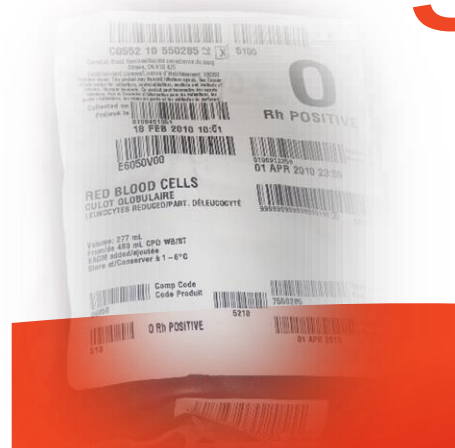
TTISS ON

Ontario Transfusion Transmitted Injuries Surveillance System



Ontario TTISS Program Report 2013 – 2014

April 2016

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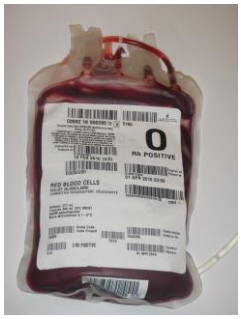

Ontario's contribution to Canada's Transfusion Transmitted Injuries Surveillance System (TTISS) relies on the voluntary involvement of hospitals to report adverse transfusion events. Ontario has created this provincial TTISS report which includes adverse transfusion events in the province during 2013 – 2014 calendar years.

We are excited for the growth in participation of TTISS Ontario (TTISS-ON) and expect to include the majority of hospitals in Ontario over the next five years.

Implementation of many new initiatives will help make TTISS-ON a valuable resource to healthcare professionals responsible for reporting these adverse transfusion events. We appreciate the involvement of healthcare professionals in the program reporting adverse transfusion reactions, as well as those medical experts who contribute their time in reviewing our program and contributing to our vision.

Thank you to the Blood Safety Contribution Program, Public Health Agency of Canada and Ontario's Blood Programs Coordinating Office at the Ministry of Health and Long-Term Care for their continued funding and guidance. In addition, many thanks to colleagues and staff at the Canadian Blood Services and ORBCoN for providing us with an avenue to grow and disseminate information on their websites and facilitating our many annual meetings with great hospitality.

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Executive Summary

Transfusion Transmitted Injuries Surveillance System (TTISS) is a national hemovigilance system implemented by the Public Health Agency of Canada (PHAC) to monitor adverse transfusion events (ATEs) related to blood components and plasma derivatives. The Ontario Ministry of Health and Long-Term Care (MOHLTC) and PHAC contracts the McMaster Centre for Transfusion Research (MCTR) at McMaster University to coordinate TTISS activity in Ontario (TTISS-ON).

The program is designed to capture ATEs related to all **blood products** comprised of ***blood components*** (red cells, plasma, platelets, cryosupernatant, cryoprecipitate) and ***plasma derivatives*** (immunoglobulin preparations, coagulation factors, albumin etc.).

There are 159 hospitals that transfuse blood products in Ontario. This report summarizes ATEs received from 58 Ontario hospitals in 2013 and 77 hospitals in 2014. All TTISS-participating hospitals submit ***reportable ATEs*** (see Appendix 1), which exclude non-reportable ATEs (i.e. febrile non-hemolytic reactions, minor allergic, delayed serological reactions). Also illustrated is the yearly trend of reportable ATEs from 2008-2014.

Transfusion activity at TTISS-ON sites in 2013-2014 represents approximately 71.7% of the blood components transfused in Ontario; an increase of 5.5% from the 66.2% reported for the 2008-2012 period. In 2014 alone, this activity reached 76.7%. We expect to increase the number of hospitals participating in TTISS-ON over the next five years.

A subgroup of 28 hospitals, referred to henceforth as ‘sentinel sites’, report ***all ATEs*** (reportable and non-reportable reactions). The comprehensive reporting by sentinel sites allows for a risk calculation for blood components only. The figures provided on the following pages of this report illustrate the risk of different types of reactions by blood component type. Health care personnel should find this information helpful when informing patients about transfusion related adverse events.

The report is divided into sections consisting of an acknowledgment, executive summary, methodology, and appendices.

There were 354 reportable ATEs (collected from all TTISS-ON sites) and 742 non-reportable ATEs (collected from sentinel sites only) for a total of 1,096 ATEs submitted to TTISS-ON from 2013 to 2014. Of the 354 reportable reactions from all TTISS-participating sites, 255 (72.0%) were related to blood components, 98 (27.7%) to plasma derivatives and 1 (0.3%) to a combination of both blood components and plasma derivatives.

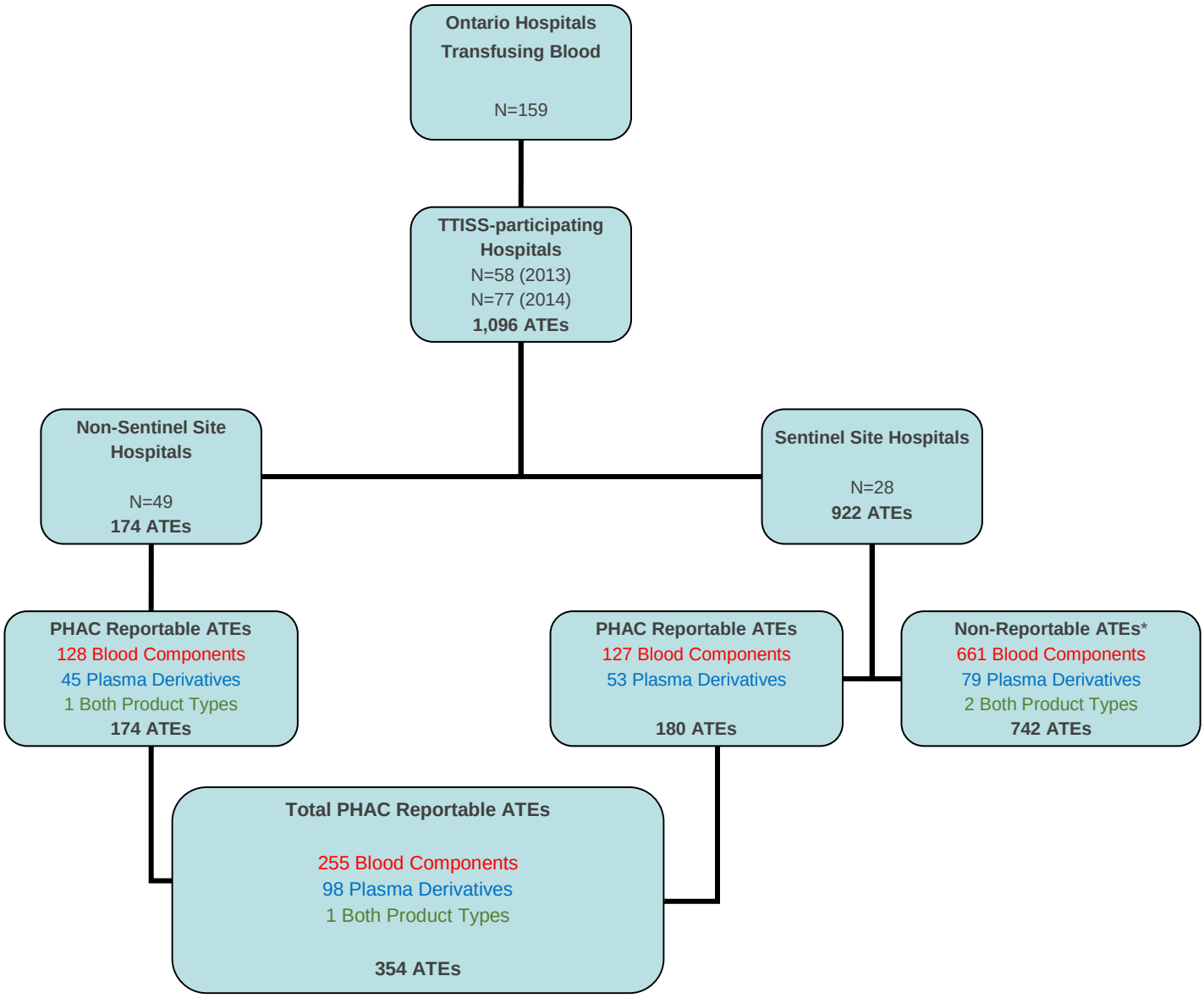
Red blood cells were implicated in 189 (74.1%) of the reactions to blood components. ATEs associated with plasma derivatives were most frequently reported with IVIg (91.8%).

In 2014, there were 7 cases of severe allergic reactions related to other plasma derivatives compared to 3 over the previous 6 years.

The most frequent ATEs reported include transfusion associated circulatory overload (TACO) reactions (118, 33.3%), severe allergic/anaphylactic/anaphylactoid reactions (63, 17.8%) and delayed hemolytic transfusion reactions (DHTR) (60, 17.0%). Forty (11.4%) ATEs were not categorized and were reported as ‘other’ or ‘unknown’ accordingly.

