Supplemental Appendix

Use of Trigger or Target Hb versus Nadir Hb

We used the nadir Hb from the preoperative period through 2 hours in the post-anesthesia care unit. Frank et al. and Ejaz et al. defined the trigger Hb as the lowest value "before the beginning of the first [intraoperative] RBC transfusion."[1,2] Missing values were recognized[1] but not reported. At our studied hospital, 18.4% of cases with transfusion had a missing trigger Hb vs 12.9% with a missing nadir Hb. Therefore, use of the trigger Hb with the same Hb threshold would have resulted in a greater than 40% larger risk (i.e., incidence) of a case being audited vs the use of the nadir Hb ($P < .0001$ for each Hb threshold).

47.8% = 6029/12616
- Numerator: 6029 cases with (1) RBC transfusion; and (2) either (2a) missing trigger Hb or (2b) trigger Hb > 9 g/dL
- Denominator: 12616 cases with RBC transfusion

32.1% = 4051/12616
- Numerator: 4051 cases with (1) RBC transfusion; and (2) either (2a) missing **nadir** Hb or (2b) **nadir** Hb > 9 g/dL
- Denominator: 12616 cases with RBC transfusion

1.49 = (6029/12616) ÷ (4051/12616)
1.43 equals one-sided lower 99% confidence limit for the ratio of 1.49
P <.0001 using ratio of proportions
P <.0001 using the ratio of counts for each year and applying Student's t-test

33.0% = 4165/12616
- Numerator: 4165 cases with (1) RBC transfusion; and (2) either (2a) missing trigger Hb or (2b) trigger Hb > 10 g/dL
- Denominator: 12616 cases with RBC transfusion

20.6% = 2594/12616
- Numerator: 2594 cases with (1) RBC transfusion; and (2) either (2a) missing **nadir** Hb or (2b) **nadir** Hb > 10 g/dL
- Denominator: 12616 cases with RBC transfusion

1.61 = (4165/12616) ÷ (2594/12616)
1.53 equals one-sided lower 99% confidence limit for the ratio of 1.61
P <.0001 using ratio of proportions
P <.0001 using the ratio of counts for each year and applying Student's t-test

They defined the target "as the last intraoperative Hb value only if it occurred after the last RBC transfusion was complete."[1,2] There was missing target Hb for 51.3% of cases (i.e., much greater risk of audit using the target Hb than nadir Hb, both P <.0001).

81.9% = 10330/12616
Numerator: 10330 cases with (1) RBC transfusion; and (2) either (2a) missing target Hb or (2b) target Hb > 9 g/dL
Denominator: 12616 cases with RBC transfusion
32.1% = 4051/12616
Numerator: 4051 cases with (1) RBC transfusion; and (2) either (2a) missing **nadir** Hb or (2b) **nadir** Hb > 9 g/dL
Denominator: 12616 cases with RBC transfusion

2.55 = (10330/12616) ÷ (4051/12616)
2.47 equals one-sided lower 99% confidence limit for the ratio of 2.55
P <.0001 using ratio of proportions
P <.0001 using the ratio of counts for each year and applying Student's t-test

68.6% = 8655/12616
Numerator: 8655 cases with (1) RBC transfusion; and (2) either (2a) missing target Hb or (2b) target Hb > 10 g/dL
Denominator: 12616 cases with RBC transfusion
20.6% = 2594/12616
Numerator: 2594 cases with (1) RBC transfusion; and (2) either (2a) missing **nadir** Hb or (2b) **nadir** Hb > 10 g/dL
Denominator: 12616 cases with RBC transfusion

3.34 = (8655/12616) ÷ (2594/12616)
3.20 equals one-sided lower 99% confidence limit for the ratio of 3.34
P <.0001 using ratio of proportions
P <.0001 using the ratio of counts for each year and applying Student's t-test

