Received: 28 October 2024 | Revised: 4 November 2024 | Accepted: 5 November 2024

DOI: 10.1111/trf.18071

ORIGINAL RESEARCH

Transfusion Practice

TRANSFUSION

Plasma transfusion in the intensive care unit

Maite M. T. van Haeren[1,2] | Senta Jorinde Raasveld[1,2] | Sanne de Bruin[1] | Merijn C. Reuland[1] | Claudia van den Oord[1] | Jimmy Schenk[1,2,3] | Cécile Aubron[4] | Jan Bakker[5,6] | Maurizio Cecconi[7] | Aarne Feldheiser[8] | Harm-Jan de Grooth[1] | Jens Meier[9] | Thomas W. L. Scheeren[10] | Zoe McQuilten[11] | Andrew Flint[11,12] | Tarikul Hamid[13] | Michaël Piagnerelli[14] | Tina Tomić Mahečić[15] | Jan Benes[16] | Lene Russell[17,18,19] | Hernan Aguirre-Bermeo[20] | Konstantina Triantafyllopoulou[21] | Vasiliki Chantziara[22] | Mohan Gurjar[23] | Sheila Nainan Myatra[24] | Vincenzo Pota[25] | Muhammed Elhadi[26] | Ryszard Gawda[27] | Mafalda Mourisco[28] | Marcus Lance[29] | Vojislava Neskovic[30] | Matej Podbregar[31] | Juan V. Llau[32] | Manual Quintana-Diaz[33] | Maria Cronhjort[34] | Carmen A. Pfortmueller[35] | Nihan Yapici[36] | Nathan D. Nielsen[37] | Akshay Shah[38] | Alexander P. J. Vlaar[1] | Marcella C. A. Müller[1] | the InPUT Study Group

Correspondence
Marcella C. A. Müller, Department of Intensive Care, Amsterdam University Medical Centers, Amsterdam, the Netherlands.
Email: m.c.muller@amsterdamumc.nl

Funding information
National Blood Authority of Australia and a National Health and Medical Research Council (NHMRC) Synergy, Grant/Award Number: GNT1189490; National Health and Medical Research Council (NHMRC) Emerging Leader Investigator, Grant/Award Number: GNT1194811; ZonMw Vidi, Grant/Award Number: 09150172010047

Abstract

Background: Current guidelines discourage prophylactic plasma use in non-bleeding patients. This study assesses global plasma transfusion practices in the intensive care unit (ICU) and their alignment with current guidelines.

Study Design and Methods: This was a sub-study of an international, prospective, observational cohort. Primary outcomes were in-ICU occurrence rate of plasma transfusion, proportion of plasma events of total blood products events, and number of plasma units per event. Secondary outcomes included transfusion indications, INR/PT, and proportion of events for non-bleeding indications.

Results: Of 3643 patients included, 356 patients (10%) experienced 547 plasma transfusion events, accounting for 18% of total transfusion events. A median of 2 (IQR 1, 2) units was given per event excluding massive transfusion protocol (MTP) and 3 (IQR 2, 6) when MTP was activated. MTP accounted for 39 (7%)

For affiliations refer to page 12

of events. Indications of non-MTP events included active bleeding (54%), prophylactic (25%), and pre-procedure (12%). Target INR/PT was stated for 43% of transfusion events; pre-transfusion INR/PT or visco-elastic hemostatic assays (VHA) were reported for 73%. Thirty-seven percent of events were administered for non-bleeding indications, 54% with a pre-transfusion INR < 3.0 and 30% with an INR < 1.5.

Discussion: Plasma transfusions occurred in 10% of ICU patients. Over a third were given for non-bleeding indications and might have been avoidable. Target INR/PT was not stated in more than half of transfusions, and pre-transfusion INR/PT or VHA was not reported for 27%. Further research and education is needed to optimize guideline implementation and to identify appropriate indications for plasma transfusion.

KEYWORDS

critically ill, ICU, intensive care unit, plasma, transfusion, transfusion practices

1 | INTRODUCTION

Plasma transfusions are commonly administered in the intensive care unit (ICU), occurring in 9%–13% of ICU patients.[1,2] Previously, it has been shown that a substantial amount of plasma is transfused to non-bleeding ICU patients.[3] However, according to guidelines, plasma transfusion is only indicated in bleeding ICU patients with or without coagulopathy.[4,5]

The global landscape of plasma transfusion practices is far from uniform. In bleeding patients, different red blood cell (RBC) to plasma ratios is used as part of (massive) transfusion protocols (MTPs),[6,7] although a higher ratio is currently recommended.[5] There are no clear indications or triggers for plasma transfusion for non-bleeding patients, except for plasmapheresis.[8,9] Moreover, current guidelines include the recommendation not to use plasma in non-bleeding patients with a coagulopathy in need of an invasive procedure or in non-bleeding patients with coagulopathy in general.[4,10,11] However, a significant portion of plasma transfusions in ICU patients is administered for non-bleeding indications.[3,12]

There are scarce prospective data from recent studies examining the utilization of plasma in ICU patients. Rather, more evidence has become available on the ineffectiveness of (prophylactic) plasma transfusions.[13–16] Therefore, this study aims to provide a current overview of global plasma transfusion practice in patients admitted to the ICU. We hypothesized that, as multiple guidelines discourage plasma transfusions in non-bleeding patients over time, the occurrence rate of plasma transfusions in non-bleeding patients has decreased compared with previous reported occurrence rates.

2 | METHODS

2.1 | Study design

This is a sub-study of the *International Point Prevalence Study of Intensive Care Unit Transfusion Practices* (InPUT) study. The InPUT was an international, multicenter, prospective observational cohort study on transfusion practices.[17] Between March 2020 and October 2022, 16 weeks were prescheduled for the study. In these weeks, all patients admitted to the ICU were included in the study and followed up until Day 28 or ICU discharge. Study procedures aligned with the Declaration of Helsinki. The protocol and Standard Operating Procedure can be found in the previously published InPUT study on RBC transfusions.[17]

2.2 | Patient population

The patient cohort included all individuals aged 18 years or older admitted to the ICU during the designated study weeks. Patients were excluded if informed consent, mandated by local or national regulations, was not obtained from the patient or their legally authorized representative.

2.3 | Data collection

Baseline demographics, daily ICU questionnaires up to discharge or up to Day 28 of ICU stay, and outcomes at Day 28 were collected. If a transfusion was administered,

a separate questionnaire for the transfusion was generated. If a patient had two transfusion events on a single day, this generated two separate transfusion forms. The transfusion questionnaire for plasma included target INR or PT, pre-transfusion INR or PT and posttransfusion INR or PT, number of units transfused, and the transfusion indication.

2.4 | Outcomes

The primary outcome was the worldwide and continent-wise occurrence rate of plasma transfusion during ICU stay, defined as receiving one or more plasma units during their ICU stay (including plasma as part of MTP). The proportion of plasma transfusion events of the total transfusion events (RBC + platelets + plasma) was assessed, and plasma units per transfusion event (excluding MTP) and per MTP event were analyzed.

Secondary outcomes included the main indications for plasma transfusion events (active bleeding, prophylactic, pre-procedure, MTP, and others). Multiple indications could be selected however for this analysis, indications were only scored once: if active bleeding was selected (with or without other indications), then the reason for transfusion was active bleeding; if pre-procedure (but not active bleeding) was selected, then the reason for transfusion was pre-procedure; if prophylactic (but not active bleeding or pre-procedure) was selected, then the reason for transfusion was prophylactic. The remaining reasons were categorized as "other." Other secondary outcomes included target INR or PT, pre- and posttransfusion INR/PT, INR/PT change per plasma transfusion event and per plasma unit (excluding MTP), INR change stratified by transfusion indication and by pre-transfusion INR (divided into three groups: <1.5, 1.5–3.0, >3.0). Lastly, as a secondary outcome, the proportion of plasma transfusion events for non-bleeding indications (being prophylactic and pre-procedure) were assessed worldwide and per continent.

2.5 | Statistical analyses

All analyses were performed with R in the R studio interface (version 4.2.1). Continuous data were expressed by mean and standard deviation (mean [±SD]) or by median and interquartile range (median [first, third interquartile]), depending on the distribution. Categorical data were expressed as counts with percentages (*n*, %). MTP events were counted in the overall in-ICU occurrence rate and the proportion of plasma of the total blood products transfused (primary outcomes) but excluded from the other analyses (plasma units per event and investigations of INR). This decision was made due to the standardized protocol inherent in MTP, which contrasts the variable nature of INR-guided plasma transfusions, making it an inadequate representation of clinical practice.

