Faculty of Medicine
University of Ottawa

INTRAOPERATIVE BLOOD TRANSFUSIONS: IDENTIFYING STAKEHOLDER INTERESTS

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Tori Lenet, MD

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CHAPTER 1. INTRODUCTION AND THESIS OUTLINE

1.1 GENERAL ABSTRACT

Close to one million red blood cell (RBC) units are transfused annually in Canadian hospitals,[1,2] with surgical inpatients accounting for up to 44% of transfusions.[3–5] There is evidence of significant variation in transfusion practice in the operating room (i.e., intraoperative).[6–9] Although variation is expected based on disease severity and patient preference, inappropriate clinical care due to either under- or over-transfusion likely also contributes to significant variation.[10–12] Indeed, estimates of unwarranted intraoperative RBC transfusions in the literature range from 19% to 49%,[8,13–20] owing partly to a lack of evidence-based consensus on RBC transfusion practice in the OR.[21] Our two systematic reviews have highlighted this gap, demonstrating a lack of evidence from trials or actionable clinical practice guidelines to inform decisions in the OR.[22,23] Perhaps more importantly, avoidance of blood product exposure is an important patient-prioritized outcome[24,25] that has yet to be studied empirically in the OR. As such, the observed variation in transfusion practice suggests that transfusion decision-making during surgery represents a clear and important knowledge and evidence gap. Transfusion decision-making in the OR is a complex and dynamic process that we cannot begin to improve without first understanding it. It is influenced by 1) physiologic parameters such as acute blood loss, the effects of general anesthesia, and surgical manipulation.[26] Decision-making is also likely heavily influenced by 2) behavioural factors in the OR (heuristics, team dynamics, institutional culture),[27–30] for which very little empirical work has been conducted.[27] Finally, the importance of 3) patient input in influencing transfusion decisions is inadequately studied,[31] given the documented disconnect between patient priorities and outcomes used in the medical literature and by clinicians.[32,33] In this context, the aim of my thesis was to develop an empirical understanding of transfusion decision-making in the OR based on stakeholder perceptions and priorities, informed by an integrated patient engagement process. With this work, I address an important knowledge gap in intraoperative blood transfusion, thereby

contributing to efforts to reduce variation in blood transfusion practice in surgery. It is my hope that this work will be influential in informing actionable perioperative tools to optimize blood management including providing both evidence and knowledge gaps for future research.

1.2 BACKGROUND AND RATIONALE

1.2.1 Red blood cell transfusions in surgery carry risk: During surgery, RBC transfusions are potentially life-saving when clinically indicated, but can also be unwarranted and associated with harm.[34] Their short-term risks are well-described[35] but often less concerning than the immediate risk of end-organ ischemia associated with under-transfusion.[36] Early risks include transfusion-associated circulatory overload (1 in 100)[35] and transfusion-related acute lung injury (1 in 10,000)[35], which have become recognized as leading causes of transfusion-related mortality.[37,38] In contrast, long-term risks are incompletely understood; evidence suggests that RBC transfusions may be associated with worse cancer outcomes[39–43] through transfusion-related immunomodulation.[44,45] RBC units need to be used appropriately as they are costly ($975 CAD/unit)[46], a scarce resource, and donated altruistically. Appropriate surgical transfusion is therefore of great concern to all stakeholders, including clinicians, healthcare administrators, funders, and, most importantly, patients.[47]

1.2.2 Significant variability in intraoperative transfusion practice suggests unwarranted transfusion: RBC transfusions in surgery range from appropriate to unwarranted). Transfusions are appropriate when given to mitigate the expected physiologic consequences of anemia and hypovolemia.[36] Although definitions vary, unwarranted transfusions are those given in the absence of an acceptable clinical indication.[48–50] There is evidence of significant variation in transfusion practice in surgical patients.[6–9] Although some variation is expected based on casemix, wide variation that cannot be explained by disease severity or patient preference likely reflects unwarranted variation in clinical care.[10–12] In Ontario, two patients with the same characteristics and risk profiles have a 30% difference in their odds of transfusion when treated by different physicians or hospitals.[51] Moreover, estimates of unwarranted intraoperative RBC transfusions range from 20% to 50%.[8,13–20] In an intraoperative transfusion audit completed by our group,[13] unwarranted intraoperative RBC transfusions were found in 22%[49], 45%[48], and 63%[50]

of patients, depending on the tool used. Importantly, 87% of patients were judged to have received excess RBC units even if the decision to transfuse was initially appropriate.[13] Considering the 250,000 RBC units transfused in surgical patients per year in Canada, of which a conservative 20% are unwarranted, 50,000 RBC units and $48,750,000 CAD could be saved annually. In addition, significant patient morbidity could be prevented by avoiding unnecessary transfusions that provide no measurable benefit. Preventing unwarranted RBC transfusions in surgery is thus an important priority for all stakeholders.

1.2.3 Transfusion practice in the operating room is unique: RBC transfusions in surgical patients occur during the intraoperative and postoperative periods. Patients undergoing surgical intervention under general anesthesia are substantively different from other patients that require RBC transfusions. This is particularly important given that well over 50% of transfusions in surgical patients occur in the OR.[13,41] Transfusion practice outside of the OR is guided by level 1 evidence supporting restrictive hemoglobin transfusion triggers of 70-80 g/L as safe and effective at reducing RBC utilization for most patients.[52–55] In the OR, there is no consensus regarding restrictive transfusion triggers.[21] Transfusion decision-making in the OR is a complex and dynamic process; patients having surgery experience acute and rapid blood loss, whereby hemoglobin concentrations may be unreliably measured with available technologies, transfusion triggers may not apply,[53] and blood loss estimates are unreliable.[56] In the non-surgical patient, hemodynamic instability can be a reflection of anemia and is used to guide transfusion following acute blood loss; however, in surgical patients, variations in hemodynamic parameters may result from several concurrent and competing factors, such as potent pharmacologic agents, patient positioning, mechanical ventilation, neuraxial anesthesia, surgical manipulation, abdominal insufflation, and surgical blood loss.[26] Importantly, end-organ ischemia (a commonly cited transfusion indication) cannot be easily assessed in the OR.[57,58]

1.2.4 Intraoperative transfusion decision-making represents a significant evidence and knowledge gap: In order to improve transfusion practice in the OR, we must first generate an understanding of its underlying governing parameters, informed by patient priorities.

Clinical parameters*:* Intraoperative transfusion decision-making relies heavily on clinician judgement, aided by physiological parameters. While this approach is passed on to trainees by apprenticeship, the observed unwarranted variability in RBC transfusion suggests that the current practice model can be improved. We have conducted a systematic review of clinical practice guidelines supporting intraoperative transfusion.[22] All identified documents failed to provide actionable guidance for clinicians, as they were either of poor quality, subspeciality specific, or made non-specific recommendations that reinforce current practice based on best judgement. The paucity of actionable recommendations highlights the lack of an evidence base to support transfusion decisions in surgery. A second systematic review we conducted identified randomized trials comparing perioperative RBC transfusion strategies.[23] Fourteen trials were identified, mainly comparing restrictive and liberal hemoglobin transfusion triggers. Variability in the chosen restrictive (70-90 g/L) and liberal (89-100 g/L) transfusion triggers was notable. Although restrictive protocols were generally safe and saved RBC units, we concluded that intraoperative transfusion trials are urgently needed, as no trial tested a protocol unique to the intraoperative period. It was thus impossible to tease out the effect of the intraoperative and postoperative components of the protocols.

Behavioural parameters: In addition to objective physiological parameters, intraoperative transfusion can be influenced by behavioural factors that underlie unwarranted variation. Behaviour science theories and models provide frameworks from which to investigate factors that drive current clinical practice and identify barriers to changing practice behaviour (work environment, patient and physician preferences, institutional pressures, etc.). For example, an anesthesiologist may be more likely to initiate transfusion if they have concerns about the

surgeon's ability to maintain hemostasis during surgery; conversely, they may be less likely to transfuse if there are institutional penalties for over-transfusion or pressure to conform to local restrictive transfusion practices. As a corollary, the roles of surgeons and anesthesiologists in intraoperative transfusion decision-making are not clearly defined. A prospective audit of intraoperative communication patterns showed that cardiac surgeons typically initiated transfusion decisions.[59] In contrast, a survey of Canadian practitioners conducted by our group identified anesthesiologists as primary decision-makers by both surgeons and anesthesiologists.[60] Thus, the influence of behavioural drivers on intraoperative transfusion is currently unknown and has not been examined empirically.

Patient parameters: Transfusions during surgery are commonly considered decisions made by clinicians without patient input. Clinicians act as the patient's surrogate in making these important decisions while they are under anesthesia. Transfusion decisions are no different from numerous other decisions made by surgeons while performing operations. However, in the former, patients have limited preoperative input, while in the latter they have lengthy consent discussions about options, alternatives, and risks/benefits. Avoidance of blood product exposure is a patient-prioritized outcome emphasized by Choosing Wisely Canada and must inform preoperative consent discussions and surgical planning.[24,25] Given the risk-benefit trade-off associated with blood transfusion during surgery, patients often express concerns about receiving blood products. A systematic review of patient perceptions of blood transfusion included a subset of six surgical studies, but none that focused on transfusions given in the OR.[31] Four of these studies focused on patients' perceptions and willingness to pay for autologous blood transfusion, a procedure that has generally fallen out of favour.[61] Another study assessed the effect of a counselling tool on patient beliefs about transfusion prior to elective surgery.[62] Finally, one study assessed patient recall of the transfusion consent process and perceived knowledge of transfusion afterwards.[63] Therefore, there remains a large knowledge gap regarding patient perspectives about

transfusions given in the operative setting. These should influence clinical practice guidelines, individual transfusion decisions, as well as preoperative consent discussions.

1.2.5 Understanding stakeholder priorities is needed to minimize unwarranted variability: The three-pronged model of intraoperative transfusion-decision making described in section 1.2.4 has formed basis for this thesis. Currently, each component lacks sufficient empirical data to develop interventions to optimize intraoperative transfusion practice and influence clinical practice guidelines. A thorough understanding of the decision-making process is required to address unwarranted variability. To this end, the Dartmouth analytic framework highlights key facets that distinguish warranted from unwarranted clinical variation.[64] Six categories of unwarranted clinical variation are defined, and include factors such as agency (where insufficient information in provided to patients to support shared decision-making), and evidence (when clinical practice is inconsistent with available knowledge base). Strategies identified therein to minimize unwarranted variation include: 1) incorporating informed patient choice into treatment decision-making, 2) rationalizing the use of supply-sensitive resources by testing clinical pathways, and 3) improving the basis for clinical decision-making using outcomes research.[64] This thesis is aligned with this framework and uniquely poised to minimize intraoperative RBC transfusion variability. We sought to understand patient priorities as an important stakeholder (Dartmouth framework 1), understand clinician priorities in choosing transfusion parameters and pathways (Dartmouth framework 2), and understand behavioural drivers that influence transfusion decisions (Dartmouth framework 2). Together, these elements will allow us to improve the scientific basis of intraoperative transfusion decision-making. These data can be incorporated into guidelines, as well as the development of targeted interventions to minimize unwarranted intraoperative transfusions (Dartmouth framework 3).

1.3 THESIS OBJECTIVES

1.3.1 Global research objective: To generate a deeper empirical understanding of the behavioural and clinical aspects that impact transfusion decision-making in the operating room based on stakeholder perceptions and priorities.

This research is fundamental to future efforts aimed directly at minimizing variation in intraoperative RBC transfusion practice, including actionable guideline development, implementation work, and targeted interventions/trials. This work will focus on RBC transfusions in the context of non-cardiac surgery for several reasons. First, there are notable differences in transfusion practice between cardiac and non-cardiac surgical procedures related to underlying patient physiology and comorbidities, the use of cardiopulmonary bypass, and baseline higher risk of perioperative bleeding and transfusion. Furthermore, but there has been significantly less published about RBC transfusion practice outside of the cardiac surgery setting.

1.3.2 Specific research aim 1 (Patients stakeholders): Patients' viewpoints and priorities are important, but currently not well understood. As a result, clinicians may make transfusion decisions on their behalf during surgery that are misaligned with patient preference. These viewpoints and perceptions can inform guideline development and help optimize transfusions (e.g., justify transfusion strategies). The aim was therefore to understand patients' perceptions of RBC transfusions during surgery and their priorities in the perioperative period.

The manuscript for Aim 1 is presented in Chapter 2. An abridged version has been accepted for publication in *Transfusion* and is currently in press:

"*Patient perspectives on intraoperative blood transfusion: a qualitative interview study with perioperative patients*"

1.3.3 Specific research aim 2 (Clinician stakeholders – behavioural factors): To understand the individual, team-based, and institutional factors that influence intraoperative transfusion decision-making among clinicians and lead to unwarranted intraoperative transfusion variability.

The manuscript for Aim 2 is presented in Chapter 3. A shortened version, due to target journal word count limits, has been submitted for publication and is under review.

"*Understanding intraoperative transfusion decision-making variability in major non-cardiac surgery: a qualitative study using the Theoretical Domains Framework*"

In my thesis proposal, we had originally planned for only three manuscripts. While undertaking the proposed thesis work, we identified a knowledge gap in the literature synthesizing the published evidence outlining the behavioural factors influencing intraoperative RBC transfusion. As such, in parallel with the physician interviews, we conducted a systematic review of this literature using the TDF as a guide. This manuscript is presented as an appendix to the three original planned manuscripts.

"*Non-clinical factors affecting intraoperative red blood cell transfusion: a systematic review using the Theoretical Domains Framework*"

1.3.4 Specific research aim 3 (Clinician stakeholders – clinical factors): To define areas of consensus among clinicians about clinical parameters leading to intraoperative transfusion. Current practice patterns, common elements of acceptable intraoperative transfusion protocols, and important research outcomes will be defined.

The manuscript for Aim 3 is presented in Chapter 4:

"*Defining appropriate intraoperative transfusion strategies: a Delphi study*"

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CHAPTER 2. PATIENT PERSPECTIVES ON INTRAOPERATIVE BLOOD TRANSFUSION: A QUALITATIVE INTERVIEW STUDY WITH PERIOPERATIVE PATIENTS

Tori Lenet,[1,2] Stephanie Skanes,[3] Joseph Tropiano,[1] Michael Verret,[2,4] Daniel I McIsaac,[5] Alan Tinmouth,[2,6,7] Julie Hallet,[8,9] Stuart G Nicholls,[2] Dean A Fergusson,[2,7] Guillaume Martel[1,2]

Affiliations:

[1]Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

[3]Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

[4]Department of Anesthesia, CHU de Québec - Université Laval, Quebec City, Quebec, Canada

[5]Departments of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[6]Department of Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[7]Canadian Blood Services, Ottawa, Ontario, Canada

[8]Department of Surgery, University of Toronto, Toronto, Ontario, Canada

[9]Division of Surgical Oncology, Odette Cancer Centre - Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

2.1 PREFACE TO CHAPTER 2

We started by studying patient perspectives about RBC transfusions that are frequently administered during major surgical interventions. We chose to interview patients both before and after major surgery, including patients who received a transfusion and those who were discharged with anemia. Although we initially planned to include a second hospital (Sunnybrook Health Sciences Centre) to improve the generalizability of our results, this was not feasible due to delays in contract negotiations and ethics approval. The goal of this work was to generate an understanding of patient perspectives about intraoperative transfusion, their recall and perception of the preoperative transfusion consent discussion, and their willingness to participate in transfusion prevention strategies.

2.2 ABSTRACT

Background: Red blood cell (RBC) transfusions are commonly given during major surgery, yet an understanding of patient beliefs and perceptions of intraoperative RBC transfusions is lacking. The aim was to understand patient perspectives about intraoperative RBC transfusion and explore their willingness to engage in transfusion prevention strategies.

Methods: Semi-structured interviews were conducted with patients before major surgery, and with other patients who had recently undergone major surgery. Purposive sampling was used to select patients from diverse backgrounds and with varying perioperative courses, including the need for perioperative transfusion and presence of postoperative anemia. Inductive thematic analysis was conducted to identify major themes.

Results: Twenty patients (nine preoperative, eleven postoperative) were interviewed. The following themes were identified: risk-benefit perception of transfusion, acceptance of transfusion prevention interventions, communication, transfusion acceptance, trust, and patient involvement in transfusion decisions. Overall, patients perceived transfusions as low-risk interventions when considered in the larger context of their surgical intervention. Major factors influencing transfusion acceptance included trust in the healthcare system and screening, and the perception of treatability of transfusion-related complications. Many patients preferred to defer intraoperative transfusion decision-making to the perioperative team, citing trust in professional judgement and a good pre-existing relationship with their surgeon. However, some wished for their preferences to be incorporated into intraoperative transfusion decisions. Some patients expressed the desire for a more detailed preoperative blood consent conversation, and most were open to hearing about and participating in strategies to minimize the risk of intraoperative transfusion.

Conclusions: Perioperative patients consider intraoperative transfusions as low-risk high-reward interventions, and generally trust the healthcare system and perioperative team to guide intraoperative transfusion decision-making. However, preoperative transfusion consent discussions were reported as superficial, brief, and lacked nuance. Targeted strategies are

required to improve preoperative blood consent discussions to integrate patient preferences into intraoperative transfusion decisions.

2.3 INTRODUCTION

Red blood cell (RBC) transfusions are commonly administered to patients undergoing major surgery.[1] Intraoperative transfusions are most often perceived as decisions made by clinicians without patient input, while patients are under anesthesia. Although it is routine practice to obtain patient consent for blood transfusions during preoperative discussions, these conversations are often brief, non-specific, and administrative in nature.[2] In an audit of information provided to patients during preoperative consent, only 50% of patients recalled having been provided with any information about blood transfusion prior to their surgery.[3] Intraoperative transfusion decision-making is generally considered by physicians to be a clinical process that is not necessarily modulated by patient preference. However, there is evidence of significant variation in intraoperative transfusion practice between physicians that is not explained by patient or operative factors.[4–7] In this context, it may be possible to integrate patient preferences into these decisions, if elicited in the preoperative period.

While thorough blood screening procedures, careful donor selection, and meticulous blood collection and processing have lowered the risk associated with RBC transfusions, recent surveys suggest that a significant proportion of patients and caregivers continue to view transfusions as harmful.[8] Avoidance of exposure to blood products has thus been emphasized as an important patient-centred outcome, which must inform preoperative consent discussions and surgical planning.[9–11] However, perceptions about risks and benefits associated with transfusion have not been adequately studied in the perioperative environment, where factors such as the potential for major bleeding including death due to bleeding, the broader context of a major surgical intervention, and the impact of anemia on postoperative recovery may influence this perception.

There are many ways the risk of intraoperative transfusion can be minimized, which collectively fall under the umbrella of perioperative blood management programs.[12] These include preoperative anemia correction, restrictive transfusion thresholds, autologous transfusion,

intraoperative cell salvage, hypovolemic phlebotomy, and the use of antifibrinolytic medications such as tranexamic acid. Many of these techniques are being increasingly used in major surgical interventions at high risk of blood transfusion. However, like many interventions that occur during surgery when the patient is under anesthesia, these transfusion alternatives are rarely discussed with the patient preoperatively and are seen as part and parcel of the operative intervention.

There is a general lack of knowledge related to patient preferences about intraoperative RBC transfusion, as well as about how to engage with patients in preoperative transfusion consent discussions and considerations. As a result, this study sought to better understand patient perspectives regarding intraoperative transfusion. Specifically, we explored: (1) patient recall and preferences regarding pre-surgical consent and discussion of transfusion possibilities; (2) patient perspectives regarding factors that would be important to them regarding decisions to transfuse or not; (3) patient perspectives about the risks and benefits of intraoperative transfusion, and (4) patient perspectives regarding areas of research in transfusion practice. These data will be critical to develop strategies to incorporate patient preferences into intraoperative transfusion decisions and incorporate patient-identified priorities into future research activities.

2.4 MATERIALS AND METHODS

Study design

Semi-structured qualitative interviews were conducted with patients to explore their perspectives about intraoperative RBC transfusion. This approach was chosen as it allows participants to discuss the topic in their own words. This study was conducted at two Canadian academic hospitals in Ottawa, Ontario (The Ottawa Hospital General Campus and The Ottawa Hospital Civic Campus). These are both tertiary care academic centres within a publicly-funded healthcare system that perform a high volume of both cancer and non-cancer surgeries for much of Eastern Ontario. The Ottawa Hospital transfuses approximately 30,000 units of red blood cells every year and serves a catchment area of approximately 1.2 million people. By including two separate centres, we sought to capture differences in patient management and blood transfusion consent processes that may affect how patients perceived intraoperative transfusion. These two centres were chosen out of convenience, given the clinical appointments of senior investigators.

Eligibility and recruitment

Adult patients that were able to provide consent were eligible for inclusion. Interviews were conducted with patients waiting to undergo surgery and those following surgical intervention to capture a range of perspectives that reflected different patient experiences.

For preoperative interviews, patients undergoing surgical procedures that confer a high risk of RBC transfusion (≥10% risk of RBC transfusion based on our previous work) were identified during clinic consultations.[10,13] Eligible preoperative patients first provided consent to their clinicians for being contacted for research purposes. These patients were then contacted by a trained research assistant for enrolment.

For postoperative interviews, patients who received an intraoperative RBC transfusion, as well as those with postoperative anemia (defined as a hemoglobin value <120 g/L on hospital discharge)[14] but who did not receive a transfusion, were eligible. Patients with postoperative

anemia were specifically selected, as anemia can be associated with symptoms that may affect postoperative quality of life (e.g., fatigue, shortness of breath) and could possibly be avoided with transfusion. Postoperative patients were identified by the research assistant from a concomitant observational study about intraoperative transfusion,[15] and those who had previously provided a global hospital consent to being approached for research were contacted and enrolled.

Postoperative interviews took place within six weeks of hospital discharge to mitigate the potential for recall bias. Purposive sampling techniques were used to select a sample of patients that would allow the exploration of different factors hypothesized to potentially affect patient perspectives surrounding intraoperative RBC transfusion.[16] Patients were selected from diverse educational and social backgrounds, as well as undergoing a variety of oncologic and non-oncologic operations. Equal gender representation was ensured among included patients. In the postoperative cohort, patients who experienced postoperative complications as well as straightforward postoperative courses were included. All interviews were conducted in English. Patients with diagnosed dementia or cognitive impairment were excluded. Thematic saturation was used to determine the number of patients to recruit.[17,18] We initially planned to recruit 15 preoperative patients and 15 postoperative patients for a total of 30 patients. We planned to recruit additional participants if needed until thematic saturation was reached.

Reflexivity

Interviews were conducted by the first author (T.L.), a graduate student and General Surgery resident physician. This work has formed the basis for a thesis project in Clinical Epidemiology. The interviewer was not known to any of the patients interviewed for this study and was outside of their clinical circle of care. She was introduced as a research assistant to avoid the perception that she could influence the patients' perioperative care.

Data collection methods

Data was collected through semi-structured interviews. Elements of the Risk Perception Attitude (RPA) framework[19] were used to create interview guides (Appendix 2). The RPA framework has been widely used to understand an individual's intent to participate in preventative behaviours based on their perception of risk and degree of personal efficacy. In this context, it was used to understand patient's perception of the risk associated with intraoperative transfusion and how that affects their willingness to participate in transfusion prevention strategies. Separate guides were produced for pre- and postoperative interviews. Preoperative interviews focused on general perceptions of blood transfusions, what the patients recall being told during their consent discussions, and identifying specific concerns related to intraoperative transfusion and clinical outcomes that would be relevant to them. This included specific prompts about known outcomes to explore the saliency of these and perspectives regarding the perceived importance for physician intraoperative transfusion decision-making. Risk perception was assessed by asking patients to rate the odds of transfusion side effects such as infection transmission, mistransfusion, and allergic reaction on a four-point Likert scale. Personal efficacy was assessed by asking about their willingness to participate in more detailed preoperative discussions about transfusion decisions, or their willingness to accept interventions to diminish their risk of intraoperative transfusion (e.g., preoperative anemia correction, tranexamic acid, intraoperative cell salvage, restrictive hemoglobin triggers). For postoperative patients, additional open-ended questions about the patient's postoperative course, focusing on their experience with RBC transfusion, were also asked. Questions were formulated in non-technical language without leading language at an 8th grade reading level.

Interview guides were drafted by a multidisciplinary team and were subsequently modified after review by an advisory committee of three patient partners. Interview guides were then piloted on five test patients and revised to ensure clarity and to establish their ability to answer the research questions.

Prior to interview initiation, baseline demographic information including age, gender, race, education level, employment status, surgical procedure, diagnosis, American Society of Anesthesiologists (ASA) classification, need for perioperative transfusion, and presence of postoperative anemia were recorded. This data was collected both from the medical record and directly from the participant prior to the interview. Consent to collect this data was obtained during the recruitment process.

All interviews were either by telephone or video conference using Microsoft Teams (Microsoft Corporation, Redmond, WA, USA). This software was also used for verbatim automatic speech-to-text transcription. These transcripts were then manually reviewed using interview audio to ensure transcription accuracy. Interview transcripts were anonymized, and each participant was assigned an identification number to preserve patient anonymity.

Data analysis

The qualitative research software NVivo (QSR International, Melbourne, Australia) was used to synthesize interview data. Interview transcripts were imported into NVivo for analysis. Data collection and analysis occurred concurrently to allow familiarity with the content of the interviews and to identify potential new topics that warranted exploration. Thematic analysis of interview transcripts was conducted using an inductive approach as outlined by Braun & Clarke to develop themes related to the research questions.[20] Recruitment stopped when no new themes were identified. Initially, three interviews were coded in duplicate by two researchers (T.L. and S.N.); these were then reviewed by T.L. to identify differences in coding and develop major themes. Subsequent interviews were coded by two researchers (T.L. and J.T.). One reviewer (T.L.) subsequently reviewed the coding of the other reviewer (J.T.) to ensure consistency in the coding process.

Techniques to enhance trustworthiness

Initial interviews were coded by a clinician with clinical expertise in surgery (T.L.), as well as a non-clinician with expertise in qualitative research and thematic analysis (S.N.). Subsequent interviews were coded by two clinicians (T.L. and J.T.).

The study protocol was prospectively registered on Open Science Framework (https://osf.io/dxpyr/?view_only=f63511427fc44615961dd49d14c58142). The Equator Network Standards for Reporting Qualitative Research (SRQR) guidelines[21] were used to describe study methods and report results.

Ethical considerations

Research protocols and interview guides were approved by local ethics board at both participating instructions (ID 20210431-01H). Interviews were conducted by an individual outside of the patient's circle of care to permit them to candidly discuss their surgical care. Verbal consent was obtained over the phone either by a research assistant or by the interviewer (T.L.). Preoperative interviews were conducted after all clinical encounters had been completed and clinical consents signed to avoid influencing clinical care decisions.

2.5 RESULTS

Of the 33 patients approached for participation in this project, 21 provided consent to participate in the interview. One participant withdrew from the study prior to their interview due to rehospitalization. Other reasons for non-participation included being discharged to a secondary facility after their acute hospital stay and were therefore unable or unwilling to participate in the interview. Patient interviews were conducted between November 2021 and January 2022. Interviews lasted between 15 and 58 minutes. Upon reaching thematic saturation at 20 patients, no further patients were contacted. Characteristics of interviewed participants are presented in Table 1.

Following thematic analysis, six major themes were identified: risk-benefit perception of transfusion, transfusion acceptance, trust, patient involvement in transfusion decisions, acceptance of transfusion prevention interventions, and communication. Below we discuss each theme in detail, with exemplar quotes provided for illustration. Additional quotes are provided in Table 2.

Risk-benefit perception of transfusion

Overall, patients expressed a varying level of concern about receiving a transfusion during their surgical intervention. A key factor in the perception of risk/benefit appeared to be the clinical or physiological outcomes associated with transfusion and the likelihood of these. Patients associated receiving a transfusion with positive effects such as faster recovery, improved energy levels, more rapid return to normalcy, and better wound healing. Some patients also perceived intraoperative transfusions as lifesaving:

> “Well, it's going to save your life if you need it. Like if you're losing a lot of blood and you receive someone else’s blood that you need to live, you're going to be OK.” (*P11, postoperative*).

Notably, some outcomes associated with transfusion were only raised in the context of postoperative interviews. These outcomes included decreased symptoms of fatigue, shortness of breath, light-headedness, and cognitive disruption. However, interviewees did acknowledge that these symptoms were likely multifactorial and not exclusively from not receiving a transfusion.

In general, patients perceived blood transfusion as a low-risk intervention, particularly in comparison with the surgical intervention itself. When specifically asked about the risk of viral transmission associated with transfusion, patients expressed that they felt this was a rare occurrence in the Canadian healthcare system. Other risks such as rejection, allergic reactions, and cancer transmission from the donor were also brought up, although were generally also perceived as low risk.

