



Original Article

Impact of a Patient Blood Management monitoring and feedback programme on allogeneic blood transfusions and related costs

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Summary

A Patient Blood Management programme was established at the University Hospital of Zurich, along with a monitoring and feedback programme, at the beginning of 2014 with a first analysis reported in 2015. Our study aimed to investigate the further impact of this Patient Blood Management monitoring and feedback programme on transfusion requirements and related costs. We included adult patients discharged between 2012 and 2017. A total of 213,882 patients underwent analysis: 66,659 patients in the baseline period (2012–2013); 35,309 patients in the year after the introduction of the Patient Blood Management monitoring and feedback programme (2014) and 111,914 patients in the continued sustainability period (2015–2017). The introduction of the Patient Blood Management monitoring and feedback programme reduced allogeneic blood product transfusions by 35%, from 825 units per 1000 hospital discharges in 2012 to 536 units in 2017. The most sustained effect was an approximately 40% reduction in red blood cell transfusions, from 535 per 1000 discharges to 319 units. Fewer patients were transfused in the periods after the introduction of the Patient Blood Management monitoring and feedback programme (6251 (9.4%) vs. 2932 (8.3%) vs. 8196 (7.3%); $p < 0.001$). Compared with 2012, the yearly OR for being exposed to any blood transfusion declined steadily after the introduction of the Patient Blood Management monitoring and feedback programme to 0.64 (95%CI 0.61–0.68; $p < 0.001$) in 2017. For patients requiring extracorporeal membrane oxygenation, transfusion requirements were also sustainably reduced. This reduction in allogeneic blood transfusions led to savings of 12,713,754 Swiss francs (£ 9,497,000 sterling; EUR 11,100,000; US\$ 12,440,000) in blood product acquisition costs over 4 years. In-hospital mortality was not affected by the programme. The Patient Blood Management monitoring and feedback programme sustainably reduced transfusion requirements and related costs, without affecting in-hospital mortality.

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Accepted: 29 July 2019

Keywords: adverse outcomes, mortality; allogeneic transfusion; healthcare costs; Patient Blood Management; patient outcomes, monitoring

Introduction

Patient Blood Management is an evidence-based multimodal treatment concept that aims to reduce transfusion of allogeneic blood products [1]. Allogeneic transfusion may cause adverse consequences; it has been shown that reduction in transfusion by implementation of a Patient Blood Management programme improves clinical outcomes and mortality rates, while saving costs [2]. The World Health Organization and European Union both support establishment of such programmes [3, 4]. Although the scale of these programmes varies between hospitals [2], the usual model is based on three pillars: comprehensive pre-operative optimisation of haematopoiesis and anaemia treatment [5]; minimisation of peri-operative blood loss and restrictive transfusion triggers; and use of intravenous iron, erythropoietin, vitamin B12 and folic acid postoperatively [1]. These three pillars require multidisciplinary hospital-wide measures [6, 7], including the development of electronic decision-making and prescribing tools [8]. At the University Hospital of Zurich, a Patient Blood Management programme was introduced in 2006. In 2014, we introduced a monitoring and feedback programme, with a first analysis of its benefits in 2015 [9]. Mehra et al. compared the period 2 years before the introduction of a Patient Blood Management programme with 1 year after, and found a 27% reduction in allogeneic blood product transfusions and estimated savings of approximately US\$ 2,000,000 in the first year [9].

Our study aimed to investigate the further impact of our Patient Blood Management monitoring and feedback programme on transfusion requirements and related costs, as well as its sustainability. We hypothesised that with more experience and better-established structures, transfusion rates and costs could be further reduced.

Methods

We conducted a retrospective impact study assessing the implementation of a hospital-wide Patient Blood Management monitoring and feedback programme. The study period lasted from January 2012 to December 2017, with the introduction of the programme occurring on 1 January 2014. We analysed three observation periods: the baseline 2 years before implementation (2012–2013); 1 year post-implementation (2014); and the sustainability period (2015–2017). During this time, every patient ≥ 18 years who was discharged from the University Hospital of Zurich was included in the study. Patients were not included if they had documentation of refusal to utilise their data for research purposes.