Analyses on INR/PT values were only performed with the transfusions on which INR/PT values were reported. No imputation was performed as a substantial amount of the INR/PT values was missing, and they were assumed to be not missing at random.

Statistical analyses included comparisons of (1) plasma-transfused versus non-transfused patients (including MTP), (2) a per continent comparison of the occurrence rate of plasma transfusion, proportion of plasma transfusion events of the total transfusion events, transfusion indications, and transfusion events for non-bleeding indications, and (3) comparisons of INR changes per transfusion indication and per pre-transfusion INR.

For comparisons between plasma transfused and non-transfused patients, differences and 95% confidence intervals (95% CIs) were estimated using an independent samples two-sided *t*-test for normally distributed continuous variables, the Wilcoxon Rank-Sum test for non-normally distributed continuous variables, and a two-sample proportion test for categorical variables. For comparisons of proportions per continent, a chi-square test was performed; when significant, a Wilcoxon Rank-Sum post hoc test was done with Bonferroni correction. To assess the effect of plasma transfusions on INR, the INR change per pre-transfusion INR category (3 categories: INR < 1.5, INR 1.5–3.0, INR > 3.0) was analyzed.

Four groups were created to compare INR change between the plasma transfusion indications (active bleeding, prophylactic, pre-procedure, or other). Depending on the distribution, the differences in INR change were tested using a one-way ANOVA or Kruskal–Wallis test. If significant, a post hoc Mann–Whitney *U* or *t*-test with Bonferroni correction was performed. The significance level for all analyses was set at a *p*-value below 0.05.

3 | RESULTS

3.1 | Plasma-transfused patients

In total, 233 centers in 30 countries and 6 continents participated (Figure 1). A total of 3643 patients were included in the InPUT database. Of those, 356 patients (10%) received one or more plasma transfusions in the ICU. These 356 patients experienced 547 plasma transfusion events including MTP, and 508 events excluding MTP (Figure 2). The occurrence rate ranged from 4% to 17% between continents, where Asia (17%) and Europe (12%) had a significantly higher plasma transfusion rate

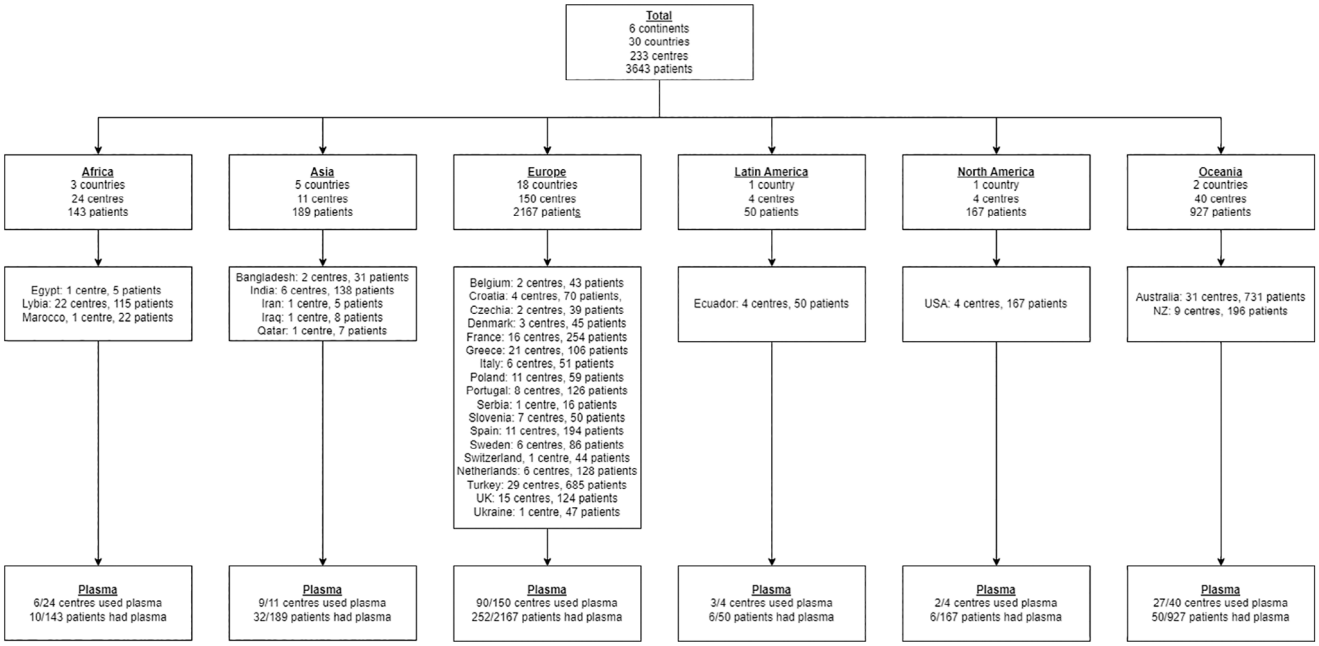


FIGURE 1 Flowchart of included countries and centers.

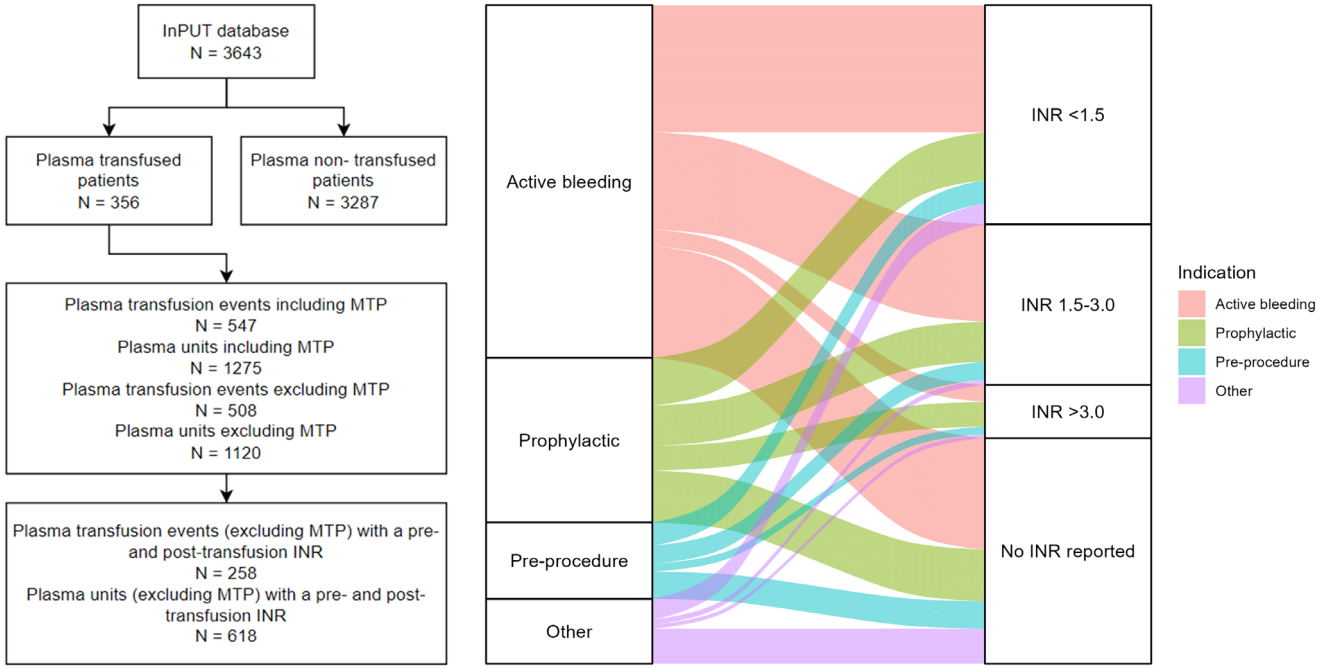


FIGURE 2 Flowchart and alluvial plot of included patients and transfusion events. On the left: a flowchart of included patients, transfusion events and plasma units; on the right: alluvial plot with on the left the transfusion indication of the event and on the right the pre-transfusion event INR.

than North America (4%, $p < 0.001$) and Oceania (5%, $p < 0.001$, Figure 3A).

