Plasma donation: Collection volumes and donor safety

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Plasma national needs (tons)

...

2020

2015

600

Recovered plasma

550-600

300

200

Source plasma

Plasmapheresis vs Whole Blood Donation

Plasmapheresis	Multicomponent apheresis	Whole blood donation
30 – 60 min.	20 – 70 min.	7 – 15 min.
Multiple cycles	Multiple cycles	Single phase collection
600 – 700 ml collected	Max 700 ml collected	405 – 495 ml collected
Gradual intravascular volume changes	Gradual intravascular volume changes	Rapid intravascular volume changes
Compensatory transcapillary refilling may occur during the procedure (0,5 – 2 ml/min.)	Compensatory transcapillary refilling may occur during the procedure (0,5 – 2 ml/min.)	Minimal compensatory transcapillary refilling during the procedure
Can include IV procedural volume replacement	Can include IV procedural volume replacement	No procedural volume replacement
Only plasma collected	Erythrocytes and/or platelets and/or plasma are collected	Erythrocytes, platelets, leucocytes, plasma are collected
Erythrocytes (almost) entirely returned to donor	Selective return. Possible reduction of erythrocytes and iron	Reduction of erythrocytes and iron
Small amount of AC returned to donor	Small amount of AC returned to donor	No AC returned to donor

Top perceived deterrents to plasmapheresis

WB ⟹✗⟸ P

WB ➡ P ➡ WB

WB ➡ P ➡ Stop

Group type	Deterrent	Number of individuals (% of sample)
DTC		
1	Apheresis donation process takes longer than WB	20 (56)
2	Expectation of donation frequency	15 (42)
3	Uncomfortable about the idea of blood replacement*	13 (36)
4	Being unclear about the plasmapheresis donation process*	12 (33)
5	Difficulty scheduling appointments	9 (25)
5	Fear of contamination of returned fluid*	9 (25)
LWB		
1	Apheresis donation process takes longer than WB	11 (41)
2	Impact on general well-being from such donations*	10 (37)
2	Excessive questioning or paperwork	10 (37)
3	Expectation of donation frequency	9 (33)
4	Eligibility requirements of plasmapheresis donation	8 (30)
5	Disorganized; unexpected delays*	5 (19)
LFP		
1	Excessive questioning or paperwork	17 (63)
2	Difficulty scheduling appointments	12 (44)
2	Being too busy*	12 (44)
2	Donating not top of mind*	12 (44)
2	Experiencing veins difficult to find*	12 (44)
3	Eligibility requirements of plasmapheresis donation	11 (41)
3	Apheresis donation process takes longer than WB	11 (41)
4	Opening hours*	10 (37)
5	Change of routine*	7 (26)

* Deterrent only appearing in the top five of this group.

Bagot 2013

Recruitment and retention strategies

- Focus on providing relevant and sufficient **information** and **educating** donors on the additional value of plasmapheresis donation to the collection agency, wider community, patients and him/her self.
- Emphasize **safety** of plasmapheresis donation, including the return process.
- Ensure **positive early experiences** with additional attention, including efficiency of the pre-donation process, providing an experienced phlebotomist and reducing perceptions of donation time.
- Offer **flexibility in scheduling** plasmapheresis appointments, tailoring to suit donors' varying schedules, initially mimiking WB frequency.
- Follow-up promptly to keep donation salient for donors to support **regular donation patterns**

Bagot 2013

Decree november 2nd 2015

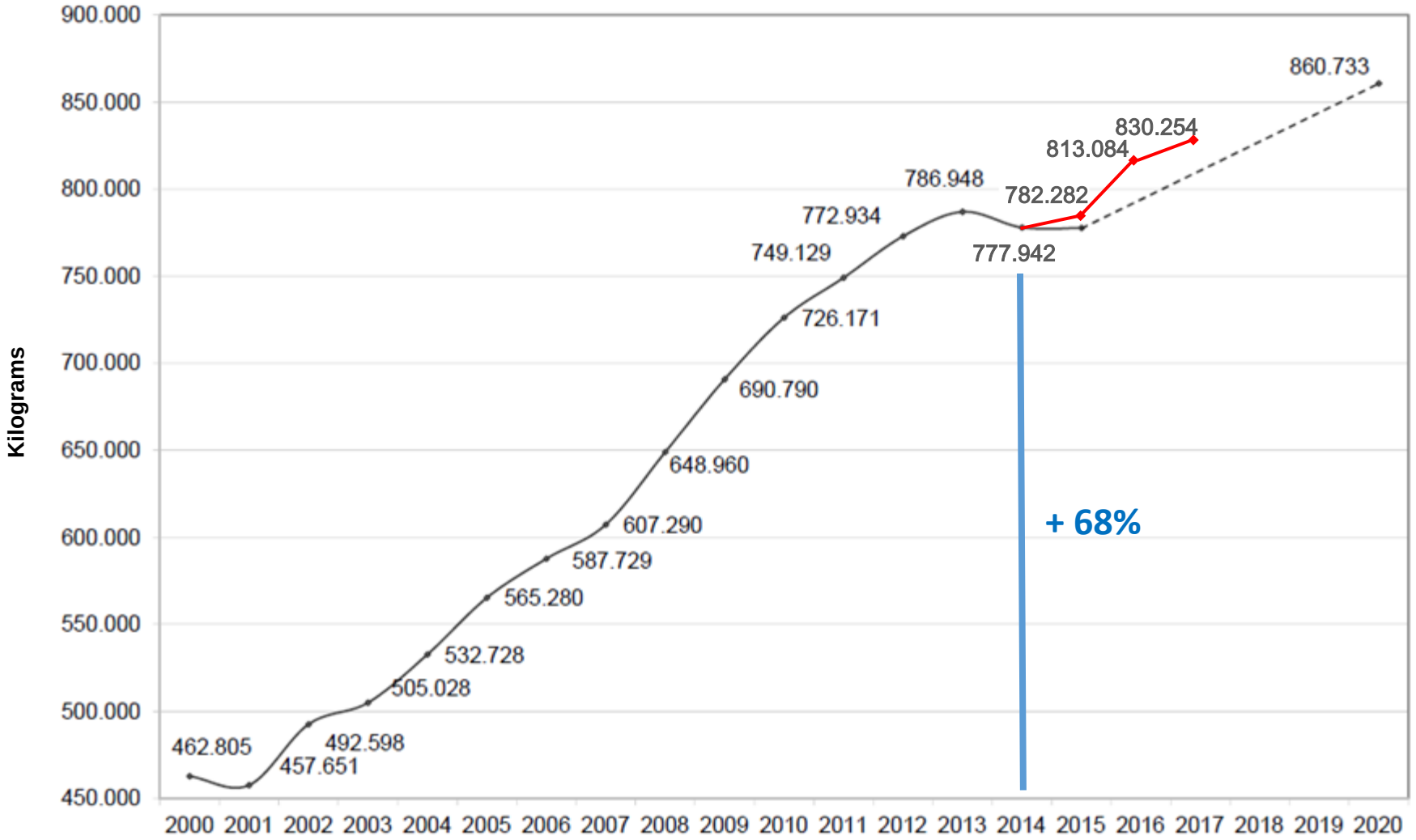
Art. 2.

Donor awareness raising and information

1. Voluntary blood donor Associations and Federations, blood establishments and collection units make available to donors **informative material** that is accurate and properly clear for donor **awareness raising and information** about the value of voluntary, non remunerated, conscious and periodic donation.

Plasma volumes issued to fractionation

Italy, 2000-2020



Plasma and PDMP programme, 2016-2020
CNS, G. Calizzani, F. Candura, 2018

Transfusion activity: quantitative indicators Italy, 2015-2017

	2015	2016	2017
Donations (whole blood+apheresis)/1000 pop	50,36	50,0	49,6
Donations (whole blood+apheresis)/Total donors N.	1,78	1,8	1,8
Whole blood donations/1000 pop	42,38	42,4	42,6
Whole blood donations/Whole blood donors N.	1,63	1,6	1,6
Apheresis donations/1000 pop	7,98	7,6	7,0
Apheresis donations/Apheresis donors N.	2,08	2,1	2,1

Rapporti ISTISAN 16/38
Programma di autosufficienza nazionale, 2017
CNS (L. Catalano 2017 - 2018)

Transfusion activity: yearly variations (%)
Italy, 2014-2017

	2014 - 15	2015 - 16	2016 - 17
New donors	+ 5,8	+ 4,0	- 4,0
Donor population	+ 0.3	- 1.7	- 0,4
Whole blood donations	- 0.4	0	+ 0,1
Plasmapheresis donations	- 1.2	- 4.8	- 6,2

Rapporti ISTISAN 16/38
Programma di autosufficienza nazionale, 2017
CNS (L. Catalano 2017 - 2018)

Plasma collection by apheresis

Decree march 3rd 2005, annex 1

450 ml minimum volume, 600-650 ml maximum (excluding anticoagulant),
max 1,5 l /month,
max 10 l /year.

14 days minimal lapse between two plasma donations.

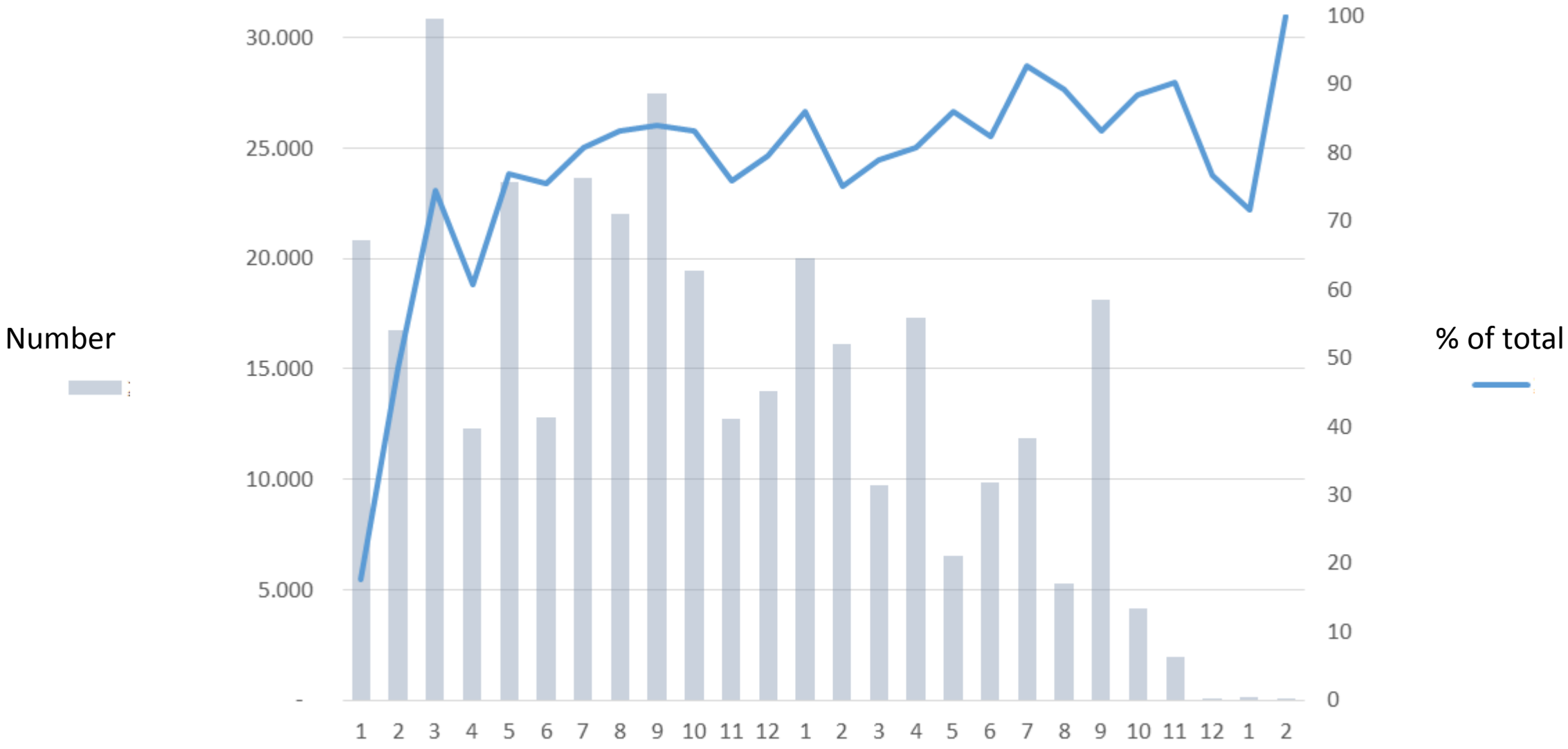
Decree november 2nd 2015, annex IV - V

600 ml minimum volume, 700 ml maximum (excluding anticoagulant),
max 1,5 l /month,
max 12 l /year.

14 days minimal lapse between two plasma donations.

Source plasma units sent to fractionation (≥ 667 g)

Italy, gen 2016 – feb 2018, per month



CNS, G. Calizzani, 2018

Principles of donor selection
Frequency of apheresis donation and maximal amount of collected plasma

Donor Weight / TBV	ECVmax	Collection Volume
• TBV of each donor should be estimated based on gender, height and weight[2] • Alternatively, collection volume based on 10.5 mL/kg of body weight broadly equates to 16% of estimated TBV	• Must never be higher than 20% of TBV with a recommended guidance of 16%	• Excluding anticoagulant, must not exceed 16% of TBV • Should not exceed 750 mL unless fluid replacement is undertaken

For donors weighing 50-65 kg, the total blood volume should be estimated.

Current recommendations are made in the absence of conclusive studies of outcomes from different regimes of volumes and frequencies of plasmapheresis. Despite some data being available from studies with several years of follow-up, further short- and long-term prospective studies are needed and should be undertaken.

EDQM, 19th Edition 2017, Chapter 2

Table 1. Blood volume of women in mL as calculated according to the ICSH formula[1]

The weights and heights corresponding to the minimum acceptable blood volumes of 3 233 mL, 3 400 mL and 3 567 mL are indicated with grey backgrounds.

kg	50	51	52	53	54	55	56	57	58	59
145 cm	3141	3167	3193	3219	3244	3269	3294	3319	3343	3367
146 cm	3157	3183	3209	3235	3260	3285	3310	3335	3359	3384
147 cm	3172	3199	3225	3251	3276	3301	3327	3351	3376	3400
148 cm	3187	3214	3240	3266	3292	3318	3343	3368	3392	3417
149 cm	3203	3230	3256	3282	3308	3334	3359	3384	3409	3433
150 cm	3218	3245	3272	3298	3324	3350	3375	3400	3425	3450
151 cm	3234	3261	3287	3314	3340	3366	3391	3416	3441	3466
152 cm	3249	3276	3303	3329	3356	3381	3407	3433	3458	3483
153 cm	3264	3291	3318	3345	3371	3397	3423	3449	3474	3499
154 cm	3279	3307	3334	3361	3387	3413	3439	3465	3490	3515
155 cm	3295	3322	3349	3376	3403	3429	3455	3481	3506	3532
156 cm	3310	3337	3365	3392	3418	3445	3471	3497	3523	3548
157 cm	3325	3353	3380	3407	3434	3461	3487	3513	3539	3564
158 cm	3340	3368	3396	3423	3450	3476	3503	3529	3555	3581
159 cm	3355	3383	3411	3438	3465	3492	3519	3545	3571	3597
160 cm	3370	3399	3426	3454	3481	3508	3535	3561	3587	3613
161 cm	3385	3414	3442	3469	3497	3524	3550	3577	3603	3629
162 cm	3400	3429	3457	3485	3512	3539	3566	3593	3619	3645
163 cm	3416	3444	3472	3500	3528	3555	3582	3609	3635	3661
164 cm	3430	3459	3487	3515	3543	3571	3598	3625	3651	3677
165 cm	3445	3474	3503	3531	3559	3586	3613	3640	3667	3693
166 cm	3460	3489	3518	3546	3574	3602	3629	3656	3683	3709
167 cm	3475	3504	3533	3561	3589	3617	3645	3672	3699	3726
168 cm	3490	3519	3548	3577	3605	3633	3660	3688	3715	3741

kg	50	51	52	53	54	55	56	57	58	59
169 cm	3505	3534	3563	3592	3620	3648	3676	3703	3731	3757
170 cm	3520	3549	3578	3607	3636	3664	3692	3719	3746	3773
171 cm	3535	3564	3593	3622	3651	3679	3707	3735	3762	3789
172 cm	3550	3579	3608	3637	3666	3695	3723	3750	3778	3805
173 cm	3564	3594	3624	3653	3681	3710	3738	3766	3794	3821
174 cm	3579	3609	3638	3668	3697	3725	3754	3782	3809	3837
175 cm	3594	3624	3653	3683	3712	3741	3769	3797	3825	3853
176 cm	3608	3639	3668	3698	3727	3756	3784	3813	3841	3868
177 cm	3623	3653	3683	3713	3742	3771	3800	3828	3856	3884
178 cm	3638	3668	3698	3728	3757	3786	3815	3844	3872	3900
179 cm	3652	3683	3713	3743	3772	3801	3830	3859	3887	3916
180 cm	3667	3698	3728	3758	3787	3816	3845	3875	3903	3931
181 cm	3682	3712	3743	3773	3803	3832	3861	3890	3919	3947
182 cm	3696	3727	3758	3788	3818	3847	3876	3905	3934	3962
183 cm	3711	3742	3772	3803	3833	3862	3892	3921	3950	3978
184 cm	3725	3756	3787	3818	3848	3878	3907	3936	3965	3994
185 cm	3740	3771	3802	3832	3863	3893	3922	3952	3981	4009

> 3750 ml

%	ml
16 : 100 = 600 : X (TBV)	
X (TBV) = 3750 ml	
20% = 750 ml	

EDQM, 19th Edition 2017, Appendix 2

kg	60	61	62	63	64	65	66	67	68	69
145 cm	3391	3414	3438	3461	3484	3507	3529	3552	3574	3596
146 cm	3408	3431	3455	3478	3501	3524	3547	3569	3591	3613
147 cm	3424	3448	3472	3495	3518	3541	3564	3587	3609	3631
148 cm	3441	3465	3489	3512	3535	3558	3581	3604	3627	3649
149 cm	3458	3482	3505	3529	3552	3576	3599	3622	3644	3667
150 cm	3474	3498	3522	3546	3570	3593	3616	3639	3662	3684
151 cm	3491	3515	3539	3563	3587	3610	3633	3656	3679	3702
152 cm	3507	3532	3556	3580	3604	3627	3650	3674	3697	3719
153 cm	3524	3548	3573	3597	3621	3644	3668	3691	3714	3737
154 cm	3540	3565	3589	3614	3638	3661	3685	3708	3731	3754
155 cm	3557	3581	3606	3630	3654	3678	3702	3725	3749	3772
156 cm	3573	3598	3623	3647	3671	3695	3719	3743	3766	3789
157 cm	3590	3615	3639	3664	3688	3712	3736	3760	3783	3807
158 cm	3606	3631	3656	3681	3705	3729	3753	3777	3801	3824

kg	60	61	62	63	64	65	66	67	68	69
159 cm	3622	3647	3672	3697	3722	3746	3770	3794	3818	3841
160 cm	3639	3664	3689	3714	3739	3763	3787	3811	3835	3859
161 cm	3655	3680	3705	3730	3755	3780	3804	3828	3852	3876
162 cm	3671	3697	3722	3747	3772	3797	3821	3845	3869	3893
163 cm	3687	3713	3738	3764	3789	3813	3838	3862	3886	3910
164 cm	3703	3729	3755	3780	3805	3830	3855	3879	3903	3928
165 cm	3720	3746	3771	3797	3822	3847	3872	3896	3921	3945
166 cm	3736	3762	3788	3813	3839	3864	3888	3913	3938	3962
167 cm	3752	3778	3804	3830	3855	3880	3905	3930	3955	3979
168 cm	3768	3794	3820	3846	3872	3897	3922	3947	3972	3996
169 cm	3784	3810	3837	3862	3888	3914	3939	3964	3988	4013
170 cm	3800	3827	3853	3879	3905	3930	3955	3981	4005	4030
171 cm	3816	3843	3869	3895	3921	3947	3972	3997	4022	4047
172 cm	3832	3859	3885	3911	3937	3963	3989	4014	4039	4064
173 cm	3848	3875	3901	3928	3954	3980	4005	4031	4056	4081
174 cm	3864	3891	3918	3944	3970	3996	4022	4047	4073	4098
175 cm	3880	3907	3934	3960	3987	4013	4039	4064	4090	4115
176 cm	3896	3923	3950	3977	4003	4029	4055	4081	4106	4132
177 cm	3912	3939	3966	3993	4019	4046	4072	4097	4123	4148
178 cm	3927	3955	3982	4009	4036	4062	4088	4114	4140	4165
179 cm	3943	3971	3998	4025	4052	4078	4105	4131	4156	4182
180 cm	3959	3987	4014	4041	4068	4095	4121	4147	4173	4199
181 cm	3975	4003	4030	4057	4084	4111	4137	4164	4190	4216
182 cm	3991	4018	4046	4073	4100	4127	4154	4180	4206	4232
183 cm	4006	4034	4062	4089	4117	4143	4170	4197	4223	4249
184 cm	4022	4050	4078	4105	4133	4160	4187	4213	4239	4266
185 cm	4038	4066	4094	4121	4149	4176	4203	4229	4256	4282

> 3750 ml

%	ml

16 : 100 = 600 : X (TBV)

X (TBV) = 3750 ml

20% = 750 ml

EDQM, 19th Edition 2017, Appendix 2

Plasmapheresis volume and frequency International overview

	Max plasma volume (ml)	AC	Minimal lapse between two donations (hours-days)	Max donations/year (N)	Max volume/year (L)
Australian Red Cross Blood Service 2012	800	excluded	14 d	26	≈ 21
FDA / CBER Guidelines 1992	880	included	48 h	104	≈ 78
EDQM 19th Edition 2017	750	excluded	48 h	33	25
German Guidelines 2017	850	included	48 h	60	≈ 45
French Arrêté 2017	750	excluded	14 d	24	≈ 18
Italian Decree 2015	700	excluded	14 d	≈ 20	12

Intermittent flow plasmapheresis (IFP) and Extra-corporeal volume (ECV)

- ECV(max) during donation **does not reliably predict the degree of hypovolemic stress**, as long as it remains below 20 % TBV (14,0 ml per Kg body weight).
- Plasmpheresis donors need not be deferred if ECV exceeds 16% TBV (10,5 ml per Kg body weight).

Karger 2006

- Hemodynamic response to intravascular volume changes of up to ≈ 20% of TBV in the setting of IFP **is sufficient to maintain cardiac function**.
- Administration of **volume replacement** as part of the source plasmapheresis donation process, using procedural saline or oral fluids, **results in a net end-ECV well below any** of the presented single unit whole blood or source plasma collection volume **guidelines**.

Becker 2015

Systemic Adverse Events

Whole blood or Apheresis donation:

Blood volume loss

- Hypotension
- Vasovagal reactions (VVR)

VVR per donation type

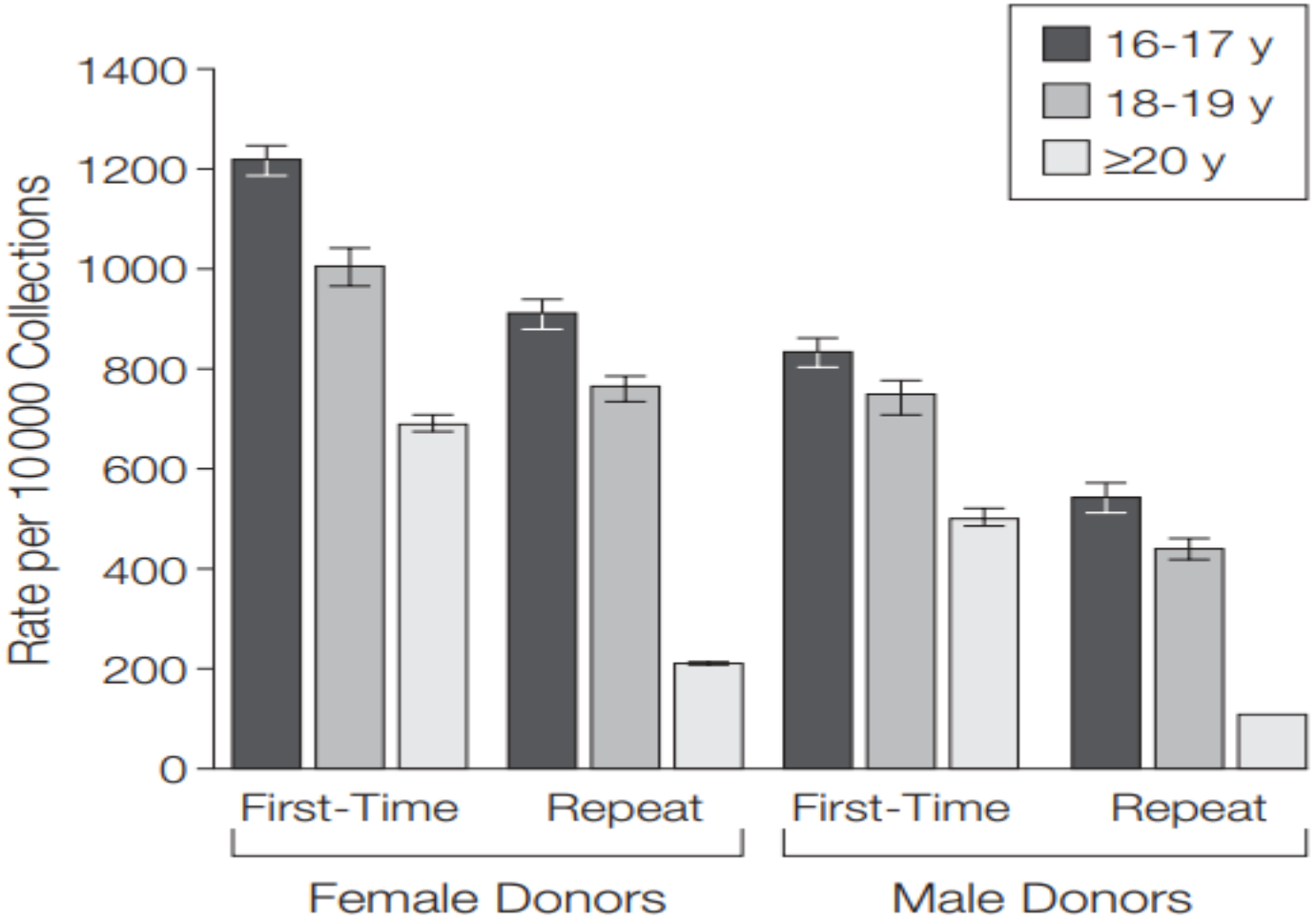
	VVR (%)
Whole blood	0,1 - 0,5
Plasmapheresis	0,2 - 0,5
Platelet apheresis	0,6 - 0,8

Despotis 1999, Crocco 2009, Amrein 2012, Burkhardt 2015

Immediate reactions	OR
Apheresis vs whole blood	1,53 (1,38-1,70) P < 0,0001
Delayed reactions	**OR**
Apheresis vs whole blood	1,61 (1,11-2,32) P < 0,0001

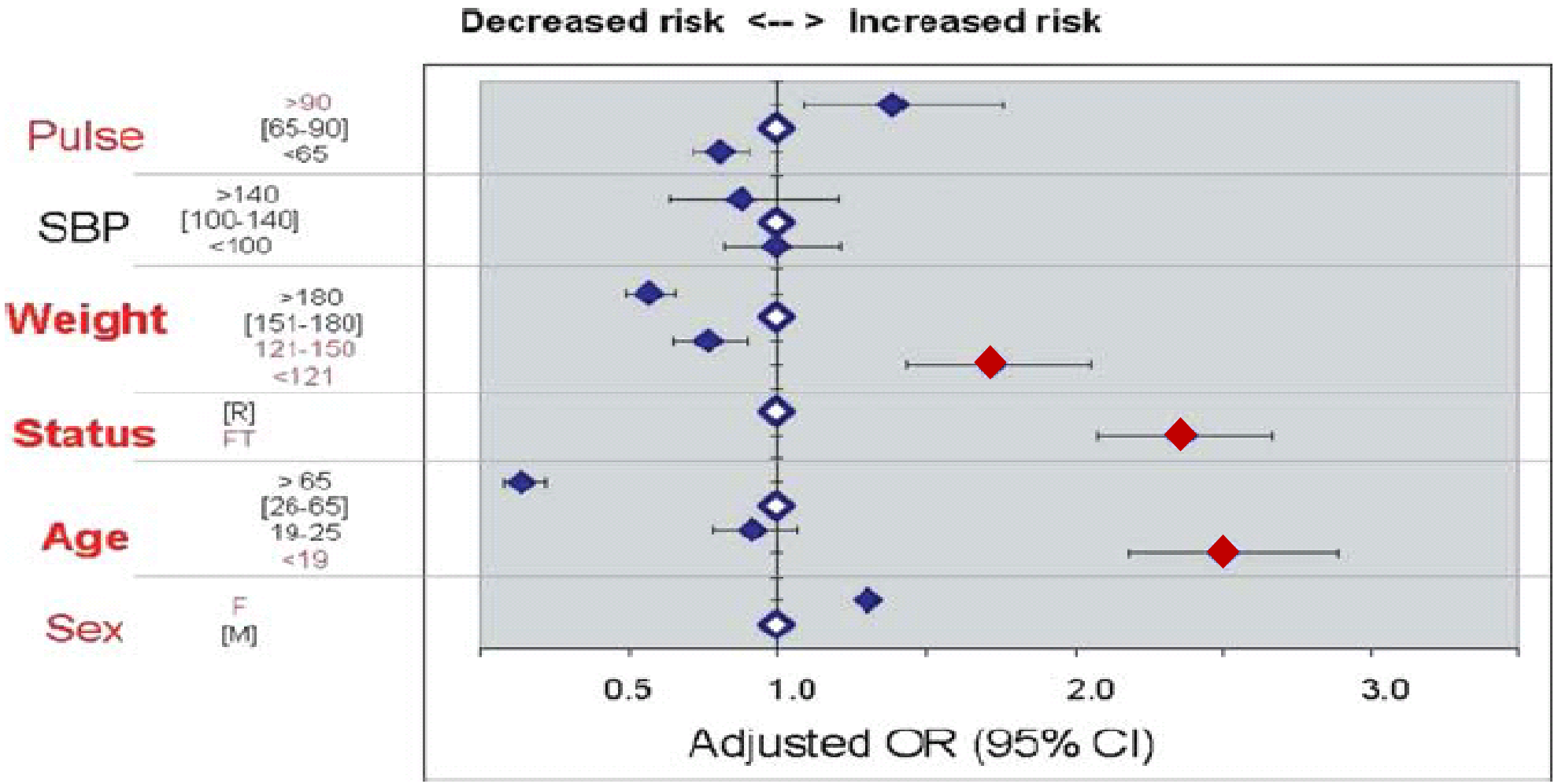
Narbey 2016

Total Systemic (Syncopal-Type) Complication Rates by Age, Sex, and Donation Status



Eder 2008

Risk factors for VVR at donation



Brodsky, Eder – Pulse Study 1997

VVR and Estimated Blood Volume

- Collection <15% of total blood volume

EBV (ml)	VVR (Adj. Hazard Ratio)
<3500	2.88
3500-4000	2.09
>4775	1

Wiltbank 2008, Eder 2009

Adverse Reaction incidence per 1000

		EBV (L)				
Symptoms		<3.5	3.5-4	4-4.5	>4.5	p value*
Total number of female donors	8784	946	2922	2919	1997	
Systemic symptoms						
Fainted	11.6	27.6	13.4	10.2	3.4	<0.0001
Felt faint or weak	78.5	135.2	91.5	69.3	45.8	<0.0001
Felt very tired	54.4	79.7	63.4	46.4	39.5	<0.0001
Any systemic symptom	110.2	171.1	127.6	97.8	73.8	<0.0001
Arm bruising	131.8	155.6	122.3	134.0	130.8	0.0721

Eder 2012

VVR
Consequences

- In 4-9% of cases: injuries from syncope and fall (Bravo 2011, Narbey 2016)
- Frequent cause of reduced donor return rates (Riga 2015, Burkhardt 2015)
- The strongest deterrent effect is seen for:
  - Repeat donors (33% vs 20% of first time donors) (France 2004)
  - Male (OR 3.95, 95% CI 2.19-7.11 vs female OR 1.78, 95% CI 1.35-2.35) (Veldhuizen 2012)
- Observing a donor being treated for VVR was associated with:
  - self-report of VVR symptoms in non-first-time blood donors,
  - slower rate of return in the following 2 years in first-time donors (Ditto 2014)

VVR
Prevention

- *Physiological strategies*
  - Pre-donation water loading
  - Applied muscle tension (AMT)
  - Consumption of caffeine
- *Psychological strategies*
  - Emotion regulation to reduce stress or anxiety
  - Audio-visual distraction
  - In situ social support
  - Experienced phlebotomist

Thijsen 2017

Plasma collection methods, PDMP yield, adverse events

Plasma characteristics	Target 750 ml No saline infusion Method 1 (n = 85)*	Target 840 ml Saline infusion 250+250 Method 2 (n = 88)*	Target 800 ml Saline infusion 500 Method 3 (n = 82)*
Number of donations	271	292	259
Mean volume collected (mL)†	657 ± 96.21 (182-753)	822 ± 79.45 (240-935)	730 ± 138.64 (0-840)
Mean collection time (min)†	40.3 ± 9.83 (14-101)	53.6 ± 9.81 (6-111)	49.2 ± 11.61 (6-144)
Total protein (g/L)‡	57.99 (57.11-58.87)	51.82 (51.06-52.59)§	53.9 (53.09-54.72)§
Average protein yield (g)¶	38.1	42.6	39.3
IgG (g/L)‡	6.14 (5.87-6.41)	5.79 (5.54-6.05)§	5.97 (5.71-6.23)§
Average IgG yield (g)¶	4.03	4.76	4.36
FVIII (IU/L)‡	1.14 (1.07-1.22)	1.03 (0.96-1.11)§	1.08 (1.00-1.15)§
Average FVIII yield (IU)¶	0.75	0.85	0.79

Adverse events: moderate/severe (%)	**3.3**	**2.0**	**0.4**
- Vasovagal: moderate/severe (%)	**0.4**	**0**	**0**
- Citrate reactions (%)	**0**	**0.7**	**0**

* The number of participants donating at least once under each method.

Buzza 2012

Criteria for saline infusion during plasmapheresis

Consider intraprocedure + end saline infusion if:
• Age < 19 • First donation • Weight 50-55 Kg • History of VVR

Conclusions

1. The increasing demand of PDMP and the observed decrease in WB donations /RBC transfusions prompt new strategies centered on plasmapheresis and improvement of its efficiency, besides strict compliance to GPG/GMP requirements.
2. The standards (about volume and donation frequency) ratified by the Italian Decree november 2nd 2015 look adequate to guarantee donor safety, PDMP quality and system sustainability.
3. Specific interventions are required focusing on donor information and support, aimed to improve his/her global donation experience, minimize adverse reaction incidence and increase intention to donate.
4. In particular, saline infusion intra and/or at the end of procedure allow to better control extracorporeal volume, within safety thresholds, even in donors at major risk of VVR (young, first time, low BMI-EBV, fear/anxiety).