Overall, 206 (58.2%) reportable ATEs were severe or life threatening, 164 were related to blood components and 41 were related to plasma derivatives and 1 related to both. There were 6 deaths related to transfusion and two deaths where the relationship was not determined. Of the 6 related deaths, 2 were due to errors causing unintentional incompatible transfusions which resulted in acute hemolytic reactions.

Figure i: Summary of ATEs to blood components and plasma derivatives reported by Ontario hospitals participating in TTISS-ON during 2013-2014



**Includes febrile non-hemolytic, minor allergic and delayed serological transfusion reactions*

Methodology

A total of 1,051,463 blood components were transfused by 159 Ontario hospitals from 2013-2014. Hospitals participating in TTISS transfused 71.2% (753,853) of those blood components over the two year period, with 77% transfusion activity for 2014.

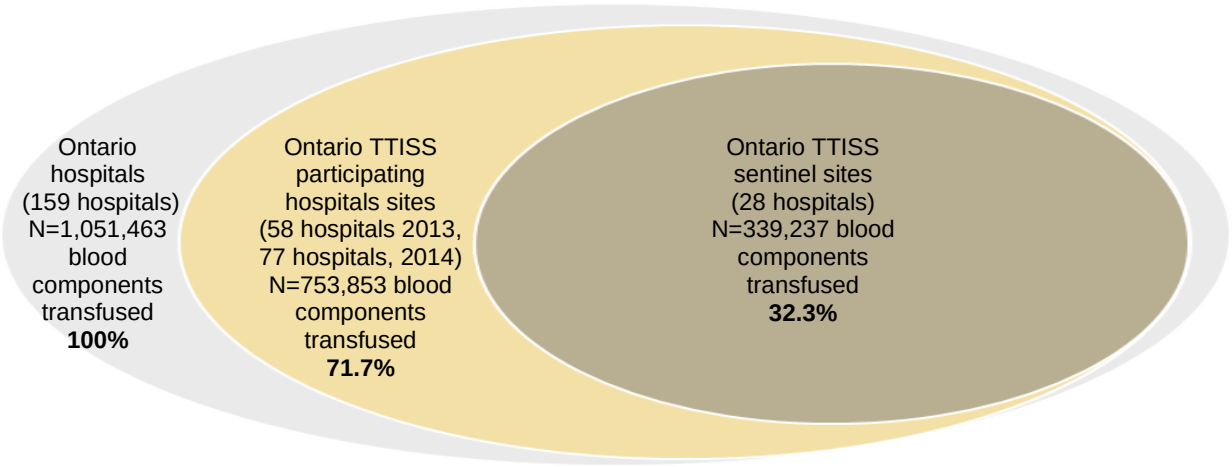
ATEs associated with blood transfusion are reported to the transfusion laboratory at the respective hospital sites. These reactions are identified, severity is established and imputability is determined using the National PHAC definitions. Imputability is categorized as 'definitely', 'probably', 'possibly', 'doubtful', 'ruled out' or 'not determined' (see Appendix 3). For the purpose of this report, those defined as 'doubtful' and 'ruled out' were not included.

If the reaction is reportable according to the TTISS guidelines provided by PHAC, it is submitted to the Ontario TTISS office either by fax or by direct entry into a web based database. Submitted data does not include personal identifying information. The data are reviewed and assessed for completeness by the Ontario TTISS staff. If additional information is required, the reporting hospital is contacted to provide the missing information. Cases initially classified as 'unknown' or 'other' are reviewed and, when possible, reclassified. In this report the remaining 'unknown' or 'other' cases have been grouped together to form a single category labeled as 'unknown pain/other'.

Adverse event data are submitted to PHAC on a biannual basis by the TTISS-ON office. There is always a 6-month delay in submitting data. This allows time for hospitals to review and complete their cases.

A subgroup of hospitals (n=28) referred to as 'sentinel sites' also submit non-reportable reactions (febrile non-hemolytic, minor allergic and delayed serological reactions). The Ontario TTISS office collects data on the number of each blood component transfused annually from Canadian Blood Services, allowing for a calculation of reaction risk per product transfused. The risk of ATEs associated with plasma derivatives is not calculated as hospitals do not report the denominator data for these products.

Figure ii: Transfusion activity in Ontario during 2013-2014



All ATEs related to blood products 2013 - 2014 (N = 354)

The ratio of reportable adverse transfusion events (not including febrile non hemolytic, delayed serological and minor allergic reactions) related to either blood components or plasma derivatives has remained constant in this 2013 - 2014 report when compared to the previous 2008 - 2012 report.

Figure 1: Number of ATEs related to blood products 2013 -2014 (N=354)

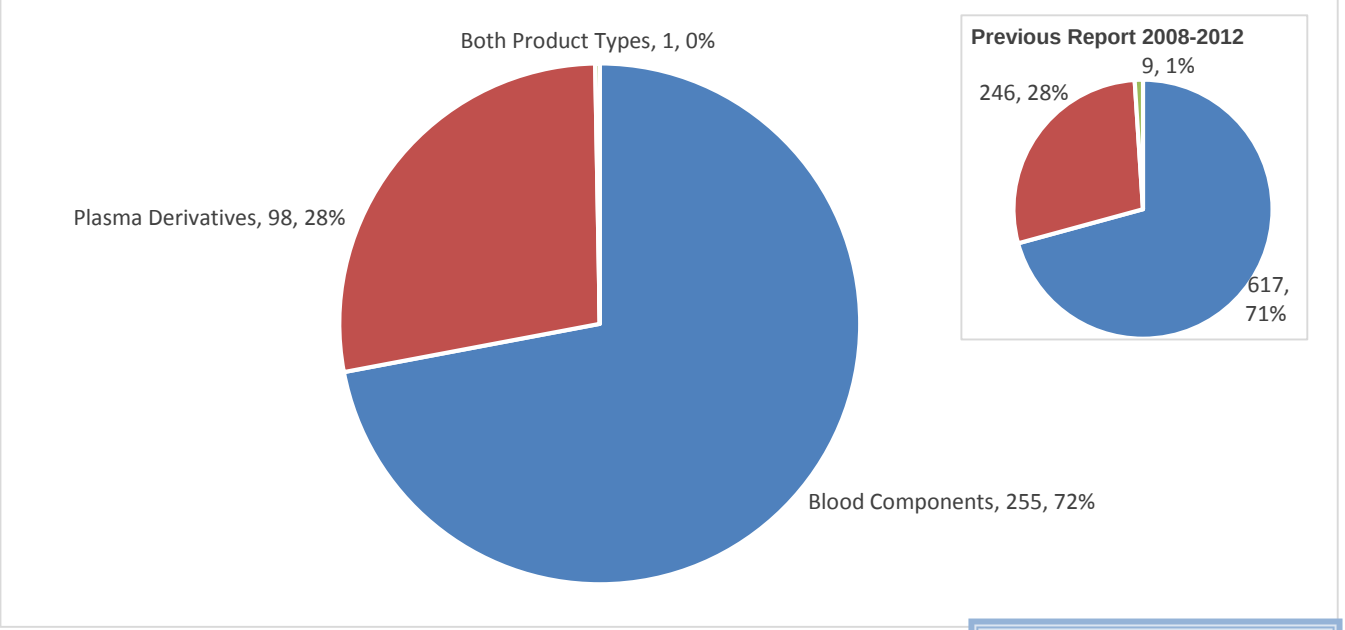


Figure 2: Number of ATEs by blood product and year

Participating hospital sites increased from 49 in 2008 - 2012 to 58 in 2013 and 77 in 2014

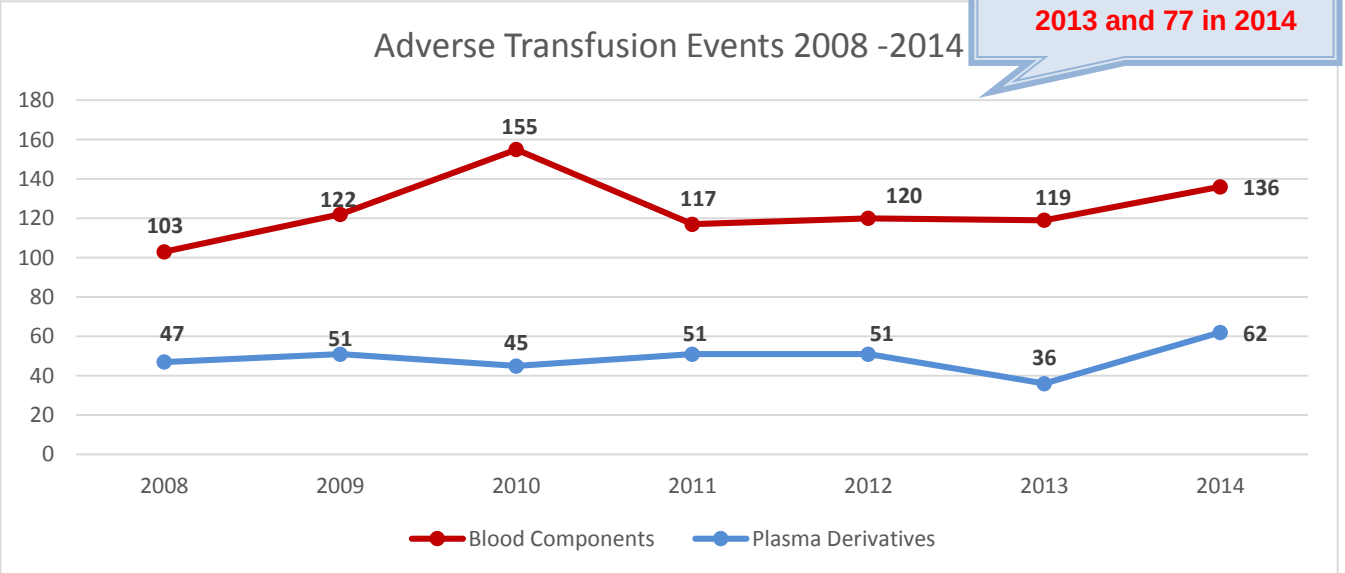


Figure 3A: Relationship of ATEs to blood products 2013 – 2014 (N = 354)

