Is intravenous iron and darbepoetin more effective than oral iron in reducing blood transfusion requirements for patients undergoing cardiac surgery (INITIATE)?

Statistical Analysis for a randomised controlled trial

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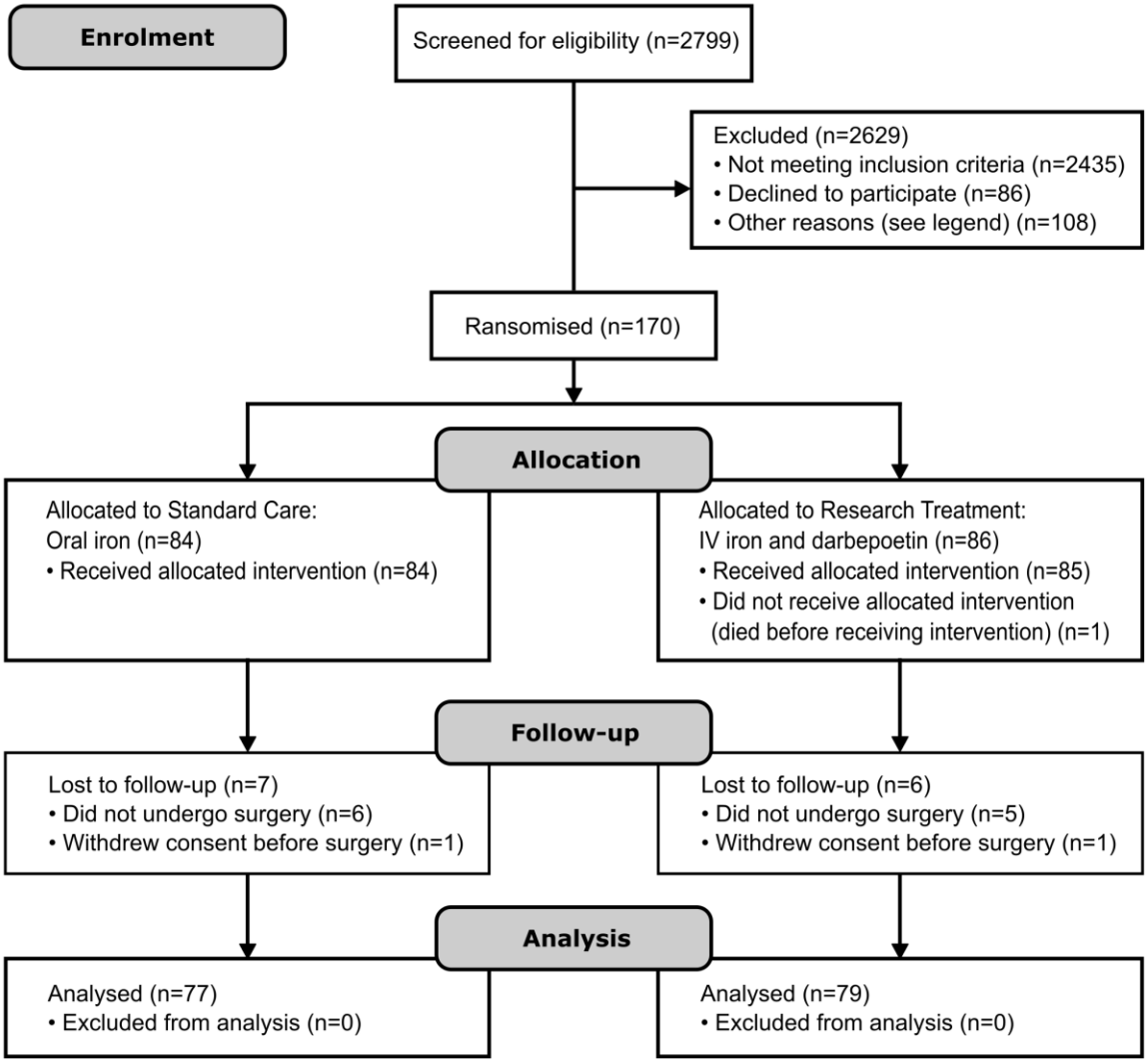
1. Participant flow

Figure 1: Study CONSORT diagram. Numbers in analysis section reflect the number in each group in the database with a primary outcome recorded. All other numbers from the 'Consort_INITIATE_v2.2' image provided. Patients not meeting the inclusion criteria include 2398 who were outside the Hb 100 to 130g/L range, 23 did not meet the ferritin and TSAT criteria, 6 were on renal replacement therapy and 8 were undergoing redo-operations. The specific reasons for the 108 excluded due to "Other reasons" are not given, but they should be described in the legend of this figure (e.g. in a paper).



