ensure that they adequately consider how the patient can easily engage with the PAIDSEM-P, and processes to support clinicians to act on deranged blood tests. More attention needs to be given to including patient consultation during development to ensure that the patient is more prominently involved. Involving the patient in the pathway development may assist by gaining greater insight into their ability to engage with the pathway and facilitate better understanding of their motivating factors to participate in PAIDSEM-P.

6 | LIMITATIONS

There are several limitations to this study, the first of which is that it was only powered to detect a difference in compliance outcomes. Future research using a hybrid effectiveness design should include sample sizes sufficient to detect clinical differences as well as improvements in compliance. In addition, an increasing understanding of iron metabolism and the impact of inflammation is highlighting the need for improved understanding of the causes and underlying mechanisms of anemia, diagnostic methods, and more nuanced etiology-specific management of anemia.[52] As CRP was the least performed test, and necessary to determine anemia type, we are unable to say with certainty if outcomes were not more improved because inflammation was not identified and factored into management.

Therefore, anemia in the presence of inflammation may require more nuanced management. A randomized controlled trial in cardiac surgery using combined therapy with intravenous iron, erythropoietin alpha, vitamin B12, and folic acid, given 1 day before surgery resulted in significantly reduced red cell transfusion and increased hemoglobin, reticulocytes, and reticulocyte hemoglobin content postoperatively in the intervention group.[15] Patients undergoing cardiac surgery have a high incidence of inflammation, and this trial suggests combined therapy may be more effective in anemia in the presence of inflammation compared to intravenous iron alone.[48] Similarly, a systematic review and meta-analysis of randomized controlled trials showed erythropoietin with iron therapy compared with iron alone significantly reduced transfusion and increased reticulocyte and hemoglobin response in patients undergoing orthopedic and cardiac surgery.[53] All this highlights the need to continue research in this area to better understand the diagnosis of anemia and its etiology, the most appropriate patient-specific therapy(s), and the most appropriate timing of therapy.

In addition to the above, the data were collected through a retrospective medical record review. A prospective study that recruited patients into the pathway may provide a clearer understanding of the clinical impact of compliance and assist in ensuring patients are more engaged in the pathway. In addition, the implementation outcomes are reported only from a health provider perspective. Reasons for reduced engagement from patients may be elicited with further qualitative research. Finally, the cost analysis should be considered with caution, as it is based on crude costs of care and may not accurately represent the savings that may be realized with a larger sample size powered to detect the difference in blood transfusion, for example. It also does not consider whether there were any impacts on the cost of care as a result of COVID-19. This may have encouraged reduced phlebotomy testing and length of stay when weighing up the risks associated with disease transmission in the acute care setting versus receiving an extended period of supportive care in hospital post-surgery.

7 | CONCLUSION

The study showed a significant improvement in compliance with PAIDSEM-P, demonstrating the effectiveness of using a theoretically informed change package to

improve practice. However, a significant reduction in RBC transfusions, anemia, and length of stay was not observed. Cost savings are shown; however, further research is needed to measure the impact of PAIDSEM-P more accurately across a wide variety of surgical specialties to determine which patient populations most benefit from the pathway treatment and when. Implementation outcomes were favorable among clinician respondents, but future iterations should better consider the patient perspective.

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CONFLICT OF INTEREST STATEMENT

The authors JD, JM, JH, KM, LG, NG, GA, HT report no conflicts of interest in this work. SF reports other from National Blood Authority (Australia), personal fees from Ethicon Biosurgery, personal fees from Baxter, other from Thieme (Stuttgart), non-financial support from Health Round Table (Australia), outside the submitted work.