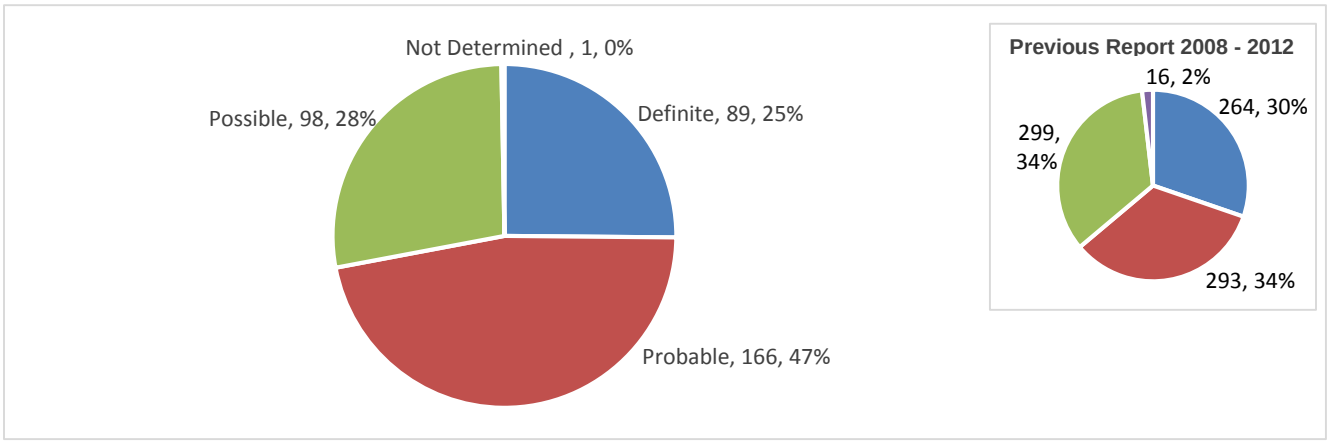


Figure 3B: Severity of ATEs to blood products 2013 – 2014 (N=354)

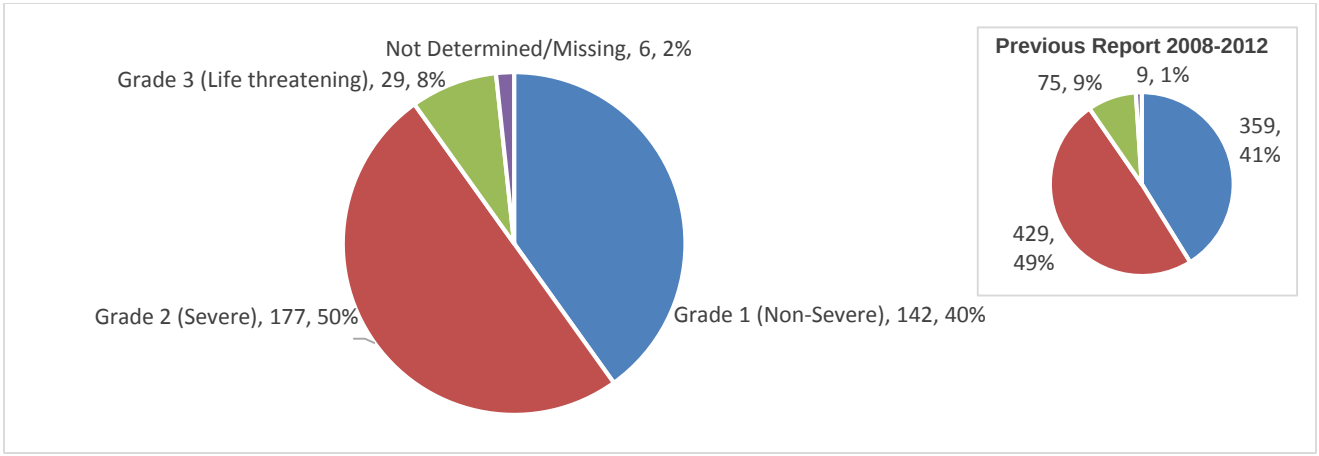
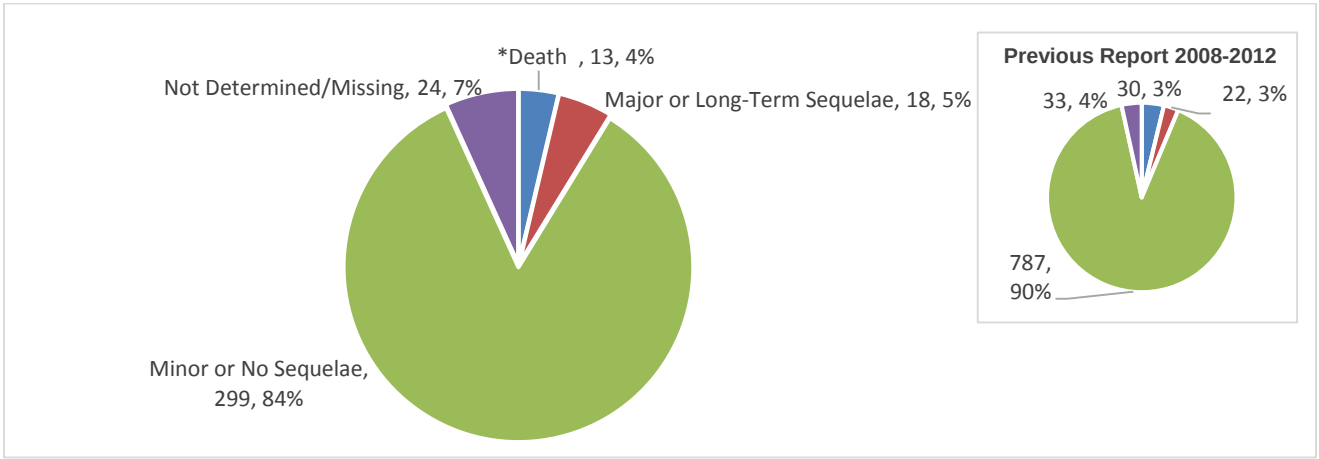


Figure 3C: Outcome of ATEs to blood products 2013 – 2014 (N=354)



***There were 6 deaths transfusion-related, 5 not related, and 2 undetermined.

A. All Blood Products

Table 1A: Blood product and severity

Blood Product	Grade 1	Grade 2	Grade 3	Not Determined	Total
Blood Components	87	140	24	4	255
Plasma Derivatives	55	37	4	2	98
Both	0	0	1	0	1
Total	**142**	**177**	**29**	**6**	**354**

Table 1B: Relationship of ATE and severity

Relationship to Product	Grade 1	Grade 2	Grade 3	Not Determined	Total
Definite	35	41	10	3	89
Probable	64	92	7	3	166
Possible	42	44	12	0	98
Not Determined	1	0	0	0	1
Total	**142**	**177**	**29**	**6**	**354**

Table 1C: Outcome and severity

Outcome	Grade 1	Grade 2	Grade 3	Not Determined	Total
Death*	0	3	9	1	13
Major or Long-Term Sequelae	3	11	4	0	18
Minor or No Sequelae	138	148	13	0	299
Not Determined	1	15	3	5	24
Total	**142**	**177**	**29**	**6**	**354**

*There were 6 deaths (out of 13 reported) that were definitely, probably or possibly related to the transfusion. There were 2 deaths where the cupability of the transfusion to the patient's death was not determined. There were 5 deaths that were doubtfully or not related to the transfusion.