Our study was approved by the local ethics board in Zurich. Results of the first part of the study from January

2012 to December 2014, and details of the study protocol, have been published previously [9].

The introduction of a systemic Patient Blood Management monitoring and feedback programme was chosen as the intervention for empirical evaluation. This consisted of two mechanisms: firstly, the monitoring programme oversees all allogeneic transfusions of blood products by examination of the electronic medical patient records; and secondly, quarterly reporting of the number of transfusions, and adherence to transfusion thresholds, to each department. If $> 10\%$ of transfusions in a department did not meet the required criteria, the department head was asked to explain each case in writing.

The Patient Blood Management monitoring thresholds were chosen to be higher than the more restrictive hospital transfusion guidelines, so that discussions on appropriateness could be minimised. The monitoring transfusion criteria consisted of a laboratory test before transfusion, taken within 24 h, showing: haemoglobin concentration $< 90 \text{ g.l}^{-1}$ for red blood cell transfusions; platelet count $< 100 \text{ g.l}^{-1}$ for platelet transfusions; and prothrombin time $> 12.7 \text{ s}$ or factor V activity $< 20\%$ for fresh frozen plasma transfusions.

The University Hospital Zurich uses the KISIM electronic medical record system (Version 5.0.6, CISTEC AG, Zurich, Switzerland). Coding and administrative data were recorded in SAP NetWeaver (Version 7400.2.7.1112; SAP AG, Walldorf, Germany). Patient variables, details of the hospital stay and case weight (the economic severity of a patient's diagnosis, using SwissDRG Catalog 1.0-6.0) were extracted. Relevant data were transferred into QlikView business intelligence software (Version 11.20.13607.0 SR 17; QlikTech International AB, Radnor, PA, USA) before being exported as a data set file (Microsoft Excel 2016 Version 16.22; Microsoft Corporation, Redmond, WA, USA) for further analysis.

Transfusion costs were calculated by multiplying the number of transfused blood products by their acquisition costs per year.

Chi-squared and Mann–Whitney tests were used as appropriate. A multiple logistic regression predicting transfusion was performed. The following covariates were included in the model: Patient Blood Management monitoring and feedback programme, sex, age groups, surgical cases, department and extracorporeal membrane oxygenation (ECMO). From this model, adjusted odds ratios (OR) with corresponding 95%CI was obtained. Statistical significance was set as a two-tailed p value < 0.05 . Statistical analysis was performed with R Version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Over the 6-year period, we screened 231,221 patients. We did not include 17,339 patients who refused consent. The remaining 213,882 included: 66,659 patients in the baseline period; 35,309 patients in the post-implementation period; and 111,914 patients in the sustainability period.

Table 1 shows the patient characteristics. The use of cell salvage increased from the post-implementation period to the sustainability period, whereas the admission haemoglobin concentration was lower.

The proportion of patients being transfused, and the number of units transfused per patient, declined significantly over the three time periods. There was a significant reduction in length of hospital stay over the study period from a mean (SD) of 7.02 (10.5) to 7.0 (10.1) days, and then to 7.0 (10.0) days, with no change in in-hospital mortality (Table 2).

The transfusion trend of all patients during the observation period is illustrated in Fig. 1, with the corresponding data presented in the Supporting Information (Appendix S1). The baseline haemoglobin concentration before red blood cell transfusion declined from a mean (SD) of 70.4 (12.3) g.l⁻¹ in the post-implementation period to 70.0 (12.3) g.l⁻¹ in the

sustainability period from 2015 to 2017 ($p < 0.001$). Adherence to monitoring and feedback thresholds improved from the post-implementation to the sustainability period (Table 2).

