Non-Anemic Iron deficiency

Fatigue/Decreased exercise capacity

Decreased cognitive function

PICA
When what you crave is not fit for human consumption

Restless leg syndrome

Panel A: Proportion of donors with absent iron stores (AIS)
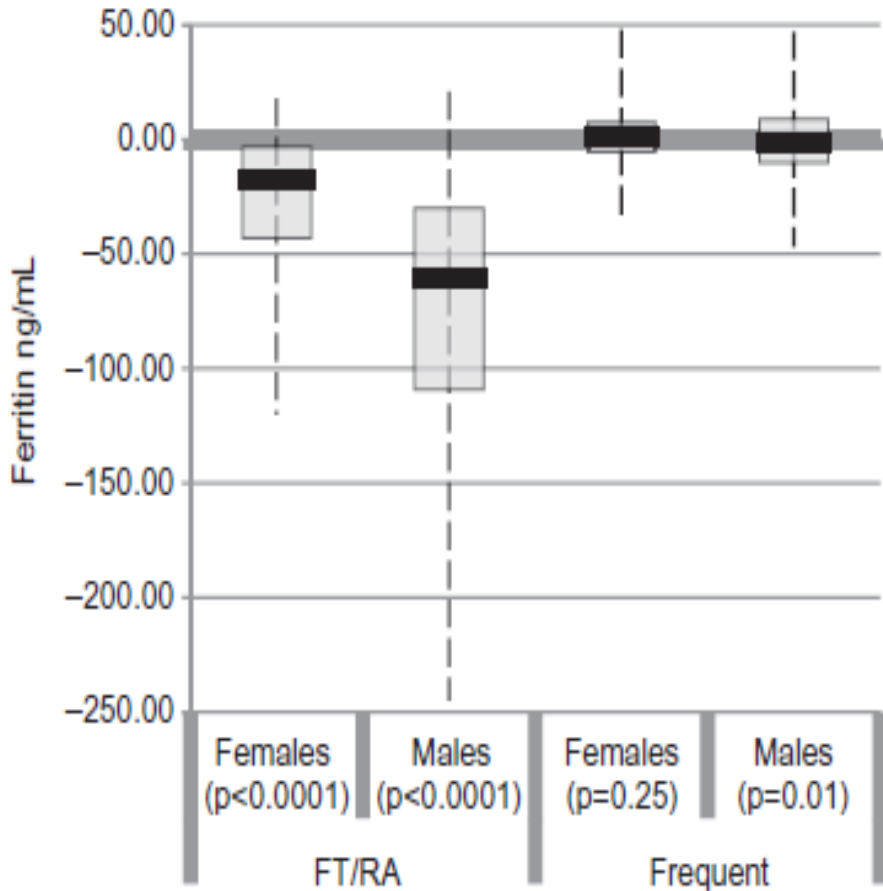
1659 donors at enrollment
1002 donors at final
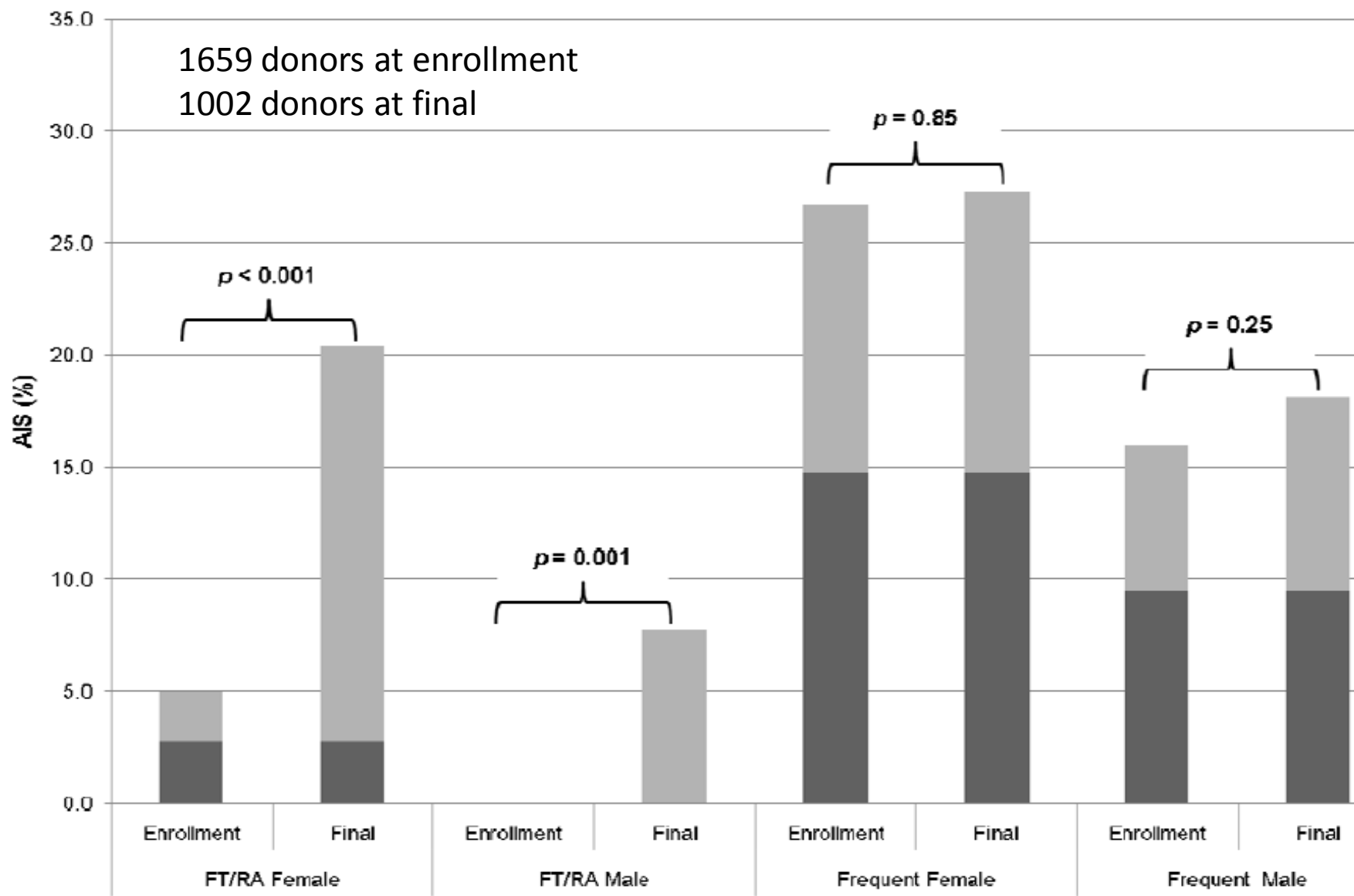
Cable, Transf. 2011

Legend:
- Donors with AIS at both visits
- Donors with AIS at that given visit (enrollment or final but not both)
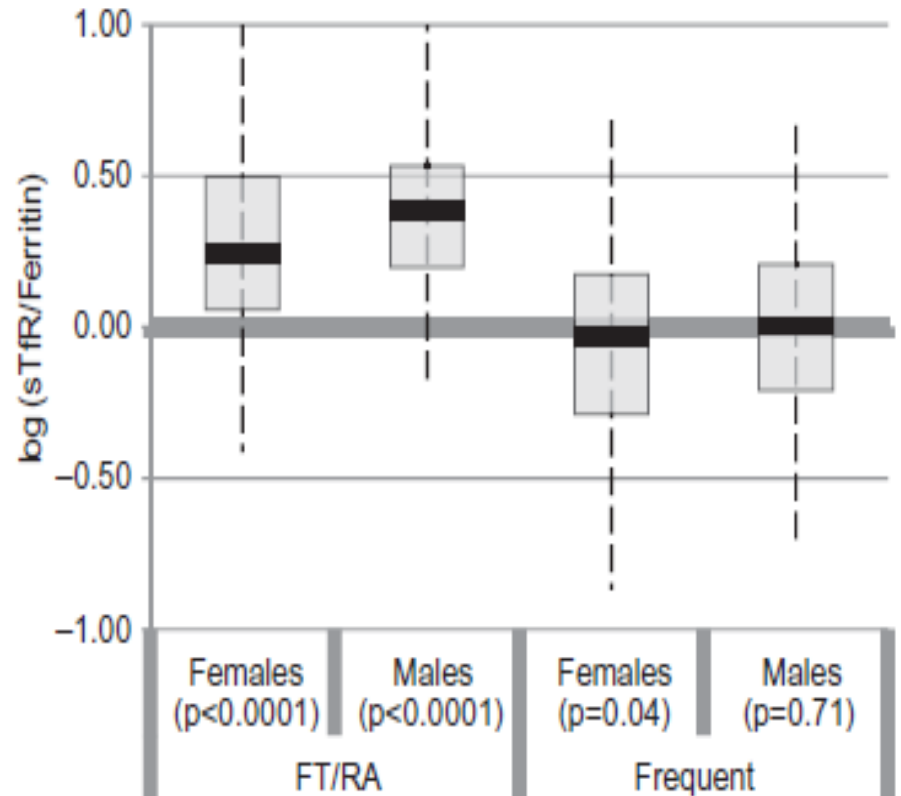
1659 donors at enrollment
1002 donors at final

A. Ferritin differential (final visit – enrollment visit)

B. Log (sTfR/Ferritin) differential (final visit – enrollment visit)

Kiss, Transf, online early

Blood Systems

Methods

- Male donors with Hb between **12.5-13.4 g/dL** and female donors with Hb between **12.5-12.9 g/dL** were screened for ferritin.

