TRANSFUSION TRANSMITTED INJURIES SURVEILLANCE SYSTEM (TTISS)

2016 – 2020 SUMMARY REPORT

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FOREWARD

The Centre for Communicable Diseases and Infection Control (CCDIC) of the Public Health Agency of Canada (PHAC) is pleased to release the *Transfusion Transmitted Injuries Surveillance System (TTISS) Summary Report, 2016-2020*. This summary report presents transfusion transmitted injury surveillance data submitted by Canadian hospitals participating in the TTISS network.

PHAC established TTISS to collect non-nominal data on adverse reactions to blood transfusions. Canadian hospitals providing transfusion services across the country participate in this surveillance system.

CCDIC, in partnership with participating provinces and territories (P/Ts), is responsible for the collection, management, and analysis of data, and the production of reports to support evidence-based public health decisions. The overarching goal of TTISS is to improve blood transfusion safety and patient safety in Canadian hospitals.

ABBREVIATIONS

AHR	Acute Haemolytic Reaction
ASPT	Aseptic Meningitis
ATE	Adverse Transfusion Event
ATR	Adverse Transfusion Reaction
BACT	Bacterial Infection
DHR	Delayed Haemolytic Reaction
DSR	Delayed Serological Reaction
FNHR	Febrile Non-Hemolytic Reaction
HYPT	Hypotensive Reaction
INCMP	Incompatible Transfusion
IVIG-HD	Intervenus Immune Globuline Headache
SAAR	Severe Anaphylactic/Anaphylactoid Reaction
TACO	Transfusion Associated Circulatory Overload
TAD	Transfusion Associated Dyspnea
TRALI	Transfusion Related Acute Lung Injury
TTISS	Transfusion Transmitted Injuries Surveillance System
BCs	Blood Components
PDs	Plasma Derivatives

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EXECUTIVE SUMMARY

Since 2001, the Transfusion-Transmitted Injuries Surveillance System (TTISS) has been collecting data on reported adverse transfusion reactions (ATRs) in Canada that are due to the transfusion of blood components and plasma derivatives. As of 2007, all provinces and territories, with the exception of Nunavut, provide data to TTISS. Currently, the TTISS network covers over 95% of total blood transfusion activities in Canada.

This report presents the number of ATRs related to the transfusion of blood components and plasma derivatives. In addition, ATR rates are reported for the transfusion of blood components (BCs) only. Rates for the transfusion of plasm a derivatives (PDs) are not shown due to the non-availability of denominator data.

The range of ATRs reported include transfusion-associated circulatory overload (TACO), severe anaphylactic or anaphylactoid reaction (SAAR), hypotensive reaction (HYPT), acute and delayed haemolytic reaction (AHR and DHR), transfusion-related acute lung injury (TRALI), transfusion-associated dyspnea (TAD), intravenous immune globulin headache or hemolysis (IVIG-HD), aseptic meningitis (ASPT), bacterial infections (BACT), incompatible transfusion (INCMP), and unusual reactions of clinical significance (Others).

Sites reported a total of 4,334 ATRs to TTISS during the five-year period of 2016 to 2020. 61.3% (2,658) of cases were due to transfusion of blood components and 38.7% (1,676) were due to transfusion of plasma derivatives. TACO, among transfusion of blood components, and IVIG-HD, among transfusion of plasma derivatives, were the most commonly reported ATRs, representing 43.7% (1,161) and 40.9% (685), respectively.

In terms of imputability (definite, probably, possible), 11.2% of ATRs were definitely imputable to transfusion. 88.8% of ATRs were probably or possibly imputable to transfusion. The severity of an ATR is defined by the level of medical care or intervention that the patient required. 68.8% of ATRS were non-severe, 25.2% were severe, and 5.0% that resulted in life-threatening injuries, including four deaths.

Of the total ATRs (n=4,334) with reported outcomes, 84.0% resulted in minimal or no harm to recipients, whereas major or long-term sequelae and deaths accounted for 2.7% and 1.4% respectively. TACO and TRALI were the leading causes of transfusion-related deaths.

Most deaths occurred in older patients (median age=72 years), so they may also be attributable to other causes. This suggests that the actual number of ATR-related deaths may be lower than the number of reported deaths. Further research is required to clarify the relationship between transfusion and death.

INTRODUCTION

Established as a pilot system in 2001, the Transfusion-Transmitted Injuries Surveillance System (TTISS) has since been reporting adverse transfusion reactions (ATRs), which are defined as undesirable and unintentional incidents that occur during or after the administration of blood, blood components, or plasma derivatives. TTISS collects non-nominal data on ATRs after the transfusion of blood components (such as red blood cells, granulocytes, platelets, plasma, and cryoprecipitate) and plasma derivatives (such as albumin, immune globulin, and coagulation factors). ATRs are voluntarily reportable to TTISS by a national network of hospitals providing transfusion services across all provinces and territories except Nunavut. The TTISS National Working Group (NWG-TTISS) is comprised of representatives from each province and territory, two blood manufacturers (Canadian Blood Services and HémaQuébec), and ex-officio representation from Health Canada's Marketed Health Products Directorate (MHPD) and Biologics and Genetic Therapies Directorate (BGTD). The NWG-TTISS advises TTISS on its operation and direction as a national surveillance system. The objective of TTISS is to identify and estimate risks and trends of ATRs in order to improve patient safety in Canadian hospitals. This report summarizes the findings of TTISS' 2016-2020 national data.

METHODS

Data collection and processing

All participating hospitals in the TTISS network are providing data to the Public Health Agency of Canada (PHAC), covering more than 95% of transfusions in Canadian hospitals.

A set of standardized case definitions and a standardized reporting form1 are used to record data and are transferred electronically to the Canadian Network for Public Health Intelligence (CNPHI), which is a centralized web-based system2. Currently, ten of the eleven participating sites enter their data into CNPHI, and one site electronically submits their data directly to PHAC. Generally, PHAC receives annual data with a time lag of six months (for example, 2020 data are received the following year by July). Data is reviewed for quality assurance and requests for verifications of any discrepancies are addressed with each site separately. After validations, some ATRs may be reclassified or excluded to comply with standardized case definitions. All data are then combined to form a national TTISS database for analysis.

ATRs are categorised based on imputability (the likelihood of being related to transfusion) and whether this relationship is definite, probable, or possible. The relationship could also be ruled out, doubtful, or undetermined, in which case the ATR is referred to as "non-transfusionrelated'. Only transfusion-related ATRs are considered for analysis. The severity (the level of intervention required to respond to the adverse event or the disability sustained) and outcome (whether the recipient sustained any physiological or physical consequence, such as damage or impairment of a bodily function) are also recorded. The outcome varies from minor to major or long-term sequelae, including death. In cases of death, further investigation is conducted to determine the ATR's imputability and to establish whether the event is definitely, probably, possibly, or doubtfully related to the transfusion, or whether imputability is undetermined or to be ruled out (Annex A).

ATRs collected in TTISS include severe anaphylactic or anaphylactoid reaction (SAAR), transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI) and possible TRALI, transfusion-associated dyspnea (TAD), hypotensive reaction (HYPT), intravenous immune globulin headache (IVIG-HD), acute and delayed haemolytic reaction (AHR and DHR), aseptic meningitis (ASPT), bacterial infection (BACT), and incompatible transfusion (INCMP). In addition to the above ATRs, when the recipient experiences any other type of adverse reaction, e.g., severe electrolyte imbalance, atypical pain

syndrome, etc., these are classified as “Other”. Minor allergic reactions, febrile nonhaemolytic reactions (FNHR), and delayed serological reactions (DSR) are not considered in the TTISS analysis. When adverse reactions are associated with both blood components and plasma derivatives, only data from the first transfusion is included in the analysis.

1. Transfusion Transmitted Injuries Surveillance System, User’s Manual, ver. 3.0, 2007. Public Health Agency of Canada.

2. CNPHI https://www.cnphi-rcrsp.ca/cnphi/DownloadUserAgreement?lang=en

Denominator Data

The number of units of blood components transfused annually in hospitals within the TTISS network is used as the denominator to calculate rates per 100,000 units of blood components transfused.

Statistical Analysis

Descriptive analyses were performed using the SAS EG 5.1 software. Counts and proportions of specific ATRs are calculated for all transfusions, transfusions of blood components, and transfusions of plasma derivatives, during the reporting period 2016-2020. Rates of specific ATRs and death are calculated per 100,000 units of blood components transfused.

RESULTS

The TTISS results are presented in five sections, each including the overall results, and where feasible, separate results for blood components and plasma derivatives:

1. Counts and proportions of ATRs, excluding those with doubtful, ruled out, or undetermined imputability, or where this information is missing

2. ATR rates associated with the transfusion of blood components

3. Counts and proportions of ATRs based on the imputability of the adverse reaction

4. Counts and proportions of ATRs by severity

5. Counts and proportions of ATRs by outcome

1. ADVERSE TRANSFUSION REACTIONS (ATRS)

Annex B provides the annual numbers of ATRs for the five-year period. Figure A presents the annual percentages of ATRs arising from the transfusion of blood components compared to from that of plasma derivatives. Of the total ATRs reported (n=4,334), nearly two-thirds (61.3%, n=2,658/4,334) are due to transfusion of blood components and a little more than one-third (38.7%, n=1,676/4,334) are due to transfusion of plasma derivatives. The annual proportions of ATRs remained consistent, with small variations in the range of 61.3 (± 4.8%) when due to transfusion of blood components and 38.7 (± 4.8%) when due to transfusion of plasma derivatives. Figure 1B presents the distribution of types of ATRs from transfusion of blood components and transfusion of plasma derivatives. Among ATRs due to transfusion of blood components, TACO is the most reported ATR (43.7%, n=1,161/2,658), followed by SAAR (11.7%, n=293/2,658) and HYPT (10.5%, n=278/2,658). Among ATRs due to transfusion of plasma derivatives, IVIG headache is the most reported (40.9%, n=685/1,676), followed by SAAR (6.9%, 115/1,676).

