

ORIGINAL ARTICLE

Multinational transfusion practices and outcomes in haematology patients admitted to the intensive care unit

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Funding information

The authors received no specific funding for
 this work.

Abstract

Background and Objectives: The number of critically ill patients with haematological conditions is increasing, yet transfusion practices in this population remain poorly defined. This study aimed to compare transfusion strategies in critically ill patients with versus without haematological conditions.

Study Design and Methods: This international, prospective observational substudy of the International Point Prevalence Study of Intensive Care Unit [ICU] Transfusion Practices (InPUT) evaluated transfusion use in ICU patients with and without haematological conditions, including benign or malignant diseases or a history of stem cell transplantation. Outcomes included use of red blood cells (RBCs), platelets, plasma, haemostatic interventions, transfusion indications and thresholds.

Caroline M. Schaap and Laurens A. Oomen contributed equally to this study.

The members of InPUT Study Group are listed in Supplementary Appendix A.

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Results: Of 3643 ICU patients, 131 (3.6%) had a haematological condition. These patients were more likely to receive RBC (odds ratio [OR] 1.58, 95% confidence interval [CI] 1.09–2.29) and platelet transfusions (OR 8.32, 95% CI 5.09–13.6), primarily due to low haemoglobin rather than physiological triggers. Platelet thresholds were lower (median $23 \times 10^9/L$ vs. $64 \times 10^9/L$) compared to non-haematology patients. Both platelet and plasma transfusions were more frequently administered prophylactically rather than for active bleeding. Haemostatic interventions were more often used in haematology patients, at higher doses and typically without viscoelastic testing. Transfused haematology patients had higher 28-day mortality and longer ICU stays.

Conclusion: ICU patients with haematological conditions receive transfusions differently, particularly regarding platelet and plasma use. These findings underscore the need for prospective studies to define optimal transfusion thresholds in this growing and vulnerable patient population, although the study's limited sample size and lack of diagnostic granularity may affect interpretation.

Keywords

critically ill, haematological patients, intensive care unit, platelet, red blood cell, transfusion practices

Highlights

- Using data from 233 centres across 30 countries, this is the first multinational study to compare transfusion practices in intensive care units for patients with haematological versus non-haematological conditions.
- Haematology patients were transfused at lower thresholds and more often based on predefined rather than physiological triggers, indicating a distinct clinical approach.
- Plasma, platelet and haemostatic interventions were more frequently administered prophylactically and at higher thresholds in haematology patients, reflecting deviations from guideline recommendations and underscoring the need for individualized transfusion strategies.

INTRODUCTION

Advancements in treating haematological malignancies and benign disorders have improved survival rates [1, 2]. However, these patients remain at high risk of intensive care unit (ICU) admission due to treatment-related toxicities, disease progression and exacerbation of chronic conditions, with respiratory failure being the most common reason for ICU admission [1]. Consequently, ICU demand for these patients is rising [1].

Transfusion of blood products is a critical component in the management of ICU patients, particularly for haematological patients [3]. Bone marrow suppression due to the haematological disease itself, progression or treatment often leads to anaemia, thrombocytopenia and coagulopathy. Therefore, haematological patients frequently require red blood cell (RBC), platelet and plasma transfusions, along with adjunct therapies like tranexamic acid or haemostatic interventions. Previous studies have reported that patients with

haematological malignancies receive more RBC and platelet transfusions than any other clinical group, even outside of the ICU [3, 4].

Despite the rising number of critically ill haematology patients and their transfusion needs, data on transfusion practices and associated outcomes in this group remain scarce. The lack of high-quality evidence tailored to this patient population has led to inconsistent, and often, conflicting guideline recommendations and uncertainty regarding transfusion efficacy [5–7]. Furthermore, there are limited data on the effectiveness of transfusions in critically ill haematology patients [4, 8]. These patients may show varying responses to blood products, such as platelet transfusions, due to their underlying haematological condition and/or treatments.

Leveraging data from an international cohort study, this study aimed to compare transfusion practices in critically ill patients with and without haematological conditions. We also aimed to study the effect of transfusion on clinical outcomes of haematologically critically ill patients, stratified by transfusion of RBCs, platelets or plasma.

MATERIALS AND METHODS

Study design and population

This planned substudy is part of the International Point Prevalence Study of ICU Transfusion Practices (InPUT) [9], a multicentre, prospective observational cohort study evaluating transfusion practices in ICUs. Data were collected during two predefined 8-week periods between March 2020 and February 2021, adhering to the main study's quality standards.

All ICU patients aged 18 years and older admitted during the study periods were eligible to be included in the study. Patients were excluded if informed consent was not obtained.

A haematological condition was identified based on medical history and included benign haematological diseases, haematological malignancies or prior stem cell transplant. Benign haematological diseases were defined as congenital or acquired disorders affecting RBCs, platelets or coagulation factors, such as sickle cell disease, haemophilia, essential thrombocythemia, polycythemia, haemochromatosis and aplastic anaemia. Haematological malignancies referred to neoplasms originating from myeloid or lymphoid cell lines. Stem cell transplantation was defined as a previous autologous or allogeneic transplant.

