**Title**. Contemporary practices around patients who decline blood component transfusion: A narrative review

**Abstract**

Blood component transfusions constitute a valuable clinical intervention and are widely used in healthcare. However, in certain situations, alternative options require consideration when transfusion is not feasible due to misalignment with an individual's wishes or beliefs. To support future research, education, and policy updates, this review has identified literature and clinical guidance on the management of individuals who decline transfusion. Searches were conducted for publications between 2013 and 2023. The publications were critically appraised and distinguished into the following four main approaches: blood management and conservation, early optimisation, synthetic compounds, and proactive management in emergencies. Applying these strategies to those who decline reduces transfusion risks and costs, preserves a limited resource, and provides a comprehensive approach to patient care and haemostasis for all individuals.

**Introduction**

Blood component transfusions are used routinely in healthcare. However, a proportion of the population will decline transfusion and healthcare providers must be aware of alternative management approaches to provide safe holistic care and maintain haemostasis. Blood transfusion carries inherent risks including, increased mortality, prolonged hospital stays, and infection (Spahn & Goodnough, 2013).

In current practice low haemoglobin (Hb) is a significant indicator for allogenic transfusion (Shander et al., 2014) and correlates with increased morbidity and mortality (Paone et al., 2014, Shander et al., 2014, Guinn et al., 2015, Delaney et al., 2016). However, similar outcomes are observed with increased transfusion use (Shander & Javidroozi, 2015, Gwam et al., 2017). Additionally, procedural errors, reactions and deaths constitute an organisational cost (Goodnough et al., 2014) and contribute to patients' decisions to decline transfusions. Patients also decline due to religious beliefs, notably Jehovah's Witnesses, numbering over 7 million worldwide (Lawson & Ralph, 2015). Exploring alternative management strategies is crucial to mitigate risk, support those who decline transfusion and enhance overall blood utilisation.

This review concentrates on strategies for managing individuals who decline transfusions for any reason. Drawing from current literature, it explores the existing alternatives, their implications for patients refusing transfusions, and their potential impact on future nursing practices. Furthermore, the review guides further research, education, and policy development.

**Methods**

Answers to two questions were sought: What alternative patient management strategies exist when allogenic blood transfusion is not feasible? How can these strategies benefit recipients who decline transfusion and the broader patient population?

The following databases were searched in January 2023: Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE, and ProQuest. The search terms were decline transfusion, refuse transfusion, decline blood, refuse blood, transfusion management, blood management, risk, and alternatives. Additionally searched were, NHS Blood and Transplant, the National Institute of Health and Care Excellence (NICE), and the World Health Organization, as they have published guidelines on current transfusion practice. For currency, the search was restricted to literature published from 2013 to 2023, except for seminal work and guidelines. The search results are reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2020).

**Findings**

The search returned 315 results, 189 records were removed due to duplication and lack of relevance, 112 were screened and 24 were removed leaving 88 records assessed for eligibility, 59 were excluded due to other factors, and 14 were identified from other sources. A total of 43 records were reviewed.

Out of the 43 reviewed studies, four broad approaches to managing patients who refuse blood component transfusions were found – namely blood management and conservation, early optimisation, the use of synthetic compounds, and proactive management in emergencies. These four approaches are discussed in the following four subsections respectively.

**Blood Management and Conservation**

Blood management and conservation is defined as a patient-centred, evidence-based approach to improving outcomes through managing and preserving a patient’s blood while promoting safety (Society for the Advancement of Patient Blood Management, 2022); and consequently, is argued by Goodnough et al. (2014) to be a key advance in transfusion care over the past half-century. Worldwide, blood management is implemented with the support of transfusion nurse specialists, who play a role in its establishment and integration (Bielby & Moss, 2018). By incorporating this into everyday patient care instances of allogenic transfusion can be reduced, thereby increasing safety. The literature identified four primary methods of blood conservation: acute normovolaemic haemodilution, cell salvage, preoperative autologous donation, and holistic methods.