FIGURE 1A: ATRs (%) from transfusion of blood components and of plasma derivatives by year

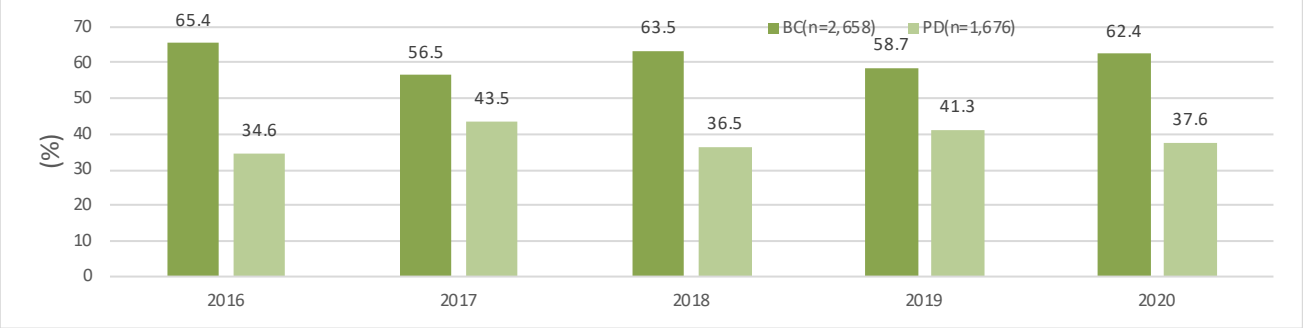
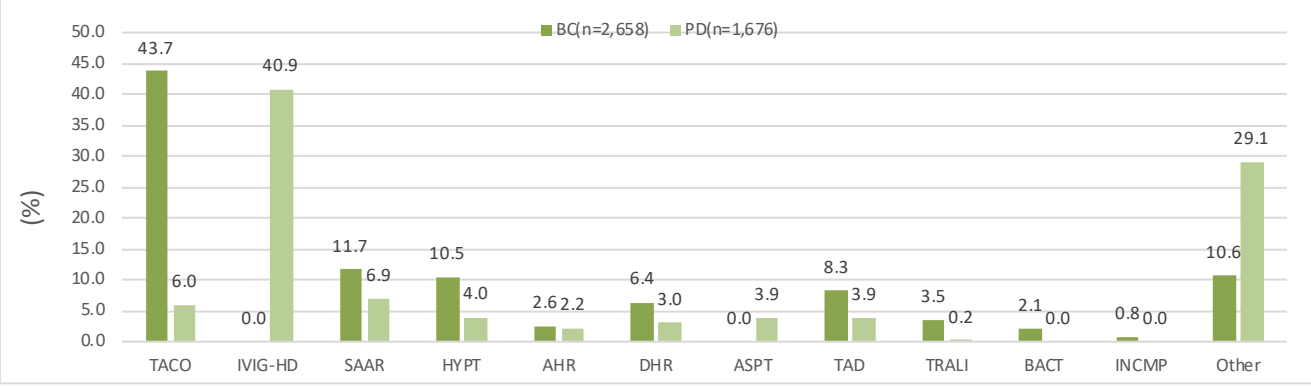


FIGURE 1B: ATRs (%) from transfusion of blood Components and of plasma derivatives by type



1. ATR RATES

ATR rates are calculated by considering the number of ATRs reported due to blood components as the numerator (Annex B) and the number of units of blood components transfused as denominator (Annex C), represented per 100,000 units of blood components transfused. TACO consistently had the highest rates with some yearly variation. ATRs including SAAR, HYPT, TAD, and TRALI had much lower rates with annual rates under 6% each. The ATR rates for BACT and INCMP are very low.

TABLE 2: ATR rates by type per year/100,000 units of blood components Transfused

ATRs	2016	2017	2018	2019	2020	TOTAL
TACO	19.0	21.1	19.0	13.6	22.8	19.1
SAAR	5.9	4.4	4.6	5.3	5.3	5.1
HYPT	4.8	4.0	5.4	2.6	6.1	4.6
AHR	1.9	1.0	1.2	0.6	0.9	1.1
DHR	3.0	1.9	3.1	2.2	3.8	2.8
TAD	4.0	2.9	3.9	3.5	3.7	3.6
TRALI	1.5	1.5	1.6	1.1	2.0	1.5
BACT	1.1	0.5	0.9	1.2	0.9	0.9
INCMP	0.4	0.9	0.2	0.1	0.0	0.3
Other	5.7	5.5	3.9	4.2	3.9	4.6
Total	47.3	43.9	43.8	34.3	49.3	43.7

2. ATRS By IMPUTABILITY

Annex A provides the definition for each imputability level and Annex D provides the numbers of ATRs in each of these levels. Table 3A to 3C displays, sorted by imputability levels, the number of ATR cases due to all transfusions, the transfusion of blood components, and the transfusion of plasma derivatives. Figure 3A exhibits the data concerning all transfusions and Figure 3B exhibits the data for transfusion of blood components and of plasma derivatives separately. Overall, one in ten (11.2%, n=484/4,334) ATRs was definitely linked to transfusions, and nine in ten (88.8%, n=3,850/4,334) were probably or possibly linked to transfusions. Whether in terms of all transfusions, just transfusions of blood components, or just transfusions of plasma derivatives, the number of ATR cases of in each imputability level remained consistent over time with small annual variations (Figure 3A, Figure 3B).

TABLE 3A: ATRs (%) from all transfusions by year and Imputability

YEAR	DEFINITE	PROBABLE	POSSIBLE	(N)
2016	11.3	47.2	41.6	888
2017	10.3	48.5	41.2	963
2018	11.6	43.1	45.3	877
2019	13.8	43.3	42.9	709
2020	9.5	46.2	44.4	897
Total	11.2	45.8	43.0	4,334

TABLE 3B: ATRs (%) from transfusions of blood components by year and Imputability

YEAR	DEFINITE	PROBABLE	POSSIBLE	(N)
2016	12.2	42.7	45.1	581
2017	9.6	43.4	47.1	544
2018	11.5	38.8	49.7	557
2019	14.6	38.8	46.6	416
2020	10.9	40.4	48.8	560
Total	11.6	40.9	47.5	2,658

TABLE 3C: ATRs (%) from transfusions of plasma derivatives by year and Imputability

YEAR	DEFINITE	PROBABLE	POSSIBLE	(N)
2016	9.4	55.7	34.9	307
2017	11.2	55.1	33.7	419
2018	11.9	50.6	37.5	320
2019	13.3	49.0	37.8	293
2020	7.1	55.8	37.1	337
Total	10.5	53.4	36.0	1,676

FIGURE 3A: ATRs (%) from all transfusions by year and imputability

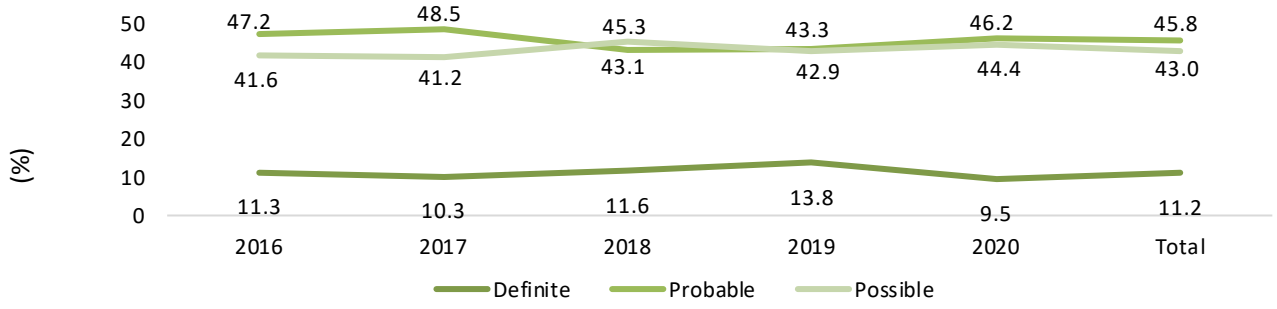
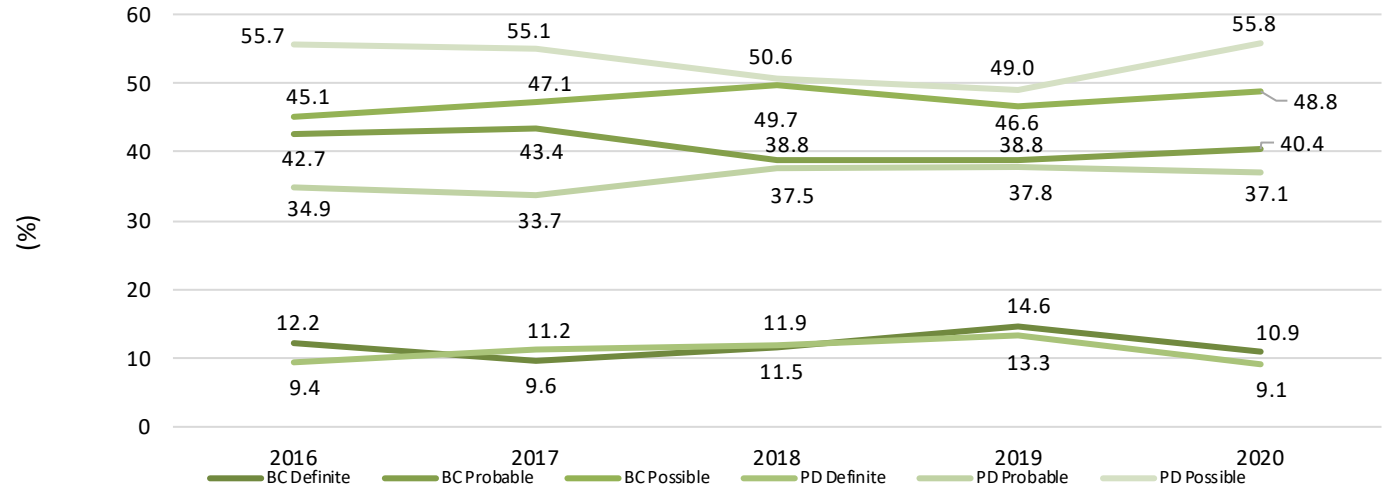


FIGURE 3B: ATRs (%) from transfusions of blood components and of plasma derivatives by year and imputability



Tables 3D to 3F present the imputability data of ATRs for all transfusions, transfusions of blood components, and transfusions of plasma derivatives for the five-year period combined. In terms of all transfusions, TACO and IVIG-HD are the most reported ATRs, representing 29.1% (n=1,261/4,334) and 15.8% (n=685/4,334) of the total. However, they have the smallest number of definitely imputable cases: 8.2% (n=104/1,261) and 9.5% (n=65/685). On the other hand, among the least reported ATRs, INCMP, AHR, and DHR represent 0.5% (n=20/4,334), 2.4% (n=105/4,334), and 5.1% (n=221/4,334) of total cases, respectively. However, a majority of these cases are definitely related to transfusion: 65.0% (n=13/20), 39.0% (n=41/105), and 46.6% (n=103/221), respectively. The ASPT and SAAR cases show almost the same relationships with definite cases making up 16.7% (n=11/66) and 18.4% (n=78/425) of their totals. The ratio between case numbers and imputability in ATR cases due to transfusions of only blood components show a similar pattern with small variations over time.

