The Hemovigilance Program of the American Red Cross:

Advancing Blood Donation and Transfusion Safety

Anne Eder, MD PhD

Executive Medical Officer

Sociedad Chilena de Hematologia

October 28, 2010

American Red Cross

Objectives

- **Describe the ARC Hemovigilance Program**
- **Examine the data-driven conclusions that have advanced blood safety**
- **Explore the strengths and limitations of the program**

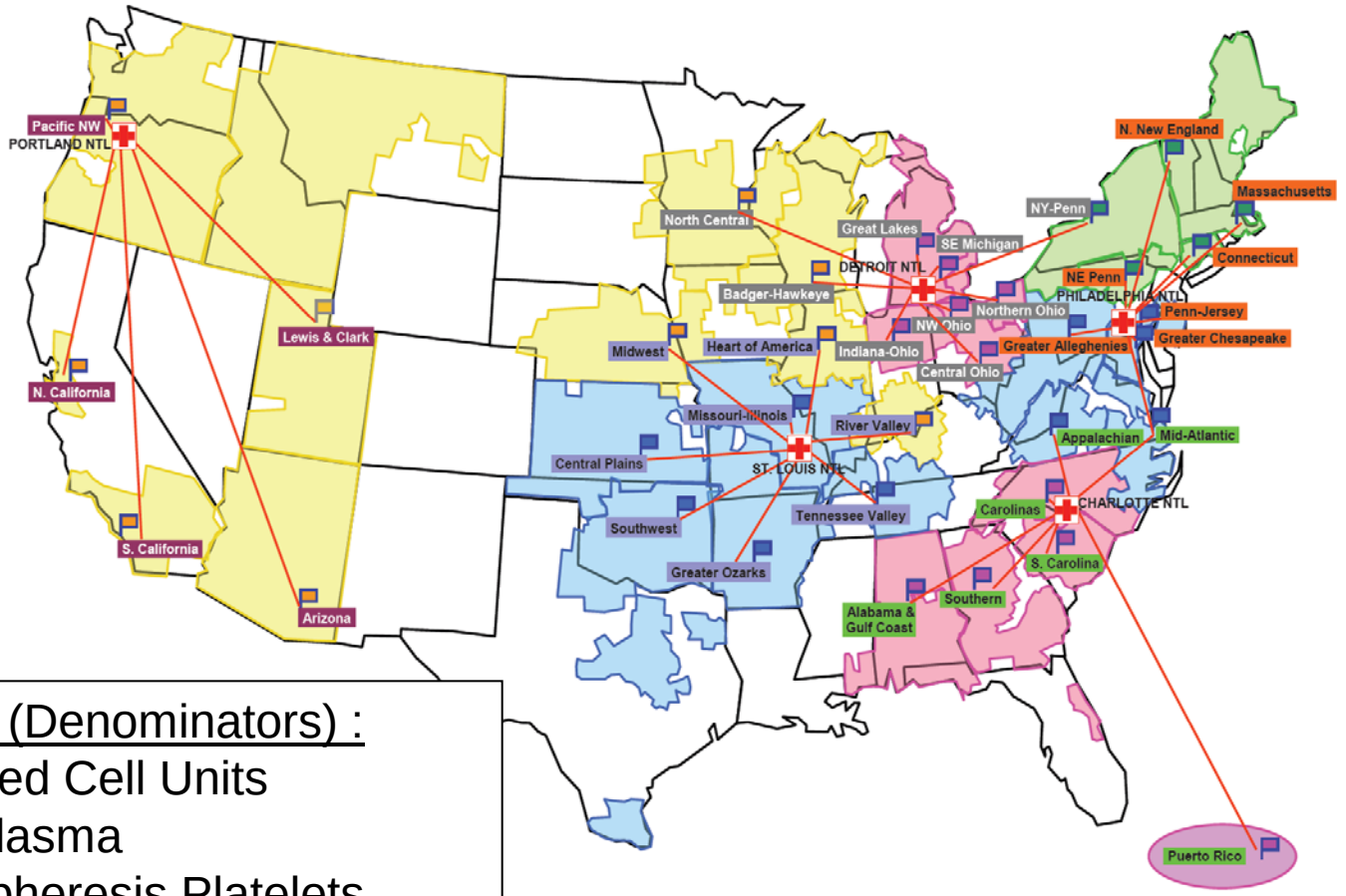
For Patient Safety

1. TRALI mitigation
2. Bacterial contamination and septic transfusion reactions

For Blood Donor Safety

3. Young Donor Initiative

American Red Cross, 2010



Distributions (Denominators) :