ORCID

Alana Delaforce https://orcid.org/0000-0002-3931-2875
Jed Duff https://orcid.org/0000-0003-1427-0303
Judy Munday https://orcid.org/0000-0003-3596-5235
Gareth Ansell https://orcid.org/0000-0002-2375-0301
Naadir Gutta https://orcid.org/0000-0002-1788-096X
Haitham Tuffaha https://orcid.org/0000-0003-2993-3480
Janet Hardy https://orcid.org/0000-0003-1127-9951
Cameron Hurst https://orcid.org/0000-0002-4577-8962

REFERENCES

1. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM. Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg. 2015;102(11):1314–24. https://doi.org/10.1002/bjs.9861
2. Farmer S, Gross I, Shander A. Blood works - an owner's guide: what every person needs to know before they are a patient. Australia: CITY POINT PR; 2022.
3. Goel R, Patel EU, Cushing MM, Frank SM, Ness PM, Takemoto CM, et al. Association of perioperative red blood cell transfusions with venous thromboembolism in a North American Registry. JAMA Surg. 2018;153(9):826–33. https://doi.org/10.1001/jamasurg.2018.1565
4. Carson JL, Stanworth SJ, Dennis JA, et al. Transfusion thresholds for guiding red blood cell transfusion. Cochrane Database Syst Rev. 2021;12:Cd002042. https://doi.org/10.1002/14651858.CD002042.pub5
5. Carson JL, Triulzi DJ, Ness PM. Indications for and adverse effects of red-cell transfusion. N Engl J Med. 2017;377(13):1261–72. https://doi.org/10.1056/NEJMra1612789
6. Delaforce A, Galeel L, Poon E, Hurst C, Duff J, Munday J, et al. Preoperative anemia screening and treatment practices in patients having total joint replacement surgery: a retrospective, observational audit. Journal of Blood Medicine. 2020;11:259–65. https://doi.org/10.2147/jbm.s254116
7. Poon E, Pache D, Delaforce A, Abdalla L, McGuire T. Anaemia in patients undergoing major bowel surgery—prevalence and current practice: a public and private institution experience. J Perioper Pract. 2021;31(6):215–22. https://doi.org/10.1177/1750458920934321
8. Patient blood management guidelines (National Blood Authority) (2012).
9. Muckenthaler MU, Rivella S, Hentze MW, Galy B. A red carpet for iron metabolism. Cell. 2017;168(3):344–61. https://doi.org/10.1016/j.cell.2016.12.034
10. Patient blood management guidelines: module 2 perioperative. Canberra, ACT, Australia: National Blood Authority; 2013. Accessed March 2020, https://www.blood.gov.au/pbm-module-2
11. World Health Organization. The urgent need to implement patient blood management: policy brief. Switzerland: World Health Organization; 2021.
12. Neef V, Choorapoikayil S, Piekarski F, Schlesinger T, Meybohm P, Zacharowski K. Current concepts in the evaluation and management of preoperative anemia. Curr Opin Anaesthesiol. 2021;34(3):352–6. https://doi.org/10.1097/ACO.0000000000000979
13. Wan S, Sparring V, Cabrales DA, Jansson KÅ, Wikman A. Clinical and budget impact of treating preoperative anemia in major orthopedic surgery—a retrospective observational study. J Arthroplasty. 2020;35:3084–8. https://doi.org/10.1016/j.arth.2020.06.018
14. National Blood Authority. National Health Medical Research Council. Patient blood management guidelines: module 2—perioperative. Canberra, ACT, Australia: National Blood Authority; 2012.
15. Spahn DR, Schoenrath F, Spahn GH, Seifert B, Stein P, Theusinger OM, et al. Effect of ultra-short-term treatment of patients with iron deficiency or anaemia undergoing cardiac surgery: a prospective randomised trial. Lancet. 2019;393(10187):2201–12. https://doi.org/10.1016/S0140-6736(18)32555-8
16. Elhenawy AM, Meyer SR, Bagshaw SM, MacArthur RG, Carroll LJ. Role of preoperative intravenous iron therapy to