Among the ATRs associated with the transfusion of plasma derivatives, nearly half of the DHR cases (47.1%, n=24/51), about one-third of the AHR cases (35.1%, n=13/37), and nearly one-fourth of the SAAR cases (23.5%, n=27/115) were considered definitely related to transfusions. TACO and IVIG-HD cases that are definitely linked to transfusions are at, respectively, 3.0% (n=3/100) and 9.5% (n=65/685) of their totals. One TRALI case is definitely associated with the transfusion and the other two cases are probably and possibly linked to the transfusions.

TABLE 3D: ATRs (%) from all transfusions by imputability

ATRS	DEFINITE	PROBABLE	POSSIBLE	TOTAL
TACO	8.7	46.1	45.2	1,161
IVIG-HD	9.5	64.2	26.3	685
SAAR	18.4	53.6	28.0	425
HYPT	3.8	34.8	61.4	345
AHR	39.0	37.1	23.8	105
DHR	46.6	27.6	25.8	221
ASPT	16.7	51.5	31.8	66
TAD	1.1	31.2	67.7	285
TRALI	9.3	29.9	60.8	97
BACT	10.9	14.5	74.5	55
INCMP	65.0	25.0	10.0	20
Other	4.9	45.4	49.7	769
Total	11.2	45.8	43.0	4334

TABLE 3E: ATRs (%) from transfusions of blood components by imputability

ATRS	DEFINITE	PROBABLE	POSSIBLE	(N)
TACO	8.7	46.1	45.2	1,161
SAAR	16.5	55.8	27.7	310
HYPT	3.6	32.7	63.7	278
AHR	41.2	30.9	27.9	68
DHR	46.5	28.8	24.7	170
TAD	1.4	32.3	66.4	220
TRALI	8.5	29.8	61.7	94
BACT	10.9	14.5	74.5	55
INCMP	65.0	25.0	10.0	20
Other	3.2	37.6	59.2	282
Total	11.6	40.9	47.5	2,658

TABLE 3F: ATRs (%) from transfusions of blood components by imputability

ATRS	DEFINITE	PROBABLE	POSSIBLE	(N)
TACO	3.0	48.0	49.0	100
IVIG-HD	9.5	64.2	26.3	685
SAAR	23.5	47.8	28.7	115
HYPT	4.5	43.3	52.2	67
AHR	35.1	48.6	16.2	37
DHR	47.1	23.5	29.4	51
ASPT	16.7	51.5	31.8	66
TAD	0.0	27.7	72.3	65
TRALI	33.3	33.3	33.3	3
Other	6.0	49.9	44.1	487
Total	10.5	53.6	35.9	1,676

4. SEVERITY OF ATRS

Annex A provides the definitions of each severity level and Annex E provides the number of yearly reported ATRs sorted by severity level. Tables 4A to 4C list the annual proportions of ATRs by severity levels. Figure 4A exhibits this data for all transfusions, and Figure 4B exhibits the data for transfusions of blood components and of plasma derivatives separately. Overall, out of the ATRs reported during 2016-2020, two-thirds (68.7%, n=2979/4,334) were non-severe, one-quarter (25.1%, n=1,090/4334) was severe, and 5.0% (n=215/4,334) were recorded as having induced life-threatening injuries. When sorted by severity levels, the ATR cases exhibit a uniform trend with small annual variations (Figure 4A).

Similarly, the distribution of cases according to severity levels in Figure 4B is also constant with small annual variations. The number of ATRs deemed to be non-severe are consistently lower for transfusion of blood components than for that of plasma derivatives, whereas the number of ATRs deemed to be severe and life-threatening injuries are consistently higher for transfusion of blood components than for that of plasma derivatives.

Table 4A: ATRs (%) from all transfusions by severity and year

YEAR	NON_SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
2016	68.8	24.0	6.5	0.7	888
2017	71.2	23.4	4.3	1.1	963
2018	69.2	25.0	4.3	1.5	877
2019	65.9	27.1	5.8	1.3	709
2020	67.8	26.9	4.1	1.2	897
Total	68.7	25.1	5.0	1.2	4,334

Table 4B: ATRs (%) from transfusions of blood components by severity and year

YEAR	NON-SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
2016	64.2	26.2	9.0	0.7	581
2017	61.6	30.1	6.8	1.5	544
2018	63.7	28.2	6.3	1.8	557
2019	55.0	34.4	9.1	1.4	416
2020	58.4	34.3	5.5	1.8	560
Total	60.9	30.4	7.4	1.4	2,658

Table 4C: ATRs (%) from transfusions of plasma derivatives by severity and year

YEAR	NON-SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
2016	77.5	19.9	2.0	0.7	307
2017	83.8	14.6	1.0	0.7	419
2018	78.8	19.4	0.9	0.9	320
2019	81.2	16.7	1.0	1.0	293
2020	83.4	14.5	1.8	0.3	337
Total	81.1	16.8	1.3	0.7	1,676

FIGURE 4A: ATRs (%) from all transfusions by severity and year

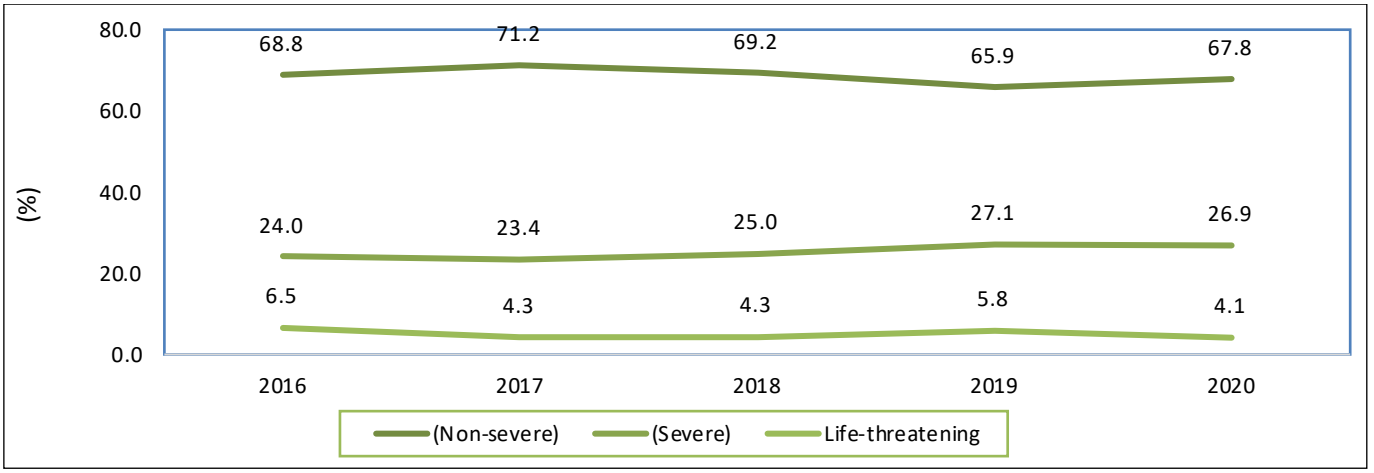
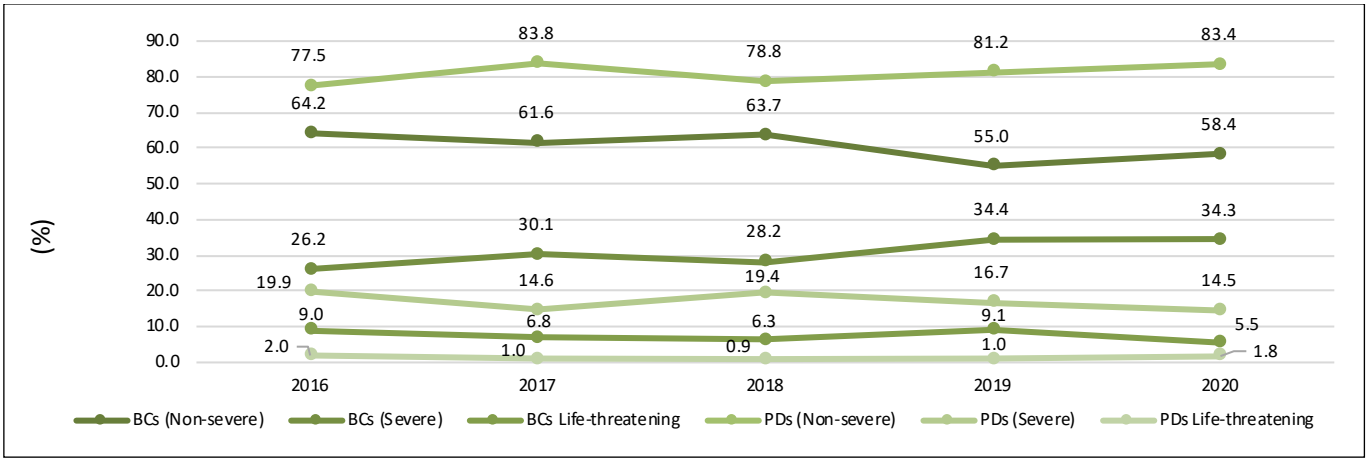


FIGURE 4B: ATRs (%) from transfusions of blood components and of plasma derivative by severity and year



Tables 4D to 4F details the percentages of cases sorted by types of ATR and by severity level for the five-year combined period. Among the ATRs related to the transfusion of blood components, TACO, SAAR, and HYPT make up a large portion of total cases. However, few cases of these ATR types were of grade 3 severity and accounted for 5.6%, 15.2%, and 5.0% of each of their totals, respectively. On the other hand, TRALI, BACT, and INCMP make up a smaller portion of the total ATRs but have higher proportions of grade 3 severity cases (35.1%, 18.2%, and 10.0% of each of their total case numbers, respectively).

