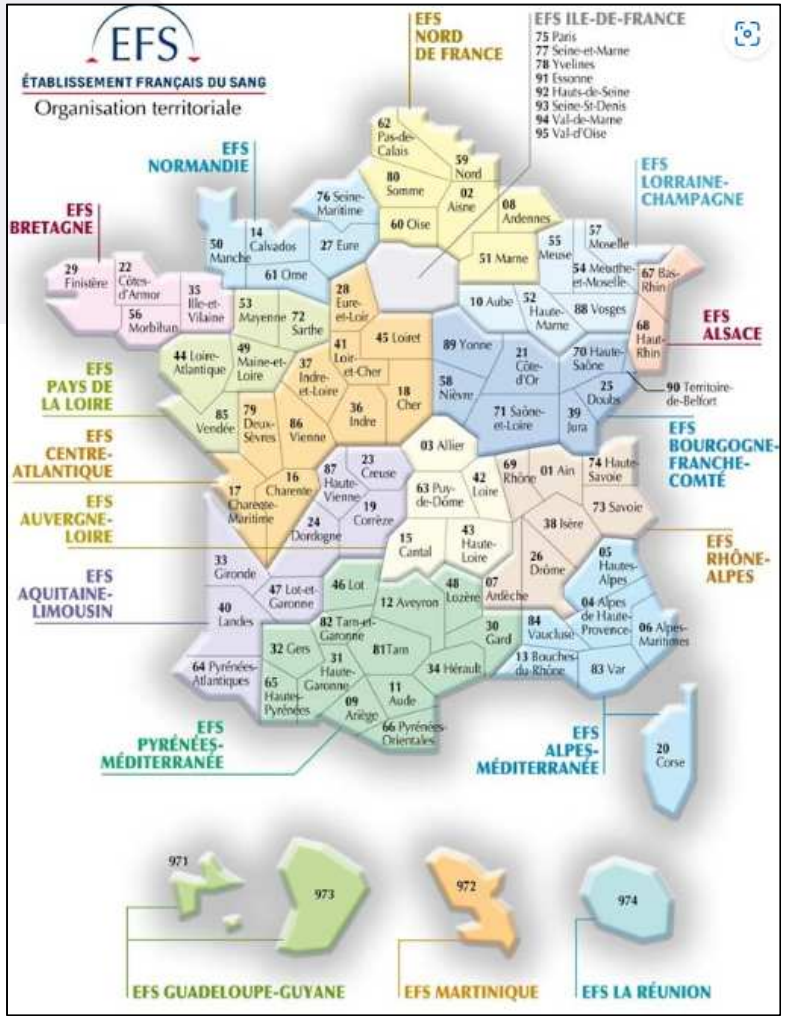
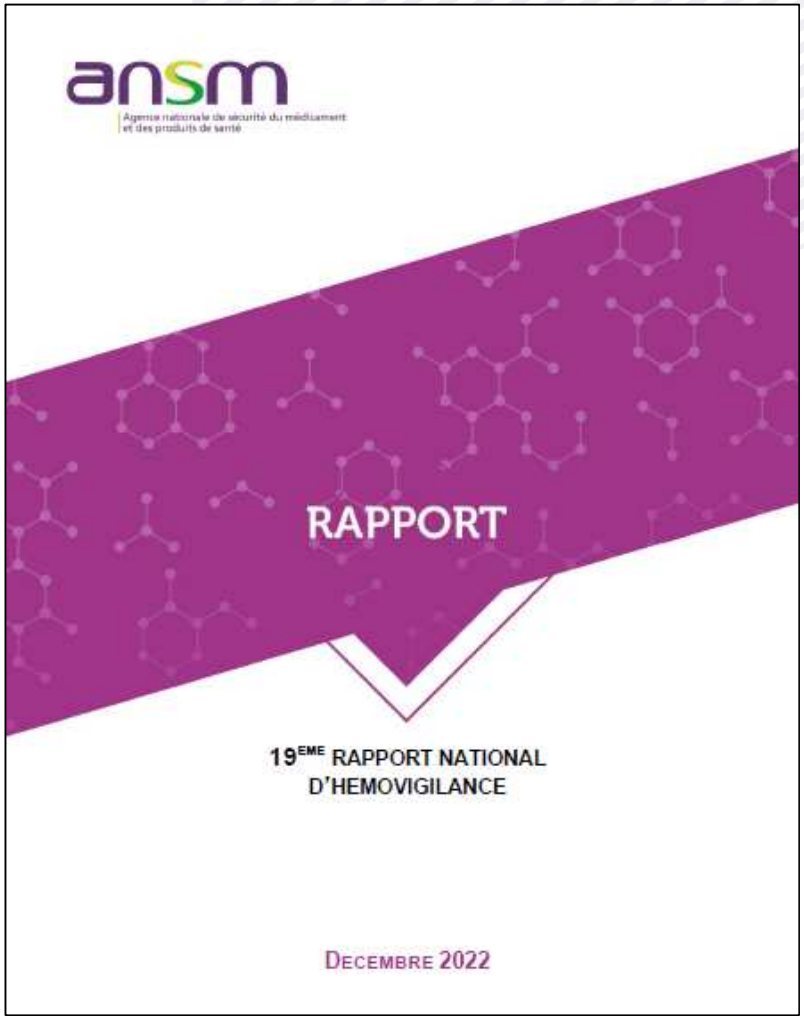
Risques pour le donneur de plasma
Risks for the plasma donor

Pierre Tiberghien
Etablissement Français du Sang
Université de Franche-Comté
European Blood Alliance