Patients who have had a transfusion previously generally had fewer concerns about the risks of transfusion compared with those who have not been transfused. When asked to consider the risks and benefits of transfusion compared to anemia, patients unanimously considered the risks of anemia higher than the risks associated with transfusion: “I think the odds [of risks associated with transfusion] are so little compared to the benefits of having a transfusion.” (*P19, postoperative*).

Transfusion acceptance

The perception of transfusion as a low-risk activity appeared to inform perspectives regarding the acceptability of a transfusion. However, patients invoked a variety of additional factors that made them more likely to accept an intraoperative transfusion. Elements such as having personal experience with previous transfusions or having a close friend or family member who had received a transfusion were cited: “I do know a couple of people who have had transfusions, so I kind of knew what to expect.” (*P12, postoperative*). A particularly salient issue was the treatability of adverse effects. For example, the perception that the complications of blood

transfusion were readily treatable was cited as a reason for transfusion acceptance: “If there was say, an infection or something, I feel that it could be cleared up in some way or another.” (*P2, preoperative*). Religious beliefs, a fear of blood or needles, and belief in their ability to recover without a transfusion were brought up as reasons why patients would be less likely to accept blood transfusion. Although no members of the Jehovah’s Witness community were interviewed, this religious group was commonly brought up as an example of patients that might refuse perioperative transfusion.

Trust

In general, patients expressed trust in the blood screening process and blood processing done by the Canadian healthcare system to prevent many of the negative side effects associated with transfusion: “In any organized country that offered me blood, I would have absolutely no trouble.” (*P10, postoperative*).

Patients also expressed a trust in the professional judgement of the surgical team to justify their willingness to delegate intraoperative transfusion decision-making to them. Patients expressed optimism that clinicians were making the right transfusion decisions in the operative room, quoting factors such as the quality of professional training, extent of medical knowledge, and a belief that they had previous experience with similar situations:

> “If this is part of what you need to do, and I respect your skills and knowledge and experience, then you know I will go along with it.” (*P10, postoperative*).

Patients referenced the quality of their relationship with their surgical team to explain their willingness to delegate transfusion decisions: “I was with a surgeon that I was very comfortable with. So, I trusted her judgment on like everything.” *(P12, postoperative)*. Patients expressed that

having a poor relationship with their surgeon would prompt them to be more involved in transfusion decision-making and may lead them to question these decisions more readily:

> "If the doctor wants to stay up in the ivory tower and lean down, occasionally tap you on the shoulder and say I want to do this, I think there would be more resistance than if there was a sort of a relationship where you felt this person knows what they're doing." *(P10, postoperative).*

Patient involvement in transfusion decisions

Although consent to receiving blood products is routinely obtained prior to surgery, patients expressed of lack of agency in participating in these discussions, believing that these decisions should solely be at the discretion of the perioperative team with little or no consideration of patient preference. Patients cited a lack of medical knowledge to participate in these decisions, and most were comfortable delegating these decisions to the surgical team, particularly while under anesthesia in the operating room:

> "They could talk to us about it, but they should be able to make the decision. I'm not the specialist of saving my own life. They have the tools. They have the education. So, they know better." (*P18, postoperative*).

However, this was not carte-blanche; and other patients expressed a desire for their preferences to be incorporated into intraoperative transfusion decisions. This perspective seemed to be more common among younger patients:

> "Personal preference [about transfusion] is something that the surgical team should be asking about in a pre-surgery conversation." (*P17, postoperative).*

As previously noted, patients with a good pre-existing relationship with their surgical team were less likely to want to be involved in transfusion decisions, believing that their surgical team would act in their best interest.

In general, participants were more willing to engage in transfusion decision-making in the postoperative period once they had made it through their surgical intervention. Patients expressed feeling uncomfortable with the lack of autonomy that accompanies a major surgical intervention, articulating a sense that things are being done to them without the explicit consent, or feeling like a “slab of meat” (*P8, preoperative*).

When asked how patient preference could be integrated into intraoperative transfusion decisions, patients had mixed feelings. Some expressed no desire to impact how those decisions are made, preferring to delegate them entire to the perioperative team: “I’m not the one who's going to tell them how to do their job.” (*P14, postoperative)*. Others thought that the perioperative team should consider patient preference when making these decisions in borderline situations where there is not a clear indication to transfuse, particularly if a patient has expressed a strong preference to not be transfused. One patient proposed having a “yellow check mark” symbolizing a preference against transfusion, rather than the binary acceptance or refusal that we currently obtain (*P17, postoperative)*. Some expressed the need and desire for a more detailed discussion of how these decisions are made in the operating room and the risks and benefits of transfusion to allow patients to participate more fully in preoperative transfusion consent discussions. They felt this would allow clinicians to have a better understanding of patient’s perioperative goals and make transfusion decisions that are in line with these goals.

Acceptance of transfusion prevention interventions

Among the patients interviewed, several underwent preoperative anemia correction using iron transfusions. Otherwise, patients generally did not recall any discussion about transfusion

alternatives during their preoperative consent with their surgical team. Most patients expressed that they would have liked to have discussed transfusion alternatives prior to their surgery: “I don't recall ever hearing anything about that, so it would be nice to know about it, just to be a potential option.” (*P11, postoperative)*. Others were amenable to delegating the decision of whether to use these techniques to the surgical team: “For myself, I would say, no, that might lead to information overload and might make things more confusing for me.” (*P8, preoperative)*. Patients brought up an interest in preoperative autologous blood donation, although this has largely fallen out of favor in recent years due to the associated cost[22] and higher intraoperative transfusion risk secondary to an increased incidence of preoperative anemia associated with autologous donation.[23] When specifically asked about their willingness to accept restrictive intraoperative transfusion strategies (such as a lower hemoglobin transfusion trigger), most indicated that they would agree if recommended by their surgeon; some expressed concerns about not receiving a transfusion if they were to need it, and preferred to defer the decision to their surgeon’s best judgement in cases of clinical uncertainty about the need for transfusion.

Communication

Communication about perioperative blood transfusions was a major theme in the interviews. Generally, patients had a very superficial recollection of their preoperative blood consent discussion and rarely recalled specific risks associated with transfusion being discussed with them. Some patients did not recall any preoperative transfusion consent discussion, even though a specific blood consent signature is required in our institution prior to any major surgical intervention. Despite this, patients were generally satisfied with this preoperative discussion, citing that in the larger context of their surgery, blood transfusion was low on their list of priorities, particularly for patients undergoing surgery for malignant indications. Other patients expressed the desire to have had more time to discuss transfusion with their surgical team, citing the need

for more than one preoperative clinic visit to digest and process the information to ask more informed questions:

> “And that's why this whole idea of not doing it in one 15-minute meeting. [You're] lying in pre-op, and all kinds of things are being thrown at [you] and consent forms and everything else because it's a hurry. There must be a way of slowing it down just a little bit. Let us absorb.” – *P8, preoperative*

Some patients felt that consent discussions lacked nuance, as consent discussions seek a binary acceptance or refusal to receive blood products:

> “I know they are pressed for time, so therefore the explanation is going to be brief, but then, do you consent to it or not? And if you say yes, I consent to it, then hey, that's it.” – *P16, postoperative*

A support person or surrogate decision-maker were also identified as essential, as patients often rely on these people to help them make decisions or interpret information given by the surgical team. Several patients did not recall being told about having received blood transfusions during their operations, even though they had; those that did recall this discussion reported it being brief, with minimal opportunity to ask questions.

2.6 DISCUSSION

This study contributes to our understanding of patient perspectives about intraoperative transfusion and the complexities involved in incorporating patient priorities into these decisions. Our findings indicate that patients had a general baseline trust in the healthcare system that could be enhanced through more thorough preoperative consent discussions and through building a positive relationship with the perioperative team. Ultimately, there was an acknowledgement of physician skill and expertise when making intraoperative transfusion decisions. Discussion of benefits and risks focused on recovery across a range of physiological and functional outcomes in the larger picture of their operative intervention, which may explain the lack of focus on the risks associated with intraoperative transfusion. However, their understanding of the risks and benefits of transfusion and how these decisions are made was reported as superficial. Given that some patients expressed a desire for preferences to be considered, and proposed mechanisms to support this, there remains the need for improvements to preoperative blood consent discussions and for further work to better integrate patient preference and priorities into intraoperative transfusion decision-making.

This study is an important novel contribution to the body of work exploring patient perspectives about transfusion. How best to communicate with patients about their choices related to blood transfusion and its alternatives has been identified as an area of uncertainty in the Blood Transfusion Priority Setting Partnership.[11] However, this area remains a significant knowledge gap. A previous review of patient perceptions of transfusion included a small subset of surgical studies.[24] Similar themes emerged to those seen here; transfusions were perceived as being of low-to-moderate risk compared with other treatments such as the surgical intervention itself. Themes such as decision-making regarding blood transfusion, negative emotions associated with receiving a blood transfusion, and safety/risk of transfusion were also identified in that review. Patients reported concerns regarding adverse events[25,26] and general apprehension about requiring transfusion in the aforementioned systematic review.[27] However,

subjects such as the incorporation of patient preference into intraoperative transfusion decision-making and patient willingness to participate in transfusion decisions or engage in transfusion prevention were not adequately explored in this review. Furthermore, no study included in this review focused on the intraoperative period. In our study, we specifically focused on the intraoperative period to elicit the aspects specific to this unique context that may influence patient perspectives about transfusion.

Beyond the binary of acceptance or refusal of transfusion, patient preferences are generally not incorporated into intraoperative transfusion decisions. Blood consent discussions often focus on identifying religious beliefs that prohibit transfusion rather than a detailed discussion of the risks and benefits of transfusion. In the operative context, preoperative consent discussions revolve around the surgical intervention itself, while transfusion is usually briefly discussed. Yet, clinicians act as the patient's surrogate in making these important decisions while they are under anesthesia. While most patients in this study reported being satisfied with the information provided about transfusion, some expressed wanting a more extensive discussion across more than one visit. Further, a recent survey study indicated that 40% of patients preferred to share transfusion decisions with the medical team.[28] A review of clinical practice guidelines of intraoperative RBC transfusion identified ten guidelines, none of which mentioned a role for considering patient preference in these decisions.[29] Furthermore, no guideline involved patients in the guideline development process. It can be argued that intraoperative transfusion guidelines are not "preference sensitive" (i.e., that these are recommendations that nearly all patients are likely to accept);[30] however, given uncertainty about the long-term risks of transfusion and the equipoise of intraoperative transfusion strategies, patient preference may be valuable to consider when making practice recommendations. Strategies to incorporate nuance into transfusion consent may help clinicians incorporate their preferences into these decisions if clinically appropriate. For example, one patient mentioned incorporating a "yellow check mark" to indicate a strong patient preference to avoid transfusion if possible. Although many physicians may find

this difficult to incorporate into intraoperative transfusion decision-making, this information may help guide physicians in borderline transfusion situations. Barriers may include time constraints and a lack of patient ability or willingness to engage in preoperative transfusion discussions. Physicians may also lack a clear understanding of how transfusion and anemia affect patients and their recovery, making it difficult to involve patients in this decision. Given that most patients trust their physicians to make transfusion decisions on their behalf, perioperative teams have a responsibility to ensure they are examining their transfusion practice and following the best available evidence. Furthermore, physicians may feel that eliciting patient opinions about intraoperative transfusion will impact their professional autonomy to make these decisions, or that they are already as restrictive as possible with intraoperative blood transfusion and there would be no way to further minimize intraoperative transfusion administration.

A major topic of discussion in the interviews was communication between the perioperative team and patients about various aspects of blood transfusion, including preoperative consent discussions and intraoperative transfusion disclosure. In the current sample, several patients who received intraoperative transfusion were unaware of having received blood products during their surgery. This is supported by another survey-based study, where 25% of patients who were transfused were unaware that they had received a transfusion, and 10% of those transfused believed they had not been transfused.[31] Importantly, in the Canadian healthcare system, patients are routinely sent a letter informing them that they have received a transfusion; it is therefore surprising that patients were unaware of this, even if it had not been disclosed by the perioperative team postoperatively. Some patients in this study also had no recollection of a blood consent discussion at all, which is again consistent with the aforementioned survey in which a third of patients were unsure or had no recollection of having had a consent discussion. This could be explained by the fact that patients are less likely to recall information that they consider to be less important, particularly given that transfusion consent discussions are generally had concurrently with the operative consent discussion. However, this

lack of recall may indicate a lack of integration of the risk and benefits of transfusion that should be discussed with patients, and points towards inadequacy of the consent process at large. Furthermore, patients in this study generally overestimated the benefits of transfusion, or even perceived that transfusions were associated with unproven benefits such as improved wound healing and infection prevention. Patients also frequently perceived intraoperative transfusions as lifesaving interventions, rather than an intervention that is frequently given in non-life-threatening situations to prevent the possible physiologic consequences of anemia. This indicates that clinicians tend to overrepresent the benefits of transfusion; this is supported by the previously referenced study, which reported that while 67% of patients were informed of the benefits of transfusion, only 28% of patients recalled being informed of the risks.[31]

A unique finding was that patients almost exclusively referenced their surgeons when discussing transfusion decisions, despite the fact that intraoperative transfusion decisions are often initiated by the anesthesiology team.[32] This is likely explained by the brief nature of the anesthesiologist-patient relationship, the fact that transfusion consent is obtained by the surgical team, and intraoperative transfusions are generally disclosed by the surgical team. This dynamic means that any preference related to intraoperative transfusion expressed to the surgeon during preoperative consent discussions would have to be communicated to the anesthesiology team at the time of the operation for it to be considered when making intraoperative transfusion decisions.

This study has limitations. First, recruited patients were mostly white, which limits the transferability of results to other racial identities; important viewpoints may not have been elicited due to the lack of racial representation.[33] For example, certain ethnic groups are reported to have lower rates of blood donation, likely due in part to historical medical mistrust.[34] Second, patients were recruited from two campuses of a Canadian academic hospital in Ottawa, Ontario; as such, viewpoints from patients undergoing surgery in other centres or other geographic regions were not captured. This may be significant, as patients expressed trust in the Canadian healthcare system as an important factor in transfusion acceptance and their willingness to delegate

intraoperative transfusion decisions to Canadian healthcare professionals, who they have confidence are appropriately trained. This may not be the case everywhere. Third, recall bias may have impacted patients' ability to remember details of their preoperative consent discussions. Although we did specifically aim to interview patients within 4-6 weeks of their hospital discharge (for postoperative patients) or of their consent discussions (for preoperative patients), the possibility of recall bias remains. Lastly, although our sample size was smaller than initially planned, purposive sampling allowed the selection of information-rich cases, allowing us to reach thematic saturation at a smaller sample size than originally anticipated.[17] Although sufficient for this exploratory study, our relatively small sample size is not surprising given the relative homogeneity of the patient population sampled. A larger, more varied sample may ensure the inclusion of a wider spectrum of patient viewpoints.

Overall, this study has provided insight into patient perceptions and priorities surrounding intraoperative blood transfusions. Although there is a general trust in the healthcare system and professional judgement with regards to intraoperative transfusion decision-making, findings point to inadequacies in the preoperative blood consent discussion and a lack of patient engagement in these important decisions made on their behalf. Future directions include initiatives to improve patient engagement in preoperative blood consent discussions, integration of patients into intraoperative transfusion guideline development, and an assessment of clinician barriers to including patients in this process.

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2.8 TABLES

Table 1: Participant characteristics

	Preoperative (n=9)	Postoperative (n=11)
Gender		
Male	6/9 (67)	4/11 (36)
Female	3/9 (33)	7/11 (64)
Age	58 [46-83]	60 [23-78]
Highest Education Level		
Primary School	0	0
High School	5/9 (56)	3/11 (27)
University Degree	4/9 (44)	8/11 (73)
Race		
White	8/9 (89)	11/11 (100)
Black	0	0
Asian	1/9 (11)	0
ASA Class		
1	0	0
2	1/9 (11)	1/11 (9)
3	8/9 (89)	10/11 (91)
4	0	0
Type of Surgery		
Colorectal	3/9 (33)	4/11 (36)
Gynecology	0	2/11 (18)
Hepatopancreaticobiliary	3/9 (33)	0
Orthopedic	1/9 (11)	2/11 (18)
Urology	1/9 (11)	2/11 (18)
Vascular	1/9 (11)	1/11 (9)
Surgical Indication		
Malignant	3/9 (33)	6/11 (55)
Benign	6/9 (67)	5/11 (45)
Intraoperative Blood Transfusion	-	7/11 (64)
Postoperative Blood Transfusion	-	3/11 (27)
Postoperative Anemia	-	10/11 (91)

ASA: American Society of Anesthesiologists
n(%), median [range]

Table 2: Patient responses according to theme

Risk-benefit perception of transfusion

- “Well, it's going to save your life if you need it. Like if you're losing a lot of blood and you receive someone else’s blood that you need to live, you're going to be OK.” – *P11, postoperative*
- “About 24 hours after the blood transfusion, I had more color, I was less fatigued, I had more of an appetite. So, I seen the benefits of blood transfusion.” – *P18, postoperative*
- “When my husband told me I had a blood transfusion, right away I didn't worry, ‘cause I knew it was gonna help me in my recovery.” – *P18, postoperative*
- "A blood transfusion can save your life, and if you need it then that's the end of it.” – *P3, preoperative*
- “On a risk basis, I wouldn't think that there would be very much risk […] the testing and the methods of screening, packaging it up and putting a star on it, that it's OK. It's pretty good.” – *P10 , postoperative*
- “I do think that tainted blood is a low enough risk that I would take the risk [of having a transfusion].”
- “The biggest concern would be to get something like hepatitis B or C or AIDS. I think that’s pretty normal. But I think the odds of that are so little compared to the benefits of having a transfusion.” – *P19, postoperative*
- “They do their best to clean up the blood that they receive from donations. But I think the risks outweigh… you know again, I'm not as worried as I would be if I wouldn't have a blood transfusion. And I think the risk is much bigger if my organs would be damaged, that would be much worse.” – *P3, preoperative*

Transfusion acceptance

- “I think age has a lot to do with the acceptance of blood transfusions and the other one is experience with other sort of invasive surgeries.” – *P10 , postoperative*
- “I'm not one that really likes hospitals, doctors, etc, and I have a pretty crippling fear of blood tests and IVs. So, I was very nervous about it.” – *P11, postoperative*
- “I was very, very, very worried about the blood transfusions, ‘cause I never had one.” – *P18, postoperative*
- “I’ve had a transfusion before and the risks were a lot higher back then than they are now.” – *P1, preoperative*
- “I do know a couple of people who have had transfusions, so I kind of knew what to expect.” – *P12, postoperative*
- “If there was say, an infection or something, I feel that it could be cleared up in some way or another.” – *P2, preoperative*

Trust

- “In any organized country, you know, that offered me blood, I would have absolutely no trouble.” – *P10, postoperative*
- “Once I’m asleep, I leave it to professionals.” – *P7, preoperative*
- “If this is part of what you need to do, and I respect your skills and knowledge and experience, then you know I will go along with it.” – *P10, postoperative*
- “If the doctor wants to stay up in the ivory tower and lean down, occasionally tap you on the shoulder and say I want to do this, I think there would be more resistance than if

there was a sort of a relationship where you felt this person knows what they're doing, I'm just going to turn myself over." – *P10, postoperative*

- "I was with a surgeon that I was very comfortable with. So, I trusted her judgment on like everything. So, there has been like some doctors where I'm like, oh I don't know about you yet, but like I was very like trusting of my surgeons so. Like I was totally comfortable." – *P12, postoperative*
- "I think it depends on your surgical team, on what kind of relationship you have with them, how much you trust in their abilities and their judgment." – *P15, postoperative*
- "I have total faith that the medical team will do it best and do what they're trained to do." – *P9, preoperative*
- "It's like when I call a carpenter to do something and I know nothing about carpentry or plumbing, I let the guy do the work." – *P7, preoperative*

Patient involvement in transfusion decisions

- "As a patient, I'm not sure that you are in the best position to make that decision. The decision to transfuse or not is with the surgeon or with the medical team." – *P10, postoperative*
- "If I said, "I'm not 100% against it, but if it's possible not to, please don't", then I would think that they would take my wishes into consideration before they made a decision." – *P17, postoperative*
- "Maybe personal preference should be something that the surgical team should be asking in a pre-surgery conversation. Maybe we could just put a yellow check mark on there. It's not a green or red." – *P17, postoperative*
- "They could talk to us about it, but they should be able to make the decision. I'm not the specialist of saving my own life. They have the tools. They have the education. So, they know better." – *P18, postoperative*
- "Just basically how that person feels about transfusion itself, but if it's something that they would rather avoid at almost all costs, or if it's something that they are comfortable with and to leave it up to like it's the doctor who going to make the decision. But they can weigh it against the patient's wishes I guess, you know within reason, but still maintaining a level of safety." – *P1, preoperative*
- "It might be that grey area where it could go either way, and then this is where the patient wishes might have an impact." – *P1, preoperative*
- "I don't know what you would call it, but I'll call it Tori's team, that would go around and do this kind of questioning of the patient beforehand. And there would be sort of a larger guidance. Right now, it's kind of a yes or no. You've given consent or no consent, and then you're leaving it up to the doctor without knowing what's happening." – *P8, preoperative*
- "I'm not the one who's going to tell them how to do their job." – *P14, postoperative*
- "If you give too much choice and information to patients, they're going make some decisions that are not so wise." – *P3, preoperative*
- "Sometimes you can feel like […] you've signed away all your right to everything. Things are being done to you not with you." – *P8, preoperative*

Acceptance of transfusion prevention interventions

- "I don't think it's any harm in having conversations if you're in a situation where you can plan for this. You can do proactive measures to try to increase [a low blood count] or stop bleeding going into a surgery." – *P19, postoperative*

- “I think that would be a good idea because a lot of patients wouldn't know that that exists. And then if they can get away with the medications or whatever it is, it'll save the blood and the blood bank for somebody who doesn't have an option and who has to have a transfusion.” – *P11, postoperative*
- “I don't recall ever hearing anything about that, so it would be nice to know about it, just to be a potential option.” – *P11, postoperative*
- “For myself, I would say, no, that might lead to information overload, and might make things more confusing for me.” – *P8, preoperative*
- “If it meant that they would hold back from giving me a transfusion if I was borderline, yeah, I would be concerned about that.” – *P17, postoperative*
- “I'm just wondering if it compromises the outcome. You know if you really in the end needed the transfusion and you didn’t get it.” – *P5, preoperative*

Communication

- “He did say there would be a possibility of blood transfusion [and that] there were risks associated with the surgery, but I don't believe he discussed any risk associated with the blood transfusion. He asked if I consented to it, and I said yes.” – *P16, postoperative*
- “I know they are pressed for time, so therefore the explanation is going to be brief, but then, do you consent to it or not? And if you say yes, I consent to it, then hey, that's it.” – *P16, postoperative*
- “They told me the possibility would be there that I may need a blood transfusion. And that's basically what it was.” – *P2, preoperative*
- “I had no discussion with the doctor about transfusion. We actually did not have a discussion, even though the form was an acknowledgement of discussion, and we haven't had that discussion.” – *P8, preoperative*
- “But we never talked about the blood transfusion [that I got during surgery]. My husband talked to me about it. So, it never crossed my mind to talk to the doctor about it.” – *P18, postoperative*
- “You know sometimes you feel that… I’m not going to be crude about it, but sometimes you can feel like you're a slab of meat on the table and they can do what they like. You signed away all your right to everything.” – *P8, preoperative*
- “[About blood transfusion consent discussion] It's like then when you go to the store, and you buy something and it's one size fits no one.” – *P8, preoperative*
- “Right now, it's kind of a yes or no. You've given consent or no consent, and then you're leaving it up to the doctor without knowing what's happening.” – *P8, preoperative*
- “I'm happy with the information I got and the decisions that were made.” – *P17, postoperative*
- “Right, and that's why this whole idea of not doing it in one 15-minute meeting. [You're] lying in pre op, and all kinds of things are being thrown at [you] and consent forms and everything else because it's a hurry. There must be a way of slowing it down just a little bit. Let us absorb.” – *P8, preoperative*

CHAPTER 3. UNDERSTANDING INTRAOPERATIVE TRANSFUSION DECISION-MAKING VARIABILITY IN MAJOR NON-CARDIAC SURGERY: A QUALITATIVE STUDY USING THE THEORETICAL DOMAINS FRAMEWORK

Tori Lenet,[1,2] Joseph Tropiano,[1] Stephanie Skanes,[3] Victoria Ivankovic,[1] Daniel I McIsaac,[4] Alan Tinmouth,[5,6] Stuart G Nicholls,[2] Andrea M Patey,[2] Dean A Fergusson,[2,6] Guillaume Martel[1,2]

Affiliations:

[1]Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

[3]Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

[4]Departments of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[5]Department of Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[6]Canadian Blood Services, Ottawa, Ontario, Canada

3.1 PREFACE TO CHAPTER 3

In the previous section, we explored the patient perspective about intraoperative RBC transfusion. The next step was to explore the clinical and behavioural factors that influence physicians to transfuse in the operating room. In doing so, we hoped to better understand the significant observed variability in intraoperative transfusion practice between physicians. This was done with the next three manuscripts. In this section, we aimed to interview experts in anesthesiology and surgery to generate a deep understanding of the factors unique to the operative context that influence RBC transfusion decision-making. To do this, an interview guide was developed using the Theoretical Domains Framework, which is widely used to explore the influences on behaviour in the context in which they occur. Participants were specifically chosen based on their expertise with transfusion medicine and perioperative care.

3.2 ABSTRACT

Introduction: Red blood cell (RBC) transfusions during major surgery are common, with evidence of significant practice variation. Although some variation is expected based on case mix, the presence of such wide variation cannot be explained by disease or case severity alone and may reflect unwarranted or inappropriate transfusions. The purpose of this work was to explore the source of this variability by eliciting the beliefs of anesthesiologists and surgeons that underlie intraoperative transfusion decisions.

Design and methods: Twenty-eight physicians with expertise in transfusion practice (sixteen anesthesiologists and twelve surgeons) were recruited internationally. An interview guide was developed based on the Theoretical Domains Framework (TDF) to identify beliefs about intraoperative RBC transfusion. Content analysis was then performed to group physicians' statements into the relevant theoretical domains. Relevant domains were selected based on the frequency of beliefs reported, the perceived influence on intraoperative transfusion behaviour, and the presence of conflicting beliefs within a domain.

Results: Eight domains were identified as relevant to intraoperative transfusion. These included 1) *Knowledge* (there is insufficient evidence to guide intraoperative transfusion), 2) *Social/professional role and identity* (both the surgeon and anesthesiologist are responsible for intraoperative transfusion decisions), 3) *Beliefs about consequences* (concerns about both the morbidity associated with both transfusion and of anemia when patient is not transfused), 4) *Environmental context/resources* (the type of surgery, availability of point of care hemoglobin testing devices, the patient's postoperative level of monitoring, concerns about local blood supply, and the cost of transfusion influencing transfusion decisions), 5) *Social influences* (institutional culture, judgement by peers, relationship with the surgeon or anesthesiologist, and patient preference influencing transfusion decisions), 6) *Behavioural regulation* (wanting better intraoperative guidelines to guide transfusion, the usefulness of individual audits and educational sessions to guide intraoperative transfusion), 7) *Nature of the behaviours* (overtransfusion

remains commonplace in the operating room, transfusion practice has become more restrictive over time), and 8) *Memory, attention, and decision processes* (a variety of patient and operative characteristics are incorporated into the decision to transfuse).

Conclusions: This study identified a range of factors that underlie intraoperative transfusion decision-making and may explain the significant observed inter-clinician variability in transfusion behaviour. Targeted theory-informed behaviour-change interventions can be derived from this work which could help reduce intraoperative transfusion variability.

3.3 INTRODUCTION

Background

Red blood cells (RBCs) are the most commonly transfused blood product, with approximately 85 million RBC units transfused each year worldwide.[1] Surgical inpatients alone account for 27-44% of RBC transfusions.[2–4] The risk of RBC transfusion can be as high as 50% in procedures at high risk of bleeding.[5,6] Transfusions are potentially lifesaving when clinically indicated, but can also be associated with unnecessary harm.[7] Short-term risks from transfusions are well-described and include infection transmission, and allergic and immunological reactions;[8–10] however, long-term risks are less well understood and likely include immunomodulation[11,12] with possible inferior cancer outcomes in oncologic surgery.[13–17]

There is evidence of significant variation in intraoperative transfusion practice between clinicians.[18–21] A large retrospective cohort study by Bennett-Guerrero and colleagues reported RBC transfusion rates between 7.8% and 92.8% among hospitals performing on-pump coronary artery bypass surgery.[21] Significant variation is also evident in non-cardiac surgery, with Qian and colleagues reporting that patients undergoing hip replacement surgery in high-transfusion hospitals have more than double the odds of being transfused with RBCs than patients treated in average-transfusion hospitals.[18]

Transfusion decision-making in the operating room is a complex and dynamic process, as physiologic parameters are influenced not only by acute blood loss, but also the effects of general anesthesia and surgical manipulation.[22] To address this, significant efforts have already been made to minimize blood transfusions in surgical patients using perioperative blood management programs.[23] However, these efforts have focused almost exclusively on traditional clinical parameters such as hemoglobin concentration. Although some variation is expected based on case mix, wide variation that cannot be explained by disease severity or patient preference likely reflects unwarranted variation in clinical care.[24–26] Consequently, intraoperative transfusions are likely also heavily influenced by socio-behavioural factors that underlie the observed variation in

transfusion care. To date the socio-behavioural factors that influence transfusion decision-making have remained largely unexplored.

