Blood donation adverse reactions and events

Annual report 2020

Denmark

Danish Hemovigilance Committee 2021

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Introduction

Hemovigilance is an important part of the transfusion quality systems covering all aspects of the transfusion chain (vein-to-vein process). The goal of hemovigilance is continuously quality improvement of the transfusion chain through corrective and preventive actions to improve donor and patient safety.

It is important to underline, that blood donation is a safe procedure. Both national and international data show that blood donation is safe with very low rates of both serious and non-serious adverse reactions or events (SARE/ARE)[1]. Even so, it is still important to monitor these. First and foremost, they must be monitored as donation is a purely altruistic gesture with no personal gain for the donor. Second, blood establishments are obliged to monitor donor safety to ensure that the risk of (S)ARE is kept on a minimal level. This is also the case when new procedures are introduced. Here, the monitoring both serves to provide a baseline risk-level for comparison but can also be used to ensure that the new procedure does not increase the risk-level.
Blood donation is an invasive procedure and involves a phlebotomy; therefore, donation-related discomfort and (S)ARE are unavoidable. Collection of data can be a tool to know more about the incidence and background of (S)ARE.

From January 1st, 2020 a national Danish donor vigilance registration was commenced to monitor adverse reactions and events in blood donors. Until 2020, only the most severe adverse reactions and events in blood donors have been monitored in Denmark on a national level and reported to the competent authorities and the EU Commission.

The overall goal of this initiative was to establish a national system to monitor *all* adverse reactions in blood donation and at the same time, to develop an easy-to-use on-site registration that could be applied to the different IT-systems used in Denmark. In addition, it was considered essential that the new system used international definitions to ease comparison to other countries and allow for international collaboration.

This registration builds on three parameters. First, the type of ARE as defined in the ISBT guideline[2]. Second, a rating of the severity from 1 (mild) to 5 (death) as defined by AABB[3]. Third, a rating of imputability, the likelihood of the donation as the dominant cause of the ARE. Here, definitions from the EU directive[4] from excluded to certain was applied. The full description of the system is available in Danish: Guideline registration of adverse reactions and events. The table of ARE categories, severity and imputability has been translated to English and can be found in the appendix. A more detailed description of the registration in the Danish Blood bank IT systems are also available in the appendix.

To our knowledge, this is the first report on a national system that relies on a simple electronic registration that combines the current international definitions. This report presents all registered AREs regardless of severity or imputability. All AREs with a severity of 2 or more, were also reported to Blood Donors in Demark, an independent organization who manage follow-up and a potential contact to the Danish Patient Compensation Association. All reactions with a severity of 3 or more were defined as severe (SAREs) and must be reported to the Danish Patient Safety Authority, who reports to the EU.

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[1] Crocco I et al. Adverse reactions in blood and apheresis donors: Experience from two Italian transfusion centres. Blood Transfus. 2009. Burkhardt T et al. Donor vigilance data of a blood transfusion service: A multicenter analysis. Transfus Apher Sci. 2015;53:180-184. Riga A et al. Blood donors - Serious adverse reactions (SAR) 2010-2014 EFS Châteauroux, France. Transfus Clin Biol. 2015;22:62-65. Sorensen BS et al. Complications related to blood donation: A population-based study. Vox Sang. 2008;94:132-137. Mikkelsen C et al. Putting the spotlight on donation-related risks and donor safety - are we succeeding in protecting donors? Vox Sang. 2021 Mar;116(3):313-323.

[2] modified according to Standard for Surveillance of Complications Related to Blood Donation, ISBT, IHN, AABB, 2014

[3] Modified according to Grading Severity of Blood Donor Adverse Events Tool, AABB 2018

[4] COMMISSION DIRECTIVE 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events

In the coming year, the Hemovigilance Committee will initiate a nation-wide survey to monitor the usefulness of the registration system and the appropriateness of the explanatory text in the guideline used. The results are expected by the end of 2022.

Postscript January 2023:
Data in this report is extracted for the first time in January 2021. Since severity grade 3 among others depend on donor having symptoms in more than 6 months, a new extraction was performed in August 2022 to catch possible donors changing in severity registration from grade 2 to 3. The updated extraction of data did not change the original numbers mentioned in this report.

Definitions:

Adverse reaction and event (ARE): The term is in this report used to describe complications of blood donation and describes unwanted symptoms in donor during or after donation. There is no international consensus regarding using the term adverse reaction (ARE) and adverse event (AE). The use of AE in the EU directives is discrepant from clinical trials and pharmacovigilance; whereas the ISBT-IHN Standard speaks of adverse events for all complications of blood donation and of reactions when they are generalized, without additional clarification.
ARE rate: The number of AREs per 100,000 donations of comparable type of donation

Blood donations in Denmark

A total of 295,637 blood donations were registered. The details are presented in table 1.
Comparing to 2019[5], the number of whole blood donations is stable, while the number of plasmapheresis and platelet apheresis has increased (2019 numbers, n = 204,817, 75,586, 1097 respectively).
In 2020 blood donors have been tested for antibodies against COVID-19 as part of the national surveillance of immunity towards COVID-19. The test was offered in spring 2020 and resulted in a larger increase in registration of new donors, but the blood establishments prioritized repeat donors to ensure the blood supply. Therefore, the number of donations from first-time donors is comparable to the number from 2019 (2019 number, n = 16,466).