2. Participant baseline data

Histograms were inspected for all continuous variables and none (except initial Hb concentration) were approximately normally distributed, so median and IQR were used to summarise all continuous variables.

Table 1: Medians and interquartile ranges/frequencies and percentages of participant characteristics at baseline by treatment group and overall.

	Intervention (n=79)		Standard (n=77)		Overall (n=156)	
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Age (years)	75.0	67.0 to 79.0	73.0	69.0 to 78.0	74.0	68.0 to 79.0
BMI (kg/m^2)	27.3	24.7 to 31.2	27.3	24.8 to 30.7	27.3	24.8 to 31.2
	No.	**%**	**No.**	**%**	**No.**	**%**
Gender						
Female	41	51.9	37	48.1	78	50.0
Male	38	48.1	40	51.9	78	50.0
Left ventricular function						
Good[>50%]	63	79.7	63	81.8	126	80.8
Fair[30-49%]	15	19.0	13	16.9	28	17.9
Poor[20-29%]	1	1.3	1	1.3	2	1.3
Diabetes						
Diet controlled	2	2.5	1	1.3	3	1.9
Insulin	6	7.6	7	9.1	13	8.3
Oral therapy	12	15.2	13	16.9	25	16.0
Not diabetic	59	74.7	56	72.7	115	73.7
Renal function						
eGFR >60	71	89.9	67	87.0	138	88.5
eGFR 30-60	8	10.1	10	13.0	18	11.5
eGFR <30	0	0.0	0	0.0	0	0.0
Type of surgery						
CABG	33	41.8	27	35.1	60	38.5
CABG+Valve	13	16.5	14	18.2	27	17.3
Valve	33	41.8	36	46.8	69	44.2
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Initial Hb concentration (g/L)	120.0	112.0 to 125.0	124.0	117.0 to 129.0	121.5	114.0 to 127.0
Serum ferritin (µg/L)	60.0	35.0 to 121.0	66.0	26.0 to 123.0	62.5	33.5 to 121.0
Transferrin saturation (%)	17.0	14.0 to 22.0	16.0	11.0 to 20.0	17.0	13.0 to 21.0
Serum B12 (pg/mL)	358.0	284.0 to 485.0	379.0	291.0 to 470.0	365.0	289.5 to 475.5
Serum folate (ng/mL)*	8.3	6.0 to 11.6	9.0	6.8 to 12.2	8.6	6.7 to 12.1
Serum thyroxine (pmol/L)	15.6	14.1 to 17.2	16.0	14.3 to 18.4	15.8	14.2 to 17.9
Serum TSH (mIU/L)	1.6	1.2 to 2.7	1.7	1.3 to 2.7	1.7	1.2 to 2.7
Serum CRP (mg/L)	2.4	1.0 to 5.3	3.0	1.6 to 7.0	2.8	1.3 to 6.4
Reticulocyte count (%)#	54.0	46.0 to 67.0	60.0	49.5 to 74.0	56.0	47.0 to 69.0
Serum hepcidin (ng/mL)	17.0	7.5 to 35.3	21.5	7.8 to 34.2	19.9	7.6 to 34.7
Serum erythropoietin (U/L)~	12.8	9.2 to 19.2	15.3	12.2 to 18.6	13.6	10.5 to 19.1
Duration of cardiopulmonary bypass (minutes)	92.0	71.0 to 127.0	88.0	67.0 to 112.0	89.0	69.5 to 124.0
*n = 68 Intervention group / 75 Standard group						
#n = 78 Intervention group / 76 Standard group						
~n = 75 Intervention group / 76 Standard group						

3. Analysis of primary outcome

3.1 Summary of primary outcome

The primary outcome 'Did participant receive one red cell transfusion on days 0-5?' (Rbc1eyn, Yes/No) was complete for all 156 participants in the dataset.

Table 2: Rbc1eyn by intervention group.

Red cell transfusion received on days 0-5	Intervention	Standard	Total
No	26	14	40
	32.9%	18.2%	25.6%
Yes	53	63	116
	67.1%	81.8%	74.4%
Total	79	77	156
	100.0%	100.0%	100.0%

3.2 Selection of covariates for primary outcome model

Not receiving a transfusion was the least common event, allowing for 40/5 = 8 variables in the logistic regression model, before accounting for any loss of participants due to data missing from any of these variables.