Purpose

In the present study, we sought to address this gap by exploring the socio-behavioural factors that clinicians identify as contributing to their transfusion decision-making. Specifically, we applied a theoretical framework to understand the beliefs of anesthesiologists and surgeons that underlie intraoperative RBC transfusion practices. By understanding these beliefs, alongside established clinical factors, it will be possible to developed targeted theory- and evidence-informed interventions to reduce intraoperative transfusion variability.

3.4 METHODS

Qualitative approach and research paradigm

The behaviour of interest was the administration of intraoperative RBC transfusion by anesthesiologists and/or surgeons for patients undergoing major non-cardiac surgical procedures in the operating room. Given the lack of prior work exploring the socio-behavioural factors that inform transfusion decision-making, we undertook an exploratory approach using a qualitative design underpinned by behaviour change theory, specifically the Theoretical Domains Framework. The Theoretical Domains Framework (TDF) is a theoretical framework that was developed to identify influences on health professional behaviour related to implementation of evidence-based recommendations into clinical practice.[27] It provides a theoretical lens through which the cognitive, affective, social, and environmental influences on behaviour can be viewed.[28] We used semi-structured interviews using the TDF as a guiding structure, but with opportunities for divergence to pursue topics arising from the interview.[29]

Researcher characteristics and reflexivity

The first author (TL) conducted all one-on-one interviews with anesthesiologists and surgeons. TL is a Resident Physician in General Surgery as well as a graduate student in Epidemiology. This study was conducted as part of her thesis work. TL was not known to any of the participants prior to the interview. While she had sufficient clinical knowledge of the subject matter to be able to probe clinicians for relevant information, she made a conscious effort not to ask biased or leading questions.

Context and sampling strategy

The population of interest were international anesthesiologists and surgeons with clinical and research expertise in perioperative and transfusion medicine. We chose to limit this study to anesthesiologists and surgeons, as they are the primary decision-makers for intraoperative

transfusion. We chose to recruit participants who were content experts, as we wished to elicit their knowledge of intraoperative transfusion behaviours. To capture the broad spectrum of socio-behavioural factors influencing intraoperative transfusion, we recruited participants both locally and internationally across a variety of surgical subspecialties. Only English- or French-speaking physicians were eligible to participate. Participants were selected if they regularly participated in or performed operations with a moderate or high risk of bleeding. Given the significant practice differences in cardiac surgery related to underlying patient physiology and comorbidities, the use of cardiopulmonary bypass, and baseline higher risk of perioperative bleeding and transfusion, we chose to focus on the non-cardiac setting; as such, no surgeons performing exclusively cardiac surgery procedures were recruited.

Purposive sampling, in which physicians were hand-selected by researchers based on their knowledge of their expertise, was used to select participants.[30,31] This assured the representation of a wide range of knowledge and experience, as well as the inclusion of participants with varying levels of RBC transfusion use, clinical backgrounds, gender, age (number of years of practice), and regional representation. These participants were then asked to suggest other individuals from their network who were reportedly knowledgeable about intraoperative transfusion using a snowball sampling method.[32,33] To include a wide range of beliefs, they were asked to suggest participants who had views that were different from their own. Authors of pertinent, high-impact publications were also considered for participation.[32]

The number of physicians to be recruited was determined using thematic saturation.[34,35] Given the range of perspectives we hoped to capture, we initially planned to recruit fifteen anesthesiologists and ten surgeons and to recruit additional participants if needed to reach thematic saturation. This is a larger sample than other comparable interview studies using the TDF.[36,37] We decided to interview more anesthesiologists than surgeons as they are generally the primary decision-makers for intraoperative transfusion.

Ethical issues

The Ottawa Health Science Network Research Ethics Board approved this study (20210707-01H). Verbal consent to participate was obtained prior to the start of the interviews.

Data collection

Participants were contacted via publicly available email addresses to determine their interest in participating in the interview. The Microsoft Teams (Microsoft Corp, Redmond, WA, United States) platform was used to conduct and record interviews. Automatic speech-to-text transcription was produced by the same software. These transcripts were then manually reviewed with the audio recording to ensure accuracy. Transcripts were then anonymized and imported into the qualitative data analysis software NVivo (QSR International, Burlington, MA, United States).

Data processing and analysis

The TDF user guide outlined by Atkins et al.[38] was used to develop an interview guide to elicits beliefs about each domain and understand how each domain influences intraoperative transfusion. Questions were adapted from a study by Islam and colleagues that explored blood transfusion in the intensive care setting using an interview guide structured around the TDF.[37] The interview guide was piloted on two surgeons and two anesthesiologists; minor changes were subsequently made to ensure clarity and avoid repetitive questions. See Appendix 3 for the interview guide.

Two researchers (TL, JT) coded participant responses into appropriate theoretical domains. The first two interviews were coded in tandem by the two coders to develop a coding scheme. This coding was then validated by a third senior author (AMP) to ensure accuracy. The remaining interviews were coded in tandem by two reviewers. Disagreements were discussed

between the two reviewers to achieve consensus. When consensus could not be achieved, the statement was either coded into two domains or adjudicated by a senior author (AMP). Given that interview transcripts were coded simultaneously by the two coders with disagreements adjudicated in real-time, interrater reliability was not calculated.

Next, statements describing similar underlying beliefs within each domain were generated by one researcher (TL). These are statements that described the perceived role of the domain in influencing intraoperative transfusion behaviour.[39] Beliefs referring to the same theme, or beliefs that were directly contradictory to one another were grouped. Belief statements were then reviewed by the second coder (JT) to ensure that they accurately represented the content of participant statements and then reviewed by a senior author (AMP). A frequency count representing the number of participants mentioning a specific belief was calculated.

Domains considered to be relevant to intraoperative transfusion were then discussed between the two coders, an expert in using the TDF (AMP), and an expert clinician (GM). Domains were deemed relevant based on the perceived impact of the beliefs on intraoperative transfusion behaviour, the presence of conflicting belief statements in a domain, and the frequency that the belief was mentioned across interviews. These three factors were considered concurrently to determine which domains influenced transfusion behaviour. For example, the domain “Beliefs about consequences” would be deemed relevant if consequences associated with intraoperative blood transfusions ranged from negative (increased risk of anemia-related complications), to neutral (transfusion does not affect patient outcomes), to positive (avoids unwarranted blood transfusion).

Techniques to enhance trustworthiness

We sought analytical rigour using multiple coders with expertise in intraoperative transfusion to capture clinically relevant beliefs that affect the behaviour of interest. The coding process was supervised by a non-clinician expert in using the TDF for similar studies (AMP).

The study protocol was published prospectively on Open Science Framework (https://osf.io/npwsh/?view_only=af124dc02c084bf29b50b4520fd34b8a). We report our research in accordance with the Standards for Reporting Qualitative Research (SRQR) guidelines.[40]

3.5 RESULTS

Participants

Forty-five participants were invited to participate. Upon reaching data saturation at 28 participants (16 anesthesiologists and 12 surgeons), no further participants were recruited. Interviews lasted between 36 and 62 minutes. Participant characteristics are presented in Table 1. Given that we recruited physicians with significant scientific and research expertise in transfusion practice, all participants practiced primarily in academic centres, and most were fellowship-trained with protected time for research during their week. As major operations at risk of intraoperative blood loss and transfusion are more commonly performed at academic rather than community or rural centres, we were confident that the majority of beliefs relevant to intraoperative transfusion would be represented by our sample. A minority (n=4) of interviewed anesthesiologists work mainly in the cardiac surgery setting; however, all are heavily involved in perioperative care and perform other types of procedures in addition to cardiac surgery (e.g., liver transplantation). Forty percent (n=11) of participants were women. A range of surgical subspecialities were represented in the sample. Most participants were Canadian (61%), while the rest were American (25%), European (11%), and Australian (4%).

Interrater reliability

A total of 1,486 utterances from the 28 interviews were coded into the 12 domains. As previously discussed, we did not calculate interrater reliability. Any disagreements were resolved either by consensus or following review with a senior author (AMP).

Key themes identified within relevant domains

Key themes emerging from interviews with surgeons and anesthesiologists were categorized in eight theoretical domains: **Knowledge**, **Social/professional role and identity**, **Beliefs about consequences**, **Environmental context/resources**, **Social influences**,

Behavioural regulation, **Nature of the behaviours**, and **Memory, attention and decisions processes** (Table 2).

State of the evidence

Physicians believed that over-transfusion remains commonplace in the operating room (**Nature of the behaviours**). While many physicians were aware of some guidelines related to RBC transfusion, most felt that there was insufficient evidence available to guide intraoperative transfusion practice (**Knowledge**). The Transfusion Requirements in Critical Care (TRICC) trial hemoglobin triggers were frequently cited.[41] Many reported that their transfusion practice had become more restrictive over time (**Nature of the behaviours**) and felt that the evidence supported implementation of restrictive intraoperative transfusion practices. However, a minority of anesthesiologist felt there was equipoise between restrictive or liberal transfusion practices (**Knowledge**). Physicians expressed a desire for intraoperative transfusion policies/guidelines to support transfusion decision-making (**Behavioural regulation**).

Surgeon-anesthesiologist dynamics

There were conflicting opinions about the relative roles of anesthesiologists and surgeons related to intraoperative transfusion decision-making (**Social/professional role & identity**). While anesthesiologists generally felt that intraoperative transfusions fell under their purview in the operating room, most physicians interviewed agreed that the decision is often shared with the surgeon. Some surgeons expressed feeling left out of intraoperative transfusion decisions. Physicians expressed that communication between anesthesiology and surgery about transfusion both pre- and intraoperatively is helpful to make the correct decision (**Behavioural regulation**).

Beliefs about consequences of anemia and transfusion

There was marked variability in beliefs about the effects of transfusion and anemia (**Beliefs about consequences**). While most physicians believed that transfusions are associated with some short- and long-term morbidity, many also expressed that they do not believe that transfusion-related morbidity significantly affects patient recovery, and do not strongly weigh the negative effects of transfusion when making intraoperative transfusion decisions. Similarly, there were varying opinions on the effects of intraoperative anemia on patient recovery, with some physicians expressing that intraoperative anemia can lead to significant postoperative morbidity, and others believing that anemia-related complications are rare and overstated. Some expressed that anesthesiologists may be less aware of the potential postoperative impact of transfusions given in the operating room, as they are generally not involved in patient care outside of the immediate postoperative period.

Environmental factors impacting intraoperative transfusion

Intraoperative transfusion decisions seemed to be heavily influenced by the operative context and environmental factors at several different levels (**Environmental context/resources**). Physicians expressed that the dynamic and unpredictable nature of the operating room impacted their transfusion decisions. Specifically, physicians expressed that they may transfuse in anticipation of future bleeding out of worry of not being able to "catch up". Physicians stated that they consider the type of surgical intervention when making transfusion decisions, stating that they may be more likely to transfuse if they perceive the operative intervention as long or complex. Some also considered the indication for surgery when making transfusion decisions; for example, some physicians stated that they are more restrictive with transfusion in patients undergoing surgery for a malignant indication out of fear of transfusion-related immunomodulation worsening cancer outcomes. The patient's postoperative level of monitoring also seemed to affect transfusion decisions, with many expressing that they would be

less likely to transfuse if the patient was going to be monitored in the intensive care unit following their surgical intervention. Access to point-of-care hemoglobin testing devices generally made physicians less likely to transfuse. Several physicians reported that concerns about institutional blood supply impacted their intraoperative transfusion decisions and considered the cost and resource utilization of transfusion when making these decisions (**Beliefs about consequences**). Other factors such as the presence of backup personnel and handing over to a new anesthesiologist were also identified as influencing transfusion decisions (**Environmental context/resources**).

Decision processes

While attention control and memory did not appear to significantly impact intraoperative transfusion decisions, physicians described well-researched clinical factors that played into the decision process underlying intraoperative transfusion (**Memory, attention and decision processes**), including pre- and intraoperative hemoglobin levels, hemodynamic stability, intraoperative blood loss, and underlying patient comorbidity.

Social influences

A variety of social influences also appeared to heavily impact transfusion decision (**Social influences**). Physicians noted that communication between the surgeon and anesthesiologist in the operating room frequently influences intraoperative transfusion decisions. Judgement by peers and patients also affected transfusion decision-making, as did institutional transfusion culture. Anesthesiologists expressed that their impression of the surgeon's technical abilities or their impression of the likelihood that the surgeon would communicate significant blood loss to the anesthesiology team impact their transfusion decisions. Personal benefit appeared to impact transfusion decisions, with some physicians expressing benefits such as worrying less about a

patient postoperatively or avoiding a phone call about low hemoglobin postoperatively (**Beliefs about consequences**).

Strategies to improve decision-making

Physicians suggested a multitude of strategies that may improve intraoperative transfusion decision-making (**Behavioural regulation**). These included individual and institutional transfusion audits, educational sessions, improved intraoperative hemoglobin measurement tools, and increased use of transfusion alternatives (e.g., intraoperative cell salvage, preoperative anemia correction, tranexamic acid). Physicians acknowledged that it is difficult to change intraoperative transfusion behaviour, as physicians are trained to intervene rather than observe (**Nature of the behaviour**), and that transfusion is routine or automatic for many physicians.

Domains reported not relevant

Four domains appeared to be less relevant: **Skills, Beliefs about capabilities, Motivation and goals, and Emotion** (Table 3). No specific technical skills necessary to perform intraoperative transfusion were mentioned (**Skills**). Physicians were generally confident making intraoperative transfusion decisions (**Beliefs about capabilities**). Overwhelmingly, the stated motivation underlying intraoperative transfusion decision-making was optimizing patient outcomes (**Motivation and goals**). Feelings and affect did not seem to impact transfusion behaviour (**Emotions**).

3.6 DISCUSSION

This study explored the influences on intraoperative RBC transfusion for patients undergoing surgery by anesthesiologists and surgeons using the TDF.[38] The results demonstrate that the most significant theoretical domains related to intraoperative RBC transfusion practice were Knowledge, Social/professional role and identity, Beliefs about consequences, Environmental context/resources, Social influences, Behavioural regulation, Nature of the behaviours, and Memory, attention and decisions processes. First, a perceived lack of high-quality evidence guiding intraoperative RBC transfusion has caused significant uncertainty about the relative risks and benefits of anemia versus RBC transfusion (**Knowledge, Beliefs about consequences**), thereby causing significant variability in intraoperative transfusion strategies between physicians. Second, there was significant uncertainty as to the role of the surgeon in making intraoperative transfusion decisions (**Social/professional role and identity**). Third, the external impact of patients, peers, and institutional culture (**Social influence**), and traditional factors such as patient comorbidity, hemoglobin level, and blood loss (**Memory, attention, and decision processes**) were identified as heavily influencing intraoperative transfusion decisions. Other physical factors affecting these decisions included concerns about local blood supply, availability of point-of-care hemoglobin testing devices, and postoperative level of monitoring (**Environmental context/resources**). Fourth, the dynamic and high-stake nature of the intraoperative environment appeared to introduce various cognitive and affective processes into intraoperative transfusion decision-making, including inaction regret and anticipated regret (**Nature of the behaviours**). Finally, several strategies were identified to help guide intraoperative transfusion and reduce inter-physician variability; these included increased routine pre-and intraoperative communication between perioperative team members, institutional transfusion audits, educational sessions, and implementing evidence-based institutional intraoperative transfusion policies (**Behavioural regulation**).

The present study is a novel contribution that explores the impact of the intraoperative setting on transfusion decision-making. Existing studies have focused largely on the non-operative context.[37,42] Several domains including Knowledge, Beliefs about consequences, and Social influences are consistently mentioned as important drivers of transfusion behaviour across studies. However, this study has elucidated factors unique to the operative context, including the surgeon-anesthesiologist relationship, the effect of the potential for rapid, life-threatening surgical bleeding, and the cognitive load of other intraoperative variables. This study has several important differences when compared to the reference study by Islam and colleagues, which explored the beliefs affecting the adoption of restrictive transfusion strategies in the intensive care setting.[37] While transfusion practice outside of the operating room is guided by level 1 evidence generally supporting the use of restrictive transfusion strategies,[41,43] no such consensus exists for the operative setting. As such, while the studied behaviour in the study by Islam et al. focused specifically on facilitators and barriers related to the adoption of restrictive transfusion strategies, the present study aimed to more broadly understand the drivers on intraoperative transfusion decision-making. The difference in environment and behaviour of interest between the two studies explain the variation in domains deemed relevant to transfusion behaviour.

The impact of the surgeon-anesthesiologist relationship is unique the intraoperative environment and appears to significantly impact intraoperative transfusion decisions. In this study, we identified conflicting views about the relative roles of anesthesiologists and surgeons in making intraoperative transfusion decisions. While most anesthesiologists felt that intraoperative transfusion was their professional role, many acknowledged that this decision is often made in consultation with surgeons. This is consistent with a previous survey of anesthesiologists and surgeons, where 76% of surgeons and 99% of anesthesiologists identified the anesthesiologist as the primary decision-maker for intraoperative transfusion.[44] This creates an interesting dynamic, as surgeons are most frequently conducting preoperative blood consent discussions with patients and are also responsible for disclosing intraoperative transfusion events to patients

following surgery. Physicians generally agreed that in borderline transfusion situations, communication with the surgeon about factors such as expected further blood loss or operative time helps them make the correct transfusion decision. Furthermore, physicians identified increasing communication between members of the perioperative team as a potential avenue to improve intraoperative transfusion decision-making. In this context, a formal policy mandating a pre-transfusion "time-out" in appropriate clinical situations might be helpful to ensure communication of relevant information from the surgical team to the anesthesia team to promote transfusion appropriateness. Adding a discussion about intraoperative transfusion to the preoperative checklist for cases at higher risk of transfusion may also be helpful to reach consensus between the perioperative team about intraoperative transfusion strategies or transfusion triggers.

Another important finding of these interviews was the degree to which social factors seem to influence intraoperative transfusion decisions. Firstly, physicians reported that judgement by peers frequently influenced whether they would transfuse in a borderline situation. Most commonly, anesthesiologists were worried about being seen as an "under-transfusers", whereas surgeons were more concerned about having high transfusion rates, as they saw this as a reflection of poor technical skill. Physicians reported a fear of judgement not only by their peers, but also by nursing staff and patients. This finding is supported by many studies in the literature that reveals the significant effect that peer pressure may have on clinical decision-making.[45,46] Secondly, anesthesiologists reported that their impression of the surgeon frequently impacted their intraoperative transfusion decisions. For example, if they perceived that a surgeon had below-average technical skill, they would be more likely to transfuse. Conversely, surgeons felt that they may be unfairly judged based on their reputation, which they perceive as impacting anesthesiologist transfusion decisions. For instance, surgeons who typically perform complex surgical oncology resections felt that this translated to their patients being transfused at a higher rate, even during less complex cases. This subconscious implicit bias has been shown to broadly

impact physician decision-making[47] and likely also influences intraoperative transfusion decisions. Thirdly, institutional transfusion culture was identified as having a significant impact on individual intraoperative transfusion decisions. This is clearly evident in the literature, with multiple studies showing significant variability in intraoperative RBC transfusion despite adjustment for patient and surgical factors.[18,20,21,48] A recent population-based analysis of patients undergoing gastrointestinal cancer surgery in Ontario, Canada revealed wide variation in hospital transfusion practice, with between 8 and 30% of patients receiving a RBC transfusion depending on the hospital.[49] Possible explanations for this observed variability were explored in the interviews, and include having local institutional transfusion policies, the use of feedback techniques such as transfusion audits, and institutional education sessions about intraoperative transfusion. Physicians expressed that there is a tendency for anesthesiologists and surgeons to "regress to the mean" when it comes to intraoperative transfusion, and the unwillingness to be an outlier compared to their peers.

Several cognitive and affective processes related to the nature of intraoperative transfusion behaviour were raised in the interviews that likely influence transfusion decisions. Both inaction regret and anticipated regret were commonly brought up as motivating factors for intraoperative transfusion. Regret is a common driver of many healthcare decisions described in the literature,[50] and is particularly important when making medical decisions involving uncertain outcomes. For example, the impact of regret has been studied in the context of ordering prostate cancer screening and administering the Human Papillomavirus (HPV) vaccine to adolescent girls.[51–53] In these situations, the level of "acceptable regret" (i.e., the regret that the individual making the decision accepts when making a potentially wrong decision) influences the likelihood of them making a certain decision.[50,54] In this study, physicians mentioned that the anticipated regret of not transfusing and subsequently not being able to "catch up" may increase the likelihood of them initiating a transfusion in the operating room, particularly in borderline transfusion situations or if they perceive that the patient may not be able to tolerate the physiological consequences of

anemia. Furthermore, many physicians expressed that inaction regret (i.e., not giving a transfusion when one was indicated) was a stronger driver than action regret (i.e., giving a transfusion when one was not indicated) in transfusion situations. In general, physicians in this study expressed that they would feel a higher degree of regret if they did not transfuse, rather than if they transfused unnecessarily. Regret therefore likely contributes to RBC overtransfusion in the intraoperative period. Moreover, physicians expressed that medical education generally teaches trainees in a way that favours intervention, making it more natural for physicians to act (i.e., order a transfusion) rather than to observe.

Interviewed physicians almost universally agreed that there is insufficient available evidence to guide intraoperative RBC transfusion. This was further evidenced by the discordant opinions as to the risks and benefits of both intra- and postoperative anemia and RBC transfusion, and the long-term effects of both of these on postoperative outcomes. There is a general lack of consensus on the ideal intraoperative RBC transfusion strategy. In a recently conducted systematic review of clinical practice guidelines related to intraoperative RBC transfusion,[55] identified guidelines failed to provide actionable guidance for clinicians, as they were either of poor quality, subspecialty specific, or made non-specific recommendations that reinforce current practice based on best judgement. This obvious dearth of actionable recommendations highlights the lack of an evidence base to support appropriate intraoperative transfusion decisions and the need for transfusion trials focusing on the intraoperative period. Furthermore, we conducted a second systematic review of randomized controlled trials comparing perioperative RBC transfusion strategies.[56] While restrictive transfusion triggers were generally safe and effectively decreased perioperative transfusion, no trial tested a protocol unique to the intraoperative period, making it impossible to determine the effect of the intraoperative and postoperative components of the protocols. It is clear from the findings of the present study that transfusion decisions made in the operating room are influenced by substantively different factors compared to the

postoperative period that have not been adequately studied in the literature, and likely explains part of the significant inter-clinician variability observed in the literature.

Physicians expressed a variety of possible methods to improve intraoperative transfusion appropriateness. Most physicians agreed that an institutional transfusion protocol to guide intraoperative transfusion would be helpful, although many emphasized that these protocols must be based on high-quality evidence which may not be available. Institutional and individual transfusion audits were also commonly brought up, and are also recommended by the American Association of Blood Banks (AABB) Patient Blood Management Standards.[57] Dexter et al. recently published an automated method for selecting cases for intraoperative transfusion audit based on missing hemoglobin measurement or recorded estimated blood loss, or transfusions above a pre-selected hemoglobin transfusion trigger.[58] This method selects for cases with a higher likelihood of inappropriate transfusion, thereby reducing the labor requirements associated with auditing procedures. Some physicians in the interviews suggested routine postoperative review of intraoperative transfusion events to discuss appropriateness on a case-by-case basis. Educational sessions to review the evidence and indications for intraoperative transfusion were also brought up as a way to decrease inappropriate transfusion, and have been used successfully in the non-operative setting.[59]

This study has provided important insights into the socio-behavioural factors that influence RBC intraoperative transfusion. However, there were several limitations. All interviewed physicians were considered content experts in the field of intraoperative transfusion or perioperative care. Given that such individuals are more likely to work in academic centres, this study may not have captured the factors that impact community or rural practice environments. For example, concerns about local blood supply may be more common in smaller centres and thus influence intraoperative transfusion decisions more than at a larger, academic centre with abundant resources. Furthermore, given that individuals were selected by study investigators and nominated by other interviewees, we may have reached thematic saturation early if all interviewed

physicians had the same transfusion philosophy. To mitigate this, we specifically selected physicians with differing opinions, and asked participating physicians to do the same when nominating other interviewees. Consequently, our results did reveal a broad spectrum of opinions from surgeons and anesthesiologists, indicating that our sampling strategy effectively selected physicians with differing viewpoints.

3.7 CONCLUSION

This study has identified a range of beliefs that underlie intraoperative transfusion decision-making and likely explain part of the observed inter-clinician variability in transfusion behaviour. Targeted theory-informed behaviour-change interventions can be derived from this work and are likely to reduce intraoperative transfusion variability. These interventions can be integrated into an intraoperative transfusion protocol and tested as part of future clinical trials.