Table 1: Blood donations divided by gender, type of blood donation, status, and age

	Female	Male	**Total**	
Type of donation			**N**	**%**
Whole blood	107,934	95,538	**203,472**	**69%**
Plasmapheresis	33,614	57,077	**90,691**	**31%**
Platelet apheresis	369	1105	**1474**	**0,5%**
Donor status				
First-time donors	10,544	6551	**17,095**	**6%**
Repeat donors	131,373	147,169	**278,542**	**94%**
Donor age				
17-18 years	2271	948	**3219**	**1%**
19-22 years	12,456	6469	**18,925**	**6%**
23-29 years	28,334	23,535	**51,869**	**18%**
≥ 30 years	98,856	122,768	**221,624**	**75%**
Total	**141,917**	**153,720**	**295,637**	

[5] Rapport over Blodproduktområdet, Styrelsen for Patientsikkerhed 2019

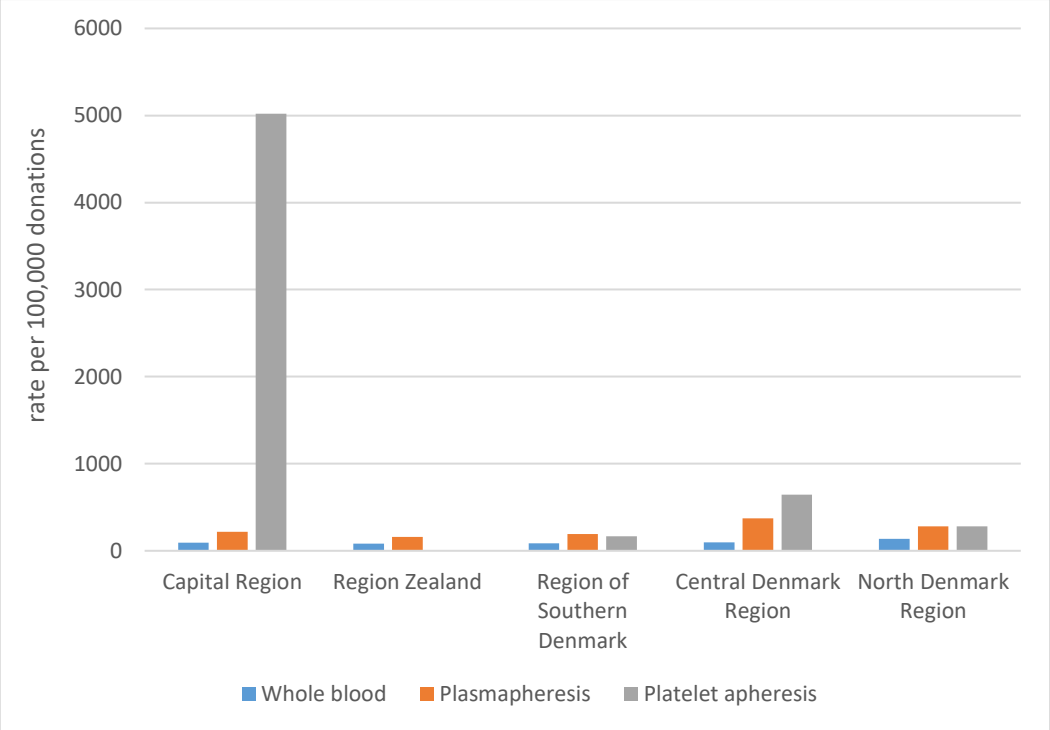
Summary of data

As expected, the overall rate of ARE is low. The rates of AREs were markedly higher for apheresis procedures. Especially platelet apheresis, however as shown in figure 1, this is due to a high number of registrations in the Capital Region. The Capital Region had registered a high number of citrate reactions during platelet apheresis compared to other regions, figure 7. If citrate reactions are excluded from the data from the Capital Region, the number of AREs on platelet apheresis in the Capital Region is comparable to the other regions and the total number of AREs for platelet apheresis in Denmark would then be 43 corresponding to a rate of 2917/100,000 donations. For all regions the rate of ARE is higher for plasmapheresis compared to whole blood. This is comparable to other countries and previous research.

Table 2: AREs by type of blood donation in Denmark

	Number of ARE	Number of blood donations	ARE proportion	ARE rate per 100,000 blood donations
Whole blood	1950	203,472	0.96%	**958**
Plasmapheresis	2208	90,691	2.43%	**2435**
Platelet apheresis	272	1474	18.45%	**18,453**
All type of donations	**4430**	**295,637**	**1.50%**	**1498**

Figure 1: ARE by type of blood donation per region



ARE divided by severity grade and imputability

The majority (89.9 %) of registrations have an imputability of definite or probable. The majority (92.8 %) are registered as grade 1 severity (symptoms < 2 weeks and no medical intervention). Only 1.6 % are registered as grade 2 severity (symptoms > 2 weeks or medical intervention). In total 8 donors (2.2 %) had a severe ARE (SARE) and of these, 7 had an imputability of definite or probable. No grade 5 severity was registered.
For definitions of severity and imputability, see appendix, table 12 and table 13, respectively.

Table 3: AREs divided by severity and imputability

	Severity						Total	
Imputability	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Grade not defined***	**N**	**%**
Definite	3553	36	3	1	0	41	3634	82%
Probable	398	25	3	0	0	4	430	10%
Possible	88	6	1	0	0	0	95	2%
Unlikely	5	0	0	0	0	0	5	0.1%
Not defined	68	2	0	0	0	196	266	6%
Total, N	4112	69	7	1	0	241	4430	100%
Total, %	92.8%	1.6%	0.2%	0.02%	0%	5.4%	100%	
Rate per 100,000 blood donations	1391	23	2	0.3	0			

***** In 1 of the 5 regions, the 3 codes are registered individually due to constraints of their IT system, consequently for some AREs only the category, but not the grade and/or imputability are registered.

AREs divided by gender, blood donation type and donor status

Table 4-6 show that the ARE rate is higher in female donors regardless of donor status, age, or donation type. Data also shows that the ARE rate is higher in first-time donors and young donors, regardless of gender. The latter is probable biased because a large proportion of young donors is first-time donors.
These results are in concordance with published literature[6].