In the logistic regression analysis, use of ECMO/assist device was associated with the second highest OR for allogeneic transfusion after haematological diseases (Table 3). The Patient Blood Management monitoring and feedback programme showed the same benefits in this patient group as for the whole study population (Fig. 2; see also Supporting Information, Appendix S2). An interaction analysis showed no additional benefit of the Patient Blood Management monitoring and feedback programme on transfusion requirements in patients with ECMO or assist device treatment compared with patients without (OR 1.33, 95%CI 0.94–1.87; $p = 0.10$).

We analysed the acquisition costs of allogeneic blood products. The price of red blood cells, fresh frozen plasma and platelets remained constant from 2012 to 2016. In 2017, the price for fresh frozen plasma declined, but increased for red blood cells and platelets (Table 4). The introduction of the Patient Blood Management monitoring and feedback programme resulted in a progressive saving from 2,680,199 to 3,660,086 Swiss francs (CHF) per year compared with the baseline. This led to a total saving of CHF

Table 1 Patient characteristics during the three study periods. Values are mean (SD) or number (proportion).

	Baseline (2012–2013) n = 66,659	Post-implementation (2014) n = 35,309	Sustainability (2015–17) n = 111,914	p value
Age; years	54.0 (19.1)	54.1 (19.2)	55.1 (19.2)	< 0.001
Sex; female	33799 (50.7%)	18128 (51.3%)	56943 (50.9%)	0.15
Diagnostic groups				< 0.001
Non-surgical	25130 (37.7%)	13504 (38.2%)	44977 (40.2%)	
Surgical	37744 (56.6%)	19735 (55.9%)	60796 (54.3%)	
Other	3628 (5.4%)	1985 (5.6%)	5868 (5.2%)	
Missing	157 (0.2%)	85 (0.2%)	273 (0.2%)	
Admission type				< 0.001
Scheduled	34850 (52.3%)	17886 (50.7%)	56302 (50.3%)	
Emergency	29540 (44.3%)	16321 (46.2%)	50846 (45.4%)	
Re-admission within 24 h	2201 (3.3%)	1044 (3.0%)	4431 (4.0%)	
Other	67 (0%)	55 (0%)	328 (0%)	
Missing	1 (0%)	3 (0%)	7 (0%)	
Case mix	1.6 (2.8%)	1.6 (2.8%)	1.6 (2.6%)	< 0.001
ECMO/assist device	307 (0.5%)	150 (0.4%)	620 (0.6%)	0.002
Cell salvage	NA	170 (0.4%)	1369 (1.1%)	< 0.001
Admission haemoglobin concentration; g.l ⁻¹	NA	131.0 (22.4)	130.4 (22.8)	0.007

ECMO, extracorporeal membrane oxygenation; NA, not applicable.

Table 2 Transfusion and patient outcomes during the three study periods. Values are number (proportion) or mean (SD).

	Baseline (2012–2013) n = 66,659	Post-implementation (2014) n = 35,309	Sustainability (2015–2017) n = 111,914	p value
Total allogeneic blood products				< 0.001
Patients transfused	6251 (9.4%)	2932 (8.3%)	8196 (7.3%)	
Units per patient	0.8 (6.2)	0.6 (4.6)	0.6 (5.2)	
Red blood cells				< 0.001
Patients transfused	5637 (8.5%)	2671 (7.6%)	7499 (6.7%)	
Units per patient	0.5 (3.2)	0.4 (2.6)	0.3 (2.7)	
Platelets				< 0.001
Patients transfused	2098 (3.1%)	879 (2.5%)	2499 (2.2%)	
Units per patient	0.1 (1.5)	0.1 (1.4)	0.1 (2.0)	
Fresh frozen plasma				< 0.001
Patients transfused	741 (1.1%)	306 (0.9%)	665 (0.6%)	
Units per patient	0.2 (3.6)	0.1 (2.1)	0.1 (2.6)	
Adherence to monitoring and feedback thresholds				
Haemoglobin $\leq 90 \text{ g.l}^{-1}$ before red blood cell transfusion	NA	11,030 (95.8%)	34,875 (96.4%)	0.002
Platelet count $\leq 100 \text{ g.l}^{-1}$ before platelet transfusion	NA	3171 (90.1%)	11,858 (93.3%)	< 0.001
Prothrombin time < 12.7 s or factor V activity < 20% before fresh frozen plasma transfusion	NA	819 (61.6%)	2699 (82%)	< 0.001
Length of stay; days	7.0 (10.5)	7.0 (10.1)	7.0 (10.0)	< 0.001
In-hospital mortality	1711 (2.6%)	908 (2.6%)	2953 (2.6%)	0.6

