



Plasma Donation in the United States: Scientific Review

Marilyn Rosa-Bray, MD
Chief Medical Officer - Grifols

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Introduction

- Just as patient's health and safety, donor health is a top priority for the plasma collection industry.
 - Globally, the industry has collected over 130,000,000 plasma donations over the past 5 years with an extraordinary safety record.
- Donor Health & Safety is addressed by:
 - Selection/Monitoring per FDA and EU Blood Directive, requirements of other countries (depending on where the final is product used)
 - Annual physical exam
 - BP / pulse / temperature / total protein / hematocrit / weight on each donation
 - Consultations with personal healthcare provider as needed
 - PPTA Voluntary Standards;
 - International Quality Plasma Program (IQPP) certification
 - Hemovigilance;

Prospective multicentre study of the effect of voluntary plasmapheresis on plasma cholesterol levels in donors

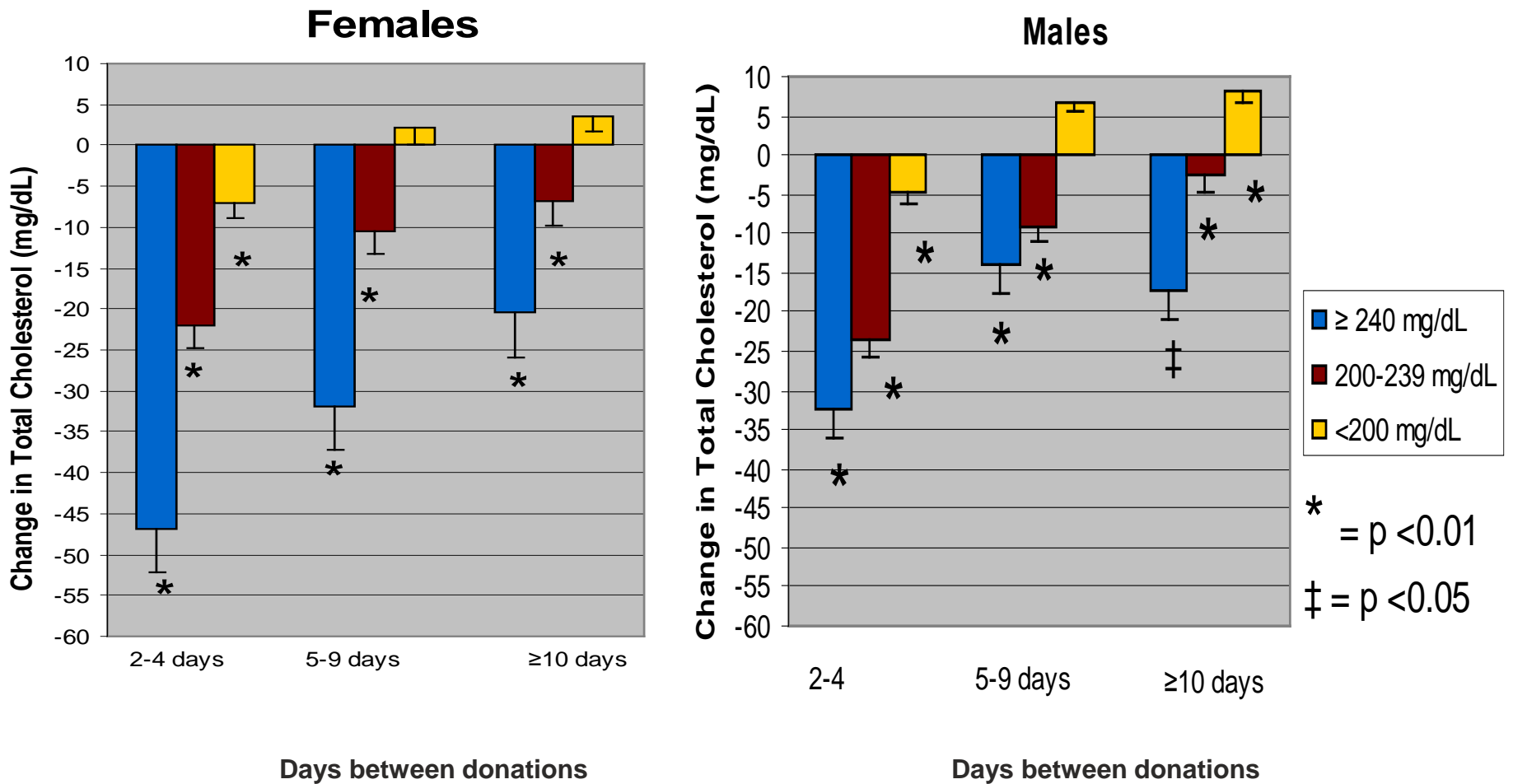
Rosa-Bray M, Wisdom C, Wada S, et. al. *Vox Sanguinis* (2013): Vol 105(2) pp 108-115;