Table 3: Priority list for potential model variables

Model variable	Priority	Completeness	No. events if variable included with all prior variables
Group (Interorstd)	Required	100%	40
Time between treatment and surgery (Treat_surgestart_time)	n/a*	100%	n/a
CRP (Crpbaseval)	1	100%	40
Ferritin (Ferbaseval)	2	100%	40
Transferrin saturation (Tsatbaseval)	3	100%	40
GFR (Gfrbaseval)	4	100%	40

*Treat_surgestart_time was not considered for inclusion for the model as it is not a baseline covariate – randomisation to either group affects the time between treatment and surgery, which is accounted for by the Group (Interorstd) variable.

None of the other potential model variables are missing any data, so no participants/events are lost from the model if all 5 variables are included. The number of events per variable for the model is therefore 40/5=8, which is acceptable (Peduzzi et. al, 1996).

3.3 Primary outcome model

There is some evidence against the null hypothesis of no difference in receiving a blood transfusion within the first 5 days after surgery between intervention groups. The odds ratio for the Intervention group vs the Standard group is 0.42 (95% CI: 0.19 to 0.91, p=0.027), indicating that the odds of receiving a blood transfusion in the Intervention group are 0.42x the odds of receiving a blood transfusion in the Standard group. Alternatively, the odds of receiving a blood transfusion are 2.39 (95% CI: 1.10 to 5.19) times greater in the Standard group. Full model output us shown in Appendix 2.

4. Secondary analyses

4.1 Summaries of secondary outcomes

Histograms were inspected for all continuous secondary outcomes and none were approximately normally distributed, so median and IQR were used to summarise all continuous secondary outcomes.

Table 4: Medians and interquartile ranges/frequencies and percentages of secondary outcome measures by treatment group and overall.

	Secondary Outcome	Intervention (n=79)		Standard (n=77)		Overall (n=156)	
		Median	IQR	Median	IQR	Median	IQR
1	Hb increase	12.0	7.0 to 17.0	0.0	-5.0 to 6.0	7.0	-1.5 to 13.5
2a	Number of packed RBCs given	2.0	0.0 to 3.0	2.0	1.0 to 3.0	2.0	1.0 to 3.0
2b	Volume of packed RBCs given	492.0	0.0 to 885.0	587.0	299.0 to 870.0	569.0	244.5 to 873.0
3a	Number of plasma units given	0.0	0.0 to 0.0	0.0	0.0 to 0.0	0.0	0.0 to 0.0
3b	Number of cryoprecipitate units given	0.0	0.0 to 0.0	0.0	0.0 to 2.0	0.0	0.0 to 1.0
3c	Number of platelet units given	0.0	0.0 to 1.0	0.0	0.0 to 1.0	0.0	0.0 to 1.0
3d	Volume of plasma units given	0.0	0.0 to 0.0	0.0	0.0 to 0.0	0.0	0.0 to 0.0
3e	Volume of cryoprecipitate units given	0.0	0.0 to 0.0	0.0	0.0 to 378.0	0.0	0.0 to 189.0
3f	Volume of platelet units given	0.0	0.0 to 188.0	0.0	0.0 to 179.0	0.0	0.0 to 183.0
4a	Postoperative blood loss by 12 hours	450.0	325.0 to 675.0	425.0	307.5 657.5	450.0	325.0 to 665.0
4b	Postoperative blood loss by 24 hours*	650.0	450.0 to 905.0	600.0	450.0 930.0	615.0	450.0 to 925.0
10	Length of hospital stay (days)	8.0	6.0 to 11.0	8.0	5.0 to 13.0	8.0	6.0 to 12.0
		No.	%	No.	%	No.	%
5	Significant postoperative myocardial injury						
	No	76	96.2	75	97.4	151	96.8
	Yes	3	3.8	2	2.6	5	3.2
6	Acute kidney injury						
	No	64	81.0	59	76.6	123	78.8
	Yes	15	19.0	18	23.4	33	21.2
7a	Death						
	No	77	97.5	75	97.4	152	97.4
	Yes	2	2.5	2	2.6	4	2.6
7b	Stroke						
	No	75	94.9	77	100.0	152	97.4
	Yes	4	5.1	0	0.0	4	2.6
7c	RRT						
	No	76	96.2	75	97.4	151	96.8
	Yes	3	3.8	2	2.6	5	3.2
7d	IABP						
	No	77	97.5	76	98.7	153	98.1
	Yes	2	2.5	1	1.3	3	1.9
7e	Debridement						
	No	76	96.2	77	100.0	153	98.1
	Yes	3	3.8	0	0.0	3	1.9
7f	Composite Death/Stroke/RRT/IABP/Debridement						
	No	69	87.3	74	96.1	143	91.7
	Yes	10	12.7	3	3.9	13	8.3
8	Re-sternotomy for bleeding within 24h of surgery						
	No	78	98.7	72	93.5	150	96.2
	Yes	1	1.3	5	6.5	6	3.8
9a	Delirium						
	No	72	91.1	71	92.2	143	91.7
	Yes	7	8.9	6	7.8	13	8.3
9b	Cerebral events						
	No	77	97.5	77	100.0	154	98.7
	Yes	2	2.5	0	0.0	2	1.3