- (Low ferritin) Males with ferritin <30 mcg/L and females with ferritin <20 mcg/L were notified, requested to comply with a 24-week deferral from any red blood cell (RBC) donation, and advised to increase their iron intake.

- Absent iron stores is defined as ferritin <12 mcg/L in male and female donors

- We determined the low ferritin (LF) rates in this group by:
  - Donation type,
  - RBC donations in the prior 6 months and also prior 2 years
  - Apheresis platelets/plasma (PP) donations in prior 2 years
  - ABO/Rh blood type and by race/ethnicity.
  - Age

- Separate multivariable logistic regression analyses (MVA) for male and female donors were fitted to identify factors associated with LF.

Blood Systems

Results

Summary of 4 months data on ferritin testing

	Male		Female		Total	
	N	%	N	%	N	%
Allogeneic donations	120208		106262		226470	
Donations tested	7064	6%	16658	16%	23722	10%
Low ferritin	3789	3%, 54%	8798	8%, 53%	12587	6%, 53%
Absent iron stores	1829	2%, 26%, 48%	5210	5%, 31%, 59%	7039	3%, 30%, 56%

Blood Systems

Number and Proportion of Tested Donations (for Ferritin) associated with Low Ferritin

WB, 2RBC, Multi component	Male		Female	
	Low Ferritin (<30)		Low Ferritin (<20)	
	N	%	N	%
RBC Donations Prior 2 years				
0	311	24	1365	33
1-3	807	39	3713	52
4-5	730	61	1830	68
6-9	1440	76	1669	69
10+	501	82	221	72
Platelets/Plasma donations prior 2 years				
0	2898	50	8147	52
1-3	176	56	265	60
4-5	57	66	68	55
6-9	117	63	73	53
10-13	76	63	64	63
=>14	465	76	181	56

Blood Systems

Number and Proportion of Low Ferritin Donations in Ferritin Tested Donations

| Donations in the past 2 years	Male		Female	
	Low Ferritin (<30)		Low Ferritin (<20)	
PP donations in prior 2 years, no prior RBC donations	N	%	N	%
0	115	12	1,195	32
1-3	2	9	13	28
4-5	0	0	8	38
6-9	8	27	11	35
10-13	8	35	23	49
=>14	178	72	115	57
Total	311	24	1,365	33
RBC donations in prior 2 years, no prior PP donations	N	%	N	%
0	115	12	1,195	32
1-3	492	32	3,474	52
4-5	561	58	1,708	68
6-9	1,267	76	1,556	69
10+	463	81	214	71
Total	2,898	50	8,147	52

Factors associated with low ferritin (<20 mcg/L) in donations from FEMALE donors compared to all allogeneic donations from females, 4 months data
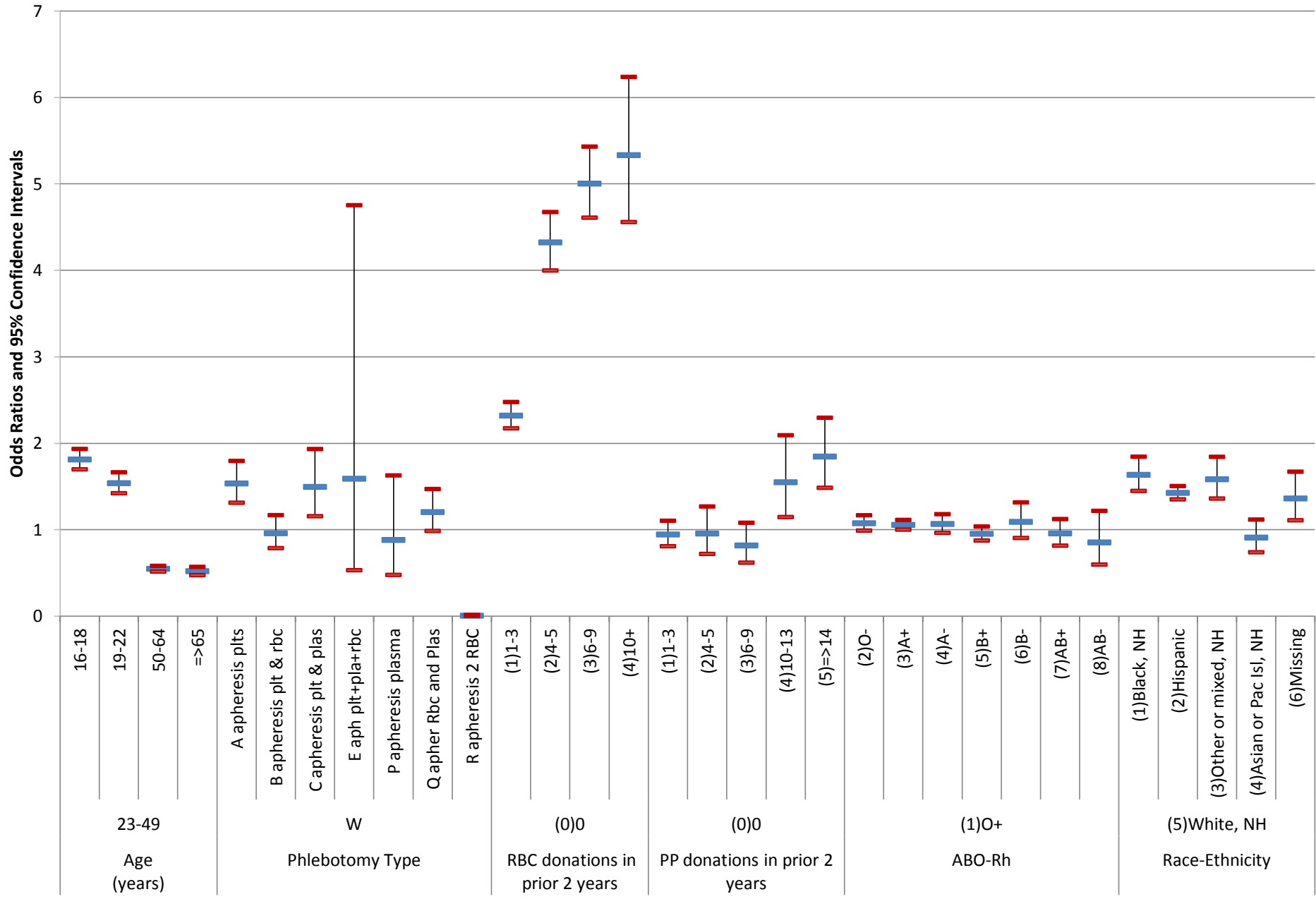
Factors associated with low ferritin (<30 mcg/L) in donations from MALE donors compared to all allogeneic donations from males, 4 months data
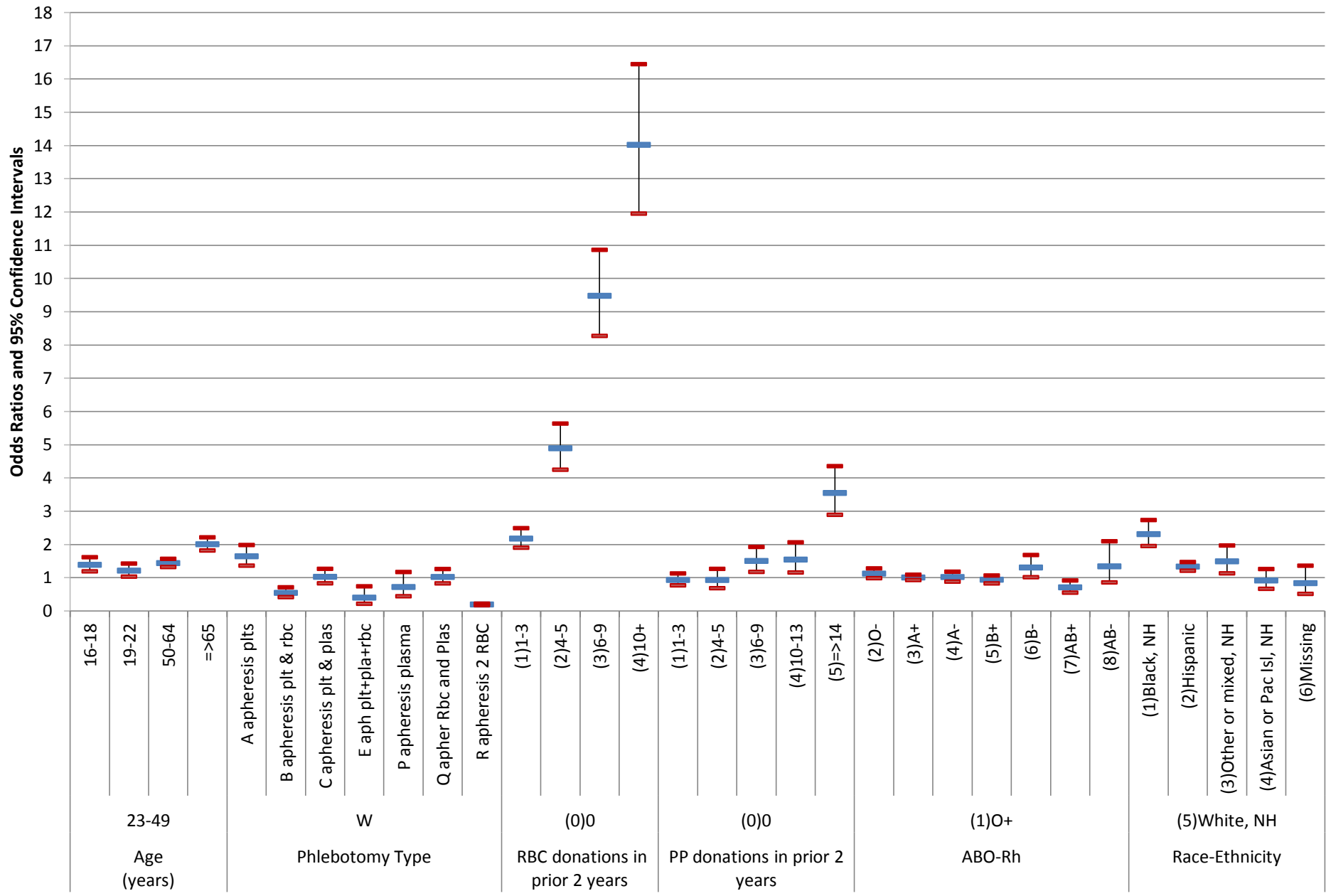
Summary of factors associated with low ferritin, 4 month analysis