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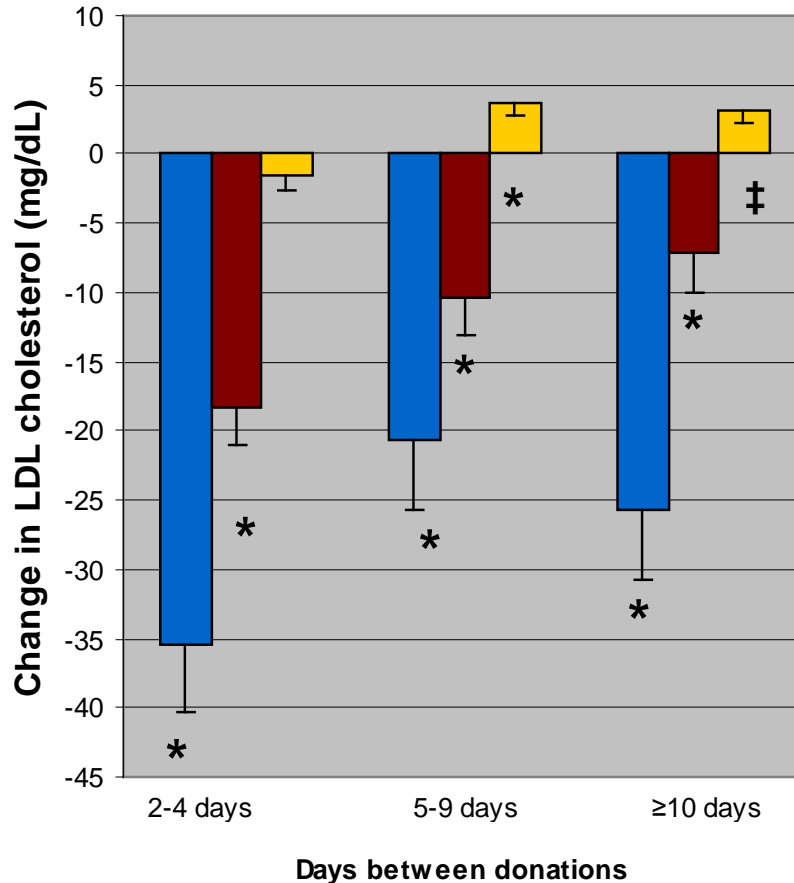
- United States; prospective, longitudinal study
- 663 new donors (9, 153 donations), followed up for 16 weeks
 - Both genders included; diverse race and weight representation
 - Ages 18-69
- Tests:
 - total cholesterol, direct LDL, HDL
 - Hematocrit, total protein, blood pressure, pulse, weight
 - adverse events and deferrals