12,713,754 (£ 9,497,000; EUR 11,100,000; US\$ 12,440,000) over 4 years (Table 4; Fig. 3; <https://www.postfinance.ch/de/privat/support/tools-rechner/waehrungsrechner.html>; accessed 08/03/2019).

Discussion

Our Patient Blood Management monitoring and feedback programme has sustainably reduced the use of allogeneic blood products and transfusion costs, and we suggest that this is an important part of each Patient Blood Management programme.

We have found a 35% reduction in all allogeneic blood transfusions during our observation period. This is better than the 27% reduction reported by Mehra et al. one year after implementation of their Patient Blood Management programme [9], and close to a figure of 41% achieved by a larger, health system-wide Patient Blood Management implementation [10]. Our results confirm the importance of a comprehensive monitoring and feedback programme as part of a more general Patient Blood Management programme. There was a continuing decline in allogeneic transfusions over the sustainability period, in spite of no changes in

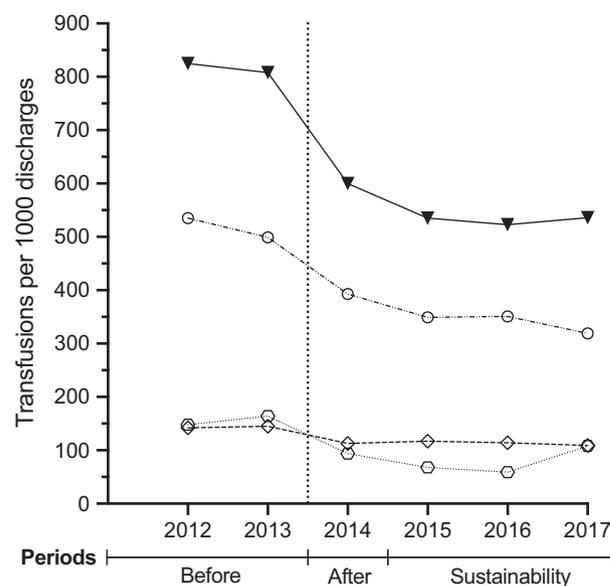


Figure 1 Impact of Patient Blood Management programme on allogeneic blood product transfusions during the study period. Vertical dotted line – introduction of Patient Blood Management monitoring and feedback programme. Total (triangles), red blood cells (circles), fresh frozen plasma (hexagons), platelets (diamonds).

Table 3 Logistic regression of factors associated with transfusion of allogeneic blood products. Patient Blood Management monitoring and feedback programme implemented at the end of 2013; reference year 2012.

	OR	95%CI	p value
Year			
2013	0.98	0.92–1.03	0.4
2014	0.87	0.82–0.92	<0.001
2015	0.71	0.67–0.75	<0.001
2016	0.72	0.68–0.77	<0.001
2017	0.64	0.61–0.68	<0.001
Sex; female	1.10	1.06–1.14	<0.001
Age			
40–59 years	1.63	1.54–1.73	<0.001
60–79 years	2.27	2.15–2.40	<0.001
> 80 years	2.57	2.40–2.75	<0.001
Surgical cases	2.09	2.01–2.18	<0.001
Department			
Haematology	41.70	38.67–44.99	<0.001
Cardiac surgery	9.67	9.18–10.19	<0.001
Oncology	8.36	7.77–8.99	<0.001
General surgery/ transplantation	2.54	2.39–2.70	<0.001
Traumatology	1.93	1.81–2.05	<0.001
Gynaecology and obstetrics	0.47	0.43–0.51	<0.001
ECMO	27.56	23.57–32.32	<0.001