Among the 12616 cases with RBC transfusion, there were 5715 cases with both documented trigger and target Hb, representing 430 procedures. Using Kruskal-Wallis (nonparametric) tests, the 5715 ratios of target/trigger, trigger/nadir, and target/nadir differed significantly among the 430 procedures; each P <.0001 after Bonferroni correction for the 3 comparisons. Therefore, the target and trigger Hb are not interpretable when pooled among procedures (e.g., each anesthesiologist's average); they are interpretable when controlled for procedure, as was done by Frank et al.'s Table 3 and Ejaz et al.'s Table 2.[1,2] The mean ratios of target to trigger Hb ± standard error of the mean (SEM) were 1.26 ± 0.04, 1.19 ± 0.04, and 1.18 ± 0.01 for abdominal hysterectomy with bilateral salpingo-oophorectomy (N = 69), pancreatectomy (N = 50), and Whipple procedure (N = 230), respectively. In contrast, the mean ± SEM were 1.03 ± 0.03, 1.00 ± 0.04, and 0.95 ± 0.04 for heart assist device insertion/removal (N = 92), repair/replace aortic valve (N = 55), and heart transplant (N = 63), respectively. The

corresponding ratios of the trigger to nadir Hb were 1.03 ± 0.01, 1.08 ± 0.02, and 1.05 ± 0.01 for the intra-abdominal procedures and 1.23 ± 0.02, 1.21 ± 0.03, and 1.38 ± 0.05 for the cardiac procedures, respectively. This systematic variation of ratios by type of procedure shows further that averaging target or trigger Hb among anesthesiologists is invalid.

References for Supplemental Appendix

1. Frank SM, Savage WJ, Rothschild JA, et al. Variability in blood and blood component utilization as assessed by an anesthesia information management system. *Anesthesiology*. 2012;117(1):99-106.

2. Ejaz A, Spolverato G, Kim Y, et al. Identifying variations in blood use based on hemoglobin transfusion trigger and target among hepatopancreaticobiliary surgeons. *J Am Coll Surg*. 2014;219(2):217-228.

Supplemental Table A. More Details of the 12,616 cases with RBC transfusion at Thomas Jefferson University Hospital, Provided in the Manuscript Table 2[a]

%	N	Statistics used in the Results (these rows are also in Table 2 of the main article)
12.9	1624	Missing Hb, within 30 days before surgery through 2 hours after operating room exit
6.4	811	Missing EBL and procedure's median EBL < 500 mL
17.7	2234	Missing Hb or missing EBL for procedure with median EBL < 500 mL
19.2	2427	Nadir Hb > 9 g/dL
7.7	970	Nadir Hb > 10 g/dL
4.8	610	Nadir Hb > 9 g/dL and procedure's median EBL ≥ 500 mL
1.9	240	Nadir Hb > 10 g/dL and procedure's median EBL ≥ 500 mL
32.1	4051	Nadir Hb > 9 g/dL or missing Hb
20.6	2594	Nadir Hb > 10 g/dL or missing Hb
36.3	4574	Nadir Hb > 9 g/dL, missing Hb, and/or missing EBL for procedure with median EBL < 500 mL
25.2	3177	Nadir Hb > 10 g/dL, missing Hb, and/or missing EBL for procedure with median EBL < 500 mL
		Most common 11 (see Results) of the 595 procedures[a]
5.1	642	Coronary artery bypass; internal mammary artery with endoscopic vein harvesting (500 mL)
5.0	636	Total hip revision (400 mL)
4.2	530	Posterior thoracic/ lumbar fusion (700 mL)
3.7	462	Exploratory laparotomy (75 mL)
3.5	440	Liver transplant (2000 mL)
3.3	421	Total hip replacement (200 mL)
2.4	298	Total knee replacement (50 mL)
2.1	264	Whipple procedure (350 mL)
1.9	241	Anterior thoracic/ lumbar fusion (300 mL)
1.8	221	Posterior lumbar fusion (350 mL)
1.7	212	Posterior cervical fusion (200 mL)
		Most common 4 procedures with missing Hb (rest have N < 50)
2.9	369	Total knee replacement
2.4	308	Total hip replacement
1.3	158	Total hip revision
1.2	147	Bilateral total knee replacement
≤0.3		All others
		Most common 10 procedures with relatively high blood loss (median EBL ≥ 500 mL)
5.1	642	Coronary artery bypass; internal mammary artery with endoscopic vein harvesting (500 mL)
4.2	530	Posterior thoracic/ lumbar fusion (700 mL)
3.5	440	Liver transplant (2000 mL)
1.9	239	Aortic valve repair/ replacement (750 mL)
1.4	174	Heart assist device insertion/ removal (785 mL)
0.9	118	Anterior/ posterior thoracic/ lumbar fusion (800 mL)