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3.9 TABLES

Table 1: Clinician characteristics

	Surgeons (n=12)	**Anesthesiologists (n=16)**
Gender		
Male	8/12 (67)	9/16 (56)
Female	4/12 (33)	7/16 (44)
Age	47.5 [38-77)	46 [36-62]
# of years of practice	14 [5-42]	15 [2-32]
Fellowship training	12/12 (100)	14/16 (88)
Region of practice		
Canada	6/12 (50)	11/16 (69)
United States	4/12 (33)	3/16 (19)
Europe	1/12 (8)	2/16 (13)
Australia	1/12 (8)	0/16 (0)
% of cases with trainees	100 [75-100]	50 [5-100]
Dedicated research time	8/11 (73)	13/16 (81)

n(%), median [range

Table 2: Summary of belief statements and sample quotes from anesthesiologists and surgeons assigned to the theoretical domains identified as relevant

Domain	Specific belief	Sample quote	Frequency out of 28
Knowledge	The evidence is not sufficient to guide intraoperative transfusion practice	"So, you know the quality of the evidence I think is troubling and certainly I think we could have better quality, better designed studies looking at some of these questions."	14
	I follow the TRICC trial recommendations or other guidelines for intraoperative transfusion	"We usually follow the TRICC trial recommendation for restrictive transfusion."	10
	Knowledge of the evidence helps guide intraoperative transfusion practice	"I think having knowledge of the evidence for when to transfuse, when not to transfuse, some of the harms of transfusion, the benefits of transfusion. You know, that kind of thing would probably be helpful."	8
	The evidence does/does not support restrictive transfusion practices	"I certainly do believe in restrictive policies based on the overall weight of the evidence."	8
		"I think there's definitely equipoise [between restrictive and liberal triggers]."	2
Social/professional role and identity	Guidelines do/do not affect my professional autonomy	"Yeah, I do. Because I think some people take them as rules. They see it as some kind of religion."	2
		"I'm not concerned when a guideline is out that it's gonna clearly affect my practice in a wrong way."	19
	Anesthesiologists are responsible for intraoperative transfusion	"I think that's part of my job."	17
	Surgeons are responsible for intraoperative transfusion	"The question is, who's in charge in the operating room? And it's the surgeon."	1
	Surgeons and anesthesiologist share responsibility for intraoperative transfusion	"I think most of the time it's a joint decision."	13
	I do not control intraoperative transfusion decisions	"I'd say quite frequently the blood is given without necessarily me knowing."	5
	Anesthesiologists are less aware of the postoperative effects of transfusion	"Yeah, we don't see enough of our patients post-op. So we don't know how good or how bad they look unless we go to see them. So, that is a problem. Anesthesia has always been accused of not thinking outside the OR."	5
Beliefs about consequences	Transfusions do/do not lead to short- and long-term morbidity	"I think there's lots of studies to support the risk associated with transfusion, whether it's infectious, febrile reaction, clerical error, incompatibility, but also immune response, possibly affecting cancer response."	16
		"I don't actually think giving a blood transfusion is actually a big deal. You know, am I worried about transfusion? No."	8
	Patients do worse when they are transfused	"We know that patients do worse in certain situations once they've gotten a transfusion."	5

	There is no advantage to transfusing	"There's no data that transfusing patients actually improves outcomes."	5
	The risks of transfusion are greater than the risks of anemia	"I worry more about the consequence of excessive transfusion. I personally haven't directly seen the cardiovascular events associated with anemia, 'cause I think that's probably the thing to worry about and I haven't seen that as a recurring theme."	4
	The risks of anemia are greater than the risks of transfusion	"I'm more worried that the patient is gonna die of hypovolemia then they are going to be if they end up a bit over transfused at the end."	3
	Anemia does/does not cause significant morbidity/mortality	"I am also aware that if you hold back, sometimes you can ultimately end up with a very unstable patient if you're not anticipating correctly what's happening in the surgery."	11
		"I think people tolerate a fair amount of hemorrhage before they need to be transfused. I think the human was designed that way."	5
	Postoperative anemia does/does not negatively impacts recovery	"We all know that if that patient goes to the ward, and they're really anemic and they go home and they're above a threshold but they're still very low, you know that they're going to be slower and they're going to be fatigued."	5
		"When you look at the quality-of-life scores and the times to discharge etc. of the more anemic vs. the less anemic patients, there really is no difference."	8
	Personal benefits are/are not considered when making transfusion decisions	"Yeah. I think there are the personal benefits, you know. [...] I don't want that phone call in three hours when I know that that hemoglobin is going to be a little bit lower, you know? So, let's just give that unit now, and just pre-empt that interruption."	4
		"That doesn't factor into my decision to transfuse."	4
	I do/do not consider the cost and resource utilization when making intraoperative transfusion decisions	"I think there's lots of studies to support the […] cost to the system, cost to supply chain. I think there's lots of reasons not to transfuse if we can avoid it."	12
		"That's not the big thing. I'm not like I want to save the blood bank one unit of blood."	3
	I will transfuse in anticipation of postoperative hemoglobin decrease	"I'm going to look at where they are in their course of their hospital stay. If they're going to be in hospital a long time and they've got a borderline hemoglobin, that might make me decide to transfuse intraoperatively 'cause I know that they're going to get the blood transfusion eventually."	5
Environmental context/resources	Point-of-care hemoglobin devices are useful to guide transfusion	"I think they're helpful. There's still helpful in all contexts. For trending, they're helpful for even the absolute number. Like I said, even though I know it's probably not perfectly accurate, it still gives me a good ballpark."	19
	The patient's postoperative disposition does/does not affect transfusion decisions	"I could see giving less blood if they're going ICU 'cause they're going to be watched more carefully."	9
		"I don't think where they go has a big impact on whether I'm going to transfuse somebody or not."	15

	Concerns about blood supply do/do not affect transfusion practice	"I think the national blood shortages have really impacted what we do, and we have certainly not given blood in situations which we probably would have prior just because we know how limited blood is currently."	9
		"I have never had that thought in my mind of what's left in the blood bank. That hasn't really occurred to me before to be honest. I've never really worried about whether the blood bank has blood or not."	11
	The type of or indication for surgery does/does not influence my transfusion decisions	"If my gestalt is that it's going to be a big surgery […] then I would say we probably tend to order blood a little bit sooner than we would otherwise."	10
		"No, not necessarily. I don't think the indication for surgery changes [my transfusion threshold]."	10
	The dynamic nature of the operating room/bleeding affects transfusion decisions	"It's the heat of the moment and you know everybody is using hemostatic resuscitation what happens is way over transfusion occurs, the hemoglobin might be 10 or 11 at the end of the case, and you know that's a problem. That's a huge problem."	5
	Using intraoperative cell salvage influences my transfusion decisions	"Access to cell salvage for a bigger case that you know is going to lose blood is a big impact for me on how much I'll transfuse."	3
	I'm more likely to transfuse if I'm handing the patient over to a new anesthetist	"I might be more likely to transfuse if I was handing over."	2
	The quality of my intravenous access influences my transfusion decisions	"And the fact that [intravenous] access was very challenging and limited, we wanted to have a softer threshold to get it started so that we didn't get too far behind and realize we couldn't really keep up. That would influence my decision."	1
	I transfuse more readily when I have less backup personnel	"I think that transfuse more readily in that case, because I had no help and I had no backup."	1
Social influences	Patient preference/judgement does/does not impact my transfusion decisions (outside of religious beliefs)	"If a patients said I realize I really might need it, but if I don't, please don't give it, then that would change my threshold where I'd be slightly less liberally inclined."	7
		"I think we generally ignore patient preference. We don't give them much chance to refuse blood unless they're a Witness."	20
	My perception of the surgeon/anesthesiologist does/does not impact transfusion decisions	"I mean, there definitely are differences in quality from one surgeon to the next, that probably will influence my decision making."	18
		"I don't think I would pre-emptively transfuse just because I think that surgeon is gonna lose more blood."	9
	Communication with the surgeon/anesthesiologists impacts my transfusion decisions	"In the borderline situation [...] the feedback of the surgeon will help me decide."	18
	Institutional culture impacts transfusion decisions	"Yeah, and to be honest I think out of all those factors, local institutional culture is by far the most important."	14
	Perception by peers does/does not influence transfusion decisions	"I think there's a fear of judgment. And I think for sure we end up maybe over transfusing rather than under transfusing."	13

		"I'm a pretty established guy and I don't really worry too much about what people think."	6
Behavioural regulation	Guidelines/transfusion policies are helpful to guide intraoperative transfusion	"I think there's a lot of value in establishing kind of institutional or in general society practice guidelines."	21
	Intraoperative transfusion should be discussed preoperatively	"If we had the discussion before the surgery would help being on the same page."	18
	Education is important to ensure best transfusion practice	"Education is the number one thing, right? And that needs to happen on both on the anesthesia and the surgical side. I think it's global education around this stuff for all the perioperative people who are involved."	17
	Transfusion audits are useful to ensure transfusion appropriateness	"I think knowing that people are auditing always helps to change behaviour. It makes you think a little bit more."	15
	Communication between team members is helpful when making transfusion decisions	"I'd say, if there's one really important thing, it's communication over anything else."	14
	I reflect on the appropriateness of my intraoperative transfusion practice	"Yes. So, I always try to, at the end of a case or when things have settled down, sort of review the appropriateness of my own transfusion practices."	14
	Patients should have more input on intraoperative transfusion decisions	"So, yeah, maybe we should have a bit more of a nuanced discussion with patients about how we're approaching transfusion."	8
	Better evidence would help guide intraoperative transfusion	"The only thing that will make me change my practice right now where it is, is data."	7
	I'd like to have more effective ways to avoid intraoperative transfusion (e.g., TXA, cell saver, pre-op anemia correction)	"I think having more effective ways to avoid transfusion, whether it's tranexamic acid, other topical coagulation agents or surgical techniques. I think if there's more support for alternative ways to reduce bleeding, people would move towards those alternative means rather than using blood."	7
	Having accurate and rapid tools to measure intraoperative hemoglobin help guide transfusion	"I mean I think maybe having more accurate point of care tests could help."	6
	Intraoperative transfusions should be a joint decision between surgeons and anesthesiologists.	"I think ideally it's a team decision."	5
	Better or more active intraoperative monitoring would help guide transfusion	"But if we have better point of care testing that don't drift too much, don't need too much maintenance, needs validation that are user friendly as much as possible, I think that could change things for sure."	5
	A tool to predict individual transfusion risk would help guide transfusion	"I wonder if some of this AI around case prediction would be helpful […] for patient with these comorbidities, starting with this hemoglobin level, having this surgery here at this institution, it's more likely, So you know to, on the balance, favour giving that unit."	3
	There should be a discussion between anesthesia and surgery prior to every transfusion	"I would not want any anesthesiologist to start blood without talking to me."	2

	Physicians should have to justify intraoperative transfusion decisions	"So I think in general, having sort of institutional checks and balances where you have to meet certain thresholds or criteria in order to transfuse blood product are justified in some way. That would definitely decrease it I think."	1
Nature of the behaviours	Transfusion practice has become more restrictive over time	"I believe that in general the movement has been towards a more restrictive."	19
	Overtransfusion is/is not common in the operating room	"But you know, as far as red cells, I think we massively over transfuse."	12
		"I just I don't think [overtransfusion] is that much of an issue. I really just don't. I think if we were having this conversation 10 years ago, it would be a very different conversation, but I'm not aware it's an issue anymore."	4
	It is easier to give a transfusion than observe	"People worry more about under transfusion because we're conditioned to give things to patients. Most doctors would rather give things than not give things to patients. It makes us feel better when you give them something. So, we're always worried about not giving a treatment."	3
	Intraoperative transfusion is routine/automatic in my practice	"I tend to have a pretty well-established series of actions based on the context that I need to do. So I actually don't think about it very often."	3
Memory, attention, and decision processes	Concerns about actual or potential blood loss, hemodynamic stability, and end organ perfusion influence my transfusion decisions	"I take into account both the hemoglobin level, the hemodynamics, and the point in the operation and anticipated future blood loss."	24
	Patient factors and preoperative hemoglobin are factors I consider when deciding whether to transfuse	"In terms of the patient factors, I better look at what they're measured hemoglobin or hematocrit is. I'm going to look at the patient's overall sort of physiologic state, comorbidities."	21
	I use a hemoglobin trigger to guide intraoperative transfusion	"Assuming the rate of bleeding is low, and the intravascular volume is normal, then I use a hemoglobin trigger of 7 to 8."	18
	Intraoperative transfusion decisions are/are not easy to make	"I think most of the time, it's pretty obvious, you know. In the OR, it's pretty straightforward."	4
		"It's not black and white and it requires a lot of judgment."	4

TRICC: Transfusion Requirements in Critical Care

Table 3: Summary of belief statements and sample quotes from anesthesiologists and surgeons assigned to the theoretical domains identified as irrelevant

Domain	Specific Belief	Sample Quote	Frequency out of 28
Skills	Clinical skills are needed to decide on intraoperative transfusion	"Clinical acumen is incredibly important in these sorts of decisions. Understanding the big picture."	10
	Communication skills are important to make transfusion decisions	"I think the number one thing is communication."	9
	Interpreting lab results is an important skill	"The knowledge to interpret the lab results that you're getting and knowing what tests you need and what reflects what."	3
	Recognizing when a patient does not fit traditional transfusion criteria is an important skill	"There will certainly be times, and this is the practice of medicine, when this situation cannot apply. And recognizing that is the skill right. Understanding what's different here."	1
	Leadership skills are important in transfusion decision	"Other leadership skills around getting buy in from other members of the team who have to live by your decision making and feel OK with it. Even if it was different than what they themselves might want to do."	1
	Technical skills are important to ensure safe intraoperative transfusion	"The next would be some technical aspects to ensure safety, you know, like filters, temperature, air embolism concerns. So, some technical issues."	1
Beliefs about capabilities	I am confident managing intraoperative transfusion	"I'm comfortable making those decisions."	7
	Clinical experience managing high risk patients increases confidence with intraoperative transfusion	"Yeah, I think that comes with experience. So, I think I have enough experience that I'm quite confident I would have a strong feeling about transfusing or not transfusing."	5
	My belief in my ability to catch up if I encounter surgical bleeding influences transfusion decisions	"It would depend on how quickly I believe I could “catch up” if I really wanted to be more… I guess I would say conservative or whatever with transfusing blood."	1
	My belief in my ability to control surgical bleeding influences transfusion decisions	"I think it depends on the individual and their belief that I can control bleeding and I will create further bleeding through the case."	1
Motivation and goals	Avoiding intraoperative transfusion is/is not important	"I think it it's fairly high for me because it's so closely related to patient’s hemodynamics, and outcomes. So, I would say it's probably at like the top third of considerations."	12

		"I would say it's not a high high priority. There are other priorities - hypotension, hemodynamic stability, maintaining renal function, good pain control. Transfusion, I'm not saying it's not important, but it's like if we have to give if we have to give it, we give it."	9
	My main motivation is optimizing patient outcomes	"Obviously, you're trying to do the right thing for the person."	10
	Physicians do not want to have a high transfusion rate	"I don't think anybody wants to have high transfusion rate for their patients."	4
	Avoiding transfusion can conflict with other goals	"[with transfusion] I'm worried about them getting into fluid overload. On the other hand, anemia may also complicate their postoperative course. And so, I mean, I'm in a goal conflict situation."	1
Emotion	Deciding when to transfuse is/is not stressful	"Yeah, especially in rapidly changing situations, there's always a fear that you make that decision and then you re-check their blood gas or something 45 minutes later and you make the wrong decision."	1
		"Yeah, I don't think that transfusion really stresses me out at all."	8
	Physicians with less experience are more stressed by intraoperative transfusion	"So, that may be more relevant for somebody that does surgery where they don't normally lose a lot of blood. You know, when I go in to help people in gynecology and they're giving a lot of blood, then everybody is upset."	2
	Stress/fear makes physicians more likely to transfuse	"Most of the time, we overshoot because we're stressed by the situation, we overshoot."	2

CHAPTER 4. A DELPHI STUDY DEFINING APPROPRIATE INTRAOPERATIVE PATIENT BLOOD MANAGEMENT STRATEGIES IN NON-CARDIAC SURGERY: THE OTTAWA INTRAOPERATIVE TRANSFUSION CONSENSUS

Tori Lenet,[1,2] Daniel I McIsaac,[2,3] Julie Hallet,[4,5] Angela Jerath,[6] Manoj M Lalu,[3] Stuart G Nicholls,[2] Justin Presseau,[2] Alan Tinmouth,[7,8] Michael Verret,[2,9] Christopher G Wherrett,[3] Dean A Fergusson,[2,7,8] Guillaume Martel,[1,2] & for the Ottawa Consensus on Intraoperative PBM*

Affiliations:

[1]Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

[3]Departments of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[4]Department of Surgery, University of Toronto, Toronto, Ontario, Canada

[5]Division of Surgical Oncology, Odette Cancer Centre - Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

[6]Department of Anesthesia, Sunnybrook Health Sciences Center, Toronto, Ontario, Canada.

[7]Department of Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[8]Canadian Blood Services, Ottawa, Ontario, Canada

[8]Department of Anesthesia, CHU de Québec - Université Laval, Québec City, Québec, Canada

*See Appendix 4 for Group authorship

4.1 PREFACE TO CHAPTER 4

In the previous two chapters, we explored the non-clinical and behavioural factors that influence RBC transfusion decision-making in the operating room. While there is extensive literature discussing the clinical drivers of intraoperative transfusion (e.g., hemoglobin triggers, blood management programs), our interviews with transfusion experts described in the previous section clearly demonstrate uncertainty about the evidence underpinning intraoperative RBC transfusion and significant variation in transfusion practice. Therefore, we aimed to perform a Delphi survey study to reach consensus on both clinical and non-clinical factors that should be integrated into intraoperative transfusion practice. These recommendations can then be used to develop local institutional transfusion protocol with the goal of minimizing intraoperative RBC transfusion variability between physicians.

4.2 ABSTRACT

Introduction: There is significant variability in red blood cell (RBC) transfusion decision-making during the intraoperative period. Existing clinical practice guidelines are insufficient to address this variability. As such, our objective was to develop an internationally endorsed consensus statement about intraoperative transfusion decision-making in major non-cardiac surgery using a Delphi consensus process.

Methods: An expert panel of surgeons, anesthesiologists, and transfusion medicine specialists was invited to participate. Thirty-eight statements were developed addressing the following domains: 1) decision-making (interprofessional communication, logistical factors, hemoglobin measurement techniques), 2) restrictive transfusion strategies, 3) integration of patient perspectives, and 4) clinical trial development (equipoise, outcomes, protocol suspension, minimal clinically important differences). Panelists were asked to score statements on a 7-point Likert scale. An anonymous three-round iterative rating and feedback process were used. Consensus was established with at least 75% agreement.

Results: The 33-member expert panel recommended routine pre- and intraoperative discussion between surgeons and anesthesiologists about intraoperative RBC transfusion, and postoperative review of intraoperative transfusion events. The use of point-of-care hemoglobin testing devices was recommended to guide RBC transfusion, along with an algorithmic transfusion protocol including a restrictive hemoglobin transfusion trigger. They recommended a detailed preoperative consent discussion of the risks and benefits of both anemia and RBC transfusion with patients, and routine disclosure of intraoperative transfusion events. Postoperative morbidity and mortality were recommended as the most relevant outcomes related to intraoperative RBC transfusion, and transfusion triggers of 70 and 90 g/L were chosen as acceptable hemoglobin triggers when evaluating restrictive and liberal transfusion strategies in clinical trials.

Discussion: This consensus statement offers internationally endorsed expert guidance on intraoperative RBC transfusion practice for non-cardiac surgical procedures at high risk of bleeding across several key domains. Future work should emphasize knowledge translation strategies to integrate these recommendations into routine clinical practice and transfusion research activities.

4.3 INTRODUCTION

Red blood cell (RBC) transfusions are commonly administered to patients undergoing major surgical procedures.[1] According to blood transfusion audits, between 40 and 70 percent of all RBC transfusions take place in the surgical setting.[2–6] These transfusions are potentially lifesaving when clinically indicated, but can also be unwarranted and associated with unnecessary harm.[7] Their short-term risks are well-described[8] and must be balanced against the immediate risk of end-organ ischemia associated with under-transfusion.[9] In contrast, long-term risks are incompletely understood; evidence suggests that RBC transfusions may be associated with worse cancer outcomes[10–14] through transfusion-related immunomodulation.[15,16] RBC transfusions are also costly ($975 CAD/unit),[17] scarce, and donated altruistically. As such, their appropriate utilization is an important priority for all stakeholders, including physicians, government funding agencies, and patients.

RBC transfusion decision-making during surgery is a complex and dynamic process that is modulated by factors that are unique to the intraoperative context. Parameters traditionally used to guide RBC transfusion in the non-operative context may not be reliable to guide intraoperative transfusion. For instance, given the possibility of acute and rapid blood loss, accurate and expeditious hemoglobin measurement to direct transfusion therapy may not be achievable with current technology.[18] Moreover, while hemodynamic instability can be a reflection of anemia requiring transfusion in the non-operative bleeding patient, several concurrent and competing factors, including potent pharmacologic agents and surgical manipulation, can lead to variations in hemodynamic parameters during surgery.[19] We also lack sensitive monitors that identify early end-organ hypoperfusion related to anemia.[20,21] Given these unique considerations, intraoperative transfusion decision-making relies heavily on clinician judgement aided by physiological parameters and is traditionally taught to trainees by apprenticeship. While perioperative blood management (PBM) programs have typically focused on strategies

implemented in the pre- and postoperative periods to reduce unwarranted RBC transfusion, the intraoperative context remains a relative black box in terms of transfusion practice.[22]

RBC transfusion outside of the operating room (OR) is guided by level 1 evidence supporting restrictive hemoglobin transfusion triggers of less than 70-80 g/L as safe and effective at reducing RBC utilization for most patients.[23–25] However, during the intraoperative period, there is no consensus and little evidence regarding the use of restrictive transfusion triggers.[26] In fact, there are reports of significant variation in intraoperative RBC transfusion practice in surgical patients.[27–30] Although some variation is anticipated based on case mix, significant variation that cannot be attributed to the disease severity or patient preference most likely represents unjustified variation in clinical care.[31–33] Estimates of unwarranted RBC transfusion given during surgery in the literature range from 19 to 49 percent,[29,34–41] highlighting the magnitude of the problem.

Furthermore, intraoperative transfusion behaviour is also influenced by cognitive, affective, social, and environmental factors, which may underlie part of the observed inter-clinician variability.[42] This has been well-studied in the intensive care unit (ICU). For instance, in a survey study of Canadian intensive care physicians, identified barriers to adopting a restrictive transfusion strategy included potential impact on other clinical goals, conflicting beliefs of other physicians, and attitudinal barriers related to denial.[43] In a similar interview study by Islam et al., factors such as the social influence of other teams members and patient's relatives, and disagreements on the importance of restrictive transfusion strategies and their compatibility with other objectives were identified as likely to influence transfusion behaviour in the ICU.[44] There is therefore a clear and pressing need for objective, easily adaptable and comprehensive consensus guidance to inform intraoperative RBC transfusion decision-making and minimize unwarranted variation in transfusion practice.

Aim

The objective of this work was to identify areas of professional consensus with regard to parameters relevant to transfusion decision-making in major non-cardiac surgery among international content experts. This work will be fundamental to future efforts aimed directly at minimizing unwarranted intraoperative RBC transfusions, including actionable guideline development, implementation work, and targeted interventions/trials.

4.4 METHODS

Study design

A Delphi methodology was used to define areas of consensus among clinicians about intraoperative RBC transfusion management, common elements of acceptable intraoperative transfusion protocols, and important research outcomes. Given the significant differences in transfusion practice in cardiac surgery related to the use of cardiopulmonary bypass and the relative paucity of data available to guide transfusion practice outside of the cardiac surgery setting, this study focused on the non-cardiac surgical context. In general, the Delphi process serves to solicit expert opinion when there exists empirical uncertainty on a topic, with a view to generating consensus.[45,46] The Delphi process, in which participants rate their agreement with statements or items across multiple survey rounds, is an iterative, anonymous approach widely used to develop consensus among relevant content experts.[47] It is classically described as having four key methodological features: (1) a group of content experts known as "panelists" are assembled and questioned about the research area of interest; (2) responses are anonymized in order to mitigate individual dominance that can occur from strong verbalization or peer pressure and allows panel members to change their responses in subsequent rounds without fear of judgement; (3) the process is iterative in nature and involves several survey rounds interspersed with controlled feedback including grouped statistical responses; and (4) subsequent survey rounds are informed by a summary of group responses from the previous round.[45,48] Delphi consensus studies are increasingly used to develop clinical practice guidelines and define core outcome sets for clinical trials.[49–51]

Ethical and institutional approval were obtained by The Ottawa Hospital Research Ethics Board. The study protocol was prospectively registered with Open Science Framework (https://osf.io/8qp7a/?view_only=6d0e714b5c3043f3bd58660bdab6dbf0). Study methods were developed and reported based on the Conducting and REporting DElphi Studies (CREDES) guidelines.[45]

Panel identification, sampling, and recruitment

The research team included a general surgeon (GM), an anesthesiologist (DIM), a hematologist (AT), a methodologist with experience conducting Delphi surveys (DAF), and a graduate student/resident physician (TL). An expert panel in perioperative care, blood management, and transfusion medicine representing the spectrum of physicians involved in intraoperative transfusion decision-making was assembled. Internationally recognized experts in transfusion practice and PBM were selected to ensure that the consensus document reflects best current available evidence. Experts were selected based on their publications in the field of transfusion medicine and the research team's personal knowledge of clinical perioperative transfusion experts. Anesthesiologists and surgeons comprised the majority of the panel, as they are the primary providers of care during surgery. Panelists were recruited through purposive sampling,[52,53] whereby investigators handpicked participants based on knowledge of their expertise. This ensured the representation of a breadth of expertise and practice profiles, different clinical backgrounds, varied age (years of practice), and geographic representation. Using a snowball sampling strategy, this group of experts were then asked to nominate additional individuals from their network who were likely to be knowledgeable about intraoperative transfusion.[47,54] They were asked to nominate authors with differing viewpoints from their own to capture a diverse spectrum of opinions. Authors of relevant high-impact publications were also considered for participation.[47] Members of relevant stakeholder agencies such as the Canadian Blood Services (CBS), Canadian Anesthesiologists' Society (CAS), American Association of Blood Banks (AABB), National Health Service Blood & Transplant, and Perioperative Anesthesia Clinical Trials Group (PACT) were represented on the panel. We selected a diverse panel and specifically ensured that the gender of selected participants was representative of the gender distribution in Canada among the medical specialties sampled.[55]

The optimal number of panelists in a Delphi has not been identified, with some studies including as many as 60 participants,[56] and others fewer than 15.[57] Although fewer participants

may be sufficient when the background and expertise of the subjects is homogeneous, more subjects are needed if various reference groups are required.[47] As such, we aimed to assemble a representative panel of 35 experts across perioperative medicine, blood management, and transfusion medicine.

Background work and statement generation

A series of statements was developed based on our extensive previous background work in understanding intraoperative transfusion including systematic reviews, as well as in-depth interviews with patients and physicians on the topic of intraoperative transfusion.[22,58–60]

Our first systematic review identified available clinical practice guidelines supporting intraoperative transfusion,[22] while the second reviewed randomized controlled trials comparing perioperative RBC transfusion strategies.[58] Interviews were conducted with perioperative patients to explore their perspectives about intraoperative RBC transfusion;[59] these results were used to identify actionable strategies to improve intraoperative transfusion that are reflective of the patient experience. Physician interviews were based on the Theoretical Domains Framework (TDF)[61] and were conducted with anesthesiologists and surgeons to identify the behavioural factors that influence intraoperative RBC transfusion;[60] the results of these interviews were used to identify potential areas of behavioural change that could be targeted in an intraoperative transfusion protocol. These were also included in the survey statements to obtain consensus on whether these interventions could be feasibly implemented in the operating room.

Statements for inclusion within the Delphi were selected and refined by our multidisciplinary research team. Statements were framed with reference to non-cardiac surgical procedures at high risk of bleeding (>5% chance of requiring a transfusion). Participants were asked to rate each statement on a seven-point Likert scale based on their agreement regarding perceived importance/relevance of the item (from completely agree [1] → neutral [4] → completely disagree [7]). A seven-point scale was used, as this has been shown in the literature to maximize

the reliability, validity, ease of use, and discriminating power of responses when compared to other numbers of response categories.[62] Participants had the option to enter statements or items that were not already under consideration. Domains of survey statements included 1) intraoperative decision-making (interprofessional communication, procedural considerations, hemoglobin measurement techniques), 2) restrictive transfusion strategies, 3) integration of patient perspectives, and 4) clinical trial development (equipoise, outcomes, protocol suspension, minimal clinically important differences). The full survey is available in Appendix 5.

Delphi survey

The surveys were distributed using a custom-made online survey platform that houses data on Canadian servers to mitigate privacy concerns. Given our extensive previous work exploring physician perspectives about intraoperative transfusion, a close-ended structured (modified) first round was used to minimize time and effort for both the study team and panelists.[63,64] Given that only clinicians with a high level of expertise in transfusion and perioperative medicine were selected for inclusion, no additional background information was provided prior to survey rounds.

Round 1

The Delphi method consisted of three survey rounds. Survey invitations which included a link to the first round of the survey were sent via e-mail. Instructions were included in this e-mail, as well as in the introductory text of the survey. Panelists were given two weeks to complete the first round of the survey. Reminder e-mails were sent out after one- and two-weeks' time. Individual e-mails were sent to non-responders to maximize survey response. Participants who had not responded to the previous round were not invited to participate in subsequent rounds. Following each statement, panelists were given the opportunity to make any comments about the statement or suggest modifications to the statement wording. It was also possible for panelists to

suggest new statements or make any general comments. These comments were amalgamated and reviewed between rounds by the research team to identify any potential new statements, and to edit existing statements to reflect consensus opinion.

Survey responses were de-identified and analyzed by categorizing responses into either disagreement (1-3 on the Likert scale), neutral (4 on the Likert scale), or agreement (5-7 on the Likert scale). Consensus was defined, *a priori,* as 75% or greater agreement or disagreement with an individual statement. Statements that achieved consensus agreement were included in the final consensus statement, while those that achieved consensus disagreement were dropped. Statements that achieved consensus agreement or disagreement in Round 1 were not included in subsequent rounds.

In addition to traditional Delphi statements, participants were also asked to rate lists of clinical factors to consider when initiating an intraoperative RBC transfusion, clinical outcomes related to intraoperative RBC transfusion, and reasons to justify suspending an intraoperative transfusion protocol as part of a clinical trial (Appendix 2). These were rated for importance on the same seven-point Likert scale.

Round 2

Statements that achieved consensus agreement or disagreement in Round 1 were not included in Round 2. Statements from Round 1 that had achieved neither consensus agreement nor disagreement were revised by the research team based on panelist feedback. The results of the previous round were presented to the panelists as the proportion of agreement and disagreement with each statement, both overall and stratified by type of physician (surgeon, anesthesiologist, or transfusion medicine specialist). For each statement represented, comments from the previous round were also provided to the panelists, as well as a copy of their responses to the previous survey round. Panelists were then asked to indicate their level of agreement for the revised statements using the same Likert scale. Again, panelists had two weeks to respond

to this survey round and were reminded in a similar fashion as previously described. Survey results were anonymized and analyzed in the same manner as round 1 using the same consensus threshold.

In addition, clinical outcomes that had reached consensus as important in the previous round were represented to participants, who were then asked to rank the five outcomes they considered most important related to intraoperative RBC transfusion.

Round 3

Statements that achieved consensus agreement or disagreement in Round 2 were not included in Round 3. As with Round 2, statements that had not reached either consensus agreement or disagreement were revised by the research team based on comments made in the previous round. The revised statements were then represented to the panelists along with the previous round's results and comments. Again, the same consensus criteria were followed.

Participants were also asked about the ideal follow-up period to measure postoperative morbidity and mortality as part of a clinical trial. Questions about their preferred study design (i.e., non-inferiority or superiority of restrictive or liberal transfusion strategies) and the corresponding minimal clinically important difference (MCID) and non-inferiority margins for clinical outcomes rated as most important in previous rounds were also included.