Plasma-transfused patients overall did not differ in comorbidities, except for a lower incidence of chronic obstructive pulmonary disease (difference of −5% [95% CI = −8 to −2]) and a higher prevalence of liver failure (difference of 6% [95% CI = 3–9], Table 1). Transfused patients had a higher APACHE IV score (difference of 12 [95% CI = 8–16]), lower hemoglobin levels (difference of −1.5 g/dL [95% CI = −1.8 to 1.2]), lower platelet

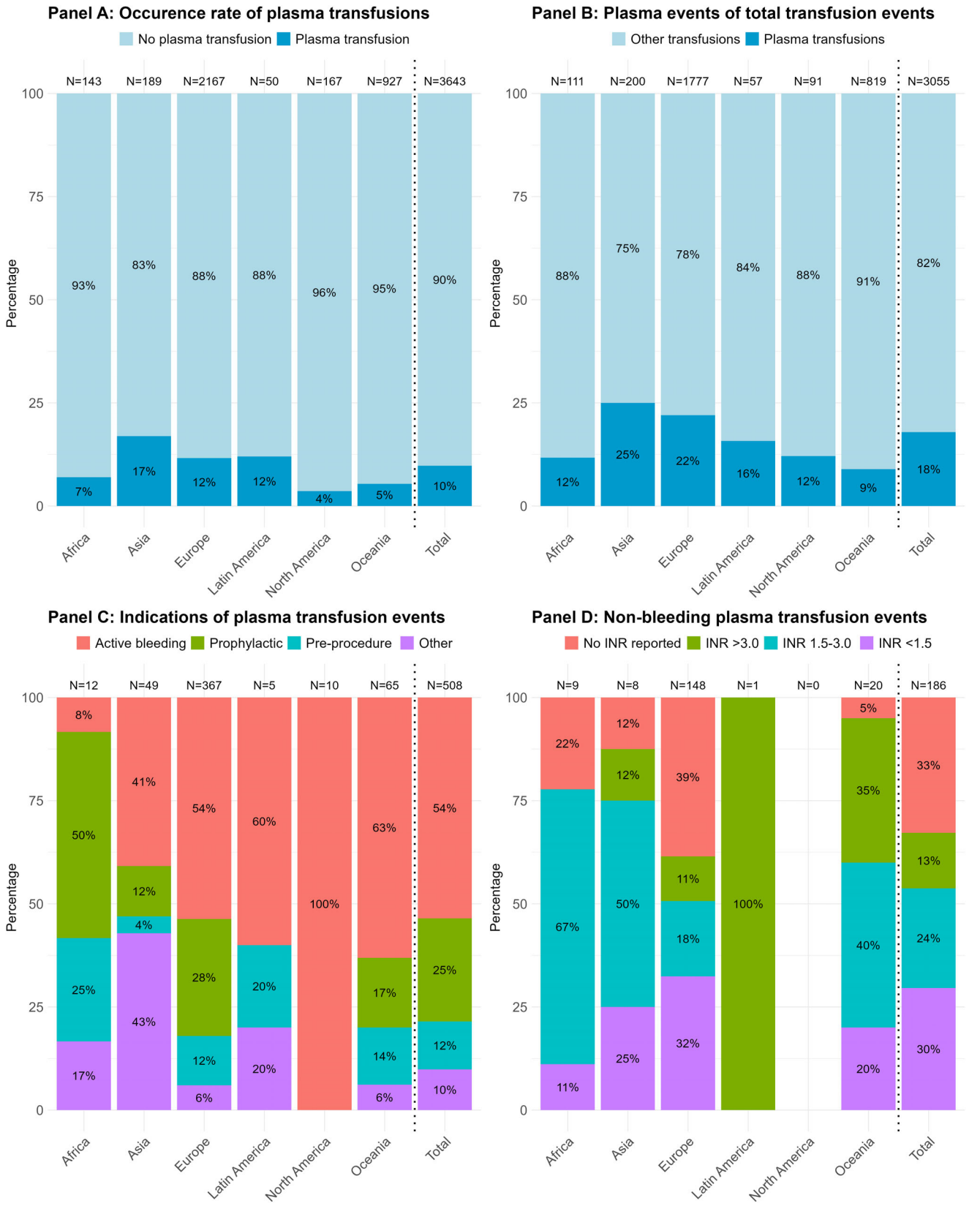


FIGURE 3 Plasma transfusion practices per continent. Panel A: Occurrence rate of plasma transfusion in the ICU per continent and in total, including as part of massive transfusion protocol (MTP). Panel B: Proportion of plasma transfusion events of the total transfusion events of all products (Red Blood Cells, Platelets and Plasma) per continent and in total, including MTP. Panel C: Distribution of proportions of transfusion indications per continent and in total, excluding MTP. Panel D: Proportions of unknown INR, INR > 3.0, INR 1.5–3.0, and INR < 1.5 of the transfusion events for a non-bleeding indication (defined as prophylatic or pre-procedure) per continent and in total, excluding MTP.

TABLE 1 ICU admission data and patient outcomes, stratified by plasma transfusion status.

	Overall $N = 3643$	Not transfused $N = 3287$	Transfused $N = 356$	Difference (95% CI)
Age, years, mean (SD)	61 (16)	61 (16)	60 (16)	−1 (−3 to 1)
Female sex, *n* (%)	1376 (38)	1248 (38)	128 (36)	−2 (−7 to 3)
Comorbidities, n (%) Multiple answers possible				
No comorbidities	1387 (38)	1244 (38)	143 (40)	2 (−3 to 8)
Solid tumor	485 (13)	443 (14)	42 (12)	−1 (−5 to 2)
Heart failure	427 (12)	380 (12)	47 (13)	2 (−2 to 6)
Chronic obstructive pulmonary disease	412 (11)	387 (12)	25 (7)	−5 (−8 to −2)
Acute coronary disease	381 (11)	340 (10)	41 (12)	2 (−3 to 5)
Chronic kidney disease	329 (9)	300 (9)	29 (8)	−1 (−4 to 2)
Liver failure	110 (3)	81 (3)	29 (8)	6 (3–9)
APACHE IV score, median [IQR]	46 [28, 70]	46 [27, 68]	60 [33, 84]	12 (8–16)
Emergency admission, *n* (%)	2372 (65)	2169 (66)	203 (57)	−9 (−15 to −3)
Laboratory values at admission				
Hemoglobin, g/dL, median [IQR]	11.9 [10.0, 13.8]	12.1 [10.2, 13.9]	10.3 [8.7, 12.7]	−1.5 (−1.8 to 1.2)
Platelet count, 10^9/L, median [IQR]	222 [163, 289]	225 [167, 291]	186 [123, 276]	33 (20–46)
INR, ratio, median [IQR]	1.10 [1.00, 1.30]	1.10 [1.00, 1.30]	1.20 [1.00, 1.60]	−0.10 (−0.20 to −0.10)
Referring specialty, *n* (%)				
Medical specialties[a]	1537 (42)	1467 (45)	70 (20)	−25 (−30 to −20)
Cardiothoracic surgery	538 (15)	426 (13)	112 (32)	19 (13–24)
Neurosurgery	291 (8)	275 (8)	16 (5)	−4 (−6 to −1)
Trauma surgery	151 (4)	126 (4)	25 (7)	3 (0–4)
Other surgical specialties[b]	1037 (29)	911 (28)	126 (35)	8 (2–13)
Other[c]	89 (2)	82 (3)	7 (2)	−1 (−2 to 1)
Referred from, *n* (%)				
Operation room	1513 (42)	1306 (40)	207 (58)	18 (13–24)
Emergency department	1145 (31)	1079 (33)	66 (19)	−14 (−19 to −10)
General ward	623 (17)	570 (17)	53 (15)	−3 (−7 to 2)
Other hospital	313 (9)	285 (9)	28 (8)	−1 (−4 to 2)
Other	47 (1)	45 (1)	2 (1)	−1 (−2 to 0)
Reason for admission, *n* (%)				
Postoperative monitoring	1305 (36)	1145 (35)	160 (45)	10 (5–16)
Respiratory insufficiency	791 (22)	748 (23)	43 (12)	−11 (−15 to −7)
Shock	432 (12)	360 (11)	72 (20)	9 (5–14)
Metabolic disturbance	268 (7)	254 (8)	14 (4)	−4 (−6 to −1)
Acute brain injury	229 (6)	214 (7)	15 (4)	−3 (−5 to 0)
Trauma	169 (5)	141 (4)	28 (8)	4 (1–7)
Cardiac arrest	133 (4)	128 (4)	5 (1)	−3 (−4 to −1)
Other	308 (9)	290 (9)	18 (5)	−4 (−6 to −1)
Shock at admission, *n* (%)				
Septic shock	335 (11)	346 (11)	49 (14)	3 (−1 to 7)
Hypovolemic shock	261 (7)	188 (6)	73 (21)	15 (10–19)
Cardiogenic shock	214 (6)	184 (6)	30 (8)	3 (0–6)
Other shock	59 (2)	52 (2)	7 (2)	0 (−1 to 2)