This manuscript follows the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines [10] (Table S1). The study was approved by the institutional review board of Amsterdam University Medical Centers and by local and national ethics committees. All procedures adhered to the Declaration of Helsinki. The study is registered under the World Health Organization's (WHO) International Clinical Trials Registry Platform (ID NL-OMON28052).

Data collection

Baseline demographics, daily ICU assessments including laboratory values, supportive treatments and complications until discharge or Day 28, and 28-day outcomes were recorded.

Transfusions included RBCs, platelets, plasma, whole blood, prothrombin complex concentrate (PCC), fibrinogen and cryoprecipitate. Administration of tranexamic acid and vitamin K was also recorded in this way. For each transfusion event, a detailed form captured clinical reasons (including low haemoglobin [Hb], age, coronary ischaemia). RBC transfusion registration included physiological triggers necessitating transfusion (e.g., hypotension, arrhythmia, electrocardiogram [ECG] changes). Pre- and post-transfusion laboratory values (<24 h) and units per event were recorded. Only transfusions given in the ICU or operating room were analysed.

Outcomes

The primary outcome was the rate of transfusions, including RBCs, platelets and plasma, along with the use of haemostatic interventions

such as cryoprecipitate, fibrinogen, PCC, tranexamic acid and vitamin K, in critically ill patients with haematological conditions compared to those without. Transfusion rate was the percentage receiving at least one transfusion during two 8-week periods.

Secondary outcomes included transfusion indications, thresholds, pre- and post-transfusion lab reports, increment rates, units per event and total transfusions, compared between groups. Haemostatic intervention use was described with a focus on reasons, dosages and viscoelastic test guidance.

Lastly, we described the 28-day survival of critically ill patients with haematological conditions, stratified by RBC, plasma or platelet transfusions.

Statistical analysis

Baseline characteristics were stratified by the haematological subtype and are presented as mean (SD) or median (interquartile range, IQR). Categorical variables are shown as counts and percentages.

To compare transfusion rates between patients with haematological conditions and the general ICU population, unadjusted transfusion occurrence rates were analysed using the Chi-square test. This was followed by mixed-effects logistic regression adjusted for age, sex, thrombocytopenia, anaemia, prolonged international normalized ratio (INR) (≥ 1.2) at ICU admission, cardiovascular comorbidity, liver failure, sepsis, surgery within the preceding 24 h, extracorporeal membrane oxygenation (ECMO), renal replacement therapy, sequential organ failure assessment (SOFA) score, hypovolaemia shock and hospital as a random effect. Renal replacement therapy included dialysis, haemofiltration, haemodiafiltration and peritoneal dialysis. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Secondary outcomes, including changes in Hb, platelet counts, INR after transfusion, number of transfused units and transfusion thresholds, were compared using the Mann-Whitney *U* test.

Twenty-eight-day survival among patients with haematological conditions was stratified by RBC, plasma or platelet transfusions (yes/no). These outcomes are presented with descriptive statistics including counts, percentages, medians and IQRs.

No sample size calculation was performed due to the observational nature of the study. All analyses were conducted using R (version 4.3.1) via RStudio.

RESULTS

Critically ill haematological patients

A total of 233 centres across 30 countries and six continents participated in the study (Figure 1), with most patients recruited in Europe. The InPUT study included 3643 ICU patients, of whom 131 (3.6%) had a history of haematological disease, the majority being haematological malignancies. Table 1 summarizes the baseline characteristics of patients with haematological conditions. Among the subgroups,

