Received: 3 February 2022 | Revised: 28 March 2022 | Accepted: 28 March 2022

DOI: 10.1111/trf.16942

TRANSFUSION PRACTICE

TRANSFUSION

Patterns and determinants of blood transfusion in intensive care in Sweden between 2010 and 2018: A nationwide, retrospective cohort study

Jacob Holmqvist[1,2] | **Anne Brynolf**[3] | **Jingcheng Zhao**[3] | **Märit Halmin**[4] | **Jacob Hollenberg**[4,5] | **Johan Mårtensson**[6,7] | **Max Bell**[6,7] | **Linda Block**[1,2] | **Gustaf Edgren**[3,4]

[1]Department of Anaestesia and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden

[2]Department of Anesthesia and Intensive Care, Sahlgrenska Academy, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden

[3]Department of Medicine, Solna, Clinical Epidemiology Division, Stockholm, Sweden

[4]Department of Cardiology, Södersjukhuset, Stockholm, Sweden

[5]Department of Clinical Science and Education, Center for Resuscitation Science, Karolinska Institutet, Södersjukhuset, Stockholm, Sweden

[6]Perioperative Medicine and Intensive Care, Karolinska University Hospital, Solna, Sweden

[7]Department of Physiology and Pharmacology, Section of Anesthesiology and Intensive Care Medicine, Karolinska Institutet, Stockholm, Sweden

Correspondence
Gustaf Edgren, Department of Medicine, Solna, Clinical Epidemiology Division, Stockholm, Sweden.
Email: gustaf.edgren@ki.se

Funding information
Vetenskapsrådet, Grant/Award Number: 2017-01954; Swedish Government, Grant/Award Number: ALFGBG-927831

Abstract

Background: Intensive care unit (ICU) patients are transfused with blood products for a number of reasons, from massive ongoing hemorrhage, to mild anemia following blood sampling, combined with bone marrow depression due to critical illness. There's a paucity of data on transfusions in ICUs and most studies are based on audits or surveys. The aim of this study was to provide a complete picture of ICU-related transfusions in Sweden.

Methods: We conducted a register based retrospective cohort study with data on all adult patient admissions from 82 of 84 Swedish ICUs between 2010 and 2018, as recorded in the Swedish Intensive Care Register. Transfusions were obtained from the SCANDAT-3 database. Descriptive statistics were computed, characterizing transfused and nontransfused patients. The distribution of blood use comparing different ICUs was investigated by computing the observed proportion of ICU stays with a transfusion, as well as the expected proportion.

Results: In 330,938 ICU episodes analyzed, at least one transfusion was administered for 106,062 (32%). For both red-cell units and plasma, the fraction of patients who were transfused decreased during the study period from 31.3% in 2010 to 24.6% in 2018 for red-cells, and from 16.6% in 2010 to 9.4% in 2018

Abbreviations: ICU, intensive care unit; SCANDAT, Scandinavian donations and transfusions; SIR, Swedish intensive care register; NRN, National registration number; SAPS3, simplified acute physiology score 3; ICD, international classification of disease; IQR, interquartile range; OR, odds ratio; CI, confidence interval.

for plasma. After adjusting for a range of factors, substantial variation in transfusion frequency remained, especially for plasma units.

Conclusion: Despite continuous decreases in utilization, transfusions remain common among Swedish ICU patients. There is considerable unexplained variation in transfusion rates. More research is needed to establish stronger critiera for when to transfuse ICU patients.

KEYWORDS

critical care, epidemiology, intensive care, transfusion

1 | BACKGROUND

Intensive care unit (ICU) patients are transfused with blood products for a number of reasons, from massive ongoing hemorrhage, to mild anemia following extensive blood sampling combined with bone marrow depression due to critical illness. Red-cell transfusion rates vary considerably between different ICUs.[1]

While the availability of blood products in most Western countries is sufficient, there are strong incentives to reduce transfusion rates since transfusion exposes patients to specific infectious,[2] immunological and non-immunological risks,[3,4] as well as nonnegligible cost.[5] In addition, evidence from large, multi-center trials supports a more conservative red-cell transfusion practice for critically ill patients.[6,7] Still, there is a concerning paucity of data on how ICU patients are transfused. Moreover, available data is often based on audits or surveys and was generally collected more than a decade ago.[8–11] Red-cell transfusion rates seem to vary greatly between different ICU units.[1,9–13] Among such studies, the SAFE-TRIPS study from 2007 demonstrated a significant residual variability in transfusion rates between 391 ICUs in 25 countries, even after adjusting for a range of predictive factors. Among included centers, the 24 reporting Swedish ICUs were found to have the most liberal transfusion practice, with an odds ratio of 4.99 for administering blood products, compared with the country with the lowest transfusion rate.[13] For plasma and platelet transfusion patterns, most studies have been small, with data from few or single centers, yielding studies with low external validity. Nonerythrocyte transfusions often lack clear indications, with unexplained practice variation.[13–17]

In light of these findings, we hypothesized that transfusion practice across Sweden would vary independently of case-mix. This nationwide descriptive study of transfusion practice in Swedish ICUs tests this hypothesis, combining data from the Scandinavian Donations and Transfusions (SCANDAT3-S) database,[18] with data from the Swedish Intensive Care register (SIR).[19]

2 | METHODS

2.1 | Setting, data sources, and record linkages

Sweden has a decentralized, almost entirely publicly financed health care system, organized in 21 regional councils. The complete range of blood services, from blood collection to component manufacture and handling, are also part of the public health care system. All inhabitants of Sweden are assigned a unique national registration number (NRN) which is used in all health care contacts, as well as in contacts with other public agencies, thus enabling the linkage of data from different sources, with little or no loss of data.[20]

Our study was based on all adult patient admissions recorded in the Swedish Intensive Care Register between January 1, 2010 and July 1, 2018.[19] Patients below age 18 were excluded. The SIR is nearly nationally complete, currently receiving data from all but two of Sweden's 84 ICUs. The register records a variety of details for patients treated in ICUs, including patient identity, demographics, indication for ICU care, baseline disease severity (expressed using the Simplified Acute Physiology Score 3 [SAPS3] score), time of death during ICU stay, as well as diagnoses (coded using the international classification of diseases, 10th revision [ICD-10], and procedures (coded using the Nordic Classification of Surgical Procedures). ICUs were broadly classified into five groups: ICUs in university hospitals, ICUs in regional hospitals, ICUs in county hospitals, neurosurgical ICUs, and cardiothoracic ICUs. Patients treated in pediatric ICUs and one extracorporeal membrane oxygenation (ECMO) ICU were excluded.