1. **Acute Normovolaemic Haemodilution**

This method aims to minimise blood loss intraoperatively. Blood is collected using gravity into an anticoagulated bag and is replaced with a crystalloid or colloid solution to restore plasma volume; finally, the blood removed from the patient is reinfused at the end of the surgery (Klein et al., 2019, Lawson & Ralph 2015). Lawson and Ralph (2015) and Roberts et al. (2021) recommended its use for those who decline transfusion for religious reasons, provided certain conditions are met, such as a continuous connection to the patient's circulation. In a meta-analysis of surgeries, Zhou et al. (2015) demonstrated those who received acute normovolaemic haemodilution required fewer transfusions but did recommend further studies to investigate its safety and efficacy.

1. **Cell Salvage**

This method includes collection, filtration, and washing of blood lost during surgery, followed by the transfusion of the treated blood back to the patient (Goel et al., 2020). According to Goel et al. (2020), this method offers several advantages: it eliminates the need for blood storage, is more cost-effective, and with pre-planning can be used in surgeries where large blood loss is expected. Jennings & Brennan (2013), Lawson & Ralph (2015), Han et al. (2019) and Klein et al. (2019) reported that patients who declined for religious reasons accepted cell salvage if there was a continuous connection to their circulation. NICE (2015) recommended its use in conjunction with tranexamic acid in surgeries where large blood loss was expected. Jennings and Brennan (2013) and Han et al. (2019) recommended cell salvage in obstetric surgeries for controlling and managing bleeding in those who decline transfusion. Goel et al. (2020) noted the use of cell salvage has reduced in recent years; further research would be required to determine the reasons for this.

1. **Preoperative autologous donation**

According to Goel et al. (2020), preoperative autologous donation (PAD) is an effective blood conservation method. An individual's blood is pre-emptively collected before elective surgery, anticipating potential intraoperative needs (Goel et al., 2020). While it may lack benefit in cases of unexpected bleeding for those who decline, PAD can prove valuable in addressing major perioperative bleeding for planned surgeries. However, Shander and Javidroozi (2015) argue the time and resources spent on blood collection are wasted if the blood is unused. Furthermore, this procedure has the potential to induce anaemia. Additionally, those who decline transfusion for religious reasons may not accept PAD as the blood has become separated from the circulation (Klein et al., 2019), so this could only be used for patients who decline for other reasons. Like cell salvage, the use of PAD has also reduced in recent years (Vassallo et al., 2015, Goel et al., 2020); however, both can still be considered viable options for patients who decline transfusion.

1. **Holistic approaches**

Blood management and conservation includes intraoperative strategies for preserving the patient’s blood and a more holistic consideration of the patient’s haemostasis (Klein et al., 2019). The literature highlights successful strategies to prevent and halt the progression of anaemia. These strategies include, obtaining blood samples only when necessary and discouraging recurring sample orders (Shander et al., 2014, Shander & Javidroozi 2015), utilising paediatric sample bottles to minimise blood volume per sample, and employing point-of-care testing (Klein et al., 2019).

**Early Optimisation**

The literature revealed proactive measures to decrease the frequency and necessity of transfusions. Berg et al. (2022) recommended early optimisation for obstetric patients, starting in early gestation. The Royal College of Obstetricians and Gynaecologists (2015) endorsed the early involvement of senior specialists to optimise haemoglobin levels and plan for potential delivery complications. Shander and Goodnough (2018) support this and emphasise early preparation in case of postpartum haemorrhage.

Shander and Javidroozi (2015) devised an algorithm for patient blood management, highlighting the importance of proactive anaemia screening four weeks before elective surgery to facilitate effective haemoglobin optimisation.

Lawson & Ralph (2015), Klein et al. (2019), and DeLoughery (2020) observed early optimisation is effective for individuals who decline transfusion due to religious reasons. They recommended proactive measures and optimisation before any intervention, including pre-operative assessment, blood management, the use of synthetic compounds, and the involvement of multidisciplinary teams.