TABLE 1 (Continued)

	Overall $N = 3643$	Not transfused $N = 3287$	Transfused $N = 356$	Difference (95% CI)
Surgery within 24 h of admission, *n* (%)				
Cardiothoracic surgery	507 (14)	403 (12)	104 (29)	17 (12–22)
Gastro-intestinal surgery	366 (10)	314 (10)	52 (15)	5 (1–9)
Neurosurgery	212 (6)	200 (6)	12 (3)	−3 (−5 to −1)
Gynecologic surgery	138 (4)	121 (4)	17 (5)	1 (−1 to 4)
Trauma surgery	108 (3)	82 (3)	26 (7)	5 (2–8)
Other surgery	393 (11)	355 (11)	38 (11)	0 (−4 to 3)
Mechanical support at admission, *n* (%)				
Mechanical ventilation	1619 (44)	1376 (42)	243 (68)	26 (21–32)
Renal replacement therapy	131 (4)	113 (3)	18 (5)	2 (−1 to 4)
Extracorporeal membrane oxygenation	15 (<1)	10 (<1)	5 (1)	1 (0–3)
Concomitant transfusion, *n* (%)				
RBC transfusion	894 (25)	626 (19)	268 (75)	56 (51–61)
Platelet transfusion	208 (6)	95 (3)	113 (32)	29 (24–34)
Other pro coagulants	208 (6)	110 (3)	98 (28)	24 (19–29)
Patient outcomes				
State of the patient at Day 28, *n* (%)				
Alive	2781 (76)	2536 (77)	245 (69)	−8 (−14 to −3)
Discharged	2248 (81)	2080 (82)	168 (69)	−13 (−20 to −7)
General ward	426 (15)	371 (15)	55 (22)	8 (2–13)
ICU	83 (3)	65 (3)	18 (7)	5 (1–8)
Readmitted to ICU	25 (1)	21 (<1)	4 (2)	1 (−1 to 3)
Death	618 (17)	523 (16)	95 (27)	11 (6–16)
Unknown	244 (7)	228 (7)	16 (5)	−2 (−5 to 0)

[a]Medical specialties included internal medicine, neurology, cardiology, and pulmonology.
[b]Other surgical specialties included general surgery, gastro-enteral surgery, gynecology, urology, and orthopedic surgery.
[c]Other specialties included psychiatry, emergency, and ENT (ear nose throat).

counts (difference of $33{\cdot}10^9$/L [95% CI = 20–46]), and higher INR (difference of −0.10 [95% CI = −0.20 to −0.10]) at admission.

Patients who underwent transfusion were more frequently referred by surgical specialties and were more often referred from the operation room and less often from the emergency department. The reason for ICU admission in transfused patients was more often postoperative monitoring, trauma, or shock. Hypovolemic or cardiogenic shock was the most common. Transfused patients were more often supported by mechanical ventilation at admission. Plasma-transfused patients more often received other blood products: RBC (difference of 56% [95% CI = 51–61]), platelets (difference of 29% [95% CI = 24–34]), or other pro-coagulants (difference of 24% [95% CI = 19–29]). Lastly, plasma-transfused patients had higher unadjusted 28-day mortality (difference of 11% [95% CI = 6–16]).

3.2 | Plasma transfusion events and units

There were 547 plasma transfusion events including MTP, involving a total of 1275 plasma units, and 508 events excluding MTP involving a total of 1120 plasma units (Figure 2). Figure 2 (on the right) presents an alluvial plot illustrating the distribution of transfusion indication categories alongside pre-transfusion INR categories. Notably, within each indication category, INR values were not reported in approximately one-third or more of the events. Furthermore, for non-bleeding indications (prophylactic and pre-procedural), a pre-transfusion INR of less than 3.0 was reported in approximately half of the events.

Of the total study cohort, plasma transfusion events accounted for 18% of all transfusion events. Per continent, this ranged from 9% to 25%, where the proportion

TABLE 2A Characteristics of the plasma transfusion events excluding massive transfusion protocol (MTP).

	Plasma transfusion events (excluding MTP) *N* = 508
Transfusion indication, *n* (%)	
Active bleeding	272/508 (54)
Prophylactic	127/508 (25)
Pre-procedure	59/508 (12)
Cardiothoracic surgery	22/59 (37)
General surgery	12/59 (20)
Neurosurgery	7/59 (12)
Other[a]	18/59 (31)
Other (asked to specify)	50/508 (10)
COVID-19	21/50 (42)
Unstable (surgical) patient	11/50 (22)
As part of a clinical trial	5/50 (10)
Solely based on visco-elastic assay (VHA) result	4/50 (8)
Other	9/50 (18)
Number of plasma units per event (median [IQR])	2 [1, 2]
INR/PT monitoring	
Proportion with a target INR stated, *n* (%)	209/508 (41)
Proportion with a target PT stated, *n* (%)	9/508 (2)
Proportion with a target INR or PT stated, *n* (%)	218/508 (43)
Proportion with a pre-transfusion INR, *n* (%)	334/508 (66)
Proportion with a pre-transfusion PT, *n* (%)	16/508 (3)
Proportion where VHA was used before transfusion, *n* (%)	24/508 (5)
Proportion with a pre-transfusion INR, PT or VHA, *n*(%)	370/508 (73)
Target INR (median [IQR])	1.30 [1.18, 1.50]
INR prior to transfusion (median [IQR])	1.48 [1.20, 2.10]
Pre-transfusion INR > 1.5, *n* (%)	148/334 (44)[b]
Pre-transfusion INR > 3.0, *n* (%)	36/334 (11)[b]
Pre-transfusion INR below target INR of patient, *n* (%)	30/209 (14)[c]
INR change per transfusion event (median [IQR])	−0.14 [−0.50, 0.00]
INR change per unit of plasma (median [IQR])	−0.08 [−0.24, 0.00]
Reversal of anticoagulants	
Proportion transfusion for reversal of anticoagulants, *n* (%)	30/508 (6)
Type of anticoagulant reversed, *n* (%) Multiple answers possible	
Vitamin K antagonist	16 (53)
Heparin	6 (20)
Low Molecular Weight Heparin	4 (13)
Direct Oral Anticoagulant	4 (13)
Other	2 (1)
Non-bleeding transfusion events, *n* (%)	
Non-bleeding (prophylactic or pre-procedure)	186/508 (37)
Non-bleeding and pre-transfusion INR < 3.0	100/334 (30)
Non-bleeding and pre-transfusion INR < 1.5	55/334 (16)

[a]Other procedures: for example, tracheostomy, lumbar puncture, thorax drain placement.
[b]Of the 508 plasma transfusion events, a pre-transfusion INR value was available for 334 events.
[c]Of the 508 plasma transfusion events, both a target INR and a pre-transfusion INR was available for 209 events.

TABLE 2B Characteristics of massive transfusion protocol (MTP) events with plasma transfusion.

	MTP events with plasma transfusion *N* = 39
Median ratio of red blood cells:plasma: platelets	1:1:0
Number of red blood cell units transfused as part of MTP	3 (2, 6)
Number of plasma units transfused as part of MTP	3 (2, 6)
Number of platelet units transfused as part of MTP	1 (0, 3)

of plasma transfusions was significantly higher for Asia (25%) and Europe (22%) as compared with Oceania (9%, $p < 0.001$), but not to the other continents (Figure 3B).