All linkages were done by technical personnel at the Swedish National Board of Health and Welfare, a government agency responsible for maintaining a range of health data registers. Vital status through December 31, 2018 was ascertained through linkage with a nationally complete, continuously updated database kept by the Swedish Tax Agency. After record linkages, all data were

de-identified by replacing NRNs with random serial numbers and transferred to Karolinska Institutet. After the two, now linked databases had been received, data underwent rigorous cleaning and were fitted into a relational database for further analysis.

The ICU register has been found to have a high level of completeness. Using NRNs, the ICU register data was linked with the Swedish portion of the third iteration of the Scandinavian Donations and Transfusions (SCANDAT3-S) database, providing data on all blood transfusions, including red-cell, plasma and platelet units, administered in conjunction with the ICU stay. Transfusions considered included units administered from the start of the day of admission until the time of discharge from the ICU. In addition to data on administered transfusions, the SCANDAT3-S database also provided ABO blood group data. Details about the SCANDAT3-S database have been published previously.[18]

Both the ICU register and the SCANDAT3-S database contain data on individuals without a known identification, registered using so-called reserve ID:s. Use of these IDs is typically maintained throughout a hospitalization, allowing the tracking of patients despite not knowing their NRN, or them not having NRNs. The two registers were also linked for patients with reserve IDs.

2.2 | Classification of indication for intensive care

As the classification of primary indication for intensive care in the ICU register had changed during the study period, we derived an alternative classification based on ICU admission diagnoses. The classification was designed to categorize patients into 16 broad groups: airway, respiratory, circulatory, metabolic/endocrine, infection, hematologic disease, intoxication, kidney failure, liver failure, neurosurgery, neurological diagnosis, obstetric, transplant surgery, other surgery, trauma, and other indications. We aimed to capture the most common indications for intensive care, but as more than 2500 different ICD-10 codes were used in the register, the classification system was nonexhaustive, assigning 95% of all diagnoses used into one of the categories and the remainder into an "other" category. See details in Tables S1 and S2.

2.3 | Statistical analyses

We first computed descriptive statistics for all ICU episodes, treating each ICU admission as a separate episode, allowing patients to contribute multiple episodes.

TABLE 1 Characteristics of ICU admissions, presented overall, and stratified by transfusion status

	Overall	Transfused	Nontransfused
Number of ICU admissions (% of total)	351,598 (100)	107,090 (30)	244,508 (70)
... with correct NRN, *N* (%)	330,938 (94)	106,062 (99)	224,876 (92)
... of whom unique persons[a]	239,406	86,419	174,295
Sex, *N* (%)			
Female	138,123 (42)	43,721 (41)	94,402 (42)
Male	192,815 (58)	62,341 (59)	130,474 (58)
Age at admission, *N* (%)			
18–29 years	28,420 (9)	4320 (4)	24,100 (11)
30–49 years	50,528 (15)	11,259 (11)	39,269 (17)
50–64 years	78,027 (24)	24,956 (24)	53,071 (24)
65–80 years	127,413 (39)	48,673 (46)	78,740 (35)
>80 years	46,550 (14)	16,854 (16)	29,696 (13)
Median (IQR)	66 (51–75)	69 (59–77)	64 (47–74)
Type of ICU, *N* (%)			
University hospital	77,409 (23)	31,312 (30)	46,097 (20)
Regional hospital	108,631 (33)	30,088 (28)	78,543 (35)
County hospital	94,938 (29)	21,905 (21)	73,033 (32)
Neurosurgical ICU	9124 (3)	3240 (3)	5884 (3)
Thoracic ICU	40,836 (12)	19,517 (18)	21,319 (9)

[a]The total number of unique patients in the transfused and non-transfused populations exceed the number in the Overall category as individual patients can contribute admissions in both categories.

TABLE 2 Clinical details, and outcomes during and following ICU admissions, stratified by transfusion status

	Transfused	Nontransfused
Number of ICU admissions with valid ID	106,062	224,876
SAPS3 score at admission, *N* (%)		
<40	7946 (7.5)	45,869 (20.4)
40–59	36,219 (34.1)	94,056 (41.8)
60–79	34,190 (32.2)	50,122 (22.3)
≥80	9703 (9.1)	11,166 (5.0)
Unknown/not reported	18,004 (17.0)	23,663 (10.5)
Median (IQR)	59 (49–70)	51 (41–62)
Indication for intensive care admission, *N* (%)		
Airway	7312 (6.9)	14,102 (6.3)
Respiratory	8741 (8.2)	24,054 (10.7)
Circulatory	19,397 (18.3)	29,835 (13.3)
Metabolic/endocrine	1664 (1.6)	12,313 (5.5)
Infection	11,253 (10.6)	20,337 (9.0)
Hematologic disease	426 (0.4)	142 (0.1)
Intoxication	914 (0.9)	28,535 (12.7)
Kidney failure	2647 (2.5)	3211 (1.4)
Liver failure	1185 (1.1)	764 (0.3)
Neurosurgery	3959 (3.7)	12,072 (5.4)
Neurological diagnosis	3370 (3.2)	24,693 (11.0)
Obstetric	1144 (1.1)	1524 (0.7)
Transplant surgery	700 (0.7)	268 (0.1)
Surgical	21,683 (20.4)	12,353 (5.5)
Trauma	6573 (6.2)	14,420 (6.4)
Other	15,094 (14.2)	26,253 (11.7)
Outcomes, *N* (%)[a]		
Dead during ICU-stay	11,552 (10.9)	14,025 (6.2)
Transferred to other ICU	10,765 (10.1)	14,233 (6.3)
Dead within 30 days of admission	22,805 (21.5)	32,687 (14.5)
Median duration of ICU stay, hours (IQR)	50 (22–138)	22 (12–45)

[a]Outcomes listed are not mutually exclusive, nor exhaustive.