Table 4: ARE divided by gender and donor status

	Female	**Male**	**Total**	**ARE rate**		
Donor status	N	N	N	Female§	Male#	Total*
First-time donor	410	217	627	3888	3312	3668
Repeat donor	2043	1760	3803	1555	1196	1365
Total	**2453**	**1977**	**4430**	**1728**	**1286**	**1498**

§ rate per 100,000 blood donations from female blood donors according to donor status
# rate per 100,000 blood donations from male blood donors according to donor status
* rate per 100,000 blood donations according to donor status

Table 5: AREs divided by gender and age

	Female	**Male**	**Total**	**ARE rate**		
Age	N	N	N	Female§	Male#	Total*
17-18 years	86	28	114	3787	2954	3541
19-22 years	327	186	513	2625	2875	2711
23-29 years	558	446	1004	1969	1895	1936
≥ 30 years	1482	1317	2799	1499	1073	1263
Total	**2453**	**1977**	**4430**	**1728**	**1286**	**1498**

§ rate per 100,000 blood donations from female donors according to age group
# rate per 100,000 blood donations from male donors according to age group
* rate per 100,000 blood donations according to age group

[6] Burkhardt T et al. Donor vigilance data of a blood transfusion service: A multicenter analysis. Transfus Apher Sci. 2015;53:180-184.

Table 6: AREs divided by blood donation type and gender

	Female	**Male**	**Total**	**ARE Rate**		
Donation type	N	N	N	Female[§]	Male[#]	Total[*]
Whole blood	1292	658	1950	1197	689	958
Plasmapheresis	1028	1180	2208	3058	2067	2435
Platelet apheresis	133	139	272	36043	12579	18453
Total	**2453**	**1977**	**4430**	**1728**	**1286**	**1498**

§ rate per 100,000 blood donations from female donors according to blood donation type
# rate per 100,000 blood donations from male donors according to blood donation type
* rate per 100,000 blood donations according to blood donation type

ARE and type of blood donations

Categories with no registrations have been omitted from the tables and figures. For a total overview of all possible categories, please see appendix, table 11.