Plasma donation in France – Hemovigilance





Plasma donation in France – Hemovigilance

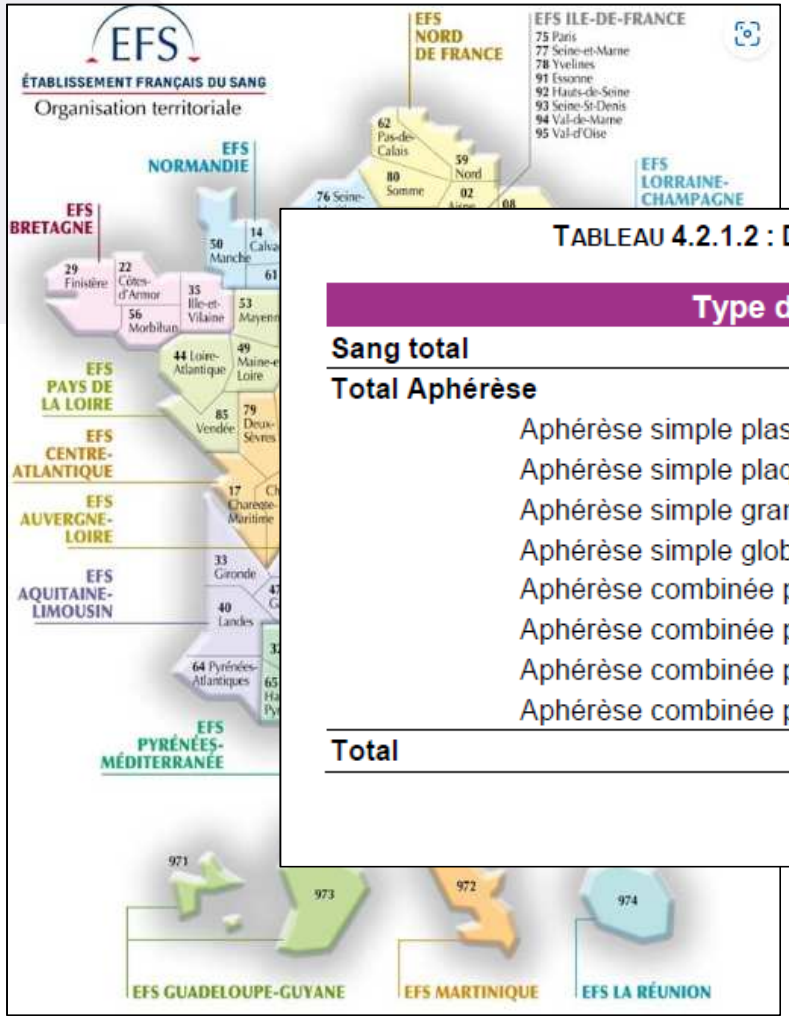


TABLEAU 4.2.1.2 : DISTRIBUTION DES DONS EN 2021 PAR TYPE DE DON

Type de dons	Nombre	% des dons
Sang total	**2 387 237**	**87.3%**
Total Aphérèse	**347 703**	**12.7%**
Aphérèse simple plasma	257 215	9.4%
Aphérèse simple plaquettes	196	0.0%
Aphérèse simple granulocytes	0	0.0%
Aphérèse simple globules rouges	0	0.0%
Aphérèse combinée plasma/plaquettes	88 070	3.2%
Aphérèse combinée plasma/plaquettes/globules rouges	2 157	0.1%
Aphérèse combinée plaquettes/globules rouges	65	0.0%
Aphérèse combinée plasma/globules rouges	0	0.0%
Total	**2 734 940**	**100%**

Source : EFS et CTSA

ansm
Agence nationale de sécurité du médicament et des produits de santé

DECEMBRE 2022

Plasma donation in France – Hemovigilance

- Up to 24 plasma donations / year
- On average, less than 5 donations / year
- Weight ≥ 55 kg
- Plasma volume harvested according to sex, weight and height (maximum 16% total blood volume, or 750 ml, excluding anticoagulant and test tubes)
- Applied muscle tension and hydration for fainting prevention
- No saline infusion of the end of the procedure
- Plasma protein level checked 1 / year (+ protein electrophoresis if protein level out of range)
- No plasma IgG determination

Plasma donation in France – Hemovigilance

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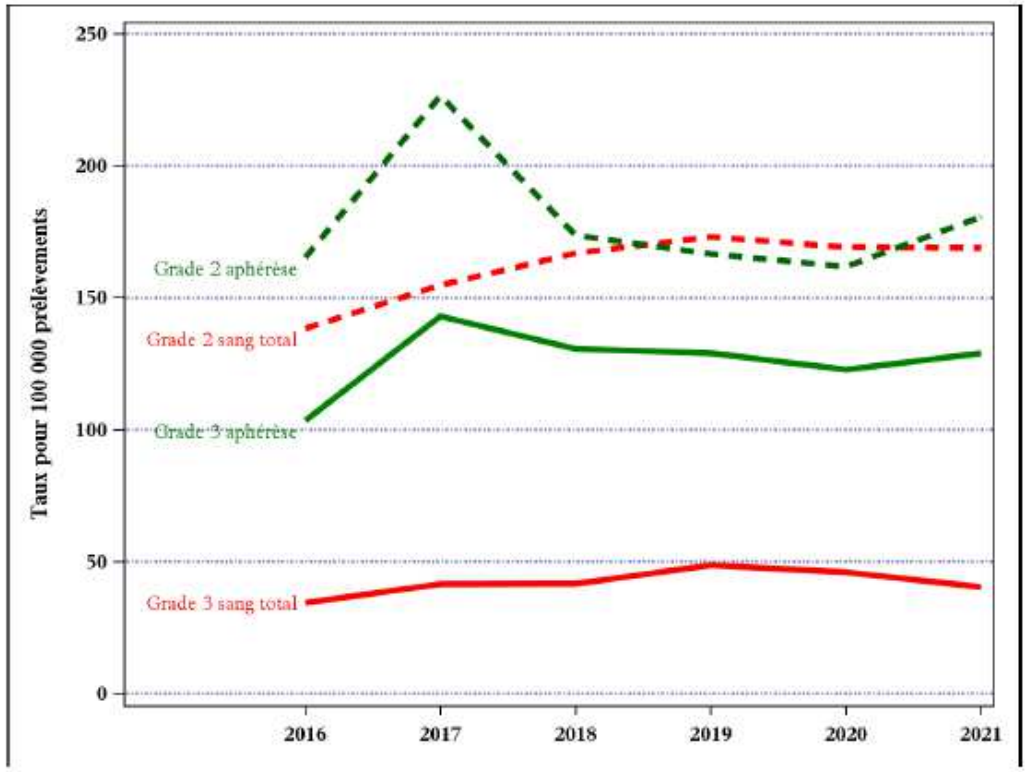
TABLEAU 6.3.2.3 : REPARTITION DES EIGD SURVENUS ET DECLARES EN 2021 D'IMPUTABILITE 1, 2, 3 OU NON EVALUABLE SELON LE TYPE DE PRELEVEMENT

Diagnostic	Sang total	Aphérèse	Non listé	Total	Taux/100 000 prélèvements (Sang total)	Taux/100 000 prélèvements (Aphérèse)	Taux/100 000 prélèvements (Ensemble)
Malaise vagal immédiat	3955	742	0	4697	164.7	212.1	170.8
Hématome	281	191	0	472	11.7	54.6	17.2
Malaise vagal retardé	329	66	0	395	13.7	18.9	14.4
Ponction artérielle	266	7	0	273	11.1	2.0	9.9
Blessure nerveuse directe par l'aiguille	82	11	0	93	3.4	3.1	3.4
Anémie (Aggravation)	51	1	0	52	2.1	0.3	1.9
Réaction au citrate	0	43	0	43	0.0	12.3	1.6
Douleur locale autre	32	7	0	39	1.3	2.0	1.4
Blessure nerveuse indirecte par l'hématome	17	4	0	21	0.7	1.1	0.8

Plasma donation in France – Hemovigilance

FIGURE 6.4.2 : EVOLUTION 2016-2021 DE L'INCIDENCE DES EIGD (ENQUETE TERMINEE) DECLARES D'IMPUTABILITE 2-3, OU NON EVALUABLE, PAR TYPE DE DON ET GRAVITE



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0		472	11.7	54.6	17.2
0		395	13.7	18.9	14.4
0		273	11.1	2.0	9.9
0		93	3.4	3.1	3.4
0		52	2.1	0.3	1.9
0		43	0.0	12.3	1.6
0		39	1.3	2.0	1.4
0		21	0.7	1.1	0.8

Hemovigilance – Fainting reactions

Case–control study of immediate and delayed vasovagal reactions in blood donors

Narbey D et al, Vox Sanguinis 2016

- Retrospective, multicenter case-control study
- Cohort of 8 800 000 donations from 2 890 000 donors
- 2011 to 2013 French hemovigilance data
- Immediate or delayed (outside the transfusion site and within 24 hours) fainting reactions with a high imputability only
- Controls drawn at random from the donor population (1 control by case) among healthy subjects free of fainting, matched on the collection site and day.
- Primary outcome: presence of an immediate and delayed fainting reaction
- Studied variables: sex, age, body mass index, donor status and collection type