Donor and Donation Characteristics	MALES	FEMALES
Age (compared to 23-49 yo)	**Increased:** Younger and older donors ≥ 65 had the highest OR in males	**Increased:** Younger donors **Decreased:** Older donors
Phlebotomy Type (compared to WB donations)	**Slightly increased :** Platelet donations **Decreased:** 2 RBC and platelet + RBC donations	**Slightly increased :** Platelet and platelet + plasma donations **Decreased:** 2 RBC donations
RBC donation in prior 2 years	**Increased:** The higher # of donations, the higher OR	**Increased:** The higher # of donations, the higher OR
PP donations in prior 2 years	**Slightly increased:** ≥ 6 PP donations	**Slightly increased:** ≥ 10 PP donations
ABORh	**Very slightly increased for Group B Rh neg**	Not significant
Race/Ethnicity (compared to white NH)	**Increased:** Black, NH, Hispanic, Other, mixed, NH	**Increased:** Black, NH, Hispanic, Other, mixed, NH

Conclusions

- More than half the males with Hb 12.5- 13.4 and females with hgb 12.5-12.9 were identified as having Low Ferritin.

- Strong associations with prior RBC donations.

- The degree of association in male and female donors appears different and may reflect underlying differences in iron homeostasis by gender in addition to the Hb subgroup eligible for ferritin testing (men may be anemic).

Hemoglobin Recovery - Methods

Data

- Between August 1, 2009 to July 31, 2012.
- First-time allogeneic donors
- Successful RBC-containing donation
- Presented to donate at least one more time
- HH donors or for therapeutic donations were excluded

Variables

- Time-interval to subsequent presentation (interdonation interval),
- Delta Hemoglobin - (Hb at 2nd presentation minus Hb at first donation)
- Hemoglobin recovery – Delta Hb of 0 or more g/dL.
- We performed separate analyses based on the donation type at initial presentation: WB 2RBC

Blood Systems

# Hemoglobin recovery proportion and median recovery time by gender and donation type

	WB		2RBC		Multi-Component		All First-time Donors
	Male	Female	Male	Female	Male	Female	
Total Donors (N)	47,936	64,097	19,362	2,403	726	516	135,040
Donors who recovered (n)	23,654 (49)	25,833 (40)	8,764 (45)	750 (31)	358 (49)	177 (34)	59,536 (44)
Donors who were deferred* (n)	163 (0.3)	6,421 (10)	47 (0.2)	183 (8)	3 (0.4)	60 (12)	6915 (5)
Median recovery time (days)	140	151	184	193.5	123.5	142	154
	147		184		128		
Median recovery time (weeks)	20	22	26	28	18	20	22
	20		26		18		

Blood Systems

# Delta Hemoglobin and Interdonation Interval –
Mean and 95% Confidence Intervals of Delta Hemoglobin by Interdonation Interval and Sex in WB and 2RBC donations