TABLE 4D: ATR types (%) from all transfusions by severity

ATRS	NON-SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
TACO	62.3	30.9	5.4	1.4	1261
IVIG-HD	94.0	6.0	0.0	0.0	685
SAAR	33.4	52.2	13.6	0.7	425
HYPT	77.4	17.4	4.1	1.2	345
AHR	45.7	50.5	2.9	1.0	105
DHR	64.3	29.4	3.2	3.2	221
ASPT	63.6	34.8	1.5	0.0	66
TAD	78.9	17.9	1.8	1.4	285
TRALI	13.4	50.5	34.0	2.1	97
BACT	38.2	40.0	18.2	3.6	55
INCMP	50.0	35.0	10.0	5.0	20
Other	83.2	13.9	1.8	1.0	769
Total	68.7	25.1	5.0	1.2	4,334

TABLE 4E: ATR types (%) from transfusions of blood components by severity

ATRS	NON-SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
TACO	61.8	31.3	5.6	1.4	1161
SAAR	35.5	48.7	15.2	0.6	310
HYPT	75.5	18.0	5.0	1.4	278
AHR	47.1	48.5	4.4	0.0	68
DHR	65.9	27.6	4.1	2.4	170
TAD	79.5	17.3	1.8	1.4	220
TRALI	12.8	50.0	35.1	2.1	94
BACT	38.2	40.0	18.2	3.6	55
INCMP	50.0	35.0	10.0	5.0	20
Other	78.0	17.7	2.8	1.4	282
Total	60.9	30.4	7.3	1.4	2,658

TABLE 4F: ATR types (%) from transfusions of plasma derivatives by severity

ATR	NON-SEVERE	SEVERE	LIFE-THREATENING	UNDETERMINED	(N)
TACO	68.0	27.0	3.0	2.0	100
IVIG-HD	94.0	6.0	0.0	0.0	685
SAAR	27.8	61.7	9.6	0.9	115
HYPT	85.1	14.9	0.0	0.0	67
AHR	43.2	54.1	0.0	2.7	37
DHR	58.8	35.3	0.0	5.9	51
ASPT	63.6	34.8	1.5	0.0	66
TAD	76.9	20.0	1.5	1.5	65
TRALI	33.3	66.7	0.0	0.0	3
Other	86.2	11.7	1.2	0.8	487
Total	81.1	16.8	1.3	0.7	1,676

4.1 Grade 2 (severe) ATRs

Tables 4.1A and B provide the annual numbers of grade 2 ATRs, sorted by ATR and transfusion types. Figure 4.1A and Figure 4.1B exhibits, respectively, the annual trends of grade 2 ATRs caused by transfusions of blood components and by transfusions of plasma derivatives. Of the total number of grade 2 ATR cases (n=1,090), approximately three-quarters (74.1%, n=808/1,090) were due to transfusion of blood components and one-fourth (25.9%, n=282/1,090) was due to transfusion of plasma derivatives. In terms of those resulting from transfusions of blood components, the total numbers of grade 2 ATR cases trended upwards for the first two years (152 in 2016 to 164 in 2017), then downwards for the next two years (157 in 2018 to 143 in 2019), followed by another upward trend to 192 cases in 2020. These numbers are relatively consistent and have small deviations within each ATR type. TACO, followed by SAAR, consistently make up most of the total number regarding the transfusion of blood components (Figure 4.1A). In terms of grade 2 ATRs that are due to the transfusion of plasma derivatives, the numbers were stable for the first three years (61 in 2016 to 62 in 2018) and then declined to 49 cases in 2019 and 2020 (Table 4.1). SAAR and IVIG headache caused grade 2 ATRs more frequently compared to other reaction types (Figure 4.1B).

TABLE 4.1A: ATR types (%) of grade 2 severity from transfusions of blood components

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	44.7	50.0	40.1	39.9	48.4	44.9
SAAR	15.8	17.7	16.6	25.9	18.2	18.7
HYPT	7.9	4.9	10.8	2.8	4.7	6.2
AHR	6.6	3.0	5.1	2.8	3.1	4.1
DHR	7.9	2.4	4.5	8.4	6.3	5.8
TAD	2.6	1.8	6.4	8.4	4.7	4.7
TRALI	3.9	5.5	7.0	3.5	8.3	5.8
BACT	2.6	1.2	2.5	4.2	3.1	2.7
INCMP	2.0	2.4	0.0	0.0	0.0	0.9
Other	5.9	11.0	7.0	4.2	3.1	6.2
(n)	152	164	157	143	192	808

TABLE 4.1B: ATR types (%) of grade 2 severity from transfusions of plasma derivatives

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	13.1	1.6	8.1	8.2	18.4	9.6
IVIG-HD	19.7	9.8	16.1	14.3	12.2	14.5
SAAR	19.7	21.3	35.5	18.4	30.6	25.2
HYPT	3.3	1.6	6.5	0.0	6.1	3.5
AHR	8.2	8.2	6.5	12.2	0.0	7.1
DHR	8.2	8.2	8.1	6.1	0.0	6.4
ASPT	4.9	4.9	4.8	16.3	12.2	8.2
TAD	4.9	6.6	0.0	8.2	4.1	4.6
TRALI	0.0	3.3	0.0	0.0	0.0	0.7
BACT	0.0	0.0	0.0	0.0	0.0	0.0
INCMP	0.0	0.0	0.0	0.0	0.0	0.0
Other	18.0	34.4	14.5	16.3	16.3	20.2
(n)	61	61	62	49	49	282

Figure 4.1A: ATR types (%) of grade 2 severity from transfusions of blood components

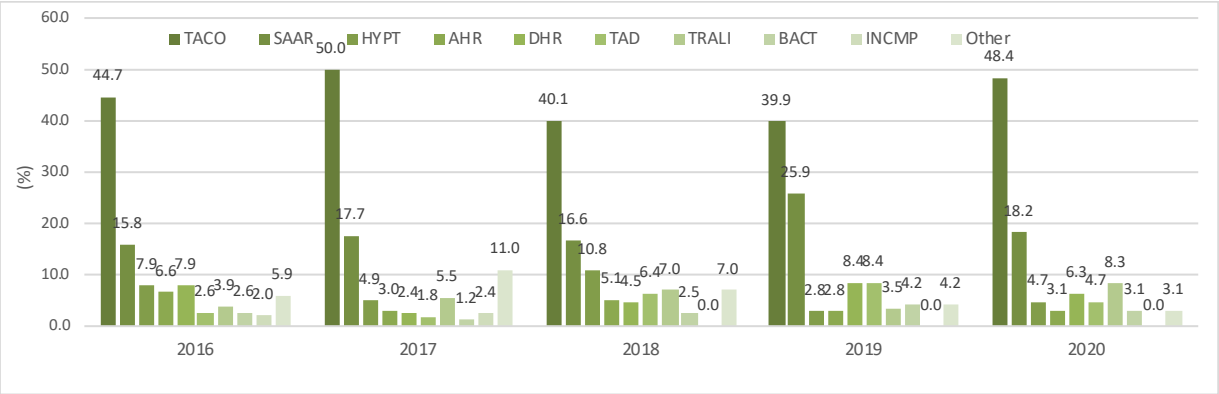
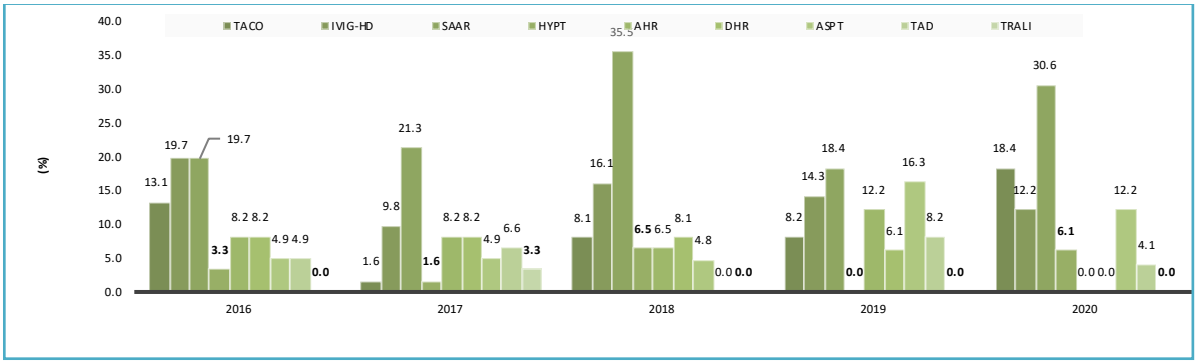


Figure 4.1B: ATR types (%) of grade 2 severity from transfusions of plasma derivatives



4.2 Grade 3 (Life-Threatening) ATRs

Out of the 211 grade 3 ATRs from 2016 to 2020, the vast majority (90.0%, n=190/211) were due to transfusion of blood components, while 10.0% (n=21/211) were due to transfusion of plasma derivatives (Table 4.2). In terms of reactions to transfusion of blood components, TACO was the most common ATR type to induce grade 3 reactions (33.7%, n=64/190), followed by SAAR (24.7%, n=47/190), TRALI (16.8%, n=32/190), and HYPT (7.4%, 14/190). Each of the remaining ATR types represents 5% or less of the total number of grade 3 ATRs. The annual numbers all have similar ratios with small variations (Figure 4.2A).

Of the grade 3 ATR cases that are due to the transfusion of plasma derivatives, SAAR accounted for more than half of the cases (52.4%, n=11/21), TACO accounted for three cases, and one case each was due to ASPT and TAD (Table 4.2). The annual numbers of grade 3 ATRs that are caused by transfusion of plasma derivatives are too small for the analysis of trends.