Hemovigilance – Fainting reactions

Case–control study of immediate and delayed vasovagal reactions in b

Narbey D et al, V

- Retrospect
- Cohort of
- 2011 to 20
- Immediate reactions v
- Controls d healthy su
- Primary ou
- Studied va

Immediate fainting:

		Univariate analysis			Multivariate analysis		
	Odds ratio crude	IC 95 %	*p*	Odds ratio Ajusted	IC 95 %	*p*
Sex						
Man	1					
Woman	1.41	[1.33 – 1.50]	*<0.0001*	-	-	-
Type of phlebotomy						
Whole blood	1			1		
Apheresis	0.63	[0.57 – 0.69]	*<0.0001*	1.26	[1.12 – 1.41]	*<0.0001*
Donation status						
Repeat	1			1		
First-time	5.80	[5.28 – 6.36]	*<0.0001*	3.72	[3.36 – 4.12]	*<0.0001*
Age group (years)						
61-70	1			1		
25-60	1.70	[1.49 – 1.93]	*<0.0001*	1.42	[1.23 – 1.64]	*<0.0001*
18-24	5.99	[5.19 – 6.92]	*<0.0001*	3.30	[2.81 – 3.87]	*<0.0001*
BMI						
Underweight	1.80	[1.41 – 2.30]	*<0.0001*	-	-	-
Normal	1			-	-	-
Overweight	0.52	[0.49 – 0.56]	*<0.0001*	-	-	-
Obesity	0.33	[0.29 – 0.38]	*<0.0001*	-	-	-

Hemovigilance – Fainting reactions

Case–control study of immediate and delayed vasovagal
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Narbey D et al,

- Retrospect
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- 2011 to 20
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Delayed fainting :

		Univariate analysis			Multivariate analysis		
		Odds ratio crude	IC 95 %	*p*	Odds ratio Ajusted	IC 95 %	*p*
Sex							
	Man	1					
	Woman	6.22	[4.71 – 8.21]	*<0.0001*	-	-	-
Type of phlebotomy							
	Whole blood	1			1		
	Apheresis	0.92	[0.69 – 1.22]	*0.56*	1.61	[1.11 – 2 .32]	*<0.0001*
Donation status							
	Repeat	1			1		
	First-time	1.70	[1.31 – 2.17]	*<0.0001*	1.70	[1.23 – 2.34]	*<0.0001*
Age group (years)							
	61-70	1			1		
	25-60	0.55	[0.40 – 0.76]	*0.0003*	0.42	[0.28 – 1.64]	*<0.0001*
	18-24	0.99	[0.69 – 1.43]	*0.69*	0.53	[2.81 – 3.87]	*<0.0001*
BMI							
	Underweight	1.05	[0.53 – 2.10]	*0.89*	-	-	-
	Normal	1			-	-	-
	Overweight	0.70	[0.56 – 0.87]	*0.0012*	-	-	-
	Obesity	0.44	[0.29 – 0.66]	*<0.0001*	-	-	-

Hemovigilance – Fainting reactions

Case–control study of immediate and delayed vasovagal reactions in b

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- Cohort
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Delayed fainting :

	Univariate analysis			Multivariate analysis		
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Normal	1			-	-	-
Overweight	0.70	[0.56 – 0.87]	*0.0012*	-	-	-
Obesity	0.44	[0.29 – 0.66]	*<0.0001*	-	-	-

Malaise retardé, grade 3

- Donneur connu de 60-65 ans (plus de 60 dons d'aphérèse plasma), 70-75 kg, 170-180 cm, IMC : 20-25
- Le xx/yy/2022 : don **d'aphérèse simple plasma**, volume prélevé : 840-860 mL.
- Après le don, environ 35 mn après la fin de l'aphérèse, alors qu'il regagne son domicile à moto, le donneur perd connaissance et percute un pont. Il est hospitalisé pour fractures membres inférieurs et fracture vertèbre cervicale avec lésion médullaire.
- L'EFS est informé un an après via un salarié de l'EFS qui croise le donneur dans la rue et apprend à cette occasion qu'il a eu accident de la voie publique après le don.

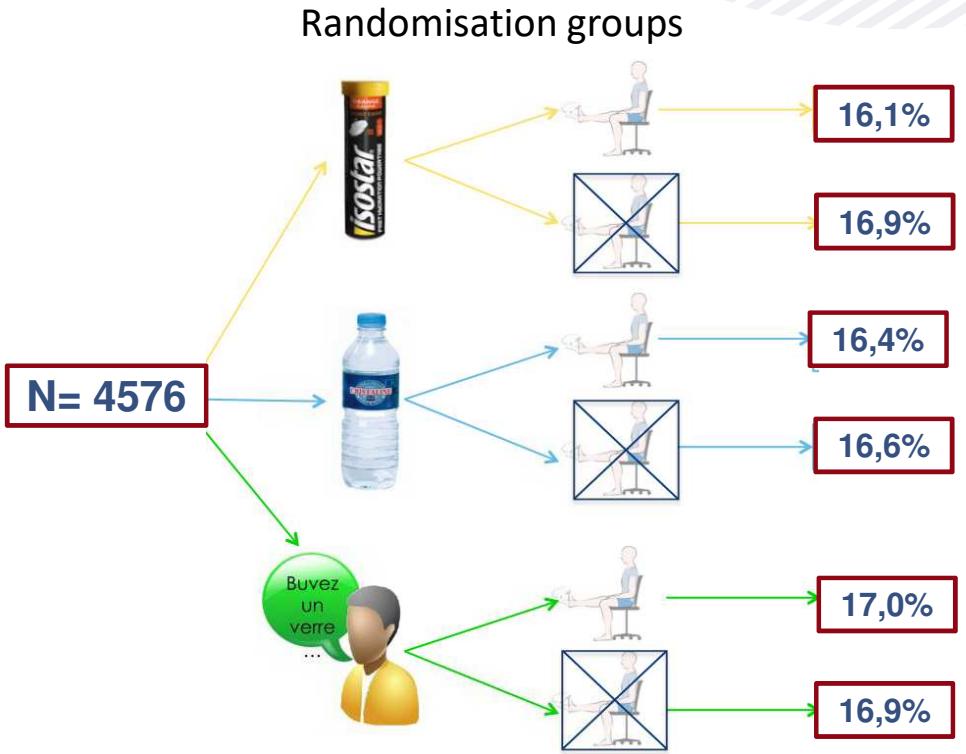
Fainting reactions - prevention

Prevention of fainting reactions and/or tiredness after whole blood donation: a randomized trial assessing hydration and/or muscle tension exercices

Evasion study, Morand et al, Transfusion, 2016

- Factorial design, cluster randomization (1 cluster = 1 blood donation unit)
- Comparison of 6 strategies regarding **hydration**:
  - ✓ 500mL of an **isotonic drink** (two tablets of Isostar power Tabs, lemon flavor) in slightly mineralized water
  - ✓ 500mL of **slightly mineralized water**
  - ✓ **advice to drink** a glass of slightly mineralized water or fruit juice)

  with or without :
  - ✓ **muscle tensing exercises**
- Donor phone interview one week after donation



