

The supply of plasma-derived medicinal products in the future of Europe

Second edition

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Donor Protection

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Disclosure

- Employed by Sanquin
- BEST Collaborative Scientific Member
- Vox Sanguinis Editorial Board Member



SUPPLY WP5: Plasma donor protection: best practices

Objective: To facilitate evidence-based plasma donor protection practices

1. Inventory of plasma donor protection practices
2. Evaluation of available evidence on plasma donation and health
3. Design a support tool on standardized donor vigilance data
4. Develop recommendations

D5.1: Inventory of plasma donor protection practices

Katja van den Hurk / Marloes Spekman, Sanquin

Survey based on previous IPFA survey, covering plasma collection, donor selection, donation procedures, vigilance, registration.

- 18 complete responses from 17 countries.
- **Donation Frequency:** Annual limits from 12 (Lux), 26 (NL), 60 (Ger) to 104 (US).
- **Selection Criteria:** Suitability (veins, tolerance), weight/height/blood volume, Hb, medication/drug use, etc.
- **Donation Procedure:** 10 different apheresis machines used. Volume limit: 400 to 896 mL, 12 organizations with sex, weight, and height-based volumes. Citrate-based anticoagulants used with varying citrate percentages. Flow rates vary.
- **Adverse Events:** Prevention methods: Hydration advice (12 organizations), trained staff (7 organizations), attention to new donors (5 organizations). Vigilance systems in place; multiple adverse event recording with severity grading.
- **Testing:** TP levels (all, with varying limits). Some: IgG, irregular antibodies, ferritin, HLA, cell counts.

T5.2: Evaluation of evidence – systematic review

Impact of plasmapheresis frequency on donor health / safety?

Studies finally included:

- 4 observational studies
- 1 RCT and 1 non-randomised trial
- 1 ongoing RCT (Haugen et al., Norway)



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Balancing donor health and plasma collection: a systematic review of the impact of plasmapheresis frequency

Tine D'aes^{a,b}, Katja van den Hurk^{c,d}, Natalie Schroyens^{a,b}, Susan Mikkelsen^e, Pieter Severijns^a,
Emmy De Buck^{a,b}, Peter O'Leary^f, Pierre Tiberghien^{g,h}, Veerle Compennolle^{ij}, Christian Erikstrup^{e,k},
Hans Van Remoortel^{a,b}

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

Alexandre Mortier¹ | Jina Khoudary² | Sophie van Dooslaer de Ten Ryen¹ | Camille Lannoy¹ | Nicolas Benoit¹ | Nancy Antoine¹ | Sylvie Copine¹ | Hans Van Remoortel^{3,4}  | Philippe Vandekerckhove^{2,4} | Veerle Compennolle^{2,5} | Louise Deldicque^{1,6} 

