LATE BREAKER ARTICLE

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Blood Transfusion Practices in Intensive Care: A Prospective Observational Binational Study

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IMPORTANCE: Blood transfusions are a common and potentially lifesaving intervention in ICU patients but are associated with harm and often transfused inconsistently with guidelines. However, it is not well known how ICU transfusion practice has recently changed and if there is variation in transfusion practice.

OBJECTIVES: To describe blood transfusion practices in ICU, the variation in practice across sites, and to compare transfusion practices against national guidelines and with prior published practice.

DESIGN, SETTING, AND PARTICIPANTS: A prospective, multicenter, binational, observational study conducted in 40 Australian and New Zealand ICUs from October 2021 to July 2022. All adult (≥ 18 yr) ICU patients admitted over 1 week were included and followed until ICU discharge or 28 days.

MAIN OUTCOMES AND MEASURES: Types of transfusion, thresholds and reasons for transfusions, the use of viscoelastic hemostatic assays (VHAs), variation in transfusion practice across sites, and changes in transfusion practice over time.

RESULTS: Of 927 patients, 217 (23.4%) received a blood transfusion during their ICU admission–192 (20.7%) received RBCs, 63 (6.8%) received platelets, 49 (5.3%) received fresh frozen plasma (FFP), and 29 (3.1%) received cryoprecipitate. Massive transfusion protocols were implemented nine times for six patients (0.7%). VHA were used in 25 of 268 (9.3%) non-RBC transfusions. Compared with national guidelines, 89.0% of RBC transfusions, 30.3% of platelet, 27.4% of FFP, and 20.0% of cryoprecipitate transfusions were consistent. Compared with ICU transfusion practices in 2008, after adjusting for confounding variables, ICU patients who received RBC and FFP were transfused more units each, and variation in total transfusions across sites increased for RBC, platelets, and FFP.

CONCLUSIONS AND RELEVANCE: Blood transfusions are common in ICU, but the practice is heterogeneous and frequently inconsistent with national guidelines, and the number of units transfused per patient has increased. More evidence is required.

KEYWORDS: blood transfusion; fresh frozen plasma; intensive care unit; red blood cell

Blood transfusions are common in ICU patients (1–3). Blood components are a precious resource and transfused appropriately have the potential to be lifesaving, but this must be weighed against their association with potential harm (2, 4–7).

Several transfusion guidelines support transfusion decisions in the ICU, such as Australia's National Blood Authority's Patient Blood Management guidelines (8–10), and other guidelines have been developed around the world (11, 12). However, for many areas, insufficient evidence has meant transfusion guidelines were often unable to make evidence-based recommendations and instead relied on expert consensus. In addition, transfusions inconsistent with

DOI: 10.1097/CCE.0000000000001197

KEY POINTS

Question: What is current transfusion practice in ICU and how has it changed since the implementation of transfusion guidelines?

Findings: In this prospective multicenter binational cohort study of 927 ICU patients, almost a quarter of ICU patients were transfused; however, transfusions were often inconsistent with guidelines, and for some blood products, patients were transfused more units compared with historical data, and variation in transfusion practice across sites increased.

Meaning: Blood transfusions are common in ICU, but more evidence to inform transfusion practice for critically ill patients is required.

guidelines (1, 3) and variation in blood transfusion practice has been reported (2, 13).

The strongest evidence base exists for RBC transfusions, with several randomized controlled trials comparing restrictive vs. liberal RBC transfusion in critically ill populations (6, 14, 15). One European study found that this led to ICU patients being transfused less frequently in 2012 compared with 1999 (16). Another study in Sweden found the proportions of patients transfused RBC and fresh frozen plasma (FFP) decreased from 2010 to 2018 (13). However, it is not known whether this trend has continued and was experienced in other parts of the world.

This study's objectives were to report current blood transfusion practices in Australia and New Zealand and how blood transfusion practices and variation across sites have changed since the publication of national guidelines in 2011–2012 (8–10).

MATERIALS AND METHODS

Study Design

The International Point Prevalence Study of ICU Transfusions Practices (InPUT) was an international, multicenter, prospective, point-prevalence study of blood transfusion practice in ICUs around the world (17). This article reports the Australian and New Zealand component.

InPUT data were compared with the Blood Observational Study data published in 2010 (1) before the publication of the National Blood Authority's guidelines (8–10), which are also considered relevant to practice in New Zealand. The Blood Observational Study was a prospective, observational study of blood transfusion practices, conducted in 47 ICUs across Australia and New Zealand over a 5-week period in 2008.

We used the STrengthening the Reporting of OBservational studies in Epidemiology checklist in the preparation of our article (**Supplementary Material**, http://links.lww.com/CCX/B448) (18).