Whole Blood

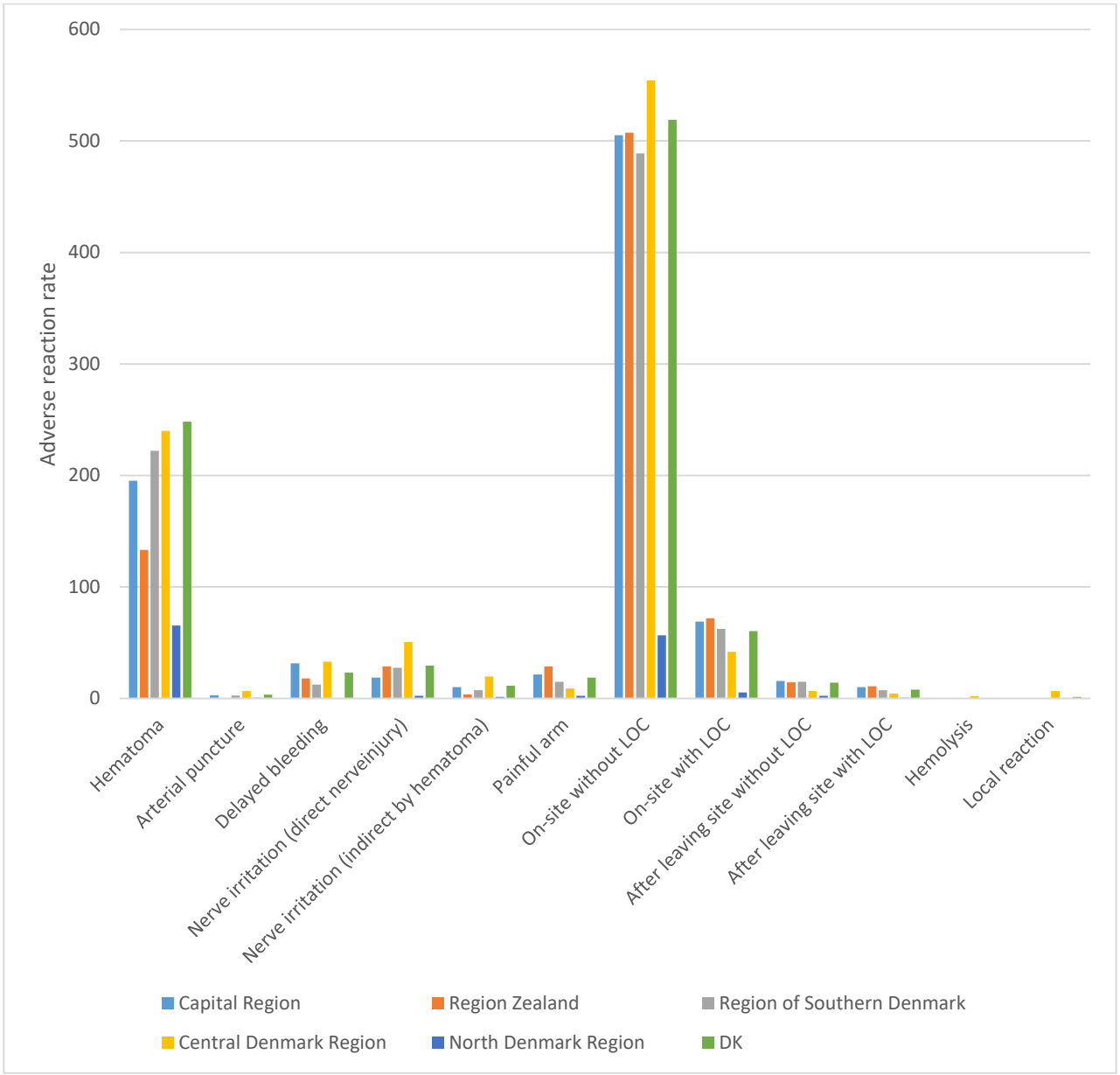
Table 7: Whole blood donations

	Severity					Total		
Category	Grade 1	Grade 2	Grade 3	Grade 4	Grade not defined	**N**	**%**	**Rate per 100,000 whole blood donations**
Vessel injury								
Hematoma	475	5	0	0	25	**505**	**25.9%**	**248**
Arterial puncture	7	0	0	0	0	**7**	**0.4%**	**3**
Delayed bleeding	45	0	0	0	2	**47**	**2.4%**	**23**
Pain								
Nerve irritation (direct nerve injury)	46	8	2	0	4	**60**	**3.1%**	**29**
Nerve irritation (indirect by hematoma)	10	7	1	0	5	**23**	**1.2%**	**11**
Painful arm	27	3	0	0	8	**38**	**1.9%**	**19**
Vasovagal reaction								
On-site withou LOC	1026	4	0	0	27	**1057**	**54.2%**	**519**
On-site with LOC	111	4	2	1	5	**123**	**6.3%**	**60**
After leaving site without LOC	25	2	0	0	2	**29**	**1.5%**	**14**
After leaving site with LOC	8	6	1	0	1	**16**	**0.8%**	**8**
Apheresis*				0				
Citrate	4	0	0	0	1	**5**	**0.3%**	**NA**
Hemolysis	1	0	0	0	0	**1**	**0.1%**	**NA**
Allergic reaction								
Local reaction	3	0	0	0	0	**3**	**0.2%**	**1**
Miscellanous								
Other	3	0	0	0	0	**3**	**0.2%**	**1**
Category not defined	29	0	0	0	4	**33**	**1.7%**	**16**
Total	**1820**	**39**	**6**	**1**	**84**	**1950**	**100%**	**958**

* registration of apheresis reaction must be a mistake

In whole blood donations the most common ARE was on-site vasovagal reactions without loss of consciousness (LOC) followed by hematoma, together accounting for 80 % of registered ARE and all with a severity of 2 or less. Only one severe ARE (grade 4) was recorded, an on-site vasovagal reaction with loss of consciousness. The ARE category distribution-pattern for all ARE in all five regions is shown in figure 5. Especially, the categories with a high proportion of mild severity are distributed unequal (hematoma, on-site vasovagal reaction without LOC). The unequal distribution could most likely be explained by differences in interpretation of the definitions of categories and different threshold for registration. We have questioned the five regions about their registration practice and threshold for these AREs. The response support that the differences could be explained by local differences in registration practice.