The RCT - IgG levels

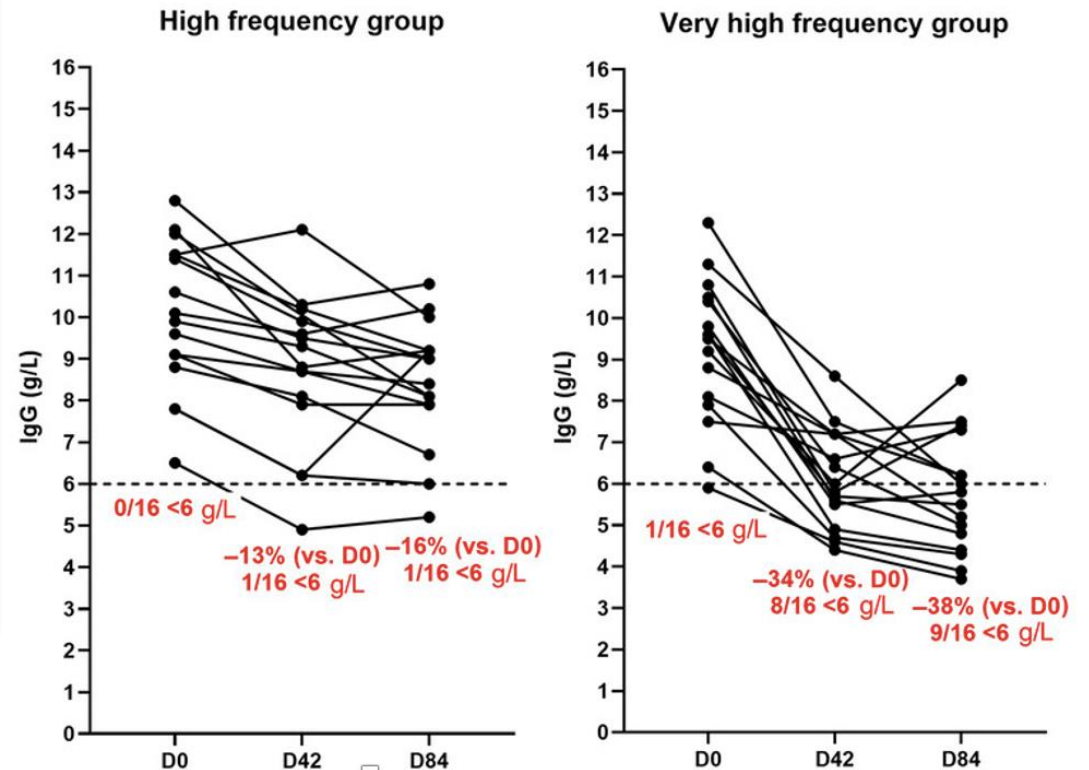
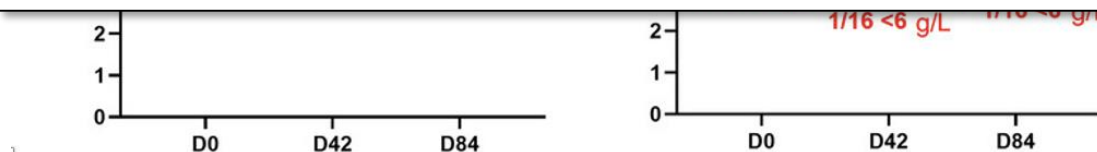
IgG decrease 38% at VHF (2/wk)

IgG decrease 16% at HF (3/M)

This well-designed study is small (n=63), short (3M)) and not designed to assess hard endpoints. LF=1/M.

- Few adverse events
- No effect on blood pressure, body composition or exercise performance.
- Hb, ferritin, IgG severely impacted at VHF, mildly impacted at HF and not impacted at LF.

Only men included!



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

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The non-randomized SIPLA

- 3,783 donors were switched from moderate to intensive plasma donations: up to 60/year for 3 years.
- No control group!
- 16% excluded for IgG, TP, or Hb below threshold levels.

Conclusion: Intensive donation safe when monitored as in the study.

”The incidence in severe cardiovascular diseases was lower in donors than in the general population”.

Table 4 Initial and final immunoglobulin G, total serum protein and Hb values and number of donors below respective thresholds in the 923 donors who completed the study

	Initial values	Final values	P-value
Females, <i>n</i> = 193			
IgG, g/l	8.8 (5.3–16.4)	8.0 (4.7–18.8)	< 0.0001 ^a
Number of donors with IgG below 5.8 g/l	2	7	0.17 ^b
TSP, g/l	68 (58–77)	69 (58–81)	0.45 ^a
Number of donors with TSP below 60 g/l	1	6	0.12 ^b
Hb, g/l	133 (120–162)	134 (116–160)	0.35 ^a
Number of donors with Hb below 115 g/l	0	0	1.0 ^b
Males, <i>n</i> = 730			
IgG, g/l	8.7 (5.5–16.0)	7.9 (5.0–17.0)	< 0.0001 ^a
Number of donors with IgG below 5.8 g/l	2	32	< 0.0001 ^b
TSP, g/l	69 (60–82)	70 (60–88)	0.10 ^a
Number of donors with TSP below 60 g/l	0	0	1.0 ^b
Hb, g/l	147 (121–171)	149 (117–184)	0.001 ^a
Number of donors with Hb below 115 g/l	0	0	1.0 ^b

Data are expressed as median values (minimum–maximum).