Patient Recruitment and Data Collection

Participating centers in Australia and New Zealand nominated a study week from October 2021 to July 2022 and collected data on all new adult (≥ 18 yr) patients that were admitted to their ICU over that week. Data were collected daily until death or discharge, or up to 28 days, and included baseline characteristics, daily physiological data, transfusion episode data (defined as ≥ 1 U requested at the same time of RBCs, platelets, FFP, and/or cryoprecipitate), laboratory data, mortality status, and ICU length of stay. Transfusion episode data included reasons for transfusion, types and quantities of transfusion, and relevant pre- and post-transfusion laboratory results, including viscoelastic hemostatic assay (VHA) results from rotational thromboelastometry and thromboelastography. Data were collected using Research Electronic Data Capture (19).

Outcomes

Our outcomes were the occurrence rate of each transfusion type during ICU stay, the documented reason and threshold for transfusion and how this compared with relevant recommendations made in the National Blood Authority's guidelines for critical bleeding, perioperative transfusions, and critical care (8–10), which involved collaboration with New Zealand groups, and are endorsed by mutual Colleges in Anaesthesia, Critical Care, Surgery, and Haematology, and are considered relevant to New Zealand (20). Other outcomes included the use of VHA, variation in transfusion practice across sites, and whether transfusion practice changed over time.

Statistical Analysis

STATA was used for all statistical analyses (21). Descriptive statistics were reported according to data distribution as either mean (SD) or median (interquartile range [IQR]). Patient groups were compared using Student *t* tests for normally distributed variables, Wilcoxon rank-sum tests for non-normally distributed variables, and chi-square for categorical variables. A two-sided p-score of *p* value of less than 0.05 was considered statistically significant.

Comparison to Historical Practice

By comparing our data to the Blood Observational Study (1) data, we statistically compared the percentage transfused using the two-sample test of proportions. We investigated changes in transfusion practice by comparing transfusion thresholds (the most recent prior hemoglobin for RBC, platelet count [PC] for platelets, international normalized ratio [INR] for FFP, and fibrinogen level for cryoprecipitate) and the total number of transfusions using multivariable linear regression. Only transfused patients from the InPUT study were included because data for nontransfused patients from the Blood Observational Study was not available. Confounding variables that were adjusted for included age, sex, postoperative status, anticoagulation, or antiplatelet agent administration before ICU admission, hematological disease, liver insufficiency, cardiovascular disease, and country. Acute coronary syndrome on ICU admission was also included in the RBC analysis. A study indicator variable was included to determine whether a statistically significant change in practice had occurred between the two studies.

Variation in transfusion practice across sites for each blood product was compared between studies using a similar methodology described in (22), by first using multivariable regression for the relevant mean pretransfusion threshold (e.g., hemoglobin for RBC transfusion) and then the total number of units transfused for each blood product. Both multivariable regressions adjusted for the same confounding variables listed above. For each analysis, two regression models were run on the same data: one with and one without the site variable. The likelihood ratio test was then used to compare the two regressions to determine the presence of significant variation across sites. Site fixed effects were then estimated using the predicted outcomes from these models and change in variation across sites was assessed using the variance ratio *F* test on the site fixed effects. We adjusted for sampling error by only including sites with more than five patients and by performing an empirical Bayes shrinkage on the site fixed effects (23). Kernel density plots were used to present outcome distributions across sites.

Ethics Approval and Consent to Participate

Following approval of the InPUT study by the Institutional Review Board of the Amsterdam University Medical Center, ethics approval for project title "International Point Prevalence Study of Intensive Care Unit Transfusion Practices" was granted in Australia by the Alfred Hospital ethics committee on June 30, 2021 (HREC/76632) and in New Zealand by the Central Health and Disability Ethics Committee on August 27, 2021 (21/CEN/213), and informed consent was waived in both countries. Study procedures aligned with the Declaration of Helsinki.

RESULTS

We recruited a total of 943 eligible patients from 40 sites. After excluding patients with incomplete data there were 927 (98.3% of eligible patients) patient records available for analysis (**Fig. 1**). There were 832 patients (89.8%) admitted to ICU in metropolitan regions (compared with rural/regional ICUs), and 895 (96.6%) admitted to public (rather than private) hospital ICU. The location of the included sites is represented in **Figure S1** (http://links.lww.com/CCX/B448).

Patient baseline demographics, clinical data, and a comparison of transfused vs. nontransfused patients are shown in **Table 1**. There were 679 transfusion episodes administered to 217 patients (23.4%). A breakdown of demographics and clinical data by transfusion type is produced in **Table S1** (http://links.lww.com/CCX/B448). The median ICU length of stay was 3 days (IQR, 2–5 d). Seventy-two patients died (7.8%) during ICU admission and 107 patients (11.5%) were reported to be deceased at 28 days.