0.9	116	Cystectomy; anterior exenteration; ileo-conduit (800 mL)
0.9	115	Heart transplant
0.8	106	Abdominal aortic aneurysm repair; endarterectomy (1200 mL)
0.7	94	Radical prostatectomy
		Most common 10 surgical specialties
29.6	3734	Orthopedics
13.0	1645	Neurological surgery
14.4	1816	Cardiothoracic (including cardiac catheterization)
12.9	1624	General surgery
4.9	618	Vascular
4.7	595	Urology
4.7	593	Transplantation
4.5	572	Otolaryngology
3.5	445	Gynecology
1.4	177	Colorectal
		Distribution of different median EBL among the procedures
12.4	1562	50 mL; most common
11.5	1454	200 mL; 2nd most common
7.9	994	100 mL; 3rd most common
7.3	920	400 mL; 4th most common
6.6	832	500 mL; 5th most common
		Incidence of transfusion among the procedures
31.2	3932	0.1% to 9.9%
19.1	2408	10.0% to 19.7%
22.7	2868	20.0% to 39.2%
17.8	2243	40.0% to 59.6%
4.5	568	61.3% to 77.8%
4.7	597	80.0% to 100%
		Distribution among the 127 anesthesiologists with at least 1 transfusion
5.8	730	Anesthesiologist with the largest number of transfusions
5.2	656	2nd largest
4.8	605	3rd largest
3.0	378	Anesthesiologist that would have had the largest number of cases with a transfusion audited based on nadir Hb > 9 g/dL, missing Hb, and/or missing EBL for procedure with median EBL < 500 mL
2.7	345	2nd largest
2.6	322	3rd largest
2.5	311	Anesthesiologist that would have had the largest number of cases with a transfusion audited based on nadir Hb > 10 g/dL, missing Hb, and/or missing EBL for procedure with median EBL < 500 mL
2.2	282	2nd largest
2.1	270	3rd largest
		Units of allogeneic blood transfused during the case
40.8	5151	1 unit
29.6	3736	2 units

10.4	1314	3 units
7.1	900	4 units
3.0	374	5 units
		American Society of Anesthesiologists' Physical Status (ASA PS)
2.0	255	1 or 2 E
14.0	1767	1 or 2
13.1	1654	ASA PS 1 or 2 and < 3 units RBC transfused
13.6	1714	ASA PS 1 or 2 and procedure's median EBL < 500 mL
44.8	5655	3
6.7	846	3 E
17.9	2260	4
14.0	1767	4E or 5
0.5	66	Missing
		Decade of age of patients
26.9	3391	60 to 69
21.1	2659	50 to 59
20.5	2583	70 to 79
11.6	1464	80 or older
10.2	1290	40 to 49
5.3	669	30 to 39
4.0	501	20 to 29

Abbreviations: Hb, hemoglobin; EBL, estimated blood loss.

[a] These data are from Thomas Jefferson University Hospital, January 1, 2006, through August 31, 2016.[a] There were 595 procedures among the 12,616 cases with at least one RBC allogeneic transfusion. There were 1891 procedures among the 400,000 cases.

Supplemental Table B. Characteristics of the 36,580 cases among adults (age > 16 years) from the University of Miami Hospital,[a] showing similar incidences of missing values as for Tables 1 and 2

%	N	Percentage of the 36,580 cases, without and with RBC transfusion
28.1	10289	Cases with missing EBL
5.2	1906	Cases with RBC transfusion
		Percentages of the 1906 cases with RBC transfusion
13.3	197	Nadir Hb > 10 g/dL
18.9	360	Missing EBL
22.2	424	Missing Hb
30.0	445	Nadir Hb > 9 g/dL
36.0	687	Missing Hb or missing EBL
44.9	856	Nadir Hb > 10 g/dL, missing Hb, and/or missing EBL
56.1	1070	Nadir Hb > 9 g/dL, missing Hb, and/or missing EBL

Abbreviations: RBC, red blood cells; Hb, hemoglobin; EBL, estimated blood loss.

[a] The University of Miami IRB declared that the quantification of the incidence of missing values for Hb and EBL among its cases with intraoperative RBC transfusion does not constitute human subjects research. These data are from September 1, 2013, through September 30, 2016, and include all cases where care was documented in the anesthesia information management system. Excluded were cases performed in the gastrointestinal endoscopy suite, as paper records were used. The Hb values include laboratories, as well as the i-Stat device (Abbott Point of Care, Inc., Princeton, New Jersey).