4.5 RESULTS

Panelists

Fifty-one physicians were invited to participate internationally. Thirty-four physicians including 16 anesthesiologists, 11 surgeons, and 7 hematologists/transfusion medicine specialists accepted the invitation to participate (Table 1). Panelists represented each of the important stakeholders. Forty-one percent (14/34) of participants identified as female. Several surgical subspecialties including gynecologic, vascular, cardiothoracic, urologic, colorectal, hepatobiliary, and orthopedic surgery were represented. Panelists had been practicing for a median of 16 years (range 2 to 50 years), and all practiced in an academic hospital setting. Most panelists practiced in a Canadian centre (53%, 18/34), while 27% (9/34) practiced in an American centre, 15% (5/34) in a European centre, and 6% (2/34) in an Australian centre.

Delphi rounds

All three electronic Delphi survey rounds were distributed. Response rates were 97% for round 1 (n=33/34), 100% for round 2 (n=33/33), and 100% for round 3 (n=33/33). During round 1, 38 statements were scored, and 26 reached consensus agreement (Figure 1, Appendix 2). Two statements were discarded as they reached consensus disagreement, and one statement was added. For round 2, the remaining 10 statements that had not achieved consensus were submitted to panelists, as well as the one additional statement. In the final round, the 7 statements that had not achieved consensus was resubmitted for voting; four statements reached consensus, while three did not (Table 2). In total, 34 statements reached consensus and were included in the final recommendations (Table 3).

Interprofessional communication

Preoperative

The panel recommends that the perioperative team formally review the patient's preoperative baseline hemoglobin prior to every case to anticipate the need for potential RBC transfusion. They also recommend that the potential for intraoperative RBC transfusion be routinely discussed between the surgeon and anesthesiologist as part of the preoperative checklist.

Intraoperative

The panel recommends that the decision to initiate an intraoperative RBC transfusion should generally be shared between the surgeon and anesthesiologist. This would not apply in cases of extreme urgency, for example during massive uncontrolled hemorrhage. The panel also recommends that every intraoperative transfusion should be discussed between the surgeon and anesthesiologist prior to initiation if the situation permits.

Postoperative

The panel recommends that a review of the appropriateness of any intraoperative transfusion event should be routinely discussed in the postoperative debrief between the anesthesiologist and surgeon.

Clinical factors

The panel recommends that the following clinical and patient-related factors are important to consider when deciding on whether to administer an intraoperative RBC transfusion: ongoing surgical bleeding and potential for additional bleeding, estimated blood loss, hemodynamic stability, signs of end-organ ischemia, and underlying patient medical comorbidity.

Hemoglobin measurement

The panel recommends the use of point-of-care testing (POCT) devices to measure hemoglobin concentration in the operating room, and agrees that they are sufficiently accurate to routinely guide intraoperative transfusion. Panelists agreed that 4 g/L is an acceptable margin of error for these devices (the Allowable Performance Limit defined by the Institute for Quality Management in Healthcare [IQMH]).[65] The panel recommends measuring intraoperative hemoglobin concentration only if clinically indicated. They also recommend measuring hemoglobin concentration routinely prior to every intraoperative RBC transfusion event, and between successive intraoperative RBC transfusions in cases where multiple units are being transfused, if the clinical situation permits.

Procedural considerations and audits

The panel recommends that a single unit of RBCs should be transfused at a time in most cases. Furthermore, they recommend that intraoperative RBC transfusions be guided by a predetermined algorithmic transfusion protocol that should include a hemoglobin transfusion trigger/threshold. The panel recommends that the physician should be prompted to provide an indication for transfusion in the electronic medical record system when ordering an intraoperative RBC transfusion except in cases of extreme urgency such as massive hemorrhage.

The panel recommends both institutional audits of intraoperative transfusion and internal audits of groups of anesthesiologists and surgeons to review the appropriateness of intraoperative transfusion events.

Restrictive transfusion strategies

The panel agrees that there is uncertainty about both the benefits and risks of using restrictive transfusion protocols in the operating room to guide RBC transfusion. However, they

agree that implementing a restrictive transfusion protocol including the use of a restrictive hemoglobin transfusion trigger would be feasible in the operating room.

Patient-centred considerations

The panel recommends routinely informing patients of any transfusion that they received during their surgical procedure. They also recommend incorporating patient preferences and previously stated perioperative goals of care regarding blood products into intraoperative transfusion decisions. They recommend that preoperative transfusion consent discussions specifically discuss the spectrum of risk associated with both RBC transfusion and perioperative anemia, and that their perception of the risks and benefits of transfusion and anemia be considered when making intraoperative transfusion decisions on their behalf.

Research considerations

The panel agrees that a stronger evidence base is needed to guide intraoperative RBC transfusion, and that expanding this evidence base is an important research priority. They were also willing to participate in a clinical trial comparing restrictive and liberal hemoglobin triggers, as well as a three-arm trial that included a usual care arm. Hemoglobin triggers of 70 g/L and 90 g/L were chosen as acceptable restrictive and liberal hemoglobin transfusion triggers.

The following were identified by the panel as legitimate reasons to suspend an intraoperative transfusion protocol during a clinical trial: massive uncontrolled hemorrhage, hemodynamic instability refractory to vasopressor support and volume resuscitation, and clear evidence of cardiac or cerebral ischemia.

The top five most important transfusion-related research outcomes in order of importance were: overall perioperative morbidity, postoperative mortality, perioperative clinically significant cardiac ischemia, postoperative functional capacity/status, and perioperative clinically significant cerebral ischemia. Panelists most commonly identified 30 days as the ideal timepoint to measure

postoperative morbidity (n=17, 52%), while 30- or 90-days were chosen as the ideal timepoint to measure postoperative mortality (n=15, 45% for both). Most panelists supported a non-inferiority clinical trial design to compare restrictive and liberal transfusion protocols (n=25, 76%). The panel chose absolute non-inferiority margins of 0.5% for postoperative mortality and 2 or 3% for overall postoperative morbidity.

4.6 DISCUSSION

This consensus arose from the need to promote standardization of intraoperative RBC transfusion practice among patients undergoing non-cardiac surgery at high risk of bleeding and transfusion. The Delphi panel of experts reached consensus on 34 statements covering several key elements of intraoperative transfusion practice, including interdisciplinary collaboration, hemoglobin measurements, the use of restrictive transfusion strategies, and the integration of patient-centred consideration into transfusion practice. Important research outcomes and elements of future intraoperative transfusion clinical trials were also defined.

The ongoing inappropriate usage of blood products that has been emphasized by numerous notable stakeholder organisations.[66,67] There are many strategies that may be used to minimize the risk of inappropriate RBC transfusion, which collectively fall under the umbrella of PBM programs.[68] This document builds on other landmark PBM consensus work, such as the Practice Guidelines for Perioperative Blood Management published by the American Society of Anesthesiologists (ASA),[20] and the Recommendations From the 2018 Frankfurt Consensus Conference on PBM.[69] While these documents focused on all phases of perioperative care including the pre- and postoperative contexts, our study focused on the intraoperative period, which remains a “black box” in terms of transfusion practice. This work is particularly topical in light of the unprecedented shortages in blood products caused by the COVID-19 pandemic.[70,71] The current lack of blood supply highlights the need for appropriate utilization of this limited resource, particularly in high-use settings like the operating room.

Perhaps one of the most effective strategies to mitigate unwarranted variation in healthcare decisions are the development and implementation of clinical practice guidelines and protocols. However, there is a relative paucity of guidance available to inform intraoperative RBC transfusion decision-making. A systematic review of clinical practice guidelines supporting intraoperative transfusion concluded that identified documents failed to provide actionable guidance for clinicians, as they were either of poor quality, subspecialty specific, or made non-

specific recommendations that reinforce current practice based on best judgement.[22] For example, in their PBM Practice Guidelines, the ASA recommend the employment of multimodal protocols or algorithms as strategies to reduce the usage of blood products.[20] Furthermore, Frankfurt Consensus Recommendations on PBM generally supports the implementation of PBM programs including computerized or electronic decision support systems to improve appropriate RBC utilization.[69] However, both of these documents do not provide any guidance as to the components that should be incorporated into such intraoperative algorithms, with the ASA document noting that "no single algorithm or protocol can be recommended at this time". Furthermore, in a survey of surgeons and anesthesiologists, 44% of all physicians surveyed stated that were unaware of any intraoperative transfusion guideline. Among those that were aware of these guidelines, 46% reported that these guidelines had little or no influence on their transfusion decisions.[42] The lack of actionable recommendations and the reluctance of physicians to implement existing clinical practice guidelines highlight the need for knowledge translation efforts of work such as this. With the expansion of the knowledge base, it will be possible to homogenize transfusion practice based on best evidence and consensus opinion.

At its core, PBM is an inherently collaborative process that involves various healthcare professionals at various points in the perioperative process. This is particularly true in the operating room, where input from various members of the perioperative team may affect transfusion decisions. While clinical practice guidelines such as those published by the ASA outline various clinical factors to consider when making intraoperative transfusion decisions, the importance of communication between the surgeon and anesthesiologist in making these decisions is not emphasized. The present document and associated recommendations clearly demonstrate a broad commitment to collaboration from transfusion experts, with a consensus that intraoperative transfusion decisions should generally be shared between the anesthesiologist and surgeon. However, this sentiment was not universal; concerns about professional autonomy and role were noted, particularly within the subgroup of Canadian anesthesiologists. This is

unsurprising, as 97% of Canadian anesthesiologists surveyed in a recent study identified anesthesiologists as the primary decision-maker for intraoperative transfusion, generally without consultation with the surgical team.[72] While this may be appropriate in situations involving sudden surgical bleeding or hemodynamic instability where the surgeon's role is to resolve the source of blood loss, most intraoperative transfusions do not take place under such circumstances. When the situation permits, increased communication between the surgical and anesthesia teams about estimated blood loss, potential for future blood loss, and estimated time of remaining surgery may minimize unwarranted transfusion in situations where the indication for transfusion is equivocal.

There has been a clear movement towards restrictive transfusion strategies that have been emphasized by several landmark PBM recommendation documents.[20,69] Likewise, this consensus document recommends the integration of restrictive transfusion strategies including a restrictive hemoglobin trigger to guide intraoperative RBC transfusion. While there is some variability in the definition of a restrictive hemoglobin trigger in the literature, this panel agreed that an intraoperative hemoglobin trigger of 70 g/L was acceptable in patients without major cardiac comorbidity. However, panelists also agreed that there remains uncertainty surrounding both the benefits and risks of implementing restrictive transfusion strategies in the operating room and identified expanding the evidence base around intraoperative transfusion as an important research priority. Concurrently, this document has generated consensus on essential aspects of trial design elements, including research outcomes, clinically-important differences and reasons for protocol suspension that can be incorporated into future research.

This work has strengths. First, statements were generated after extensive background evidence gathering into intraoperative RBC transfusion practice. This included systematic reviews of clinical practice guidelines[22] and of intraoperative hemoglobin transfusion trigger trials,[58] and a systematic review of the behavioural factors influencing intraoperative transfusion practice.[73] Importantly, we also conducted in-depth qualitative interviews with both patients and physicians to develop a thorough understanding of stakeholder priorities and opinions.[59,60] Although patients

were not involved in the survey process, statements specifically addressing the integration of patient perspectives into transfusion decision-making and consent processes were included. These reflect our understanding of the patient experience with intraoperative RBC transfusion that was generated from the aforementioned qualitative interview study. Second, international leaders in intraoperative transfusion practice with experience in previous collaborative PBM activities were recruited from the spectrum of specialties involved in transfusion decision-making. This increases the credibility and applicability of recommendations to most non-cardiac surgical contexts. Finally, the high and sustained response rate across the three survey rounds ensured the validity of study results and minimized the introduction of bias due to non-response.[64]

This study also has limitations. First, although experts in transfusion were solicited internationally, the proportion of participants from outside of North America was relatively low; as such, recommendations may be less applicable to other geographic locations with different environmental context and resource considerations. Second, as all included panelists worked in academic centres, recommendations may be less applicable to community centres. Third, while all included statements reached agreement consensus by 75% of panelists, there were variations in opinions between surgeons, anesthesiologists, and hematologist in several statement categories. This means that while overall consensus may have been achieved, individual specialties may not have agreed with all included statements. Fourth, given that all panelists were content experts with a clinical and research interest in intraoperative RBC transfusion, many with experience working on similar collaborative PBM consensus work, we likely selected individuals who are more vocal and opinionated about intraoperative transfusion than the average physician in their specialty. Recommendations may therefore be less reflective of the opinions of physicians with less expertise. Finally, anesthesiologists were more heavily represented in the panel than surgeons or hematologists; however, both surgeons and hematologists were heavily involved in the study design and conduct. Anesthesiologists were considered an essential group to target in

standardising transfusion practice since they are considered the primary decision-makers for intraoperative RBC transfusion most cases.

4.7 CONCLUSIONS

This consensus statement offers expert guidance on intraoperative RBC transfusion practice for non-cardiac surgical procedures at high risk of bleeding across several key domains. By addressing an important knowledge gap, it is an advance toward minimizing unwarranted RBC transfusion variability and standardizing intraoperative RBC transfusion practice. It has also generated consensus on several salient elements of future clinical trials. Future work should emphasize knowledge translation strategies to integrate these recommendations into routine clinical practice and transfusion research activities.

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4.9 TABLES

Table 1: Expert panel participants

Last Name	First Name	Specialty	Location of Practice
Aucoin	Sylvie	Anesthesia	Ontario, Canada
Auer	Rebecca	General surgery	Ontario, Canada
Bartoszko	Justyna	Anesthesia	Ontario, Canada
Blitz	Jeanna	Anesthesia	North Carolina, USA
Breau	Rodney	Urology	Ontario, Canada
Callum	Jeannie	Transfusion medicine/hematology	Ontario, Canada
Carrier	François	Anesthesia	Quebec, Canada
Carson	Jeffrey	Transfusion medicine/hematology	New Jersey, USA
Chow	Lorraine	Anesthesia	Calgary, Canada
Ferraris	Victor	Cardiothoracic surgery	Kentucky, USA
Flexman	Alana	Anesthesia	British Columbia, Canada
Foss	Nicolai	Anesthesia	Copenhagen, Denmark
Frank	Steven	Anesthesia	Maryland, USA
Grocott	Hilary	Anesthesia	Manitoba, Canada
Hallet	Julie	General surgery	Ontario, Canada
Jerath	Angela	Anesthesia	Ontario, Canada
Jones	Philip	Anesthesia	Ontario, Canada
Karanicolas	Paul	General surgery	Ontario, Canada
McCluskey	Stuart	Anesthesia	Ontario, Canada
Meybohm	Patrick	Anesthesia	Frankfurt, Germany
Murphy	Michael	Transfusion medicine/hematology	Oxford, UK
Napolitano	Lena	General surgery	Michigan, USA
Ness	Paul	Transfusion medicine/hematology	Maryland, USA
Palmer	Antony	Orthopedic surgery	Oxford, UK
Pawlik	Timothy	General surgery	Ohio, USA
Prescott	Lauren	Obstetrics/gynecology	Tennessee, USA
Richards	Toby	Vascular surgery	Perth, Australia
So-Osman	Cynthia	Transfusion medicine/hematology	Leiden, Netherlands
Spence	Jessica	Anesthesia	Ontario, Canada
Tinmouth	Alan	Transfusion medicine/hematology	Ontario, Canada
Turgeon	Alexis	Anesthesia	Quebec, Canada
Waters	Jonathan	Anesthesia	Pennsylvania, USA
Wood	Erica	Transfusion medicine/hematology	Melbourne, Australia

Table 2: Results of Delphi survey

Statement	Consensus (>75%) reached		
	Round 1	*Round 2*	*Round 3*
The patient's baseline hemoglobin should be formally reviewed prior to every case.	88%		
The potential for intraoperative transfusion should be discussed as part of the preoperative checklist prior to every case.	97%		
The decision to initiate an intraoperative blood transfusion should be shared between the anesthesiologist and surgeon, except in cases of uncontrolled massive hemorrhage.		82%	
The anesthesiologist and surgeon should pause and discuss the indication for transfusion prior to every intraoperative transfusion event, situation permitting.			76%
In the operating room, a single unit of blood should be transfused at a time in most cases.	79%		
The ordering clinician should be prompted to provide an indication when ordering an intraoperative transfusion using an electronic medical record (EMR) system, except in cases of massive transfusion.			76%
The indication for intraoperative transfusion should be approved by the institutional blood bank and/or a transfusion medicine specialist prior to release (situation permitting).	Discarded		
The decision to administer an intraoperative transfusion should be made by the attending physician, except in cases of extreme urgency e.g., massive hemorrhage.			53%
A review of the appropriateness of intraoperative transfusion events should be formally included in the postoperative debrief.	79%		
Hospitals should establish audits of institutional intraoperative transfusion practice.	91%		
Groups of anesthesiologists and/or surgeons should review the appropriateness of their intraoperative transfusion events regularly.	91%		
Point-of-care devices to measure hemoglobin (e.g.: HemoCue, iSTAT, non-invasive pulse co-oximeters, blood gas analyzers) are accurate enough to guide intraoperative transfusion.	88%		
Point-of-care hemoglobin devices should be routinely used to measure hemoglobin to guide intraoperative transfusion.	78%		
Point-of-care hemoglobin measurements should be confirmed with a central lab measurement (i.e., CBC) prior to intraoperative transfusion except in cases of extreme urgency e.g., massive hemorrhage.			39%
A margin of error of 4 g/L (0.4 g/dL) (the Allowable Performance Limit defined by the Institute for Quality Management in Healthcare [IQMH]) is acceptable for point-of-care hemoglobin testing devices in the operating room.		78%	
Hemoglobin should routinely be measured at set time points in the operating room.	Discarded		
Hemoglobin should only be measured in the operating room if determined to be clinically indicated.	76%		
Hemoglobin should be routinely measured before every intraoperative transfusion if the situation permits.	85%		
When the situation permits, hemoglobin should be routinely measured within 1 hour after an intraoperative transfusion episode (which could include more than 1 unit).			67%

Hemoglobin should be measured between successive intraoperative transfusions in cases where multiple units are being transfused (situation permitting).	76%		
In general, intraoperative transfusions should be guided by a predetermined algorithmic transfusion protocol.	79%		
A hemoglobin threshold or trigger should generally be used to guide intraoperative transfusion as part of a broader transfusion strategy.		82%	
Restrictive transfusion strategies should be adopted for intraoperative transfusions, which would include a restrictive hemoglobin transfusion threshold/trigger.		82%	
Patients should always be informed that they received a blood transfusion during their surgery.	97%		
Patient preferences should be incorporated into intraoperative transfusion decision-making.	88%		
Transfusion decisions made in the operating room should take into account the patients' previously stated perioperative goals of care regarding blood products.	91%		
Preoperative consent to intraoperative blood transfusion should include a presentation of the risks and benefits.	97%		
Preoperative consent discussions should emphasize the spectrum of risk associated with transfusion.	94%		
Preoperative consent discussions should emphasize the spectrum of risks associated with anemia.	91%		
Patient's perception of the spectrum of risk associated with transfusion and anemia should be explicitly considered when making intraoperative transfusion decisions on their behalf.	79%		
A stronger evidence base is needed to guide intraoperative transfusion decision-making.	91%		
Expanding the evidence base around intraoperative transfusion is an important research priority.	94%		
There is uncertainty surrounding the benefits of restrictive transfusion protocols in the operating room.	76%		
There is uncertainty surrounding the risks of restrictive transfusion protocols in the operating room.	79%		
A restrictive transfusion protocol including a restrictive hemoglobin transfusion trigger would be feasible to implement in the operating room.	76%		
I would be willing to participate in a two-arm interventional trial evaluating restrictive and liberal transfusion protocols.	87%		
I would be willing to participate in a 3-arm randomized trial evaluating restrictive and liberal transfusion strategies that includes a usual care arm.			76%
70 g/L (7 g/dL) is an acceptable restrictive hemoglobin trigger to use in the operating room in patients without major cardiac comorbidities.	79%		
90 g/L (9 g/dL) is an acceptable liberal hemoglobin trigger to use in the operating room as part of a clinical trial.			79%

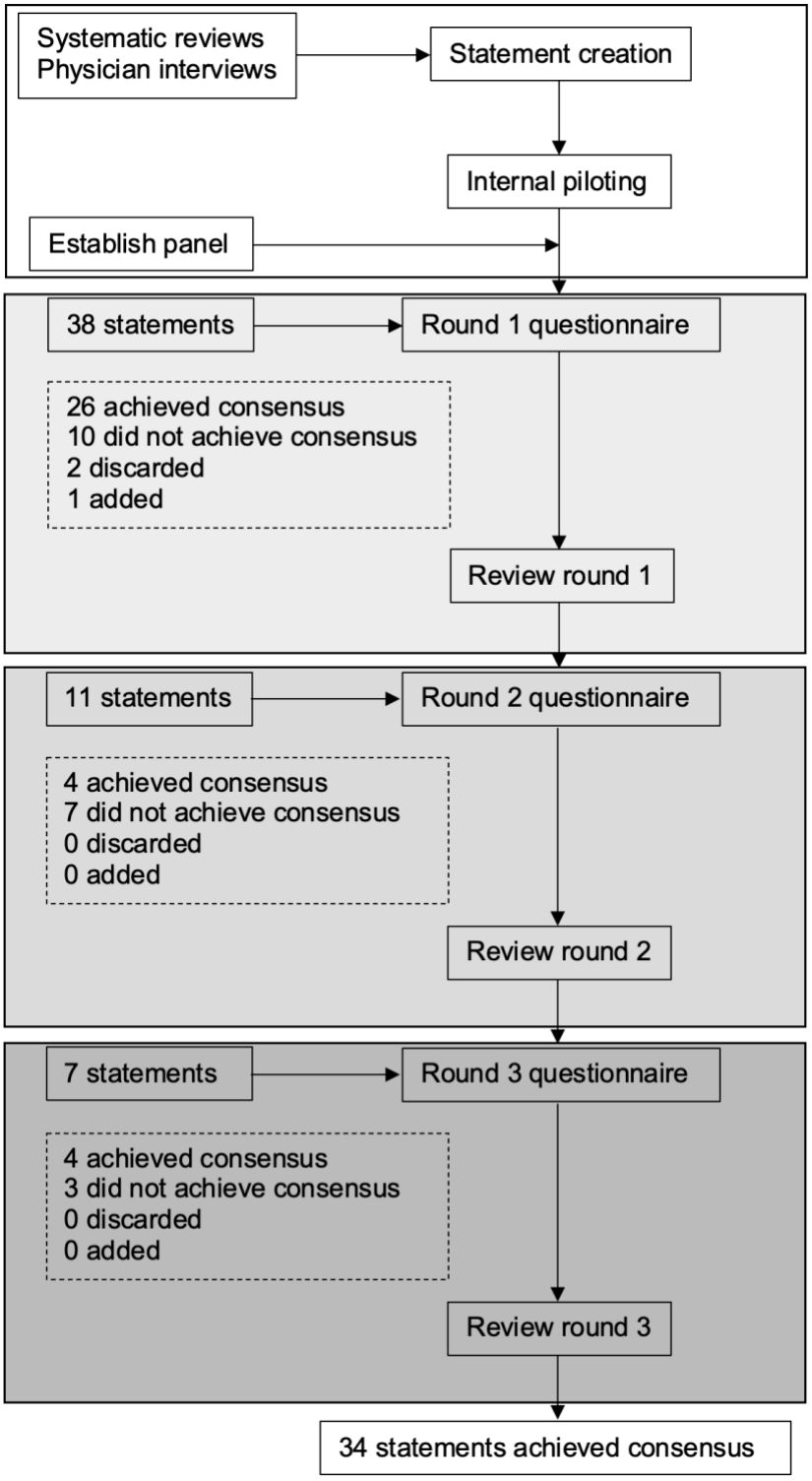
Table 3: Summary of recommendations for intraoperative RBC transfusion

	Recommendations
Interprofessional communication	The patient's baseline hemoglobin should be formally reviewed prior to every case.
	The potential for intraoperative transfusion should be discussed as part of the preoperative checklist prior to every case.
	The decision to initiate an intraoperative blood transfusion should be shared between the anesthesiologist and surgeon, except in cases of uncontrolled massive hemorrhage.
	The anesthesiologist and surgeon should discuss the indication for transfusion prior to intraoperative transfusion, except in cases of extreme urgency e.g., massive hemorrhage.
	A review of the appropriateness of intraoperative transfusion events should be formally included in the postoperative debrief.
Hemoglobin measurement	Point-of-care devices to measure hemoglobin (e.g.: HemoCue, iSTAT, non-invasive pulse co-oximeters, blood gas analyzers) are accurate enough to guide intraoperative transfusion.
	Point-of-care hemoglobin devices should be routinely used to measure hemoglobin to guide intraoperative transfusion.
	A margin of error of 4 g/L (0.4 g/dL) (the Allowable Performance Limit defined by the Institute for Quality Management in Healthcare [IQMH]) is acceptable for point-of-care hemoglobin testing devices in the operating room.
	Hemoglobin should only be measured in the operating room if determined to be clinically indicated.
	Hemoglobin should be routinely measured before every intraoperative transfusion if the situation permits.
	Hemoglobin should be measured between successive intraoperative transfusions in cases where multiple units are being transfused (situation permitting).
Procedural considerations and audits	In the operating room, a single unit of blood should be transfused at a time in most cases.
	The ordering clinician should be prompted to provide an indication when ordering an intraoperative transfusion using an electronic medical record (EMR) system, except in cases of massive transfusion.
	Hospitals should establish audits of institutional intraoperative transfusion practice.
	Groups of anesthesiologists and/or surgeons should review the appropriateness of their intraoperative transfusion events regularly.
	A hemoglobin threshold or trigger should generally be used to guide intraoperative transfusion as part of a broader transfusion strategy.
	In general, intraoperative transfusions should be guided by a predetermined algorithmic transfusion protocol.
Restrictive transfusion strategies	There is uncertainty surrounding the benefits of restrictive transfusion protocols in the operating room.
	There is uncertainty surrounding the risks of restrictive transfusion protocols in the operating room.
	A restrictive transfusion protocol including a restrictive hemoglobin transfusion trigger would be feasible to implement in the operating room.
	Restrictive transfusion strategies should be adopted for intraoperative transfusions, which would include a restrictive hemoglobin transfusion threshold/trigger.

Patient-centered considerations	Patients should always be informed that they received a blood transfusion during their surgery.
	Patient preferences should be incorporated into intraoperative transfusion decision-making.
	Transfusion decisions made in the operating room should take into account the patients' previously stated perioperative goals of care regarding blood products.
	Preoperative consent to intraoperative blood transfusion should include a presentation of the risks and benefits.
	Preoperative consent discussions should emphasize the spectrum of risk associated with transfusion.
	Preoperative consent discussions should emphasize the spectrum of risks associated with anemia.
	Patient's perception of the spectrum of risk associated with transfusion and anemia should be explicitly considered when making intraoperative transfusion decisions on their behalf.
Research considerations	A stronger evidence base is needed to guide intraoperative transfusion decision-making.
	Expanding the evidence base around intraoperative transfusion is an important research priority.
	I would be willing to participate in a 2-arm interventional trial evaluating restrictive and liberal transfusion protocols.
	I would be willing to participate in a 3-arm randomized trial evaluating restrictive and liberal transfusion strategies that includes a usual care arm.
	70 g/L (7 g/dL) is an acceptable restrictive hemoglobin trigger to use in the operating room in patients without major cardiac comorbidities.
	90 g/L (9 g/dL) is an acceptable liberal hemoglobin trigger to use in the operating room as part of a clinical trial.

4.10 FIGURES

Figure 1: Process used to achieve consensus for statements



CHAPTER 5. INTEGRATED DISCUSSION

The operating room remains a black box regarding red blood cell (RBC) transfusion. My thesis work has explored various facets of intraoperative RBC transfusion and elicited crucial stakeholder perspectives with the overarching goal of minimizing unwarranted intraoperative RBC transfusion variability.

In Chapter 2, I used patient interviews to explore previously under-researched perspectives about intraoperative transfusion. Given the significant observed intraoperative transfusion variability between hospital and individual physicians, these perspectives may be incorporated into individual transfusion decisions and more broadly into future guideline development. There is a clear need for improvements to our preoperative blood consent discussions and to increase patient engagement in transfusion prevention strategies.

In Chapter 3 and Appendix 1, physician interviews and a systematic review based on the Theoretical Domains Framework (TDF) provided valuable insights about the behavioural drivers of intraoperative transfusion that likely explain a significant portion of the observed variability in transfusion practice. They highlighted that intraoperative transfusion continues to be perceived as a knowledge gap and identified several modifiable factors that influence intraoperative RBC transfusion. The findings will allow for the implementation of evidence- and theory-based interventions aimed at decreasing intraoperative transfusion variability.