Per event, a median of 2 plasma units (IQR 1, 2) was administered, excluding MTP (Table 2A). When MTP was activated, a median of 3 (IQR 2, 6) plasma units was

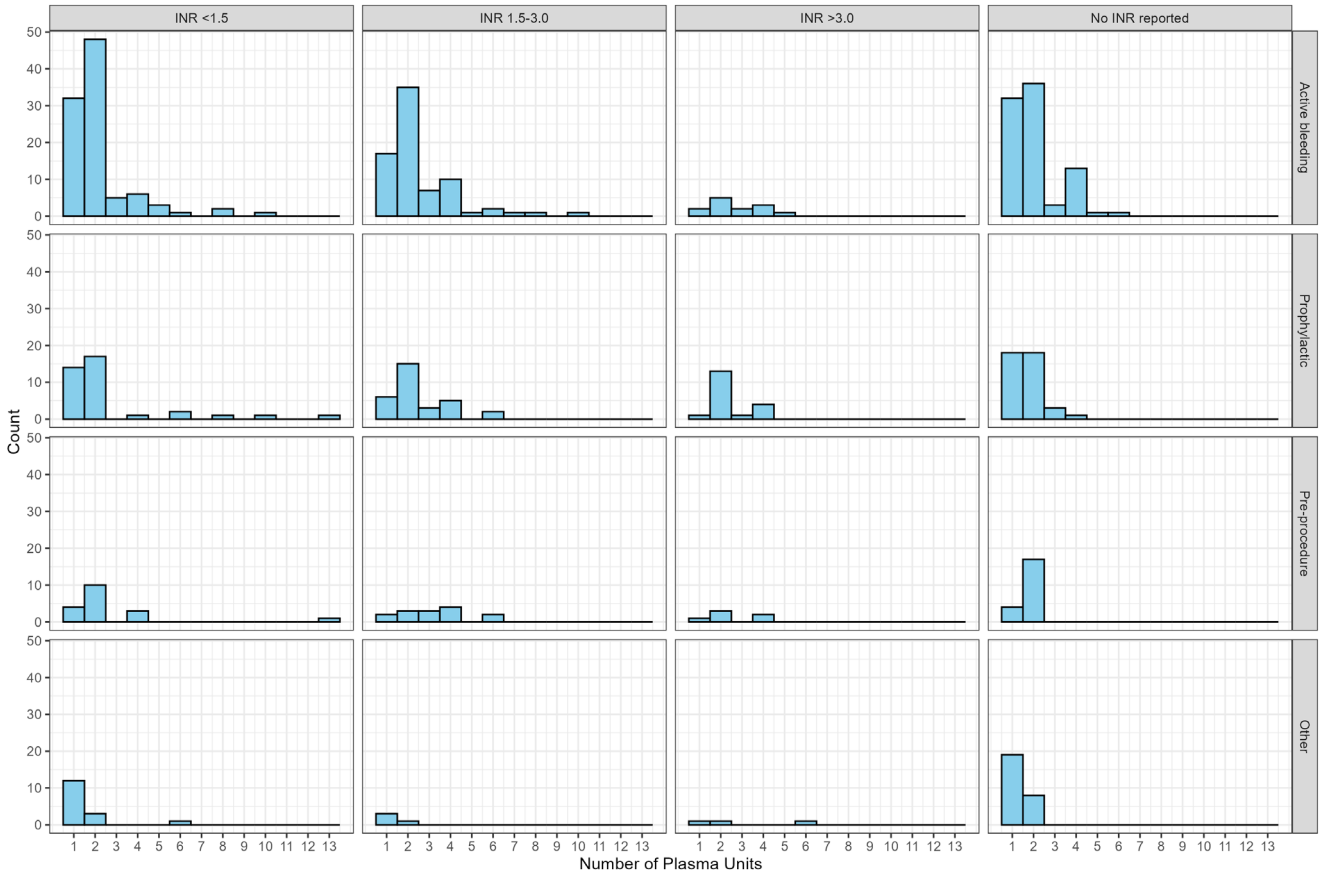


FIGURE 4 Histograms of plasma units by transfusion indication and pre-transfusion INR.

administered, with a median ratio RBC:plasma:platelets of 1:1:0 (Table 2B). One or two units per event was the most frequent administered dose of plasma for prophylactic transfusions, in the pre-procedure group there was more variability in dose (Figure 4).

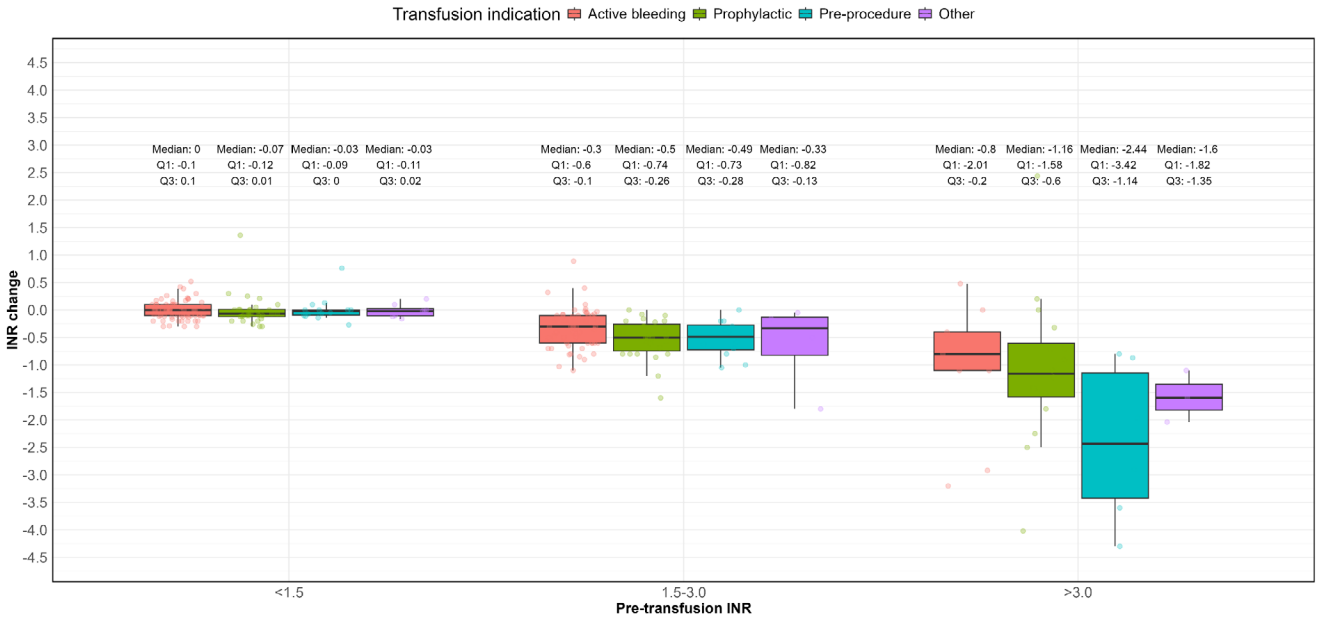
3.3 | Transfusion indications

In the 508 non-MTP transfusion events, active bleeding was the most common transfusion indication for plasma (54%), followed by prophylactic transfusion without bleeding (25%). Pre-procedure plasma transfusion was the indication in 12% of events (Table 2A and Figure 3C). Intercontinental differences in transfusion indications are shown in Figure 3C. Of note, Africa, Latin America, and North America had too few plasma transfusion events to reliably analyze differences in indications ($N = 12$, $N = 5$, and $N = 10$, respectively). The "other" category was much more prevalent in Asia than Europe and Oceania, due to 21 events transfused with the reason "COVID-19." Transfusion for a prophylactic indication made up 28% of transfusion events in Europe, 17% in Oceania, and 12% in Asia. Pre-procedural transfusions made up 12% of transfusion events in Europe, 14% in Oceania, and 4% in Asia.

3.4 | INR values

Target INR or PT was stated for 43% of the plasma transfusion events, and pre-transfusion INR, PT, or viscoelastic hemostatic assays (VHA) were reported in 73% of events, indicating that in 27% these might not have been performed (Table 2A). As no VHA values were collected and no International Sensitivity Index (ISI) factor was known to compare PT across centers, further analyses were only performed on INR values. The median target INR was 1.30 (IQR 1.18, 1.50), and the median pre-transfusion INR was 1.48 (IQR 1.20, 2.10). Of the 334 transfusion events for which a pre-transfusion INR was available, only 11% had a pre-transfusion INR above 3.0. Of the 209 transfusion events of which a target INR and a pre-transfusion INR were known, 14% had a pre-transfusion INR below the individual target INR.

INR change (posttransfusion INR − pre-transfusion INR) was available for 258 plasma transfusion events (618 plasma units). The median INR change was −0.14



	INR <1.5	INR 1.5-3.0	INR > 3.0	Total
Active bleeding	69	57	11	137
Prophylactic	31	27	16	74
Pre-procedure	14	12	6	32
Other	8	4	3	15
Total	122	100	36	258

FIGURE 5 INR change per pre-transfusion INR and per transfusion indication.

(IQR −0.50, 0.00) per transfusion event and −0.08 (IQR −0.24, 0.00) per plasma unit (Table 2A). The median INR change was larger as the pre-transfusion INR was higher (−0.01 median INR change when the pre-transfusion INR was below 1.5, −0.40 when the pre-transfusion INR was between 1.5 and 3.0, −1.10 when the pre-transfusion INR was above 3.0, $p < 0.001$, Figure S1). The INR change did not differ significantly by transfusion indication in any of the pre-transfusion INR categories, although this may be due to the small sample size, especially in the group with pre-transfusion INR > 3.0 (Figure 5).