* n=76 for Standard group

4.2 Secondary outcome models

Sufficient data were available to fit models for secondary outcomes 1, 2, 3, 4, 6 and 10. Normality of residuals was checked for each linear regression model and the residuals were not normally distributed from any of these. Bootstrapping (5000 replicates with seed 695674803) was used for these models to calculate appropriate 95% CIs and p-values. Models could not be fitted for secondary outcomes 5, 7, 8 or 9 due to the low number of events for each. The proportional hazards assumption was checked for secondary outcome model 10.

Table 5: Effect of intervention group (Intervention vs Standard) in secondary outcome models

Secondary outcome		Intervention group effect	Effect type	95% CI	p-value
1	Hb increase	10.54	Linear regression β coefficient	7.90 to 13.18	<0.001
2a	Number of packed RBCs given	0.14	Negative binomial regression coefficient	-0.25 to 0.52	0.486
2b	Volume of packed RBCs given	-168.43	Linear regression β coefficient	-369.59 to 32.72	0.101
3a	Number of plasma units given	-0.57	Negative binomial regression coefficient	-2.57 to 1.42	0.573
3b	Number of cryoprecipitate units given	0.08	Negative binomial regression coefficient	-0.70 to 0.87	0.835
3c	Number of platelet units given	-0.04	Negative binomial regression coefficient	-0.67 to 0.60	0.909
3d	Volume of plasma units given	-0.24	Linear regression β coefficient	-85.57 to 85.10	0.996
3e	Volume of cryoprecipitate units given	-12.68	Linear regression β coefficient	-96.40 to 71.06	0.767
3f	Volume of platelet units given	-7.20	Linear regression β coefficient	-75.72 to 61.31	0.837
4a	Postoperative blood loss by 12 hours	13.16	Linear regression β coefficient	-115.11 to 141.44	0.841
4b	Postoperative blood loss by 24 hours	1.01	Linear regression β coefficient	-160.00 to 162.03	0.990
6	Acute kidney injury	0.81	Logistic regression Odds Ratio	0.36 to 1.81	0.606
10	Length of hospital stay (days)	0.93	Cox Regression Hazard Ratio	0.67 to 1.29	0.668

4.2.1 Model interpretations

For secondary outcome model 1, there is strong evidence against the null hypothesis of no difference between intervention and standard groups. The value of Hb increase is 10.54g/L (95% CI: 7.90 to 13.18) greater in the Intervention group compared to the Standard group. There is no evidence against any of the other null hypotheses of no difference between intervention and standard groups for any of the other secondary outcomes. Full secondary outcome models are shown in Appendix 2.

5. Appendix 1: Derived variables

Variable name	Variable type	Range/categories	Derivation	Description
Treat_surgestart_time	Continuous	>0	For patients in the standard group (Interorstd2==0): Surgdate – Orironstartdate For patients in the intervention group (Interorstd2==1): Surgdate – Ivirondate	Days between treatment start and surgery
CompinhospAE	Binary	0= No, 1= Yes	Yes if any of Hospdeadyn, Strtiahospyn, Rrtyn, Iabpyn, Woundebyn are 'Yes'	Secondary outcome 7: Composite in-hospital adverse events
renal_function_cat	Categorical	1=eGFR >60 2=eGFR 30-60 3=eGFR <30	Categorisation of Gfrbaseval variable	Categorisation of kidney function measured by eGFR