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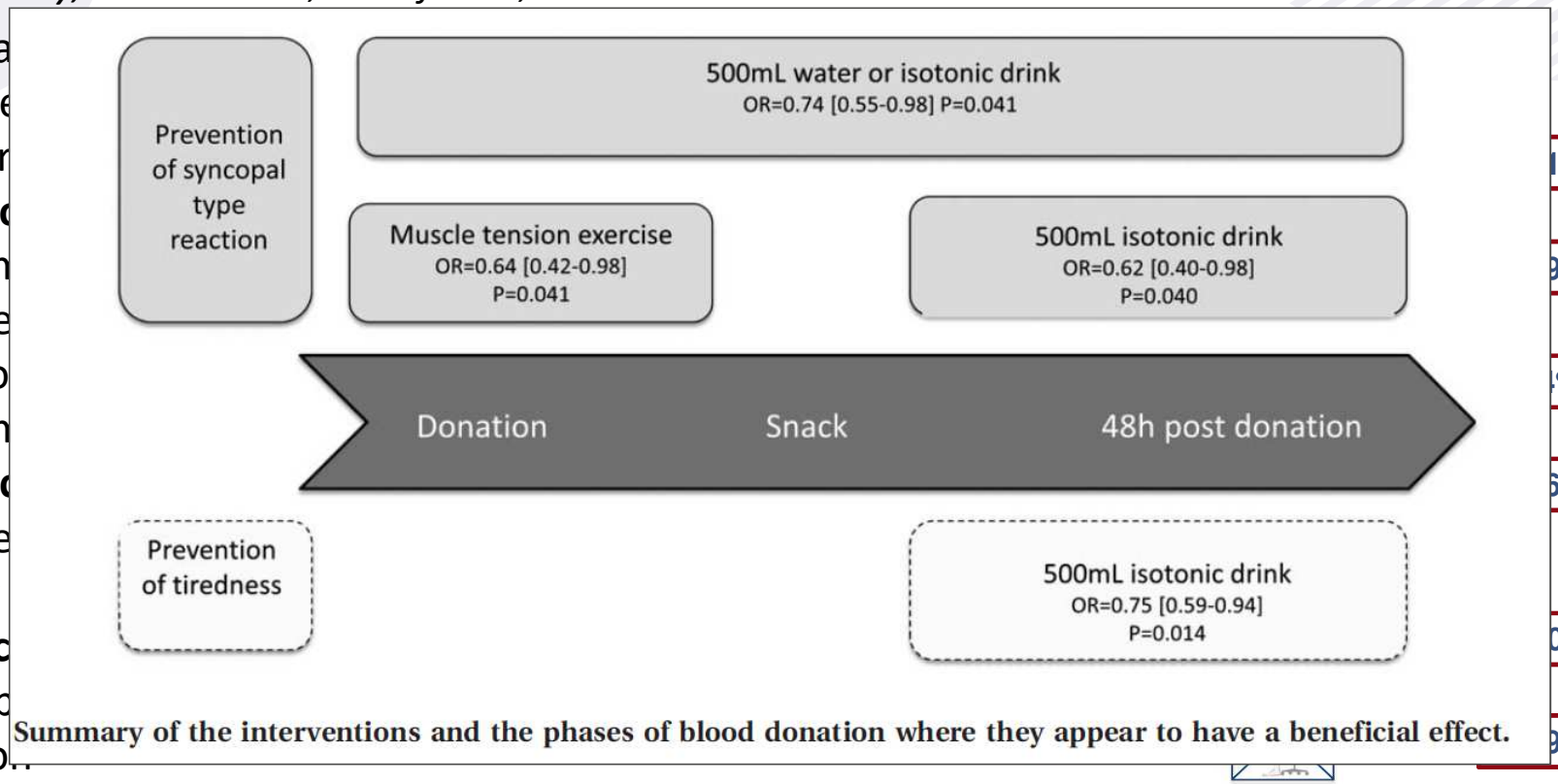

Summary of the interventions and the phases of blood donation where they appear to have a beneficial effect.

Fainting reactions – prevention

Frequency of vasovagal reactions with large volume plasma donation in Canada

Khandelwal et al, AABB, 2023

Current Vasovagal Reaction Mitigation Strategy for Plasmapheresis Donors at Canadian Blood Services

- Minimum weight criteria to be an eligible donor
- Pre-donation meal and fluids
- Step-wise TEBV based donation volume
- Saline infusion 500mL if over 562mL donated
- Post-donation 500mL fluid, salty snack
- Active surveillance of vasovagal reactions

- 19185 donors made 78401 donations.
- Progression to 18% TEBV was completed by 18.5% of female donors and 24.3% of male donors
- Saline was administered in 52906 (67.4%) of donations

TEBV: total estimated blood volume

Fainting reactions – prevention

Frequency of vasovagal reactions with large volume plasma donation in Canada

Khandelwal et al. AABB, 2022

Current Va
Plasmaph

- Minimum
- Pre-donat
- Step-wise
- Saline infu
- Post-dona
- Active sur

e 78401 donations.
TEBV was completed
donors and 24.3% of male

tered in 52906 (67.4%)

Figure 3: Rate of VVR per 10,000 donations by blood volume

TEBV: total estimated blood volume

Hemovigilance – Iron depletion / anemia
What about protein depletion in plasma donors?

TABLEAU 6.3.2.3 : REPARTITION DES EIGD SURVENUS ET DECLARES EN 2021 D'IMPUTABILITE 1, 2, 3 OU NON EVALUABLE SELON LE TYPE DE PRELEVEMENT

Diagnostic	Sang total	Aphérèse	Non listé	Total	Taux/100 000 prélèvements (Sang total)	Taux/100 000 prélèvements (Aphérèse)	Taux/100 000 prélèvements (Ensemble
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Hématome	281	191	0	472	11.7	54.6	17.2
Malaise vagal retardé	329	66	0	395	13.7	18.9	14.4
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Blessure nerveuse directe par l'aiguille	82	11	0	93	3.4	3.1	3.4
Anémie (Aggravation)	51	1	0	52	2.1	0.3	1.9
Réaction au citrate	0	43	0	43	0.0	12.3	1.6
Douleur locale autre	32	7	0	39	1.3	2.0	1.4
Blessure nerveuse indirecte par l'hématome	17	4	0	21	0.7	1.1	0.8

- Iron depletion and anemia is often severely underreported in hemovigilance systems
- Means to reduce this risk in plasma apheresis donors:
  - Saline rinse back to flush back residual RBC
  - Optimizing test tubes collection

- Protein depletion is not reported
- IgG levels are not measured

Hemovigilance – Protein / Immunoglobulin depletion

A prospective multicentre study on the safety of long-term intensive plasmapheresis in donors (SIPLA)

Schulzki et al, Vox Sanguinis, 2006

Twenty-one plasma centers recruited **experienced 3783 plasma donors** who were switched from a moderate to an intensive plasmapheresis program and observed over a 3-year period. Individuals weighing < 70 kg and ≥ 70 kg donated 750 ml and 850 ml of plasma per session, respectively. The maximum of annual donations was limited to 60.