correct anemia before major surgery: a systematic review and meta-analysis. Syst Rev. 2021;10(1):36. https://doi.org/10.1186/s13643-021-01579-8
17. Shander A, Corwin H, Meier J, et al. Recommendations from the International Consensus Conference on Anemia Management in Surgical Patients (ICCAMS). Ann Surg. 2022. https://journals.lww.com/annalsofsurgery/Fulltext/9900/Recommendations_from_the_International_Consensus.277.aspx
18. So-Osman C, Wal DE, Allard S. Patient blood management initiatives on a global level: the results of an International Society of Blood Transfusion Survey. ISBT Sci Ser. 2017;12(3):327–35. https://doi.org/10.1111/voxs.12356
19. Hofmann A, Shander A, Blumberg N, Hamdorf JM, Isbister JP, Gross I. Patient blood management: improving outcomes for millions while saving billions. What Is holding it up? Anesth Analg. 2022;135(3):511–23. https://doi.org/10.1213/ANE.0000000000006138
20. 2020 Preoperative anaemia assessment and management in elective surgical procedures survey report (Victorian Government) (2020).
21. Delaforce A, Duff J, Munday J, Hardy J. Overcoming barriers to evidence-based patient blood management: a restricted review. Implement Sci. 2020;15(1):6. https://doi.org/10.1186/s13012-020-0965-4
22. Delaforce A, Duff J, Munday J, Hardy J. Preoperative anemia and iron deficiency screening, evaluation and management: barrier identification and implementation strategy mapping. J Multidiscip Healthc. 2020;13:1759–70. https://doi.org/10.2147/JMDH.S282308
23. Delaforce A, Duff J, Munday J, Farmer S, Miller K, Glover L, et al. A theoretically informed approach to support the implementation of pre-operative anemia and iron deficiency screening, evaluation, and management pathways: protocol for a type two hybrid-effectiveness study. J Multidiscip Healthc. 2021;14:1037–44. https://doi.org/10.2147/JMDH.S313309
24. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Prof. 2006;26(1):13–24. https://doi.org/10.1002/chp.47
25. Wensing M, Bosch M, Grol R. Selecting, tailoring, and implementing knowledge translation interventions. In: Straus S, Tetroe J, Graham ID, editors. Knowledge translation in health care: moving from evidence to practice. Canada: Wiley-Blackwell BMJ Books; 2009.
26. Graham ID, Tetroe J. Some theoretical underpinnings of knowledge translation. Acad Emerg Med. 2007;14(11):936–41. https://doi.org/10.1111/j.1553-2712.2007.tb02369.x
27. Waltz TJ, Powell BJ, Fernandez ME, Abadie B, Damschroder LJ. Choosing implementation strategies to address contextual barriers: diversity in recommendations and future directions. Journal article. Implement Sci. 2019;14(1):42. https://doi.org/10.1186/s13012-019-0892-4
28. Damschroder LJ. Clarity out of chaos: use of theory in implementation research. Psychiatry Res. 2020;283:112461. https://doi.org/10.1016/j.psychres.2019.06.036
29. Powell BJ, Waltz TJ, Chinman MJ, et al. A refined compilation of implementation strategies: results from the expert recommendations for implementing change (ERIC) project. Implement Sci. 2015;10(1):21. https://doi.org/10.1186/s13012-015-0209-1
30. 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. https://doi.org/10.1186/1748-5908-4-50
31. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care. 2012;50(3):217–26. https://doi.org/10.1097/MLR.0b013e3182408812
32. Weiner BJ, Lewis CC, Stanick C, Powell BJ, Dorsey CN, Clary AS, et al. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci. 2017;12(1):108. https://doi.org/10.1186/s13012-017-0635-3
33. Isbister JP, Pearse BL, Delaforce AS, Farmer SL. Patients' choice, consent, and ethics in patient blood management. Anesth Analg. 2022;135(3):489–500. https://doi.org/10.1213/ane.0000000000006105
34. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Switzerland; 2011. https://apps.who.int/iris/handle/10665/85839.
35. Trentino K, Mace H, Symons K, Sanfilippo FM, Leahy MF, Farmer SL, et al. Screening and treating pre-operative anaemia and suboptimal iron stores in elective colorectal surgery: a cost effectiveness analysis. Anaesthesia. 2020;76(3):357–65. https://doi.org/10.1111/anae.15240
36. Trentino KM, Mace H, Symons K, et al. Associations of a preoperative anemia and suboptimal iron stores screening and management clinic in colorectal surgery with hospital cost, reimbursement, and length of stay: a net cost analysis. Anesth Analg. 2021;132(2):344–52. https://doi.org/10.1213/ANE.0000000000005241
37. Trentino KM, Farmer SL, Swain SG, Burrows SA, Hofmann A, Ienco R, et al. Increased hospital costs associated with red blood cell transfusion. Transfusion. 2015;55(5):1082–9. https://doi.org/10.1111/trf.12958
38. Jin L, Kapadia TY, Von Gehr A, et al. Feasibility of a preoperative anemia protocol in a large integrated health care system. Perm J. 2019;23:17–200. https://doi.org/10.7812/TPP/17-200
39. Liao A, Burgess M, Barritt-Eyles R, Trompf L, Crispin P. Perceptions on consumer information in transfusion. A qualitative study of consumers and prescribers. Vox Sang. 2020;116:81–7. https://doi.org/10.1111/vox.12934
40. Warner MA, Hanson AC, Frank RD, Schulte PJ, Go RS, Storlie CB, et al. Prevalence of and recovery from anemia following hospitalization for critical illness among adults. JAMA Netw Open. 2020;3(9):e2017843. https://doi.org/10.1001/jamanetworkopen.2020.17843
41. Richards T, Baikady RR, Clevenger B, Butcher A, Abeysiri S, Chau M, et al. Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, double-blind, controlled trial. Lancet. 2020;396:1353–61. https://doi.org/10.1016/S0140-6736(20)31539-7
42. Meyer J, Cirocchi R, Di Saverio S, Ris F, Wheeler J, Davies RJ. Pre-operative iron increases haemoglobin concentration before abdominal surgery: a systematic review