Anemia and RBC Transfusion

The mean ICU admission hemoglobin was 113 g/L (SD, 24 g/L) for females and 124 g/L (SD, 27 g/L) for males. Five hundred twenty-nine patients (57.1%) were anemic

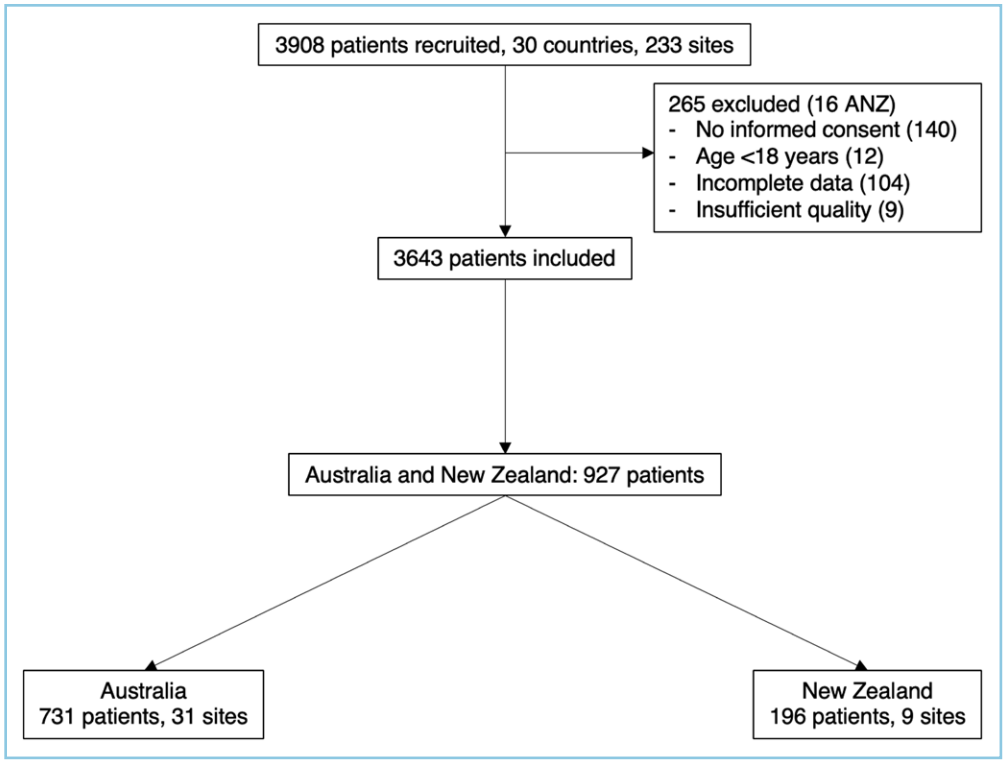

Figure 1. Final dataset for Australia and New Zealand (ANZ) after exclusions.

(hemoglobin < 120 g/L for females and hemoglobin < 130 g/L males) on ICU admission and 779 (84.0%) were anemic at some point during their ICU admission.

Of 679 transfusion episodes, 420 (61.9%) included RBC and there was a total of 625 U transfused to 192 patients (20.7%), with a median of 1 U (IQR, 1–1 U) per transfusion episode, and a maximum of 16 U. Ninety-nine patients (10.7%) received RBC more than once during their ICU admission and received a median total of 3 U (IQR, 2–5 U).

A hemoglobin threshold was reported in almost all (403, 96.0%) RBC transfusions. The mean hemoglobin before RBC transfusion was 76 g/L (SD, 11 g/L) and hemoglobin thresholds were less than 70 g/L for 98 (23.3%), 70–79 g/L for 202 (48.1%), 80–89 g/L for 83 (19.8%), 90–99 g/L for 8 (1.9%), and greater than or equal to 100 g/L for 12 (2.9%) patients. Following transfusion of 1 U, the median increment in hemoglobin was 9 g/L (IQR, 6–14 g/L).

Documented clinical reasons for RBC transfusions are listed in **Table 2**. One hundred four RBC transfusion episodes (24.8%) were given therapeutically to bleeding patients, but most (316, 75.2%) were given to nonbleeding patients. Most RBC transfusions (372, 89.0%) were consistent with the guidelines (**Table 3**).

Thrombocytopenia and Platelet Transfusion

The mean ICU admission PC was 231 × 10^9/L (SD, 108). On ICU admission, 183 patients (19.7%) were thrombocytopenic (PC < 150 × 10^9/L) and 16 (1.7%) had severe thrombocytopenia (PC < 50 × 10^9/L). At any point during ICU admission, 349 (37.7%) and 49 (5.3%) patients were thrombocytopenic and severely thrombocytopenic, respectively.

One hundred fifty-eight transfusion episodes (23.2%) involved platelet transfusions and a total of 213 U were transfused to 63 patients (6.8%), with a median of 1 U (IQR, 1–2 U) per transfusion episode, and a maximum of 5 U. Twenty-three patients (2.5%) received platelet transfusions on more than one occasion and received a median total of 2 U (IQR, 2–6 U).

A PC threshold was reported for 136 (86.1%) platelet transfusions and the mean PC before platelet transfusion was in the category less than 20 × 10^9/L for 26 (16.5%), 20–49 × 10^9/L for 44 (27.9%), 50–149 × 10^9/L for 44 (27.9%), and greater than or equal to 150 × 10^9/L for 22 (13.9%) of platelet transfusions. The PC increment following 1 U was 20 × 10^9/L (IQR, 9–36) and 17.9% of single unit platelet transfusions did not increment greater than 5 × 10^9/L.