ECMO, extracorporeal membrane oxygenation.

management. Although the use of cell salvage increased over the period, it was used in only a small fraction of patients and does not explain the continued improvements regarding allogeneic blood transfusion. These are more likely to be attributable to increased adherence to monitoring and feedback thresholds.

The most important reduction in transfusion was for red blood cells, continuing from the period after implementation of the programme [9]. We found a 40% reduction in red blood cell unit transfusions, which accords with a recent meta-analysis that showed an average reduction of 39% in red blood cell transfusions by implementation of a Patient Blood Management programme [2]. There has been an increase in fresh frozen plasma transfusions in the last year of analysis, which led to notification to the departmental heads and requests to reduce the use of allogeneic blood products.

Calculating the savings from the reduction of blood products, the Patient Blood Management monitoring and feedback programme lowered blood product acquisition costs by CHF 12,713,754 over 4 years, with annual savings

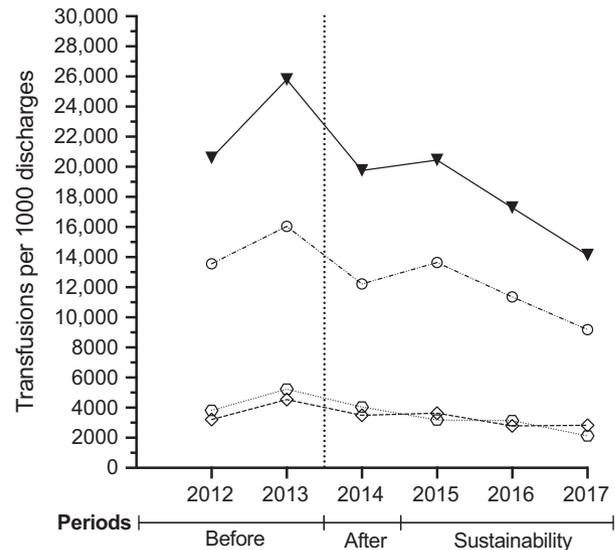


Figure 2 Impact of Patient Blood Management programme on allogeneic blood product transfusions in patients with extracorporeal membrane oxygenation or assist device during the study period. Vertical dotted line – introduction of Patient Blood Management monitoring and feedback programme. Total (triangles), red blood cells (circles), fresh frozen plasma (hexagons), platelets (diamonds).

increasing over the whole study period. Reductions in healthcare costs are well known from other established Patient Blood Management programmes [9, 10]. However, the extent of saving varies widely between studies. This depends on the pre-existing situation, length of assessment, type of patients, as well as what factors are included in the calculations [2]. In our study, savings were calculated based on blood product acquisition costs. Others have used activity-based costs of blood products, which typically is at least three times higher than pure acquisition costs [10–12]. Activity-based costing includes all costs related to the administration of an allogeneic blood product [11–15]. Thus, our yearly saving of over CHF 2,500,000 are just a fraction of the total cost benefits. However, even activity-based costing does not include the costs of prolonged hospitalisation, or treatment of any postoperative complication [16]. Appropriate system-wide analysis of Patient Blood Management cost-effectiveness should be the focus of future studies.

After patients with haematological disease, patients requiring ECMO/assist device had the highest risk for any type of allogeneic blood transfusion. ECMO devices were used in about 0.5% of all patients. Coagulopathy and anticoagulation, with subsequent bleeding, are common complications [17]. Besides the cost aspect, allogeneic blood transfusions may be associated with septicaemia in ECMO patients [18, 19]. Even in

Table 4 Analysis of allogeneic blood product acquisition costs over time.