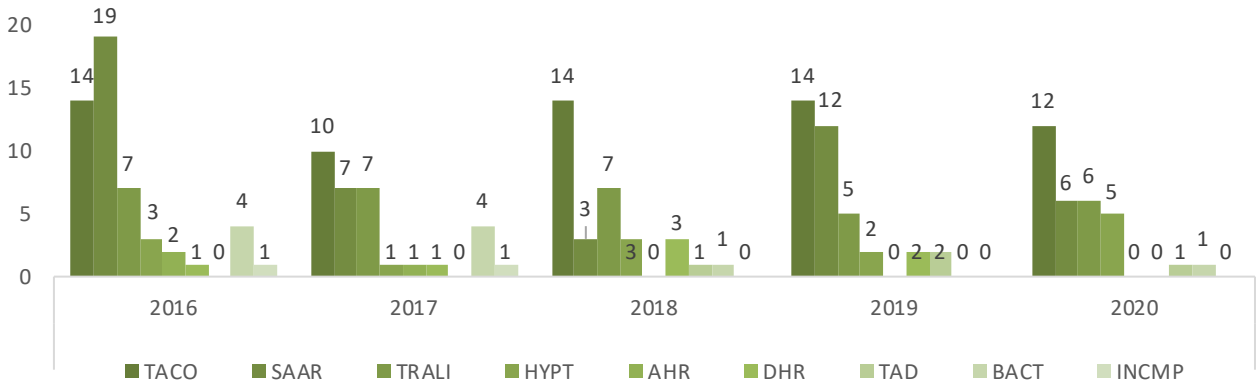
Table 4.2A: ATRs of Life-threatening) Severity by Year from transfusions of blood components

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	14	10	14	14	12	64
SAAR	19	7	3	12	6	47
HYPT	3	1	3	2	5	14
AHR	2	1	0	0	0	3
DHR	1	1	3	2	0	7
ASPT	0	0	0	0	0	0
TAD	0	0	1	2	1	4
TRALI	7	7	7	5	6	32
BACT	4	4	1	0	1	10
INCMP	1	1	0	0	0	2
Other	1	2	3	1	0	7
Total	52	34	35	38	31	190

Table 4.2B: ATRs of life-threatening severity by year from transfusions of plasma derivatives

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	1	1	0	1	3
SAAR	3	2	1	2	3	11
ASPT	0	0	1	0	0	1
TAD	1	0	0	0	0	1
Other	1	1	0	1	2	5
Total	5	4	3	3	6	21

Figure 4.2A: ATRs of life-threatening) severity by year from transfusions of blood components



5. ATRS BY OUTCOME

Annex A provides the detailed definitions of different outcome levels; Annex F lists the number of ATR cases throughout 2016-2020 according to their outcomes. Table 5A to 5C present the percentages of ATR cases that resulted in each outcome category. The figures demonstrate this data in graph-form, with 5A displaying the annual trends of ATR outcomes of all transfusions, and 5B displaying the trends of ATR outcomes of transfusions of blood components and of plasma derivatives separately. The vast majority of ATRs resulted in minor or no sequelae (91.4%, n=3,961/4,334), 3.3% (n=141/4,334) resulted in major or long-term sequelae, and 1.9% (n=81/4,334) resulted in death. The outcome patterns are consistent with small annual variations (Figure 5A). Outcomes associated with only transfusions of blood components or with only that of plasma derivatives demonstrate a similar pattern (Figure 5B). Compared to ATRs resulting from transfusion of plasma derivatives, ATRs resulting from transfusion of blood components have fewer cases with "minor or no-sequelae" and more cases with "major or long-term sequelae" (Table 5, Figure 5B). Of the ATRs resulting in death, the vast majority (96.3%, 78/81) were due to transfusions of blood components and only three deaths (3.7%, 3/81) were due to transfusions of plasma derivatives.

TABLE 5A: ATRs (%) from all transfusions by outcome and year

OUTCOME LEVELS	2016	2017	2018	2019	2020	TOTAL
Minor or no sequelae	92.7	92.2	89.3	91.0	91.6	91.4
Major or long-term sequelae	2.8	3.2	2.7	4.7	3.1	3.3
Death	2.3	1.6	2.6	1.1	1.7	1.9
Undetermined	2.3	3.0	5.4	3.2	3.6	3.5
Total (n)	888	963	877	709	897	4,334
Median age (years) of recipients who reported ATRs	65	64	65	62	66	65
Median age (years) of male recipients who reported ATRs	66	65	67	62.5	66	66
Median age (years) of female recipients who reported ATRs	67	63	62	61	66	63

TABLE 5B: ATRs (%) from transfusions of blood components by outcome and year

OUTCOME LEVELS	2016	2017	2018	2019	2020	TOTAL
Minor or no sequelae	90.7	88.2	85.8	89.2	88.2	88.4
Major or long-term sequelae	2.9	4.2	4.1	6.3	3.8	4.1
Death	3.3	2.8	3.9	1.7	2.7	2.9
Undetermined	3.1	4.8	6.1	2.9	5.4	4.5
Total (n)	581	544	557	416	560	2,658
Median age (years) of recipients who reported ATRs	70	68	68	67	69	69
Median age (years) of male recipients who reported ATRs	69	68	70	67	68	68
Median age (years) of female recipients who reported ATRs	70	68	67	67.5	71	69

TABLE 5C: ATRs (%) from transfusions of plasma derivatives by outcome and year

OUTCOME LEVELS	2016	2017	2018	2019	2020	TOTAL
Minor or no sequelae	96.4	97.4	95.3	93.5	97.3	96.1
Major or long-term sequelae	2.6	1.9	0.3	2.4	2.1	1.8
Death	0.3	0.0	0.3	0.3	0.0	0.2
Undetermined	0.7	0.7	4.1	3.8	0.6	1.8
Total (n)	307	419	320	293	337	1,676
Median age (years) of recipients who reported ATRs	53	58	57	55	62	57
Median age (years) of male recipients who reported ATRs	55	58	56	58	63	59
Median age (years) of female recipients who reported ATRs	52	59	57	52.5	59	57

FIGURE 5A: ATRs (%) from all transfusions by outcome and year

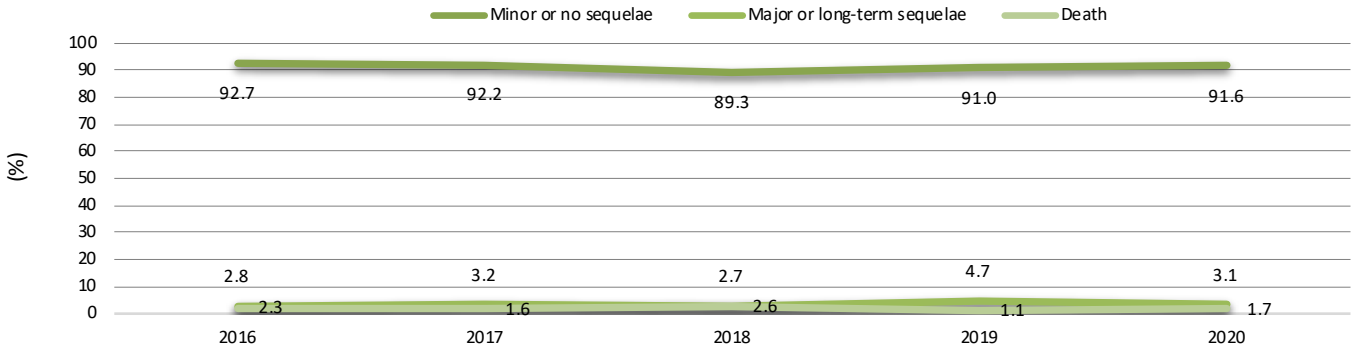
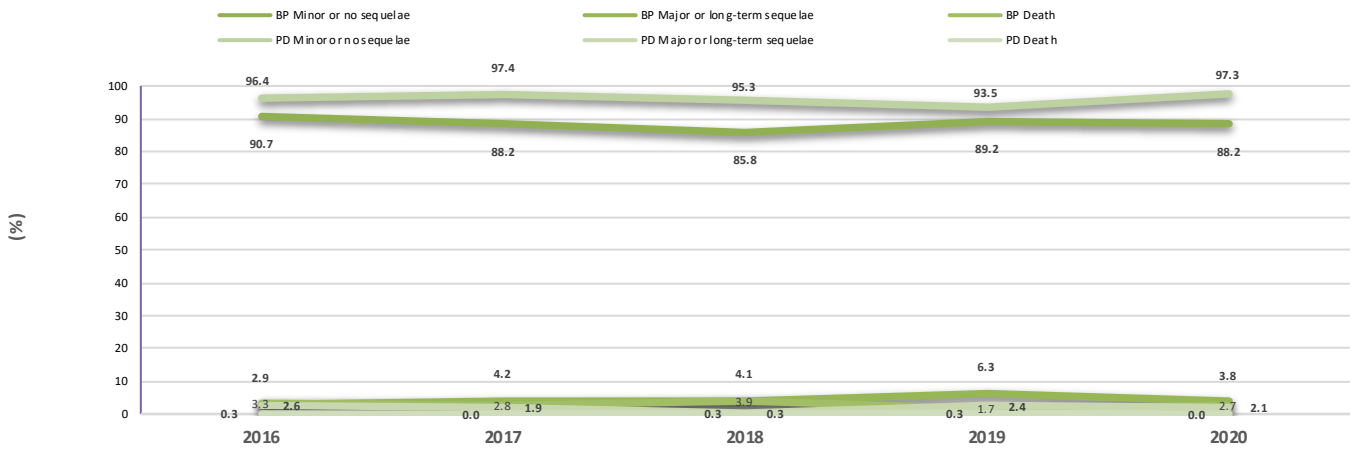


FIGURE 5B: ATRs (%) from transfusions of blood components and plasma derivatives by outcome and year



5.1 ATRs leading to major or long-term sequelae

Of the ATRs that resulted in major or long-term sequelae, the majority (78.0%, n=110/141) were related to transfusions of blood components and 22.0% (n=31/141) were related to transfusions of plasma derivatives (Table 5.1A-5.2C). In terms of all transfusions (Table 5.1A), one-quarter of the ATRs that resulted in major or long-term sequelae was due to TACO (28.4%, n=40/141). Other ATR types that often caused major or long-term sequelae are TRALI (11.3%, n=16/141), SAAR (9.9%, n=14/141), DHR (9.9%, n=14/141), and AHR (9.2%, n=13/141). ATRs due to transfusions of blood components (Table 5.2B) have similar ratios, with TACO representing one-third of the cases (35.5%, n=39/110), followed by TRALI (13.6%, n=15/110), DHR (12.7%, n=14/11), and SAAR (10.0%, n=11/110).