Delta Hb after successful RBC donation

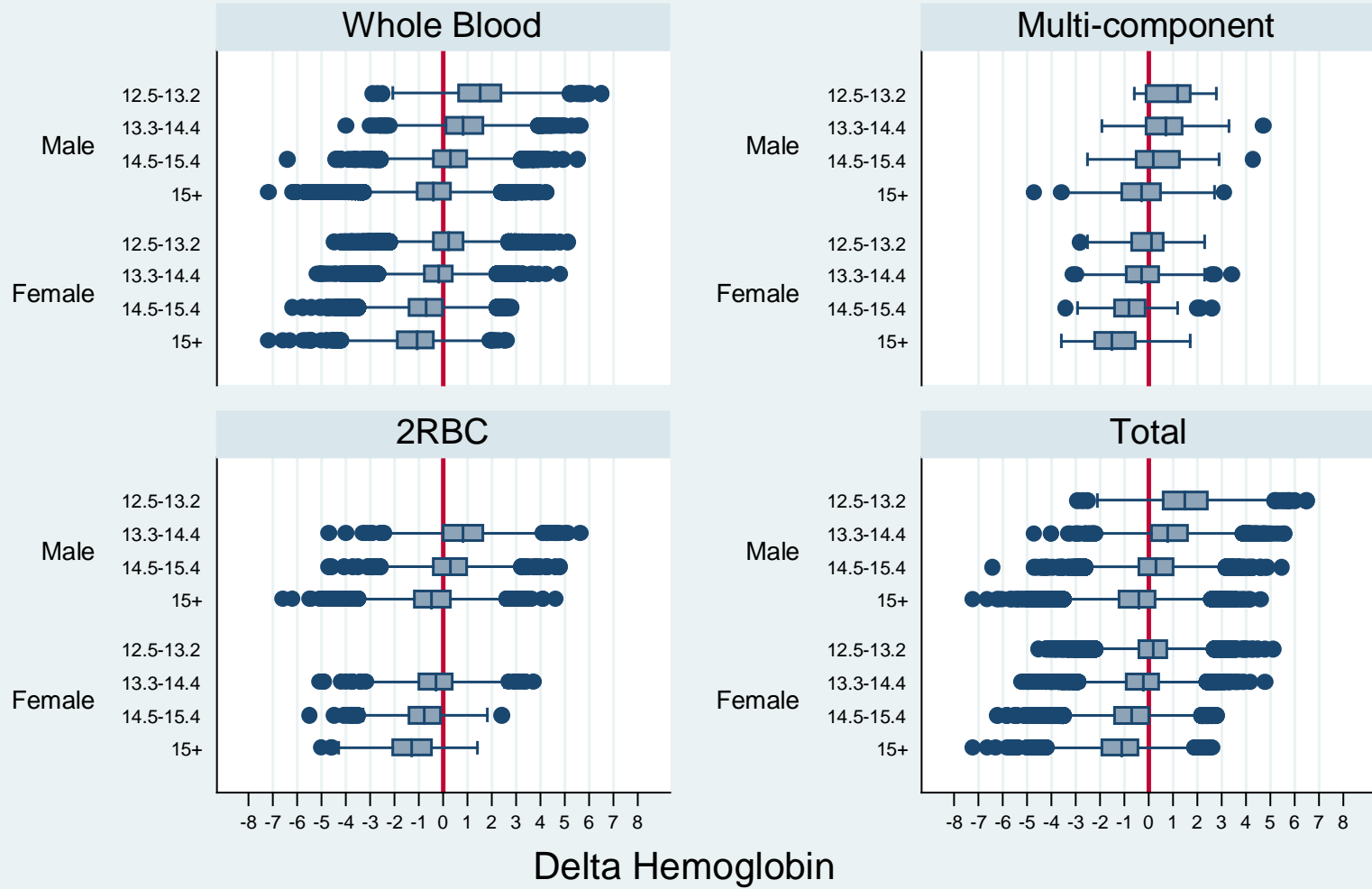BSI data - August 2009 to July 2012
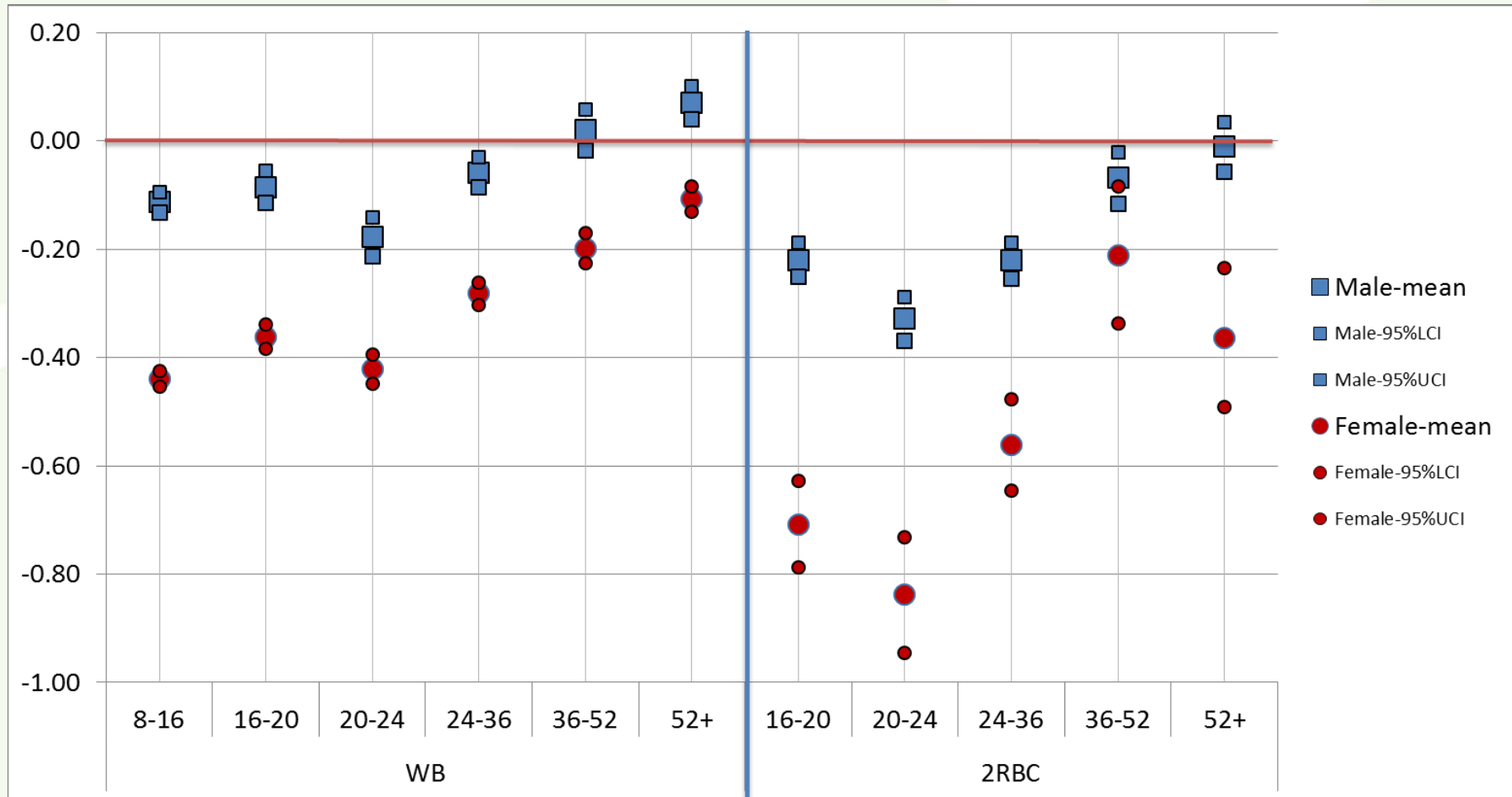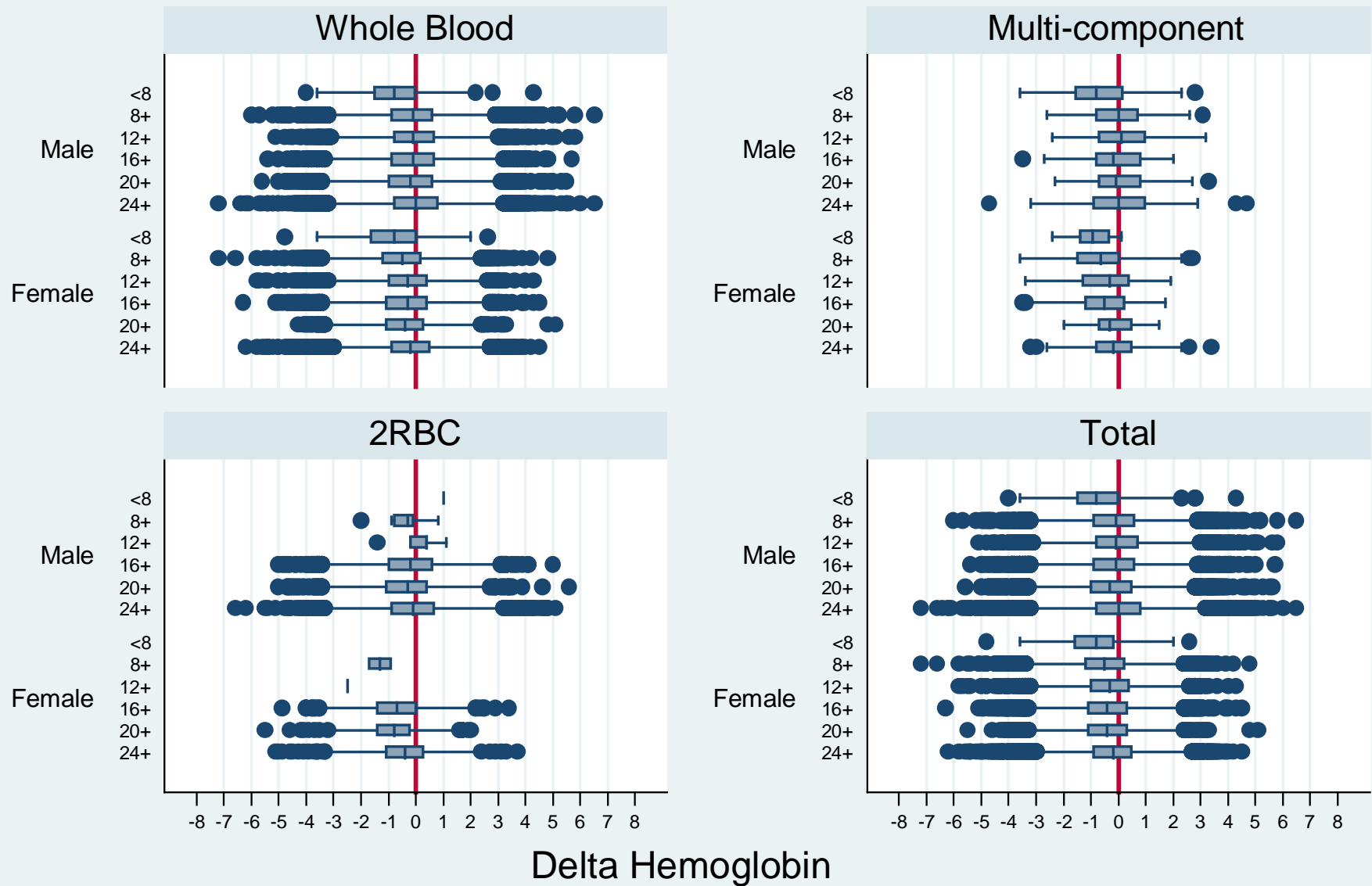
Delta Hemoglobin and Index Hemoglobin values -