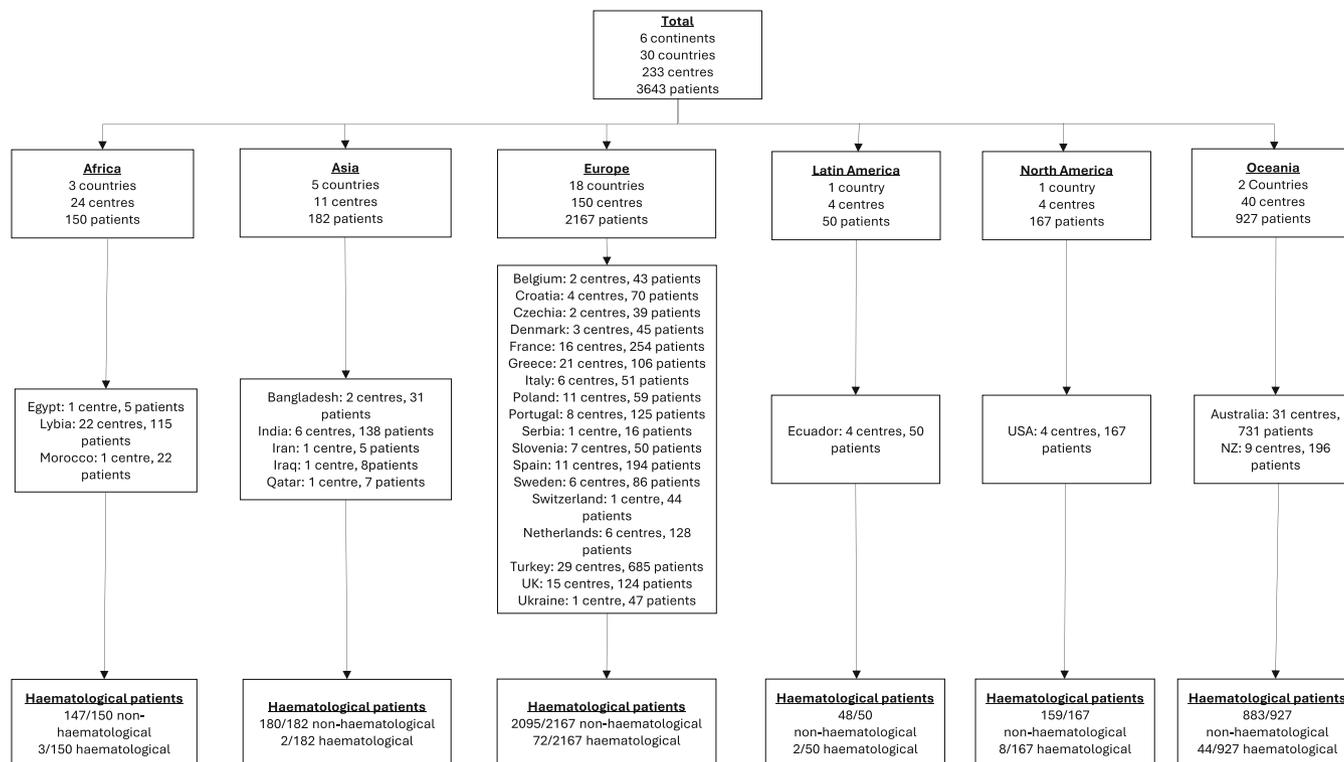


FIGURE 1 Flowchart of participating countries and centres and haematological patients per continent. Figure adapted from previous International Point Prevalence Study of Intensive Care Unit Transfusion Practices (InPUT) substudy [17]. NZ, New Zealand.

patients with haematological malignancies had the lowest Hb levels and platelet counts at ICU admission.

Transfusion rates

Table 2 shows that patients with haematological conditions had significantly higher odds of receiving RBC transfusions (OR 1.58, 95% CI: 1.09–2.29, $p = 0.019$), platelet transfusions (OR 6.13, 95% CI: 4.00–9.38, $p < 0.001$) and cryoprecipitate (OR 3.63, 95% CI: 1.40–9.37, $p = 0.015$) compared to the general ICU population.

After adjusting for covariates, the increased odds of RBC (OR 2.00, 95% CI: 1.36–2.92, $p < 0.001$) and platelet transfusions (OR 8.32, 95% CI: 5.09–13.60, $p < 0.001$) remained. In contrast, the odds of receiving cryoprecipitate decreased (OR 0.04, 95% CI: 0.01–0.18, $p < 0.001$), while the likelihood of receiving vitamin K increased (OR 4.17, 95% CI: 2.19–7.93, $p < 0.001$).

RBC transfusion events

A total of 1607 RBC transfusions were given to 850 of 3512 (24%) non-haematological patients, while 120 transfusions were given to 44 of 131 (34%) haematological patients (Table S2).

The number of RBC units per event was similar between groups, but haematological patients had a lower transfusion threshold, reflected in a lower pre-transfusion Hb level (median 7.15 g/dL [IQR:

6.53–7.68] vs. 7.60 g/dL [IQR: 6.90, 8.40], $p < 0.001$). Post-transfusion Hb levels followed the same trend (median 8.30 g/dL [IQR: 7.50–9.38] vs. 9.00 g/dL [IQR: 8.20, 9.80], $p < 0.001$), although Hb delta was comparable.

The reasons and triggers for RBC transfusion, stratified by the presence of a haematological condition, are illustrated in Figure 2a,b. Patients with a haematological condition had ‘low Hb’ more often cited as a reason for RBC transfusion. ‘None’ refers to the absence of any overt physiological signs necessitating a transfusion at that point, and these cases were reported more frequently in this group. When a clinical reason was given, ‘hypotension’ was most often reported.

Platelet transfusion events

A total of 301 platelet transfusions were given to 176 of 3512 (5%) non-haematological patients, while 155 transfusions were given to 32 of 131 (24%) haematological patients (Table S1). A higher number of platelet units were administered to haematological patients, accounting for 155 of 456 total platelet units (34.0%). Haematological patients received more platelet units per event and had significantly lower transfusion thresholds. The median pre-transfusion platelet count was significantly lower in patients with haematological conditions compared to those without ($23 \times 10^9/L$ [IQR: 15–49] vs. $64 \times 10^9/L$ [IQR: 33–125], $p < 0.001$). Similarly, post-transfusion platelet counts remained lower in the haematological group ($45 \times 10^9/L$ [IQR:

TABLE 1 Baseline characteristics of haematological patients.