In terms of transfusions of plasma derivatives, ATRs resulting in major or long-term sequelae were rare and sparsely distributed during the five-year reporting period. AHR and IVIG-HD accounted for 22.6% (n=7/31) and 12.9% (n=4/31), respectively, whereas only one case each of TACO and TRALI were reported for this category (Table 5.1C).

TABLE 5.1A: ATRs from all transfusions resulting in major or long-term sequelae

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	5	6	8	12	9	40
IVIG-HD	1	0	0	1	2	4
SAAR	3	3	3	2	3	14
HYPT	0	1	1	0	0	2
AHR	5	1	1	4	2	13
DHR	5	1	5	2	1	14
TAD	0	0	3	2	1	6
TRALI	2	4	1	3	6	16
BACT	0	4	1	4	0	9
INCMP	0	1	0	0	0	1
Other	4	10	1	3	4	22
Total	25	31	24	33	28	141

TABLE 5.1B: ATRs from transfusions of blood components resulting in major or long-term sequelae

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	5	5	8	12	9	39
SAAR	3	3	2	2	1	11
HYPT	0	1	1	0	0	2
AHR	1	1	1	1	2	6
DHR	5	1	5	2	1	14
TAD	0	0	3	1	1	5
TRALI	2	3	1	3	6	15
BACT	0	4	1	4	0	9
INCMP	0	1	0	0	0	1
Other	1	4	1	1	1	8
Total	17	23	23	26	21	110

TABLE 5.1C: ATRs from transfusions of plasma derivatives resulting in major or long-term sequelae

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	1	0	0	0	1
IVIG-HD	1	0	0	1	2	4
SAAR	0	0	1	0	2	3
AHR	4	0	0	3	0	7
TAD	0	0	0	1	0	1
TRALI	0	1	0	0	0	1
Other	3	6	0	2	3	14
Total	8	8	1	7	7	31

5.2 ATRs leading to death

Among the total number of reported deaths, half (49.4%, 40/81) were deemed to have "definite, probable or possible" relationships to transfusion, while the other half (50.6%, n=41/81) were deemed to be "doubtful, ruled out, or not determined" in relationship to transfusions (Table 5.2A). This latter group of non-transfusion-related deaths were not considered further.

Table 5.2A: ATRs resulting in transfusion-related deaths by imputability

ATRS	DEFINITE	PROBABLE	POSSIBLE	N (%)
TACO	1	6	8	15 (37.5)
SAAR	1	1	0	2 (5.0)
DHR	0	1	1	2 (5.0)
TAD	0	0	2	3 (5.0)
TRALI	0	6	6	12 (30.0)
BACT	1	0	2	3 (7.5)
Other	0	0	4	4 (10.0)
Total	3	14	23	40 (100)

TABLE 5.2B: ATRs resulting in non-transfusion-related deaths by imputability

ATRS	DOUBTFULE	RULED OUT	UNDETERMINED	N(%)
TACO	7	8	4	19 (46.3)
SAAR	0	2	0	2 (4.9)
HYPT	0	3	0	3 (7.3)
AHR	3	0	0	3 (7.3)
TAD	1	1	0	2 (4.9)
TRALI	4	0	2	6 (14.6)
BACT	2	0	0	2 (4.9)
Other	2	2	0	4 (9.8)
Total	19	16	6	41 (100)

Of transfusion-related deaths, 95.0% (n=38/40) were due to transfusion of blood components while 5.0% (n=2/40) were due to plasma derivatives (Table 5.2C & Table 5.2D).Three deaths were deemed definitely related to transfusions (two due to that of blood components and one due to that of plasma derivatives), and the remaining 37 deaths were deemed probably or possibly related to transfusions (36 due to blood components, 1 due to plasma derivatives). Among transfusions of blood components, TACO and TRALI were the leading causes of death, the exact numbers being 39.5% (n=15/38) and 31.6% (n=12/38) respectively. In terms of other ATR types, BACT caused three deaths, DHR and TAD caused two deaths each, SAAR caused two deaths (1 due to transfusion of blood components and 1 due to that of plasma derivatives). Four more deaths are categorized as "Other" since the causes are not classifiable among the listed ATRs (Table 5.2B).

TABLE 5.2C: ATRs resulting in transfusion-related deaths by imputability (transfusions of blood components)

ATRS	DEFINITE	PROBABLE	POSSIBLE	TOTAL
TACO	1	6	8	15
SAAR	0	1	0	1
DHR	0	1	1	2
TAD	0	0	2	2
TRALI	0	6	6	12
BAC	1	0	2	3
Other	0	0	3	3
Total	2	14	22	38

TABLE 5.2D: ATRs resulting in transfusion-related deaths by imputability (transfusions of plasma derivatives)

ATRS	DEFINITE	PROBABLE	POSSIBLE	TOTAL
SAAR	1	0	0	1
Other	0	0	1	1
Total	1	0	1	2

The number of deaths by ATR type and year are detailed in Table 5.2E and F. The average number of deaths was 7.6 per year, varying from nine deaths in 2016 to seven deaths in 2020. TACO and TRALI were the leading causes of death with, respectively, an average of three deaths per year (Range: 1 to 5 deaths) and 2.4 deaths per year (Range: 1 to 4 deaths). Of the two deaths due to transfusions of plasma derivatives, one reported in 2016 was due to “Other causes” and one reported in 2019 was due to SAAR (Table 5.2D). The changes over time in the number of deaths should be interpreted with caution given the small number of cases reported and inherent variations in annual reporting.

In order to consider the relationship between age and transfusion-related deaths, the median age was calculated by sex for patients who experienced ATRs (Table 5) and death (Table 5.2E and F). The overall median age of patients with ATRs was 65 years. The male and female median ages were 66 and 63 years, respectively (Table 5). The overall median age of patients who passed away was 73 years. The male and female median ages at the time of death were, respectively, 73 and 72 years (Table 5.2E). Of the two deaths due to plasma derivatives, one involved a female infant in 2016 and the other was a 72-year-old male in 2019. These findings suggest that ATR-related deaths generally occur at much older ages where other underlying morbidities may play a role.

TABLE 5.2E: Annual number of deaths, median age (years) at death, and death rates (transfusions of blood components)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	2	3	5	1	4	15
SAAR	0	1	0	0	0	1
DHR	0	1	1	0	0	2
TAD	1	0	1	0	0	2
TRALI	4	2	3	1	2	12
BACT	2	0	0	0	1	3
Other	0	1	1	1	0	3
All deaths (med. age)	9 (73.0)	8 (73.0)	11 (73.0)	3 (42.0)	7 (74.0)	38 (73.0)
Male deaths (med. age.)	5 (73.0)	4 (69.0)	7 (73.0)	0	5 (74.0)	21 (73.0)
Female deaths (med. age.)	4 (71.0)	4 (79.0)	4 (74.5)	3 (42.0)	2 (77.0)	17 (72.0)
BC units transfused	1,227,593	1,240,351	1,272,609	1,210,631	1,133,937	6,086,778
Death rate per million units transfused	7.3	6.4	8.6	2.5	6.2	6.2

TABLE 5.2F: Annual number of deaths and median age (years) at death (transfusions of plasma derivatives)

ATRS	2016	2017	2018	2019	2020	TOTAL
SAAR	0	0	0	1	0	1
Other	1	0	0	0	0	1
All deaths (med age)	1	0	0	1	0	2
Male deaths (med age)	n/a	n/a	n/a	1 (72)	n/a	1 (72)
Female death (med age)	1 (0)	n/a	n/a	n/a	n/a	1 (0)

SUMMARY

Among the ATRs reported during the five-year period of 2016-2020:

- In total, 60% of ATRs were related to the transfusion of blood components and forty percent were related to that of plasma derivatives.
- TACO and IVIG-HD were, respectively, the most reported ATRs among recipients of blood components and of plasma derivatives.
- One in ten ATRs was definitely related to transfusion; nine in ten were probably or possibly related to transfusion.
- Of the reported deaths, one-half was transfusion-related and the other half were non-transfusion-related.
- Among the transfusion-related deaths, 95.0% were due to transfusion of blood components and 5.0% were due to transfusion of plasma derivatives.
- TACO and TRALI were the leading causes of deaths.
- TTISS findings demonstrate trends and outcomes similar to that of other industrialized countries.

ANNEX A: DEFINITIONS OF SEVERITY, IMPUTABILITY, AND OUTCOME LEVELS

SEVERITY LEVELS OF ATRS

SEVERITY LEVEL	DEFINITIONS
Grade 1 (Non-severe)	No permanent damage or impairment of a bodily function.
Grade 2 (Severe)	Patient required in-patient hospitalization or prolongation of hospitalization directly attributable to the reaction; or the adverse reaction resulted in persistent/ significant disability or incapacity; or it necessitated medical/surgical intervention to preclude permanent/significant damage or impairment of a bodily function.
Grade 3 (Life-threatening)	Patient required major intervention following the transfusion (vasopressors, intubation, transferred to intensive care).
Grade 4 (Death)	Patient's death was suspected to be the consequence of the transfusion reaction.
Not determined	Consequences of the transfusion reaction were not certain.

IMPUTABILITY LEVELS OF ATRS

IMPUTABILITY LEVEL	DEFINITIONS
Definite	Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives and was proven by investigation to have been caused by transfusion.
Probable	Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives and did not seem to be explainable by any other cause.
Possible	Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives but could be explained by concurrent disease(s) or by the administration of a drug or other agent.
Doubtful	Clinical and/or laboratory event occurred within a reasonable time frame in relation to the transfusion but the preponderance of data supports an alternative explanation.
Ruled out	Clinical and/or laboratory event occurred within a time frame inconsistent with the administration of the blood, blood component, or plasma derivatives or, if it occurred within a consistent time period but it was proven to have no relationship to the transfusion.
Not determined	It remains to be determined whether the event was related to the administration of the blood, blood component or plasma derivatives. Further information is forthcoming however was not available at time of data provision.

OUTCOME LEVELS OF ATRS

OUTCOME LEVEL	DEFINITION
Minor sequelae	Patient had no sequelae or permanent disability from the reaction or developed antibodies to low/medium frequency antigens (< 95%).
Major sequelae	Patient developed either an infection with a persistent infectious agent (HIV, HBV or HCV), or a transfusion reaction with major or long-term sequelae; or the anticipation of difficulties with future transfusions (e.g., development of antibodies to antigens present in more than 95% of donations).
Death	n/a
Not determined	The outcome of the adverse event was deemed uncertain.