Episodes where patients were transferred between different ICUs were also treated as separate observations to allow all transfusions to be assigned to one distinct unit. We used medians with interquartile range [IQR] and frequencies, with percentages, as appropriate. Analyses were stratified by whether the patient was transfused or not. Because these analyses revealed a lower-than-expected transfusion rate among patients with an unknown identity (i.e., coded using a reserve ID), we interpreted this as evidence of under-ascertainment of transfusions in this group, and therefore, restricted all further analyses to patients with a known ID.

The distribution of blood use comparing different ICUs was investigated by computing the observed proportion of hospitalizations where a transfusion was administered in each ICU, together with an exact, binomial 95% confidence interval for the proportion. In addition, we estimated the expected transfusion proportion for each ICU using a series of logistic regression models. These models included patient age (categorized as 18–29, 30–49, 50–64, 65–79, ≥80 years), sex (as a categorical term), year of admission (as a categorical term), SAPS3 score at admission (categorized as <40, 40–59, 60–79, ≥80), and indication for ICU admission (as a categorical term with 16 levels). Separate models were run for red-cells, plasma and platelets. C statistics with 95% confidence limits were used to summarize model discrimination. To provide more interpretable and more representable odds ratio [OR] estimates, the models were also run restricted to patients admitted either to a university hospital, regional hospital, or county hospital ICU. 95% confidence intervals for the ORs were constructed using likelihood ratio tests.

Lastly, because transfusion use varied over time during ICU stay, we also calculated the transfusion-free survival following patients from admission to ICU until time of first transfusion, death, or discharge from ICU. Analyses were done using the Kaplan–Meier method, assessing red-cell, plasma, and platelet transfusions in separate analyses, stratified by ICU category.

All data processing and statistical analyses were performed using SAS Statistical Analysis Software, version 9.4 (Cary, North Carolina). The creation of the SCANDAT3 database and the conduct of this study was approved by the regional ethics committee in Stockholm, Sweden (ref.nr. 2018/167-31).

3 | RESULTS

A total of 351,598 ICU admissions were identified. Of these, 20,660 (5.9%) were registered to patients without a valid NRN and thus excluded. In the remaining 330,938 admissions, 42% were female, the median age was 66, and the median SAPS3 score was 53. At least one transfusion was administered in 106,062 (32%) of the admissions. The sex distribution was similar in the transfused and nontransfused groups, with 41 and 42% being female, respectively. Transfused patients were older than nontransfused patients, with median ages of 69 (IQR, 59–77) and 64 (IQR, 47–74). There were some notable

differences in the distribution of ICU category between the transfused and nontransfused patient categories, with a higher proportion of transfused patients being treated in University hospitals (30 vs. 20%), and cardio-thoracic ICUs (18 vs. 9%), than nontransfused patients (Table 1).

Further clinical details about the patients are presented in Table 2. Transfused patients had a higher median (IQR) SAPS3 score at admission than nontransfused patients (59 [IQR, 49–70] vs. 51 [IQR, 41–62] points). The probability of death during ICU stay (10.9 vs. 6.2%), or within 30 days (21.5 vs. 14.5%) was higher among transfused than nontransfused patients. The distribution of indication for ICU care was mostly similar between transfused and nontransfused patients, but with some notable exceptions. The proportion of patients with surgical and hematological ICU admission diagnoses was higher among transfused patients while the proportion of patients with metabolic or respiratory ICU admission diagnosis was higher among nontransfused patients (Table 2).

Figure 1 presents the observed (colored points with error bars representing confidence limits) proportion of patients in each ICU, who received at least one red-cell (Panel A), plasma (Panel B), or platelet unit (Panel C) during their ICU stay. In addition Figure 1 also includes the expected proportions (gray circles) estimated using logistic regression. There was substantial variation between ICUs for all three component types. Although there were instances where the observed and expected counts were in close agreement, there was substantial variation in blood use between ICUs which was not