IgG threshhold : 5,8 g/l

Hemovigilance – Protein / Immunoglobulin depletion

A prospective multicentre study on the safety of long-term intensive plasmapheresis in donors (SIPLA)

	All *n* = 3783	Arm I *n* = 2402	Arm II *n* = 1381	Females *n* = 897	Males *n* = 2886	*P*-value Arm I vs. arm II	*P*-value F vs. M
Age, in years	35 (20–55)	34 (20–55)	36 (21–54)	35 (21–54)	35 (20–55)	**0·003**	0·51
Female/male ratio	0·31 (897/2886)	0·44 (738/1680)	0·13 (159/1206)			**< 0·0001**	
Body weight, in kg	79 (60–105)	74 (59–100)	86 (72–111)	70 (56–102)	81 (65–106)	**< 0·0001**	**< 0·0001**
Initial IgG, g/l	8·4 (6·4–12·1)	8·3 (6·4–11·9)	8·7 (6·5–12·5)	8·5 (6·5–12·4)	8·4 (6·4–12)	**< 0·0001**	0·20
Initial total serum protein, g/l	69 (63–76)	69 (63–75)	70 (64–77)	68 (63–75)	70 (64–76)	**< 0·0001**	**< 0·0001**
Initial Hb, g/l	146 (127–162)	145 (126–161)	149 (132–163)	132 (122–146)	150 (136–163)	**< 0·0001**	**< 0·0001**
Initial Hct, v/v	43 (38–49)	43 (37–48)	44 (39–49)	39 (36–44)	45 (40–49)	**< 0·0001**	**< 0·0001**
Observation period, in days	475 (39–1093)	476 (42–1093)	466 (37–1093)	475 (45–1094)	475 (38–1093)	0·70	0·60
Absolute number of donations	304 836	195 411	109 425	68 099	236 737		
Number of donations per donor during observation period	65 (6–180)	65 (6–180)	63 (5–180)	63 (6–178)	65 (6–180)	0·88	0·023
Plasma donated per donor per year, in litres	43 (27–63[a])	41 (26–59[a])	47 (30–71[a])	40 (27–57[a])	44 (28–65[a])	**< 0·0001**	**< 0·0001**
Plasma donated per donation and per kilogram of body weight, in ml	10 (7·4–12·4)	10·1 (7·5–12·7)	9·9 (7·7–11·8)	10·9 (7·9–13·4)	9·8 (7·5–11·8)	**< 0·0001**	**< 0·0001**
Individual average time interval between two donations, in days	6·5 (4·3–10)	6·6 (4·4–10)	6·5 (4–10)	6·9 (4·7–10)	6·5 (4·2–10)	**0·002**	**< 0·0001**

Data are expressed as median values (5th–95th percentiles). Bold numbers indicate *P*-values below the significance level of 0·01.
[a]Values greater than 45 and 51 l per year, respectively, result from projecting periods with high donation frequency to a 1-year period.
IgG, immunoglobulin G; Hb, haemoglobin; Hct, haematocrit.

IgG threshhold : 5,8 g/l

Hemovigilance – Protein / Immunoglobulin depletion

A prospective multicentre study … intensive plasmapheresis in donc

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[a]Values greater than 45 and 51 l per year, respectively, result from projecting perio
IgG, immunoglobulin G; Hb, haemoglobin; Hct, haematocrit.

Table 3 Reasons for cessation of participation in the 2860 donors who dropped out of the study

Subgroup, *n* (%)	All *n* = 3783	Arm I *n* = 2402	Arm II *n* = 1381	Females *n* = 897	Males *n* = 2886	*P*-value Arm I vs. arm II	*P*-value F vs. M
Donors completing the study	923 (24·4)	587 (24·4)	336 (24·3)	193 (21·5)	730 (25·3)	0·97	0·023
Total number of dropouts	**2860 (75·6)**	**1815 (75·6)**	**1045 (75·7)**	**704 (78·5)**	**2156 (74·7)**		
~~Socioeconomic reasons~~	~~1360 (49·2)~~	~~1159 (48·3)~~	~~701 (50·8)~~	~~396 (44·1)~~	~~1464 (50·7)~~	~~0·14~~	~~0·0007~~
Lack of time or work schedule conflicts	686 (18·1)	416 (17·3)	270 (19·6)	114 (12·7)	572 (19·8)	0·090	**< 0·0001**
Moving from the area	121 (3·2)	81 (3·4)	40 (2·9)	31 (3·5)	90 (3·1)	0·48	0·69
Other personal reasons	1053 (27·8)	662 (27·6)	391 (28·3)	251 (28)	802 (27·8)	0·64	0·94
Medical reasons unrelated to plasmapheresis	**393 (10·4)**	**247 (10·3)**	**146 (10·6)**	**122 (13·6)**	**271 (9·4)**	0·82	**0·0004**
Medical diseases	138 (3·6)	85 (3·5)	53 (3·8)	43 (4·8)	95 (3·3)	0·70	0·056
Surgery, accidents, injuries	88 (2·3)	54 (2·2)	34 (2·5)	23 (2·6)	65 (2·3)	0·75	0·67
Malaise, disturbed well-being	65 (1·7)	46 (1·9)	19 (1·4)	24 (2·7)	41 (1·4)	0·27	0·024
Pregnancy	16 (0·4)	10 (0·4)	6 (0·4)	16 (1·8)		0·93	
Diagnostic endoscopy	11 (0·3)	9 (0·4)	2 (0·1)	5 (0·6)	6 (0·2)	0·34	0·17
Laboratory findings not related to plasmapheresis	75 (2)	43 (1·8)	32 (2·3)	11 (1·2)	64 (2·2)	0·31	0·083
Dropouts because of low IgG, TSP or Hb/Hct and clinical events related to plasmapheresis	**607 (16)**	**409 (17·0)**	**198 (14·3)**	**186 (20·7)**	**421 (14·6)**	0·031	**< 0·0001**
Low IgG	468 (12·4)	300 (12·5)	168 (12·2)	99 (11·0)	369 (12·8)	0·80	0·18
Low total serum protein	77 (2·0)	58 (2·4)	19 (1·4)	38 (4·2)	39 (1·4)	0·039	**< 0·0001**
Low Hb or Hct	56 (1·5)	46 (1·9)	10 (0·7)	48 (5·4)	8 (0·3)	**0·005**	**< 0·0001**
Others[a]	5 (0·1)	5 (0·2)	(0·0)	1 (0·1)	4 (0·1)	0·21	0·84

[a]Four haematomas, one metacarpal fracture.
IgG, immunoglobulin G; Hb, haemoglobin; Hct, haematocrit.
Bold numbers indicate total numbers and percentages of donors completing the study all drop-outs, main drop-out subcategories and *P*-values below the significance level of 0·01.

IgG threshhold : 5,8 g/l

Hemovigilance – Protein / Immunoglobulin depletion

Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations

Laub et al, Vox Sanguinis, 2010

- Levels of tot
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- Both **recove**
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In comparison to pools of **unpaid EU or US whole-blood or plasmapheresis donors**, pools from **paid US plasmapheresis donors** showed significantly lower:

- total protein (-9%)
- albumin (-15%)
- total IgG (-24%)
- IgM (-28%)
- hemopexin (-11%)
- and retinol-binding protein (-10%)

and higher C1-inhibitor, pre-albumin and C-reactive protein contents.

Hemovigilance – Protein / Immunoglobulin depletion

Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations

Laub et al, Vox Sanguinis, 2010

- Levels of total protein, 15 main relevant plasma protein markers, and anti-B19 and anti-Streptococcus pneumoniae IgG were compared in single-type pools of donations from different countries (Belgium, Finland, France, the Netherlands, Germany, United States).
- Both **recovered plasma from non-remunerated donors** and **apheresis plasma from remunerated and non-remunerated donors** were studied.