IMPUTABILITY LEVELS OF TRANSFUSION-RELATED DEATHS

IMPUTABILITY LEVEL	DEFINITION
Definite	Death occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives and was proven by investigation to have been caused by transfusion.
Probable	Death occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives and did not seem to be explainable by any other cause.
Possible	Death occurred within a time frame consistent with the administration of the blood, blood component, or plasma derivatives but could be explained by concurrent disease(s) or by the administration of a drug or other agent.
Doubtful	Death occurred within a reasonable time frame in relation to the transfusion but the preponderance of data supports an alternative explanation.
Ruled out	Death occurred within a time frame inconsistent with the administration of the blood, blood component, or plasma derivatives, if it occurred within a consistent time period but it was proven to have no relationship to the transfusion.
Not determined	It could not be determined if the death was related to transfusion.

ANNEX B: ANNUAL NUMBERS OF ATRS ACCORDING TO KIND OF TRANSFUSION

ANNUAL NUMBERS OF ATRS FROM ALL TRANSFUSIONS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	251	284	260	186	280	1261
IVIG-HD	95	207	141	128	114	685
SAAR	94	72	89	82	88	425
HYPT	67	67	90	34	87	345
AHR	35	22	20	18	10	105
DHR	59	37	46	35	44	221
TAD	63	53	66	54	49	285
TRALI	19	21	20	14	23	97
ASPT	29	9	7	11	10	66
BACT	13	6	12	14	10	55
INCMPT	5	11	3	1	0	20
Other	158	174	123	132	182	769
Total	888	963	877	709	897	4,334

ANNUAL NUMBERS OF ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	233	262	242	165	259	1161
SAAR	73	55	58	64	60	310
HYPT	59	50	69	31	69	278
AHR	23	13	15	7	10	68
DHR	37	24	39	27	43	170
TAD	49	36	50	43	42	220
TRALI	19	19	20	13	23	94
BACT	13	6	12	14	10	55
INCMPT	5	11	3	1	0	20
Other	70	68	49	51	44	282
Total	581	544	557	416	560	2,658

ANNUAL NUMBER OF ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	18	22	18	21	21	100
IVIG-HD	95	207	141	128	114	685
SAAR	21	17	31	18	28	115
HYPT	8	17	21	3	18	67
AHR	12	9	5	11	0	37
DHR	22	13	7	8	1	51
TAD	14	17	16	11	7	65
TRALI	0	2	0	1	0	3
ASPT	29	9	7	11	10	66
Other	88	106	74	81	138	487
Total	307	419	320	293	337	1,676

ANNEX C: ANNUAL NUMBERS OF UNITS OF BLOOD COMPONENTS TRANSFUSED

Province / Territory	2016	2017	2018	2019	2020
British Columbia	176,681	172,513	170,373	161,296	159,779
Yukon Territory	535	636	579	733	884
Alberta	131,755	121905	118,626	111,431	104,762
Saskatchewan	42,575	37,000	50,379	48,197	40,882
Manitoba	52,181	50,364	35,979	31,603	30,460
Ontario	427,494	473,810	513,301	475,493	438,286
Québec	303,262	295452	297,780	299,880	280,487
New Brunswick	28,021	27,320	26,812	27,674	26,442
Nova Scotia	38,614	35,473	20,288	17,426	15,680
Prince Edward Island	4,220	3,911	34,213	34,213	33,087
Newfoundland & Labrador	21,809	21,546	3,791	3,824	3,502
Northwest Territories	446	421	488	518	635
Total	1,227,593	1,240,351	1,272,609	1,212,288	1,134,886

ANNEX D: ANNUAL NUMBERS OF ATRS BY IMPUTABILITY LEVELS

ATRS FROM ALL TRANSFUSIONS (DEFINITE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	16	15	22	30	21	104
IVIG-HD	4	19	13	18	11	65
SAAR	15	15	15	22	11	78
HYPT	1	0	6	2	4	13
AHR	16	8	10	3	4	41
DHR	33	12	22	14	22	103
TAD	1	0	0	1	1	3
TRALI	0	4	0	2	3	9
ASPT	6	1	1	2	1	11
BACT	2	3	0	0	1	6
INCMPT	3	8	2	0	0	13
Other	3	14	11	4	6	38
Total	100	99	102	98	85	484

ATRS FROM ALL TRANSFUSIONS (PROBABLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	124	134	116	78	131	583
IVIG-HD	67	140	87	78	68	440
SAAR	44	39	52	43	50	228
HYPT	24	27	28	11	30	120
AHR	9	9	9	8	4	39
DHR	18	12	12	11	8	61
TAD	21	17	18	15	18	89
TRALI	9	7	5	1	7	29
ASPT	16	4	1	7	6	34
BACT	3	1	1	1	2	8
INCMPT	2	2	1	0	0	5
Other	82	75	48	54	90	349
Total	419	467	378	307	414	1,985

ATRS FROM ALL TRANSFUSIONS (POSSIBLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	111	135	122	78	128	574
IVIG-HD	24	48	41	32	35	180
SAAR	35	18	22	17	27	119
HYPT	42	40	56	21	53	212
AHR	10	5	1	7	2	25
DHR	8	13	12	10	14	57
TAD	41	36	48	38	30	193
TRALI	10	10	15	11	13	59
ASPT	7	4	5	2	3	21
BACT	8	2	11	13	7	41
INCMPT	0	1	0	1	0	2
Other	73	85	64	74	86	382
Total	369	397	397	304	398	1,865

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS (DEFINITE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	16	14	22	28	21	101
SAAR	13	9	9	16	4	51
HYPT	1	0	5	2	2	10
AHR	12	3	8	1	4	28
DHR	21	8	18	10	22	79
TAD	1	0	0	1	1	3
TRALI	0	4	0	1	3	8
BACT	2	3	0	0	1	6
INCMPT	3	8	2	0	0	13
Other	2	3	0	1	3	9
Total	71	52	64	60	61	308

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS (PROBABLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	115	123	108	70	119	535
SAAR	35	32	34	34	38	173
HYPT	20	19	18	11	23	91
AHR	4	6	6	1	4	21
DHR	14	8	11	8	8	49
TAD	18	12	13	14	14	71
TRALI	9	6	5	1	7	28
BACT	3	1	1	1	2	8
INCMPT	2	2	1	0	0	5
Other	28	27	19	21	11	106
Total	248	236	216	161	226	1087

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS (POSSIBLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	102	125	112	67	119	525
SAAR	25	14	15	14	18	86
HYPT	38	31	46	18	44	177
AHR	7	4	1	5	2	19
DHR	2	8	10	9	13	42
TAD	30	24	37	28	27	146
TRALI	10	9	15	11	13	58
BACT	8	2	11	13	7	41
INCMPT	0	1	0	1	0	2
Other	40	38	30	29	30	167
Total	262	256	277	195	273	1263

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES (DEFINITE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	1	0	2	0	3
IVIG-HD	4	19	13	18	11	65
SAAR	2	6	6	6	7	27
HYPT	0	0	1	0	2	3
AHR	4	5	2	2	0	13
DHR	12	4	4	4	0	24
TRALI	0	0	0	1	0	1
ASPT	6	1	1	2	1	11
Other	1	11	11	3	3	29
Total	29	47	38	38	24	176

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES (PROBABLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	9	11	8	8	12	48
IVIG-HD	67	140	87	78	68	440
SAAR	9	7	18	9	12	55
HYPT	4	8	10	0	7	29
AHR	5	3	3	7	0	18
DHR	4	4	1	3	0	12
TAD	3	5	5	1	4	18
TRALI	0	1	0	0	0	1
ASPT	16	4	1	7	6	34
Other	54	48	29	33	79	243
Total	171	231	162	146	188	898

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES (POSSIBLE IMPUTABILITY)

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	9	10	10	11	9	49
IVIG-HD	24	48	41	32	35	180
SAAR	10	4	7	3	9	33
HYPT	4	9	10	3	9	35
AHR	3	1	0	2	0	6
DHR	6	5	2	1	1	15
TAD	11	12	11	10	3	47
TRALI	0	1	0	0	0	1
ASPT	7	4	5	2	3	21
Other	33	47	34	45	56	215
Total	107	141	120	109	125	602

ANNEX E: ANNUAL NUMBERS OF ATRS BY SEVERITY LEVELS

NON-SEVERE ATRS FROM ALL TRANSFUSIONS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	160	185	172	110	158	785
IVIG-HD	83	201	131	121	108	644
SAAR	35	21	37	20	29	142
HYPT	48	56	65	28	70	267
AHR	18	11	8	7	4	48
DHR	41	25	29	18	29	142
TAD	55	46	54	33	37	225
TRALI	5	2	2	4	0	13
ASPT	26	6	3	3	4	42
BACT	4	0	6	8	3	21
INCMPT	1	5	3	1	0	10
Other	135	128	97	114	166	640
Total	611	686	607	467	608	2,979

SEVERE ATRS FROM ALL TRANSFUSIONS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	76	83	68	61	102	390
IVIG-HD	12	6	10	7	6	41
SAAR	36	42	48	46	50	222
HYPT	14	9	21	4	12	60
AHR	15	10	12	10	6	53
DHR	17	9	12	15	12	65
TAD	7	7	10	16	11	51
TRALI	6	11	11	5	16	49
ASPT	3	3	3	8	6	23
BACT	4	2	4	6	6	22
INCMPT	3	4	0	0	0	7
Other	20	39	20	14	14	107
Total	213	225	219	192	241	1,090

LIFE-THREATENING ATRS FROM ALL TRANSFUSIONS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	14	12	15	14	13	68
SAAR	22	9	4	14	9	58
HYPT	3	1	3	2	5	14
AHR	2	1	0	0	0	3
DHR	1	1	3	2	0	7
TAD	1	0	1	2	1	5
TRALI	7	8	7	5	6	33
ASPT	0	0	1	0	0	1
BACT	4	4	1	0	1	10
INCMPT	1	1	0	0	0	2
Other	3	4	3	2	2	14
Total	58	41	38	41	37	215