Figure 4: ATEs reported for blood products 2013 – 2014 (N = 354)

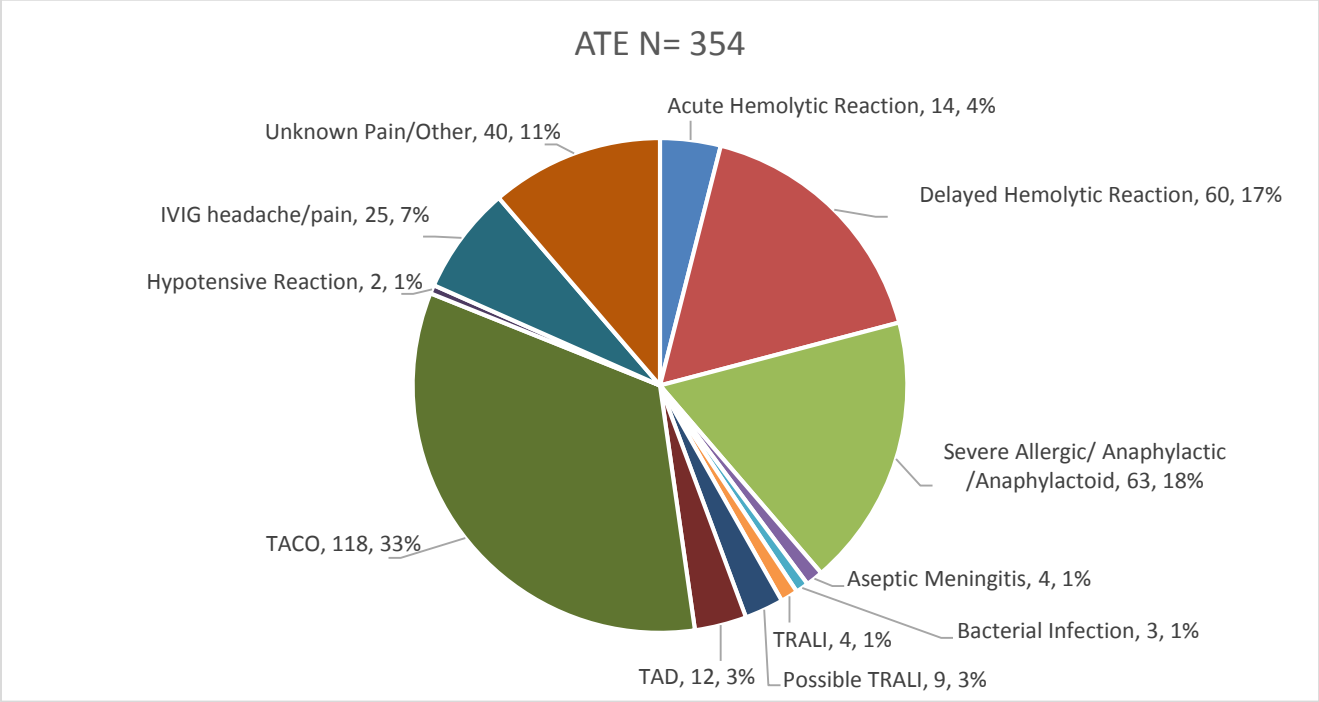
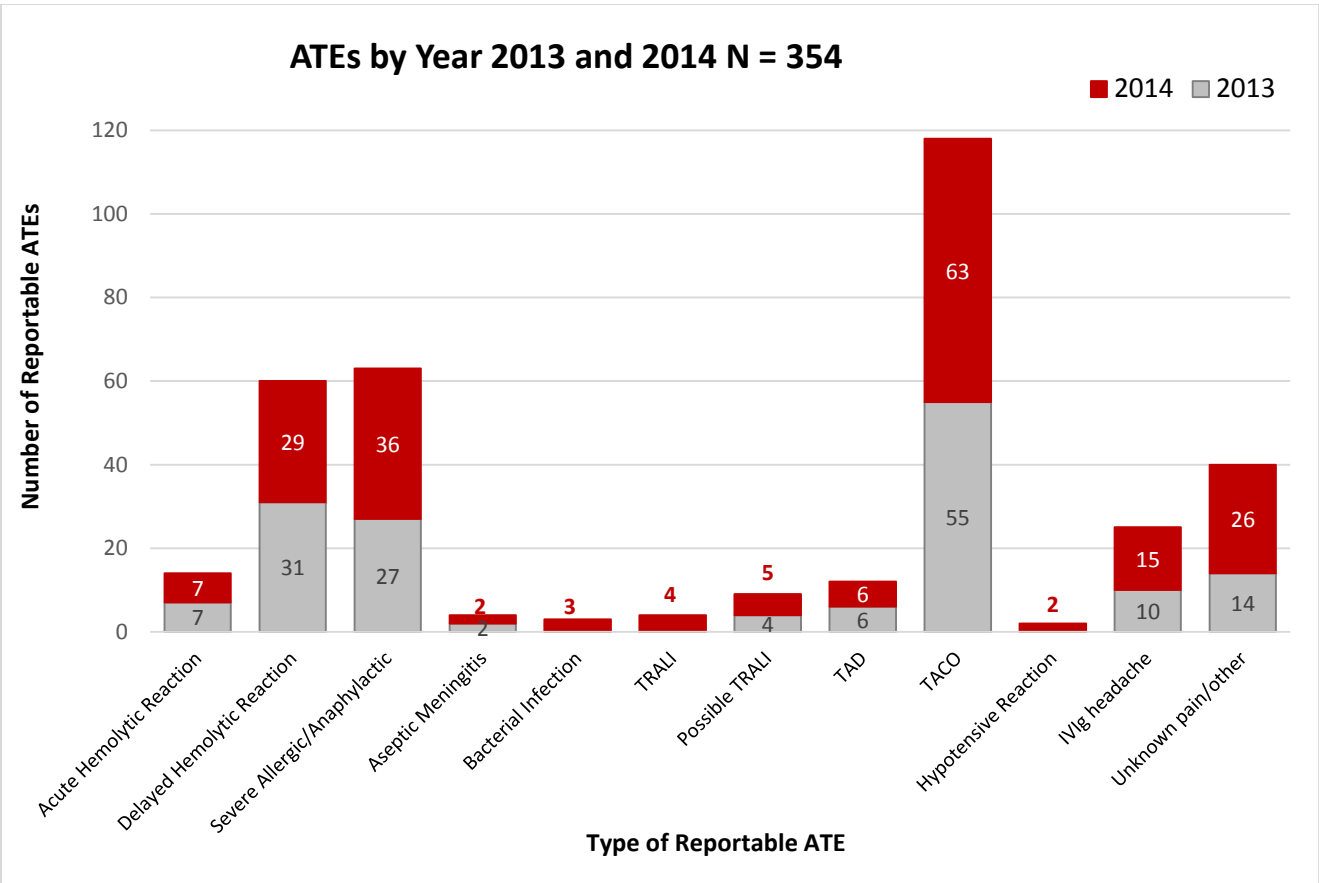


Figure 5: Number of ATEs per year by reaction type for blood products 2013 – 2014



Type of ATE by Blood Product

The majority of ATEs are associated with blood components. As indicated in Table 3, Transfusion Associated Circulatory Overload (TACO) is the most frequently reported type of ATE to a blood component (45.5%). The reporting of TACO has seen a marked increase of 28.3% from the previous Report (2008-2012). IVIg Headache and Delayed Hemolytic Transfusion Reaction is the most frequently reported type of ATE to a plasma derivative.

Table 2: ATE and blood product (N=354)

Adverse Transfusion Event (ATE)	Blood Component		Plasma Derivative		Both Product Types		Total of All Products	
	N	%	N	%	N	%	N	%
Acute Hemolytic Transfusion Reaction	6	2.4	8	8.2	0	0.0	14	3.9
Delayed Hemolytic Transfusion Reaction	36	14.1	23	23.5	1	100.0	60	17.0
Severe Allergic/ Anaphylactic/Anaphylactoid	46	18.0	17	17.3	0	0.0	63	17.8
Aseptic Meningitis	0	0.0	4	4.1	0	0.0	4	1.1
Bacterial Infection	3	1.2	0	0.0	0	0.0	3	0.9
TRALI	4	1.6	0	0.0	0	0.0	4	1.1
Possible TRALI	9	3.5	0	0.0	0	0.0	9	2.5
TAD	12	4.7	0	0.0	0	0.0	12	3.4
TACO	116	45.5	2	2.0	0	0.0	118	33.3
Hypotensive Reaction	2	0.8	0	0.0	0	0.0	2	0.6
IVIg Headache/Pain	0	0.0	25	25.5	0	0.0	25	7.1
Unknown Pain/Other	21	8.2	19	19.4	0	0.0	40	11.3
Total	**255**	**100**	**98**	**100**	**1**	**100**	**354**	**100**

A. All Blood Products

Table 3: Type of ATE and severity (N=354)