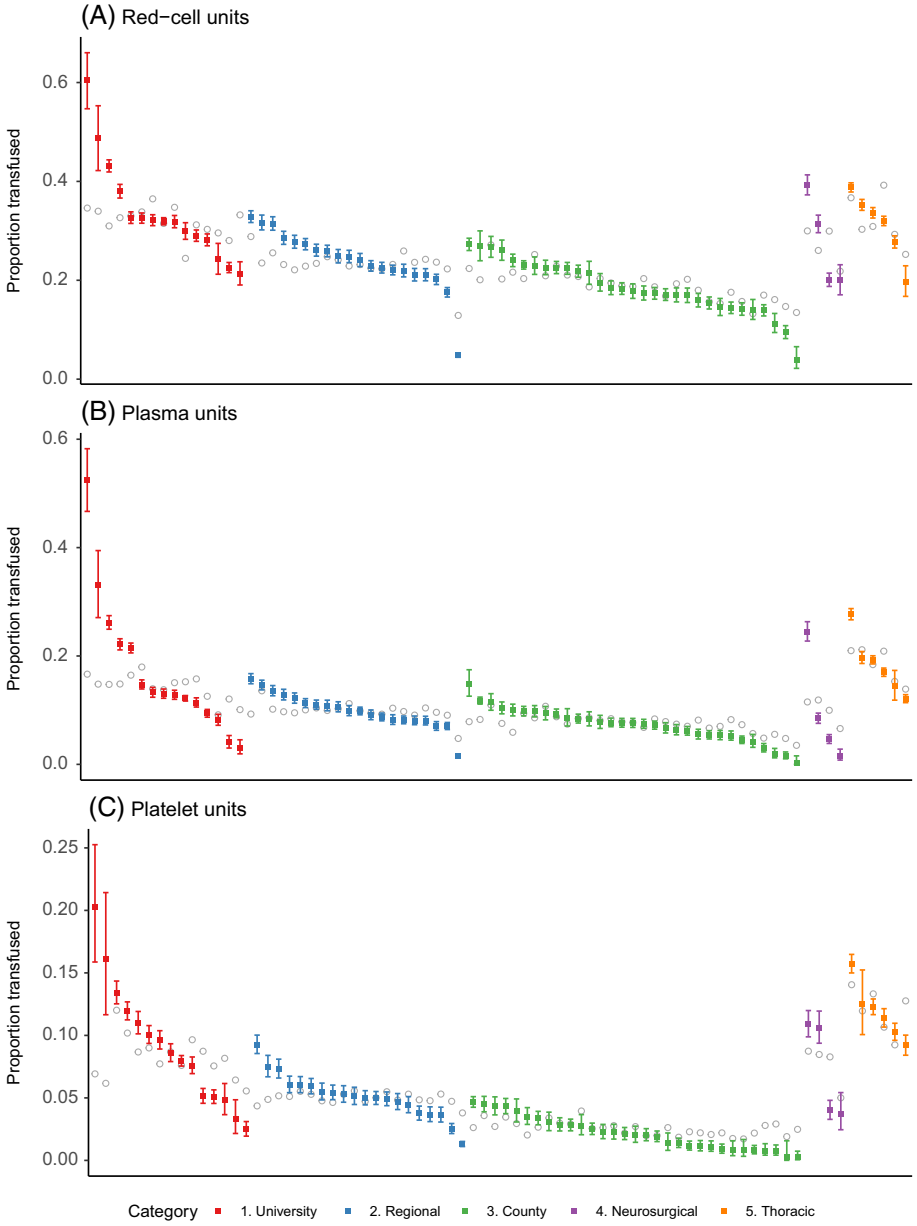

FIGURE 1 Observed (solid square, with error bars indicating 95% confidence intervals) and expected (gray circles) transfusion proportions for red-cell units (A), plasma units (B), and platelet units (C), presented for all 81 ICUs contributing data to the study. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Odds ratios for the administration of red-cell, plasma or platelet transfusion, in relation to selected clinical parameters for patients treated in a university, regional or county hospital ICU

	Red-cell transfusion		Plasma transfusion		Platelet transfusion	
Parameter	**Transfused episodes (%)**	**Odds ratio (95% CI)**	**Transfused episodes (%)**	**Odds ratio (95% CI)**	**Transfused episodes (%)**	**Odds ratio (95% CI)**
Sex						
Female	28,923 (23.6)	1.00 (ref)	11,405 (9.3)	1.00 (ref)	5507 (4.5)	1.00 (ref)
Male	38,817 (24.5)	0.88 (0.86–0.90)	17,789 (11.2)	1.05 (1.02–1.08)	8927 (5.6)	1.07 (1.03–1.11)
Age at admission						
18–29 years	2788 (10.4)	1.00 (ref)	1531 (5.7)	1.00 (ref)	792 (2.9)	1.00 (ref)
30–49 years	7117 (15.8)	1.16 (1.11–1.22)	3640 (8.1)	1.01 (0.95–1.08)	2129 (4.7)	1.07 (0.98–1.17)
50–64 years	15,487 (24.4)	1.33 (1.27–1.40)	7008 (11.0)	0.95 (0.89–1.02)	3948 (6.2)	0.87 (0.80–0.95)
65–80 years	30,352 (29.4)	1.24 (1.18–1.30)	12,280 (11.9)	0.76 (0.72–0.81)	5912 (5.7)	0.57 (0.52–0.62)
>80 years	11,996 (28.4)	0.93 (0.88–0.98)	4735 (11.2)	0.55 (0.51–0.59)	1653 (3.9)	0.29 (0.26–0.32)
SAPS3 score at admission						
<40	4068 (8.2)	0.36 (0.35–0.38)	1888 (3.8)	0.35 (0.33–0.37)	575 (1.2)	0.23 (0.21–0.25)
40–59	25,465 (21.1)	1.00 (ref)	11,009 (9.1)	1.00 (ref)	4334 (3.6)	1.00 (ref)
60–79	27,320 (34.1)	2.01 (1.97–2.06)	11,289 (14.1)	1.90 (1.84–1.96)	6135 (7.7)	2.77 (2.66–2.90)
≥80	8004 (39.6)	2.62 (2.53–2.72)	3697 (18.3)	2.74 (2.61–2.87)	2798 (13.8)	5.74 (5.42–6.08)
Unknown	2883 (27.0)	1.42 (1.35–1.50)	1311 (12.3)	1.18 (1.10–1.26)	592 (5.5)	1.77 (1.60–1.95)