Effect of Plasmapheresis in Total Cholesterol (mg/dL) in Female and Male Donors

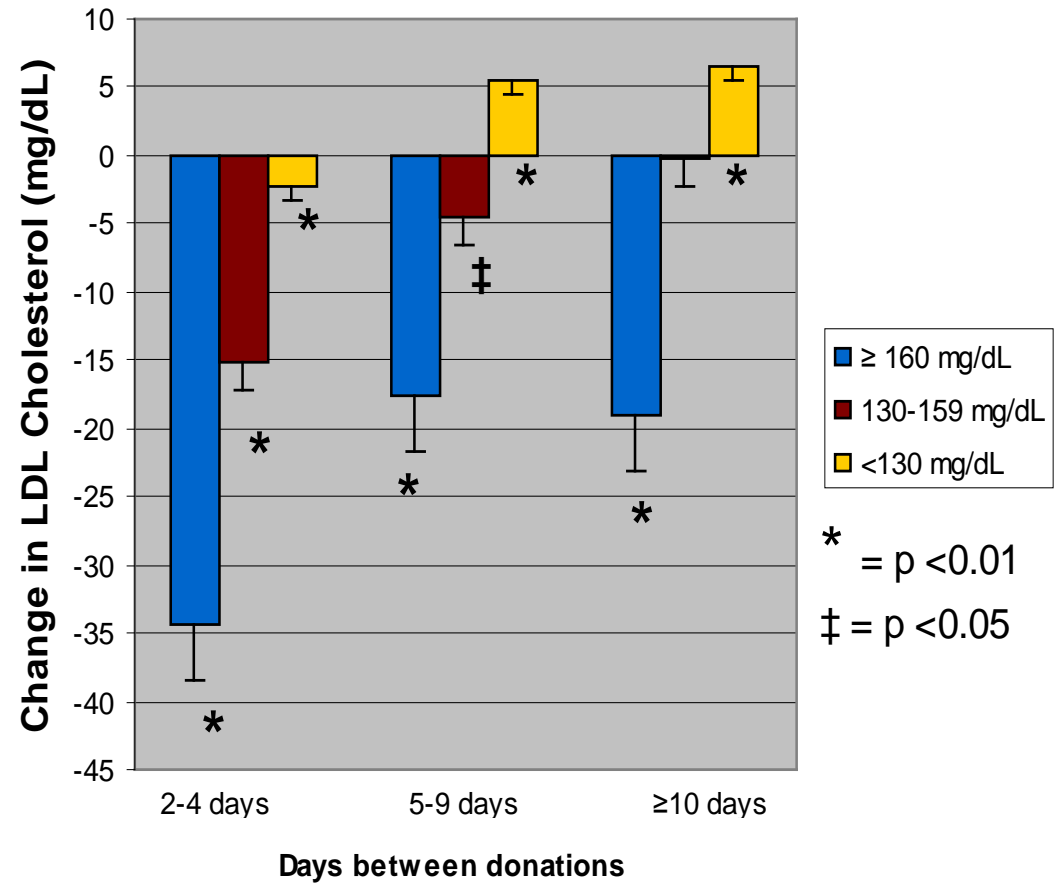


Effect of Plasmapheresis in LDL (mg/dL) in Female and Male Donors

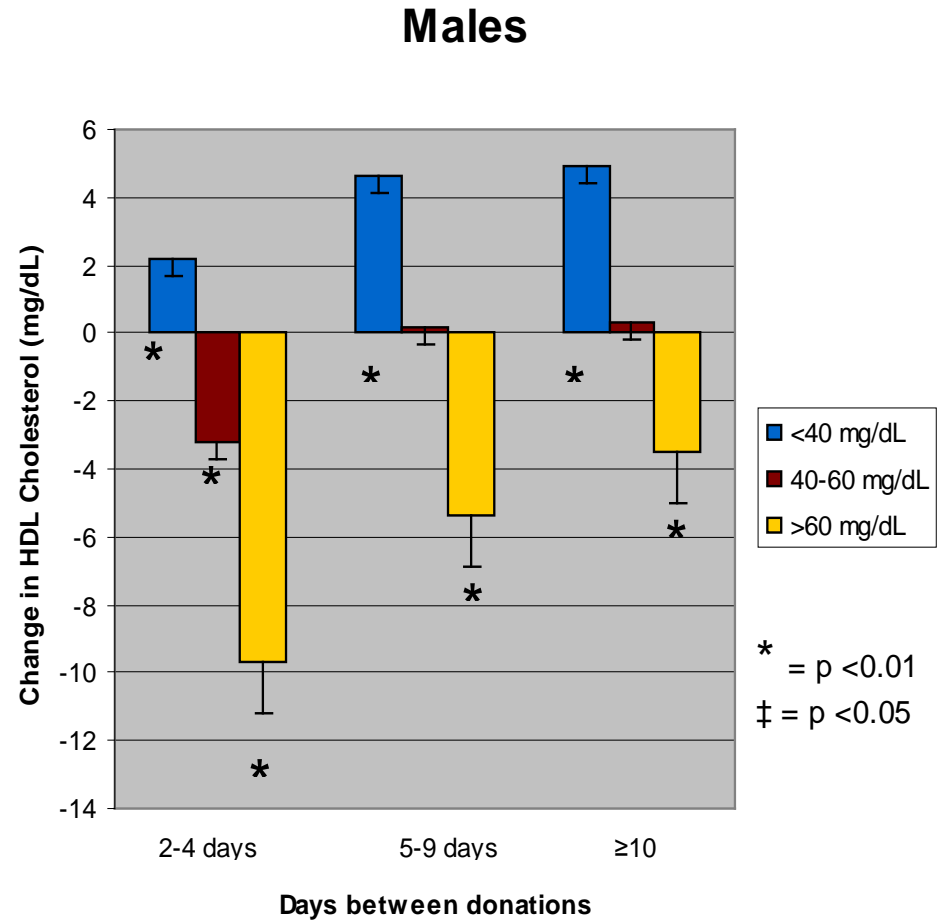
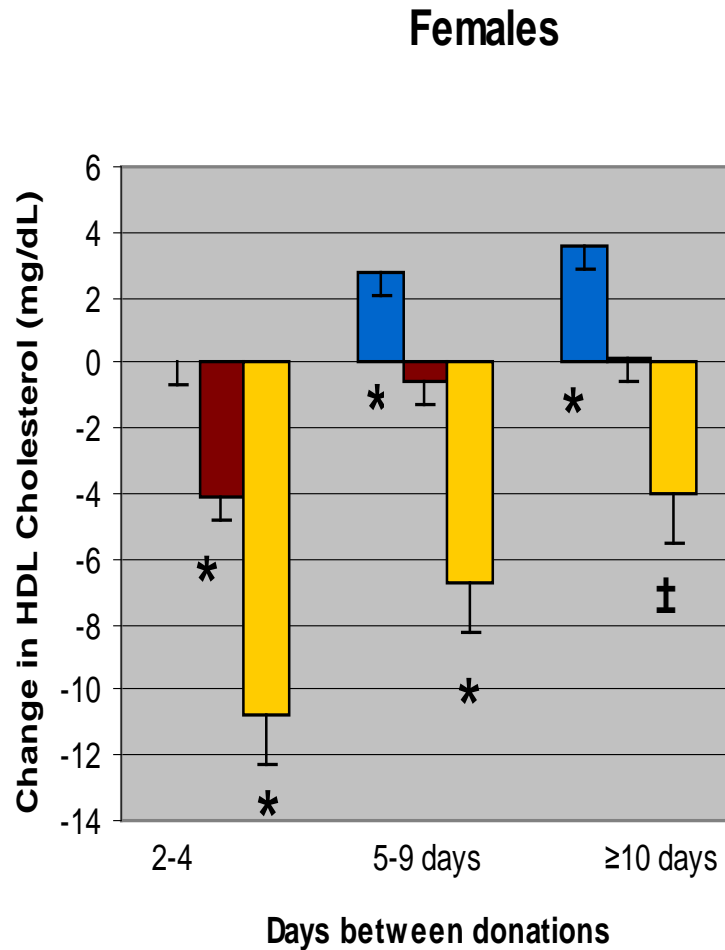
Females



Males



Effect of Plasmapheresis in HDL (mg/dL) in Female and Male Donors



Adverse Events

Symptoms	Severity	
	Mild	Moderate
Hematoma	4	0
Dizziness	4	4
Nausea	3	4
Loss of consciousness	3	3
Blurred vision	2	2
Pallor	2	2
Vomiting	1	4
Chest pain (non-cardiac)	0	1

- Adverse events were observed in 0.15% of the donations (14 events/9,135 donations) by 14 donors
- Donors typically present more than one symptom during an adverse event.
- No severe or serious adverse events were reported.
- Deferrals monitored. No correlation between donation frequency and deferrals

Prospective multicentre study of the effect of voluntary plasmapheresis on plasma cholesterol levels in donors

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- Donors with high TC or LDL showed a significant decrease with repeated donations
 - Similar results in both genders but to a greater extent in females
 - Smaller decreases when donation intervals increased
 - Decrease was *not observed if baseline cholesterol was at normal range*
- Small increase in HDL in donors with low HDL and donation interval of ≥ 10 days
- Additional studies would be needed to evaluate the possible clinical implications of these findings.
- No correlation between number of donations and number of deferrals for parameters measured
- Adverse events 0.015% (14 / 9,135 donations); no severe events

The effect of plasmapheresis on blood pressure in voluntary plasma donors

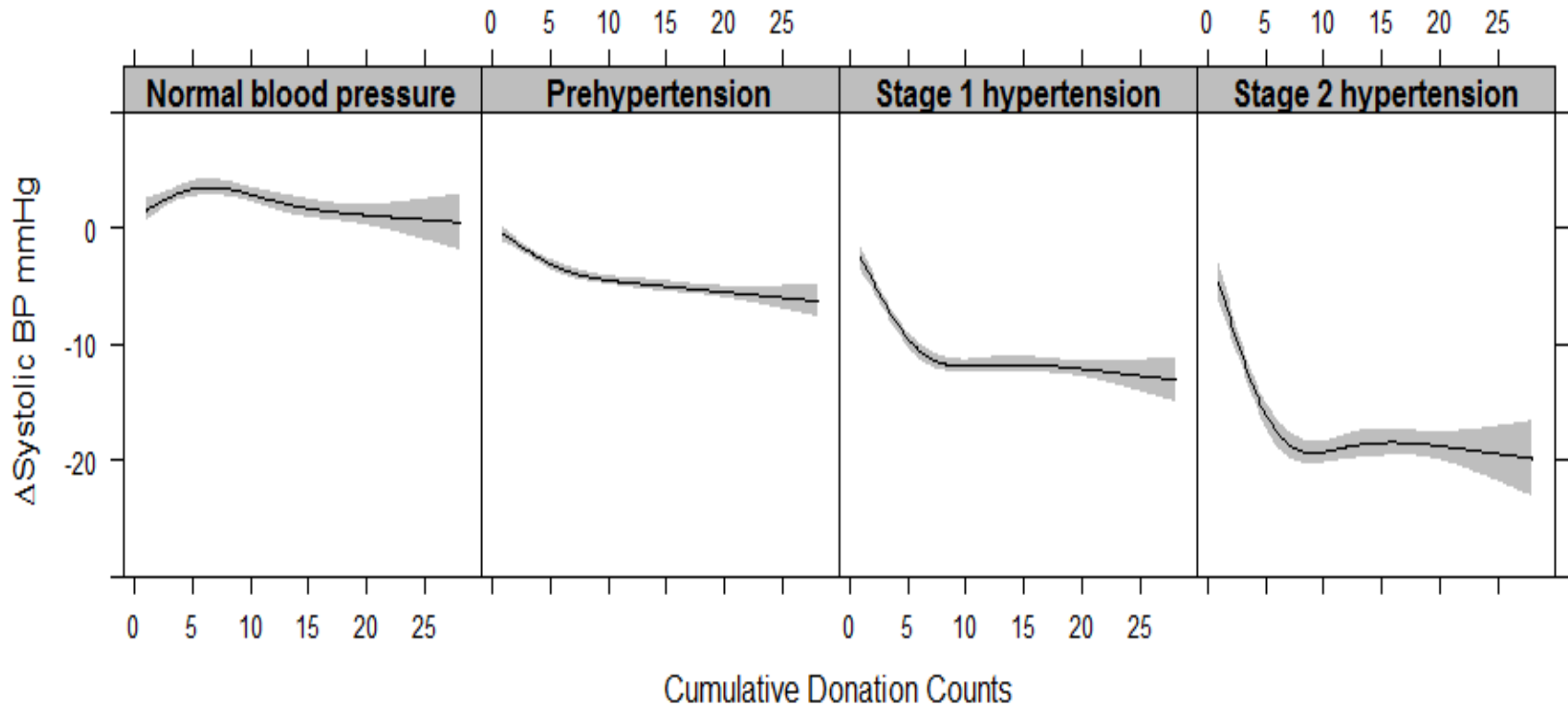
Rosa-Bray M, Wisdom, C, Marier, et. al.; *Vox Sanguinis* (2015), 108(1): 11-17;

The effect of plasmapheresis on blood pressure in voluntary plasma donors

Vox Sanguinis (2015), 108(1): 11-17; Rosa-Bray M, Wisdom, C, Marier, JF, et. al.

- United States; prospective, longitudinal study
- 666 new donors (9, 153 donations), followed up for 16 weeks
 - Both genders included; diverse race and weight representation
 - Ages 18-69
 - Blood pressure, pulse measured prior to donation
 - Digital equipment, with daily calibration; no manual blood pressure measurements

Effect of Donation on Change from Baseline for SBP by Baseline BP Category*



* Rosa-Bray M, et. al. The effect of plasmapheresis on blood pressure in voluntary plasma donors *Vox Sanguinis* (2015), 108(1): 11-17;

The effect of plasmapheresis on blood pressure in voluntary plasma donors

Vox Sanguinis (2015), 108(1): 11-17; Rosa-Bray M, Wisdom, C, Marier, JF, et. al.

- Donors with high blood pressure showed a significant decrease when donating at intervals of less than 14 days
 - Smaller decreases when donation intervals increased
- Decrease in blood pressure was not observed in donors with normal blood pressure or pre-hypertension levels.

Frequent Source Plasma Donors are not at Risk of Iron Depletion: The Ferritin Levels in Plasma Donor Study (FLIPD)

Transfusion, submitted, under review.

Frequent Source Plasma Donors are not at Risk of Iron Depletion: The Ferritin Levels in Plasma Donor Study (FLIPD)

Transfusion, submitted for publication

- United States, cross sectional
- 1254 plasma donors from four (4) groups based on number of donations in the last 12 months;
 - males and females included
- Groups:
 - New donors (no previous donations)
 - 1-24 donations in last 12 months (low frequency)
 - 25-69 donations in last 12 months (high frequency)
 - ≥ 70 donations in last 12 months (very high frequency)
- Tests:
 - ferritin

Frequent Source Plasma Donors are not at Risk of Iron Depletion: The Ferritin Levels in Plasma Donor Study (FLIPD)

Transfusion, submitted for publication

- Iron depletion (low ferritin levels) is not common in plasma donors and is not higher in frequent donors.
- Frequent plasma donation does not adversely impact iron stores
- Absent Iron Stores (ferritin <12 ng/ml),
 - Whole blood donors have higher rates of AIS than plasma donors, for both males and females, even at high frequency donations (WB= > 2donations/yr (F), >3 donations/yr (M); plasma = >25 donations/yr)

Donor Adverse Events

Plasma donor Adverse Events

Unpublished Data (2014)*

- 2014 data analysis:
 - five (5) year data collection of adverse events
 - One (1) year data collection of adverse events + donor demographics (gender, age, weight, hematocrit, nomogram group, donation volume); >15 million donations
- Analysis of rate of AE based on gender, weight, BMI, donation volume
- Results:
 - Donors with lower collection volume had a higher rate of vasovagal events
 - Lower collection volume corresponds with lower weight
 - Females > males
 - First time donors 10-15x higher than repeat donors
 - 5 yr analysis overall rate for VV events is 10.68 per 10,000donations
 - 1 yr analysis overall rate for VV events is 8 per 10,000 donations
 - Differences most likely due to no standard definitions for minor/moderate events

* PPTA data, 2014

Vasovagal Event (VVE) Rates* by Gender and Weight

Weight Group (lbs)	Nomogram Volume (ml) + AC	Female	Male	Total
<150	690	19.90	6.01	13.37
150-174	825	21.34	5.38	10.64
175+	880	16.63	3.72	6.43
TOTAL		16.63	4.30	8.32

*Rate by 10,000 donations

Donor Adverse Event Categorization Standard

(2016)

- New iQPP Standard effective on April 2015 with a 6 month implementation window (Oct 2015)
- Uniform definitions and categorization to capture the granularity of the spectrum of donor adverse events seen in the plasma industry
 - Includes categories for events occurring after the donor leaves the facility
- Pilot data collection corresponding to 4 months (Summer 2016); 5 months after implementation of standard to assess clarity of categorization
 - 7.6 million donations (86% industry; not all automated)
 - Findings:
 - Most of the categories in the Standard were clear
 - Still learning curve
 - Identified need to provide further clarification as there is variability in the interpretation of the minor/moderate hypotensive events and categorization of phlebotomy events
 - Revision of the standard is in progress