First results from the Study on Intensive Plasmapheresis II (SIPLA II)

Kiessig et al, ISBT congress 2013 (Vox Sanguinis, 2013)

- 71,006 donations (65,118 plasma, 4,251 whole blood, 1,637 incomplete donations from **both first-time and experienced donor**s),
- An average of 29.8 plasma donations and 1.9 whole blood donations per donor.
- Total plasma volume per donor of 19.1 L and an average **interval of 9.3±11.2 days between donations.**
- **IgG levels below threshold were in 19.9% of males and in 20.9% of females**
- **Total protein below thresholds in 31.2% o**

Authors reported that results of this study w
first SIPLA trial and the even when first time
plasmapheresis under intensified conditio
appears to be safe.

Unresolved questions:

- How long does it take for a low (depletion-mediated) Ig level to return to a normal level?
- Are there inter-individual variations?
- What are the long term health effects of chronic or intermittent (depletion-mediated) hypo Ig?
- Are there risks associated with the depletion of other known and less know plasma proteins ?

Why do US source plasma donors stop donating?

Fransen et al, Transfusion, 2023

Abstract

Background: In the United States, source plasma (SP) donors can donate up to 104 times per year. Considering the global need for SP and plasma-derived medicinal products, it is critical to maintain the health of frequent donors. This study explores SP donors' self-reported reasons for a lapse in donating.

Study Design and Methods: There were 5608 SP donors from 14 SP centers who enrolled in a longitudinal cohort study to assess self-reported functional health and well-being. Donors were assigned to one of four groups, according to the frequency of SP donation in the 12 months before enrollment. One thousand four hundred forty-eight SP donors who lapsed in donating during 6 months or greater during the study follow-up were asked to complete a survey.

Results: There were 545 lapsed SP donors who returned surveys (37.6%); 63% were female. Most responses given for stopping SP donation were categorized as convenience reasons (69.1%). Self-reported health concerns, including being deferred multiple times, which were categorized as possibly related or unable to determine a relationship to plasmapheresis, represented 45.5% of the responses.

Discussion: Primary reasons US SP donors report for a lapse in donation were categorized as convenience (e.g., schedule conflicts/lack of time). Donor responses categorized as health concerns which have a possible or uncertain relationship to plasmapheresis were less frequent but present in all frequency groups. This study adds to the body of evidence that SP donors cease donating for a variety of self-reported reasons with the majority not directly related to a perceived negative impact on their health.

Reason[a]	Category[b]	All donors		Male donors		Female donors	
		Number of responses	Percentage of responses	Number of responses	Percentage of responses	Number of responses	Percentage of responses
I was deferred multiple times during the screening process	HP	78	14.3	22	11.1	56	16.1
I was concerned about my health	HP	54	9.9	21	10.6	32	9.2
I did not feel well after donating plasma	HP	42	7.7	16	8.0	26	7.5
I was told I had low or abnormal protein levels	HP	35	6.4	10	5.0	25	7.2
Issues with phlebotomy or veins	HP	23	4.2	9	4.5	14	4.0
I had an unexpected reaction donating plasma	HP	10	1.8	5	2.5	5	1.4
A health care provider told me to stop donating	HP	7	1.2	3	1.5	4	1.2
Subtotal (health issues possibly related or unable to determine relationship to plasmapheresis)	Any HP	249	45.5	86	43.2	162	46.6
I found donating plasma was too painful	P	18	3.3	6	3.0	12	3.5

Effects of donation frequency on U.S. source plasma donor health

Fransen et al, Transfusion, 2023

Study Design and Methods: A total of 5608 SP donors from 14 US SP centers were enrolled in a cross-sectional study to assess self-reported health related quality of life (HRQoL) and well-being. By sex, donors were assigned to one of four groups, according to their frequency of SP donation in the 12 months before enrollment. The SF-36v2® Health Survey (SF-36v2) and a survey assessing the frequency of various health conditions that may be associated with impaired immune function over different time periods were used.

Results: There were no statistically significant differences in SF-36v2 scores between any of the donor frequency groups, compared with new donors after controlling for potential confounding and accounting for multiple comparisons among males and females. Cough, cold, occasional fatigue, and sore throat were the most reported health conditions or symptoms, but there was no clear difference among sex or frequency groups.

Finally, the so-called "healthy donor effect" documented in the blood donor literature may be a factor to consider.[29,30] The donors participating in the study self-selected by the SP donation process itself. Thus, we cannot extend our observations to the population from which the donors were drawn; our frequent donors passed multiple health screenings to reach the higher frequency groups. In addition, the commitment to the SP donation program may represent a process by which healthier individuals donate SP, compared with the general population.

Safety and protection of plasma donors: A scoping review and evidence gap map

Schroyens et al, Vox Sanguinis, 2023

Identifying the existing evidence (gaps) on adverse events (AEs) and other health effects in plasmapheresis donors, as well as factors that may be associated with such events/effects.

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such events/effects.

- Ninety-four research articles and five registrations were identified.
- **Around 90% were observational studies**
- Ten studies investigating the association between donation frequency and donor health, only one experimental study
- More than 30 studies analyzed donors during or after a specified period (1 month–23 years) in which multiple donations were given (without control group in 10).
- Among the controlled studies, the majority were observational (n = 16) and retrospective (n = 11).
- **Such studies are often subject to bias**, given that long-term donors are self-selected to withstand the donation frequency under evaluation.
- **Studies on preventive interventions against AEs or other health effects are scarce**

Safety and protection of plasma donors: A scoping review and evidence gap map

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Scoping review - Take home messages?

Research gaps

- Preventive measures
- Factors potentially affecting the occurrence of adverse events
- Long-term health effects of plasma donation
- Different donation frequencies and the effect on donor safety

Future directions

More high-quality controlled ((quasi-)experimental) studies

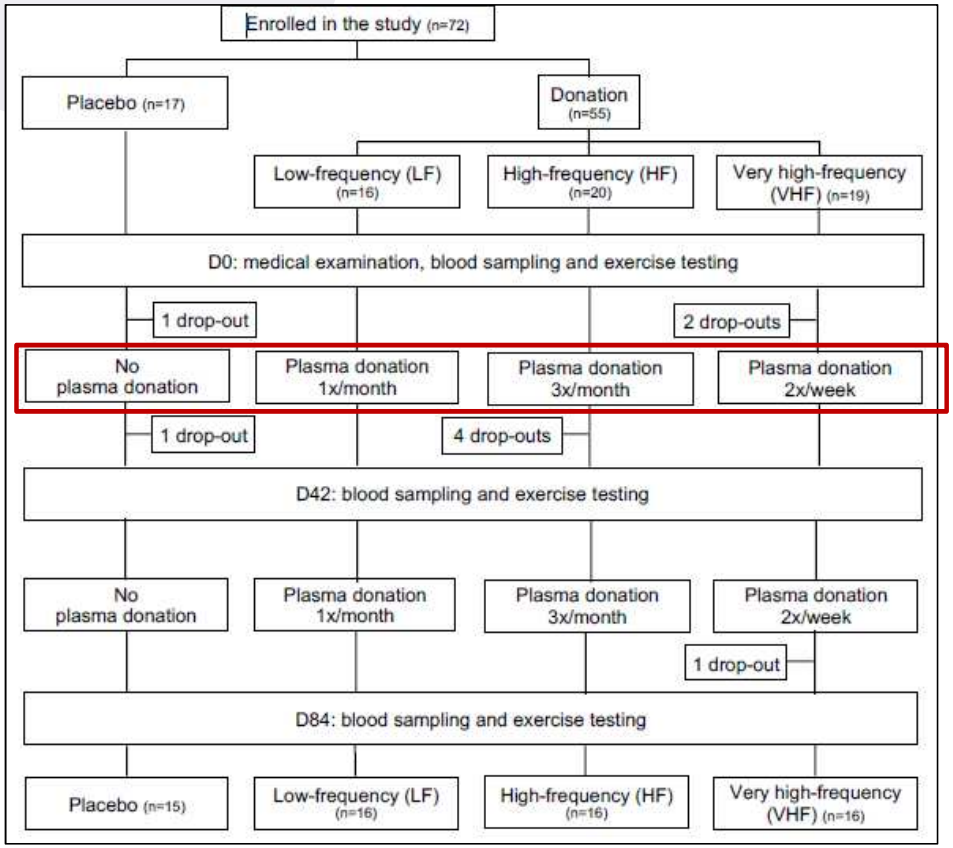
SUPPLY | Co-funded by the European Union