**Synthetic Compounds**

Medications known as synthetic compounds are alternatives to blood components. These can include oral and intravenous (IV) iron, erythropoietin (EPO) and haemoglobin-based oxygen carriers (HBOCs).

1. **Iron**

One primary reason for utilising transfusion is to treat anaemia, a condition linked to higher mortality rates (Paone et al., 2014, Shander et al., 2014, Guinn et al., 2015, Delaney et al., 2016). Treating anaemia with oral and IV iron is acceptable to those who decline transfusions for religious reasons (Lawson & Ralph, 2015). Klein et al. (2019) recommended oral iron at least six weeks before surgery if the patient’s Hb is <130 g/L. Closer to surgery, IV iron should be used (Shander & Javidroozi 2015, Klein et al., 2019). Additionally, folate and vitamin B12 can be used to treat anaemia and optimise Hb (Resar & Frank, 2014, Langhi et al., 2018).

1. **Erythropoietin**

Anaemia can also be treated with EPO (Paone et al., 2014, Shander et al., 2014, Guinn et al., 2015, Delaney et al., 2016). However, NICE (2015) discourages this unless the patient has anaemia, refuses blood, or if suitable blood is unavailable; consequently, this has resulted in limited utilisation in the UK. The Royal College of Obstetricians and Gynaecologists (2015) recommended only using EPO in clinical trials or under the expert advice of a haematologist. Nevertheless, studies have demonstrated EPO’s use for those who decline transfusion has been beneficial. Shander and Goonough (2018) argued it is essential for Hb recovery. Moreover, Duce et al. (2018) advocated for EPO preoperatively in patients who are anaemic and decline for religious reasons, and NICE (2014) recommended epoetin beta to increase Hb and avoid allogenic blood when pre-donating. However, the use of EPO requires frequent injections over weeks to induce a rise in Hb (NICE, 2014); thus, whilst beneficial for early optimisation, it is less useful in emergencies.

1. **Haemoglobin-based oxygen carriers**

HBOCs are synthetic drugs utilised as alternatives to red blood cells. They are synthesised from chemically modified human or bovine haemoglobin, or developed through genetic engineering (Meng et al., 2018) and can be acceptable to those who decline transfusion for religious reasons (Lawson & Ralph, 2015, Weiskopf et al., 2017). HBOCs are only currently licenced in a few countries due to concerns over risks (Weiskopf & Silverman, 2013). HBOCs were reported to be toxic and could potentially lead to myocardial infarction and pulmonary hypertension (Chand et al., 2014). However, in severely anaemic patients who are haemorrhaging with the risk of severe or fatal tissue hypoxia, HBOCs are considered a viable alternative to blood (Weiskopf et al., 2017). Weiskopf et al. (2017) stated more research is required in this area as benefits have only been demonstrated by laboratory experiments, not clinical trials. Furthermore, no HBOC has been approved by any British, European, or American regulatory body following studies and trials (Belcher et al., 2020). Thus, further research is required.

**Proactive Emergency Management**

During emergencies or significant haemorrhage scenarios, navigating management without resorting to a blood transfusion becomes challenging. Obstetric haemorrhage is the world’s leading cause of maternal mortality (Berg et al., 2022), responsible for a quarter of annual maternal deaths worldwide (World Health Organization, 2012). Berg et al. (2022) reviewed 52 years’ worth of data from women during labour who declined blood components for religious reasons and identified 15 deaths from haemorrhage. They recommended once delivery is underway to consider early surgical intervention (Berg et al., 2022). Kim et al. (2015) support this recommendation suggesting caesarean, hysterectomy, volume expanders, EPO, tranexamic acid, IV iron, and intensive care admission.

During a haemorrhage, Shander and Goodnough (2018) recommended first stopping the cause of the bleeding. Lawson and Ralph (2015) suggested stopping anticoagulants and using vasopressors, clotting factors, and fluid resuscitation, and Jennings and Brennan (2013) recommended cell salvage in obstetric emergencies.