Finally, in Chapter 4, I present the results of a Delphi study that was used to generate consensus among international blood transfusion experts about intraoperative transfusion strategies that could be implemented to improve transfusion practice in the operating room. It has also allowed the identification of important research priorities and outcomes. Having obtained expert consensus on critical study design elements and important research outcomes, the findings of this Delphi study will be useful to the conduct of future clinical trials.

One of the mains themes of this thesis was the role of integrating patient preferences into intraoperative transfusion decisions. Patients in the perioperative interviews expressed a desire for their opinions and perspectives to be considered when transfusion decisions are made on their behalf in the operating room. However, patient preferences were not identified by physicians as a significant influence when making intraoperative transfusion decisions. This was reinforced in the systematic review presented in Appendix 1, wherein only one study addressed the influence of patient preference on these decisions, noting that less than 25% of physicians reported that their transfusion decisions were significantly impacted by patient preference.[1] Interestingly, in the Delphi study, physicians reached consensus on a range of statements reinforcing the importance of incorporating preferences and perioperative goals of care regarding blood products into intraoperative transfusion decisions. As such, there is a clear discrepancy as to what patients and physicians believe should be done and what is done in practice. There may be several explanations for this discrepancy. For instance, preoperative blood consent discussions are likely inadequate to generate a detailed understanding of patient preferences regarding intraoperative transfusion. This was clearly demonstrating during patient interviews, where many had no recollection of their transfusion consent discussion. Furthermore, some patients were unwilling to participate in these discussions, preferring to delegate transfusion decisions entirely to the perioperative team. Second, physicians may feel uncomfortable having these discussions with patients, as we lack high-quality evidence as to the ideal intraoperative transfusion strategy. However, it is clear that both patients and physicians alike recognize the importance of incorporating patient preferences and opinion into intraoperative transfusion decisions, and that transfusion consent and decisions must be personalized to individual patient values.

Although this work is relevant to all stakeholders including surgeons, anesthesiologists, blood bankers, and policy-makers, surgical patients are the ones most affected by transfusion decisions made on their behalf during surgical interventions. As such, we have ensured the integration of patient perspectives throughout all aspects of this work. For instance, a committee

of three patient advisors was assembled to review study materials for the patient interview study presented in Chapter 2. The impact of patient preference on intraoperative transfusion decisions was explicitly explored in the physician interviews, and consensus was obtained on a variety of patient-centred items in the Delphi process. This included recommendations to improve preoperative transfusion consent discussions and explicitly considering patient preferences and values when making intraoperative transfusion decisions. We plan to continue engaging these patient advisors by having them review the recommendations put forth from the Delphi consensus and including them in the dissemination of research findings to the public.

The importance of interdisciplinary collaboration when making intraoperative transfusion decisions and the relative roles of anesthesiologists and surgeons in making these decisions were also major themes identified in this thesis. In the Delphi study, physicians demonstrated a clear commitment to collaboration, agreeing that input from both anesthesiologists and surgeons is essential to optimize intraoperative transfusion decision-making. This sentiment was also echoed in the physician interviews, wherein physicians expressed that communication between surgery and anesthesiology teams is helpful to make the correct transfusion decision, particularly in situations where the transfusion indication is equivocal. The professional role of surgeons and anesthesiologists in making intraoperative transfusion decisions was identified in the systematic review, where there appeared to be variability as to the primary decision-maker for intraoperative transfusion. On the whole, this thesis identified anesthesiologists as the main group responsible for intraoperative transfusion, particularly in situations of uncontrolled surgical bleeding. However, incorporating the surgical team into these decisions is essential and strategies to do so should be integrated into routine clinical practice. The Delphi study identified several such strategies to improve intraoperative communication about transfusion between perioperative team members, including adding a discussion about transfusion into the preoperative surgical pause, instituting a mandatory time-out prior to each intraoperative transfusion to discuss the indication (situation permitting), and a routine review of intraoperative transfusion events in the postoperative debrief

to discussion transfusion appropriateness. Improving intraoperative collaboration between the anesthesiology and surgical teams as it related to transfusion decisions is likely to facilitate decision-making and reduce unwarranted intraoperative RBC transfusion.

In addition to the interaction between anesthesiologists and surgeons, this thesis has explored various other factors unique to the intraoperative environment that affect transfusion decisions. In the physician interviews and systematic review based on the TDF, a variety of environmental, social, and cognitive factors were identified as impacting intraoperative transfusion decision-making. While patient blood management strategies have largely focused on clinical factors such as hemoglobin transfusion triggers, patient hemodynamics, and surgical blood loss to guide intraoperative RBC transfusion, it is clear that the observed variability in transfusion practice cannot be addressed without considering these so-called "non-clinical" socio-behavioural factors that heavily impact transfusion decision-making. Strategies to improve intraoperative transfusion decision-making taking these factors into account were discussed in both the physician interviews and the Delphi study. These include provider- and institution-level intraoperative transfusion audits and implementing educational sessions to review the evidence underlying best transfusion practice. Perhaps the most impactful method to standardize intraoperative transfusion practice would be the implementation of a transfusion algorithm specific to the intraoperative period. Existing intraoperative transfusion guidelines are limited, and do not adequately consider the impact of the operative environment on transfusion decisions. A systematic review of clinical practice guidelines supporting intraoperative transfusion conducted by our research group found that the identified documents were either of poor quality, subspecialty specialised, or gave non-specific suggestions that reinforced current practice based on best judgement.[2] In our physician interviews, anesthesiologists and surgeons identified a clear need for evidence-based protocols to guide intraoperative RBC transfusion. However, they also expressed that the evidence base underlying intraoperative transfusion is currently insufficient to guide transfusion practice. This was reflected in a wide variety of beliefs about the effects of both

intraoperative transfusion and anemia. This was also identified among several articles included in the systematic review presented in Appendix 1. This significant variability in beliefs likely explains the substantial transfusion practice heterogeneity observed in the literature. Uncertainty about the benefits and risks of implementing restrictive transfusion strategies in the operating room was identified in both the physician interviews and Delphi consensus studies. Despite this, in the Delphi study, transfusion experts were able to reach consensus on various aspects of an intraoperative transfusion protocol, including the implementation of a restrictive hemoglobin transfusion trigger of 70 g/L. There is clearly a need for expanding the evidence base underlying intraoperative transfusion and to develop intraoperative transfusion decision-making aids specific to the intraoperative context to decrease transfusion variability and unwarranted transfusion. The Delphi study provides guidance as to salient elements of future research studies that would help to do this, having obtained consensus on aspects such as study design, elements of an intraoperative transfusion algorithm, and relevant transfusion-related outcomes.

Overall, my thesis has evaluated and synthesized important stakeholder perspectives about intraoperative RBC transfusion and expanded our understanding of how and why these decisions are made in the operating room. This work is a crucial step towards homogenizing intraoperative transfusion practice with the goal of minimizing unwarranted intraoperative transfusion.

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CHAPTER 6. ACKNOWLEDGEMENTS

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CHAPTER 8. APPENDICES

8.1 APPENDIX 1: Non-clinical factors affecting intraoperative red blood cell transfusion: A systematic review using the Theoretical Domains Framework

Tori Lenet,[1,2] Pauline Berthelot,[3] Alexa L Grudzinski,[4] Alexander Banks,[1] Joseph Tropiano,[1] Daniel I McIsaac,[4] Alan Tinmouth,[5,6] Andrea M Patey,[2] Dean A Fergusson,[2,6] Guillaume Martel[1,2]

Affiliations:

[1]Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

[3]Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada

[4]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[5]Department of Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada

[6]Canadian Blood Services, Ottawa, Ontario, Canada

PREFACE

In conjunction with the interview study presented in Chapter 3, we performed a systematic review of studies that discussed the non-clinical drivers of intraoperative RBC transfusion practice using the Theoretical Domains Framework to organize these factors. The following manuscript is presented as an addition to the main three manuscripts presented in Chapters 2, 3, and 4 as an appendix, as it was not initially included in the thesis outline.

ABSTRACT

Introduction: There is significant variability in intraoperative red blood cell (RBC) transfusion practice. The non-clinical and behavioural factors underlying this variability have not been comprehensively investigated. Our aim was to systematically review the literature to identify the non-clinical and behavioural drivers of RBC transfusion practice in the operating room and categorize these factors using the Theoretical Domains Framework (TDF).

Methods: MEDLINE, Embase, and Web of Science were searched from inception until August 2021 to identify studies evaluating non-clinical factors influencing intraoperative RBC transfusion. Title, abstract, and full text screening were conducted in duplicate independently. The quality of included studies was assessed using the Mixed Methods Appraisal Tool (MMAT). Non-clinical factors deemed to be relevant to intraoperative RBC transfusion decision-making were identified and coded into the appropriate domain of the TDF using NVivo by two independent reviewers. Common themes were then identified within the domains. Domains were sorted based on the number of studies reporting factors within those domains.

Results: Nineteen studies including nine retrospective cohort studies, six cross-sectional survey studies, three before-and-after studies, and one review article were identified for inclusion. Factors most frequently reported in the included studies pertained to the **Social influences, Behavioural regulation, Environmental context/resources,** and **Beliefs about consequences** domains of the TDF. Key factors underlying the observed variability in transfusion practice included the social effects of peers, patients, and local institutional culture on decision-making (**Social influences**), and various environmental characteristics of the practice environment such as case volume, geographic location, and case start time (**Environmental context/resources**). Studies reported a variety of beliefs about the consequences of both intraoperative transfusion and anemia among physicians (**Beliefs about consequences**). Provider- and institutional-level audits, educational sessions, and increased communication

between surgeons and anesthesiologists were identified as useful strategies to optimize intraoperative transfusion decision-making (**Behavioural regulation**).

Discussion: Our review has synthesized the literature describing non-clinical and behavioural factors underlying intraoperative transfusion decision-making and categorized these factors using the TDF. These results can be used to design future evidence- and theory-based interventions aimed at decreasing intraoperative RBC transfusion variability.

INTRODUCTION

Background and rationale

Red blood cell (RBC) transfusions are a common intervention among patients undergoing major surgery. Transfusion decision-making during surgery is a complex and dynamic process, as physiological and biochemical markers traditionally used to guide transfusion decision-making can be influenced by acute blood loss, surgical manipulation and positioning, and potent pharmacological agents.[1] There is evidence of significant variation in transfusion practice during surgery.[2–5] Although some variation is expected based on case mix, the bulk of variation not explained by disease severity or patient preference likely reflects inappropriate clinical care due to under- or over-transfusion.[6–8] In one study, two patients with the same characteristics and risk profiles had a 30% difference in their odds of transfusion when treated by different physicians or hospitals.[9] Efforts to standardized intraoperative transfusion have focused mainly on objective physical parameters such as hemoglobin transfusion triggers.[10] However, little research has been done to explore non-clinical and behavioural factors that underlie intraoperative transfusion decision-making. There are complex interpersonal, environmental institutional, and psychological factors that influence the decision to transfuse RBCs in the operating room and likely explain much of the observed inter-physician variability in transfusion behaviour.

The theoretical domains framework (TDF) is a framework that was developed to explore factors influencing clinical behaviour.[11] The TDF is increasingly being used to structure systematic reviews by synthesizing influences on behaviours across studies according to theoretical domains. Findings can then be used to design theory-informed implementation interventions, which in this case would aim to decrease intraoperative RBC transfusion variability.

Purpose

The aim of this review is to identify non-clinical and behavioural factors that influence intraoperative RBC transfusion decision-making. More specifically, we seek to understand the psychological, social, environmental, and contextual factors that influence transfusion decisions made in the operating room.

METHODS

This systematic review was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Appendix 1).[12] The protocol was developed prospectively and registered with Open Science Framework and is available at: https://osf.io/pm8zs/?view_only=166299ed28964804b9360c429b1218c1.

Search strategy

The search strategy was developed in consultation with an experienced librarian in the healthcare field and is presented in Appendix 2. The term "blood transfusion" was combined using the Boolean operator "or" with terms related to the following topics: shared care (e.g., team-based cared), behaviour (e.g., intention-behaviour relation, decision-making) and non-technical skills (e.g., prognostic factors, attitudes). Similarly, these latter terms were combined with each other using the same Boolean operator "or".

Information sources

The following databases were searched from inception until August 5th, 2021: Ovid MEDLINE, Embase, and Web of Science. The first 100 hits of Google Scholar were also reviewed to include the grey literature. Reference lists of any relevant systematic reviews were also reviewed to identify eligible studies. All citations identified from the literature searches were de-duplicated and exported into Covidence.

Eligibility criteria

Studies describing any non-clinical or behavioural factor influencing intraoperative RBC transfusion decisions were included. Studies were eligible only if they specifically focused on the intraoperative period, rather than the pre-, post-, or any non-operative context. Studies of healthcare professionals (i.e., anesthesiologists and surgeons) involved in intraoperative

transfusion decisions and studies using patient transfusion data were both eligible for inclusion. All study designs were considered for inclusion except editorials and systematic reviews. Published abstracts were considered for inclusion provided they reported enough information to contribute to the review. Only studies published in English or French were considered for inclusion. Studies that reported clinical factors only influencing intraoperative transfusion were excluded; this included studies reporting on hemoglobin triggers, preoperative autologous transfusion, intraoperative cell salvage, intraoperative tranexamic acid, or thromboelastometric testing. Studies exclusively reporting on transfusion of blood products other than RBCs were excluded.

Study Screening

Titles and abstracts were screened independently and in duplicate by a team of three reviewers (PB, AB, TL). Full texts of potentially eligible studies identified in the first stage of screening were then obtained reviewed for eligibility independently and in duplicate by the same team of reviewers. Disagreements were resolved either by consensus or in consultation with a senior investigator (GM).

Data collection

Following full text review assessment of eligibility, included studies were imported into NVivo (QSR International Pty Ltd). Data on study characteristics including year of publication, location, study design, aim, study population, setting, and data collection method were extracted. Next, using the NVivo coding software, factors deemed to be relevant intraoperative RBC transfusion decision-making were identified from included studies and coded into the appropriate theoretical domain of the TDF. Coding was performed independently and in duplicate by two reviewers (PB, AG) and subsequently reviewed with a third author (TL). Disagreements were resolved by consensus or by a senior author.

Quality assessment

The quality of studies was assessed independently and in duplicate using the Mixed Methods Appraisal Tool (MMAT).[13] The MMAT is designed to be used as a checklist for concurrently rating and/or describing papers in systematic reviews that include various study designs (i.e., reviews including qualitative, quantitative and mixed methods studies). Non-randomized studies were assessed using Section 3; it includes items pertaining to participant recruitment, outcome measurements, group comparability, and completeness of outcome data. Descriptive studies were assessed using Section 4, which has components pertaining to appropriate sampling procedure, the representativeness of the sample, outcome measurements, and an acceptable response rate. The overall quality score is calculated based on the percentage of quality criteria met by each study.

Data synthesis and analysis

Factors deemed to be relevant to intraoperative transfusion decision-making were extracted from included studies and listed. Each extracted factor was then classified according to the TDF into one of its 14 domains. A description of the theoretical domains is presented in Appendix 3. The domains were then sorted based on the number of studies reporting a factor related to that domain. The number of studies describing the same theme within a domain was also considered when analyzing the data to determine which non-clinical factors have been most reported to influence intraoperative transfusion decision-making.

RESULTS

Following deduplication, 3089 unique citations were identified by the literature searches. After title and abstract screening, 114 full text articles were assessed for final eligibility, and 19 studies were included in this review (Table 1). Reasons for full text exclusion are detailed in Figure 1. Included studies were published between 1990 and 2020. The majority of studies were conducted in the United States (n=12), with the others being conducted in Canada (n=3), Asia (n=2), Europe (n=1), and Australia (n=1). Study designs included nine retrospective cohort studies,[2,5,14,15,15–19] six cross-sectional survey-based studies,[20–25] three before-and-after studies,[26–28] and one narrative review.[29] Cross-sectional studies used a variety of survey administration techniques including self-administration and interviewer-assisted, involving both electronic, paper, and mailed formats. Ten studies included patients as the unit of study,[2,14–20,28,30] while seven surveyed a variety of physicians including surgeons and anesthesiologists,[20,22–27] and one surveyed institutions about organizational-level blood management practices.[21] Eleven studies focused only on physicians or patients performing or undergoing cardiac surgery procedures.[5,14–19,21,25,26,30] All but one included study were full text papers, with one published abstract included.[28]

Study quality assessment

The MMAT tool was used to assess the quality of 18 studies. The quality of the narrative review by Irita et al.[29] was not assessed, as the MMAT cannot be used to assess this type of study. The results are presented in Table 2. Of the 18 studies assessed, three met 100% of the quality criteria,[5,15,30] 11 met 80%,[2,14,16,17,19–25] three met 60%,[18,26,27] and one met 20%.[28] Non-randomized quantitative comparative studies were most commonly downgraded for not reporting missing outcome data (criteria 3.3) and not adequately controlling for confounding in their statistical analysis (criteria 3.4). Quantitative non-comparative studies were most frequently downgraded for not adequately describing the characteristics of their sample relative to their

target population (criteria 4.2) and for the possibility of non-response bias impacting their results (criteria 4.4).

Factors affecting intraoperative transfusion

A total of 53 behavioural factors influencing intraoperative RBC transfusion were identified and categorized into ten domains (Table 3). Domains are reported in descending order based on the number of studies that reported factors related to each domain (Figure 2).

Social influences

Twelve studies reported the impact of **Social influences** on intraoperative transfusion decision-making.[2,5,15–21,23–25] These included the influence of colleagues on transfusion decisions, as well as the impact of patient preferences on these decisions. The effect of local institutional culture on intraoperative transfusion decisions was reported by 10 studies, the most of any factor in this review.

Behavioural regulation

Eight studies described factors related to the **Behavioural regulation** domain.[14,17,21,23,26–29] Several strategies to improve intraoperative transfusion decision-making were described and/or tested. Institutional transfusion guidelines were reported to be helpful in guiding intraoperative transfusion practice in four studies.[14,21,27,29] Effective communication between the anesthesiologist and surgeon was noted to be essential to guide intraoperative transfusion,[17,29] and was shown to decrease intraoperative transfusion and postoperative anemia in one study.[28] Provider-level intraoperative transfusion audits were reported to decrease transfusion rates in two studies,[21,26] with another two studies discussing the importance of hospital-level transfusion audits and feedback.[17,29] Educational sessions were also reported to reduced unwarranted RBC transfusion.[23]

Environmental context/resources

The effects of **Environmental context and resources** on intraoperative transfusion practice were discussed by seven studies.[2,5,14,21,23,29,30] Several environmental factors were associated with increased rates of intraoperative transfusion including later case start times,[14] academic hospital settings,[5] geographic region,[5] and lower hospital case volumes.[2,5] Other factors such as team changeover did not appear to affect intraoperative transfusion.[30] Resource considerations including local blood product availability and the presence of RBC units in the operating room also did not appear to significantly affect intraoperative transfusion decisions.[21,23]

Beliefs about consequences

Beliefs about the consequences of transfusing and not transfusing were reported by seven studies.[2,2,14,22–24,27] Beliefs reported to affect intraoperative transfusion decisions included the legal repercussions of not transfusing[27] and the morbidity associated with transfusion.[22] Physicians tended to overestimate the consequences of both transfusing and not transfusing; physicians reporting personal experience with anemia-related complications were more likely to both overestimate the risks associated with anemia and to have higher rates of appropriate transfusion.[23] Physicians were reported to weigh the benefits of intraoperative transfusion more heavily than the risks.[14,23] The financial cost of intraoperative transfusion did not appear to affect transfusion decisions.[23] Significant variability in beliefs about the effects of transfusion and anemia was identified, resulting in substantial practice heterogeneity.[2,27]

Knowledge

Knowledge of the evidence underlying intraoperative transfusion decision-making was reported by five studies.[2,17,23,24,27] The evidence underlying intraoperative transfusion practice was reported as poor and was thought to contribute to increased variability in transfusion practice.[2,27]

Physicians felt that transfusion-related education provided during medical training was insufficient, and that it was difficult to stay up to date with the published evidence underlying intraoperative transfusion.[27] Poor transfusion knowledge was associated with higher rates of inappropriate transfusion.[24] Knowledge deficiencies about intraoperative transfusion were reported as widespread, with most physicians not routinely using published intraoperative RBC transfusion guidelines.[17,23]

Social/professional role and identity

The **professional role** of surgeons and anesthesiologists in making intraoperative transfusion decisions was discussed in five studies.[15,20,22,24,27] There appeared to be variability among studies as to the primary decision-maker for intraoperative transfusion. One study identified the anesthesiologist as the primary decision-maker,[20] another reported that transfusion decisions are multidisciplinary,[15] and another reported uncertainty regarding the primary decision-maker, even within a single institution.[24] One study reported that surgeons are more likely to transfuse at higher hemoglobin values compared to anesthesiologists.[22]

Nature of the behaviours

Five studies reported factor categorized into the **Nature of the behaviours** domain.[15,20,22,23,27] Physicians reported that their transfusion practice has become more restrictive over the course of their careers.[20] Physicians appeared to be more concerned about committing errors of omission than errors of commission, leading them to be more likely to transfuse rather than to observe in situations where the indication for transfusion is equivocal.[23] These individual differences in transfusion practice were reported to be related to the degree of interventionism or non-interventionism of the physician.

Memory, attention, and decision processes

Four studies discussed factors related to the **Memory, attention, and decision processes** domain,[2,14,27,29] including the effect of decision fatigue[14] and mental stress[29] on intraoperative transfusion decision-making. The observed variability in intraoperative transfusion practice between physicians was attributed to errors in reasoning and oversimplification,[27] and difficulty predicting future blood loss.[29] The decision processes underpinning intraoperative transfusion were noted to be a complex sequence of decisions involving numerous healthcare professionals.[2]

Beliefs about capabilities

Factors associated with belief about individual capability to make intraoperative transfusion decisions were reported in two studies.[23,27] Lack of self-efficacy was associated with higher rates of inappropriate intraoperative transfusion, and higher levels of confidence were associated with lower transfusion knowledge. Older physicians were reported to be more confident in their transfusion practice.

Motivation and goals

Only one study discussed factors that motivated intraoperative transfusion decision-making, stating that physicians are generally motivated to make decisions that they deem are in the patient's best interest.[27]

DISCUSSION

Factors most frequently reported in the included studies pertained to the **Social influences, Behavioural regulation, Environmental context/resources,** and **Beliefs about consequences** domains of the TDF. Key factors underlying the observed variability in transfusion practice included the social effects of peers, patients, and local institutional culture on decision-making (**Social influences**), as well as various environmental characteristics of the practice environment such as volume, geographic location, and case start time (**Environmental context/resources**). Physicians often held varying beliefs about the consequences of both intraoperative transfusion and anemia (**Beliefs about consequences**). Studies reported several strategies to optimize intraoperative transfusion decision-making including provider- and institutional-level audits, educational sessions, and increased communication between surgeons and anesthesiologists (**Behavioural regulation**).

The social influences and environmental factors underlying intraoperative RBC transfusion decisions were among the most cited factors in included studies. Social norms have a significant impact on human behaviour; people constantly gauge and shape their actions based on those of their peers, rarely departing from social standards. Accordingly, this also governs clinical decisions made by physicians, wherein social norms are formed at the levels of the profession, institution, and peer group.[31] The effect of peers on intraoperative transfusion decisions was commonly discussed in included studies. For instance, one survey-based study reported that half of all attending physicians reported having changed their minds about whether or not to give a patient a transfusion at least once a month based on the advice of colleagues.[23] The importance of joint decision-making was further highlighted by another study, which implemented a mandatory discussion of intraoperative transfusion strategies in the pre-operative timeout between the anesthesiologist and surgeon,[28] resulting in a 40% reduction of the rate of intraoperative RBC transfusion. Peer pressure from other physicians has been reported as an

influential factor for other healthcare decisions, including physician hand hygiene[32] and patient disposition in the emergency department.[33]

The effect of local institutional culture was also commonly discussed in included studies. Medical trainees are exposed to practice standards through a combination of local practice styles, specialty-specific techniques, and general professional behavioural norms.[34] In this review, local institutional culture was the most studied non-clinical factor driving intraoperative transfusion practice, with included studies reporting that hospital characteristics accounted for between 20%[25] and 70%[17] of the observed variability in RBC transfusion practice in the operating room. This underlines the importance of institutional norms and hospital-wide blood management programs in optimizing intraoperative transfusion practice and minimizing unwarranted transfusion.

Interestingly, only one study discussed the influence of patient preference on intraoperative transfusion decision-making. In this survey study by Salem-Schatz, while the majority of physicians (85%) agreed that the patient's wishes should be taken into account when deciding whether or not to order an RBC transfusion in the intraoperative period, only 23% said that their transfusion decisions were significantly influenced by patient preference.[23] Thus, there appeared to be a discrepancy between what physicians think should be done compared to what is actually done. The Blood Transfusion Priority Setting Partnership has highlighted the best communication with patients regarding their options related to transfusion and its alternatives as an area of uncertainty.[35] While some patients may wish to defer intraoperative transfusion decisions entirely to the surgical team, others wish for their preferences to be incorporated into transfusion decisions made on their behalf while under anesthesia. For instance, a recent survey study found that 40% of patients wanted to discuss transfusion choices with the medical staff.[36] Therefore, there is likely a role for incorporating patient preferences and values into transfusion decisions, particularly when the indication for transfusion is equivocal.

While many studies focused on the social and environmental factors influencing intraoperative transfusion behaviour, others emphasized the impact of individual practice patterns

on intraoperative transfusion variability. Despite published intraoperative transfusion guidelines by prominent organizations,[37–39] provider-level factors continue to heavily influence transfusion decisions; one study by Shehata et al. reported that up to 80% of the variance in transfusion practice is due to individual physician characteristics.[25] Included studies describe a variety of factors that may underlie this practice variation. Firstly, physicians generally perceive the quality of the available evidence guiding intraoperative transfusion practice as poor, preventing uptake of published transfusion guidelines and perpetuating so-called "inertia" of previous practice.[27] Furthermore, variation in beliefs about the consequences of both intraoperative transfusion and anemia compounded with individual previous experience with the complications of both are also described as influencing transfusion practice. Other factors related to the nature of transfusion behaviours that underlie physician-level practice variation include the general interventionist or noninterventionist tendencies of physicians and the propensity for physicians to be more concerned about errors of omission (i.e., the consequences of non-transfusion) rather than errors of commission (i.e., the consequences of giving a transfusion). Finally, transfusion decisions may also be modified by factors such as decision fatigue, errors in reasoning, oversimplification, and mental stress. The influence of these physician-level factors may be minimized by using strategies such as educational sessions about the evidence underlying intraoperative transfusion or implementing evidence-based intraoperative transfusion algorithms to guide decision-making.

The main strengths of this review lie in its methodological rigour. Using the TDF to synthesize and categorize the behavioural factors underlying intraoperative transfusion decision-making has allowed for the identification of modifiable behaviours which can be integrated into future interventions aimed at reducing transfusion variability and unwarranted RBC transfusion. These include individual and hospital-wide transfusion audits, educational programs, institutional intraoperative transfusion algorithms, and strategies to increase intraoperative communication between physicians involved in transfusion decision-making. Each of these were shown to significantly decrease transfusion rates in the operating room, underscoring the influence of these

behavioural factors on transfusion decisions. Unfortunately, given the limited number of studies testing each strategy, we were unable to calculate an aggregate effect size to quantify the degree to which they reduce intraoperative transfusion.

The limitations of this review are largely related to the nature of the available data published in the literature. While there has been extensive research into the clinical factors that influence intraoperative transfusion (including hemoglobin triggers), relatively little attention has been paid to the effects of non-clinical and behavioural factors on these decisions. These factors likely have a stronger influence on transfusion decisions in the intraoperative context than in the non-operative environment because of the unique nature of the intraoperative setting. For example, while these decisions are usually made by a single healthcare provider in the nonoperative setting, multiple individuals including surgeons, anesthesiologists, and perfusionists may influence transfusion decision-making in the operating room. Further, factors such as the potential for major surgical blood loss and the perceived consequences of intraoperative anemia are not present in the non-operative setting and are likely to significantly impact the decision processes underlying intraoperative transfusion. Only 19 studies were identified in this review, and the majority of those studies only examined a small number of the non-clinical factors that influence transfusion decision-making. Furthermore, there is an even greater paucity of data regarding transfusion practice in non-cardiac surgery, as greater than half of included studies focused on transfusions administered in the context of cardiac surgical procedures. Factors impacting intraoperative transfusion decisions made in the context of cardiac surgery, particularly among patients undergoing cardiopulmonary bypass, are not necessarily transferrable to the non-cardiac setting given the significant differences in transfusion practice between these two settings.