3.5 | Plasma transfusion for non-bleeding indications

A total of 186 of the 508 transfusion events (37%) were administered for a non-bleeding indication (prophylactic or pre-procedure). Of the 334 transfusion events with a pre-transfusion INR available, 100 events were for a non-bleeding indication with a pre-transfusion INR below 3.0 (30%), and 55 with a pre-transfusion INR below 1.5 (16%, Table 2A). Of the 186 non-bleeding transfusion events involving 432 units, 33% had an unknown pre-transfusion INR (105 plasma units), 30% had an INR < 1.5 (144 plasma units), and 54% had an INR < 3.0 (266 plasma units) (Figure 3D).

4 | DISCUSSION

This study aimed to describe current global practices of plasma transfusions in the ICU. We found that one in 10 patients received a plasma transfusion during their ICU stay, with indications being active bleeding in half of the events and prophylactic in a quarter of the evens. Per transfusion event (excluding MTP), a median of 2 plasma units per event was administered and a median of 3 units when MTP was activated. A target INR or PT was not stated for most events, and a pre-transfusion INR, PT or VHA was not reported in approximately a quarter of all non-MTP events. The INR change was minimal per transfusion event and per unit, though the change was larger when the pre-transfusion INR exceeded 3.0. Thirty-seven percent of transfusion events were administered for non-bleeding indications. In Europe, higher occurrence rates compared with other continents were observed for plasma transfusion overall and plasma transfusion for a non-bleeding indication.

4.1 | Occurrence rate of plasma transfusions

In the past decades, multiple studies have been published on the occurrence rate of plasma transfusions in the ICU. Studies from before 2008 report 19%–30% occurrence

rates in the United Kingdom,[18] India,[19] and Canada.[20] From 2008 onward, studies report lower occurrence rates of 7%–9%,[1,2,21–23] including a Swedish study from 2010 to 2018 reported a decreasing rate from 17% to 9%.[23] Our study, which used data from 2020 to 2022, found a similar rate of 10%. Geographical differences are present in the literature and our study. The higher occurrence rates of Europe and Asia and the lower rates of Oceania are consistent with previous studies from the United Kingdom,[1] Sweden,[23] India,[19] and Australia/New Zealand.[21] The low occurrence rate for North America found, consisting of US centers, is lower than previously reported,[2] possibly due to the small sample size of US patients in our study.

Overall, while previous literature indicated a potential decrease in the occurrence rate of plasma transfusions from 1999 to 2018, our analysis reveals no additional decline when comparing our data to earlier studies. Moreover, global differences are present and seem unchanged.

4.2 | Plasma transfusion for non-bleeding indications

In previous studies, "inappropriate" plasma transfusions have been investigated. The definition of "inappropriate" plasma transfusion changed over time and varied per study. Despite the variability in the definition of "inappropriate," all studies consistently labeled *non-bleeding* as an "inappropriate" indication, albeit with or without an added INR below a certain threshold. These studies reported rates of 'inappropriate' use of plasma transfusions ranging from 29% to 48%,[3,12,20,24,25] consistent with our findings, and do not show a decreasing trend over time. There have been attempts to reduce "inappropriate" plasma transfusion in a study setting, which was not always successful.[26,27]

Previous studies reporting transfusion indications are in line with our observations. A prophylactic indication was observed in 24%–45%,[2,21] and a pre-procedure indication was present in 24%–27%.[28,29] In this current study 25% of plasma was transfused for a prophylactic indication and 12% for a pre-procedure indication, adding up to a total of 37% for a non-bleeding indication, consistent and seemingly unchanged when compared with previous literature.

4.3 | Effect on INR

A notable finding of our study is the large proportion of non-stated targets and missing pre-transfusion INR/PT values, especially in non-bleeding patients. This indicates that a considerable part of plasma transfusions is not INR-driven. Previous studies have shown that the effect of plasma transfusion on INR is minimal.[1,3,30] Moreover, plasma transfusion mostly fails to correct INR to below 1.5.[13,31–33]

Furthermore, plasma transfusion usually fails to produce a more procoagulant state in ICU patients.[14,34] Indeed, multiple studies have shown that prophylactic plasma transfusions do not prevent bleeding complications or RBC transfusions after a procedure in the ICU.[2,13,15,29,31,32] More evidence from trials on the effectiveness of plasma transfusions on INR and bleeding complications in the ICU is not likely to arise, as two trials were never published,[35,36] one trial ended prematurely,[13] and multiple RCTs in other settings outside of the ICU failed to show effectiveness of plasma transfusion.[16]

Further investigation into the barriers to participation in one of the ICU trials found that the most important barriers were mostly physician-driven, making a future trial likely not feasible.[37] Of note, plasma transfusions are not without harm, and associations of plasma transfusions with increased mortality in sepsis patients[38] and ECMO patients,[39] longer length of stay,[2] and increased incidence of acute lung injury after plasma transfusion[32,40,41] have been established.

As a considerable part of the events in our study do not seem INR-driven, other indications for plasma transfusion might have been at play, such as plasma to improve hemodynamics in traumatic shock[42] or to enhance endothelial condition for example in sepsis patients.[43] These indications might be promising and indeed would need different monitoring than INR. Unfortunately, these specific indications, which might be considered prophylactic, were not individually captured in the records of the current study. More research is needed to acquire evidence for effectiveness for other indications of plasma transfusion in non-bleeding patients, for instance, in sepsis.

To conclude, from 1999 until 2019, although the incidence of plasma transfusions might show a decreasing trend, the incidence of plasma transfusion in non-bleeding patients still ranges from 24% to 48%, in line with our observation and has not changed the last decade. This is worrisome, as since 2010, several published guidelines around the world advise against pre-procedure or prophylactic plasma transfusions (in 2010 in the US,[44] in 2012 in Australia,[45] in 2016 and 2018 in Europe,[46–48] in 2017 by EACTS/EACTA,[49] and in 2020 by ESICM[4]). We therefore urge the implementation of existing guidelines in clinical practice. Further research to identify the possible barriers to implement and adhere to these guidelines is warranted.

A key strength of this study lies in its considerable sample size and global reach, providing a comprehensive

overview of plasma transfusion practices in the ICU setting. This enhances the generalizability of the findings, allowing for meaningful insights into transfusion patterns across diverse patient populations and healthcare settings. However, Europe was overrepresented in this database. A notable limitation of the study is that we do not have a further subdivision on the reason for prophylactic transfusions and can therefore not be certain that the reason is a coagulopathy (without bleeding) or another prophylactic reason or, for example, plasmapheresis. We observed a substantial proportion of missing INR values. This limitation leads to smaller subgroups, decreasing the statistical power and precision of conclusions drawn regarding INR changes per transfusion indication. Consequently, interpretations regarding INR changes should be approached with caution, considering them as primarily descriptive. However, they are in line with previously published studies.

5 | CONCLUSION

Plasma transfusions occurred in 10% of ICU patients. Over a third of these transfusions were given for non-bleeding indications and might have been avoidable. Future research should identify possible barriers to implementing current guidelines that advise against transfusing plasma for non-bleeding indications and acquire evidence for effectiveness for other indications of plasma transfusion in non-bleeding patients.

AUTHOR CONTRIBUTIONS

Concept and design: Maite M. T. van Haeren, Marcella C. A. Müller, Senta Jorinde Raasveld, Sanne de Bruin, Cécile Aubron, Bakker, Maurizio Cecconi, Aarne Feldheiser, Harm-Jan de Grooth, Jens Meier, Zoe McQuilten, Thomas W. L. Scheeren, Jimmy Schenk, Alexander P. J. Vlaar. *Drafting of the manuscript*: Maite M. T. van Haeren, Senta Jorinde Raasveld, Marcella C. A. Müller, Alexander P. J. Vlaar. *Critical review of the manuscript*: all authors. *Supervision*: Senta Jorinde Raasveld, Marcella C. A. Müller, Alexander P. J. Vlaar. *Statistical analysis*: Maite M. T. van Haeren. *Acquisition*: all authors.