Figure 5 Distribution of ARE in relation to whole blood donation per region



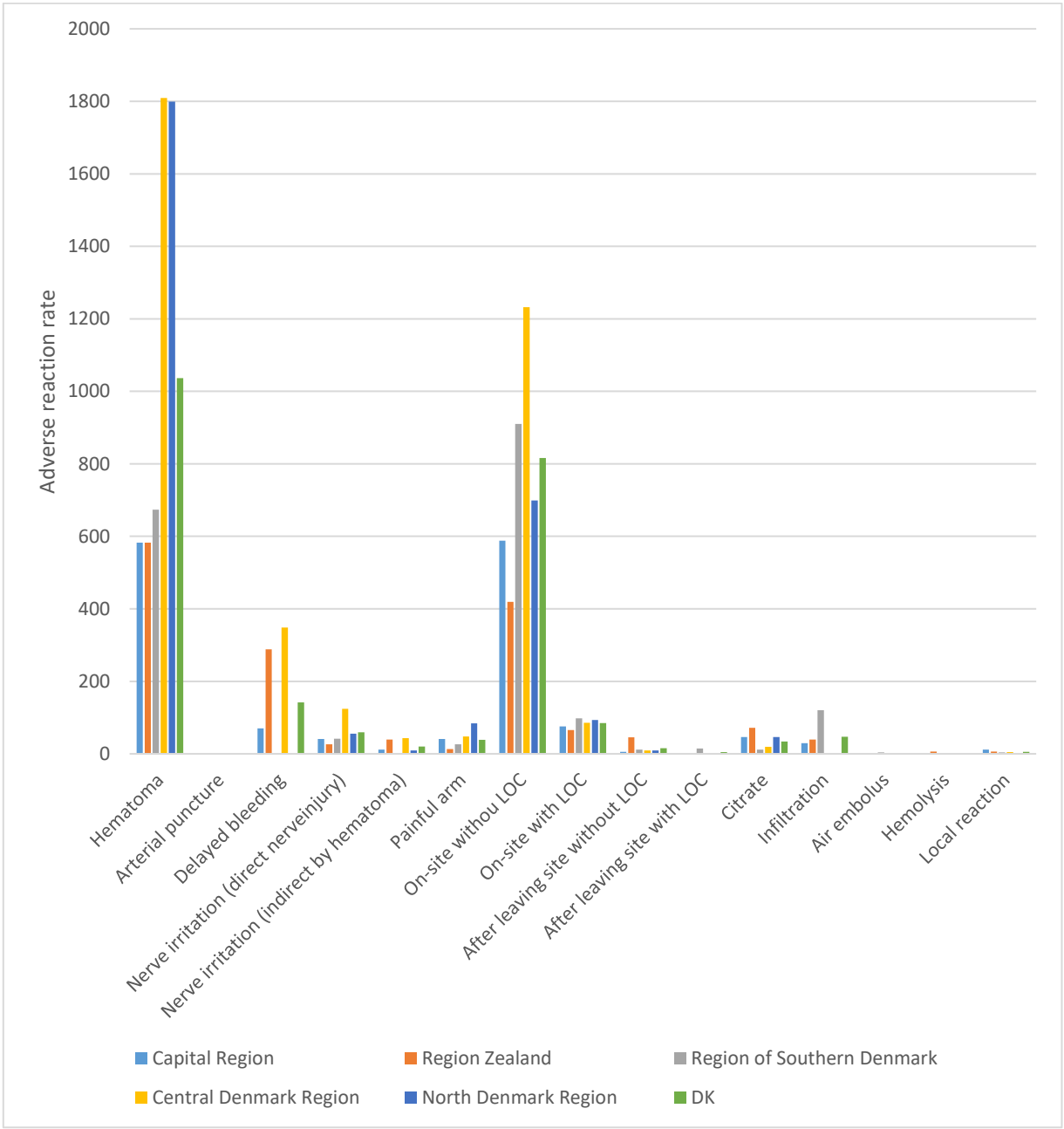
Plasmapheresis

Table 8: Plasmapheresis

	Severity					Total		
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade not defined**	**N**	**%**	**Rate per 100,000 plasmapheresis**
Vessel injury								
Hematoma	901	8	0	0	31	**940**	**42.6%**	**1036**
Arterial puncture	0	0	0	0	0			
Delayed bleeding	123	0	0	0	6	**129**	**5.8%**	**142**
Thrombophlebitis	0	0	0					
Deep venous thrombosis	1	0	0	0	0	**1**	**0%**	**1**
Pain								
Nerve irritation (direct nerveinjury)	48	4	0	0	2	**54**	**2.4%**	**60**
Nerve irritation (indirect by hematoma)	14	3	0	0	1	**18**	**0.8%**	**20**
Painful arm	31	2	0	0	2	**35**	**1.6%**	**39**
Vasovagal reaction								
On-site without LOC	728	3	1	0	8	**740**	**33.5%**	**816**
On-site with LOC	70	3	0	0	4	**77**	**3.5%**	**85**
After leaving site without LOC	11	3	0	0	0	**14**	**0.6%**	**15**
After leaving site with LOC	3	1	0	0	0	**4**	**0.2%**	**4**
Apheresis								
Citrate	27	0	0	0	4	**31**	**1.4%**	**34**
Infiltration	39	0	0	0	4	**43**	**1.9%**	**47**
Air embolus	1	0	0	0	0	**1**	**0%**	**1**
Hemolysis	1	0	0	0	0	**1**	**0%**	**1**
Allergic reaction								
Local reaction	4	1	0	0	0	**5**	**0.2%**	**6**
Miscellanous								
Other	14	1	0	0	67	**82**	**3.7%**	**90**
No category	23	0	0	0	10	**33**	**1.5%**	
Total	**2039**	**29**	**1**	**0**	**139**	**2208**	**100.0%**	**2434**

Like the ARE distribution recorded in relation to whole blood donations, hematoma and on-site vasovagal reactions without loss of consciousness accounted for the majority (75%) of the registered ARE in relation to plasmapheresis donations. The ARE category distribution-pattern for all five regions is shown in figure 6. Again, local differences in distribution is noted and being even more pronounced than for AREs in relation to whole blood donations. Also, we find the same trend, that unequal distribution primarily is related to the categories with a high proportion of AREs with a mild severity. Especially hematoma, delayed bleeding and VVR without LOC show an unequal distribution. The unequal distribution could most likely be explained by differences in interpretation of the definitions of categories and different threshold for registration. We have questioned the five regions about their registration practice and threshold for these AREs. The response support that the differences could be explained by local differences in registration practice.

Figure 6 Distribution of AREs in relation to plasmapheresis per region



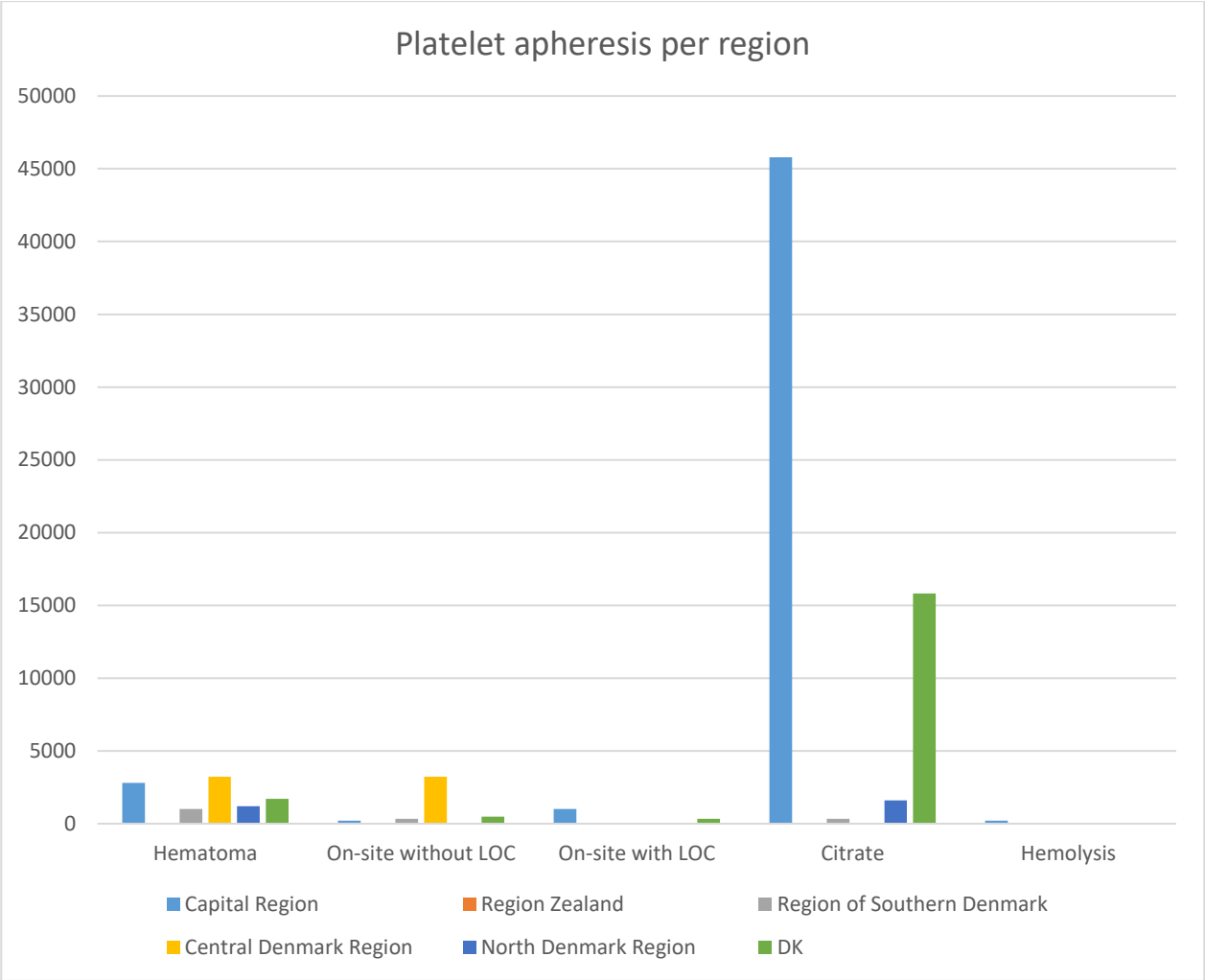
Platelet apheresis

Table 9: Platelet apheresis

	Severity					Total		
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade not defined**	**N**	**%**	**Rate per 100,000 platelet apheresis**
Vessel injury								
Hematoma	24				1	**25**	**9.2%**	**1696**
Vasovagal reaction								
On-site withou LOC	6				1	**7**	**2.6%**	**475**
On-site with LOC	5					**5**	**1.8%**	**339**
After leaving site without LOC								
After leaving site with LOC								
Apheresis								
Citrate	219				14	**233**	**85.7%**	**15.807**
Hemolysis					1	**1**		
Miscellanous								
category not assigned					1			
Total	**254**				**18**	**272**	**99.3%**	**18.453**