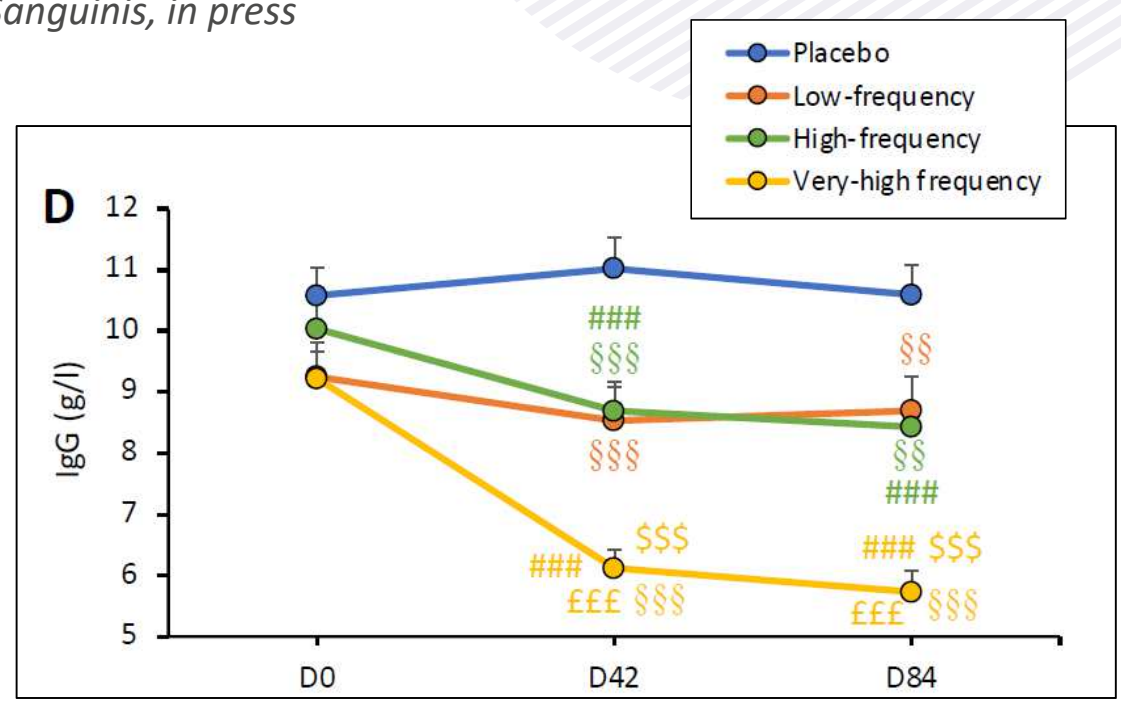
This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union.
The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Protein / immunoglobulin depletion in plasma donors: relation with donation frequency

Effects of plasmapheresis frequency on health status and exercise performance in men: a randomized controlled trial

Mortier et al, MedRxiv, 2023, Vox Sanguinis, in press





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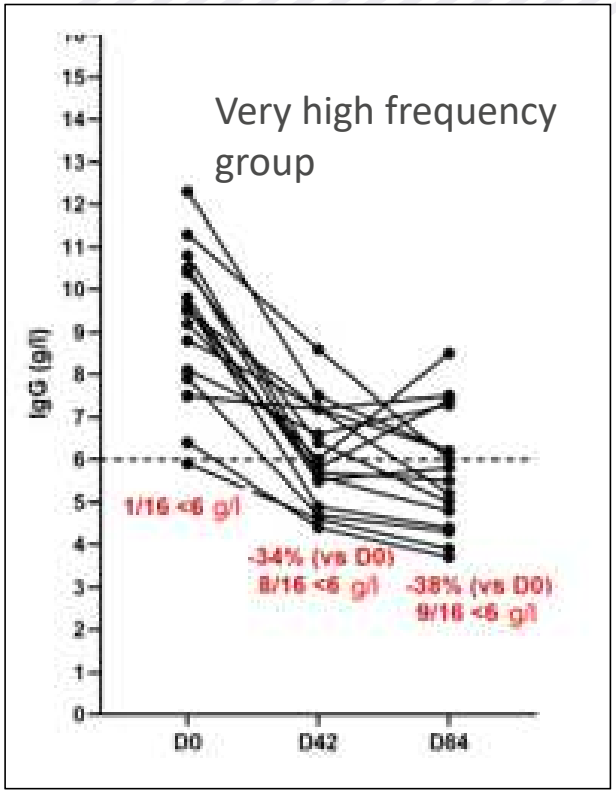
- In the **very high frequency group**, albumin, IgG, IgA and IgM levels dropped from D0 to D42 and remained lower at D84 than D0. **The IgG level fell below the 6g/liter in 9 /16 donors**
- In the **high frequency group**, IgG, IgA and IgM levels were lower at D42 and IgG and IgM were lower at D84 compared to D0.
- In the **low frequency group**, IgG levels were lower at day 42 compared to D0
- In the **very high frequency group**, red blood cells, haemoglobin and haematocrit levels decreased while reticulocyte levels increased from D0 to D84
- Repeated plasma donation had **no effect on blood pressure, body composition or exercise performance**.