AFFILIATIONS

[1]Department of Intensive Care, Amsterdam University Medical Centers, Amsterdam, the Netherlands
[2]Department of Anesthesiology, Amsterdam University Medical Center, Amsterdam, the Netherlands
[3]Department of Epidemiology and Data Science, Amsterdam University Medical Centre, Amsterdam Public Health, University of Amsterdam, Amsterdam, The Netherlands
[4]Médecine Intensive Réanimation, CHU de Brest, Université de Bretagne Occidentale, Brest, France
[5]Department of Intensive Care Adults, Erasmus MC University Medical Centers, Rotterdam, the Netherlands
[6]Department of Intensive Care, Pontificia Universidad Católica de Chile, Santiago, Chile
[7]Department of Anesthesiology and Intensive Care, IRCCS Humanitas Research Hospital, Milan, Italy
[8]Department of Anesthesiology, Intensive Care Medicine and Pain Therapy, Evang. Kliniken Essen-Mitte, Huyssens-Stiftung/Knappschaft, Essen, Germany
[9]Department of Anesthesiology and Intensive Care, Kepler University Clinic, Linz, Austria
[10]Department of Anesthesiology, University Medical Center Groningen, Groningen, the Netherlands
[11]School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[12]The Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[13]Department of Critical Care, Asgar Ali Hospital, Dhaka, Bangladesh
[14]Department of Intensive Care, CHU Charleroi Marie Curie, Charleroi, Belgium
[15]Department of Anesthesiology and Intensive Care, University Clinical Hospital Center Zagreb, Zagreb, Croatia
[16]Department of Anesthesiology and Intensive Care Medicine, University Hospital and Faculty of Medicine in Plzen – Charles University, Plzen, Czech Republic
[17]Department of Intensive Care, Copenhagen University Hospital, Rigshospitalet Copenhagen, Copenhagen, Denmark
[18]Department of Anesthesia and Intensive Care Medicine, Copenhagen University Hospital – Gentofte, Hellerup, Denmark
[19]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark
[20]Unidad de Cuidados Intensivos, Hospital Vicente Corral Moscoso, Cuenca, Ecuador
[21]Department of Cardiothoracic Surgery, Interbalkan Medical Center, Thessaloniki, Greece
[22]Department of Respiratory Medicine, National and Kapodistrian University of Athens, Sotiria Chest Hospital, Athens, Greece
[23]Department of Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
[24]Department of Anesthesiology, Critical Care and Pain, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, India

[25]Department of Child, General and Specialistic Surgery, University of Campania, "Luigi Vanvitelli", Naples, Italy
[26]Faculty of Medicine, University of Tripoli, Tripoli, Libya
[27]Department of Anesthesiology and Intensive Care, Institute of Medical Sciences, University of Opole, Opole, Poland
[28]Department of Intensive Care, Centro Hospitalar de Entro o Douro e Vouga, Santa Maria da Feira, Portugal
[29]Department of Anesthesiology, Aga Khan University Hospital, Nairobi, Kenya
[30]Department of Anesthesia and Intensive Care, Military Medical Academy Belgrade, Belgrade, Serbia
[31]Department for Internal Medicine, University of Ljubljana, Ljubljana, Slovenia
[32]Department of Anesthesiology and Post-surgical Critical Care, University Hospital Doctor Peset, Valencia, Spain
[33]Intensive Care Service, Hospital Universitario La Paz, Madrid, Spain
[34]Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden
[35]Department of Intensive Care, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland
[36]Department of Anesthesiology and Reanimation, Dr Siyami Ersek Thoracic and Cardiovascular Surgery Center, University of Health Sciences, Istanbul, Turkey
[37]Division of Pulmonary, Critical Care and Sleep Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico, USA
[38]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

FUNDING INFORMATION

No additional funding was received for this sub-study. The InPUT study was endorsed, but not financially supported, by the European Society of Intensive Care Medicine. Monash University, Australia, received a project grant by the National Blood Authority of Australia and a National Health and Medical Research Council (NHMRC) Synergy Grant (GNT1189490) to conduct the InPUT study in Australia and New Zealand (ID508). In addition, Dr. McQuilten is supported by an National Health and Medical Research Council (NHMRC) Emerging Leader Investigator Grant (GNT1194811). Dr. Vlaar is supported by a ZonMw Vidi grant (09150172010047). The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

CONFLICT OF INTEREST STATEMENT

Dr. Cecconi reported receiving personal fees from Edwards Lifesciences, GE Healthcare, and Directed Systems outside the submitted work. Dr. Shah reported receiving consultancy fees from Pharmacosmos UK outside of the submitted work. Dr. Feldheiser reported receiving personal fees from Baxter and Medtronic outside the submitted work. Dr. Scheeren reported serving as senior medical director for Edwards Lifesciences (Garching, Germany). Dr. McQuilten reported receiving grants from Australian National Blood Authority and National Health and Medical Research Council during the conduct of the study. Dr. Flint reported receiving grants from the Australian National Blood Authority and Blood Synergy (Monash University) during the conduct of the study. Dr. Piagnerelli reported receiving grants from Centre Federal d'Expertise Belge–KCE grant for COVID-19 study outside the submitted work. Dr. 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. 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. Nielsen reported receiving personal fees from Adrenomed outside the submitted work. Dr. Vlaar reported receiving personal fees from a Vidi grant (ZonMW: 09150172010047). No other disclosures were reported.

ORCID

Maite M. T. van Haeren https://orcid.org/0009-0009-2674-0668
Merijn C. Reuland https://orcid.org/0009-0009-3738-0397
Zoe McQuilten https://orcid.org/0000-0001-9698-7185
Andrew Flint https://orcid.org/0000-0001-9183-7882
Lene Russell https://orcid.org/0000-0001-7352-8728
Konstantina Triantafyllopoulou https://orcid.org/0009-0008-3039-6727
Vojislava Neskovic https://orcid.org/0000-0003-3583-7129