6 M	Red Cell Units
1.7 M	Plasma
850,000	Apheresis Platelets
250,000	WB derived Platelets
40,000	Pooled WB Platelets

American Red Cross

Overview

ARC Hemovigilance Program

DONOR

RECIPIENT

Regional Blood Centers

ASSESSMENT

- Collection staff
- Medical Directors

INPUT

Biomedical Headquarters

MONITORING

- Medical Director
- Program Manager

ANALYSIS

INTERVENTION, FEEDBACK

American Red Cross

ARC Hemovigilance

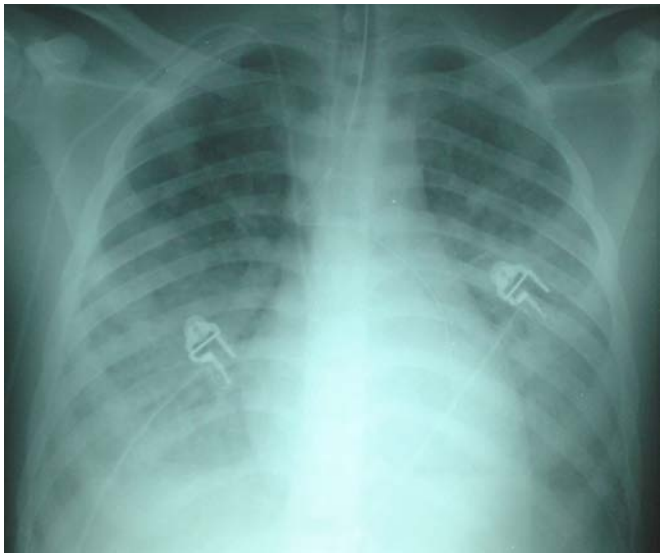
Program Goals

- To improve blood safety for recipients
- To minimize procedure risk for donors
- To identify significant trends that emerge from analysis of reports of uncommon events
- To implement changes aimed to reduce the risk of complications
- To monitor effectiveness of interventions

Transfusion-related Acute Lung Injury

Acute lung injury with hypoxemia

- Acute onset (within 6 hours)
- Hypoxemia
- Bilateral diffuse infiltrates on CXR
- No evidence of pulmonary overload
- No preexisting lung injury
- No temporal relationship to ALI



TRALI is a clinical diagnosis

Does NOT depend on laboratory results on donors

- Donor testing is performed for donor management to determine future eligibility in an effort to reduce the risk