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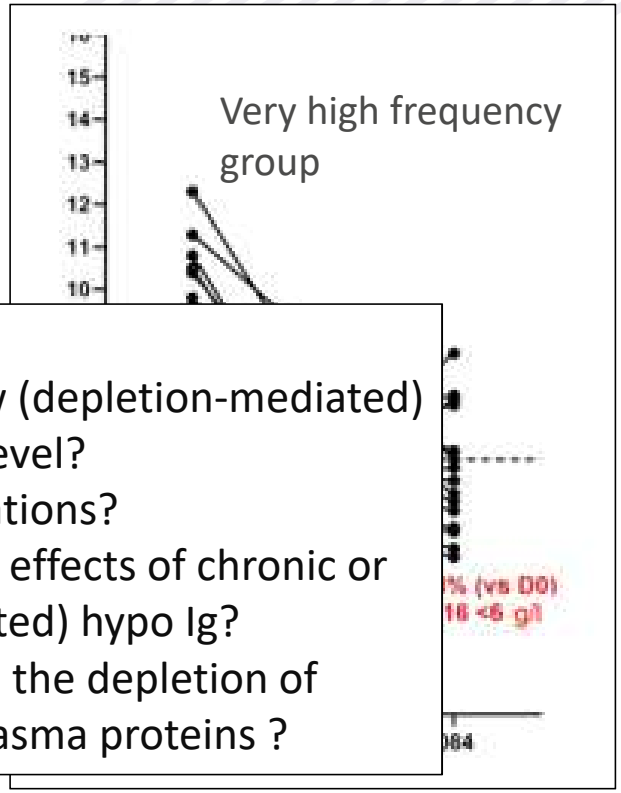

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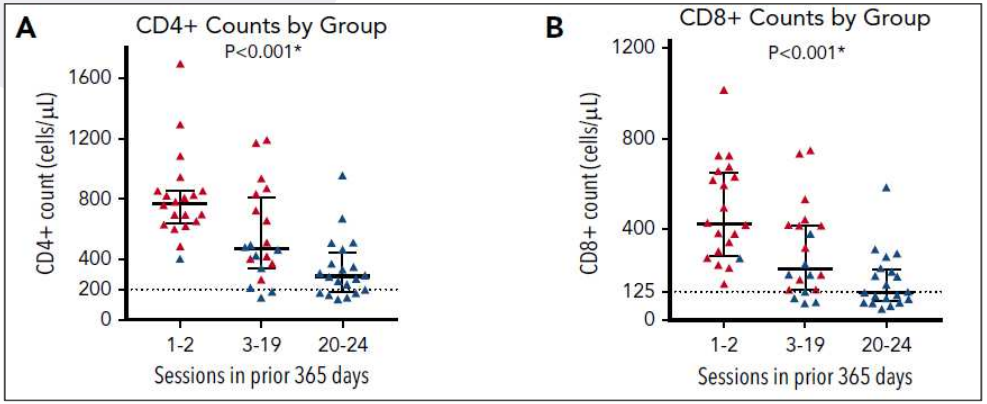
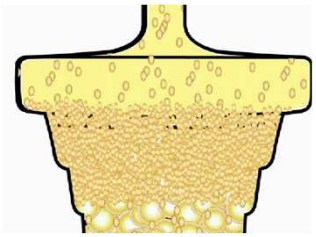
Lymphopenia in platelet donors: long-term effects on donor health?

Plateletpheresis-associated lymphopenia in frequent platelet donors

Gansner et al, Blood, 2018





Leukoreduction system (LRS) chamber (elutriation)

Frequent platelet donation is associated with lymphopenia and risk of infections: A nationwide cohort study

Zhao et al, Transfusion, 2021

Linkage between the Swedish portion of the Scandinavian Donations and Transfusions (SCANDAT3-S) database and the national patient register (which had complete nationwide coverage of in-hospital and hospital-associated out patient care).

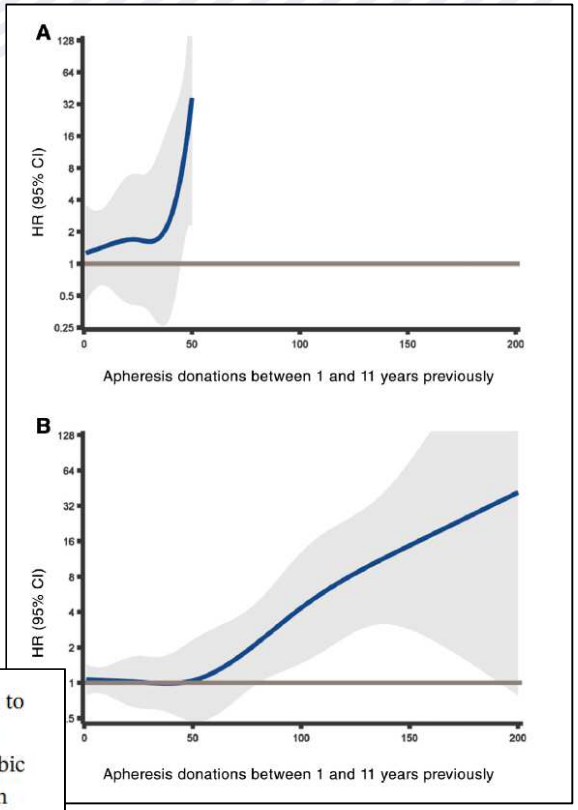


FIGURE 2 Risk of infections comparing LRS donations to non-LRS donations, in relation to number of past donations between 1 and 11 years previously modeled as a restricted cubic spline. A, Immunosuppression-related infections. B, Common bacterial infections. The range of the y axes is restricted to 128 for legibility [Color figure can be viewed at wileyonlinelibrary.com]

A European Health Data Space (EHDS) to facilitate the access to secondary health data across the EU

Main objectives of the European Health Data Space

- Proposal by the **European Commission**
- Regulation creating the **European Health Data Space** (EHDS) - May 2022

A **health-specific ecosystem** comprised of rules, common standards and practices, infrastructures and a governance framework that aims **to facilitate data exchange of health data** in the EU, with two dimensions:

- **Allowing easier access to personal health data for citizens that can be shared with health professionals anywhere in the EU.**
  - Member States will ensure that patient summaries, ePrescriptions, images, … are issued and accepted in a common European format.
  - Interoperability and security will become mandatory requirements.
- **Improving the use of health data across the EU for researchers, public institutions and industry.**
  - Connection of health data access bodies to the new decentralised **EU-infrastructure for secondary use (HealthData@EU**) which will be set up to support cross-border projects.

https://ec.europa.eu/commission/presscorner/detail/en/ip_22_2711

A European Health Data Space (EHDS) to facilitate the access to secondary health data across the EU

With the help of the upcoming Substances of Human Origin (SOHO) regulation?

- Proposal for a regulation on standards of quality and safety for SOHO intended for human application (European Commission – July 2022): SOHO regulation
- To replace the **Blood / Tissues and Cells Directives** (2002 / 2004)

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EUROPEAN BLOOD ALLIANCE

EBA submission on the European Health Data Space proposal, 26 July 2022

- EBA **welcomes this proposal**
- Long-standing request for **more and better data to increase donor protection and reinforce patient care**
- Calling on the EU and Member States to **reinforce donor vigilance requirements** through **a pan-European donor vigilance program**.
- Reporting of data on Substances of Human Origin (SOHO) should be further developed to provide **public access to key anonymized data on European registries**
- **EHDS regulation and the SoHO Regulation need to be well aligned**
- Necessity to include methods to **unambiguously identify and trace individuals (donors or transfused patients) as they come in contact with the health care system**
- However, implementing must ensure that **EHDS does not become a burden to healthcare professionals**
- Lastly, concerns regarding **varying interpretation** of the **General Data Privacy Regulation** (GDPR) across EU countries that may hinder data sharing.

https://europeanbloodalliance.eu/resources/eba-response-the-european-commissions-proposal-for-a-european-health-data-space-ehds-july-2022/

EUROPEAN BLOOD ALLIANCE

High frequency plasmapheresis and donor health – Absence of evidence is not equal to evidence of absence

Hans Van Remoortel, Katja van den Hurk, Veerle Compernolle, Peter O'Leary, Pierre Tiberghien, Christian Erikstrup