6. Appendix 2: Full primary and secondary outcome models

6.1 Primary outcome: blood transfusion within the first 5 days after surgery

Logistic regression — Number of obs = 156; LR chi2(5) = 8.69; Prob > chi2 = 0.1223; Log likelihood = -84.46285; Pseudo R2 = 0.0489

Rbcleyn2	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	.4177005	.1648512	-2.21	0.027	.19272	.9053224
Crpbaseval	1.056828	.0394585	1.48	0.139	.982253	1.137065
Ferbaseval	.9967431	.0030043	-1.08	0.279	.9908723	1.002649
Tsatbaseval	1.044249	.0332893	1.36	0.174	.9809996	1.111576
Gfrbaseval	.994986	.0080911	-0.62	0.536	.9792534	1.010971
_cons	3.420942	2.968603	1.42	0.156	.6244469	18.74114

Note: _cons estimates baseline odds.

6.2 Secondary outcome 1: Hb increase

Linear regression — Number of obs = 156; Replications = 5,000; Wald chi2(5) = 98.58; Prob > chi2 = 0.0000; R-squared = 0.3447; Adj R-squared = 0.3228; Root MSE = 8.7144

Hbchgbase2s~l	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	10.54064	1.3481	7.82	0.000	7.89841	13.18287
Crpbaseval	-.154974	.0622256	-2.49	0.013	-.276934	-.0330141
Ferbaseval	-.0053693	.0123928	-0.43	0.665	-.0296587	.01892
Tsatbaseval	-.5566565	.1159385	-4.80	0.000	-.7838919	-.3294212
Gfrbaseval	.0226804	.0321259	0.71	0.480	-.0402851	.085646
_cons	10.30721	2.875374	3.58	0.000	4.671578	15.94284

6.3 Secondary outcome 2a: Number of packed RBCs given

Negative binomial regression — Number of obs = 156
LR chi2(5) = 8.90
Dispersion = mean — Prob > chi2 = 0.1132
Log likelihood = -336.39459 — Pseudo R2 = 0.0131

Rbcdistotalnum	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	.1354576	.1944659	0.70	0.486	-.2456886	.5166039
Crpbaseval	-.0014341	.0106357	-0.13	0.893	-.0222797	.0194116
Ferbaseval	-.0015062	.001518	-0.99	0.321	-.0044814	.001469
Tsatbaseval	-.0149195	.0157829	-0.95	0.345	-.0458534	.0160144
Gfrbaseval	-.0078678	.0041235	-1.91	0.056	-.0159496	.000214
_cons	1.991863	.4071262	4.89	0.000	1.19391	2.789816
/lnalpha	.0257735	.1592224			-.2862967	.3378437
alpha	1.026108	.1633795			.7510397	1.401921

LR test of alpha=0: chibar2(01) = 348.20 — Prob >= chibar2 = 0.000

6.4 Secondary outcome 2b: Volume of packed RBCs given

Linear regression — Number of obs = 156
Replications = 5,000
Wald chi2(5) = 3.70
Prob > chi2 = 0.5931
R-squared = 0.0231
Adj R-squared = -0.0095
Root MSE = 634.1557

Rbcdistot~lum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	-168.4329	102.6313	-1.64	0.101	-369.5867	32.7208
Crpbaseval	.8496486	5.078601	0.17	0.867	-9.104227	10.80352
Ferbaseval	-.3615826	.6874202	-0.53	0.599	-1.708901	.9857362
Tsatbaseval	3.999277	8.961278	0.45	0.655	-13.5645	21.56306
Gfrbaseval	-1.893741	2.51836	-0.75	0.452	-6.829635	3.042154
_cons	847.4506	259.4377	3.27	0.001	338.962	1355.939

6.5 Secondary outcome 3a: Number of plasma units given

Negative binomial regression — Number of obs = 156
LR chi2(5) = 4.89
Dispersion = mean — Prob > chi2 = 0.4301
Log likelihood = -75.879226 — Pseudo R2 = 0.0312

Ffpdistotalnum	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	-.5743628	1.018896	-0.56	0.573	-2.571362	1.422636
Crpbaseval	-.2382902	.1547471	-1.54	0.124	-.541589	.0650085
Ferbaseval	.002504	.0084761	0.30	0.768	-.0141089	.0191168
Tsatbaseval	.0752523	.0792829	0.95	0.343	-.0801394	.230644
Gfrbaseval	.0052821	.0219789	0.24	0.810	-.0377958	.04836
_cons	-2.104938	2.266873	-0.93	0.353	-6.547928	2.338052
/lnalpha	3.033926	.3688878			2.310919	3.756933
alpha	20.77865	7.664993			10.08369	42.81691