Mean and 95% Confidence Intervals of Delta Hemoglobin by Index Hemoglobin and Gender, WB and 2RBC donations
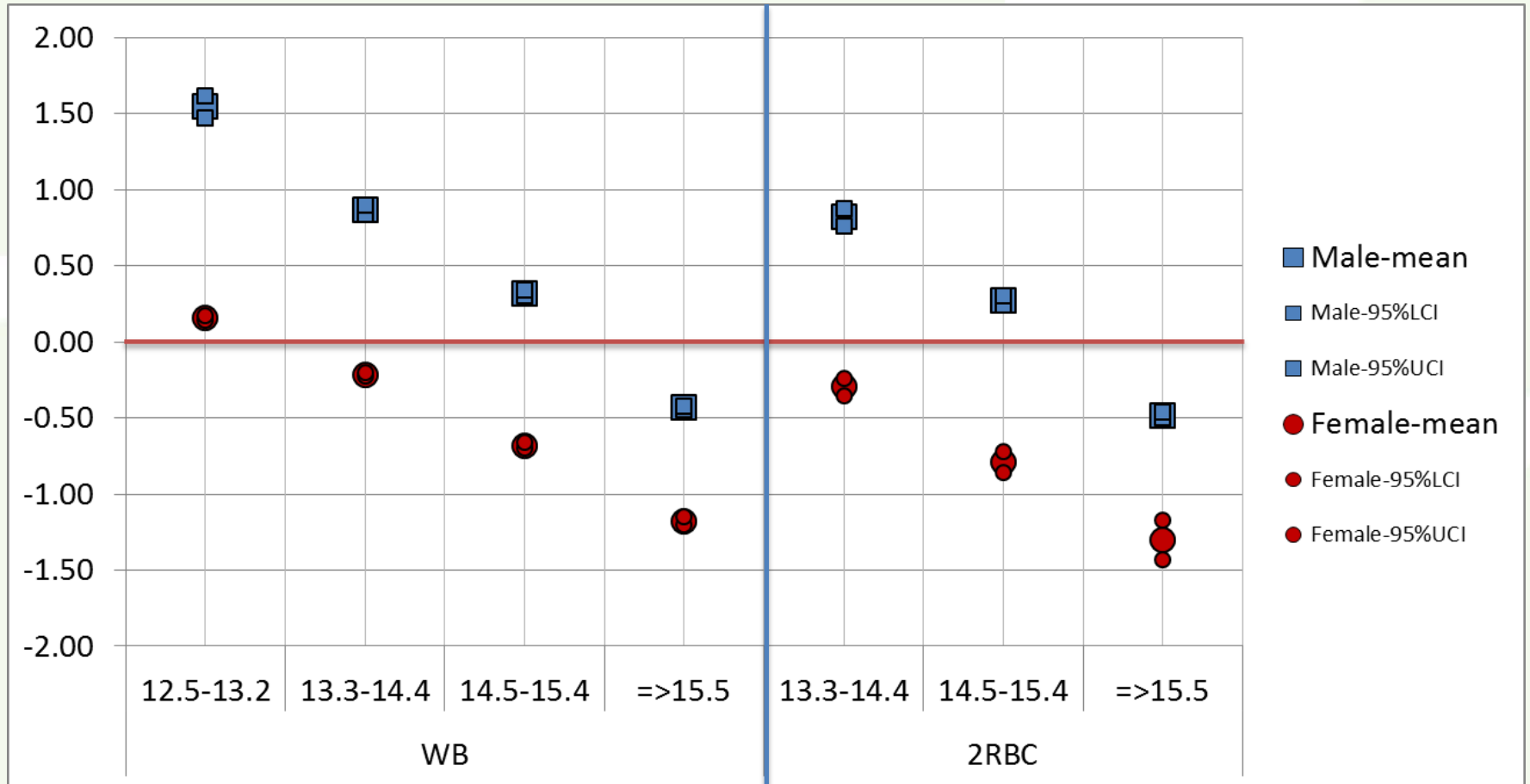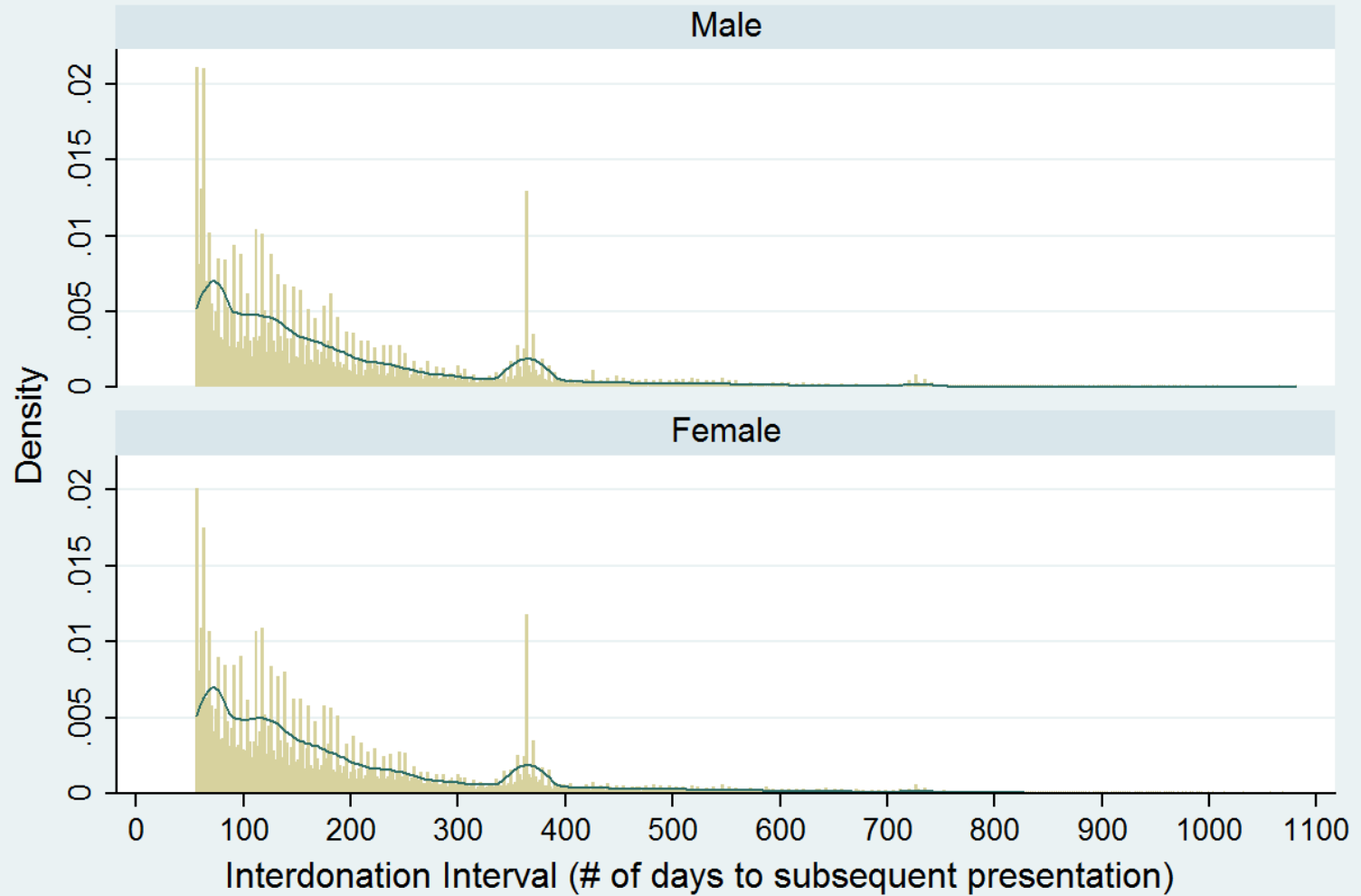
By index Hb group