There were 66 (41.8%) therapeutic platelet transfusions to bleeding patients and 92 (58.2%) prophylactic platelet transfusions (Table 2). Only 48 (30.4%) platelet transfusions were consistent with the guidelines (Table 3).

Coagulopathy and Plasma Product Transfusion

The ICU admission INR and activated partial thromboplastin time (APTT) were available for 728 (78.5%) and 754 (81.3%) patients, respectively. Coagulopathy on ICU admission (INR > 1.5 and/or APTT > 40 s) was found in 163 patients (17.6%) and at any point during ICU admission in 274 patients (29.6%).

TABLE 1.
Patient Demographics and Clinical Data[a]

Variable	All Patients ($n = 927$)	Any Transfusion ($n = 217$)	No Transfusion ($n = 710$)	p
Age, yr	59.4 (17.1)	61.8 (16.6)	58.6 (17.2)	0.02
Sex, female	341 (36.8)	94 (43.3)	247 (34.8)	0.02
Comorbidities (multiple possible)				
Acute coronary syndrome	87 (9.4)	24 (11.1)	63 (8.9)	0.33
Benign hematological disease	9 (1.0)	2 (0.9)	7 (1.0)	0.93
Bone marrow transplant	4 (0.4)	2 (0.9)	2 (0.3)	0.21
Chronic kidney disease	67 (7.2)	20 (9.2)	47 (6.6)	0.20
Chronic obstructive pulmonary disease	82 (8.9)	14 (6.5)	68 (9.6)	0.16
Hematological malignancy	33 (3.6)	11 (5.1)	22 (3.1)	0.17
Heart failure	58 (6.3)	10 (4.6)	48 (6.8)	0.25
Liver failure	23 (2.5)	13 (6.0)	10 (1.4)	< 0.01
Organ transplant recipient	19 (2.1)	8 (3.7)	11 (1.6)	0.05
Solid tumor diagnosis	92 (9.9)	19 (8.8)	73 (10.3)	0.51
Acute Physiology and Chronic Health Evaluation IV score	59.9 (29.0)	69.6 (29.1)	57.2 (28.5)	< 0.01
Emergency admission	668 (72.1)	162 (74.7)	506 (71.3)	0.33
Surgery < 24 hr before admission	461 (49.7)	131 (60.4)	330 (46.5)	< 0.01
Reason for admission				
Acute brain injury	49 (5.3)	10 (4.6)	39 (5.5)	
Cardiac arrest	40 (4.3)	7 (3.2)	33 (4.7)	
Metabolic disturbance	101 (10.9)	16 (7.4)	85 (12.0)	
Postoperative monitoring	331 (35.7)	85 (39.2)	246 (34.7)	
Respiratory failure	130 (14.0)	20 (9.2)	110 (15.5)	
Shock	142 (15.3)	45 (20.7)	97 (13.7)	
Trauma	45 (4.9)	10 (4.6)	35 (4.9)	
Other/unknown	89 (9.6)	24 (11.1)	65 (9.2)	0.03
Shocked state at admission[b]	286 (30.9)	94 (43.3)	193 (27.0)	< 0.01
Severe acute respiratory syndrome coronavirus 2 suspected or confirmed	64 (6.9)	7 (3.2)	57 (8.0)	0.02
Supportive therapies at admission (multiple possible)				
Mechanical ventilation	370 (39.9)	102 (47.0)	268 (37.8)	0.02
Renal replacement therapy	30 (3.2)	15 (6.9)	15 (2.1)	< 0.01
Extracorporeal membrane oxygenation	4 (0.4)	2 (0.9)	2 (0.3)	0.21
Other mechanical cardiac support	8 (0.9)	6 (2.8)	2 (0.3)	< 0.01
Other support	26 (2.8)	11 (5.1)	15 (2.1)	0.02
Antiplatelet administration before admission	15 (1.6)	15 (6.9)	0 (0.0)	< 0.01
Anticoagulation before admission	25 (2.7)	19 (8.8)	6 (0.9)	< 0.01

[a]Results are reported in mean (SD) for normally distributed variables and *n* (%) for categorical variables.
[b]This includes cardiogenic, distributive, obstructive, and hypovolemic shock.