	2012	2013	2014	2015	2016	2017
Discharges	33,186	33,473	35,309	35,984	37,506	38,424
Red blood cells						
Units transfused per 1000 discharges	535	499	393	349	351	319
Price per unit (CHF)	212.5	212.5	212.5	212.5	212.5	217.8
Costs per 1000 discharges (CHF)	113,659	105,999	83,510	74,260	74,527	69,454
Platelets						
Units transfused per 1000 discharges	142	145	113	117	114	109
Price per unit (CHF)	1334.3	1334.3	1334.3	1334.3	1334.3	1349.2
Costs per 1000 discharges (CHF)	189,695	193,331	151,081	156,108	151,517	147,161
Fresh frozen plasma						
Units transfused per 1000 discharges	148	164	94	68	59	108
Price per unit (CHF)	146.5	146.5	146.5	146.5	146.5	114.17
Costs per 1000 discharges (CHF)	21,724	24,006	13,709	10,032	8,636	12,337
Overall						
Units transfused per 1000 discharges	825	808	600	535	523	536
Costs per 1000 discharges (CHF)	325,078	323,336	248,300	240,400	234,680	228,952
Savings per 1000 discharges (CHF)	Reference (mean of 2012/2013)		75,907	83,806	89,526	95,255
Total savings per year (CHF)	Reference (mean of 2012/2013)		2,680,199	3,015,690	3,357,779	3,660,086

CHF, Swiss francs.

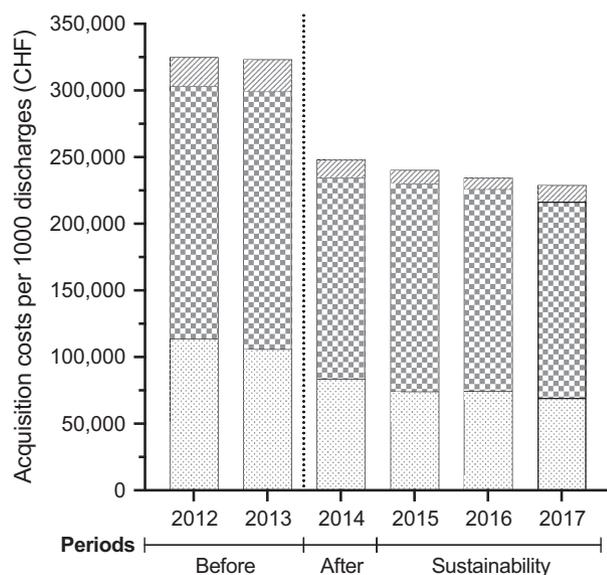


Figure 3 Impact of Patient Blood Management programme on adjusted acquisition costs of allogeneic blood products during the study period. Vertical dotted line – introduction of Patient Blood Management monitoring and feedback programme. Fresh frozen plasma (diagonal bars), platelets (checks), red blood cells (dots). CHF, Swiss francs.

this population with higher transfusion triggers, a Patient Blood Management monitoring programme substantially reduced transfusion rates.

In-hospital mortality did not change during the study period. We did not assess adverse outcomes such as stroke, myocardial infarction or kidney failure, as there were changes in diagnostic coding over the periods with a risk of bias in the data. It has been shown by large meta-analyses that Patient Blood Management programmes, with restrictive transfusion triggers of haemoglobin $< 70 \text{ g.l}^{-1}$, are both safe and improve a variety of patient outcomes [2, 7, 20, 21]. Althoff et al. showed a risk ratio of 0.89 (95%CI 0.80–0.98) for all-cause mortality with the introduction of comprehensive Patient Blood Management programmes [2].

Clinical decision support systems have been shown to help reduce allogeneic blood transfusions by notifying physicians if they are not complying with guidelines [8]. Our monitoring and feedback programme contains a structured, quarterly report to all departments. Mere implementation of transfusion guidelines may not achieve the desired effect [22]. This non-adherence may be due to a lack of knowledge and missing feedback on non-compliance. Education on guidelines, with feedback programmes to ensure continued application, is an important part of Patient Blood Management [23].