Delta Hb after successful RBC donation

BSI data - August 2009 to July 2012

Donation Interval in First-time Donors, Male and Female with WB Index Donation

Hb recovery - FT donors with succ. WB donation

MALES: M12.5-13.2, M13.3-14.4, M14.5-15.4, M=>15.5

BSI data August 2009 to July 2012

Blood Systems

Hb recovery - FT donors with succ. WB donation

FEMALES

F12.5-13.2 · F13.3-14.4 · F14.5-15.4 · F=>15.5

BSI data August 2009 to July 2012

Blood Systems

Donation Interval in First-time Donors, Male and Female with 2RBC Index Donation
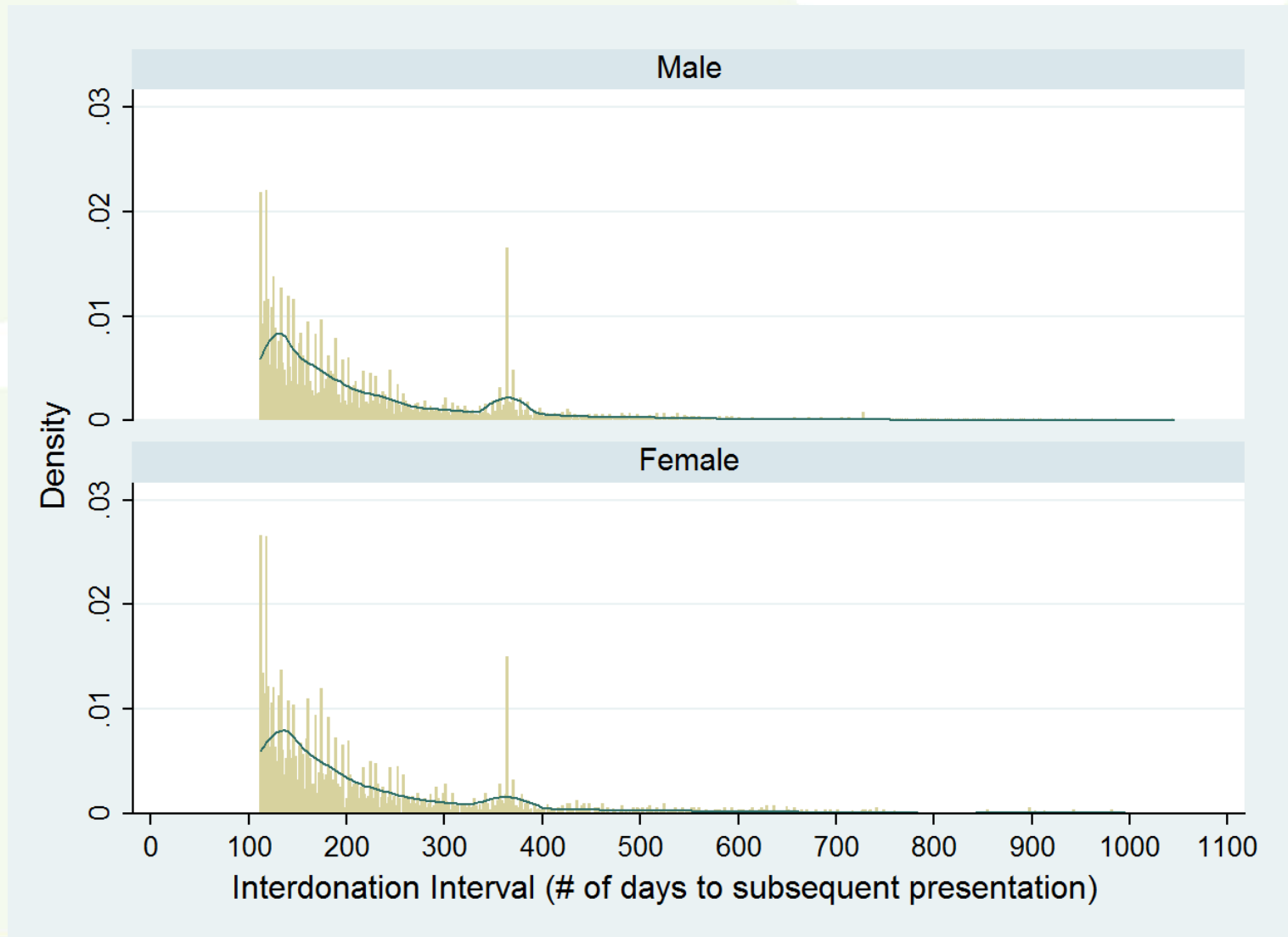
Time to recovery Kaplan-Meier graphs
by Index Hb and Sex in 2RBC Index Donation
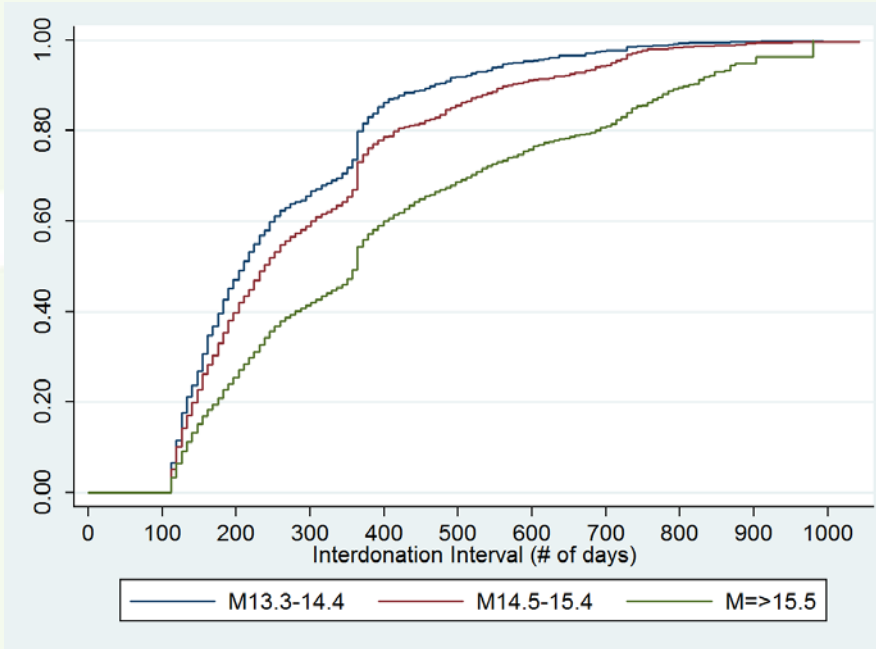
MALES
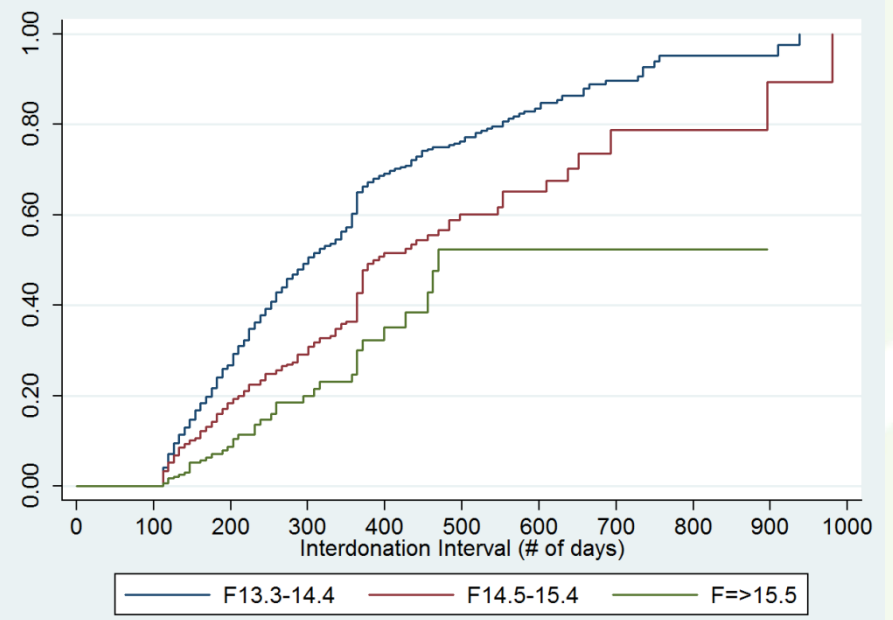
FEMALES