ATRS FROM ALL TRANSFUSIONS WITH UNDETERMINED SEVERITY

ATRS	**2016**	**2017**	**2018**	**2019**	**2020**	**Total**
TACO	1	4	5	1	7	18
SAAR	1	0	0	2	0	3
HYPT	2	1	1	0	0	4
AHR	0	0	0	1	0	1
DHR	0	2	2	0	3	7
TAD	0	0	1	3	0	4
TRALI	1	0	0	0	1	2
BACT	1	0	1	0	0	2
INCMPT	0	1	0	0	0	1
Other	0	3	3	2	0	8
Total	6	11	13	9	11	50

NON-SEVERE ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS

ATRS	**2016**	**2017**	**2018**	**2019**	**2020**	**TOTAL**
TACO	151	165	160	93	148	717
SAAR	30	19	29	13	19	110
HYPT	42	40	48	25	55	210
AHR	11	7	7	3	4	32
DHR	24	19	28	13	28	112
TAD	45	33	38	27	32	175
• **TRALI**	5	2	2	3	0	12
BACT	4	0	6	8	3	21
INCMPT	1	5	3	1	0	10
Other	60	45	34	43	38	220
Total	373	335	355	229	327	1,619

SEVERE ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	68	82	63	57	93	363
SAAR	24	29	26	37	35	151
HYPT	12	8	17	4	9	50
AHR	10	5	8	4	6	33
DHR	12	4	7	12	12	47
TAD	4	3	10	12	9	38
TRALI	6	9	11	5	16	47
BACT	4	2	4	6	6	22
INCMPT	3	4	0	0	0	7
Other	9	18	11	6	6	50
Total	152	164	157	143	192	808

LIFE-THREATENING ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	14	11	14	14	12	65
SAAR	19	7	3	12	6	47
HYPT	3	1	3	2	5	14
AHR	2	1	0	0	0	3
DHR	1	1	3	2	0	7
TAD	0	0	1	2	1	4
TRALI	7	8	7	5	6	33
BACT	4	4	1	0	1	10
INCMPT	1	1	0	0	0	2
Other	1	3	3	1	0	8
Total	52	37	35	38	31	193

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS WITH UNDETERMINED SEVERITY

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	4	5	1	6	16
SAAR	0	0	0	2	0	2
HYPT	2	1	1	0	0	4
DHR	0	0	1	0	3	4
TAD	0	0	1	2	0	3
TRALI	1	0	0	0	1	2
BACT	1	0	1	0	0	2
INCMPT	0	1	0	0	0	1
Other	0	2	1	1	0	4
Total	4	8	10	6	10	38

NON-SEVERE ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	9	20	12	17	10	68
IVIG-HD	83	201	131	121	108	644
SAAR	5	2	8	7	10	32
HYPT	6	16	17	3	15	57
AHR	7	4	1	4	0	16
DHR	17	6	1	5	1	30
TAD	10	13	16	6	5	50
TRALI	0	0	0	1	0	1
ASPT	26	6	3	3	4	42
Other	75	83	63	71	128	420
Total	238	351	252	236	281	1,360

SEVERE ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	8	1	5	4	9	27
IVIG-HD	12	6	10	7	6	41
SAAR	12	13	22	9	15	71
HYPT	2	1	4	0	3	10
AHR	5	5	4	6	0	20
DHR	5	5	5	3	0	18
TAD	3	4	0	4	2	13
TRALI	0	2	0	0	0	2
ASPT	3	3	3	8	6	23
Other	11	21	9	8	8	57
Total	61	61	62	49	49	282

LIFE-THREATENING ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	1	1	0	1	3
SAAR	3	2	1	2	3	11
TAD	1	0	0	0	0	1
TRALI	0	0	0	0	0	0
ASPT	0	0	1	0	0	1
Other	2	1	0	1	2	6
Total	6	4	3	3	6	22

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES OF UNDETERMINED SEVERITY

ATRS	2016	2017	2018	2019	2020	TOTALOTAL
TACO	1	0	0	0	1	2
SAAR	1	0	0	0	0	1
DHR	0	2	1	0	0	3
TAD	0	0	0	1	0	1
Other	0	1	2	1	0	4
Total	2	3	3	2	1	11

ANNEX F: ANNUAL NUMBERS OF ATRS BY OUTCOME LEVELS ATRS FROM ALL TRANSFUSIONS RESULTING IN MINOR OR NO SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	233	260	151	126	249	1019
IVIG-HD	94	207	121	117	112	651
SAAR	90	67	58	51	85	351
HYPT	63	66	63	26	83	301
AHR	27	17	12	9	6	71
DHR	53	33	28	18	39	171
TAD	61	52	42	41	46	242
TRALI	8	10	8	3	9	38
ASPT	29	8	5	9	10	61
BACT	10	2	3	4	8	27
INCMPT	5	7	3	1	0	16
Other	150	159	107	103	175	694
Total	823	888	601	508	822	3,642

ATRS FROM ALL TRANSFUSIONS RESULTING IN MAJOR OR LONG-TERM SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	5	6	6	7	9	33
IVIG-HD	1	0	0	1	2	4
SAAR	3	3	1	2	3	12
HYPT	0	1	0	0	0	1
AHR	5	1	1	2	2	11
DHR	5	1	1	2	1	10
TAD	0	0	1	2	1	4
TRALI	2	4	1	2	6	15
BACT	0	4	0	2	0	6
INCMPT	0	1	0	0	0	1
Other	4	10	0	1	4	19
Total	25	31	11	21	28	116

ATRS FROM ALL TRANSFUSIONS RESULTING IN DEATH

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	4	7	3	2	10	26
SAAR	1	1	0	0	0	2
HYPT	1	0	0	0	1	2
AHR	1	1	0	0	0	2
DHR	0	1	1	0	0	2
TAD	1	0	1	0	0	2
TRALI	6	3	1	1	3	14
BACT	3	0	1	0	1	5
Other	3	2	0	1	0	6
Total	20	15	7	4	15	61

ATRS FROM ALL TRANSFUSIONS WITH AN UNDETERMINED OUTCOME LEVEL

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	9	11	100	51	12	183
IVIG-HD	0	0	20	10	0	30
SAAR	0	1	30	29	0	60
HYPT	3	0	27	8	3	41
AHR	2	3	7	7	2	21
DHR	1	2	16	15	4	38
TAD	1	1	22	11	2	37
TRALI	3	4	10	8	5	30
ASPT	0	1	2	2	0	5
BACT	0	0	8	8	1	17
INCMPT	0	3	0	0	0	3
Other	1	3	16	27	3	50
Total	20	29	258	176	32	515

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS RESULTING IN MINOR OR NO SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	215	239	141	114	228	937
SAAR	69	50	36	45	59	259
HYPT	55	49	46	23	65	238
AHR	19	9	7	5	6	46
DHR	32	20	25	14	38	129
TAD	47	35	29	37	39	187
TRALI	8	9	8	3	9	37
BACT	10	2	3	4	8	27
INCMPT	5	7	3	1	0	16
Other	67	60	40	45	42	254
Total	527	480	338	291	494	2,130

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS RESULTING IN MAJOR OR LONG-TERM SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	5	5	6	7	9	32
SAAR	3	3	1	2	1	10
HYPT	0	1	0	0	0	1
AHR	1	1	1	1	2	6
DHR	5	1	1	2	1	10
TAD	0	0	1	1	1	3
TRALI	2	3	1	2	6	14
BACT	0	4	0	2	0	6
INCMPT	0	1	0	0	0	1
Other	1	4	0	1	1	7
Total	17	23	11	18	21	90

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS RESULTING IN DEATH

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	4	7	3	2	10	26
SAAR	1	1	0	0	0	2
HYPT	1	0	0	0	1	2
AHR	1	1	0	0	0	2
DHR	0	1	1	0	0	2
TAD	1	0	1	0	0	2
TRALI	6	3	1	1	3	14
BACT	3	0	1	0	1	5
Other	2	2	0	1	0	5
Total	19	15	7	4	15	60

ATRS FROM TRANSFUSIONS OF BLOOD COMPONENTS WITH AN UNDETERMINED OUTCOME LEVEL

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	9	11	92	42	12	166
SAAR	0	1	21	17	0	39
HYPT	3	0	23	8	3	37
AHR	2	2	7	1	2	14
DHR	0	2	12	11	4	29
TAD	1	1	19	5	2	28
TRALI	3	4	10	7	5	29
BACT	0	0	8	8	1	17
INCMPT	0	3	0	0	0	3
Other	0	2	9	4	1	16
Total	18	26	201	103	30	378

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES RESULTING IN MINOR OR NO SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	18	21	10	12	21	82
IVIG-HD	94	207	121	117	112	651
SAAR	21	17	22	6	26	92
HYPT	8	17	17	3	18	63
AHR	8	8	5	4	0	25
DHR	21	13	3	4	1	42
TAD	14	17	13	4	7	55
TRALI	0	1	0	0	0	1
ASPT	29	8	5	9	10	61
Other	83	99	67	58	133	440
Total	296	408	263	217	328	1,512

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES RESULTING IN MAJOR OR LONG-TERM SEQUELAE

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	1	0	0	0	1
IVIG-HD	1	0	0	1	2	4
SAAR	0	0	0	0	2	2
AHR	4	0	0	1	0	5
TAD	0	0	0	1	0	1
TRALI	0	1	0	0	0	1
Other	3	6	0	0	3	12
Total	8	8	0	3	7	26

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES RESULTING IN DEATH

ATRS	2016	2017	2018	2019	2020	TOTAL
Other	1	0	0	0	0	1
Total	1	0	0	0	0	1

ATRS FROM TRANSFUSIONS OF PLASMA DERIVATIVES WITH AN UNDETERMINED OUTCOME LEVEL

ATRS	2016	2017	2018	2019	2020	TOTAL
TACO	0	0	8	9	0	17
IVIG-HD	0	0	20	10	0	30
SAAR	0	0	9	12	0	21
HYPT	0	0	4	0	0	4
AHR	0	1	0	6	0	7
DHR	1	0	4	4	0	9
TAD	0	0	3	6	0	9
TRALI	0	0	0	1	0	1
ASPT	0	1	2	2	0	5
Other	1	1	7	23	2	34
Total	2	3	57	73	2	137