Calendar year						
2010	8389 (27.0)	1.00 (ref)	4290 (13.8)	1.00 (ref)	1442 (4.6)	1.00 (ref)
2011	8792 (26.2)	0.98 (0.95–1.02)	4200 (12.5)	0.90 (0.86–0.94)	1773 (5.3)	1.17 (1.09–1.27)
2012	8441 (25.0)	0.92 (0.88–0.95)	4034 (12.0)	0.85 (0.80–0.89)	1741 (5.2)	1.18 (1.10–1.28)
2013	8299 (24.4)	0.88 (0.84–0.91)	3711 (10.9)	0.75 (0.71–0.79)	1798 (5.3)	1.19 (1.11–1.29)
2014	8054 (24.0)	0.85 (0.82–0.89)	3356 (10.0)	0.67 (0.64–0.71)	1802 (5.4)	1.20 (1.12–1.30)
2015	7759 (22.9)	0.79 (0.76–0.83)	3153 (9.3)	0.62 (0.59–0.66)	1827 (5.4)	1.23 (1.14–1.33)
2016	7574 (23.1)	0.78 (0.75–0.82)	2823 (8.6)	0.56 (0.53–0.59)	1689 (5.1)	1.13 (1.05–1.22)
2017	6973 (21.6)	0.71 (0.69–0.74)	2494 (7.7)	0.50 (0.47–0.52)	1568 (4.9)	1.05 (0.97–1.14)
2018	3459 (21.4)	0.69 (0.66–0.73)	1133 (7.0)	0.44 (0.41–0.47)	794 (4.9)	1.05 (0.96–1.16)
Indication for intensive care admission						
Airway	1001 (11.0)	0.98 (0.89–1.06)	364 (4.0)	2.08 (1.77–2.45)	159 (1.7)	1.98 (1.56–2.54)
Respiratory	6449 (21.1)	1.64 (1.54–1.75)	1325 (4.3)	1.84 (1.61–2.12)	704 (2.3)	1.90 (1.56–2.32)
Circulatory	13,659 (30.9)	2.48 (2.34–2.63)	6002 (13.6)	5.76 (5.07–6.56)	3312 (7.5)	5.03 (4.19–6.11)
Metabolic/ endocrine	1460 (10.5)	1.00 (ref)	254 (1.8)	1.00 (ref)	115 (0.8)	1.00 (ref)
Infection	9028 (29.7)	2.56 (2.41–2.73)	2957 (9.7)	4.16 (3.66–4.75)	1594 (5.2)	4.16 (3.45–5.06)
Hematologic disease	350 (62.4)	10.4 (8.65–12.5)	131 (23.4)	10.7 (8.44–13.5)	216 (38.5)	42.4 (32.9–55.0)
Intoxication	719 (2.4)	0.27 (0.25–0.30)	248 (0.8)	0.50 (0.42–0.60)	117 (0.4)	0.51 (0.39–0.66)
Kidney failure	1962 (37.0)	3.68 (3.40–3.99)	455 (8.6)	3.78 (3.23–4.44)	244 (4.6)	3.87 (3.10–4.87)
Liver failure	965 (49.7)	4.81 (4.32–5.35)	557 (28.7)	11.7 (9.95–13.7)	495 (25.5)	14.9 (12.1–18.6)
Neurosurgery	1503 (12.8)	0.98 (0.91–1.06)	528 (4.5)	1.99 (1.71–2.32)	532 (4.5)	3.87 (3.17–4.77)
Neurological disease	1676 (6.7)	0.53 (0.49–0.57)	558 (2.2)	1.06 (0.92–1.24)	390 (1.6)	1.49 (1.21–1.84)