	Overall	Benign haematological disease	Stem cell transplant	Malignant haematological disease
Number of patients	131	32	9	90
Age, mean (SD)	63 (16)	61 (18)	53 (20)	65 (14)
Female, <i>n</i> (%)	50 (38.2)	12 (37.5)	4 (44.4)	34 (37.8)
APACHE score, median [IQR]	66 [43, 85]	66 [40, 82]	54 [36, 62]	72 [47, 88]
Medical history				
Solid tumour, <i>n</i> (%)	20 (15.3)	5 (15.6)	2 (22.2)	13 (14.4)
Chronic kidney failure, <i>n</i> (%)	19 (14.5)	9 (28.1)	3 (33.3)	7 (7.8)
Acute coronary syndrome, <i>n</i> (%)	11 (8.4)	3 (9.4)	0 (0.0)	8 (8.9)
Heart failure, <i>n</i> (%)	15 (11.5)	6 (18.8)	0 (0.0)	9 (10.0)
COPD, <i>n</i> (%)	11 (8.4)	3 (9.4)	0 (0.0)	8 (8.9)
Liver failure, <i>n</i> (%)	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)
Organ transplant, <i>n</i> (%)	3 (2.3)	1 (3.1)	0 (0.0)	2 (2.2)
Other, <i>n</i> (%)	29 (22.1)	11 (34.4)	2 (22.2)	16 (17.8)
Code status				
Do not transfuse, <i>n</i> (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Do not resuscitate, <i>n</i> (%)	14 (10.7)	4 (12.5)	0 (0.0)	10 (11.1)
Do not intubate, <i>n</i> (%)	11 (8.4)	2 (6.2)	0 (0.0)	9 (10.0)
Emergency admission, <i>n</i> (%)	94 (71.8)	20 (62.5)	7 (77.8)	67 (74.4)
Organ support at admission (multiple options possible)				
Mechanical ventilation, <i>n</i> (%)	36 (27.5)	10 (31.2)	0 (0.0)	26 (28.9)
Renal replacement therapy, <i>n</i> (%)	6 (4.6)	1 (3.1)	0 (0.0)	5 (5.6)
Laboratory parameters (mean, SD) at admission				
Haemoglobin (g/dL)	10.3 (2.6)	10.9 (2.8)	11.6 (3.1)	9.9 (2.4)
Platelet count ($\times 10^9/L$)	137 (118)	173 (112)	174 (162)	118 (113)
INR	1.3 (0.3)	1.4 (0.3)	1.3 (0.3)	1.3 (0.4)
Prothrombin time (s)	15 (4)	NA (NA)	NA (NA)	15 (4)
Activated partial thromboplastin time (s)	32 (6)	34 (7)	30 (6)	31 (6)

Note: Patients with the combination of a benign haematological disease and haematological malignancy are categorized in the group haematological malignancy. Patients with the combination of stem cell transplant and haematological malignancy are categorized in the stem cell transplant group. Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; IQR, interquartile range; NA, not available.

21–70] vs. $88 \times 10^9/L$ [IQR: 55–143], unadjusted $p < 0.001$). The increment was lower in haematological patients (median 11×10^9 [IQR: 1–24] vs. 18×10^9 [IQR: 4–42], unadjusted $p = 0.024$).

Platelet transfusion reasons varied (Figure 2d). Haematological patients more often received transfusions prophylactically based on a predefined value, while ‘active bleeding’ was cited less frequently compared to non-haematological patients.

Plasma transfusion events

A total of 519 plasma transfusions were given to 319 of 3512 (9%) non-haematological patients, compared to 32 transfusions in 18 of 131 (14%) haematological patients (Table S2). Excluding those under

the massive transfusion protocol, 28 transfusions occurred in 16 haematological patients.

INR was assessed more often before plasma transfusion in haematological patients than in non-haematological patients (84.4% vs. 65.1%, $p = 0.041$), although pre- and post-transfusion INR assessments were otherwise similar. About half of the patients in both groups had INR measured post-transfusion or both pre- and post-transfusion. The target INR was lower in haematological patients than in non-haematological patients (median 1.00 [IQR 1.00–1.33] vs. 1.30 [IQR 1.20–1.50], $p = 0.015$). No differences were found in pre- or post-transfusion INR values or in their increments.

Reasons for plasma transfusion differed: haematological patients more often received prophylactic transfusions, while active bleeding was less frequently cited (Figure 2c).

TABLE 2 Transfusion and haemostatic intervention occurrence by the presence of haematological condition.

	Overall	No	Yes	Unadjusted		Adjusted	
				Odds ratio	p-value	Odds ratio	p-value
Number of patients	3643	3512	131				
RBC, n (%)	894 (24.5)	850 (24.2)	44 (33.6)	1.58 (1.09–2.29)	0.019	2.00 (1.36–2.92)	<0.001
Plasma, n (%)	337 (9.3)	319 (9.1)	18 (13.7)	1.60 (0.96–2.66)	0.098	1.35 (0.85–2.15)	0.199
Platelet, n (%)	208 (5.7)	176 (5.0)	32 (24.4)	6.13 (4.00–9.38)	<0.001	8.32 (5.09–13.60)	<0.001
Cryoprecipitate, n (%)	43 (1.2)	38 (1.1)	5 (3.8)	3.63 (1.40–9.37)	0.015	0.04 (0.01–0.18)	<0.001
Fibrinogen, n (%)	27 (0.7)	25 (0.7)	2 (1.5)	2.16 (0.51–9.23)	0.583	0.68 (0.14–3.30)	0.628
Prothrombin complex concentrate, n (%)	34 (0.9)	32 (0.9)	2 (1.5)	1.69 (0.40–7.11)	0.797	0.13 (0.04–0.42)	<0.001
Tranexamic acid, n (%)	92 (2.5)	88 (2.5)	4 (3.1)	1.23 (0.44–3.39)	0.913	0.97 (0.51–1.85)	0.922
Vitamin K, n (%)	80 (2.2)	74 (2.1)	6 (4.6)	2.23 (0.95–5.22)	0.111	4.17 (2.19–7.93)	<0.001

Note: Unadjusted rates were analysed with Chi-squared tests; mixed-effects logistic regression was used for modelling. Abbreviation: RBC, red blood cell.

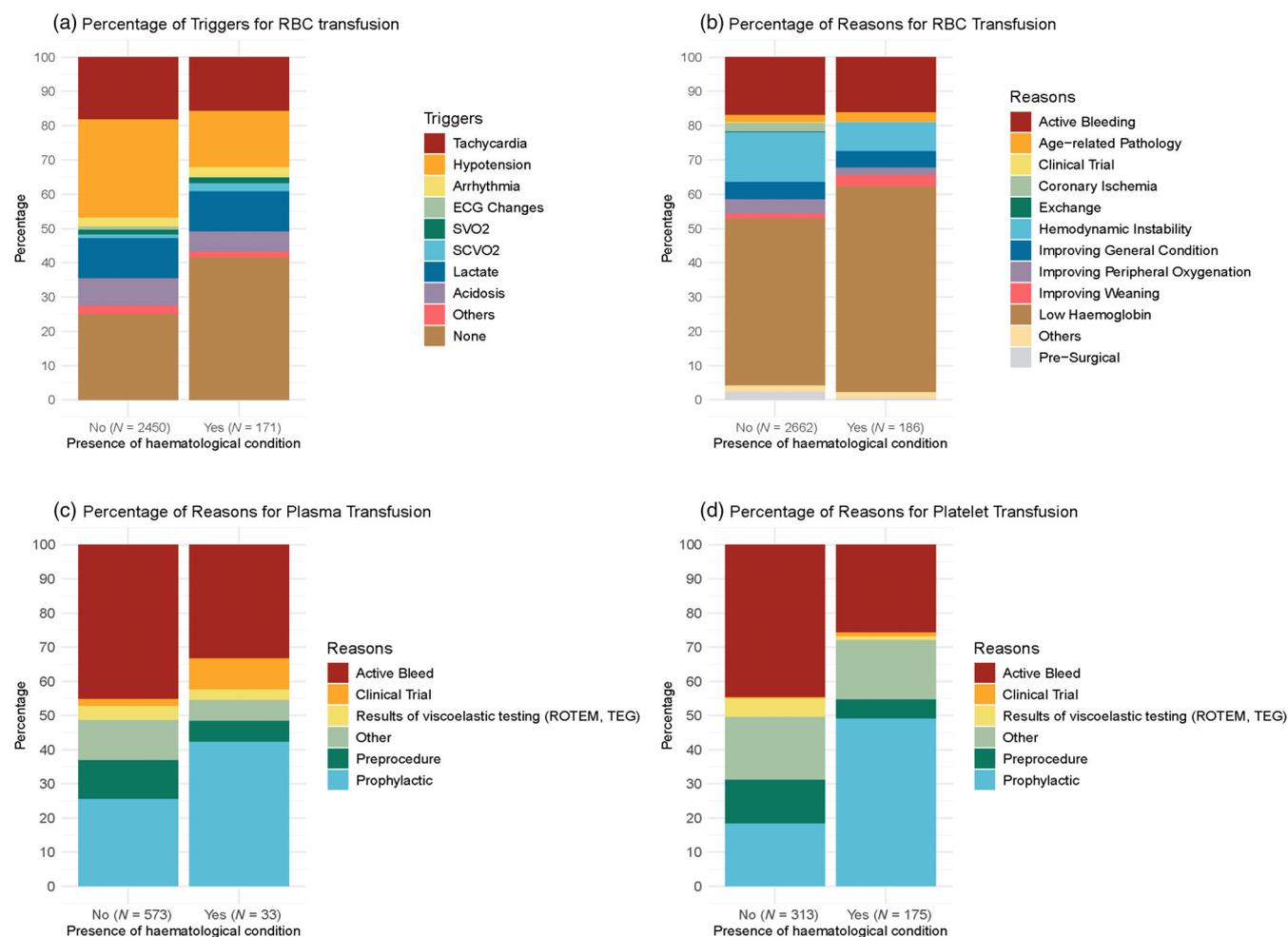


FIGURE 2 Reasons and triggers for red blood cell (RBC), platelet and plasma transfusion, stratified by the presence of a haematological condition. Triggers are defined as: Physiological parameters necessitating transfusion. Reasons are defined as: Clinical reason provided for transfusion. ECG, electrocardiogram; ROTEM, rotational thromboelastometry; SCVO2, central venous oxygen saturation; SVO2, mixed venous oxygen saturation; TEG, thromboelastography.

TABLE 3 Outcomes of patients with haematological conditions, stratified by transfusion status (red blood cell, plasma and platelet).

RBC transfusion	No	Yes
Number of patients, <i>n</i>	87	44
APACHE-IV upon admission, mean (SD)	72.28 (26.77)	75.24 (24.95)
Mean SOFA score during ICU stay, mean (SD)	4.68 (3.42)	7.56 (4.31)
Support during ICU stay, <i>n</i> (%)		
Invasive mechanical ventilation	21 (24.1)	26 (59.1)
Renal replacement therapy	22 (25.3)	14 (31.8)
Non-invasive mechanical ventilation	9 (10.3)	5 (11.4)
Extracorporeal membrane oxygenation	0 (0.0)	1 (2.3)
State of patient at Day 28, <i>n</i> (%)		
Dead	19 (21.8)	20 (45.5)
Alive	66 (75.9)	23 (52.3)
Unknown	2 (2.3)	1 (2.3)
Total number of days ICU stay, median [IQR]	3 [2, 5]	6 [3, 11]
Plasma transfusion	No	Yes
Number of patients, <i>n</i>	113	18
APACHE-IV upon admission, mean (SD)	73.70 (26.37)	70.83 (24.62)
Mean SOFA score during ICU stay, mean (SD)	5.08 (3.46)	8.93 (5.13)
Support during ICU stay, <i>n</i> (%)		
Invasive mechanical ventilation	33 (29.2)	14 (77.8)
Renal replacement therapy	32 (28.3)	4 (22.2)
Non-invasive mechanical ventilation	11 (9.7)	3 (16.7)
ECMO	0 (0.0)	1 (5.6)
State of patient at Day 28, <i>n</i> (%)		
Dead	30 (26.5)	9 (50.0)
Alive	80 (70.8)	9 (50.0)
Unknown	3 (2.7)	-
Total number of days ICU stay, median [IQR]	3 [2, 6]	8 [3, 15]
Platelet transfusion	No	Yes
Number of patients, <i>n</i>	99	32
APACHE-IV upon admission, mean (SD)	71.85 (26.92)	77.36 (23.53)
Mean SOFA score during ICU stay, mean (SD)	4.84 (3.55)	8.69 (4.04)
Support during ICU stay, <i>n</i> (%)		
Invasive mechanical ventilation	28 (28.3)	19 (59.4)
Renal replacement therapy	25 (25.3)	11 (34.4)
Non-invasive mechanical ventilation	10 (10.1)	4 (12.5)
ECMO	0 (0.0)	1 (3.1)
State of patient at Day 28, <i>n</i> (%)		
Dead	19 (19.2)	20 (62.5)
Alive	78 (78.8)	11 (34.4)
Unknown	2 (2.0)	1 (3.1)
Total number of days ICU stay, median [IQR]	3 [2, 6]	5 [3, 10]

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; RBC, red blood cell; SOFA, sequential organ failure assessment.

Haemostatic interventions

Haemostatic interventions were carried out 34 times in 19 of 131 haematological patients (14.5%) and 373 times in 208 of 3512 non-haematological patients (5.9%). In haematological patients, the most commonly administered haemostatic intervention was tranexamic acid (13, 38.2%), whereas in non-haematological patients, it was vitamin K (132, 35.4%) (Table S3).

In haematological patients, haemostatic intervention administration was less frequently guided by viscoelastic tests and was more often by prophylactic or pre-procedural tests to prevent bleeding. While tranexamic acid and vitamin K dosages were similar between groups, fibrinogen, cryoprecipitate and PCC were given in higher doses to non-haematological patients (Table S2).

Outcomes

Outcomes of patients with a haematological condition stratified by transfusion status (RBC, plasma or platelet) are displayed in Table 3. Across all transfusion types, patients who received transfusions (RBC, plasma or platelet) had higher mortality rates at 28 days and longer ICU stays compared to those who did not receive transfusions.

DISCUSSION

The key findings of this study were that in critically ill patients with a haematological condition, approximately one-third received an RBC transfusion during their ICU stay. Compared to the general critically ill population, haematological patients have 1.5 times higher odds of receiving an RBC transfusion and 6 times higher odds of receiving a platelet transfusion. Haematological patients exhibited lower transfusion thresholds for RBCs and platelets and more frequently received plasma and platelet transfusions for prophylactic or procedural purposes rather than for active bleeding. Furthermore, the presence of a haematological condition was associated with differences in the administration of haemostatic interventions, including less frequent use of viscoelastic testing, more frequent prophylactic administration prior to procedures and higher doses of fibrinogen, cryoprecipitate and PCC compared to non-haematological patients. Finally, across all transfusion types, haematological patients who received a transfusion had a higher 28-day mortality rate and a longer ICU stay compared to patients with a similar condition who did not receive any transfusions.

A primarily threshold-based decision to transfuse, rather than one based on physiological triggers, may reflect the predominance of chronic bone marrow failure disorders in this population [1]. Importantly, the efficacy of RBC transfusions, measured by Hb increment post-transfusion, was comparable between the groups.

Data on the optimal transfusion threshold for critically ill patients with haematological conditions are scarce, as noted in recent guidelines and reviews [5–7]. While both literature and guidelines make no strict recommendation to adhere to a restrictive or liberal threshold, in our study, transfusions are generally based upon a restrictive threshold.

Three small studies examined restrictive (7 g/dL) versus liberal (8 or 12 g/dL) transfusion thresholds [11–13] but they were underpowered to assess clinical or transfusion-related outcomes. A recent systematic review showed that single-unit transfusions in haematological malignancy patients significantly reduced the total RBC use per admission without increasing hospital stay, severe bleeding or mortality, although discharge Hb levels were lower [14]. This practice aligns with our findings, where a median of one RBC unit was used per transfusion event in haematological patients in our cohort.

Our findings align with previously reported data on plasma transfusion practices, including an InPUT substudy [15–17], showing frequent prophylactic plasma use despite limited supporting evidence. Of note, there is no evidence for the efficacy of plasma transfusion in critically ill patients to prevent procedure-related bleeding complications except during lumbar punctures in those at high risk of bleeding, where the potential for catastrophic complications supports a more cautious approach [6, 18–21]. Our observations underline the need to identify potential challenges in implementing and adhering to these guidelines in haematological patients.

The findings of our study likely reflect severe hypoproliferative thrombocytopenia common in haematological patients, caused by bone marrow failure due to haematological malignancies, aplastic anaemia or their treatments [22]. Although previous research has shown prophylactic platelet transfusion is also common in non-haematological critically ill patients [4], haematological patients often have lower nadir platelet counts compared to the general ICU population, possibly reflecting differences in indications. However, transfusion triggers in haematological patients in our study remain higher than found in recent literature and professional guidelines advise [6, 7, 23]. The reduced post-transfusion increment was consistent with previous studies in haematological patients admitted to the ICU, suggesting altered platelet utilization, more frequent allo-antibody formation and decreased production or increased consumption depending on the underlying pathology necessitating ICU admission [4, 24]. An ongoing trial evaluating different platelet transfusion thresholds prior to procedures, the Thresholds for Platelets-trial, may provide further insight into the optimal platelet transfusion threshold in this subgroup [25].

The findings regarding the occurrence of haemostatic interventions should be interpreted cautiously because of the low event occurrence rate in haematological patients. Nonetheless, they align with earlier research [26, 27] suggesting that haematological patients receive haemostatic interventions more prophylactically, although those studies primarily focused on benign haematological conditions.

Patients with haematological conditions who received transfusions had longer ICU stays and higher mortality, although these associations may be confounded by factors such as disease severity, organ failure and comorbidities, which could not be fully adjusted for due to the limited sample size. Furthermore, multiple factors, including frailty, allogeneic haematopoietic stem cell transplantation, kidney injury and cardiac complications, also contribute to poorer outcomes [1, 2]. Bone marrow failure may contribute to both transfusion need and higher mortality, potentially confounding the outcomes [2].

This study has several strengths. It offers a unique, multicentre prospective analysis of transfusion practices in critically ill haematology patients, providing broad insights into ICU management. The inclusion of diverse centres reduced regional treatment bias and improved generalizability. To our knowledge, it is among the first to comprehensively assess RBCs, platelets, plasma, haemostatic interventions, transfusion thresholds and clinical indications in this population. To address the heterogeneity of haematological conditions, patients were stratified into malignant, benign and post-stem cell transplant groups for baseline characterization. However, the limited sample size prevented more detailed stratified analyses.

An important limitation is the broad classification of haematological conditions. The InPUT dataset, as part of the main study, did not capture specific diagnoses, grouping patients into ‘benign’ or ‘malignant’ categories that often overlap clinically. For example, myeloproliferative neoplasms may present with high counts, while aplastic anaemia can resemble malignancy in terms of cytopenia’s. Some disorders classified as benign are in fact considered malignant by the WHO criteria, limiting the interpretability of comparisons. Furthermore, because of the broad classification and limited sample size, a more granular subgroup analysis was not possible. These factors, along with the observational design of the study, introduce the potential for confounding by indication, as patients receiving transfusions were more likely to be sicker or have more complex clinical presentations, making it difficult to disentangle the effects of transfusion itself from the effects of the underlying severity of illness. Therefore, while our study shows an association between transfusion and worse outcomes, we cannot draw causal conclusions, and the findings should be interpreted as hypothesis-generating. Nevertheless, together with prior studies showing no consistent outcome differences between liberal and restrictive transfusion strategies [13, 28, 29], our findings underscore the need for further prospective research to define optimal transfusion thresholds in this population.

The descriptive analysis of transfusion rates provides a foundation for further research. Regarding RBC transfusion, the optimal RBC transfusion threshold remains uncertain, especially for patients with bone marrow failure, and the relative benefits of Hb-triggered versus physiological transfusion strategies are unclear. The efficacy of plasma, haemostatic interventions and fibrinogen in reducing procedure-related bleeding is also unknown. Recent guidelines made conditional recommendations, which were made on a low level of evidence [6, 7]. Our study and prior data suggest that prophylactic plasma and platelet use remains common. Higher thresholds are used for platelets in our study than recent guidelines advise, whereas RBC transfusion thresholds for anaemia were more consistently followed. Future research should focus on accurately assessing bleeding risk, identifying effective alternative strategies to reduce bleeding complications, and addressing barriers to guideline implementation at the centre level for prophylactic plasma and platelet transfusions. A better understanding of institutional practices and the reasons for deviations from guidelines will help reduce unwarranted variation and improve consistency in care.

In conclusion, haematological ICU patients more frequently receive RBC transfusions than non-haematological patients, primarily due to low Hb levels rather than physiological triggers. The

predominance of prophylactic plasma, platelet and haemostatic interventions underscores the urgent need for prospective studies to define optimal transfusion strategies in this vulnerable population.

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ACKNOWLEDGEMENTS

C.M.S. performed the analysis and drafted the manuscript. L.A.O. drafted the manuscript. J.S. epidemiologist involved in the original InPUT study and part of the steering committee of the original InPUT study. S.J.R., S. d.B., M.C.R. and C.v.d.O. contributed to the design and establishment of the original InPUT study. J.Ba., Mau.C., A.F., J.M., Z.M., T.W.L.S. and C.A. are the part of the steering committee of the original InPUT study. A.W.J.F., T.H., Mi.P., T.T.M., J.Be., L.R., H.A.-B., K.T., V.C., M.G., S.N.M., V.P., M.E., R.G., M.M., M.L., V.N., Ma.P., J.V.L., M.Q.-D., Mar.C., C.A.P., N.Y. and N.N. are the national coordinators during data collection of the original InPUT study. H.-J.d.G. is the part of the steering committee of the original InPUT study. A.P.J.V. is the principal investigator during the original InPUT study and participated in manuscript writing. B.J.B. supervised and contributed to manuscript writing. A.S. is the national coordinator during data collection of the original InPUT study,

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CONFLICT OF INTEREST STATEMENT

Dr. Bart J. Biemond reported receiving research grants from Sanquin, Novartis, Pfizer and BMS and received honoraria for advisory board meetings/podcasts from Pfizer, Celgene, Novo Nordisk and Sanofi. Dr. Maurizio Cecconi reported receiving personal fees from Edwards Lifesciences, GE Healthcare, and Directed Systems outside the submitted work. Dr. Aarne Feldheiser reported receiving personal fees from Baxter and Medtronic outside the submitted work. Dr. Thomas W. L. Scheeren reported serving as senior medical director for Edwards Lifesciences (Garching, Germany). Dr. Zoe McQuilten reported receiving grants from the Australian National Blood Authority and National Health and Medical Research Council during the conduct of the study. Dr. Andrew W. J. Flint reported receiving grants from the Australian National Blood Authority and Blood Synergy (Monash University) during the conduct of the study. Dr. Michaël Piagnerelli reported receiving grants from Centre Federal d'Expertise Belge—KCE grant for COVID-19 study outside the submitted work. Dr. Mohan Gurjar reported receiving royalties for edited books (*Manual of ICU Procedures and Textbook of Ventilation, Fluids, Electrolytes and Blood Gases*) from the publisher Jaypee Brothers Medical Publishers (Pvt) Ltd., New Delhi. Dr. Carmen A. Pfortmueller reported receiving grants from Orion Pharma, Abbott Nutrition International, B Braun Medical AG, CSEM AG, Edwards Lifesciences Services GmbH, Kenta Biotech Ltd., Maquet Critical Care AB, Omnicare Clinical Research AG, Nestle, Pierre Fabre Pharma AG, Pfizer, Bard Medica SA, Abbott AG, Anandic Medical Systems, Pan Gas AG Healthcare, Bracco, Hamilton Medical AG, Fresenius Kabi, Getinge Group Maquet AG, Dräger AG, Teleflex Medical GmbH, GlaxoSmithKline, Merck Sharp and Dohme AG, Eli Lilly and Co, Baxter, Boehringer Ingelheim, Aseptuva, Astellas, AstraZeneca, CSL Behring, Novartis, Covidien and Nycomed outside the submitted work; the funds were paid into departmental funds and no personal financial gain applied. Dr. Nathan Nielsen reported receiving personal fees from Adrenomed outside the submitted work. Dr. Alexander P. J. Vlaar reported receiving personal fees from a Vidi grant (ZonMW: 09150172010047). No other disclosures are to be reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Schaap CM, Oomen LA, Raasveld SJ, Schenk J, de Bruin S, Reuland MC, et al. Multinational transfusion practices and outcomes in haematology patients admitted to the intensive care unit. *Vox Sang.* 2026;121:169–79.