LR test of alpha=0: chibar2(01) = 144.59 — Prob >= chibar2 = 0.000

6.6 Secondary outcome 3b: Number of cryoprecipitate units given

Negative binomial regression — Number of obs = 156
LR chi2(5) = 5.98
Dispersion = mean — Prob > chi2 = 0.3084
Log likelihood = -158.30906 — Pseudo R2 = 0.0185

Cryodistotalnum	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	.083805	.4013798	0.21	0.835	-.7028849	.8704949
Crpbaseval	-.0456886	.0338639	-1.35	0.177	-.1120606	.0206834
Ferbaseval	-.0009143	.0030531	-0.30	0.765	-.0068982	.0050697
Tsatbaseval	-.0658889	.0370503	-1.78	0.075	-.1385062	.0067284
Gfrbaseval	.0001367	.0096685	0.01	0.989	-.0188132	.0190866
_cons	.9238684	.925832	1.00	0.318	-.8907289	2.738466
/lnalpha	1.38451	.2709626			.8534326	1.915586
alpha	3.992867	1.081918			2.347692	6.79092

LR test of alpha=0: chibar2(01) = 86.97 — Prob >= chibar2 = 0.000

6.7 Secondary outcome 3c: Number of platelet units given

Negative binomial regression — Number of obs = 156; LR chi2(5) = 5.94; Dispersion = mean; Prob > chi2 = 0.3119; Log likelihood = -133.97436; Pseudo R2 = 0.0217

Platdistotalnum	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	-.036956	.3234639	-0.11	0.909	-.6709336	.5970217
Crpbaseval	-.0749589	.0392315	-1.91	0.056	-.1518512	.0019334
Ferbaseval	.0023533	.0023812	0.99	0.323	-.0023138	.0070204
Tsatbaseval	-.0150362	.0257784	-0.58	0.560	-.065561	.0354886
Gfrbaseval	-.0015887	.0068908	-0.23	0.818	-.0150945	.0119171
_cons	-.2918663	.7128697	-0.41	0.682	-1.689065	1.105333
/lnalpha	.2923813	.4053844			-.5021575	1.08692
alpha	1.339614	.5430585			.6052235	2.965128

LR test of alpha=0: chibar2(01) = 17.75 — Prob >= chibar2 = 0.000

6.8 Secondary outcome 3d: Volume of plasma units given

Linear regression — Number of obs = 156; Replications = 5,000; Wald chi2(5) = 4.61; Prob > chi2 = 0.4653; R-squared = 0.0282; Adj R-squared = -0.0042; Root MSE = 280.3276

Ffpdistot~lum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	-.2400236	43.53923	-0.01	0.996	-85.57536	85.09531
Crpbaseval	-.9428808	1.909959	-0.49	0.622	-4.686332	2.800571
Ferbaseval	-.2179339	.2884216	-0.76	0.450	-.7832298	.3473619
Tsatbaseval	4.834071	3.713518	1.30	0.193	-2.44429	12.11243
Gfrbaseval	.7715351	.9505875	0.81	0.417	-1.091582	2.634652
_cons	-47.20343	111.3974	-0.42	0.672	-265.5382	171.1314

6.9 Secondary outcome 3e: Volume of cryoprecipitate units given

Linear regression

Number of obs	= 156
Replications	= 5,000
Wald chi2(5)	= 6.78
Prob > chi2	= 0.2376
R-squared	= 0.0414
Adj R-squared	= 0.0094
Root MSE	= 266.9423

Cryodisto~lum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	-12.67616	42.72175	-0.30	0.767	-96.40925	71.05692
Crpbaseval	-2.305315	1.728886	-1.33	0.182	-5.69387	1.083241
Ferbaseval	-.2552862	.3225126	-0.79	0.429	-.8873993	.3768268
Tsatbaseval	-6.590382	2.948702	-2.24	0.025	-12.36973	-.8110315
Gfrbaseval	.0328745	.7363377	0.04	0.964	-1.410321	1.47607
_cons	287.4549	94.46475	3.04	0.002	102.3074	472.6024