(Continues)

TABLE 3 (Continued)

Parameter	Red-cell transfusion		Plasma transfusion		Platelet transfusion	
	Transfused episodes (%)	Odds ratio (95% CI)	Transfused episodes (%)	Odds ratio (95% CI)	Transfused episodes (%)	Odds ratio (95% CI)
Obstetric	711 (26.6)	5.99 (5.37–6.67)	498 (18.7)	19.4 (16.5–22.9)	326 (12.2)	29.2 (23.4–36.7)
Transplant surgery	320 (51.4)	8.44 (7.96–8.96)	135 (21.7)	22.3 (19.7–25.4)	187 (30.0)	14.9 (12.4–18.1)
Surgical	17,387 (52.5)	10.2 (8.57–12.1)	10,431 (31.5)	14.7 (11.7–18.6)	4064 (12.3)	44.7 (34.6–58.1)
Trauma	5356 (26.4)	4.32 (4.05–4.61)	2767 (13.6)	10.3 (9.09–11.8)	1285 (6.3)	10.0 (8.31–12.2)
Other	5194 (23.7)	2.93 (2.75–3.12)	1984 (9.0)	5.81 (5.10–6.65)	694 (3.2)	4.30 (3.54–5.27)

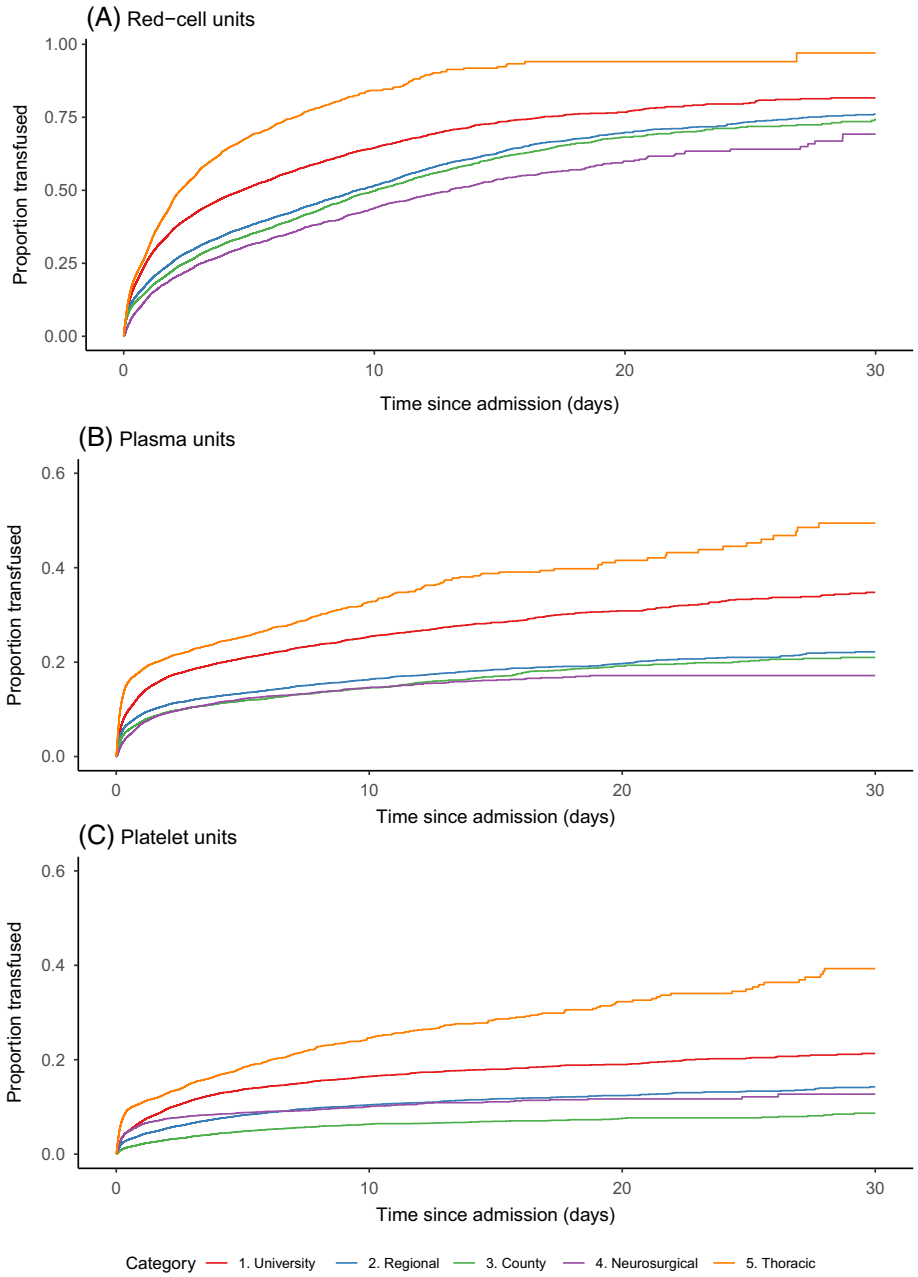

FIGURE 2 Cumulative proportion transfused as a function of days since admission to ICU, for red-cell units (A), plasma units (B), and platelet units (C), stratified by ICU category. [Color figure can be viewed at wileyonlinelibrary.com]

accounted for, despite logistic regression models achieving at least modest discriminative performance with C-statistics of 0.75 (95% CI, 0.75–0.75) for red-cell, 0.78 (95% CI, 0.77–0.78) for plasma, and 0.79 (95% CI, 0.79–0.79) for platelet transfusions.

Table 3 present odds ratios extracted from logistic regression models that were run for the three main ICU categories (university, regional, and county hospital ICUs). The probability of receiving each of the three types of blood transfusion was associated with all considered clinical parameters, with weak or modest associations seen for sex, age and calendar year. More pronounced associations were seen for ICU admission diagnosis and pre-admission surgery. For the former of these, the probability of receiving at least one red-cell unit ranged more than 20-fold, from 2.7% for patients admitted for intoxication (OR, 0.28; 95% CI, 0.25–0.30, compared with metabolic/endocrine disease) to 66.8% for patients with hematologic disease (OR, 12.3; 95% CI, 10.2–14.9, again compared with metabolic/endocrine disease). Other indications that stood out were different types of surgical indications. Similar, but partly more pronounced patterns were seen for plasma and platelet transfusions, where—as expected—patients with hematological disease, liver failure, obstetric patients, or patients who had undergone transplant surgery, all had a very high probability of being transfused.

Figure 2 depicts the cumulative incidence of being transfused as a function of time since admission. Again,