For platelet apheresis, the registration was dominated by the reports of citrate reactions in one region. If citrate reactions from the Capital Region were deleted from the dataset the number of citrate reactions would be 5 corresponding to a rate of 1200/100,000 platelet apheresis. Aside from citrate reaction, only hematomas and vasovagal reactions were recorded. All recorded ARE was grade 1 severity. The total number of platelet apheresis procedures are low and therefore, the likelihood for donor of having a rare ARE is also low and would not be expected to be recorded every year e.g. if we assume that the rate of direct needle injury is comparable to plasmapheresis, we would expect less than 1 case per year. The ARE category distribution-pattern for all ARE in all five regions is shown in figure 7. The distribution is even more unequal than for the other two types of donations. The unequal distribution could most likely be explained by differences in interpretation of the definitions of categories and different threshold for registration. We have questioned the five regions about their registration practice and threshold for these AREs. The response support that the differences could be explained by local differences in registration practice.

Figure 7: ARE in platelet apheresis per region



Vasovagal reaction in relation to blood donation

As the most common ARE, vasovagal reactions were of particular interest. Data on vasovagal reactions divided by severity, donation type, gender, age, and donor status are shown in table 10.
Overall, across all blood donation types, vasovagal reactions were found to be in general mild (96 % grade 1). Vasovagal reactions after leaving the blood bank has a potential for severe consequences, due to the risk of accidents and therefore one of the most feared ARE. Data shows that only 3 % (N=63) of all vasovagal reactions are happening after donor has left the donation site. Of these, only 20 cases have a loss of consciousness (LOC) (data not shown). Notably, data does not show any clear difference between vasovagal reaction on site or after leaving the site in relation to severity. In our data, vasovagal reactions are clearly associated with younger age, female gender and first-time donors, corresponding to what is already described in the literature[7] Also, the rate of vasovagal reaction was highest in plasmapheresis donors. This contrasts with a previous report[8], but the data in the referenced report is also very heterogenic. First-time plasmapheresis donors had a 5 times higher rate than repeat plasmapheresis donors (5263/100,000 first-time plasmapheresis and 859/100,000 repeat plasmapheresis, data not shown).

[7] Gillet P et al. First-time whole blood donation: A critical step for donor safety and retention on first three donations. Transfus Clin Biol. 2015 Oct-Dec;22(5-6):312-7. Wiersum-Osselton, J.C. et al. Risk factors for complications in donors at first and repeat whole blood donation: a cohort study with assessment of the impact on donor return. Blood Transfusion 2014, 12 (Suppl. 1), s28–s36. Bravo, M. et al. Factors associated with fainting: before, during and after whole blood donation. Vox Sanguinis 2011, 101, 303–312. Tondon, R. et al. vasovagal reactions in 'at risk' donors: a univariate analysis of effect of age and weight on the grade of donor reactions. Transfusion and Apheresis Science 2008, 39, 95–99.

[8] Wiersum-Osselton, J.C. et al. Complications of blood donation reported to haemovigilance systems: analysis of eleven years of international surveillance. Vox Sang. 2020 Dec 5..

Table 10: Vasovagal reactions divided by severity, blood donation type, gender, age, and donor status

	On-site		After leaving the blood bank		Total		
	N	%	N	%	N	%	**ARE Rate***
Severity							
Grade 1	1944	94%	47	2%	1991	96%	**673**
Grade 2	16	1%	12	1%	28	1%	**9**
Grade 3	3	0%	1	0%	4	0%	**0**
Grade 4	1	0%	0		1	0%	**0**
Not specified	45	2%	3	0%	48	2%	**16**
Type of blood donation							
Whole blood	1180	57%	45	2%	1225	59%	**602**
Plasmapheresis	817	39%	18	1%	835	40%	**921**
Platelet apheresis	12	1%	0	0%	12	1%	**814**
Gender							
Female	1226	59%	55	3%	1281	62%	**903**
Male	783	38%	8	0%	791	38%	**515**
Blood donation type and gender							
Female							
Whole blood	516	25%	40	2%	556	27%	**772**
Plasmapheresis	368	18%	15	1%	383	18%	**1318**
Platelet apheresis	5	0%	0	0%	5	0%	**1355**
Men							
Whole blood	264	13%	5	0%	269	13%	**410**
Plasmapheresis	335	16%	3	0%	338	16%	**687**
Platelet apheresis	4	0%	0	0%	4	0%	**633**
Age and gender							
Female							
17-18 years	75	4%	3	0%	78	4%	**3435**
19-22 years	286	14%	7	0%	293	14%	**2352**
23-29 years	387	19%	17	1%	404	19%	**1426**
> 30 years	478	23%	28	1%	506	24%	**512**
Male							
17-18 years	19	1%	0	0%	19	1%	**2004**
19-22 years	126	6%	0	0%	126	6%	**1948**
23-29 years	234	11%	0	0%	234	11%	**994**
> 30 years	404	19%	8	0%	412	20%	**336**
Donor status							
First-time	496	24%	13	1%	509	25%	**2977**
Repeat	1513	73%	50	2%	1563	75%	**561**
Total	**2009**	**97%**	**63**	**3%**	**2072**	**100%**	**701**

* ARE rate is calculated as per 100,000 donations in the same category as the corresponding ARE

Conclusion

It is safe to donate blood in Denmark. The majority of AREs are mild (grade 1 severity). In line with other international reports, hematoma and vasovagal reactions were the most common ARE regardless of donation type. ARE is most frequent in female donors and in first-time donors.

As expected, the rate of vasovagal reactions in apheresis procedures are higher than in whole blood donations, but the severity is comparable between the two types of donations and found to be mild. The plasmapheresis program will increase in the coming years with opening of several plasmapheresis centers and this registration will be a tool to monitor if any negative effects occur.

The year 2020 was in many ways defined by the SARS-cov2 pandemic. This is the first annual report on blood donation related AREs. Comparing the number of donations with the annual report made by the Danish Patient Safety Authority, the total number of donations was comparable to 2019 and we consider this report representative for the incidence of ARE in blood donors. The number of plasmapheresis has increased but this has been a deliberate effort to increase the self-sufficiency of plasma-derived medicinal products in Denmark.

This first national report revealed substantial differences in reporting of hematomas, delayed bleeding, vasovagal reaction onsite without LOC, and citrate reactions. The guideline will in 2021 be updated with a revised definition of these categories and with a clearer definition of the registration threshold. We expect this will even out the regional differences in the 2021 report

Appendix

Description of registration in blood bank IT system

The registration ensures that the following information can be exported from the system:
Nominator:
Type of donation (whole blood, plasmapheresis, platelet apheresis)
Gender and age of donor
First-time donation or repeat donation
If plasmapheresis, volume collected
Category of complication, severity grade and imputability
Denominator:
Total number of donations (whole blood, plasmapheresis, platelet apheresis)
Total number of donations in relation to gender, first-time donations/repeat donations
Total number of donations divided on age groups (17-18, 19-22, 23-29, 30-69, >70 år)

In Denmark, 2 blood bank IT systems are used (Prosang and Blodflödet). The registration can be done on-site when the reaction is noticed, days/months after the donation when donor informs the blood bank. The registration can be updated at every time e.g. at follow-up.

Prosang:
The blood bank staff register a clinical value on donor ("medicinsk værdi"). A clinical value is set up in the system dedicated for registration of donor complication and named "bivirk". The registration consists of 3 values, the unique personal identification number of the donor (cpr.no), the date of the donation, and the 3-digit code of the ARE. By using the personal identification number, we can in the export of data, get all information related to the donor, e.g. age, gender, number of donations etc. The date is set to the date of the respective donation and in this way we can in the export combine data on the actual donation with the adverse reaction. The 3-digit combination is the combination of category, severity and imputability ref. table 11-13. The system only accepts a 3-digit combination. A barcode is made of all combinations that can be scanned and used instead of manually entering the 3 digits. If more complications are registered on the same donation, the clinical values "bivirk2" and "bivirk3" must be used and the registration is performed in the same way as "bivirk". When a follow-up is done and the registration should be changed, a new clinical value is registered. This clinical value is named "bivirk opfolg". The registration is again done the same way. It is possible to export data related to the clinical value and the result on the clinical value is searchable. If more than one clinical value is registered on the donation, then the followup clinical value and the primary clinical value must be in concordance, e.g. if "bivirk2" is registered then "bivirk opfolg2" must be used.

Blodflödet:
The blood bank staff register the ARE in the donation-charts ("tappejournal"). A clinical value is set up in the system dedicated for registration of donor complication and named "Komplikation". The registration consists of three separate registrations. A K-code (Category), an S-code (severity) and I-code (Imputability) as illustrated in table 11-13. The date is set to the date of the respective donation and in this way we can in the export combine data on the actual donation with the adverse reaction. The system is not able to detect if one or more codes are missing and the user is responsible for ensuring correct registration themselves. If more ARE are registered, then they are added to the same

list. When a follow-up is done and the registration should be changed, a new clinical value is registered. An example of registration is shown below.

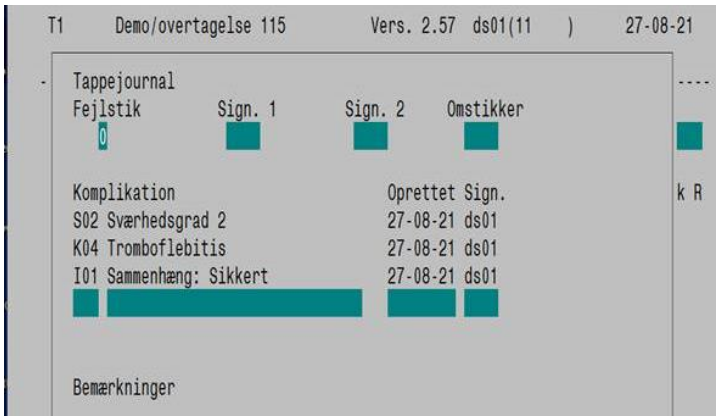


TABLE 11 (translated from Danish): Categories[9]

Categories AREs (the code is used as first element in the registration)				
Code		**Category**	**subcategory**	**Symptoms**
Prosang	Blodflödet	Injury to vessel		
A	K01		Hematoma (bruise)	Bruising, discolouration, swelling and local pain
B	K02		Arterial puncture	A lighter red colour than usual of the collected blood can be seen. The needle and tubing may appear to pulsate; the blood bag fills very quickly. Local pain
C	K03		Delayed bleeding	Spontaneous recommencement of bleeding from the venepuncture site, after pressure has been applied and the initial dressing has been removed, or leaking through the dressing
D	K04		Thrombophlebitis	Redness, swelling, and tenderness extend along the course of the vein
E	K05		Deep venous thrombosis (DVT)	Swelling and pain in the upper arm. May be accompanied by symptoms of superficial inflammation and thrombosis.
F	K06		Compartment syndrome	Painful arm, particularly on movement; swelling, paresthesias and partial paralysis.
G	K07		Pseudoaneurysm	Pulsating mass in the arm. May be accompanied by pain and paraesthesias.
H	K08		Arteriovenous fistula	Pulsating mass with a palpable thrill and associated bruit. The affected area may be warm, and the distal part of the arm may be cool if significant shunting of blood is present. The distal veins may be dilated and may pulsate
		Pain in the arm		
I	K09		Nerve injury/irritation (caused by direct nerve injury)	Symptoms arise **immediately** when the needle is inserted or withdrawn: Radiating, often 'electrical' sharp pain moving away from the venepuncture site, and/or paraesthesias such as tingling, burning sensations in the hand, wrist or shoulder area but away from the venepuncture site. Symptoms may be worse in certain positions or with certain arm motions
J	K10		Nerve injury/irritation (caused by hematoma)	Symptoms arise **after** the needle has been removed: Radiating, often 'electrical' sharp pain moving away from the venepuncture site, and/or paraesthesias such as tingling, burning sensations in the hand, wrist or shoulder area but away from the venepuncture site. Symptoms may be worse in certain positions or with certain arm motions.