Adverse Transfusion Event (ATE)	Grade 1 (Non-Severe)		Grade 2 (Severe)		Grade 3 (Life Threatening)		Not Determined		Total of All Blood Products	
	%	N	%	N	%	N	%	N	N	%
Acute Hemolytic Transfusion Reaction	7	49.3	2	1.1	1	16.7	4	1.4	14	3.9
Delayed Hemolytic Transfusion Reaction	30	21.1	26	1.5	2	33.3	2	6.9	60	17.0
Severe Allergic/ Anaphylactic/ Anaphylactoid	5	3.5	56	2.8	0	0.0	2	6.9	63	17.8
Aseptic Meningitis	1	0.7	3	1.7	0	0.0	0	0.0	4	1.1
Bacterial Infection	0	0.0	1	0.6	0	0.0	2	6.9	3	0.9
TRALI	1	0.7	2	0.6	0	0.0	1	3.4	4	1.1
Possible TRALI	0	0.0	2	1.1	0	0.0	7	24.1	9	2.5
TAD	7	4.9	5	2.8	0	0.0	0	0	12	3.4
TACO	48	33.8	60	34.0	1	16.7	9	31.0	118	33.3
Hypotensive Reaction	0	0.0	2	1.1	0	0.0	0	0.0	2	0.6
IVIg Headache	20	14.1	5	2.8	0	0.0	0	0.0	25	7.1
Unknown Pain/Other	23	16.2	13	7.3	2	33.3	2	6.9	40	11.3
Total	**142**	**100**	**177**	**100**	**6**	**100**	**29**	**100**	**354**	**100**

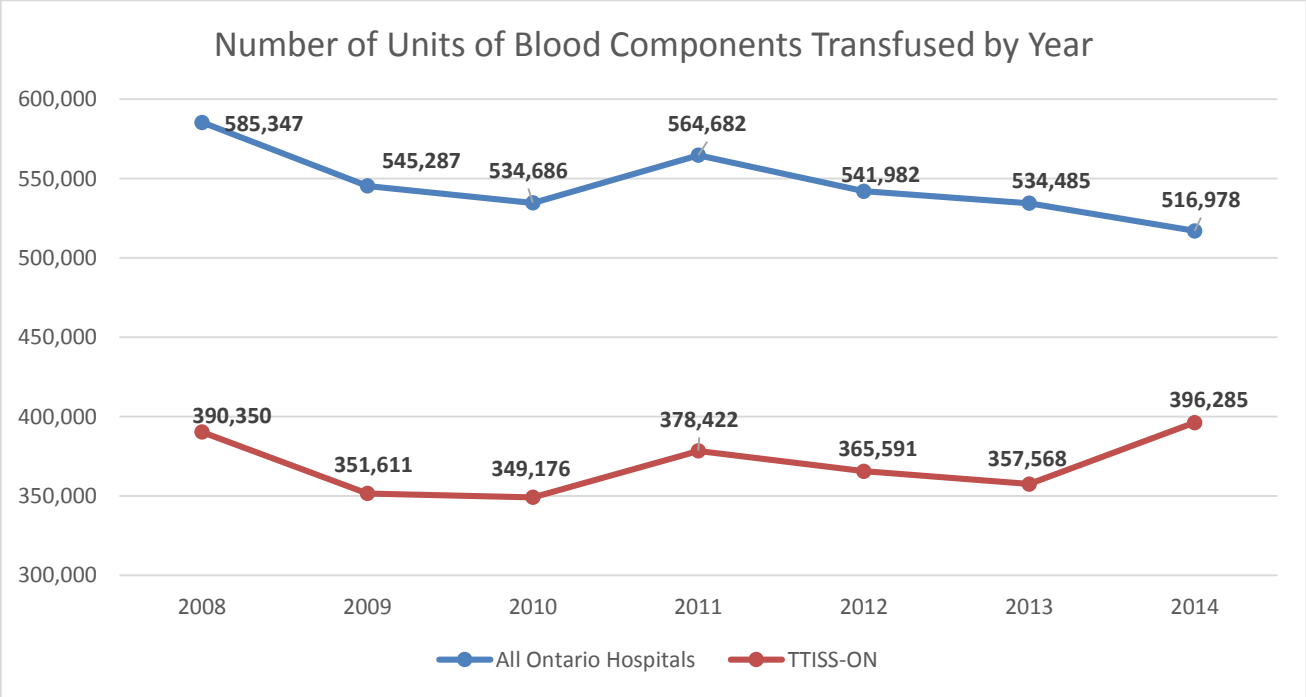
Transfusion Activity:

Ontario transfuses approximately 37.7% of all the blood components transfused in Canada. 1,051,463 blood components were transfused in Ontario from 2013 - 2014. TTISS-participating hospitals account for 71.7% of blood components transfused within the province, an increase of almost 10% since the previous report for the years 2008-2012.

Table 4: Transfusion activity in all Ontario hospitals compared to those participating in TTISS

Blood Component	Units Transfused by All Ontario Hospitals (159)	Units Transfused by All TTISS-Participating Hospitals (58 in 2013, 77 in 2014)		Units Transfused by TTISS Sentinel Site Hospitals (28)	
		N	%	N	%
Red Blood Cells (RBC)	772,921	519,884	67.3	224,805	29.1
Plasma	124,311	103,660	84.3	52,172	42.0
Platelets (Buffy Coat)	65,950	52,884	76.2	21,275	40.2
Platelets (Apheresis)	27,420	23,857	87.0	11,245	32.2
Cryoprecipitate	60,861	53,568	88.0	29,740	48.9
Total	**1,051,463**	**753,853**	**71.7**	**339,237**	**32.3**

Figure 6: Transfusion activity by year



Risk Estimates: Transfusion Activity and Number of ATEs

There are 28 sentinel site hospitals participating in TTISS-ON. These sites report all transfusion reactions. In total, there were 788 ATEs; 127 reportable ATEs and 661 PHAC non-reportable ATEs collected from sentinel sites during 2013-2014.

Table 5: Risk Estimates (± 0% to 15% range)

ATE	Red Blood Cell Units		Plasma Units		Platelets		Cryo-Precipitate		All Blood Component Units	
	N	Risk	N	Risk	N	Risk	N	Risk	N	Risk
AHTR	3	1:75,000	0		0		0	0	3	1:100,000
DHTR	21	1:10,000	0		0		0	0	21	1:15,000
Severe Allergic/ Anaphylactic/ Anaphylactoid	6	1:40,000	10	1: 5,000	13	1:2,500	0	0	29	1:10,000
Possible TRALI	2	1:100,000	1	1:50,000	2	1:15,000	0	0	5	1:70,000
TAD	2	1:100,000	0		0		0	0	2	1:170,000
TACO	51	1:4,000	3	17,000	4	1:8000	0	0	51	1:6,500
Hypotensive Reaction	1	1:200,000	0		0	0	0	0	1	1:300,000
Other /Unknown Pain	7	1:30,000	0		1	32,000	0	0	8	1:40,000
Febrile Non-Hemolytic	230	1:1000	8	1:6,500	46	1:700	1	1:30,000	285	1:1,000
Delayed Serological	141	1:600	0		1	1:32,500	0	0	142	1:2,000
Minor Allergic Reaction	76	1:3,000	39	1:1,500	118	1:300	1	1:30,000	234	1:450
Total	**540**	**1:400**	**61**	**1:850**	**185**	**1:175**	**2**	**1:15,000**	**788**	**1:400**

Plasma Derivative 2013 – 2014 (N = 98)

There are 98 (of 354) ATEs associated with transfusion of plasma derivatives. Of these, 93.9% are due to IVIg.

Table 6: Number (%) of ATEs by plasma derivatives and year

Plasma Derivative	2013		2014		Total	
	N	%	N	%	N	%
IVIg	35	97.2	55	88.8	90	93.9
Albumin	0	0	3	4.8	3	3.1
Other Ig	1	2.8	3	4.8	4	4.0
SD Plasma	0	0	1	1.6	1	1.0
Total	**36**	**100**	**62**	**100**	**98**	**100**

Table 7: Type of ATE by plasma derivative (N=98)

Adverse Transfusion Event	IVIg	Other Ig	Albumin	SD Plasma	Total
Acute Hemolytic Reaction	8	0	0	0	8
Delayed Hemolytic Reaction	23	0	0	0	23
Severe Allergic/Anaphylactic/Anaphylactoid	11	3	3	0	17
Aseptic Meningitis	4	0	0	0	4
Bacterial Infection	0	0	0	0	0
TRALI	0	0	0	0	0
Possible TRALI	0	0	0	0	0
TACO	2	0	0	0	2
TAD	0	0	0	0	0
Hypotensive Reaction	0	0	0	0	0
IVIg Headache	25	0	0	0	25
Unknown Pain/Other	17	1	0	1	19
Total	**90**	**4**	**3**	**1**	**98**

D. Types of ATEs by year 2008 - 2014

Figure 7: Number of Acute Hemolytic Transfusion Reactions (AHTR) by year 2008 -2014