Interdonation interval (by index hemoglobin group) for first-time donors (recovered - yes or no) with a subsequent donation **after successful WB donation**

Index Hb Group	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	12.5-13.4		13.5-14.4		14.5-15.4		=>15.5		12.5-13.4		13.5-14.4		14.5-15.4		=>15.5	
Sex	Male								Female							
Mean	181	164	189	172	187	176	189	174	195	166	195	170	193	174	191	171
Lower 95 % CI	174	146	184	164	183	172	186	172	192	163	192	168	189	171	181	167
Upper 95 % CI	188	183	193	180	190	181	191	176	198	169	198	172	198	176	201	174

Interdonation interval (by index hemoglobin group) for first-time donors (recovered - yes or no) with a subsequent donation **after successful 2RBC donation**

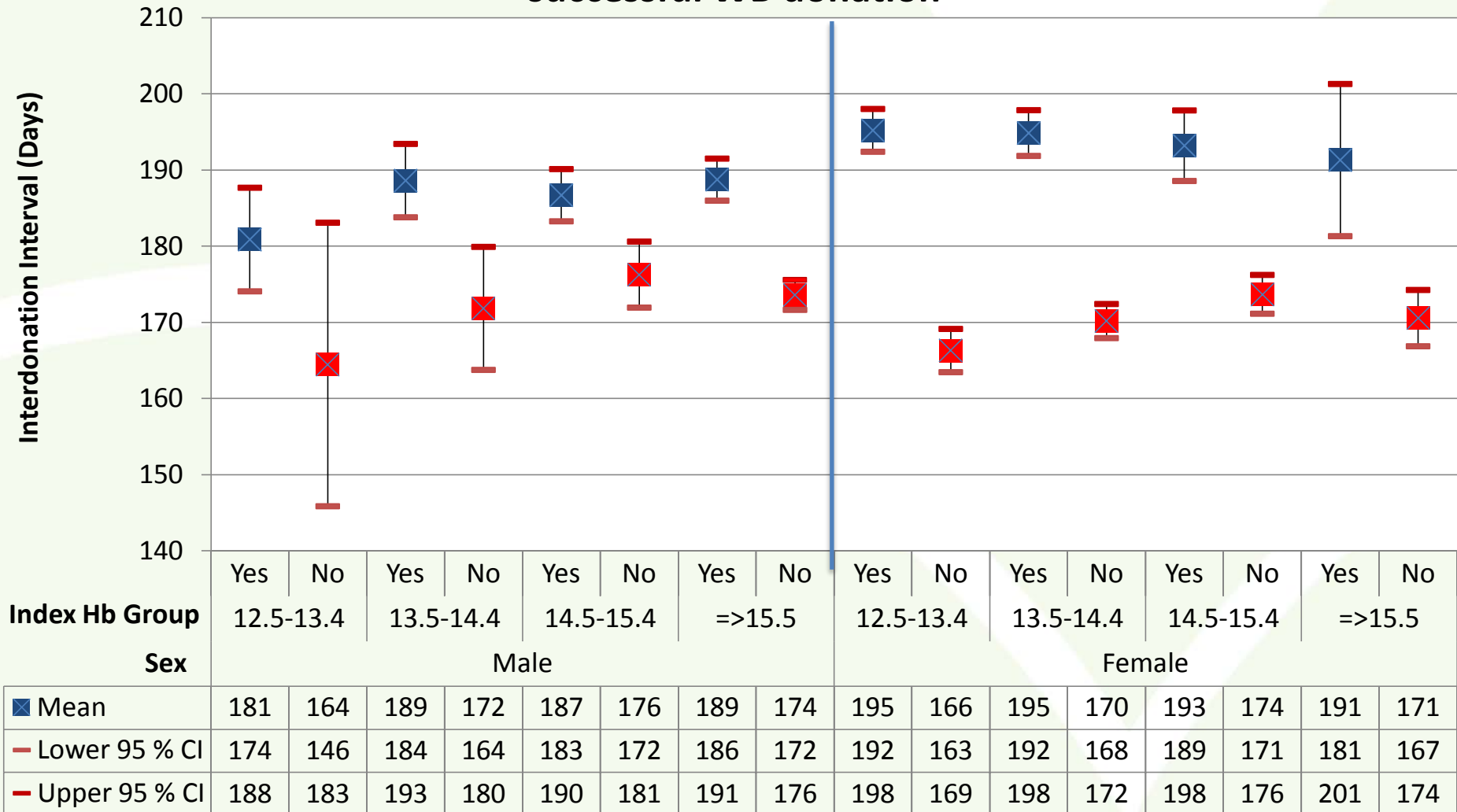| Index Hb Group	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	12.5-13.4		13.5-14.4		14.5-15.4		=>15.5		12.5-13.4		13.5-14.4		14.5-15.4		=>15.5	
Sex	Male								Female							
Mean	223	219	226	205	227	210	224	208	220	202	232	194	226	202	249	188
Lower 95% CI	202	177	219	195	222	204	220	206	197	181	219	186	207	193	210	176
Upper 95 % CI	243	262	233	215	232	215	228	211	243	223	246	202	245	212	289	200