CONCLUSIONS

In summary, our study has synthesized the literature describing non-clinical and behavioural factors underlying intraoperative transfusion decision-making and categorized these factors using the Theoretical Domains Framework. These results can help in the design of future evidence- and theory-based interventions aimed at decreasing intraoperative RBC transfusion variability.

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TABLES

Table 1: Study Characteristics

First author	Year	Country	Design	Aim	Setting	Data collection method	Participants
Addis[14]	2020	USA	Retrospective cohort study	Investigate the role time of day plays in perioperative outcomes	Single academic centre	Retrospective chart review	Adult cardiac surgery patients involving CPB
Bennett-Guerrero[5]	2010	USA	Retrospective cohort study	Assess hospital-level variation in use of allogeneic RBCs	798 American hospitals	Retrospective chart review (STS database)	Patients undergoing primary isolated CABG with CPB
Bennett[20]	2018	Canada	Cross-sectional survey study	Describe current practices in perioperative blood management and explore differences between surgeons and anesthesiologists	31 Canadian hospitals	Web-based survey	Canadian liver surgeons and anesthesiologists
Brown[30]	2011	USA	Retrospective cohort study	Examine the impact of team changeover and unfamiliar teams in cardiovascular surgery on clinical outcome measures	Single academic centre	Retrospective chart review (institutional databases)	Patients undergoing elective or urgent cardiovascular surgery
Camaj[21]	2017	USA	Cross-sectional survey study	Improve understanding of “organizational contributors” to hospital variation in low volume intra-operative transfusion rates	Cardiac surgical programs	Electronic survey	The Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative institutions
Cote[15]	2015	Canada	Retrospective cohort study	Determine whether differing practice patterns had an impact on variation in perioperative transfusion	Single hospital	Retrospective chart review (cardiac surgery database)	All patients who underwent cardiac surgery at the Saint John Regional Hospital
Fischer[27]	2015	Germany	Before-and-after study	Analyze barriers to PBM implementation and outlines a strategy to introduce and manifest PBM	Single academic centre	Self-administered questionnaire	Physicians (surgeons and anesthesiologists) attending the introduction session of PBM and the PBM lecture 1 year thereafter
Goodnough[16]	1991	USA	Retrospective cohort study	Describe the variability in transfusions among institutions and to determine factors that may account for variability	18 academic tertiary-care hospitals	Audit of 30 consecutive adult patients in each 18 programs	540 patients undergoing elective first-time CABG
Hensley[26]	2019	USA	Before-and-after study	Describe effective methods for audits with feedback to the cardiac anesthesiologists	Single academic centre	Retrospective chart review (electronic record system)	Attending cardiac anesthesiologists
Irita[29]	2011	Japan	Review article	Discuss how critical hemorrhage can be prevented and how to deal with those cases caused by surgical procedures	-	-	-

Jin[17]	2013	USA	Retrospective cohort study	Quantitate the contribution of hospital influence on individual surgeons' transfusion practices	12 American hospitals	Retrospective chart review (STS database)	Patients who underwent CABG operations
Maddux[18]	2009	USA	Retrospective cohort study	Assess institutional variability of intraoperative RBC utilization in on-pump CABG surgery	144 American hospitals	Retrospective chart review (Hospital Clinical Services Group quality indicator database)	Patients undergoing isolated CABG surgery
Matot[22]	2004	Israel	Cross-sectional survey study	Evaluate the attitude of anesthesiologists and gynecologists to the use of blood during cesarian section	7 university hospitals and 3 nonteaching hospitals	Scenario-based survey	Hospital-based anesthesiologists and gynecologists
McQuilten[19]	2014	Australia	Retrospective cohort study	Investigate the differences in perioperative transfusion rates in cardiac surgery and what hospital factors may contributes	25 Australian hospitals	Retrospective chart review (cardiac surgery database)	Adults undergoing cardiac surgery
Qian[2]	2013	USA	Retrospective cohort study	Examine the hospital variability in use of RBCs in patients undergoing major noncardiac surgery	American academic medical centres	Retrospective chart review (University Health System Consortium database and the American Hospital Association Annual Survey File)	Patients who underwent elective or urgent primary THR, colectomy and pancreaticoduodenectomy surgeries
Rodrigues[28]	2015	USA	Before-and-after study	To reduce the number of patients transfused and the utilization of blood by 10% by improving interdisciplinary communication about transfusion.	Single academic centre	Retrospective chart review	Patients undergoing surgery
Salem-Schatz[23]	1990	USA	Cross-sectional survey study	Evaluate the influence of several clinical and nonclinical factors on transfusion decision making	3 American hospitals	Face-to-face survey	122 general and orthopedic surgeons and anesthesiologists
Salem-Schatz[24]	1993	USA	Cross-sectional survey + retrospective cohort study	Explore the relationship between physicians' knowledge and attitudes regarding the use of blood products and the quality of their transfusion practice	2 large American teaching hospitals	Mixed-methods design including face-to-face survey and chart review	17 attending orthopedic and general surgeons
Shehata[25]	2007	Canada	Cross-sectional survey study	Quantify hospital variation in RBC transfusion decisions perioperatively for patients undergoing CABG	32 Canadian hospitals	Self-administered mailed questionnaires	All anesthesiologists and cardiac surgeons involved in CABG in Canada

Table 2: Quality of included studies

First author	Year	Criteria from the Mixed Methods Appraisal Tool[13]										% of quality criteria met
		3.1	3.2	3.3	3.4	3.5	3.1	4.2	4.3	4.4	4.5	
Addis[14]	2020	1	1	0	1	1						80%
Bennett-Guerrero[5]	2010	1	1	1	1	1						100%
Bennett[20]	2018						1	1	1	0	1	80%
Brown[30]	2011	1	1	1	1	1						100%
Camaj[21]	2017						1	0	1	1	1	80%
Cote[15]	2015	1	1	1	1	1						100%
Fischer[27]	2015						1	0	1	0	1	60%
Goodnough[41]	1991	1	1	1	0	1						80%
Hensley[26]	2019	1	1	0	0	1						60%
Irita[29]	2011											
Jin[17]	2013	1	1	0	1	1						80%
Maddux[18]	2009	1	1	0	0	1						60%
Matot[22]	2004						1	0	1	1	1	80%
McQuilten[19]	2014	1	1	0	1	1						80%
Qian[2]	2013	1	1	1	1	0						80%
Rodrigues[28]	2015	0	0	0	0	1						20%
Salem-Schatz[23]	1990						1	0	1	1	1	80%
Salem-Schatz[24]	1993						1	0	1	1	1	80%
Shehata[42]	2007						1	1	1	0	1	80%

1: criteria met, 0: criteria not met

Table 3: Intraoperative transfusion behavioural factors distributed to the TDF domains

TDF domain	Factors	Studies citing the domain
Social influences	Influence of other physicians affects intraoperative transfusion decisions	14–17,19
	Patient preference affects intraoperative transfusion decisions	16
	Local institutional culture affects intraoperative transfusion decisions	2,5,14,15,17,18,20–23
Behavioural regulation	Institutional transfusion guidelines are helpful to guide intraoperative transfusion practice	18,24–26
	Communication between anesthesiologists and surgeons is essential to guide transfusion in the operating room	15,26
	Educational programs would improve intraoperative transfusion practice	16
	Hospitals should assess their intraoperative transfusion practice routinely	15,26
	Transfusion audits decrease intraoperative transfusion	18,25,27
Environmental context/resources	Later case start times increase the intraoperative transfusion rate	24
	Academic hospital settings transfuse at higher rates than community sites in the operating room	5
	Hospital with higher volumes transfuse less frequently in the operating room	2,5
	Geographic region influences intraoperative transfusion rates	5
	Linkage of the operating room with blood transfusion services are essential for intraoperative transfusion	26
	Team changeover does not affect intraoperative transfusion	28
	Institutional pressure to avoid ordering blood products delays intraoperative transfusion	26
	Blood product availability does not affect intraoperative transfusion decisions	16
	The presence of RBC units in the OR does not increase intraoperative transfusion	18
Beliefs about consequences	Blood product cost does not affect intraoperative transfusion decisions	16
	Concerns about legal repercussions lead to overtransfusion in the operating room	25
	Variations in belief about consequences of transfusion/anemia lead to practice variation in intraoperative transfusion	2,25
	Concerns about the risks of intraoperative transfusion affect transfusion practice	29
	Physicians overestimate the risks of anemia in the operating room	16
	Physicians overestimate the risks of intraoperative transfusion	16
	Personal experience with anemia complications lead to overestimation of the risks of anemia	16
	Personal experience with anemia complications lead to higher rates of appropriate transfusion.	17
	Physicians weigh the benefits of intraoperative transfusion more heavily that the risks	16,24
Knowledge	It is difficult to keep up to date with transfusion evid ence	25

	There is not enough transfusion education given during training	25
	The evidence base underlying intraoperative transfusion is poor, leading to increased variability in transfusion practice	25, 2
	Poor knowledge leads to higher rates of inappropriate transfusion	17
	Knowledge deficiencies about intraoperative transfusion are widespread	16
	Most physicians do not used published transfusion guidelines	15,16
Social/professional role and identity	Anesthesiologists are the primary transfusion decision-makers	19
	Transfusion decisions are multidisciplinary	14
	Intraoperative transfusion clinical practice guidelines threaten professional autonomy	25
	Surgeons are more likely to transfuse at higher hemoglobin levels in the operating room than anesthesiologists	29
	There is uncertainty as to the primary decision maker for intraoperative transfusion	17
Nature of the behaviours	Physicians become more restrictive with intraoperative transfusion over the course of their careers	19
	Rates of intraoperative transfusion are rising	14
	It is difficult to change transfusion behaviour in the operating room	25
	Most physicians transfuse 2 units of RBCs at a time in the operating room	29
	Physicians are more worried about errors of omission than errors of commission related to intraoperative transfusion	16
Memory, attention and decision processes	Decision fatigue leads to overtransfusion in the operating room	24
	Errors in reasoning and oversimplification leads to variation in intraoperative transfusion practice	25
	Overwhelming clinical responsibility leads to mistransfusion in the operating room	25
	Difficulty predicting future blood loss delays intraoperative transfusion	26
	Intraoperative transfusion decisions are complex	2
	Mental stress affects intraoperative transfusion decisions	26
Beliefs about capabilities	Lack of self-efficacy is associated with a worse intraoperative transfusion practice	25
	Greater confidence in intraoperative transfusion practice is associated with lower knowledge levels	16
	Older physicians are more confident in their intraoperative transfusion practice	16
Motivation and goals	Physicians want to make the right intraoperative transfusion decisions to optimize patient health/recovery	25

FIGURES

Figure 1: PRISMA flow diagram

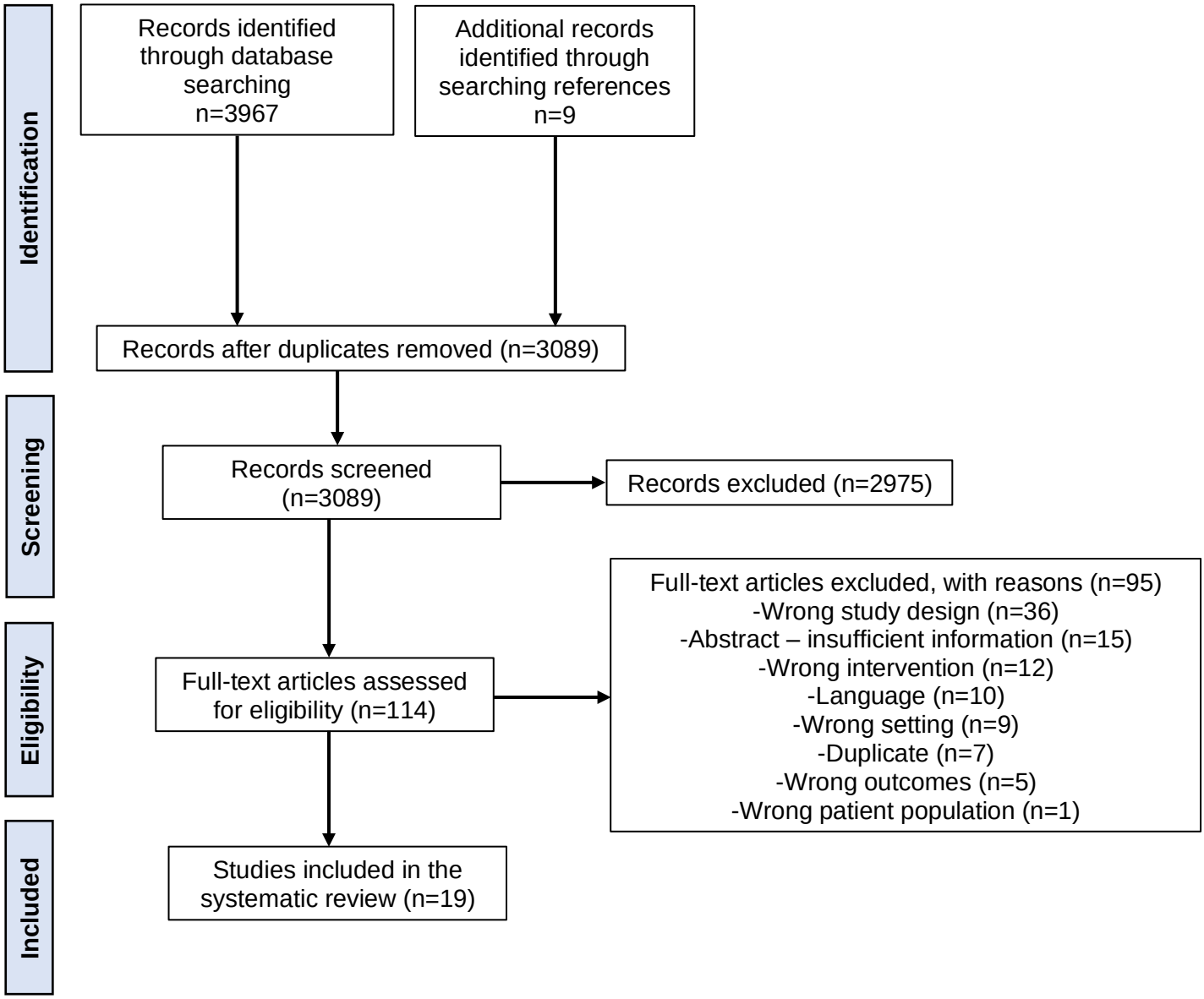
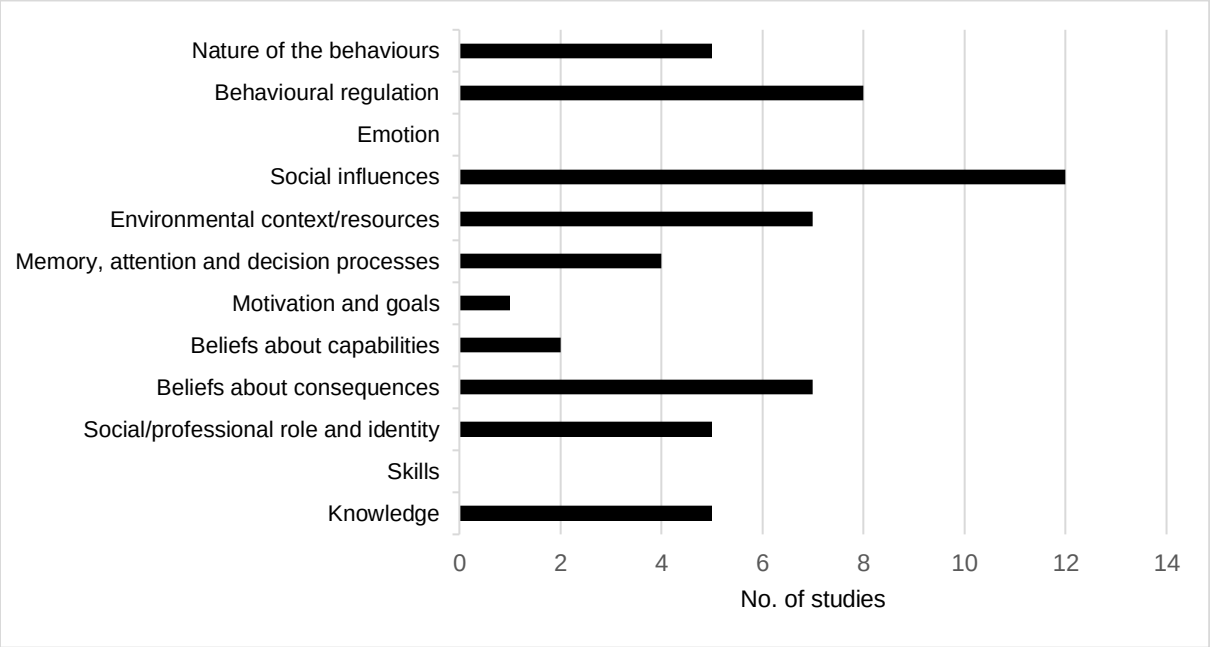


Figure 2: Number of studies attributed to each Theoretical Domain



APPENDIX 1: PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5-6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5, appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6-7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8, fig 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Fig 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8, Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	N/A
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	14
	23b	Discuss any limitations of the evidence included in the review.	17
	23c	Discuss any limitations of the review processes used.	N/A
	23d	Discuss implications of the results for practice, policy, and future research.	17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

APPENDIX 2: Search strategy

Ovid MEDLINE(R) ALL <1946 to August 05, 2021>

1 *blood transfusion/ or blood component transfusion/ or erythrocyte transfusion/ (39579)

2 ((red blood cell* or rbc or erythrocyte* or red cell*) adj3 (transfus* or infus* or retransfus*)).tw,kf. (12787)

3 (blood adj4 transfus*).tw,kf. (69716)

4 RBCT.tw,kw. 111

5 (hemotransfus$ or haemotransfus$).tw,kf. (252)

6 1 or 2 or 3 or 4 or 5 (89702)

7 INTRAOPERATIVE COMPLICATIONS/ or INTRAOPERATIVE CARE/ or INTRAOPERATIVE PERIOD/ or Perioperative Care/ (77915)

8 (intraoperat* or intra-operat* or perioperat* or peri-operat*).tw,kf. (259444)

9 (surg* or operat*).ti. (821189)

10 (transfus* adj5 (operat* or surg*)).tw,kf. (10442)

11 ((undergoing or during) adj4 (surg* or operat*)).tw,kf. (220777)

12 or/7-11 (1136869)

13 6 and 12 (22247)

14 decision making/ or choice behavior/ or judgment.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword

heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (167780)

15 (judgment or choice*).tw,kf. (382386)

16 (decision* making or deciding).tw,kf. (174529)

17 Practice Patterns, Physicians'/ (63658)

18 (behaviour or behavior).ti. (201588)

19 decision*.ti. (71121)

20 physician* practice.tw,kf. (2777)

21 Health Knowledge, Attitudes, Practice/ (118963)

22 ((physician* or doctor* or surgeon* or an?esthesiolog* or neurosurg*) adj2 (belief* or attitude* or behavio?r* or choice* or decision*)).tw,kf. (14129)

23 (teamwork or team work).tw,kw. (12941)

24 (team or teams).ti. (28134)

25 ((nontechnical or non-technical or nonmedical or non-medical) adj2 (skill* or performance)).tw,kf. (1319)

26 (team adj2 (performance or management or skill*)).tw,kf. (4868)

27 Patient Care team/ (67498)

28 Cooperative Behavior/ or communication/ or clinical competence/ or Verbal Behavior/ or Interdisciplinary Communication/ or Interprofessional Relations/ (288342)

29 Interdisciplinary Communication/ or Communication/ or Professionalism/ or Leadership/ or Cooperative Behavior/ or Interprofessional Relations/ or Awareness/ or Clinical Decision-Making/ (252053)

30 (nontechnical skill* or non-technical skill*).tw,kf. (1239)

31 (task management or situation* awareness or professionalism or teamwork or team work).tw,kw. (22863)

32 ((interpersonal or communication or leadership) adj2 skill*).tw,kf. (16733)

33 ((share* or sharing or informed or collaborative) adj2 (decid* or decision*)).tw. (21343)

34 or/14-33 (1384204)

35 13 and 34 (1090)

APPENDIX 3: Theoretical domains from the TDF and their descriptions

Table 1 Domains from the TDF [30] and their descriptions adapted from Francis et al. [47]

Knowledge *Patey et al. (2017)*	Existing procedural knowledge, knowledge about guidelines, knowledge about evidence and how that influences what the participants do
Skills	Competence and ability about the procedural techniques required to perform the behaviour
Social/professional role and identity	Is the behaviour something the participant is supposed to do or someone else's? (When discussing 'we'/the collective) Boundaries between professional groups
Beliefs about capabilities	Perceptions about competence and confidence in doing the behaviour
Beliefs about consequences	Perceptions about outcomes and advantages and disadvantages of performing the behaviour or pervious experiences that have influenced whether the behaviour is performed or not
Motivation and goals	Priorities, importance, commitment to a certain course of actions or behaviours Intentions
Memory, attention and decision processes	Attention control, decision-making, memory, i.e. is the target behaviour problematic because people simply forget?
Environmental context/resources	How factors related to the setting in which the behaviour is performed (e.g. people, organisational, cultural, political, physical and financial factors) influence the behaviour
Social influences	External influence from other people, views of other professions, patients and families, doing what you are told and how that influences what you do
Emotion	How feelings, affect (positive or negative) may influence behaviour
Behavioural regulation	Ways of doing things that relate to pursuing and achieving desired goals, standards or targets
	Strategies the participants have in place to help them perform the behaviour
	Strategies the participants would like to have in place to help them
Nature of the behaviours	What is the participant's history of the behaviour, have they any experience (done it often or not at all in the past), is the behaviour routine or automatic?

Adapted from: Patey, A.M., Curran, J.A., Sprague, A.E. et al. Intermittent auscultation versus continuous fetal monitoring: exploring factors that influence birthing unit nurses' fetal surveillance practice using theoretical domains framework. BMC Pregnancy Childbirth 17, 320 (2017). https://doi.org/10.1186/s12884-017-1517-z

Available at: https://rdcu.be/cS7A6

8.2 APPENDIX 2A: Pre-operative patient interview guide

Introduction

Thank you for agreeing to participate in this interview. You are being approached because you have an upcoming major surgery. We are interviewing you to understand what patients think about receiving blood transfusions during their surgical care, and how we can improve the way we provide care for people undergoing surgery. There are no right or wrong answers to any of the interview questions; we are only interested in your opinions and experiences.

Participation in this study is voluntary and your decision to participate will not affect the care you currently receive from the surgical team. Importantly, transfusion decisions during your surgical care will not be impacted by your responses. The interview will take approximately 30 minutes but could take longer (up to one hour) depending on how much information you choose to share. With your permission, I would like to audio record the interview because I don't want to miss any of your comments. Your responses will be kept confidential. Your anonymized interview responses will be shared only with the research team. Any information included in our report will not identify you as the respondent. You may decline to answer any question or stop the interview at any time and for any reason. Do you have any questions about what I have just explained?

May I turn on the digital recorder?

Establishing Rapport

Before we begin, would you be willing to tell me a little bit about why you were seen in the surgery clinic and what surgery you will be having?

1. Experience with and knowledge about blood transfusions

Blood transfusion is a procedure during which blood is put into a patient's bloodstream through a narrow tube placed in a vein. Patients having surgery may require a blood transfusion in cases of major blood loss. Sometimes during surgery, a doctor might have to decide whether to give the patient a blood transfusion

Q: Have you thought about or heard about blood transfusions that may need to be given to patients during their operations?

PROMPT: If YES, can you tell me a little bit about what you have heard about blood transfusions?

Q: Have you ever had a blood transfusion yourself?

IF YES: Can you tell me a little bit more about that? What do you remember about it? Did you experience any side effects (positive or negative) from it?

Q: Have you ever refused to receive a blood transfusion?

IF YES: Would you mind telling me a bit more about that and some of the factors that weighed into your decision?

IF NO, PROMPT: Thinking about this; what might be a situation where you might refuse a blood transfusion?

Q: Do you remember your surgeon or anesthesiologist discussing the possibility of a blood transfusion with you?

IF YES: What do you remember from that discussion?

IF YES: Do you recall any specific risks or benefits that were mentioned (IF SO PROBE FOR DETAILS).

Q: Do you remember if you were asked to agree to receive blood transfusions during or after your surgery?

IF YES: Did you agree to receive blood transfusions during or after your surgery?

PROMPT: How did you feel about that discussion? Would there have been any part of the discussion that could have been improved?

2. Trade-off

During surgery, doctors must weigh the risk of low blood levels, which may cause organ damage from lack of oxygen delivery, against the risk of a blood transfusion, which are associated with rare but possibly serious side effects, when deciding whether to start a blood transfusion.

Based on what I have just told you, what is your immediate reaction?

PROMPT: Do you find yourself weighing one of those risks more or less than the other? Overall, do you think the risks of low blood levels are higher than the risk associated with a transfusion?

<u>IF PATIENT RECALLS SURGEON MENTIONING BLOOD TRANSFUSION</u>

Q: You mentioned that your surgeon or anesthesiologist discussed the possibility of a blood transfusion with you and that they discussed [INSERT RISKS THAT THEY MENTIONED IN SECTION 1]. Which of those risks would you say were more important to you?

PROMPT: What is it about that risk that is important for you?

<u>IF PATIENT DOES NOT RECALL SURGEON MENTIONING BLOOD TRANSFUSION</u>

There might be a number of risks that surgeons or anesthesiologist consider when making a decision. These include allergic reactions and fevers, and more rarely, injury to the lungs, transmission of bacteria/viruses, and having too much fluid in the body causing shortness of breath.

Q: Which of those risks would you say were more important to you?

PROMPT: What is it about that risk that is important for you?

Q: Would there be anything, if it were a side effect, that would really bother you? Why?

Although the risks of having low blood levels can be very serious, more common and less severe side effects include fatigue, weakness, and shortness of breath.

Q: Would you be willing to accept these less severe side effects of low blood levels if it meant avoiding a blood transfusion? What about a very small chance of serious side effect like heart attack or kidney damage?

A challenge for doctors is that they may need to make a quick decision about whether to start a blood transfusion during surgery. Because the patient is asleep, the doctor cannot ask the patient about what they would prefer and the decision can depend on a lot of factors, and different doctors may make different decisions in a given scenario.

Q: What do you think the doctors should ask the patient *before* their surgery that might help the doctor make this decision?

There are some medications and techniques that can be used to minimize the chance of blood transfusion during surgery.

Q: What do you know about these techniques/medications? Were any of these strategies discussed with you prior to your surgery? Do you think these should be discussed with patients prior to surgery?

3. Subjective risk assessment

Q: How do you feel about the possibility of receiving a blood transfusion during your surgery?

PROMPT: What do you think is the biggest benefit of getting a blood transfusion during surgery? What is your biggest concern about getting a blood transfusion?

Please use the following scale to rate the likelihood of experiencing the following adverse events from blood transfusion: no risk, low risk, medium risk, high risk (*order to be randomized)*

Overall: _____

HIV: _____

Hepatitis: _____

Bacterial infection: _____

Receiving the wrong blood type: _____

Allergic reaction: _____

4. Research priorities

Because blood is a rare resource, and because there may be both benefits and risks to blood transfusions, researchers are interested in doing studies that test strategies to minimize the amount of blood transfused during and after operations.

Q: Do you think this area of research is worthwhile to pursue? Why or why not?

PROMPT: What would be your thoughts on such a trial? Would you have any specific concerns if someone approached you about such a trial?

Conclusion

Have you ever donated blood before?

Is there anything else you would like to comment on about receiving blood transfusions during your surgical care that we haven't discussed today?

Thank you very much for your time and the information you shared today.

8.3 APPENDIX 2B: Post-operative patient interview guide

Introduction

Thank you for agreeing to participate in this interview. You are being approached because you have recently undergone major surgery. We are interviewing you to understand what patients think about receiving blood transfusions during their surgical care, and how we can improve the way we provide care for people undergoing surgery. There are no right or wrong answers to any of the interview questions; we are only interested in your opinions and experiences.

Participation in this study is voluntary and your decision to participate will not affect the care you currently receive from the surgical team. The interview will take approximately 30 minutes, but could take longer (up to one hour) depending on how much information you choose to share. With your permission, I would like to audio record the interview because I don't want to miss any of your comments. Your responses will be kept confidential. Your de-identified interview responses will be shared only with the research team. Any information included in our report will not identify you as the respondent. You may decline to answer any question or stop the interview at any time and for any reason. Do you have any questions about what I have just explained?

May I turn on the audio recording?

1. Perioperative Course

Q: Before we begin, would you be willing to tell me a little bit about how your surgery went and how you're feeling now?

PROMPT: Did you have any complications after your surgery?