TABLE 2.
Reasons for Transfusion[a]

Transfusion Type	Reason	*n* (%)
RBC	Low hemoglobin value	373 (88.8)
	Active bleeding	104 (24.8)
	Hemodynamic instability	65 (15.5)
	Improving general state	16 (3.8)
	Preoperative	15 (3.6)
	Improving peripheral oxygen	7 (1.7)
	Age of patient	6 (1.4)
	New coronary ischemia	4 (1.0)
	Improving weaning	3 (0.7)
	Clinical trial	2 (0.5)
	Other	23 (5.5)
	No reason stated	9 (2.1)
Platelets	Active bleeding (including MTP)	66 (41.8)
	Preprocedure	16 (10.1)
	Abnormal VHA results	4 (2.5)
	Thrombocytopenia, coagulopathy, and/or platelet dysfunction	22 (13.9)
	Hematology advice	7 (4.4)
	Perioperative transfusion	6 (3.8)
	Other	37 (23.4)
	No reason stated	8 (5.1)
Fresh frozen plasma	Active bleeding (including MTP)	49 (67.1)
	Preprocedure	12 (16.4)
	Perioperative	11 (15.1)
	Coagulopathy	6 (8.2)
	Abnormal VHA results	5 (6.9)
	Hemodynamic instability	2 (2.7)
	Local protocol	1 (1.4)
	Other	10 (13.7)
	No reason stated	8 (11.0)
Cryoprecipitate	Active bleeding (including MTP)	25 (50.0)
	Abnormal VHA results	5 (10.0)
	Preprocedure	4 (8.0)
	Coagulopathy	4 (8.0)
	Perioperative	4 (8.0)
	Other	9 (18.0)
	No reason stated	6 (12.0)

MTP = massive transfusion protocol, VHA = viscoelastic hemostatic assay.
[a]Multiple reasons for each transfusion were possible.

There were 73 (10.8%) transfusion episodes involving FFP and a total of 181 U of FFP were transfused to 49 patients (5.3%), who received a median of 2 U (IQR, 1–3 U) per transfusion. FFP was transfused therapeutically in 49 (67.1%) transfusions (Table 2). An INR threshold was documented for 64 (87.7%) FFP

TABLE 3.
Reasons/Thresholds for Transfusions Compared With Guidelines

Transfusion Type	Consistent Transfusions	*n* (%)	Inconsistent Transfusions	*n* (%)
RBC	Total consistent	372 (89.0)	Total inconsistent	46 (11.0)
	Critical bleeding[a]	9 (2.2)	Noncritical bleeding, hemoglobin ≥ 70	26 (6.2)
	Hemoglobin < 70	96 (23.0)	Elderly or to improve general state, hemoglobin > 70	2 (0.5)
	Acute coronary syndrome and hemoglobin < 80	2 (0.5)	Perioperative, hemoglobin > 80	3 (0.7)
	Hemoglobin 70–90 and clinical anemia	265 (63.4)	No other consistent indication/threshold	15 (3.6)
Platelets	Total consistent	48 (30.4)	Total inconsistent	110 (69.6)
	PC count < 20	26 (16.5)	PC 20–150	29 (18.4)
	Critical bleeding[a]	8 (5.1)	No other consistent indication/threshold	22 (13.9)
	Specialist advice/local guidelines	8 (5.1)	Noncritical bleeding, PC 50–149	21 (13.3)
	PC count 20–49 and undergoing a procedure	6 (3.8)	Noncritical bleeding, PC 20–49	15 (9.5)
			Noncritical bleeding, PC ≥ 150	14 (8.9)
			Preprocedure, PC ≥ 50	5 (3.2)
			Perioperative, normal/unknown PC	4 (2.5)
Fresh frozen plasma	Total consistent	20 (27.4)	Total inconsistent	53 (73.6)
	Critical bleeding[a]	8 (11.0)	Noncritical bleeding, coagulopathic	14 (19.2)
	INR > 2 and preprocedure	7 (9.6)	Noncritical bleeding, not coagulopathic	21 (28.8)
	Local guidelines/specialist advice	5 (6.9)	Preprocedure, INR < 2	3 (4.1)
			Coagulopathy	13 (18.8)
			No other consistent indication/threshold	2 (2.7)
Cryoprecipitate	Total consistent	11 (22.0)	Total inconsistent	39 (78.0)
	Critical bleeding[a]	6 (12.0)	Noncritical bleeding, fibrinogen level < 1.5	3 (6.0)
	Local guidelines	5 (10.0)	Noncritical bleeding, normal fibrinogen level	17 (34.0)
			Preprocedure, fibrinogen level < 1.5	1 (2.0)
			Coagulopathy, no bleeding/procedure	8 (16.0)
			Perioperative	2 (4.0)
			No other consistent indication/threshold	10 (20.0)

INR = international normalized ratio, PC = platelet count (× 10^9/L).

[a]Critical bleeding was defined as major hemorrhage that is life threatening and likely to result in the need for massive transfusion—critical bleeding patients were identified as those who received massive transfusion protocols and had their reason for transfusion reported as active bleeding.

transfusions and was less than or equal to 1.5 for 32 (43.8%) transfusions, 1.6–2 for seven (9.6%) transfusions, and greater than 2 for 25 (34.3%) transfusions. Twenty FFP transfusions (27.4%) were transfused consistently with the guidelines (Table 3).