Notably, multiple pharmacological agents and patient monitoring techniques are available in an emergency, including prothrombin complex concentrate, recombinant factor VIIa, fibrinogen concentrate, thrombopoietin agonists, interventional radiology, and thromboelastography (Klein et al., 2019, DeLoughery, 2020). However, further research is required to determine how frequently they are used and their effect on patient outcomes. Weiskopf et al. (2017) argued that without red cell transfusion, HBOCs could be used in life-threatening circumstances, however, clinical trials would be needed to prove this.

Immediate treatment is needed in urgent situations and emergencies when a patient’s wishes are unknown (British Medical Association, 2019) and appropriate support is given to those who have received a transfusion if they may have otherwise declined.

**Summary**

Recognised for its holistic approach to haemostasis, patient blood management emerged as the predominantly utilised and widely accepted strategy. It prevents anaemia, reducing the need for transfusions and minimising the demand for blood components while mitigating risks.

Synthetic compound use reduces instances of allogeneic and autologous blood transfusion and the associated complications. Patients who decline transfusion for religious reasons accept synthetic compounds, suggesting a viable option for all those who decline. However, more research and trials are required before wider patient use.

Early optimisation is beneficial for patients refusing transfusion at the beginning of their care journey. It can prevent the need for transfusion and its associated complications in obstetric patients throughout pregnancy, birth, and postpartum. It is also effective for elective surgery, allowing preoperative optimisation. Applicable to early-stage situations, this approach holds potential benefits for all patients by minimising the need for blood component transfusions.

In emergencies, many blood management strategies cannot be used. The literature confirms the optimal strategy for correcting critically low blood volume includes blood component transfusion, and patients who decline this procedure may not survive a major bleed. Nevertheless, proactive strategies for minimising bleeding can be used. Knowledge of the available strategies, alongside the use of blood management and optimisation throughout the care journey, would provide the best chance of survival for patients in emergencies.

**Conclusion**

This review has highlighted the main strategies used to manage patients who decline blood component transfusions for any reason. Patient blood management, synthetic compounds, early optimisation, and proactive emergency management collectively contribute to minimising the need for blood component transfusions. These approaches, when integrated into the patient's care journey, can benefit all those who decline. Knowledge of alternative management strategies and techniques is essential for healthcare practitioners. All practitioners must provide a person-centred approach in conjunction with their clinical expertise and judgement to implement safe and effective care, without compromising the health and clinical management of their patients. These findings can now influence healthcare education and the development of policies to incorporate these strategies in everyday practice.

**Further Research**

Further research is needed to enhance the understanding and viability of alternative strategies to blood component transfusions for all patients. Exploring additional reasons for patient refusal can contribute to a more patient-centred and holistic approach to transfusion care. Healthcare practitioners equipped with this knowledge can empower patients to make more informed choices about their care.

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**Identification**

**Screening**

Records identified from:

CINAHL (n = 100)

MEDLINE (n = 170)

ProQuest (n = 31)

Records removed *before screening*:

Duplicate records removed (n = 11)

Records removed for other reasons (n = 178)

Records screened

(n = 112)

Records excluded

(n = 24)

Reports sought for retrieval

(n = 88)

Reports not retrieved

(n = 0)

Reports assessed for eligibility

(n = 88)

Records identified from:

Websites (n = 2)

Organisations (n = 5)

Citation searching (n = 7)

Reports excluded: (n = 0)

Reports excluded:

Not associated with refusal alone (n = 22)

Patients unsuitable for transfusion (n = 6)

Low-quality paper/study (n = 12)

Lack of relevance to review (n = 19)

**Identification of studies via databases and registers**

**Identification of studies via other methods**

Reports assessed for eligibility

(n = 14)

Reports not retrieved

(n = 0)

Reports sought for retrieval

(n = 14)

Studies included in review

(n = 43)

Reports of included studies

(n = 43)

**Included**

**Figure 1.** PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources.