Plasmavigilance – Adverse Events Among U.S. Source Plasma Donors

George B. Schreiber, Mark Becker, Michelle Fransen,
Janet Hershman, James Lenart, Guang Song and Toby Simon

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Background

- Plasma Protein Therapeutics Association (PPTA) is the global trade association that represents private sector manufacturers of plasma therapies and plasma collection centers in Europe and the United States (US)
- Source Plasma (SP) is the primary starting material for 87% of plasma-derived products globally
- PPTA also administers standards that help ensure the quality and safety of plasma protein therapies, donors, and patients

Background

- Plasmavigilance is a program designed to collect, analyze, and monitor donor adverse events (AE) across the SP collection industry
- Donor retention depends on donors having a safe and satisfactory experience
- This study analyzes AE rates and SP donor characteristics that may be predictors of an AE

Investigators

- Toby Simon, Co-Investigator
- Mark Becker, Co-Investigator
- Janet Hershman, Co-Investigator
- James Lenart, Co-Investigator
- Guang Song, Data Analysist
- George Schreiber, Principal Investigator
- Michelle Fransen, Co-Investigator

Donor Health and Safety

- For US plasma donors, 21 CFR 640.65 (8) states: ". . collection shall not occur less than 2 days apart or more frequently than twice in a 7-day period"
- To determine eligibility, a donor must have a pre-donation screening before **every** donation consisting of:
  - Completing the Donor History Questionnaire
  - Providing Informed Consent
  - Having a physical exam performed by Physician Substitute
- Every donor is screened for health and infectious disease risks
- Not every individual that is interested in donating is eligible

Donor Health and Safety

Throughout the plasmapheresis procedure, there are several safety measures to protect the donor's health:

- Donor education on importance of healthy lifestyle (fluid intake, nutrition, rest, etc.)
- The plasmapheresis process is monitored by trained phlebotomists
- RBCs are returned with each cycle and at the end of the procedure
- Industry standard 500mL of saline is administered at the end of the procedure to enhance return of intravascular fluid balance

International Quality Plasma Program

- The International Quality Plasma Program (IQPP) provides global leadership for the plasma protein industry's goal of continuous improvement with a focus on safety and quality from the donor to the patient.
- This voluntary Standards Program will be transparent, credible, innovative, and responsive to stakeholder and industry needs.
- The *Standard for Recording Donor Adverse Events* provides a common language to classify AE within the plasma industry with easy to use, objective definitions based on simple and common signs and symptoms.
- Standard Version 2.0 implemented April 1, 2018, and was in effect for the duration of this study.
  - https://www.pptaglobal.org/images/IQPP/Standards_Revisions/2018/IQPP_DAERS_V2.pdf

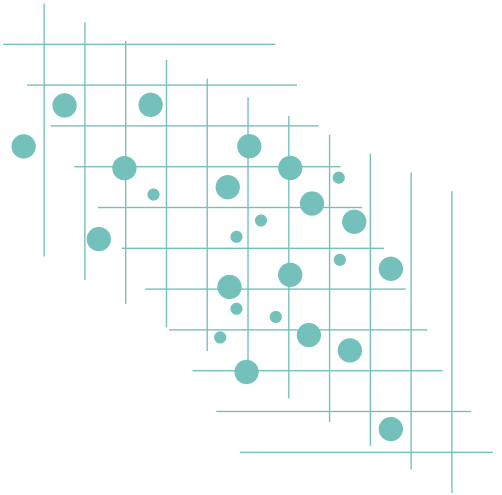
Donor Adverse Event Classifications & Subcategories

Category	Subcategory	Recording Requirement (Yes/No)	Category	Subcategory	Recording Requirement (Yes/No)
Hypotensive Event (Vasovagal/ Hypovolemia)	Prefaint, no loss of consciousness (LOC) (Minor)	No	Hemolysis/ Hemoglobinuria Event	Uncomplicated	Yes
	Prefaint, no LOC, (Moderate)	Yes		Complicated	Yes
	LOC approximately ≤ 60 seconds	Yes			
	LOC approximately > 60 seconds	Yes	Air Embolus Event	Uncomplicated	No
	Severe (with or without LOC)	Yes		Complicated	Yes
	Injury	Yes			
			Hyperventilation Event	--	Yes
Major Cardiovascular or Respiratory Event	--	Yes			
			Allergic Event	Local	Yes
Local Injury Related to Phlebotomy Event	Nerve irritation	Yes		Generalized	Yes
	Hematoma/bruise (uncomplicated)	No		Anaphylaxis	Yes
	Hematoma/bruise (complicated)	Yes			
	Infection	Yes	Immunization Event	Local, mild	No
	Arterial puncture	Yes		Local, severe	Yes
	Infiltration	No		Systemic, mild	No
	Major blood vessel injury	Yes		Systemic, severe	Yes
				Hypotensive, no LOC	Yes
Citrate Reaction Event	Minor	No		Hypotensive, LOC	Yes
	Moderate	Yes			
	Severe	Yes	Other Event	--	Yes

Results

Donor Adverse Event Analysis

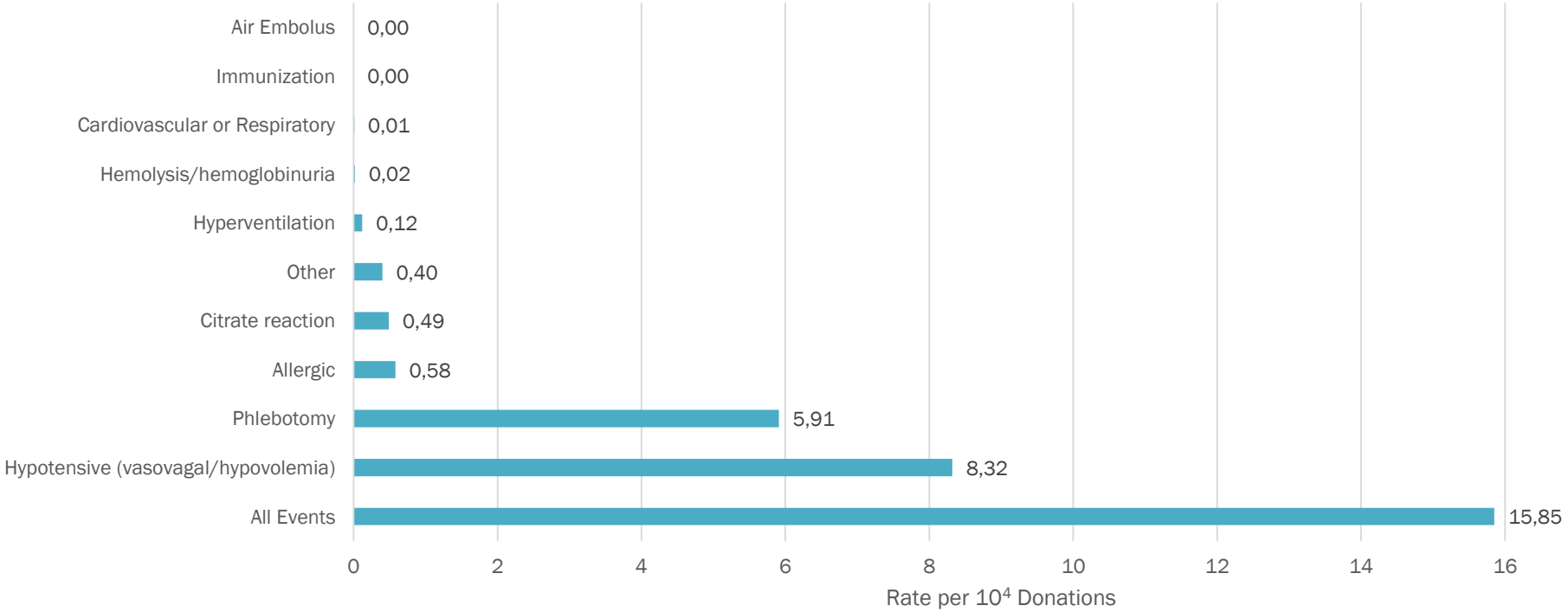
- Donation data for ≈1.1 million US donors from 3 PPTA member companies making 12,183,183 SP donations over a 4-month period from 513 plasma centers in 41 states were analyzed
- This represented approximately 72% of the donations collected by the US plasma industry
- The large, geographically diverse data should be representative of the US SP donor population



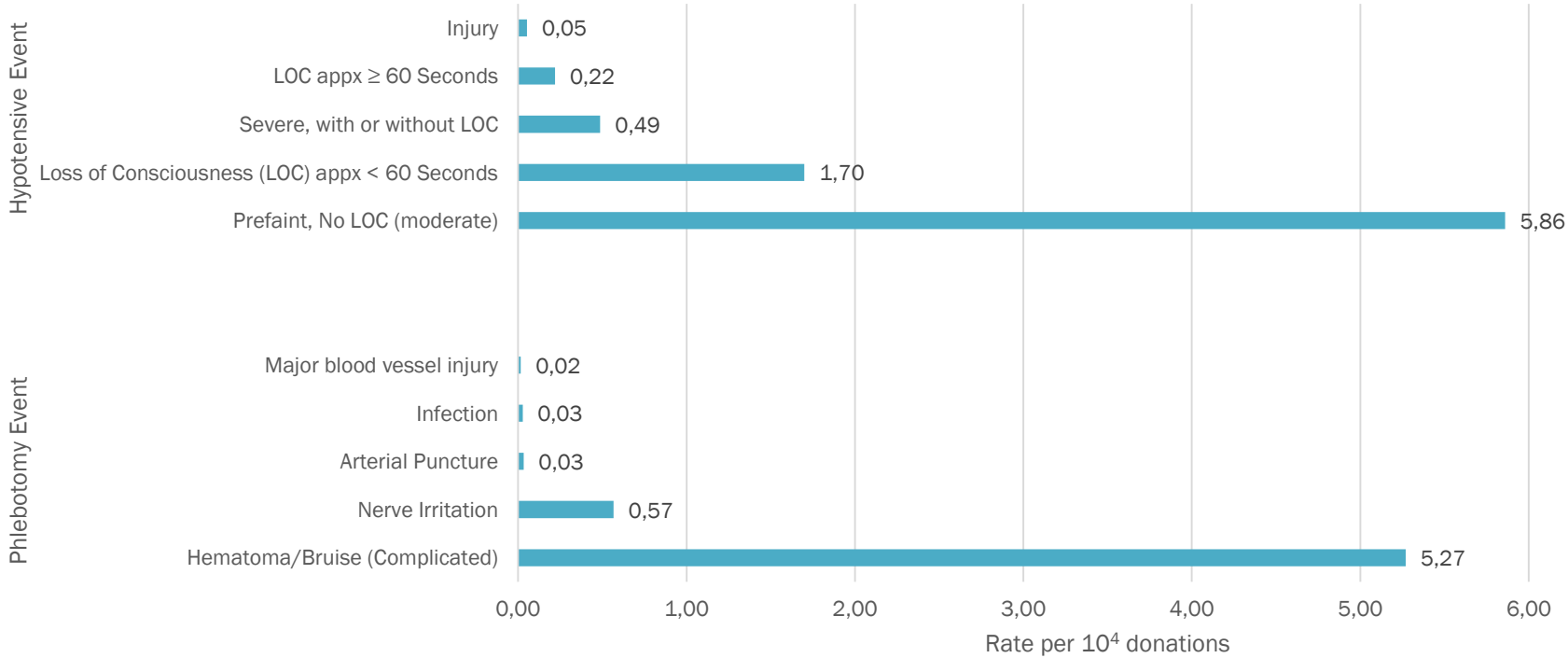
Donor Adverse Event Analysis

- 19,305 AE were recorded over the 4-month period
- Adverse events were rare: 15.85 per 10^4 donations
  - **0.16% of ALL donations resulted in an AE**
- 18,700 donors had at least one AE (1.74% of all donors) and 570 donors (0.05%) experienced more than one event
- Donors who had a full donation (≥ 90% of the target donation volume) had a significantly lower AE rate than donors who had a partial donation
- Overall, there is a **very low risk** of having an AE when donating with automated plasmapheresis

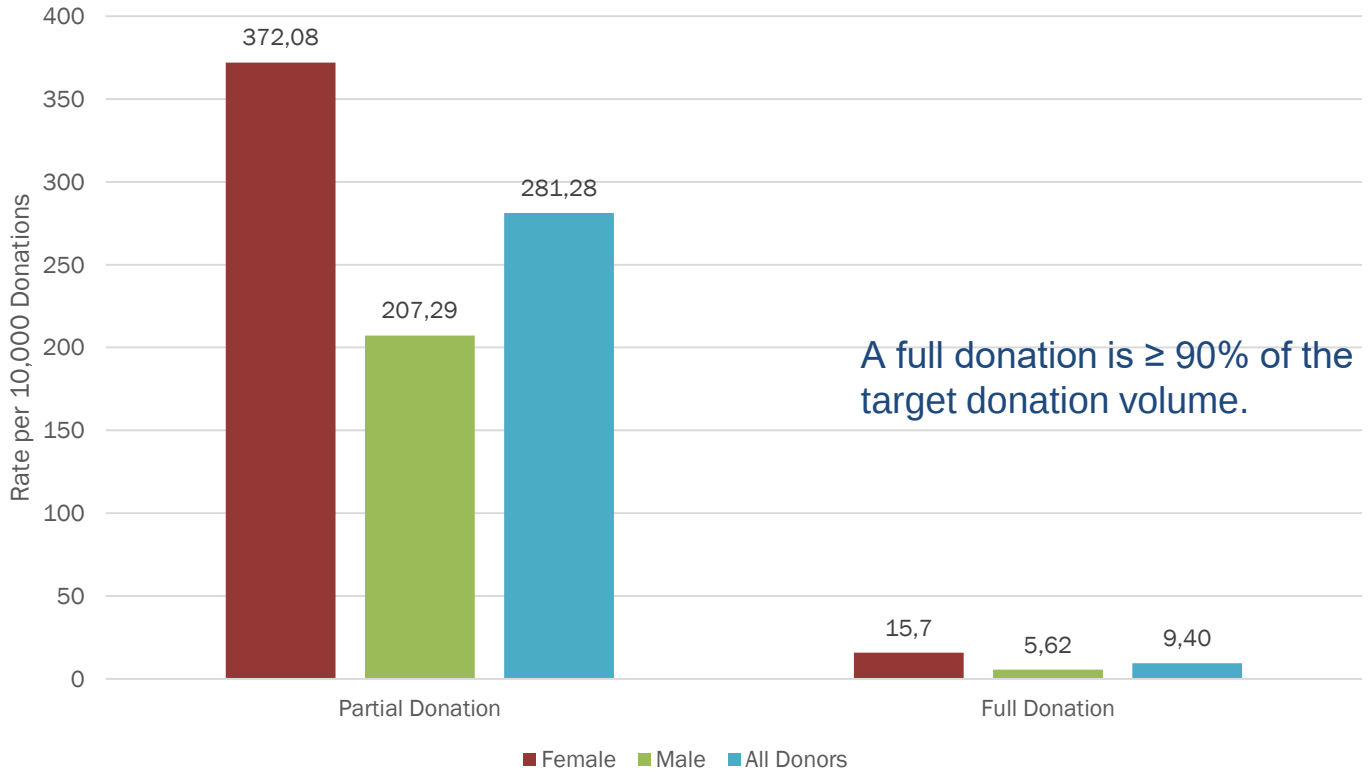
Donor Adverse Event (AE) Rates (per 10^4 donations) by Event Category



Hypotensive and Phlebotomy Subcategory AE Rates (per 10^4 donations)



AE Rates (per 10^4 donations) by Full and Partial Donations by Gender



Detailed Analysis

AE Rates (per 10^4 donations) by Gender, Donation Status and Age

Category	Hypotensive			Phlebotomy			All Events		
	All Donors	Female	Male	All Donors	Female	Male	All Donors	Female	Male
Gender									
	8.32	16.18	3.56	5.91	7.09	5.20	15.85	25.76	9.85
Donor status									
First-time	87.48	140.62	37.25	40.47	37.84	42.96	136.66	191.37	84.95
Repeat	6.04	11.53	2.76	4.92	5.94	4.31	12.37	19.56	8.07
Age (years)									
≤20	23.24	46.07	8.54	9.80	11.56	8.66	35.81	61.74	19.13
21-24	13.39	27.15	5.68	6.38	7.13	5.96	22.00	37.59	13.27
25-44	6.71	12.71	3.15	5.32	6.39	4.69	13.55	21.42	8.86
45-64	5.65	11.11	2.13	5.91	7.37	4.96	12.78	20.53	7.78
≥65	6.8	12.33	2.69	12.97	12.33	13.45	21.62	26.83	17.76

AE Rates (per 10^4 donations) by Gender, Weight and Body Mass Index (BMI)

Category	Hypotensive			Phlebotomy			All Events		
	All Donors	Female	Male	All Donors	Female	Male	All Donors	Female	Male
Weight (pounds)									
110-124	25.98	33.85	7.53	8.21	8.94	6.51	38.05	47.70	15.45
125-149	11.16	17.13	4.88	6.79	7.96	5.55	19.94	27.54	11.93
150-174	11.37	22.44	4.67	5.94	7.77	4.83	19.21	33.03	10.84
≥175	6.35	12.74	3.02	5.67	6.51	5.24	13.41	21.48	9.21
BMI									
<18	10.14	23.79	8.44	6.76	13.60	5.91	18.40	37.39	16.05
18-24	8.53	19.06	4.54	5.76	8.15	4.85	16.18	30.11	10.90
25-29	8.41	19.09	3.66	5.75	7.49	4.97	15.74	29.45	9.63
30-34	9.27	19.67	3.12	6.00	7.91	5.30	16.86	29.47	9.41
≥35	7.27	11.13	2.61	5.94	6.18	5.64	14.72	19.39	9.06

US Food and Drug Administration Nomograms

Plasma Volume and Total Collected Volume, by Donor's Weight

Donor's Weight	Plasma Volume (mL)	Total Collection Volume (mL)
110 – 149 (lbs) (50 kg - 68 kg)	625	690
150 – 174 (lbs) (69 kg -79 kg)	750	825
≥ 175 (lbs) (≥ 80 kg)	800	880