Fifty transfusions episodes (7.4%) involved cryoprecipitate and a total of 235 U were transfused to 29 patients (3.1%) at a median of 5 U (IQR, 3–6 U). A pre-transfusion fibrinogen level was documented for 36 (72.0%) transfusions and was less than 1.5 g/L in 12 (33.3%) transfusions and greater than or equal to 1.5 g/L in 24 (66.7%) transfusions. Twenty-five cryoprecipitate transfusions (50.0%) were transfused therapeutically to bleeding patients (Table 2). Eleven

cryoprecipitate transfusions (22.0%) were transfused consistently with the guidelines (Table 3).

Patients Who Did Not Receive RBC Transfusions

Only 25 of 217 transfused patients (11.5%) did not receive RBC transfusions. This included 18 of 63 patients (28.9%) who received platelets—they received just 22 (10.3%) of the total platelet units. Similarly, ten of 49 (20.4%) who received FFP and six of 29 (20.7%) who received cryoprecipitate did not receive RBC transfusions: they received 25 of 181 (13.8%) FFP units and 25,235 (10.6%) cryoprecipitate units, respectively.

Massive Transfusion Protocol

There were nine instances of massive transfusion protocol (MTP) administration administered to six patients (0.7%).

Viscoelastic Hemostatic Assays

VHA was used in 25 of 268 non-RBC transfusions (9.3%), including eight platelet transfusions (5.1%), nine FFP transfusions (12.3%), and eight cryoprecipitate transfusions (16.0%). It was also used in three MTPs (33.3%).

Comparison to Historical Practice

In this study, fewer patients received RBC transfusions (20.7%) compared with the Anemia and Blood Transfusion in Critical Care (ABC) study in 1999 (37.0%) (24), the Anemia and blood transfusion in the critically ill – current clinical practice in the United States (CRIT study) in 2001–2002 (44.1%) (25), and the Intensive Care Over Nations (ICON) study in 2012 (26.3%) (2). Additionally, the mean hemoglobin before RBC transfusion (76 g/L) was lower than that reported in the ABC study (84 g/L) (24), the CRIT study (86 g/L) (25), and the ICON study (83 g/L) (2).

Twenty-three of the 40 sites (57.5%) in the InPUT study were also in the Blood Observational Study (1). Compared with Blood Observational Study's patients in 2008, more patients in this study received transfusions of RBC ($p < 0.01$), platelets ($p < 0.01$), and cryoprecipitate ($p < 0.01$), but not FFP ($p < 0.14$) (**Table 4**). However, for all blood products the pre-transfusion thresholds were not significantly different (Table 4).

After restricting InPUT data to only the transfused patients, a comparison of patients from the InPUT study vs. the Blood Observational Study is presented in Table 4. Comparing the two studies, there was no significant difference after adjusting for confounders in the mean pre-transfusion thresholds (mean hemoglobin $p = 0.11$, mean PC $p = 0.08$, mean INR $p = 0.78$, mean fibrinogen level $p = 0.11$), but for those who received each blood product type, InPUT patients compared with Blood Observation Study patients were significantly more likely to receive more units of RBC ($p < 0.01$) and FFP ($p < 0.01$), but not platelets ($p = 0.10$). Cryoprecipitate was not included in the total transfusion analysis because we were uncertain if the small median number of units in the Blood Observational Study represented different volumes or multiple units.

Finally, significant variation in transfusion practice across sites for pre-transfusion thresholds was found for each blood product in the Blood Observational Study, but only for platelet and cryoprecipitate transfusions in the InPUT study (Table 4). This variation significantly decreased for pre-FFP INR ($p < 0.01$) but increased for pre-cryoprecipitate fibrinogen level ($p < 0.01$). Significant variation in the total number of units per patient was only found in the Blood Observational Study for RBC and not in the InPUT study for any blood products (Table 4). However, variation in total units per patient was significantly greater in the InPUT study for RBC ($p < 0.01$), platelets ($p < 0.01$), and FFP ($p < 0.01$) and was not investigated for cryoprecipitate. Kernel density plots are shown in **Figures S2** and **S3** (http://links.lww.com/CCX/B448).

DISCUSSION

We performed a prospective, multicenter, observational study of blood transfusions in ICUs of Australia and New Zealand. We found that transfusions for RBC were mostly consistent with guidelines, but other products were frequently transfused inconsistently with guidelines. Compared with historical practice, a greater proportion of all transfusions (except cryoprecipitate) were inconsistent with guidelines, patients were less likely to receive FFP, those who received transfusions were more likely to receive more units of RBC and FFP, and there was more variation across sites in the total number of transfusions administered for RBC, FFP, and platelets.

Compared with earlier studies of RBC transfusion in ICU (2, 24, 25), the percentage of patients transfused RBC and the mean hemoglobin before RBC transfusion

TABLE 4.