In summary, we found that a Patient Blood Management monitoring and feedback programme sustainably reduced transfusion requirements and related costs, without affecting in-hospital mortality.

Acknowledgement

No funding declared. Local ethics board of Zurich reference KEK-ZH-Nr. 2015-0175. AK and JR contributed equally to this manuscript.

The academic department of DS is receiving grant support from the Swiss National Science Foundation, Berne, Switzerland; the Swiss Society of Anesthesiology and Reanimation (SGAR), Berne, Switzerland; the Swiss Foundation for Anesthesia Research, Zurich, Switzerland, CSL Behring, Berne, Switzerland; Vifor SA, Villars-sur-Glâne, Switzerland. DRS is co-chair of the ABC-Trauma Faculty, sponsored by unrestricted educational grants from Novo Nordisk Health Care AG, Zurich, Switzerland; CSL Behring GmbH, Marburg, Germany; LFB Biomédicaments, Courtaboeuf Cedex, France and Octapharma AG, Lachen, Switzerland. DRS has received honoraria or travel support for consulting or lecturing from: Danube University of Krems, Austria; US Department of Defense, Washington, USA; European Society of Anesthesiology, Brussels, BE; Korean Society for Patient Blood Management, Seoul, Korea; Korean Society of Anesthesiologists, Seoul, Korea; Baxter AG, Volketswil, Switzerland; Baxter S.p.A., Roma, Italy; Bayer AG, Zürich, Switzerland; Bayer Pharma AG, Berlin, Germany; B. Braun Melsungen AG, Melsungen, Germany; Boehringer Ingelheim GmbH, Basel, Switzerland; Bristol-Myers-Squibb, Rueil-Malmaison Cedex, France and Baar, Switzerland; CSL Behring GmbH, Hattersheim am Main, Germany and Berne, Switzerland; Celgene International II Sàrl, Couvet, Switzerland; Curacyte AG, Munich, Germany; Daiichi Sankyo AG, Thalwil, Switzerland; GlaxoSmithKline GmbH & Co. KG, Hamburg, Germany; Haemonetics, Braintree, MA, USA; Instrumentation Laboratory (Werfen), Bedford, MA, USA; LFB Biomédicaments, Courtaboeuf Cedex, France; Merck Sharp & Dohme, Kenilworth, New Jersey, USA; Octapharma AG, Lachen, Switzerland; Organon AG, Pfäffikon/SZ, Switzerland; PAION Deutschland GmbH, Aachen, Germany; Pharmacosmos A/S, Holbaek, Denmark; Photonics Healthcare B.V., Utrecht, Netherlands; Pierre Fabre Pharma, Alschwil, Switzerland; Roche Diagnostics International Ltd, Reinach, Switzerland; Roche Pharma AG, Reinach, Switzerland; Sarstedt AG & Co., Sevelen, Switzerland and Nümbrecht, Germany; Schering-Plough International, Inc., Kenilworth, New Jersey, USA; Tem International GmbH, Munich, Germany; Verum Diagnostica GmbH, Munich, Germany; Vifor Pharma, Munich, Germany, Vienna, Austria and Villars-sur-Glâne, Switzerland; Vifor (International) AG, St. Gallen, Switzerland. All other authors declare no competing interests.