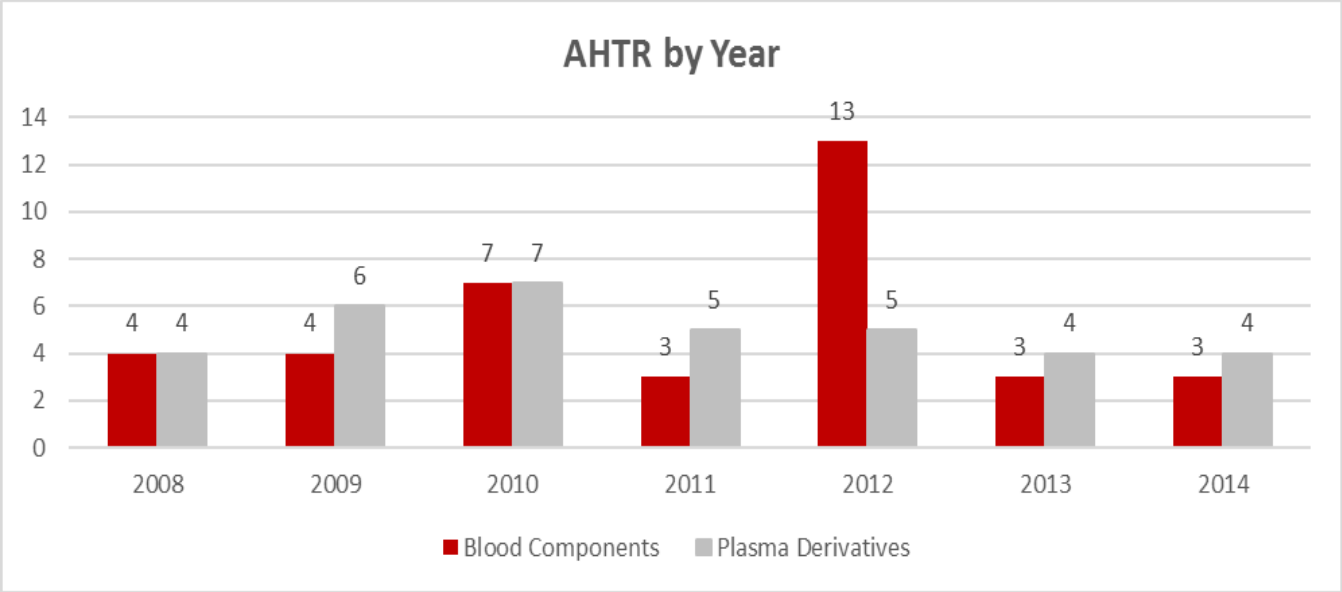
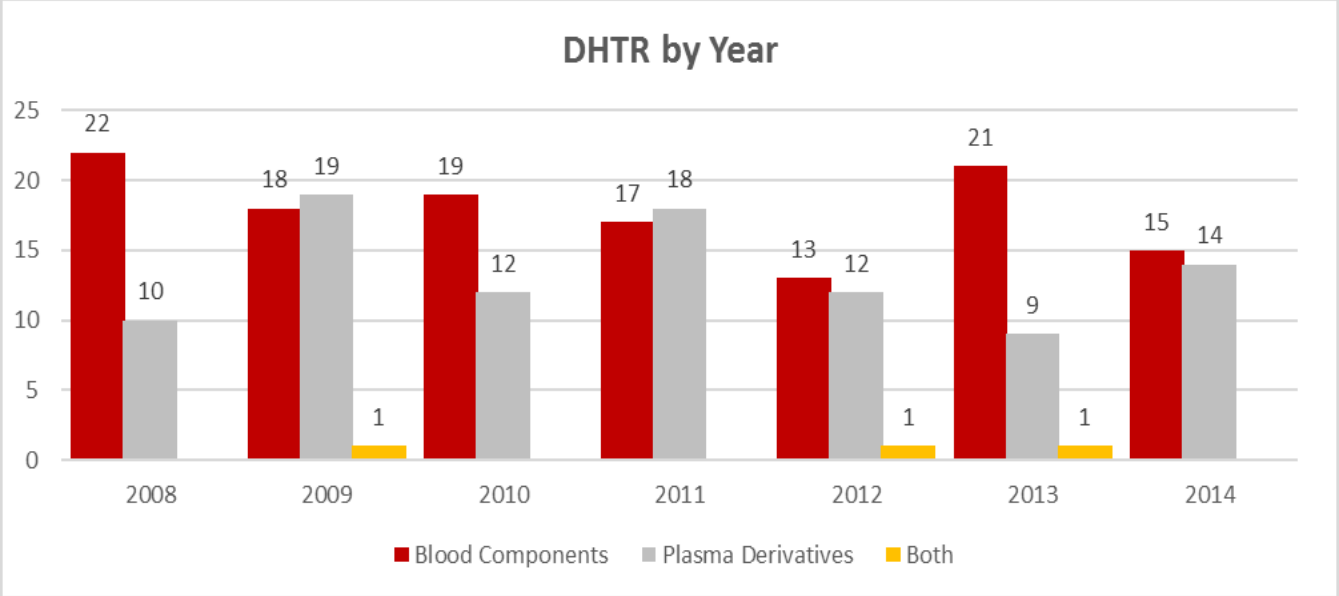


Figure 8: Number of Delayed Hemolytic Transfusion Reactions (DHTR) by year 2008 - 2014



D. Types of ATEs by year 2008 - 2014

Figure 9: Number of Severe Allergic/Anaphylactic/Anaphylactoid by year 2008 - 2014

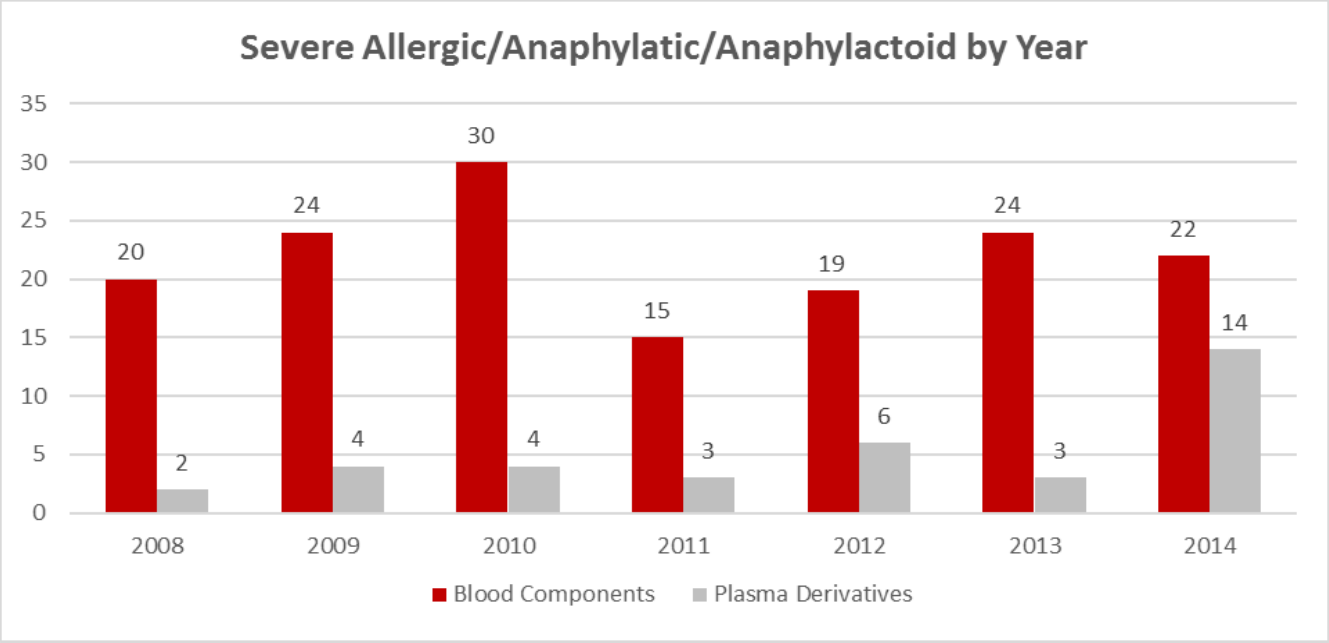
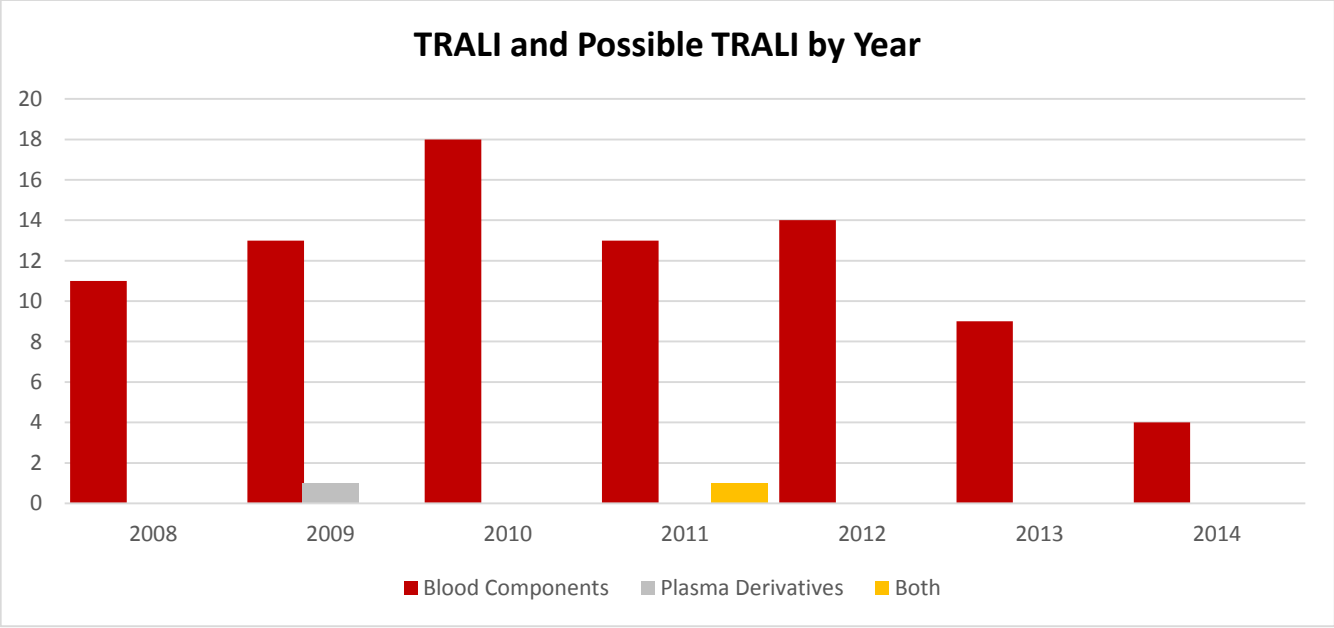