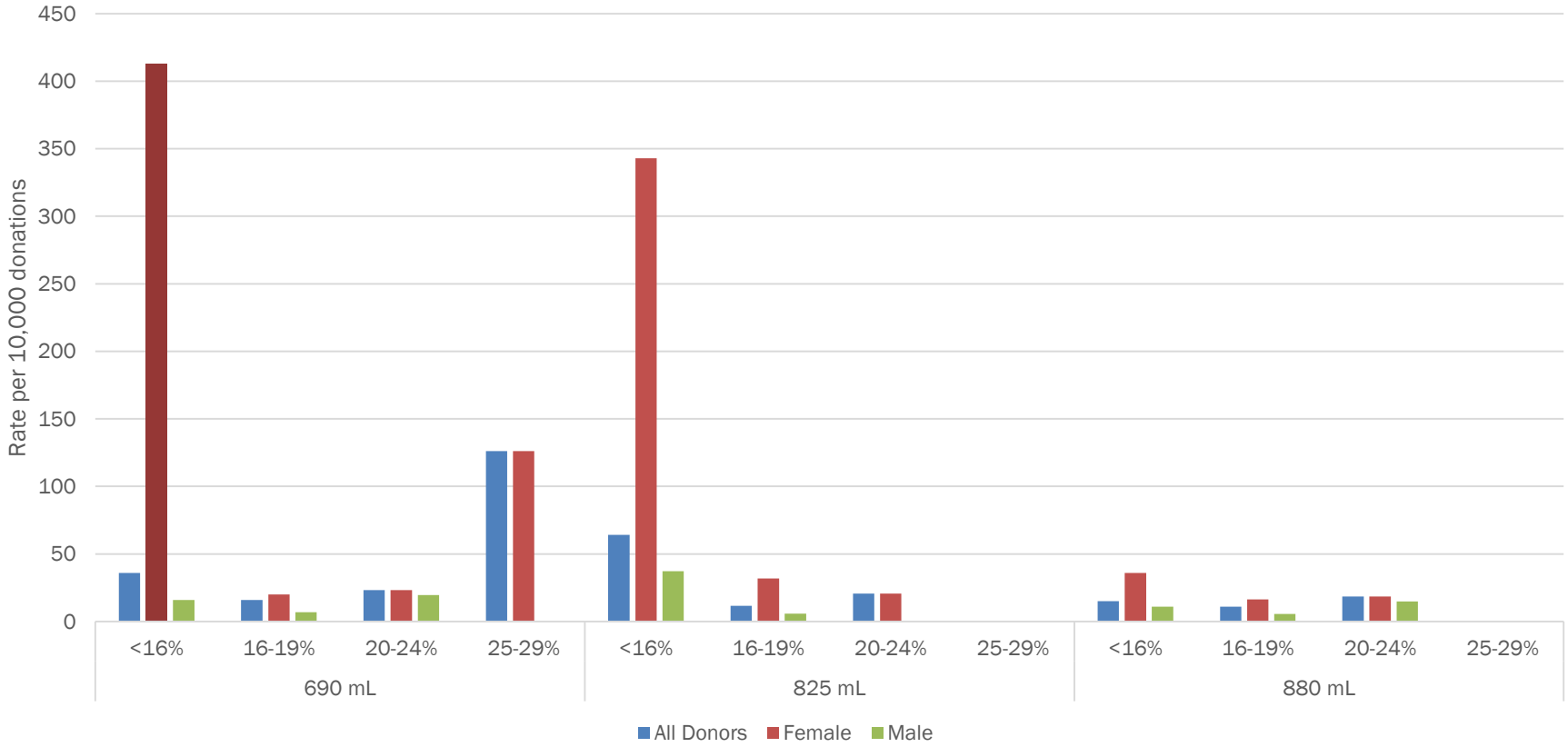
Anticoagulant is approximately 9% of the total collection volume