[9] modified according to Standard for Surveillance of Complications Related to Blood Donation, ISBT, IHN, AABB, 2014

K	K11		Other painful arm	Pain in the arm that **canno**t be characterized as: Radiating, often 'electrical' sharp pain and/or paraesthesias such as tingling, burning sensations in the hand, wrist or shoulder area
		Vasovagal reactions/loss of consciousness		Usually several of the following: discomfort, weakness, anxiety, light-headedness/dizziness, nausea, chills, sweating, vomiting, pallor, hyperventilation, rapid or a slow pulse, hypotension, loss of consciousness (LOC), loss of bladder or bowel control or convulsive movements
L	K13		On collection facility, without loss of consciousness	
M	K14		On collection facility, with loss of consciousness	
N	K15		Outside collection facility, without loss of consciousness	
O	K16		Outside collection facility, with loss of consciousness	
		Complications related to apheresis		
P	K17		Citrate reaction	Numbness or tingling of lips, feelings of vibrations, numbness or tingling in the fingers, metallic taste, chills, shivering, light-headedness, feeling of tightness, muscle twitching
Q	K18		Infiltration	Swelling of the tissues at the venipuncture site (fluids enter the surrounding tissues)
R	K19		Air embolism	Bubbling sound or feeling at the venipuncture site. Cough, dyspnea, apprehension, sweating, chest pain, confusion, tachycardia, hypotension, nausea and vomiting.
S	K20		Haemolysis	Pink or red plasma, blood in lines or filter may appear dark. The donor may notice pink or red urine after collection
		Allergic reactions		
T	K21		Allergy (local)	Itching and redness at the venepuncture site, the bandage site, or the entire skin disinfection area. In a true allergic reaction, there may be a raised rash or hives in these areas that may expand to cover a larger area of the arm. The reaction may occur soon after donation or in the hours to days post-donation
U	K22		Generalised allergic reaction (anaphylactic reaction)	Apprehension, anxiousness, flushing, swelling of eyes, lips or tongue, cyanosis, cough, wheezing, dyspnea, chest tightness, cramps, nausea, vomiting, diarrhoea, tachycardia, hypotension, and altered mentation.
		Other serious complications		Hjertesymptomer, cerebrovaskulær event, fraktur, involvering i ulykker.
Z	K23		Rare complication	

TABLE 12 (translated from Danish): Severity[10]

Severity of ARE (the code is used as the second element in the registration)			
Code		**Severity**	**Explanation**
Prosang	Blodflödet		
1	S01	Grade 1	Symptoms that resolves with no or minimal intervention in the blood bank **and** do not require Outside Medical Care (OMC) **and** persist ≤ 2 weeks/expected to persist ≤ 2 weeks **and** has no limitation on Activities of Daily Living (ADL) Donor must contact the blood bank if the symptoms persist more than 2 weeks, if any medical care/hospitalization or limitation on activities on daily living.
2	S02	Grade 2	Outside Medical Care (OMC) without hospitalization **or** duration of symptoms more than 2 weeks but less than 6 months **or** limitations on Activities of Daily Living in less than 2 weeks. Outside Medical Care (OMC) without hospitalization: e.g. examination/treatment at GP, physiotherapist, observation in the Emergency Room
3	S03	Grade 3	Hospitalization **or** duration of symptoms more than 6 months **or** limitations on Activities of Daily Living in more than 2 weeks **or** surgery of any kind. *Hospitalization:* inpatient admission to the hospital; does NOT include being seen and discharged from urgent care or hospital emergency department
4	S04	Grade 4	Immediate medical intervention required to prevent death
5	S05	Grade 5	Death
		Definitions:	*limitation on Activities of Daily Living (ADL):* Include everyday household chores, doing necessary business, shopping, going to work or school, or getting around for other purposes. ADL is impacted if the donor • needs the help of other persons with bathing or showering, dressing, eating, getting in or out of bed or chairs, using the toilet, and getting around the home (Self-care ADL) • cannot work, attend school or manage routine personal/family activities because of the Donor Adverse Event (Instrumental ADL).
		ARE with severity grade 3, 4 and 5 must also be reported to the Danish Patient Safety Authority *ARE with severity grade 2, 3, 4 and 5 must also be reported to Blood Donors in Denmark. ARE with severity grade 1 is reported to the Blood Donors in Denmark if donor is entitled to reimbursement*	

TABLE 13 (translated from Danish): Imputability

Imputability (the code is used as the third element in the registration)			
Code		**Imputability**	**Explanation**
prosang	Blodflódet		
9	I05	Not assessable	When there is insufficient data for causality assessment
0	I04	Unlikely	When the evidence is clearly in favour of attributing the ARE to causes other than the blood or blood components
1	I03	Possible	When the evidence is indeterminate for attributing the ARE to the blood donation or to alternative causes
2	I02	Probable (likely)	When the evidence is clearly in favour of attributing the ARE to the blood donation
3	I01	Definite (certain)	When there is conclusive evidence beyond reasonable doubt for attributing the ARE to the blood donation

[10] Modified according to Grading Severity of Blood Donor Adverse Events Tool, AABB 2018