Alexander P. J. Vlaar https://orcid.org/0000-0002-3453-7186

REFERENCES

1. Stanworth SJ, Walsh TS, Prescott RJ, Lee RJ, Watson DM, Wyncoll D, et al. A national study of plasma use in critical care: clinical indications, dose and effect on prothrombin time. Crit Care. 2011;15:R108.
2. Warner MA, Chandran A, Jenkins G, Kor DJ. Prophylactic plasma transfusion is not associated with decreased red blood cell requirements in critically ill patients. Anesth Analg. 2017; 124:1636–43.
3. Stanworth SJ, Grant-Casey J, Lowe D, Laffan M, New H, Murphy MF, et al. The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. Transfusion. 2011;51:62–70.
4. Vlaar AP, Oczkowski S, de Bruin S, Wijnberge M, Antonelli M, Aubron C, et al. Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Intensive Care Med. 2020; 46:673–96.
5. Vlaar APJ, Dionne JC, de Bruin S, Wijnberge M, Raasveld SJ, van Baarle F, et al. Transfusion strategies in bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Intensive Care Med. 2021;47: 1368–92.
6. de Bruin S, Eggermont D, van Bruggen R, de Korte D, Scheeren TWL, Bakker J, et al. Transfusion practice in the bleeding critically ill: an international online survey-the TRACE-2 survey. Transfusion. 2022;62:324–35.
7. Rossaint R, Afshari A, Bouillon B, Cerny V, Cimpoesu D, Curry N, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care. 2023;27:80.
8. de Bruin S, Scheeren TWL, Bakker J, van Bruggen R, Vlaar APJ, Cardiovascular Dynamics Section and Transfusion Guideline Task Force of the ESICM. Transfusion practice in the non-bleeding critically ill: an international online survey-the TRACE survey. Crit Care. 2019;23:309.
9. Watson DM, Stanworth SJ, Wyncoll D, McAuley DF, Perkins GD, Young D, et al. A national clinical scenario-based survey of clinicians' attitudes towards fresh frozen plasma transfusion for critically ill patients. Transfus Med. 2011;21: 124–9.
10. Federatie Medisch Sepcialisten. Bloedtransfusiebeleid. Available from: https://richtlijnendatabase.nl/richtlijn/bloedtransfusiebeleid/plasmatransfusies/profylactische_plasmatransfusie_bij_patienten_met_verbruikscoagulopathie.html. [Accessed 12th November 2024].
11. McMichael ABV, Ryerson LM, Ratano D, Fan E, Faraoni D, Annich GM. 2021 ELSO adult and pediatric anticoagulation guidelines. ASAIO J. 2022;68:303–10.
12. Tinmouth A, Thompson T, Arnold DM, Callum JL, Gagliardi K, Lauzon D, et al. Utilization of frozen plasma in Ontario: a provincewide audit reveals a high rate of inappropriate transfusions. Transfusion. 2013;53:2222–9.
13. Muller MC, Arbous MS, Spoelstra-de Man AM, Vink R, Karakus A, Straat M, et al. Transfusion of fresh-frozen plasma in critically ill patients with a coagulopathy before invasive procedures: a randomized clinical trial (CME). Transfusion. 2015;55:26–35. quiz 25.
14. Muller MC, Straat M, Meijers JC, Klinkspoor JH, de Jonge E, Arbous MS, et al. Fresh frozen plasma transfusion fails to influence the hemostatic balance in critically ill patients with a coagulopathy. J Thromb Haemost. 2015;13:989–97.
15. Veelo DP, Vlaar AP, Dongelmans DA, Binnekade JM, Levi M, Paulus F, et al. Correction of subclinical coagulation disorders before percutaneous dilatational tracheotomy. Blood Transfus. 2012;10:213–20.
16. Yang L, Stanworth S, Hopewell S, Doree C, Murphy M. Is fresh-frozen plasma clinically effective? An update of a systematic review of randomized controlled trials. Transfusion. 2012; 52:1673–86. quiz 1673.
17. Raasveld SJ, de Bruin S, Reuland MC, van den Oord C, Schenk J, Aubron C, et al. In PUTSG. Red blood cell transfusion in the intensive care unit. JAMA. 2023;330:1852–61.
18. Rao MP, Boralessa H, Morgan C, Soni N, Goldhill DR, Brett SJ, et al. Blood component use in critically ill patients. Anaesthesia. 2002;57:530–4.
19. Makroo RN, Mani RK, Vimarsh R, Kansal S, Pushkar K, Tyagi S. Use of blood components in critically ill patients in the medical intensive care unit of a tertiary care hospital. Asian J Transfus Sci. 2009;3:82–5.
20. Lauzier F, Cook D, Griffith L, Upton J, Crowther M. Fresh frozen plasma transfusion in critically ill patients. Crit Care Med. 2007;35:1655–9.
21. Blood Observational Study Investigators of A-CTG, Westbrook A, Pettila V, Nichol A, Bailey MJ, Syres G, Murray L, et al. Transfusion practice and guidelines in Australian and New Zealand intensive care units. Intensive Care Med. 2010;36:1138–46.
22. Vlaar AP, in der Maur AL, Binnekade JM, Schultz MJ, Juffermans NP. A survey of physicians' reasons to transfuse plasma and platelets in the critically ill: a prospective single-centre cohort study. Transfus Med. 2009;19:207–12.
23. Holmqvist J, Brynolf A, Zhao J, Halmin M, Hollenberg J, Martensson J, et al. Patterns and determinants of blood transfusion in intensive care in Sweden between 2010 and 2018: a nationwide, retrospective cohort study. Transfusion. 2022;62: 1188–98.
24. Schofield WN, Rubin GL, Dean MG. Appropriateness of platelet, fresh frozen plasma and cryoprecipitate transfusion in New South Wales public hospitals. Med J Aust. 2003;178: 117–21.
25. Khandelwal A, Minuk L, Liu Y, Arnold DM, Heddle NM, Barty R, et al. Plasma transfusion practices: A multicentre electronic audit. Vox Sang. 2022;117:1211–9.
26. Arnold DM, Lauzier F, Whittingham H, Zhou Q, Crowther MA, McDonald E, et al. A multifaceted strategy to reduce inappropriate use of frozen plasma transfusions in the intensive care unit. J Crit Care. 2011;26(636):636.e7–636.e13.
27. Leal-Noval SR, Arellano-Orden V, Maestre-Romero A, Munoz-Gomez M, Fernandez-Cisneros V, Ferrandiz-Millon C, et al. Impact of national transfusion indicators on appropriate blood usage in critically ill patients. Transfusion. 2011;51:1957–65.
28. Argyrou A, Valsami S, Pouliakis A, Gavalaki M, Aggelidis A, Voulgaridou V, et al. Current practice in FFP preparation and use in Greece: a national survey. Turk J Haematol. 2021;38: 22–32.

29. Ren Q, Zhao J, He X, Su L, Chai J, Bai L, et al. Plasma transfusion in critically ill patients with abnormal coagulation tests before invasive procedures: a propensity-adjusted cohort study. Transfus Apher Sci. 2023;62:103700.
30. Abdel-Wahab OI, Healy B, Dzik WH. Effect of fresh-frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion. 2006;46:1279–85.
31. Biu E, Beraj S, Vyshka G, Nunci L, Cina T. Transfusion of fresh frozen plasma in critically ill patients: effective or useless? Open Access Maced J Med Sci. 2018;6:820–3.
32. Dara SI, Rana R, Afessa B, Moore SB, Gajic O. Fresh frozen plasma transfusion in critically ill medical patients with coagulopathy. Crit Care Med. 2005;33:2667–71.
33. Triulzi D, Gottschall J, Murphy E, Wu Y, Ness P, Kor D, et al. A multicenter study of plasma use in the United States. Transfusion. 2015;55:1313–9. quiz 1312.
34. Segal JB, Dzik WH, Transfusion Medicine/Hemostasis Clinical Trials Network. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion. 2005; 45:1413–25.
35. Tinmouth A, Chatelain E, Fergusson D, McLntyre L, Giulivi A, Hébert P. A randomized controlled trial of high and standard dose frozen plasma transfusions in critically ill patients. Transfusion. 2008;48:26A–27A.
36. ClinicTrials.gov [Internet]. Database Provider: National Library of Medicine (US) 2009. Identifier NCT00953901, Restrictive Versus Liberal Fresh Frozen Plasma Transfusion Prior to Low-Risk Invasive Procedures in Hospitalized Patients; 2009 Nov 16 [cited 2024 Nov 12]. Available from: https://clinicaltrials.gov/study/NCT00953901.
37. Muller MC, de Haan RJ, Vroom MB, Juffermans NP. Evaluation of a multi-center randomised clinical trial on prophylactic transfusion of fresh frozen plasma: implications for future trials. Transfus Med. 2014;24:292–6.
38. Qin X, Zhang W, Zhu X, Hu X, Zhou W. Early fresh frozen plasma transfusion: is it associated with improved outcomes of patients with sepsis? Front Med. 2021;8:754859.
39. Luo Z, Qin L, Xu S, Yang X, Peng Z, Huang C. Impact of fresh frozen plasma transfusion on mortality in extracorporeal membrane oxygenation. Perfusion. 2022;2676591221137034: 294–303.
40. Rana R, Fernandez-Perez ER, Khan SA, Rana S, Winters JL, Lesnick TG, et al. Transfusion-related acute lung injury and pulmonary edema in critically ill patients: a retrospective study. Transfusion. 2006;46:1478–83.
41. Vlaar AP, Binnekade JM, Prins D, van Stein D, Hofstra JJ, Schultz MJ, et al. Risk factors and outcome of transfusion-related acute lung injury in the critically ill: a nested case-control study. Crit Care Med. 2010;38:771–8.
42. Sperry JL, Guyette FX, Brown JB, Yazer MH, Triulzi DJ, Early-Young BJ, et al. Prehospital plasma during air medical transport in trauma patients at risk for hemorrhagic shock. N Engl J Med. 2018;379:315–26.
43. Kravitz MS, Kattouf N, Stewart IJ, Ginde AA, Schmidt EP, Shapiro NI. Plasma for prevention and treatment of glycocalyx degradation in trauma and sepsis. Crit Care. 2024;28:254.
44. Roback JD, Caldwell S, Carson J, Davenport R, Drew MJ, Eder A, et al. Evidence-based practice guidelines for plasma transfusion. Transfusion. 2010;50:1227–39.
45. National Blood Authority. Australia. Patient Blood Management Guidelines. 2012. https://blood.gov.au/pbm-module-4
46. Kozek-Langenecker SA, Ahmed AB, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: first update 2016. Eur J Anaesthesiol. 2017;34:332–95.
47. Green L, Bolton-Maggs P, Beattie C, Cardigan R, Kallis Y, Stanworth SJ, et al. British Society of Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. Br J Haematol. 2018;181:54–67.
48. Klein AA, Arnold P, Bingham RM, Brohi K, Clark R, Collis R, et al. AAGBI guidelines: the use of blood components and their alternatives 2016. Anaesthesia. 2016;71:829–42.
49. Pagano D, Milojevic M, Meesters MI, Benedetto U, Bolliger D, von Heymann C, et al. 2017 EACTS/EACTA guidelines on patient blood management for adult cardiac surgery. Eur J Cardiothorac Surg. 2018;53:79–111.

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: van Haeren MMT, Raasveld SJ, de Bruin S, Reuland MC, van den Oord C, Schenk J, et al. Plasma transfusion in the intensive care unit. Transfusion. 2024. https://doi.org/10.1111/trf.18071