Comparison of Transfused Patients From the Australian and New Zealand International Point Prevalence Study of ICU Transfusions Practices Study and the Blood Observational Study[a]

Variable	Blood Observational Study ($n = 5128$)	Australian and New Zealand International Point Prevalence Study of ICU Transfusions Practices Study ($n = 927$)	p
Year	2008	2021–2022	
Transfused patients, n[b]	874 (17.0)	217 (23.4)	< 0.01
Country, Australia	700 (80.1)	180 (83.0)	0.34
Age, yr	62.5 (16.4)	61.8 (16.6)	0.57
Sex, female	330 (37.8)	94 (43.3)	0.13
Postoperative admission	500 (57.2)	131 (60.4)	0.40
Comorbidities (multiple possible)			
Hematological disease	26 (3.0)	14 (6.5)	0.02
Liver insufficiency	69 (7.9)	13 (6.0)	0.34
Cardiovascular disease	395 (45.2)	28 (12.9)	< 0.01
Anticoagulation or antiplatelet agent before admission	463 (53.0)	29 (13.4)	< 0.01
RBC transfusion, n[b]	763 (14.8)	192 (20.7)	< 0.01
Proportion inconsistent with guidelines, %	2	11	
Mean hemoglobin before RBC transfusion, g/L	78 (8.9)	76 (10.6)	0.12
Variation in pre-transfusion hemoglobin, p	< 0.01	0.37	0.21
Total RBC for patients transfused RBCs, U	1 (1–2)	2 (1–4)	< 0.01
Variation in total RBC per patient, p	0.04	0.62	< 0.01
Platelet transfusion, n[b]	231 (4.5)	63 (6.8)	< 0.01
Proportion inconsistent with guidelines, %	53	70	
Median PC before platelet transfusion, × 10^9/L	76 (44–13)	69 (41–152)	0.96
Variation in pre-transfusion PC, p	< 0.01	< 0.01	0.34
Total platelets for patients transfused platelets, U	1 (1–2)	2 (1–2)	< 0.01
Variation in total platelets per patient, p	0.81	0.17	< 0.01
FFP transfusion, n[b]	341 (6.6)	49 (5.3)	0.14
Proportion inconsistent with guidelines, %	26	74	
Median INR before FFP transfusion	1.7 (1.4–2)	1.6 (1.3–2.6)	0.52
Variation in pre-transfusion INR, p	< 0.01	0.08	< 0.01
Total FFP for patients transfused FFP, U	1 (1–2)	2 (2–4)	< 0.01
Variation in total FFP per patient, p	0.61	0.30	< 0.01
Cryoprecipitate transfusion, n[b]	78 (1.5)	29 (3.1)	< 0.01
Proportion inconsistent with guidelines, %	85	78	
Median fibrinogen level before cryoprecipitate transfusion, g/L	1.6 (1.3–2.1)	1.9 (1.4–2.7)	0.13
Variation in pre-transfusion fibrinogen level, p	< 0.05	< 0.01	< 0.01
Total cryoprecipitate for patients transfused, U	1 (1–2)	5 (2–10)	< 0.01

(*Continued*)

TABLE 4. (*Continued*)

Comparison of Transfused Patients From the Australian and New Zealand International Point Prevalence Study of ICU Transfusions Practices Study and the Blood Observational Studya

Variable	Blood Observational Study (*n* = 5128)	Australian and New Zealand International Point Prevalence Study of ICU Transfusions Practices Study (*n* = 927)	*p*
Mortality, hospital/28 d[c]	146 (16.7)	37 (17.1)	0.90
ICU length of stay, d	4 (2–8)	5 (3–8)	< 0.01

FFP = fresh frozen plasma, INR = international normalized ratio, PC = platelet count.

[a]Results are reported in mean (SD) for normally distributed variables, median (interquartile range) for non-normally distributed variables, and *n* (%) for categorical variables.

[b]Percentage of the total population (not transfused population).

[c]Hospital mortality was reported for the Blood Observational Study, and 28-d mortality was reported for the International Point Prevalence Study of ICU Transfusions Practices study.

were lower. However, compared with the Blood Observational Study (1), which was published before the National Blood Authority's guidelines (8–10), despite similar pre-transfusion thresholds, a greater proportion of patients in this study received RBC, platelet, and cryoprecipitate transfusions, and there was a nonsignificant decrease for FFP. Less patients being transfused FFP was also found in Sweden over a similar time period (13). This could be due to the use of other plasma products in place of FFP, such as prothrombin complex concentrate. More common transfusion of cryoprecipitate might reflect appreciation of the association between low fibrinogen and poor outcomes, and benefits of timely supplementation in certain patient populations (26). After adjusting for confounding variables, we did not find evidence that transfusion thresholds were becoming more restrictive, which has been reported previously (16). Instead, we found evidence of some transfusion practices becoming more liberal: if a patient was transfused RBC or FFP, they received more units, despite the pre-transfusion threshold not significantly differing over time. This might suggest that after an initial movement toward more restrictive practice from at least 1999 to 2012 (16), the trend to more restrictive transfusion practice has reached a stable point. Another possibility is that an increase in the severity of clinical illness affected our results—although patients in the InPUT study had longer hospital stays, the mortality rates were comparable to those in the earlier study, casting doubt on the notion of increased clinical illness severity.