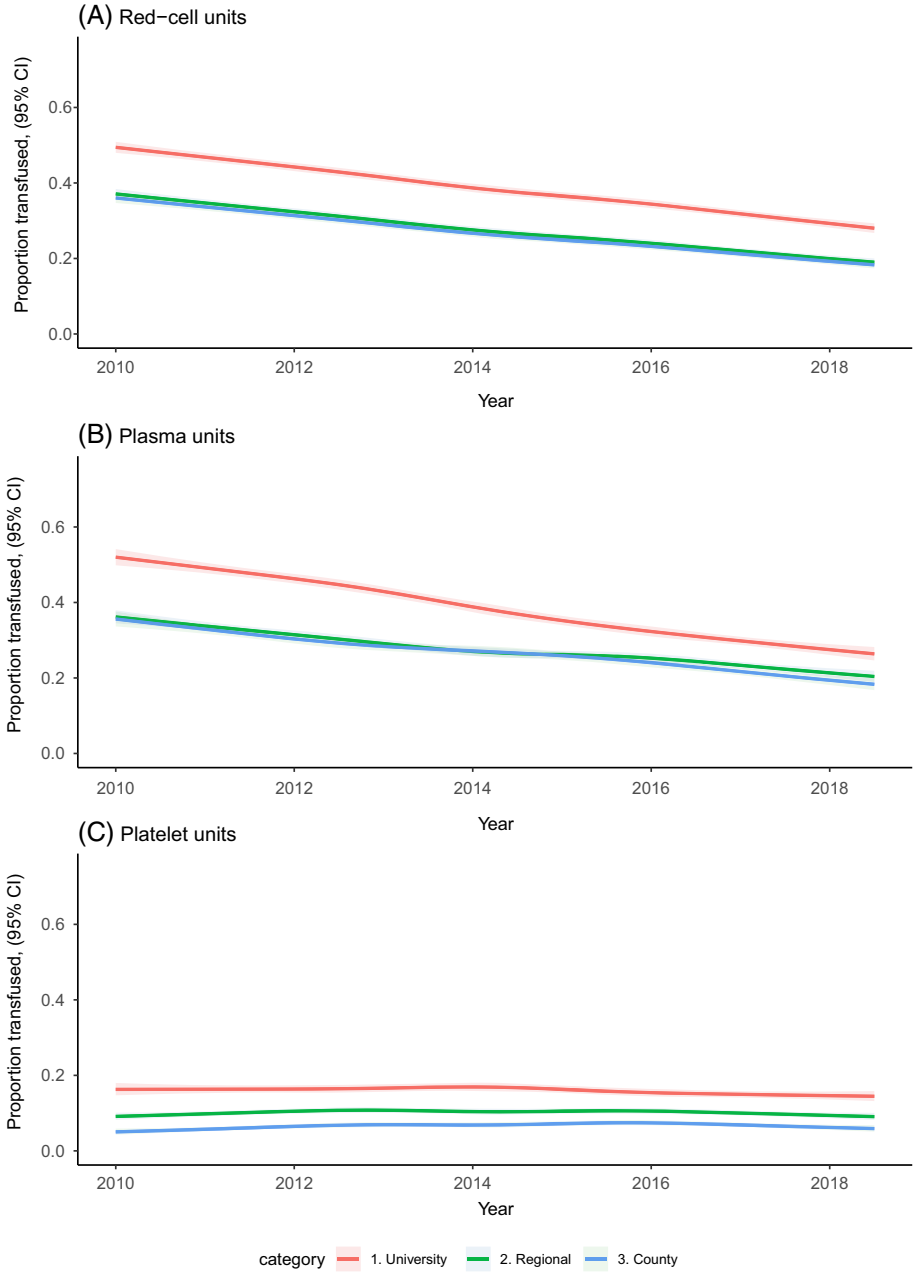

FIGURE 3 Proportion of patients transfused with red-cell units (A), plasma units (B), and platelet units (C), over time from 2010 to 2018 and stratified by ICU category. Shaded areas indicate 95% confidence intervals. [Color figure can be viewed at wileyonlinelibrary.com]

there was substantial variation between the different ICU categories. Patients treated in cardiothoracic ICUs persistently had the highest probability of being transfused. Indeed, among cardiothoracic ICU patients, close to 100% of patients had received at least one red-cell unit after 30 days, more than 50% had received at least one plasma unit, and almost 50% had received at least one platelet unit. In all ICU categories, for all three component types, there was a general pattern with rapidly increasing cumulative incidence in the first day, and then a more gradual increase.

Lastly, Figure 3 demonstrates the proportion of patients transfused over time with red cells, plasma and platelets, stratified on ICU category. For both red-cell units and plasma, there was a continuous reduction in the probability of patients being transfused during the study period, where the probability of receiving at least one red-cell unit decreasing from 31.3% in 2010 to 24.6% in 2018 (OR, 0.67; 95% CI, 0.64–0.70, comparing 2018 to 2010), and the probability of receiving at least one plasma unit decreasing from 16.6% in 2010 to 9.4% in 2018 (OR, 0.50; 95% CI, 0.47–0.53, comparing 2018 to 2010).

4 | DISCUSSION

With data on more than 300,000 intensive care admissions for almost 250,000 individual patients and nearly 100% coverage of Swedish ICUs, we are able to present a complete and contemporary picture of transfusion practice in Swedish intensive care. Using this data, we present detailed data on transfusion determinants and show that the transfusion frequency has decreased gradually over the past decade, for red-cell and especially plasma units, but still remains high. Of particular relevance for future research, is the striking heterogeneity in transfusion practice between different centers, which was not accounted for by a wide range of clinical parameters.

A similar practice heterogeneity, with large differences in transfusion frequency both between ICUs and between different countries have been described before, but not in such a complete data set.[1,9–13] Since this study was based on all ICU episodes in Sweden over a several years, a key strength is that we are able to confidently show that the heterogeneity was not driven by fluctuations in blood use, but rather seems to be an inherent phenomenon. Effectively, this means that it is likely difficult to draw wider conclusions about transfusion patterns in a region or country based on individual practice in one ICU, which needs to be kept in mind in interpreting findings from studies with more limited scope. Moreover, few reports on transfusion frequency in ICUs have been presented in the past decade. As to total transfusion frequency, we observed a decline from 31 to 24% between 2010 and 2018, which is in line with a general decrease in blood utilization seen in many western countries both in general[21] and among ICU patients in particular.[22] The transfusion frequency we observe at the end of the study period is thus similar to the 26% frequency reported from 2012 in the ICON study,[1] but higher than for example the 17% observed in Australia and New Zeeland in 2008.[12]

The most important strengths of the study stem from the qualities of the data, which were nationwide, longstanding and detailed, allowing us to characterize transfusion practice for a complete country in great detail. Still, there were some limitations in the data, relating for example to lack of specific information on the indication for transfusion, why we instead resorted to using indications for intensive care and discharge diagnoses. Other limitations include the inability to include data for the 6% of episodes where the patient was coded with a reserve number instead of an NRN. Although this issue should not affect the internal validity of our findings, it may affect the generalizability for patient categories who commonly present without a known identity (i.e., unconscious or nonSwedish patients). The lack of detailed, time-varying data on disease severity and complications throughout the ICU stay, for example, makes it mostly irrelevant to try to compare outcomes of transfused and nontransfused patients as such comparisons would invariably suffer residual confounding.[23] Still, for the purpose of describing the overall patterns of transfusion therapy in intensive care patients, the available data should mostly be sufficient. Another slight limitation is the lack of data on use of products such as albumin and prothrombin complex concentrate. These products potentially affect transfusion needs and patterns.

Among our findings, the most striking was perhaps the considerable variation in transfusion practice between seemingly similar ICU's and for the same types of patients, despite adjusting for a range of predictors including indication for ICU care, SAPS score and demographics. The proportion of patients who were transfused differed severalfold for all three component types and in all ICU categories. Unfotunately, the lack of granular data on transfusion indications and clinical nuances makes it difficult to identify clear determinants of the heterogeneity. However, we interpret it as an indication of a lack of adherence to established guidelines for transfusion therapy, and no clear consensus as to whom to transfuse and when, it clearly demonstrates that relying on audits, surveys and point prevalence studies in only a selection of ICUs is likely to result in findings that are not representative of the wider ICU population. Although considerable practice variation was seen for all three

component sites, it was especially pronounced for plasma units. It is thus perhaps encouraging that plasma was the component type for which we observed the greatest reduction in utilization during the study period. Viewed together, we believe that this signals a need for further refinement of indications for all types of transfusion therapy, but especially for plasma.