Figure 10: Number of TRALI and Possible TRALI by year 2008 -2014



D. Types of ATEs by year 2008 - 2014

Figure 11: Number of Transfusion Associated Dyspnea (TAD) by year 2008 - 2014

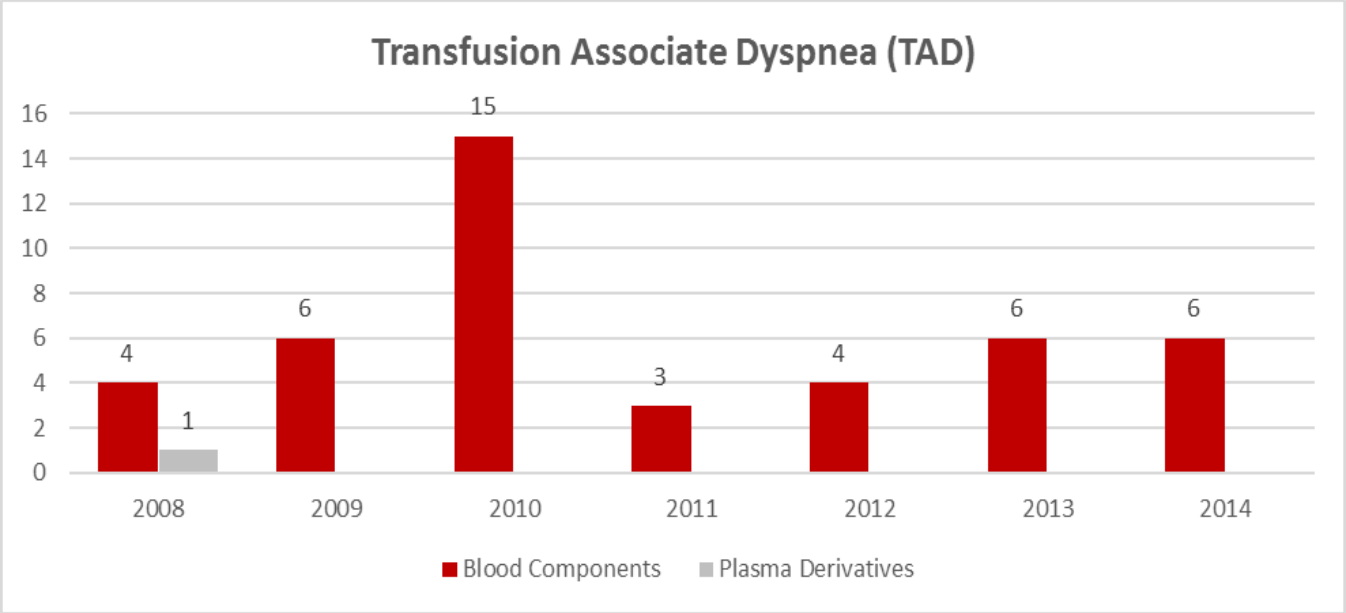
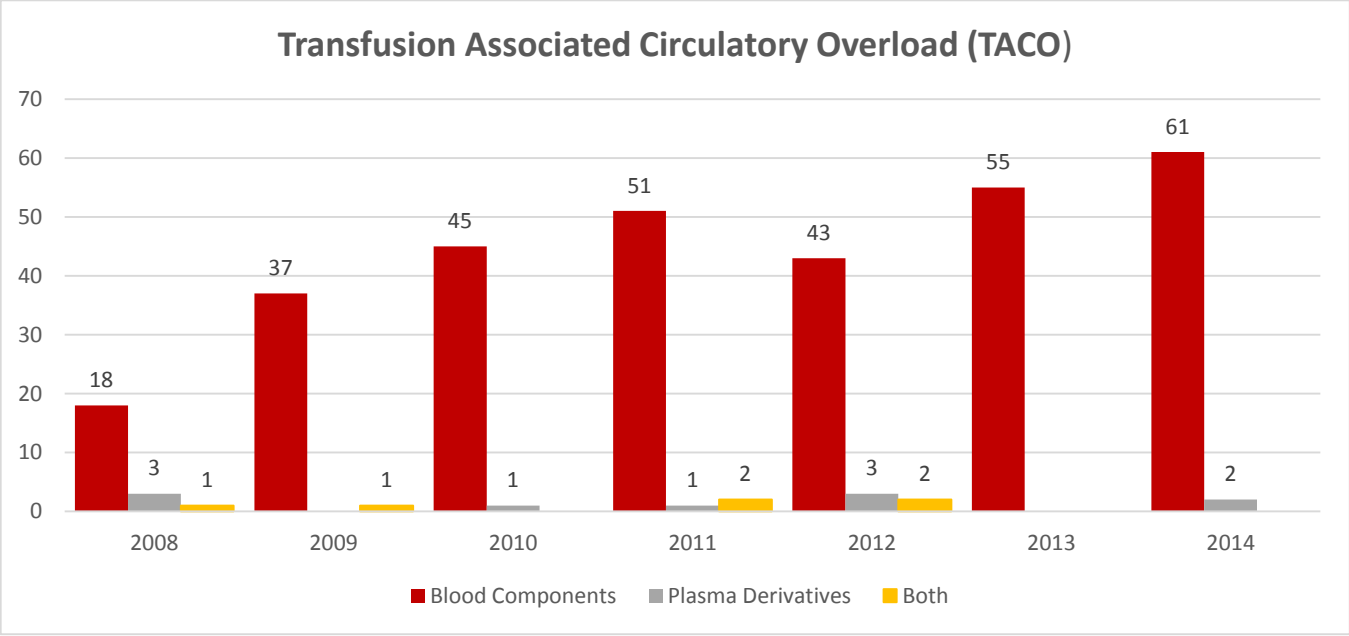


Figure 12: Number of Transfusion Associated Circulatory Overload (TACO) by year 2008 - 2014



ATEs and Deaths:

Figure 13A: 2008-2014

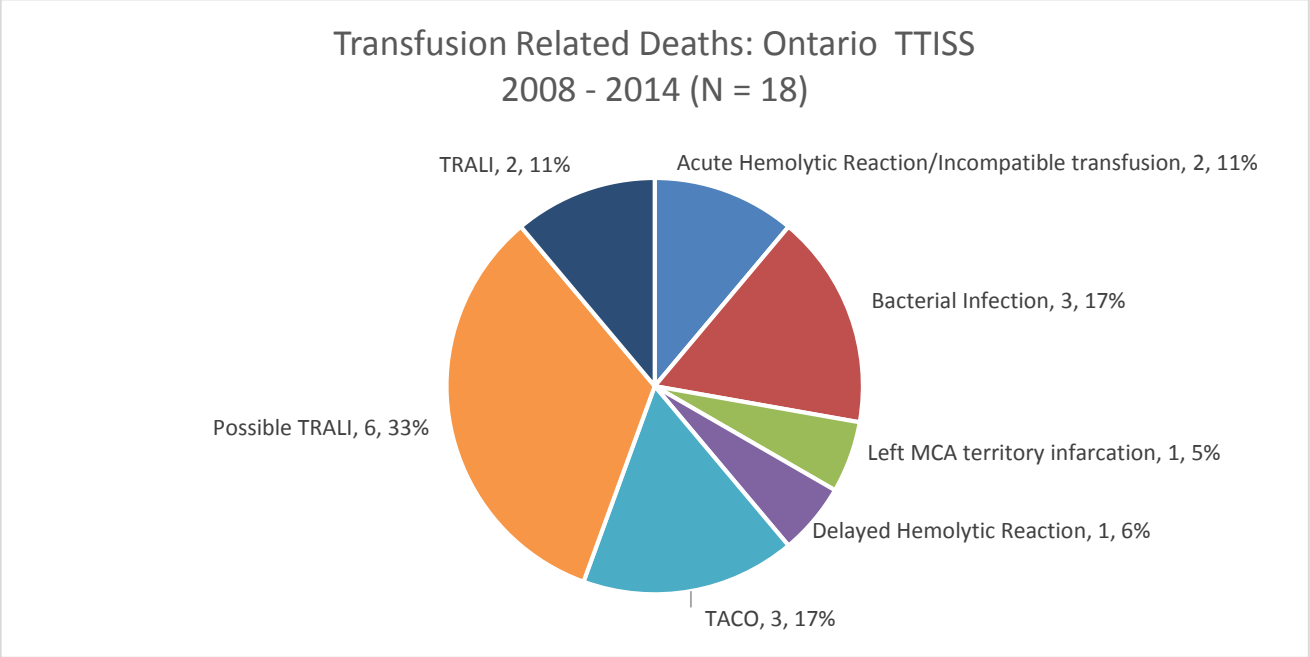


Figure 13B: Previous Report 2008 -2012

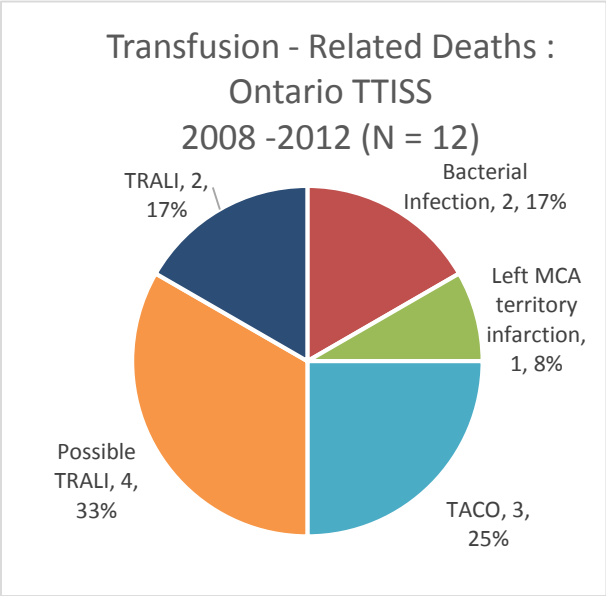
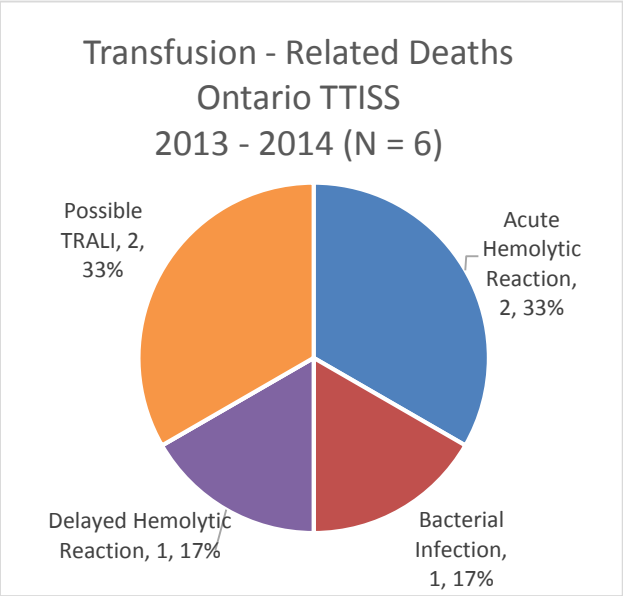


Figure 13C: Current Report 2013-2014



Death Specifics 2013 - 2014

Table 8: Relationship of death to the blood product.

ATE	Definite	Probable	Possible	Total
Acute Hemolytic Reaction	1	0	1	2
Delayed Hemolytic Reaction	0	0	1	1
Bacterial Infection	0	1	0	1
Possible TRALI	0	1	1	2
Total	**1**	**2**	**3**	**6**

Table 9: Number of deaths by ATE and blood product.

ATE	Red Blood Cells	Multiple components	Platelets	IVIg	Total
Acute Hemolytic Reaction	1	0	0	1	2
Delayed Hemolytic Reaction	1	0	0	0	1
Bacterial Infection	0	0	1	0	1
Possible TRALI	0	1	1	0	2
Total	**2**	**1**	**2**	**1**	**6**

Table 10: Deaths related to transfusions.

ATE	Relationship to Transfusion	Blood Component	Comments
AHTR	Definite	Red Blood Cells	Unintentional Incompatible Transfusion
AHTR	Possible	Red Blood Cells	Unintentional Incompatible Transfusion
DHTR	Possible	Red Blood Cells	Fatal hyper hemolysis and severe multiple organ dysfunction
Bacterial Infection	Probable	Platelets	Sepsis, post splenectomy
Possible TRALI	Probable	Massive blood transfusion	Polytrauma, second degree MVA, an infiltration on CXR
Possible TRALI	Possible	Platelets	Patient previously unwell with relapsed AML on palliative chemotherapy.

Appendix 1: List of Reportable and Non Reportable Transfusion Reactions

Reportable ATEs	Reportable ATEs
Acute Hemolytic Transfusion Reaction	Severe Allergic/Anaphylactic/Anaphylactoid
Anaphylactic Shock	Transfusion Associated Circulatory Overload (TACO)
Aseptic Meningitis	Transfusion Associated Dyspnea (TAD)
Bacterial Infection	Transfusion Associated Graft Versus Host Disease (TA-GVHD)
Delayed Hemolytic Transfusion Reaction	Transfusion Related Acute Lung Injury (TRALI)
Hemochromatosis	Unknown Pain/ Other - This was combined here for this report of TTISS "unknown" and TTISS "other results of investigation
Hypotensive Reaction	Viral Infection
Incompatible Transfusion Reactions	**Non-Reportable ATEs**
Intravenous immunoglobulin (IVIg) headache	
Other Infection	Delayed Serological Transfusion Reaction
Possible TRALI	Febrile Non Hemolytic Reaction
Post Transfusion Purpura (PTP)	Minor Allergic Reaction

Appendix 2: Abbreviations

Abbreviation	Description
AHTR	Acute Hemolytic Transfusion Reaction
ATE	Adverse Transfusion Event
CBS	Canadian Blood Services
DHTR	Delayed Hemolytic Transfusion Reaction
Ig	Immunoglobulin
IVIg	Intravenous Immunoglobulin
MOHLTC	Ministry of Health and Long-term Care
ORBCoN	Ontario Regional Blood Coordinating Network
PHAC	Public Health Agency of Canada
Possible TRALI	Possible Transfusion Related Acute Lung Injury
PTP	Post-Transfusion Purpura
RBC	Red Blood Cells
SD	Solvent Detergent
TACO	Transfusion Associated Circulatory Overload
TAD	Transfusion Associated Dyspnea
TRALI	Transfusion Related Acute Lung Injury
TTISS	Transfusion Transmitted Injuries Surveillance System

Appendix 3: Surveillance Definitions[1]

Relationship to Product (Imputability)	
Definite	Clinical and/or laboratory event within a time frame consistent with the administration of the blood, blood component or plasma derivative 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 derivative 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 derivative but could be explained by concurrent disease(s) or by the administration of a drug or other agent.

Severity: Severity was initially classified into four categories including death (as Grade 4) which was subsequently reclassified as life-threatening. The death was categorized as an outcome and relationship between transfusion and death was assessed.	
Life-threatening (Grade 3)	The recipient required major intervention following the transfusion (i.e. vasopressors, intubation, and transfer to intensive care).
Severe (Grade 2)	The recipient required in-patient hospitalization or prolongation of hospitalization directly attributable to the event; or the adverse event resulted in persistent or significant disability or incapacity; or the adverse event necessitated medical or surgical intervention of preclude permanent/significant damage or impairment of body function.
Non-severe (Grade 1)	The recipient may have required medical intervention (i.e. symptomatic treatment) but lack of such would not result in permanent damage or impairment of body function.

Outcome	
Death	Death was directly or indirectly transfusion-related.
Major or long-term sequelae	Transfused patient developed an infection with persistent infectious agent or any other long-term sequelae including difficulties with future transfusions.
Minor or no sequelae	Transfused patient developed antibodies to low-medium frequency antigens or any other minor reaction

[1]Public Health Agency of Canada. TTISS -2006-2012 Report, Centre for Communicable Diseases and Infection Control, PHAC, 2014