AE Rates (per 10^4 donations) by Nomogram Volume, Weight and Gender

Nomogram Volume	Weight (pounds)	Female			Male		
		AE Rate	% of all AE	AE Rate / (%)	AE Rate	% of all AE	AE Rate / (%)
690 mL	110-119.9	53.32	3.10		19.67	0.39	
	120-129.9	38.48	4.26	31.54 / (16.90)	13.89	0.92	12.28 / (5.57)
	130-139.9	27.81	4.58		11.82	1.69	
	140-144.9	26.45	2.59		11.53	1.16	
	145-149.9	22.71*	2.38		11.37*	1.40	
825 mL	150-154.9	40.21	3.95		12.59	1.86	
	155-159.9	34.46	3.57	33.03 / (17.15)	10.04	1.62	10.84 / (9.28)
	160-164.9	31.66	3.33		10.22	1.76	
	165-169.9	31.35	3.32		11.17	2.03	
	170-174.9	28.01*	2.98		10.41*	2.01	
880 mL	175-179.9	34.77	3.50		10.49	2.01	
	180-189.9	29.51	5.92		9.85	3.87	
	190-199.9	26.69	5.07		9.82	3.73	
	200-224.9	22.25	9.19		9.33	7.59	
	225-249.9	17.99	5.41	21.48 / (29.10)	8.53	4.81	9.21 / (22.00)
	250-274.9	14.59	2.78		8.62	2.95	
	275-299.9	13.96	1.50		8.75	1.70	
	300-349.9	11.07	0.94		8.27	1.36	
	350-399.9	11.80*	0.22		9.38	0.44	
	≥400	10.07[b]	0.01		9.61	0.02	

[b] only 993 donations in the 880mL, ≥400 pounds group with one AE *p<0.001

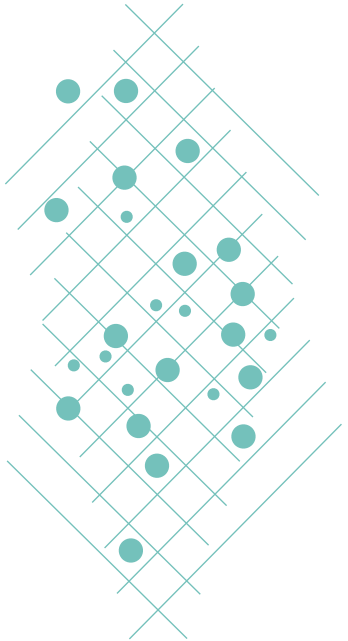
AE Rates (per 10^4 donations) by Percent (%) Estimated Blood Volume (EBV) Drawn by Nomogram Volume



Summary

Donor Characteristics Associated with Higher AE Rates

- First time donors
  - 11 times more likely to experience an AE than repeat donors
  - 14.5 times more likely to experience a hypotensive AE than repeat donors
- Females
  - 2.6 times more likely than males to experience any AE
  - 4.5 times higher for Hypotensive AE
- Younger age
  - ≤20 years old were 1.74 times more likely than donors aged 45-64
- Lower pre-donation EBV



Comparison to Blood Community AE Rates

- Blood collection industry has a similar donor hemovigilance program to the IQPP Standard.
- This analysis does not include minor subcategories as they are not recorded for the Standard. Thus, our findings are not directly comparable to other hemovigilance programs.
- While all AEs that occurred may not have been captured, in most cases these events are minor and resolve without further donor complications.
- As Cho & Hiskey conclude in their 2021 editorial review of this study, “this very large study demonstrates that SP collection presents a low risk to donors, similar to blood donation.”

References

Schreiber GB, Becker M, Fransen M, Hershman J, Lenart J, Song G, et al. Plasmavigilance—Adverse events among US Source plasma donors. Transfusion. 2021;1–17. https://doi.org/10.1111/trf.16612

Cho J, Hiskey M. Plasmavigilance: Source plasma joins the call to arms, Transfusion. 2021;61:2803–2805.

The ***Plasmavigilance—Adverse events among US Source plasma donors*** is an Open Access publication. It is available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/trf.16612.

The ***Plasmavigilance: Source plasma joins the call to arms*** editorial is a Free Access publication and can be found here: https://onlinelibrary.wiley.com/doi/epdf/10.1111/trf.16668.

Thank You

Michelle Fransen, MPH, MPS

mfransen@pptaglobal.org

@PlasmaProteins
@PPTAEurope

www.PPTAGlobal.org
www.DonatingPlasma.org

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