and meta-analysis of randomized controlled trials. Sci Rep. 2022;12(1):2158. https://doi.org/10.1038/s41598-022-05283-y
43. Krishnasivam D, Trentino KM, Burrows S, Farmer SL, Picardo S, Leahy MF, et al. Anemia in hospitalized patients: an overlooked risk in medical care. Transfusion. 2018;58(11):2522–8. https://doi.org/10.1111/trf.14877
44. Wiciński M, Liczner G, Cadelski K, Kołnierzak T, Nowaczewska M, Malinowski B. Anemia of chronic diseases: wider diagnostics-better treatment? Nutrients. 2020;12(6):1–17. https://doi.org/10.3390/nu12061784
45. Ganz T. Anemia of inflammation. N Engl J Med. 2019;381(12):1148–57. https://doi.org/10.1056/NEJMra1804281
46. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood. 2019;133(1):40–50. https://doi.org/10.1182/blood-2018-06-856500
47. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. Lancet. 2021;397(10270):233–48. https://doi.org/10.1016/S0140-6736(20)32594-0
48. Rossler J, Hegemann I, Schoenrath F, et al. Efficacy of quadruple treatment on different types of pre-operative anaemia: secondary analysis of a randomised controlled trial. Anaesthesia. 2020;124(1):25–34. https://doi.org/10.1111/anae.15062
49. Warner MA, Goobie SM. Preoperative anemia screening and treatment: is it worth the return on investment? Anesth Analg. 2021;132(2):341–3. https://doi.org/10.1213/ane.0000000000005313
50. Li J, Smyth SS, Clouser JM, McMullen CA, Gupta V, Williams MV. Planning implementation success of syncope clinical practice guidelines in the emergency department using CFIR framework. Medicina. 2021;57(6):1–11. https://doi.org/10.3390/medicina57060570
51. Farmer S, Gross I, Shander A. Blood works: an owner's guide. Australia: City Point Press; 2022.
52. McSorley ST, Anderson JH, Whittle T, et al. The impact of preoperative systemic inflammation on the efficacy of intravenous iron infusion to correct anaemia prior to surgery for colorectal cancer. Periop Med (London, England). 2020;9:17–7. https://doi.org/10.1186/s13741-020-00146-4
53. Kei T, Mistry N, Curley G, Pavenski K, Shehata N, Tanzini RM, et al. Efficacy and safety of erythropoietin and iron therapy to reduce red blood cell transfusion in surgical patients: a systematic review and meta-analysis. Can J Anaesth. 2019;66(6):716–31. https://doi.org/10.1007/s12630-019-01351-6

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