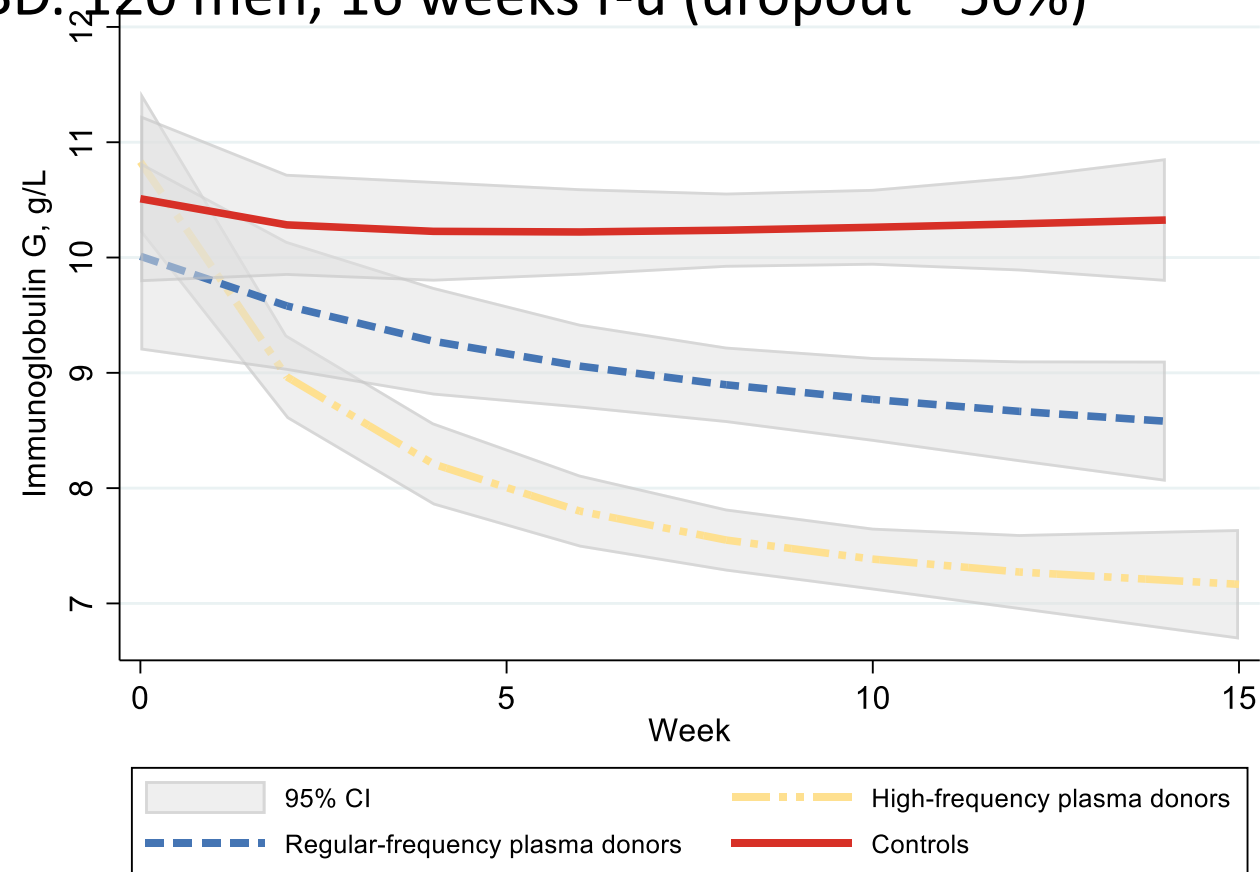
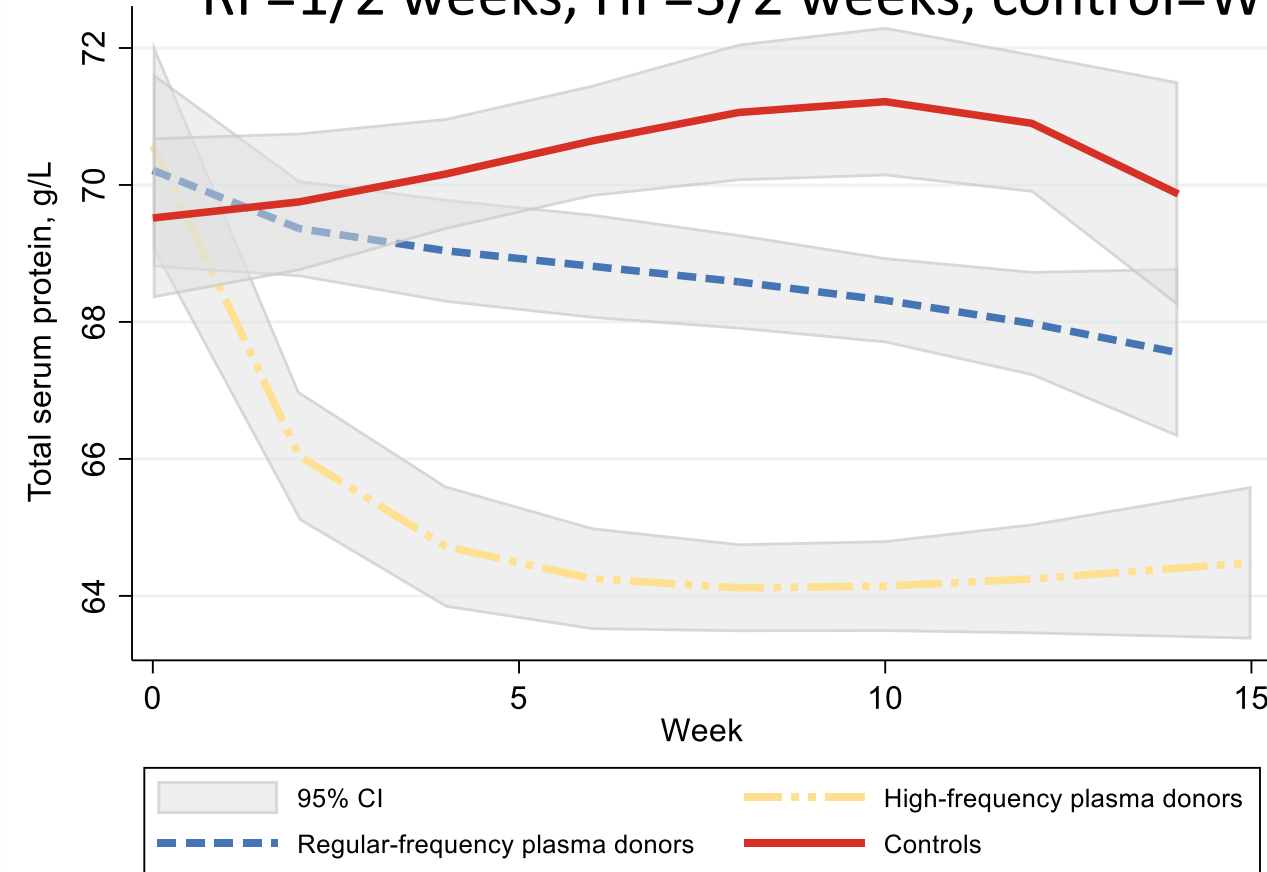
^aWilcoxon matched pairs test; ^bFisher's exact test.