Mortality was, as expected, higher in transfused patients with a 30-days mortality of 21% in transfused patients versus 14% in nontransfused patients, with median SAPS3 score 59 versus 51 and median ICU length of stay 50 versus 22 h. The extent to which transfusion therapy increases mortality is beyond the scope of this study, given limitations in available data and likely confounding by indication that cannot be removed by adjustment for available data. It can however be noted that plasma is a therapy not without risk or cost, and that it should primarily be used to correct coagulopathy when needed.[24]

5 | CONCLUSIONS

To conclude, we present data on transfusion patterns in almost 300,000 ICU admissions over a 10-year period in Sweden. Overall, we see high, but mostly decreasing transfusion rates as well as striking and unexplained variation between centers. The latter finding is the key observation for the practicing ICU physician, reinforcing the need for adherence to practice guidelines and self-criticism as to the indication of each transfusion. Swedish, or Scandinavian guidelines geared specifically to blood product transfusion in intensive care would be of value and could be based on existing European guidelines.[25]To further add to knowledge on the subject, data from patient data management databases could be used, providing data on Hb and coagulation parameters upon transfusion as well as use of other products and medications affecting coagulation and transfusion needs.

ORCID

Jacob Holmqvist https://orcid.org/0000-0002-2902-3324
Anne Brynolf https://orcid.org/0000-0003-4151-8263
Gustaf Edgren https://orcid.org/0000-0002-2198-4745

ACKNOWLEDGMENTS

We are greatly indebted to the ICU register and to all blood banks and transfusion medicine clinics in Sweden who contributed data to this study.

FUNDING INFORMATION

The conduct of this study and the creation of the SCANDAT database was made possible by a grant to Dr Edgren from Swedish Research Council (2017-01954). Dr Holmqvist is supported by a grant from the Swedish Government under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBG-927831). Dr Edgren is supported by Region Stockholm (clinical research appointment). Dr Zhao is supported by the Clinical Scientist Training Program and the Research Internship Program, both at Karolinska Institutet.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

The conduct of this study has been approved by regional Stockholm County Board of Ethics Committee (ref nr: 2018/167-31). All procedures performed were in accordance with the ethical standards of the regional ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Swedish register-based research informed consent, when involving a large number of individuals, does not need to be obtained.

REFERENCES

1. Vincent JL, Jaschinski U, Wittebole X, Lefrant JY, Jakob SM, Almekhlafi GA, et al. Worldwide audit of blood transfusion practice in critically ill patients. Crit Care. 2018;22:102.
2. Alter HJ, Klein HG. The hazards of blood transfusion in historical perspective. Blood. 2008;112:2617–26.
3. Roubinian NH, Triulzi DJ. Transfusion-associated circulatory overload and transfusion-related acute lung injury: etiology and prevention. Hematol Oncol Clin North Am. 2019;33:767–79.
4. Roubinian NH, Hendrickson JE, Triulzi DJ, Gottschall JL, Michalkiewicz M, Chowdhury D, et al. Contemporary risk factors and outcomes of transfusion-associated circulatory overload. Crit Care Med. 2018;46:577–85.
5. Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion. 2010;50:753–65.
6. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med. 1999;340:409–17.
7. Holst LB, Haase N, Wetterslev J, Wernerman J, Guttormsen AB, Karlsson S, et al. Lower versus higher hemoglobin threshold for transfusion in septic shock. N Engl J Med. 2014;371:1381–91.
8. Sakr Y, Lobo S, Knuepfer S, Esser E, Bauer M, Settmacher U, et al. Anemia and blood transfusion in a surgical intensive care unit. Crit Care. 2010;14:R92.
9. Corwin HL, Gettinger A, Pearl RG, Fink MP, Levy MM, Abraham E, et al. The CRIT study: anemia and blood transfusion in the critically ill—current clinical practice in the United States. Crit Care Med. 2004;32:39–52.

10. 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.
11. Hebert PC, Wells G, Martin C, Tweeddale M, Marshall J, Blajchman M, et al. Variation in red cell transfusion practice in the intensive care unit: a multicentre cohort study. Crit Care. 1999;3:57–63.
12. Group BOSIoA-CT, Westbrook A, Pettila V, Nichol A, Bailey MJ, Syres G, et al. Transfusion practice and guidelines in Australian and New Zealand intensive care units. Intensive Care Med. 2010;36:1138–46.
13. Finfer S, Liu B, Taylor C, Bellomo R, Billot L, Cook D, et al. Resuscitation fluid use in critically ill adults: an international cross-sectional study in 391 intensive care units. Crit Care. 2010;14:R185.
14. 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.
15. 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.
16. 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.
17. Stanworth SJ, Walsh TS, Prescott RJ, Lee RJ, Watson DM, Wyncoll DL, et al. Thrombocytopenia and platelet transfusion in UKcritical care: a multicenter observational study. Transfusion. 2013;53:1050–8.
18. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727–33.
19. Sjoberg F, Walther S. Intensive care registries and the evolution of the concept of "quality of care": reflections from the 10-year anniversary symposium of the Swedish Intensive Care Registry. Acta Anaesthesiol Scand. 2012;56:1073–7.
20. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. Eur J Epidemiol. 2009;24:659–67.
21. Auvinen MK, Zhao J, Lassen E, Lubenow N, Seger Mollen A, Watz E, et al. Patterns of blood use in Sweden from 2008 to 2017: a nationwide cohort study. Transfusion. 2020;60:2529–36.
22. Cavalcante Dos Santos E, Bakos P, Vincent JL. How have red blood transfusion practices changed in critically ill patients? A comparison of the ICON and ABC studies conducted 13 years apart. Transfusion. 2020;60:2801–6.
23. Edgren G, Hjalgrim H. Epidemiology of donors and recipients: lessons from the SCANDAT database. Transfus Med. 2019;29-(Suppl 1):6–12.
24. Gorlinger K, Saner FH. Prophylactic plasma and platelet transfusion in the critically ill patient: just useless and expensive or even harmful? BMC Anesthesiol. 2015;15:86.
25. 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.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Holmqvist J, Brynolf A, Zhao J, Halmin M, Hollenberg J, Mårtensson 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(6):1188–98. https://doi.org/10.1111/trf.16942