6.10 Secondary outcome 3f: Volume of platelet units given

Linear regression

Number of obs	= 156
Replications	= 5,000
Wald chi2(5)	= 3.21
Prob > chi2	= 0.6669
R-squared	= 0.0155
Adj R-squared	= -0.0173
Root MSE	= 224.7687

Platdisto~lum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	-7.204325	34.95771	-0.21	0.837	-75.72019	61.31154
Crpbaseval	-2.681313	1.758034	-1.53	0.127	-6.126996	.7643693
Ferbaseval	.2047309	.3185463	0.64	0.520	-.4196084	.8290703
Tsatbaseval	-.0877393	2.401943	-0.04	0.971	-4.795462	4.619983
Gfrbaseval	.0520927	.7333383	0.07	0.943	-1.385224	1.489409
_cons	109.1056	81.48172	1.34	0.181	-50.59562	268.8069

6.11 Secondary outcome 4a: Postoperative blood loss by 12 hours

Linear regression

Number of obs	= 155
Replications	= 5,000
Wald chi2(5)	= 2.06
Prob > chi2	= 0.8407
R-squared	= 0.0103
Adj R-squared	= -0.0229
Root MSE	= 381.6815

Bloss12hvolum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	13.16325	65.44821	0.20	0.841	-115.1129	141.4394
Crpbaseval	-3.148432	2.616543	-1.20	0.229	-8.276761	1.979898
Ferbaseval	-.0087058	.4260753	-0.02	0.984	-.8437981	.8263864
Tsatbaseval	-3.715764	5.307677	-0.70	0.484	-14.11862	6.687091
Gfrbaseval	.4208696	1.450377	0.29	0.772	-2.421816	3.263556
_cons	595.2381	164.7362	3.61	0.000	272.361	918.1151

6.12 Secondary outcome 4b: Postoperative blood loss by 24 hours

Linear regression

Number of obs	= 155
Replications	= 5,000
Wald chi2(5)	= 4.03
Prob > chi2	= 0.5457
R-squared	= 0.0237
Adj R-squared	= -0.0091
Root MSE	= 478.7555

Bloss24hvolum	Observed Coef.	Bootstrap Std. Err.	z	P>|z|	Normal-based [95% Conf.	Interval]
Interorstd2						
Intervention	1.014601	82.1538	0.01	0.990	-160.0039	162.0331
Crpbaseval	-3.819436	3.346956	-1.14	0.254	-10.37935	2.740478
Ferbaseval	-.2628972	.5225023	-0.50	0.615	-1.286983	.7611886
Tsatbaseval	-5.584677	6.600058	-0.85	0.397	-18.52055	7.351198
Gfrbaseval	2.141872	1.985903	1.08	0.281	-1.750426	6.034171
_cons	714.1721	214.8705	3.32	0.001	293.0336	1135.311

6.13 Secondary outcome 6: Acute kidney injury

Logistic regression — Number of obs = 156; LR chi2(5) = 7.72; Prob > chi2 = 0.1724; Log likelihood = -76.634537; Pseudo R2 = 0.0479

Rifleyn2	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2						
Intervention	.8096153	.3315663	-0.52	0.606	.3628118	1.806658
Crpbaseval	1.010422	.0184335	0.57	0.570	.9749316	1.047205
Ferbaseval	1.002965	.0030089	0.99	0.324	.9970849	1.00888
Tsatbaseval	1.018581	.0352975	0.53	0.595	.9516968	1.090167
Gfrbaseval	.9781789	.0097255	-2.22	0.026	.9593018	.9974275
_cons	.9592611	.935405	-0.04	0.966	.1418744	6.48589

Note: _cons estimates baseline odds.

6.14 Secondary outcome 10: Length of hospital stay

Cox regression -- Breslow method for ties

No. of subjects = 156; No. of failures = 156; Time at risk = 1678; Number of obs = 156; LR chi2(5) = 8.68; Log likelihood = -643.66486; Prob > chi2 = 0.1225

_t	Haz. Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Interorstd2	.9310536	.1550416	-0.43	0.668	.6717849	1.290384
Crpbaseval	1.003985	.0087047	0.46	0.646	.987068	1.021191
Ferbaseval	1.001025	.0013326	0.77	0.442	.9984165	1.00364
Tsatbaseval	.9982237	.0137088	-0.13	0.897	.9717133	1.025457
Gfrbaseval	1.009607	.0035203	2.74	0.006	1.00273	1.01653

7. References

Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR (1996) A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 49:1373-9.