Blood transfusion is a procedure during which blood is put into a patient's bloodstream through a narrow tube placed in a vein. Patients having surgery may require a blood transfusion in cases of major blood loss. Sometimes during surgery, a doctor might have to decide whether to give the patient a blood transfusion

Q: Have you thought about or heard about blood transfusions that may need to be given to patients during their operations?

PROMPT: If YES, can you tell me a little bit about what you have heard about blood transfusions?

Q: Do you recall if you received a blood transfusion during or after your surgery? Were you informed if you received a transfusion during your surgery?

IF YES*:* Were they during or after your surgery? Did you experience any side effects (positive or negative) from them? Would you have preferred not to have gotten a blood transfusion? Were you satisfied with the reasons the surgery team used to decide on the need for a transfusion? Were you given the opportunity to ask questions about getting a blood transfusion? Were you asked how you felt about getting a blood transfusion?

IF NO: How do you feel knowing that you did not receive a blood transfusion during your surgical care?

Q: At any point, did you make a conscious decision not to have a blood transfusion? (IF YES: Were there any specific reasons why you had made a conscious decision to refuse a transfusion? Did you experience any side effects (positive or negative) due to not receiving blood transfusions?)

For patients identified as anemic:

PROMPT: Did you know about your blood levels after surgery? Were you aware that your blood levels after surgery were considered low? Did you associate any side effects from low blood levels after your surgery? If so, what were they? Have these symptoms resolved? How did these symptoms impact your recovery? Would you have preferred to have received a blood transfusion to avoid these symptoms?

2. Knowledge about blood transfusions

Q: Do you remember your surgeon or anesthesiologist discussing the possibility of a blood transfusion with you?

IF YES: What do you remember from that discussion? Do you recall any specific risks or benefits that were mentioned (IF SO PROBE FOR DETAILS).

IF NO: Do you wish blood transfusion had been discussed before your surgery? Why or why not?

Q: Do you remember if you were asked to agree to receive blood transfusions during or after your surgery?

IF YES: Did you agree to receive blood transfusions during or after your surgery?

PROMPT: How did you feel about that discussion? Would there have been any part of the discussion that could have been improved?

3. Subjective risk assessment

In general, can you describe how you feel about receiving a blood transfusion?

Prompt: What do you think is the biggest benefit of getting a blood transfusion during surgery? What is your biggest concern about getting a blood transfusion?

Please use the following scale to rate the likelihood of experiencing the following adverse events from blood transfusion: no risk, low risk, medium risk, high risk

Overall: _____

HIV: _____

Hepatitis: _____

Bacterial infection: _____

Receiving the wrong blood type: _____

Allergic reaction: _____

4. Trade-off scenarios

During surgery, doctors have to weigh the risk of low blood levels, which may cause organ damage from lack of oxygen delivery, against the risk of a blood transfusion, which are associated with rare but possibly serious side effects, when deciding whether to start a blood transfusion.

Based on what I have just told you, what is your immediate reaction?

PROMPT: Do you find yourself weighing one of those risks more or less than the other? Overall, do you think the risks of low blood levels are higher than the risk associated with a transfusion?

IF PATIENT RECALLS SURGEON MENTIONING BLOOD TRANSFUSION

Q: You mentioned that your surgeon or anesthesiologist discussed the possibility of a blood transfusion with you and that they discussed [INSERT RISKS THAT THEY MENTIONED IN SECTION 1]. Which of those risks would you say were more important to you?

PROMPT: What is it about that risk that is important for you?

IF PATIENT DOES NOT RECALL SURGEON MENTIONING BLOOD TRANSFUSION

There might be a number of risks that surgeons or anesthesiologist consider when making a decision. These include allergic reactions and fevers, and more rarely, injury to the lungs, transmission of bacteria/viruses, and having too much fluid in the body causing shortness of breath.

Q: Which of those risks would you say were more important to you?

PROMPT: What is it about that risk that is important for you?

Q: Would there be anything, if it were a side effect, that would really bother you? Why?

Although the risks of having low blood levels can be very serious, more common and less severe side effects include fatigue, weakness, and shortness of breath.

Q: Would you be willing to accept these less severe side effects of low blood levels if it meant avoiding a blood transfusion? What about a very small chance of serious side effect like heart attack or kidney damage?

A challenge for doctors is that they may need to make a quick decision about whether to start a blood transfusion during surgery. Because the patient is asleep, the doctor cannot ask the patient

about what they would prefer and the decision can depend on a lot of factors, and different doctors may make different decisions in a given scenario.

Q: What do you think the doctors could ask the patient *before* their surgery that might help the doctor make this decision?

There are some medications and techniques that can be used to minimize the chance of blood transfusion during surgery.

Q: What do you know about these techniques/medications? Were any of these strategies discussed with you prior to your surgery? Do you think these should be discussed with patients prior to surgery?

5. Research priorities

Because blood is a rare resource, and because there may be both benefits and risks to blood transfusions, researchers are interested in doing studies that test strategies to minimize the volume of blood transfused during and after operations.

Q: Do you think this area of research is worthwhile to pursue? Why or why not?

PROMPT: What would be your thoughts on such a trial? Would you have any specific concerns if someone approached you about such a trial?

Conclusion

Have you ever donated blood before?

Is there anything else you would like to comment about blood transfusions that we haven't discussed today?

Thank you very much for your time and the information you shared today.

8.4 APPENDIX 3: Physician interview guide

Introduction

Thank you for agreeing to participate in this interview. You have been approached because you are a physician involved in making intraoperative transfusion decisions. We are interviewing you to understand the factors that influence your decision to initiate transfusion in the operating room. We are hoping to understand the behavioural factors that affect transfusion. For example, the impact of communication between members of the operating team or the effect of local institutional culture on transfusion behaviour. There are no right or wrong answers to any of the interview questions; we are interested in your opinions and experiences.

We are interested in several different theories, covering several domains, and therefore, some questions may seem repetitive. You may give the same answer for different questions if you feel it most appropriate.

Your participation in this study is voluntary. The interview will take approximately one hour, depending on how much information you choose to share. With your permission, I would like to audio record the interview because I don't want to miss any of your comments. Your responses will be kept confidential. Your anonymized interview responses will be shared only with the research team. Any information included in our report will not identify you as the respondent. You may decline to answer any question or stop the interview at any time and for any reason. Do you have any questions about what I have just explained?

May I begin audio recording?

Establishing Rapport

Before we begin, would you be willing to tell me a little bit about how you normally decide to initiate blood transfusion in the operating room?

1. Knowledge

What do you think of the available evidence guiding intraoperative transfusion? Do you use any specific guideline to inform your intraoperative transfusion practice?

Prompt: If so, which one? Do you ever refer back to the guidelines to see if your transfusion was compliant? If not, why not?

Do you think guidelines are important in this context? Why or why not? What are they important for? Who are they important for?

Do you think the evidence base supporting these guidelines is sufficient? Do you think the guidelines need updating? What further studies or trials do you think would be helpful to guide intraoperative transfusion?

2. Social/professional role and identity

Do you feel constrained by guidelines or transfusion protocols? How do you feel this affects your professional autonomy?

Who do you think should be responsible for transfusion decision-making in the operating room? Do you usually consult with the surgeon/anesthetist before initiating transfusion?

Is there anything about your role as an anesthesiologist/surgeon that influences your intraoperative transfusion practice?

Prompt: for example, is this something you are trained to do; consensus in your profession; standard of practice

3. Social influences

I'd like you to imagine the following scenario where you are managing a patient in the operating room in a borderline transfusion situation.

A 60-year-old woman is undergoing a combined liver-first resection and right hemicolectomy for metastatic colorectal cancer. She is otherwise healthy and has no major cardiac comorbidities. Her preoperative hemoglobin is 100 g/L. After the liver resection, her hemoglobin has dropped to 80 g/L measured by a point-of-care hemoglobin device. She is hemodynamically normal and not requiring vasopressors.

How do the other team members influence your behaviour? In what circumstances? How does your impression of the surgeon/anesthetist influence your decision to transfuse? How would communication with other team members help you manage these patients?

Prompt: How does consensus in your profession regarding intraoperative transfusion influence your behaviour? Does acceptance/perception by your peers affect your behaviour?

How does local institutional culture change your transfusion practice?

Prompt: How should intraoperative transfusion strategies be discussed amongst the surgical team in the perioperative period? (examples could include preoperative hemoglobin, availability of cross-matched blood, conditions under which transfusion will be initiated, regular communication between surgeon/anesthetist during heavy blood loss) Should it be discussed in the preoperative time-out? Why or why not?

Prompt: How do you think intraoperative transfusion decision-making could be improved? Logistically, how should intraoperative transfusion decision-making occur? How can communication between physicians improve?

How do patient preferences impact your intraoperative transfusion decisions?

Prompt: Do you think patient preferences should be incorporated into intraoperative transfusion decision-making? How?

4. Beliefs about capabilities

How confident are you in your ability to manage a patient in the operating room in a borderline transfusion situation? Are you generally confident in your intraoperative transfusion decisions?

Prompt: What difficulties do you encounter when managing such a patient? What would help overcome these difficulties?

5. Beliefs about consequences

In your opinion, what are the benefits of transfusing a patient in the operating room in a borderline scenario?

Prompt: What harms might be avoided to the patient? Benefits to yourself, your colleagues, your institution, the healthcare system? Short- and long-term benefits?

In your opinion, what are the risks of transfusing a patient in a borderline situation?

Prompt: What are the risks to the patient? Risk to yourself, your colleagues, your institution, the healthcare system? Short- and long-term risks?

6. Environmental context and resources

How is your intraoperative transfusion practice affected by different clinical/environmental situations?

Prompt: for example, how much time it would take to get a unit of blood to the OR, concerns about local blood supply or cost of transfusion, complexity or remaining length of the surgical procedure, surgical indication (benign/malignant, transplant), availability of rapid hemoglobin testing, the patient's postoperative disposition (ICU/ward), biologic sex

Prompt: Do you think that point-of-care hemoglobin testing devices are helpful to make transfusion decisions? Why or why not? In what contexts?

7. Motivation and goals

What are your motivations when deciding whether to initiate transfusion in a borderline situation?

Do you think it is important to avoid transfusing patients in a borderline situation?

Prompt: In relation to other priorities required to treat patients in the OR, how high is the priority of avoiding excessive transfusion?

Would the goal of avoiding transfusion in a borderline patient be incompatible with achieving another objective?

Prompt: For example, slower time to recovery/discharge

8. Memory, Attention, and Decision processes

What thought processes might guide your decision to manage a patient in a borderline situation without transfusing?

Prompt: for example, patient preferences about transfusion, uncertainty about the evidence

9. Skills

What formal training did you receive about intraoperative transfusion?

What skills are required to manage a patient in a borderline transfusion situation in the OR? How easy or difficult is it to decide to initiate a transfusion?

Prompt: for example, understanding of physiology, knowledge of evidence, preoperative discussion about risks and benefits of transfusion, communication, clinical experience

10. Emotion

In general, how does intraoperative transfusion influence your work stress during an operation?

In what situations would you be worried about observing a patient in a borderline situation rather than transfusing? What would worry you about?

Does anticipated regret about the consequences of anemia impact your decision to transfuse?

In general, how optimistic are you that patients are transfused appropriately in the operating room? Do you think that physicians generally make the correct intraoperative transfusion decisions? Why or why not?

11. Nature of the behaviour

Can you think of a time when you've changed your transfusion practice? If so, what did you change and what are you doing differently?

If you were to change your intraoperative transfusion practice, how would you go about doing this?

What procedures or ways of working would change the way you decide to initiate intraoperative transfusion?

Prompt: for example, a set intraoperative transfusion protocol or institutional policy, increased frequency of intraoperative hemoglobin testing, etc.

Are intraoperative transfusion decisions automatic or do you spend a lot of mental energy thinking about them?

12. Behavioural regulation

The evidence in the literature suggests that intraoperative transfusion practice is variable. However, there is evidence to support restrictive intraoperative transfusion practices.

With this in mind, what might need to be done differently to observe a patient in a borderline situation rather than transfuse?

Prompt: What would you do differently? Who needs to do what differently?

What incentives are there to avoid unnecessary transfusion? What punishments are there for prescribing unnecessary transfusion?

Prompt: Role of educational sessions? Transfusion audits?

Conclusion

Is there anything else you would like to comment on about intraoperative transfusion decision-making that we haven't discussed today?

Thank you very much for your time and the information you shared today.

8.5 APPENDIX 4: Group authorship

Sylvie Aucoin, Rebecca Auer, Justyna Bartoszko, Jeanna Blitz, Rodney Breau, Jeannie Callum, François Carrier, Jeffrey Carson, Lorraine Chow, Victor Ferraris, Alan Flexman, Nicolai Foss, Steven Frank, Hilary Grocott, Julie Hallet, Angela Jerath, Philip Jones, Paul Karanicolas, Stuart McCluskey, Patrick Meybohm, Mike Murphy, Lena Napolitano, Paul Ness, Antony Palmer, Timothy Pawlik, Lauren Prescott, Toby Richards, Cynthia So-Osman, Jessica Spence, Alan Tinmouth, Alexis Turgeon, Jonathan Waters, Erica Wood

8.6 APPENDIX 5: Delphi surveys

A: Round 1

Please note that all questions are referring to allogeneic red blood cell transfusions given in the operating room while the patient is undergoing surgery (intraoperative) ONLY. These questions refer to any NON-CARDIAC surgical procedure at medium or high risk of red blood cell transfusion (>5%).

Please add any comments about the wording of the statement or item content in the optional comment boxes following each statement. Please suggest any additional statements or general comments in the box at the end of each page.

Intraoperative transfusion decision-making

Please rate your agreement with the following statements from completely disagree to completely agree.

1. The patient's baseline hemoglobin should be formally reviewed prior to every case.

2. The potential for intraoperative transfusion should be discussed as part of the preoperative checklist prior to every case.

3. The decision to initiate an intraoperative blood transfusion should be shared between the anesthesiologist and surgeon, situation permitting.

4. The anesthesiologist and surgeon should pause and discuss the indication for transfusion prior to every intraoperative transfusion event, situation permitting.

5. In the operating room, a single unit of blood should be transfused at a time in most cases. (7) completely agree

6. Anesthesiologists and/or surgeons should be prompted to provide an indication when ordering an intraoperative transfusion.

7. The indication for intraoperative transfusion should be approved by the institutional blood bank and/or a transfusion medicine specialist prior to release (situation permitting).

8. The decision to initiate intraoperative transfusion should be made by the attending anesthesiologist and/or surgeon.

9. A review of the appropriateness of intraoperative transfusion events should be formally included in the postoperative debrief.

10. Hospitals should establish audits of institutional intraoperative transfusion practice. (7) completely agree

11. Groups of anesthesiologists and/or surgeons should review the appropriateness of their intraoperative transfusion events regularly.

Please rate the importance of the following factors when determining whether to start an intraoperative red blood cell transfusion:

1. Hemoglobin level

2. Hemodynamic stability

3. Estimated blood loss

4. Underlying medical comorbidities

5. Urine output

6. Cerebral oximetry

7. Signs of end-organ ischemia

8. Ongoing bleeding

9. Potential for additional surgical bleeding

10. Surgical indication (e.g., cancer, benign disease, solid organ transplantation, etc.)

11. Patient age

12. Postoperative destination level of monitoring

13. Fluid balance

14. Intravascular volume status

15. Patient sex

16. Non-invasive cardiac output monitoring (NICOM)

17. Local availability of blood

18. Availability of rapid hemoglobin testing

Hemoglobin measurement

Please rate your agreement with the following statements from completely disagree to completely agree.

1. Point-of-care devices to measure hemoglobin (e.g.: HemoCue, iSTAT, non-invasive pulse co-oximeters, blood gas analyzers) are accurate enough to guide intraoperative transfusion.

2. Point-of-care hemoglobin devices should be routinely used to measure hemoglobin to guide intraoperative transfusion.

3. All point-of-care hemoglobin measurements should be confirmed with a central lab measurement (i.e., CBC) prior to initiating intraoperative transfusion if the situation permits.

4. A margin of error of 4 g/L (0.4 g/dL) (the Allowable Performance Limit defined by the Institute for Quality Management in Healthcare [IQMH]) is acceptable for point-of-care hemoglobin testing devices in the operating room.

5. Hemoglobin should routinely be measured at set time points in the operating room.

6. Hemoglobin should only be measured in the operating room if determined to be clinically indicated.

7. Hemoglobin should be routinely measured before every intraoperative transfusion if the situation permits.

8. Hemoglobin should be routinely measured after every intraoperative transfusion (within 1 hour of the end of transfusion) if the situation permits.

9. Hemoglobin should be measured between successive intraoperative transfusions in cases where multiple units are being transfused (situation permitting)

Restrictive Transfusion Strategies

Please rate your agreement with the following statements from completely disagree to completely agree.

1. In general, intraoperative transfusions should be guided by a predetermined algorithmic transfusion protocol.

2. A hemoglobin threshold trigger should be routinely used in the operating room to guide transfusion.

3. Intraoperative transfusions should be compliant with restrictive transfusion strategies.

Integrating patient perspectives

Please rate your agreement with the following statements from completely disagree to completely agree.

1. Patients should always be informed that they received a blood transfusion during their surgery.

2. Patient preferences should be incorporated into intraoperative transfusion decision-making.

3. Transfusion decisions made in the operating room should take into account the patients' previously stated perioperative goals of care regarding blood products.

4. Preoperative consent to intraoperative blood transfusion should include a presentation of the risks and benefits.

5. Preoperative consent discussions should emphasize the spectrum of risk associated with transfusion.

6. Preoperative consent discussions should emphasize the spectrum of risks associated with anemia.

7. Patient's perception of the spectrum of risk associated with transfusion and anemia should be explicitly considered when making intraoperative transfusion decisions on their behalf.

Trial questions

Please rate your agreement with the following statements from completely disagree to completely agree.

1. A stronger evidence base is needed to guide intraoperative transfusion decision-making.

2. Expanding the evidence base around intraoperative transfusion is an important research priority.

3. There is uncertainty surrounding the benefits of restrictive transfusion protocols in the operating room.

4. There is uncertainty surrounding the risks of restrictive transfusion protocols in the operating room.

5. A restrictive transfusion protocol including a restrictive hemoglobi transfusion trigger would be feasible to implement in the operating room.

6. I would be willing to participate in a two-arm interventional trial evaluating restrictive and liberal transfusion protocols.

7. I would be willing to participate in a three-arm interventional trial evaluating the following interventions: (1) restrictive transfusion protocol, (2) liberal transfusion protocol, (3) usual care.

8. 70 g/L (7 g/dL) is an acceptable restrictive hemoglobin trigger to use in the operating room in patients without major cardiac comorbidities.

9. 90 g/L (9 g/dL) is an acceptable liberal hemoglobin trigger to use in the operating room. (5) somewhat agree

Outcomes

Please rate the importance of the following outcomes related to intraoperative transfusion:

1. Overall perioperative morbidity

2. Postoperative mortality

3. Length of hospital stay

4.Length of ICU stay

5. Need for reoperation

6. Need for readmission

7. Perioperative acute kidney injury

8. Perioperative need for dialysis

9. Perioperative clinically significant cardiac ischemia

10. Perioperative clinically significant cerebral ischemia

11. Infectious complications

12. Cancer recurrence

13. Global quality of life

14. Surgery-specific quality of life

15. Functional capacity/status

16. Need for postoperative transfusion

17. Total perioperative transfusion events

Protocol suspension

Please rate the legitimacy of the following events in justifying the suspension of any intraoperative transfusion protocol algorithm

1. Hemodynamic instability refractory to vasopressor support and volume resuscitation

2. Massive uncontrolled hemorrhage

3. Clinician judgement

4. Clear evidence of cardiac ischemia

5. Clear evidence of cerebral ischemia

6. Very low urine output

7. Significant estimated blood loss (e.g., >1,500 mL)

B: Round 2

Please note that all questions are referring to allogeneic red blood cell transfusions given in the operating room while the patient is undergoing surgery (intraoperative) ONLY. These questions refer to any NON-CARDIAC surgical procedure at medium or high risk of red blood cell transfusion (>5%).

Please add any comments about the wording of the statement or item content in the optional comment boxes following each statement. Please suggest any additional statements or general comments in the box at the end of each page.

Intraoperative transfusion decision-making

Please rate your agreement with the following statements from completely disagree to completely agree.

1. The decision to initiate an intraoperative blood transfusion should be shared between the anesthesiologist and surgeon, except in cases of uncontrolled massive hemorrhage.

2. The anesthesiologist and surgeon should pause and discuss the indication for transfusion prior to every intraoperative transfusion, except in cases of massive hemorrhage.

3. The ordering clinician should be prompted to provide an indication when ordering an intraoperative transfusion using an electronic medical record (EMR) system, except in cases of massive transfusion.

4. The decision to administer an intraoperative transfusion should be made by the attending anesthesiologist and/or surgeon, except in cases of massive hemorrhage.

Hemoglobin measurement

Please rate your agreement with the following statements from completely disagree to completely agree.

1. When the situation permits, point-of-care hemoglobin measurements should be confirmed with a central lab measurement (i.e., CBC) prior to initiating intraoperative transfusion.

2. A margin of error of 4 g/L (0.4 g/dL) (the Allowable Performance Limit defined by the Institute for Quality Management in Healthcare [IQMH]) is acceptable for point-of-care hemoglobin testing devices in the operating room.

3. When the situation permits, hemoglobin should be routinely measured within 1 hour after every intraoperative transfusion.

Restrictive Transfusion Strategies

Please rate your agreement with the following statements from completely disagree to completely agree.

1. A hemoglobin threshold or trigger should generally be used to guide intraoperative transfusion as part of a broader transfusion strategy.

2. Restrictive transfusion strategies should be adopted for intraoperative transfusions, which would include a restrictive hemoglobin transfusion threshold/trigger.

Trial questions

Please rate your agreement with the following statements from completely disagree to completely agree.

1. I would be willing to participate in a randomized trial evaluating restrictive and liberal transfusion strategies that includes a usual care arm.

2. 90 g/L (9 g/dL) is an acceptable liberal hemoglobin trigger to use in the operating room.

Outcomes

Please rank the top five outcomes related to intraoperative transfusion that you consider to be the most important. (NOTE: only rank 5 outcomes, leave the others blank)

Overall perioperative morbidity Postoperative mortality

Perioperative clinically significant cardiac ischemia

Perioperative clinically significant cerebral ischemia

Functional capacity/status Global quality of life Surgery-specific quality of life Perioperative acute kidney injury Infectious complications

Cancer recurrence

Total perioperative transfusion events

Perioperative need for dialysis

Need for postoperative transfusion

Length of hospital stay

C: Round 3

Please note that all questions are referring to allogeneic red blood cell transfusions given in the operating room while the patient is undergoing surgery (intraoperative) ONLY. These questions refer to any NON-CARDIAC surgical procedure at medium or high risk of red blood cell transfusion (>5%).

Please add any comments about the wording of the statement or item content in the optional comment boxes following each statement. Please suggest any additional statements or general comments in the box at the end of each page.

Intraoperative transfusion decision-making

Please rate your agreement with the following statements from completely disagree to completely agree.

1. The anesthesiologist and surgeon should discuss the indication for transfusion prior to intraoperative transfusion, except in cases of extreme urgency e.g., massive hemorrhage.

2. The ordering clinician should be prompted to provide an indication when ordering an intraoperative transfusion using an electronic medical record (EMR) system, except in cases of massive transfusion.

3. The decision to administer an intraoperative transfusion should be made by the attending physician, except in cases of extreme urgency e.g., massive hemorrhage.

Hemoglobin measurement

Please rate your agreement with the following statements from completely disagree to completely agree.

1. Point-of-care hemoglobin measurements should be confirmed with a central lab measurement (i.e., CBC) prior to intraoperative transfusion except in cases of extreme urgency e.g., massive hemorrhage.

2. When the situation permits, hemoglobin should be routinely measured within 1 hour after an intraoperative transfusion episode (which could include more than 1 unit).

Trial Questions

Please rate your agreement with the following statements from completely disagree to completely agree.

1. I would be willing to participate in a 3-arm randomized trial evaluating restrictive and liberal transfusion strategies that includes a usual care arm.

2. 90 g/L (9 g/dL) is an acceptable liberal hemoglobin trigger to use in the operating room as part of a clinical trial.

3. When should overall perioperative morbidity be measured in the context of a clinical trial implementing a restrictive intraoperative transfusion protocol?

1. During hospital admission
2. 30 days
3. 60 days
4. 90 days
5. Other (specify)

4. When should postoperative mortality be measured in the context of a clinical trial implementing a restrictive intraoperative transfusion protocol?

1. During hospital admission
2. 30 days
3. 60 days
4. 90 days
5. Other (specify)

Minimal clinically important difference (MCID)

1. When designing an intraoperative transfusion protocol comparing liberal and restrictive transfusion protocols, which primary trial objective do you support:

1. Demonstrating that a restrictive transfusion protocol is superior to a liberal transfusion protocol
2. Demonstrating that a liberal transfusion protocol is superior to a restrictive transfusion protocol
3. Demonstrating that a restrictive transfusion protocol is non-inferior to liberal transfusion protocol

Consider the following questions in the context of a surgical intervention at high risk of bleeding with a baseline postoperative morbidity of 40% and postoperative mortality of 2% (e.g., pancreaticoduodenectomy, open AAA repair, pelvis exenteration).

2a. In designing a randomized clinical trial to evaluate whether a restrictive intraoperative protocol improves overall perioperative morbidity compared to a liberal intraoperative transfusion protocol, what is the minimal clinically important difference you would consider in terms of overall perioperative morbidity improvement with a restrictive intraoperative transfusion protocol (i.e., to change practice, a restrictive transfusion protocol needs to decrease overall perioperative morbidity by an absolute X% compared to a liberal protocol)?

1. 1%
2. 2%
3. 3%
4. 4%
5. 5%
6. 6%
7. 7%
8. 8%

9. 9%
10. 10%
11. Other (please specify)
12. I don't know

2b. In designing a randomized trial to evaluate whether a liberal intraoperative transfusion protocol improves overall perioperative morbidity compared to a restrictive intraoperative transfusion protocol, what is the minimal clinically important difference you would consider in terms of overall perioperative morbidity improvement with a liberal intraoperative transfusion protocol? (i.e., to change practice, a liberal transfusion protocol needs to decrease overall perioperative morbidity by an absolute X% compared to a restrictive protocol)

1. 1%
2. 2%
3. 3%
4. 4%
5. 5%
6. 6%
7. 7%
8. 8%
9. 9%
10. 10%
11. Other (please specify)
12. I don't know

2c. In designing a randomized trial to evaluate whether a restrictive intraoperative transfusion protocol is non-inferior (as effective as) to a liberal intraoperative transfusion protocol, what is the margin for non-inferiority you would consider in terms of overall perioperative morbidity improvement with a restrictive intraoperative transfusion protocol (i.e., a restrictive transfusion protocol would be considered not worse than a liberal protocol if within an absolute margin of X%)?

1. 1%
2. 2%
3. 3%
4. 4%
5. 5%
6. 6%
7. 7%
8. 8%
9. 9%
10. 10%
11. Other (please specify)
12. I don't know

3a. In designing a randomized clinical trial to evaluate whether a restrictive intraoperative protocol improves postoperative mortality compared to a liberal intraoperative transfusion protocol, what is the minimal clinically important difference you would consider in terms of postoperative mortality improvement with a restrictive intraoperative transfusion protocol (i.e., to

change practice, a restrictive transfusion protocol needs to decrease postoperative mortality by an absolute X% compared to a liberal protocol)?

1. 0.25%
2. 0.5%
3. 0.75%
4. 1%
5. 1.25%
6. 1.5%
7. 1.75%
8. Other (please specify)
9. No response

3b. In designing a randomized trial to evaluate whether a liberal intraoperative transfusion protocol improves postoperative mortality compared to a restrictive intraoperative transfusion protocol, what is the minimal clinically important difference you would consider in terms of postoperative mortality improvement with a liberal intraoperative transfusion protocol? (i.e., to change practice, a liberal transfusion protocol needs to decrease postoperative mortality by an absolute X% compared to a restrictive protocol)

1. 0.25%
2. 0.5%
3. 0.75%
4. 1%
5. 1.25%
6. 1.5%
7. 1.75%
8. Other (please specify)
9. No response

3c. In designing a randomized trial to evaluate whether a restrictive intraoperative transfusion protocol is non-inferior (as effective as) to a liberal intraoperative transfusion protocol, what is the margin for non-inferiority you would consider in terms of postoperative mortality improvement with a restrictive intraoperative transfusion protocol (i.e., a restrictive transfusion protocol would be considered not worse than a liberal protocol if within an absolute margin of X%)?

1. 0.25%
2. 0.5%
3. 0.75%
4. 1%
5. 1.25%
6. 1.5%
7. 1.75%
8. Other (please specify)
9. No response