Donor Adverse Events, pilot data results

Post implementation of iQPP Standard Categorization

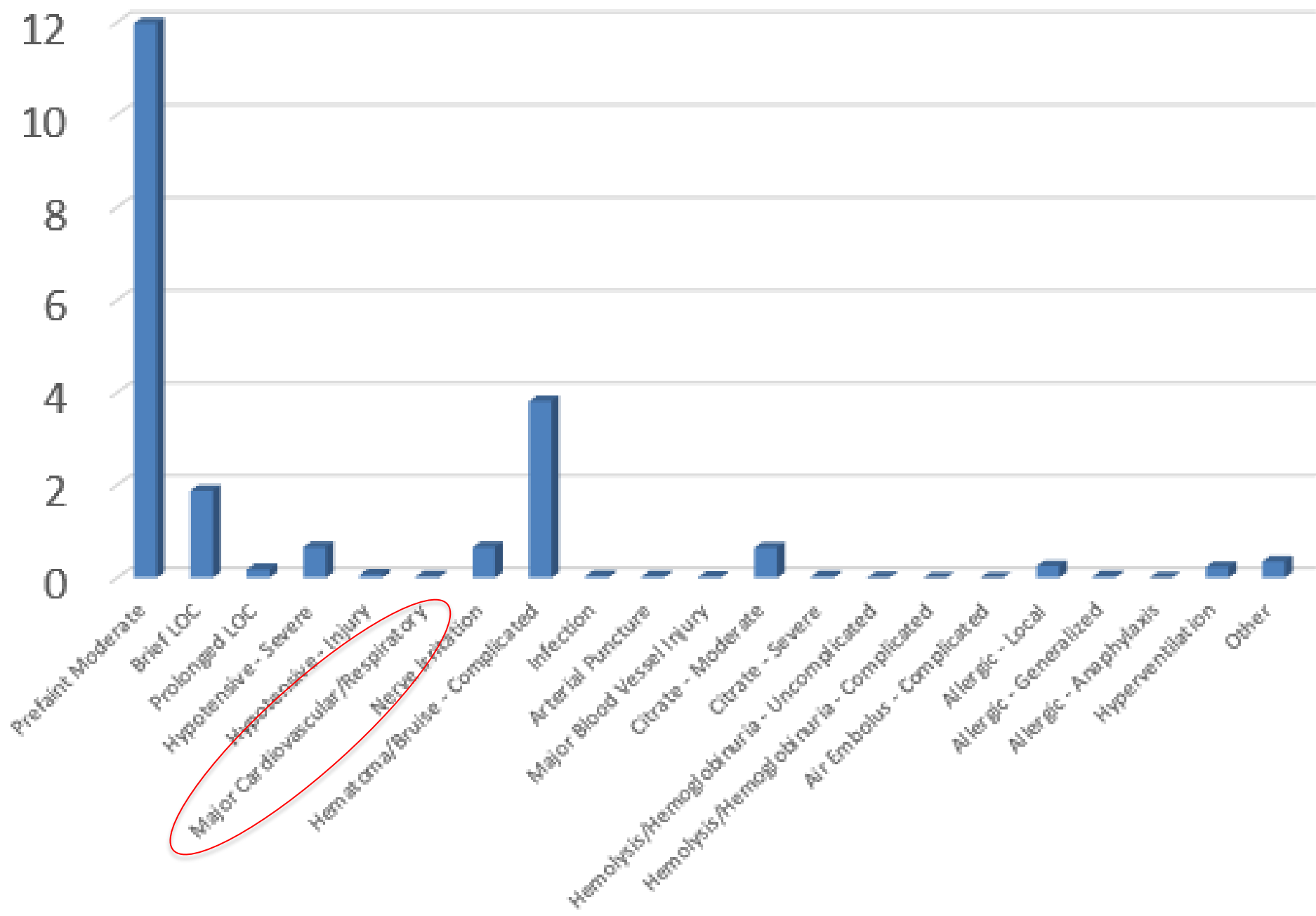
Incidence of all adverse events was rare: 0.209% (rate of 20.93 per 10,000 donations)

- Incidence of hypotensive adverse events: 0.148% (rate of 14.77 per 10,000 donations)
- Incidence of phlebotomy adverse events: 0.046% (rate of 4.56 per 10,000 donations)

All DAE rate/10,000 donations	% DAE Hypotensive	Hypotensive DAE rate/10,000 donations	% DAE Phlebotomy	Phlebotomy DAE rate/10,000 donations
20.93	70.59	14.77	21.80	4.56

*PPTA, 2016

Events per 10,000 donations



Summary

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- The rate of donor adverse events of Normal Source Plasma donors is very low and does not increase with donation frequency or collected volume.
 - Most common AE is vasovagal reactions
- Iron depletion is not common in plasma donor and is not higher in frequent donors
- Plasma donation may help reduce cholesterol levels and blood pressure in donors whose baseline is elevated. This decrease is not seen in donors whose baseline is within the normal range.
- Some biological markers increase in repeat plasma donors. This highlights that the body's physiological response to plasmapheresis is still not well understood. It is possible that it does not follow a linear synthesis and removal relationship, and more studies are needed,
- The clinical implications of a change in laboratory tests are not clear. It is important to utilize data in order to claim impact on donor health.

THANK YOU!