IgG, immunoglobulin G; TSP, total serum protein; Hb, haemoglobin.

The unpublished RCT - confidential

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RF=1/2 weeks, HF=3/2 weeks, control=WBD. 120 men, 16 weeks f-u (dropout ~50%)



Papers published after the systematic review

Fransen M. et al., Transfusion 2023: Effects of donation frequency on U.S. source plasma donor health.

SRQL assessed in 5,608 plasmapheresis donors, 14 US centers.

No differences in SRQL across donation frequency groups compared with new donors.

Conclusion: Remunerated,
high-frequency donations are safe.

BUT: Healthy Donor Effect may
counteract negative effects.

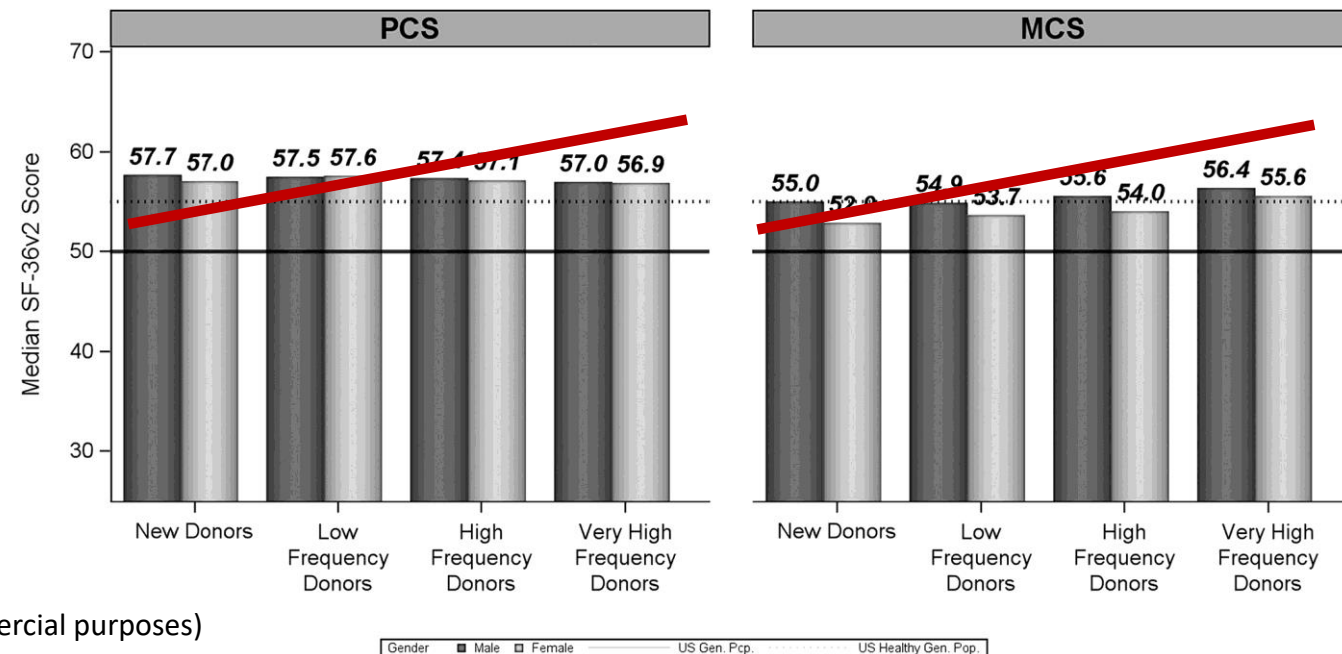


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Continued: Papers published after the systematic review

Fransen M. et al., Transfusion 2023: Why do US source plasma donors stop donating?

- Survey among 545 lapsing (6M) plasmapheresis donors
- Primary reason to stop: “convenience” (schedule/time conflicts, n = 377, 69.1%),
- Less-frequent: self-reported health concerns, possible/uncertain relationship to plasmapheresis (45.5%)

Conclusion: Additional evidence supporting the safety of frequent plasmapheresis (up to 104/year)

BUT: 45.5% is far from negligible

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COMMENTARY	TRANSFUSION
Very-high frequency plasmapheresis and donor health –absence of evidence is not equal to evidence of absence	
Hans Van Remoortel ^{1,2} Katja van den Hurk ^{3,4} Veerle Compernelle ^{5,6} Peter O’Leary ⁷ Pierre Tiberghien ^{7,8,9} Christian Erikstrup ^{10,11}	

D5.3: Develop recommendations on plasma donor health protection

- Adherence to Blood Guide (21st edition 2023) awaiting further evidence.
- Based on expert opinion, reflecting the view of a WP5 majority*: **max 2 plasma donations/month**, pending evidence confirming the safety of higher frequencies.

**Alternative recommendation, supported by two WP5 members: max 2 plasma donations/month, unless a donor health and IgG management system is established.*

- IgG levels should be monitored (evidence optimal IgG algorithms/ intervals lacking!).
- Prospective studies on health effects of varying plasma donation frequencies needed.
- Implementation of register for standardized haemovigilance data > mandatory basis.
- These recommendations stem from the precautionary principle, prioritizing donor safety until more evidence is available.

Thank you!



Belgian
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Evidence-based
by **CEBaP**

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