Regarding anemia and RBC transfusion, nearly all patients were anemic at some point during their ICU admission, and this was more common than thrombocytopenia and coagulopathy. To what extent and at what hemoglobin anemia becomes clinically important in ICU patients, and how best to treat the underlying cause other than with RBC transfusion alone, needs to be determined.

Variation in transfusion practice across regions has been reported previously (2, 13, 17). Raasveld et al (17) reported considerable variation across sites around the world in the lowest hemoglobin before RBC, and Vincent et al (2) reported variation in transfusion practice across geographic regions for total RBC transfusions. Similarly, significant variation in the pre-RBC hemoglobin and total RBC transfused per patient was reported in the Blood Observational Study (1). This was not, however, found for RBC transfusion in this study: variation across sites significantly decreased. This might be due to new published evidence for RBC transfusions over that time and investigating two countries in a similar geographic region with the same set of national guidelines (8–10).

We found low rates of inconsistency of RBC transfusions with transfusion guidelines but higher rates of inconsistent transfusions for non-RBC transfusions, like our previous studies (1, 3). This reflects the evidence and guidelines for RBC transfusions in ICU being the most established, compared with the evidence for non-RBC transfusions and corresponding weak guidelines. We hope that this study brings attention to the lack of

evidence guiding non-RBC transfusions and the need for further research.

This study has several limitations. Using documented reasons and thresholds for transfusion, and comparing against transfusion guidelines, may be an oversimplification of the transfusion decision process, and transfusions we found to be inconsistent with guidelines may have been indicated in their clinical context. Second, in the comparison to the Blood Observational Study, although we attempted to adjust for clinically relevant variables, there were variables we were unable to adjust for in all patients because they were not common to both datasets. In addition, in our comparison we only included the transfused patient subgroup because nontransfused patient data were not available. Third, our variation analysis was unable to quantify the size of the variation, only if it was present or not, and it did not characterize how variation differed across sites and regions. Fourth, sites participated at different times over a 10-month period and temporal changes in transfusion practice over the year, as well as clinician knowledge of the study and potential behavior change, may have confounded our results. Finally, most sites were metropolitan hospitals in the public health system spread across a large geographic region, and the impact of different health systems, local guidelines, and blood supply challenges to regional hospitals potentially limits the generalizability of the findings.

CONCLUSIONS

Blood transfusions in ICU are common, frequently transfusions are administered for indications inconsistent with guidelines, and there is heterogeneity in transfusion practice across sites. Patients are being transfused greater quantities and with increasing variation compared with historical practice. More evidence to inform transfusion practice for critically ill patients is required.

ACKNOWLEDGMENTS

We thank the National Blood Authority, the Australian and New Zealand Intensive Care Society Clinical Trials Group, and the National Health and Medical Research Council Blood Synergy for their support. Also, we thank the site-based contributors listed in the Supplementary Material (http://links.lww.com/CCX/B448) and everyone else who contributed to this study.

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Drs. Flint, Raasveld, Brady, Cooper, French, Higgins, Irving, Winearls, Reade, Wood, Vlaar, and McQuilten were involved in the concept and design. Dr. Flint, Dr. Poole, Dr. Brady, Dr. Cooper, Dr. French, Dr. Higgins, Dr. Irving, Mr. Waters, Dr. Winearls, Dr. Reade, Dr. Wood, Dr. Vlaar, and Dr. McQuilten obtained funding. Ethics approval was conducted by Drs. Flint, Poole, and McQuilten. The acquisition of data were overseen by Dr. Flint, Dr. Poole, Dr. Raasveld, Dr. Brady, Ms. Chen, Dr. Higgins, Dr. Irving, Mr. McAllister, Dr. Neto, Mr. Trapani, Dr. Wood, Dr. Vlaar, and Dr. McQuilten. Data analysis and statistical analysis were done by Drs. Flint, Bailey, Chen, Higgins, Irving and McQuilten. Drafting of the article was done by Dr. Flint, and all authors were involved in reviewing the final article. Figures were produced by Drs. Flint and Brady. Administrative support was provided by Drs. Flint, Poole, Raasveld, Vlaar, and McQuilten.

This study was funded in part by a National Blood Authority National Blood Sector Research and Development Grant (No. ID508), along with support from the Australian National Health

and Medical Research Council funded Blood Synergy (No. 1189490).

Drs. Wood and Cooper are supported by a National Health and Medical Research Council (NHMRC) Leadership Fellowship (Nos. 1177784, 2016324). Drs. McQuilten and Higgins are supported by NHMRC Emerging Leadership Fellowships (Nos. 1194811, 2008447). Dr. Vlaar is supported by a Landsteiner Foundation for Blood Research fellowship grant (No. 1931F) and by a personal grant from the Dutch Research Council (Vidi grant number 09150172010047). The remaining authors have disclosed that they do not have any potential conflicts of interest.

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