References

1. Isbister JP. The three-pillar matrix of patient blood management. *International Society of Blood Transfusion Science Series* 2015; **10**: 286–94.
2. Althoff FC, Neb H, Herrmann E, et al. Multimodal patient blood management program based on a three-pillar strategy. A systematic review and meta-analysis. *Annals of Surgery* 2019; **269**: 794–804.
3. Publications Office of the European Union. Supporting Patient Blood Management (PBM) in the EU. A Practical Implementation Guide for Hospitals. 2017. <https://publications.europa.eu/en/publication-detail/-/publication/93e1bbb1a8b-11e7-808e-01aa75ed71a1/language-en> (accessed 23/07/2019).
4. World Health Organization. WHA63.12 Agenda item 11.17 Availability, safety and quality of blood products. 2010. http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R12-en.pdf (accessed 23/07/2019).
5. Muñoz M, Acheson AG, Auerbach M, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. *Anaesthesia* 2017; **72**: 233–47.
6. Meybohm P, Richards T, Isbister J, et al. Patient blood management bundles to facilitate implementation. *Transfusion Medicine Reviews* 2017; **31**: 62–71.
7. Mueller MM, Van Remoortel H, Meybohm P, et al. Patient Blood Management. Recommendations from the 2018 Frankfurt Consensus Conference. *Journal of the American Medical Association* 2018; **2019**: 983–97.
8. Butler CE, Noel S, Hibbs SP, et al. Implementation of a clinical decision support system improves compliance with restrictive transfusion policies in hematology patients. *Transfusion* 2015; **55**: 1964–71.
9. Mehra T, Seifert B, Bravo-Reiter S, et al. Implementation of a patient blood management monitoring and feedback program significantly reduces transfusions and costs. *Transfusion* 2015; **55**: 2807–15.
10. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion* 2017; **57**: 1347–58.
11. 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.
12. Shander A, Ozawa S, Hofmann A. Activity-based costs of plasma transfusions in medical and surgical inpatients at a US hospital. *Vox Sanguinis* 2016; **111**: 55–61.
13. Charleston SC. The cost of blood: multidisciplinary consensus conference for a standard methodology. *Transfusion Medicine Reviews* 2005; **19**: 66–78.
14. Abraham I, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. *Transfusion* 2012; **52**: 1983–8.
15. Shander A, Hofmann A, Gombotz H, Theusinger OM, Spahn DR. Estimating the cost of blood: past, present, and future directions. *Best Practice and Research Clinical Anaesthesiology* 2007; **21**: 271–89.
16. Kleinerüschkamp A, Meybohm P, Straub N, Zacharowski K, Choorapoikayil S. A model-based cost-effectiveness analysis of patient blood management. *Blood Transfusion* 2019; **17**: 16–26.
17. Esper SA, Levy JH, Waters JH, Welsby IJ. Extracorporeal membrane oxygenation in the adult: a review of anticoagulation monitoring and transfusion. *Anesthesia and Analgesia* 2014; **118**: 731–43.
18. Menaker J, Galvagno S, Rabinowitz R, et al. Epidemiology of blood stream infection in adult extracorporeal membrane

- oxygenation patients: a cohort study. *Heart and Lung* 2019; **48**: 236–9.
19. Na SJ, Chung CR, Choi HJ, et al. Blood stream infection in patients on venovenous extracorporeal membrane oxygenation for respiratory failure. *Infection Control and Hospital Epidemiology* 2018; **39**: 871–4.
 20. Simon GI, Craswell A, Thom O, Fung YL. Outcomes of restrictive versus liberal transfusion strategies in older adults from nine randomised controlled trials: a systematic review and meta-analysis. *Lancet Haematology* 2017; **4**: e465–74.
 21. Carson JL, Stanworth SJ, Roubinian N, et al. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *Cochrane Database of Systematic Reviews* 2016; **10**: CD002042.
 22. Thakkar RN, Lee KHK, Ness PM, et al. Relative impact of a patient blood management program on utilization of all three major blood components. *Transfusion* 2016; **56**: 2212–20.
 23. Zuckerberg GS, Scott AV, Wasey JO, et al. Efficacy of education followed by computerized provider order entry with clinician decision support to reduce red blood cell utilization. *Transfusion* 2015; **55**: 1628–36.

Supporting Information

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

Appendix S1. Details of transfusion trends during the study period. Values are number.

Appendix S2. Details of transfusion trends in patients having extracorporeal membrane oxygenation during the study period. Values are number.