Blood Systems
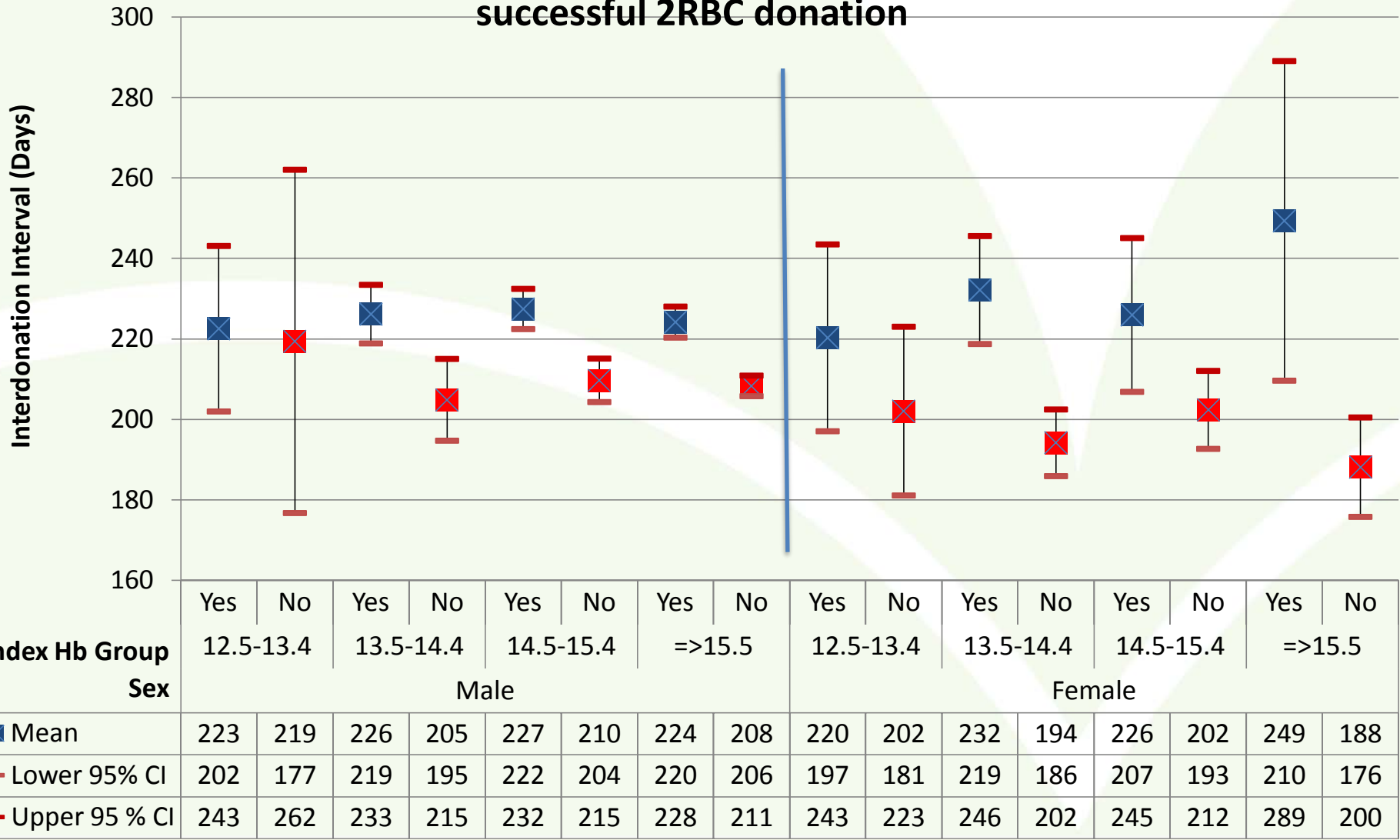
Comparison of median interdonation interval of those who recovered (green) vs. those who did not recover (red) in WB donors
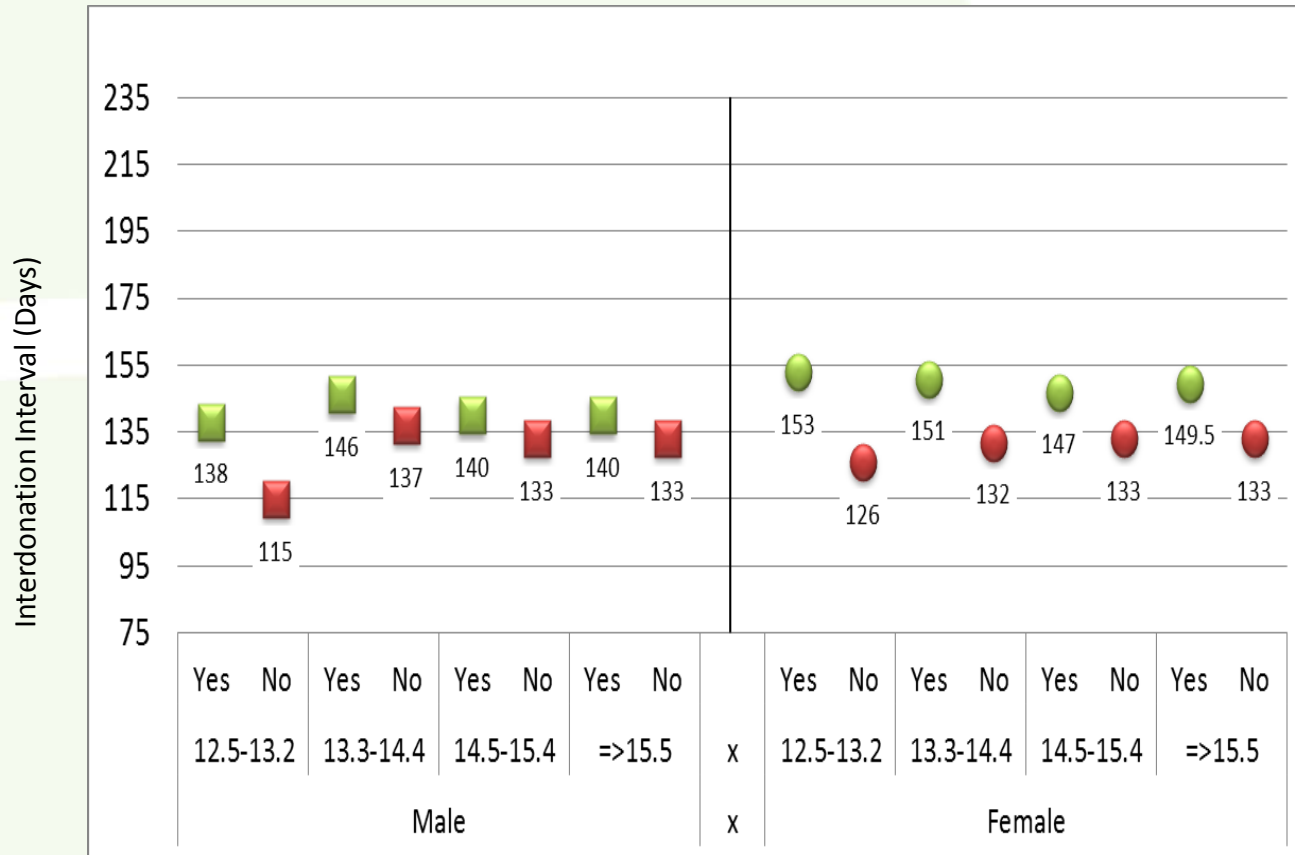
Donors who did not recover had shorter median interdonation interval compared to those who recovered.

Comparative logistic regression analysis on factors of hemoglobin deferral and recovery among first-time donors with a subsequent presentation **after a successful WB donation**

Donor and Donation Characteristics		Deferral	Recovery
Reference Group	Factors	After successful WB donation	
Index Hgb:'=>15	12.5-13.2	16.3 (13.2-20.3)	15.5 (14.6-16.5)
	13.3-14.4	5.7 (4.6-7.1)	7 (6.7-7.4)
	14.5-15.4	2 (1.6-2.5)	3.1 (3-3.2)
Sex: Female	Male	0.1 (0.1-0.1)	4.8 (4.5-5.1)
Interdonation interval: 24-36	<8		
	8-16	1.6 (1.4-1.7)	0.8 (0.8-0.8)
	16-20	1.2 (1.1-1.3)	0.9 (0.9-0.94)
	20-24	1.2 (1.1-1.4)	0.9 (0.8-0.9)
	36-52	0.9 (0.8-0.93)	1.2 (1.2-1.3)
	52+	0.8 (0.7-0.9)	1.4 (1.3-1.5)
Ethnicity: Hispanic	Non-Hispanic	0.7 (0.6-0.8)	0.9 (0.8-0.9)
Race: White	Black-AA	2.2 (2-2.4)	0.8 (0.7-0.91)
	Native Indian-Alaskan	1.8 (1.5-2.1)	1 (0.9-1.1)
	Asian-Pacific Islander	1.2 (0.93-1.4)	1.1 (0.95-1.3)
	Other	1.1 (0.93-1.2)	1.2 (1.1-1.2)
Age: 23-49	16-18	1.2 (1.1-1.3)	1.2 (1.1-1.2)
	19-22	1.2 (1.1-1.3)	1 (0.9-1)
	50-64	0.8 (0.7-0.9)	1 (1-1)
	=>65	1.1 (0.9-1.3)	1.1 (1.1-1.2)

Blood Systems

Comparative logistic regression analysis on factors of hemoglobin deferral and recovery among first-time donors with a subsequent presentation **after a successful WB donation**

Donor and Donation Characteristics		Deferral	Recovery
Reference Group	Factors	After successful WB donation	
Index Hgb:'=>15	12.5-13.2	16.3 (13.2-20.3)	15.5 (14.6-16.5)
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	Native Indian-Alaskan	1.8 (1.5-2.1)	1 (0.9-1.1)
	Asian-Pacific Islander	1.2 (0.93-1.4)	1.1 (0.95-1.3)
	Other	1.1 (0.93-1.2)	1.2 (1.1-1.2)
Age: 23-49	16-18	1.2 (1.1-1.3)	1.2 (1.1-1.2)
	19-22	1.2 (1.1-1.3)	1 (0.9-1)
	50-64	0.8 (0.7-0.9)	1 (1-1)
	=>65	1.1 (0.9-1.3)	1.1 (1.1-1.2)
BMI:<18.5	18.5-22.49	0.9 (0.7-1.1)	1 (1-1.2)
	22.5-24.99	0.8 (0.6-1)	1.1 (1-1.2)
	25-29.99	0.7 (0.6-0.9)	1.1 (1-1.2)
	30-39	0.8 (0.6-1)	1 (0.9-1.2)
	=>40	0.9 (0.7-1.2)	0.9 (0.8-0.94)

Blood Systems

Summary (Preliminary)

- A history of multiple donations is associated with iron deficiency

- Young women and young and old men at risk

- Donors with low hgb recover hgb faster than donors with high hgb (recovery time ~ 20 weeks)

- Donors with low hgb sometimes overshoot and those with high hgb sometimes don't return to index level

- The combination of donor iron status and donor behavior suggests individual donor management

Blood Systems

Summary (Preliminary)

- Need more information on clinical significance of non-anemic iron deficiency

- Need more information on donor iron metabolism
  - Factors influencing absorption
  - Variations in absorption
  - Effective acceptable supplemental therapy
  - Will ferritin recovery data look like hemoglobin recovery data?

- Need more information on detecting donors at risk
  - Screening tests
  - Batch testing
  - Less expensive testing
  - Correct levels for action

Blood Systems