Kleinman SH et al. Transfusion 44, 1774; 2004

American Red Cross

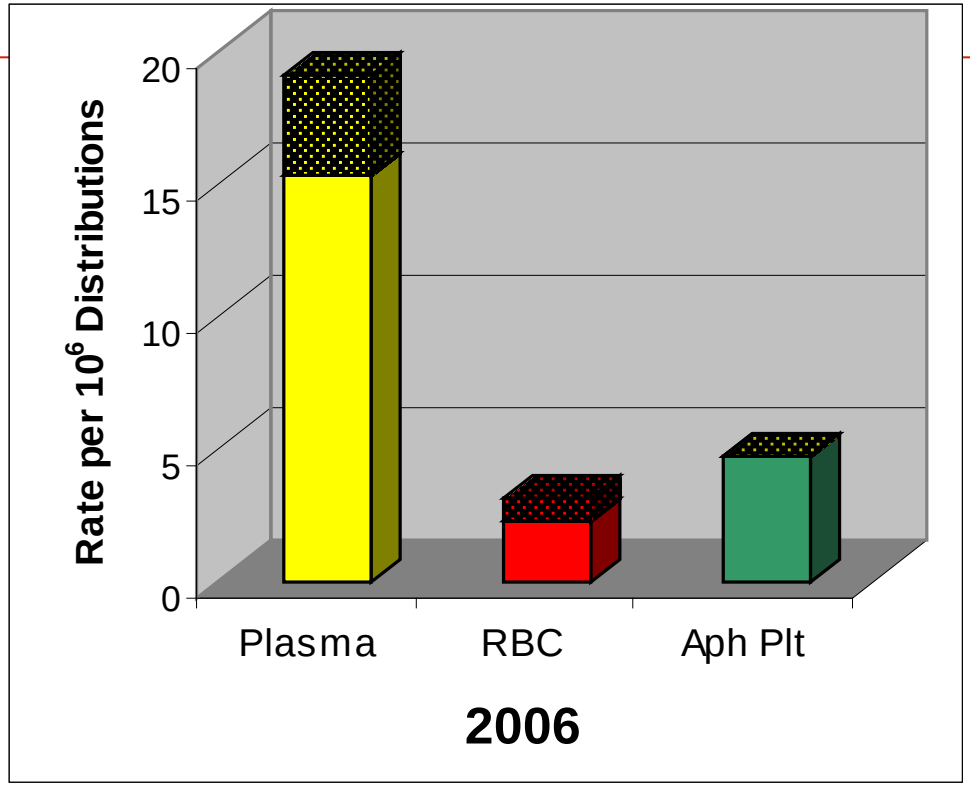
Background

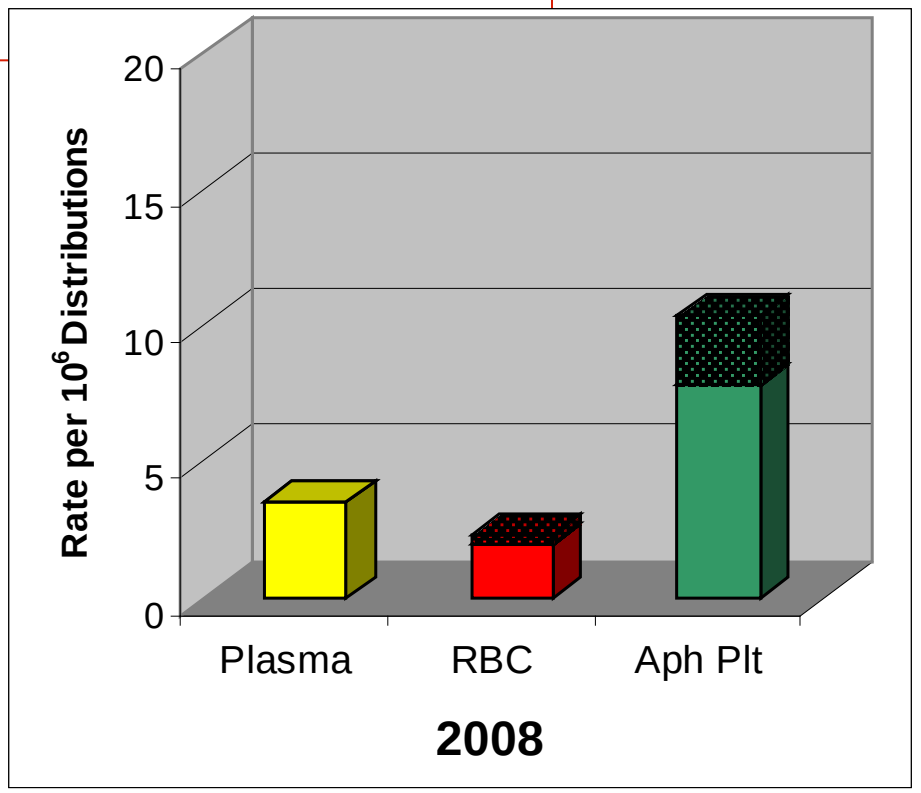
TRALI, reported fatalities 2003-5

- Plasma was responsible for the majority of TRALI cases
- Female HLA/HNA antibody-positive donors were implicated in the majority of probable TRALI cases among reported fatalities
- In 2006, we switched to a male-predominant plasma strategy
- By the end of 2008, 95% of plasma distributed for transfusion was from male donors

Eder et al. Transfusion. 2007 Apr;47(4):599-607.

Effect of Male-Predominant Plasma





Conclusion: TRALI involving plasma transfusion was significantly reduced in 2008 [OR 95% CI 0.2 (0.07-0.4)], to a level that was no longer different from the rate of TRALI observed for RBC transfusion

Eder et al. Transfusion, 2010; 50:1732-1742

American Red Cross

Jefferson Memorial, Washington DC

Septic Transfusion Reactions

Bacterial Detection, Apheresis Platelets

Within 4 hours of transfusion, any of the following:

- Fever ≥ 39°C (102.2°F) or change of ≥ 2°C from pre- value
- Rigors
- Tachycardia ≥ 120 bpm or change in heart rate ≥ 40 bpm
- Blood pressure changes (rise or fall) of ≥ 30 mmHg B

And….

- Positive culture of residual component (not lab contamination) or:
- Culture of residual component & patient reveal identical strains

Wendel et al.Transfusion Medicine Illustrated; Transfusion.2005; 45.

American Red Cross

Background

Bacterial Detection, Apheresis Platelets

American Red Cross implemented routine, quality-control (QC) bacterial culture of all apheresis platelet donations in 2004

Data from the first 15 months (Period 1):

Bacterial contamination (Confirmed QC Culture)	1 in 5,399 donations
Septic reactions (Reported by hospitals; false negative QC culture)	1 in 66,000 distributed units

3/2004 – 05/2006

Eder et al Transfusion. 2007 Jul;47(7):1134-42.

American Red Cross

Background

Period 1 (3/2004 – 05/2006)

- Two-arm apheresis platelet procedures had a statistically higher rate of bacterial contamination and septic transfusion reactions

Two-arm

One-arm

Eder et al Transfusion. 2007 Jul;47(7):1134-42.

American Red Cross

Process Improvement

Reduce bacterial contamination

- Inlet-line sample diversion for all apheresis platelet collections (100% vs. 39% procedures)
- Predicted to decrease bacterial detection rates

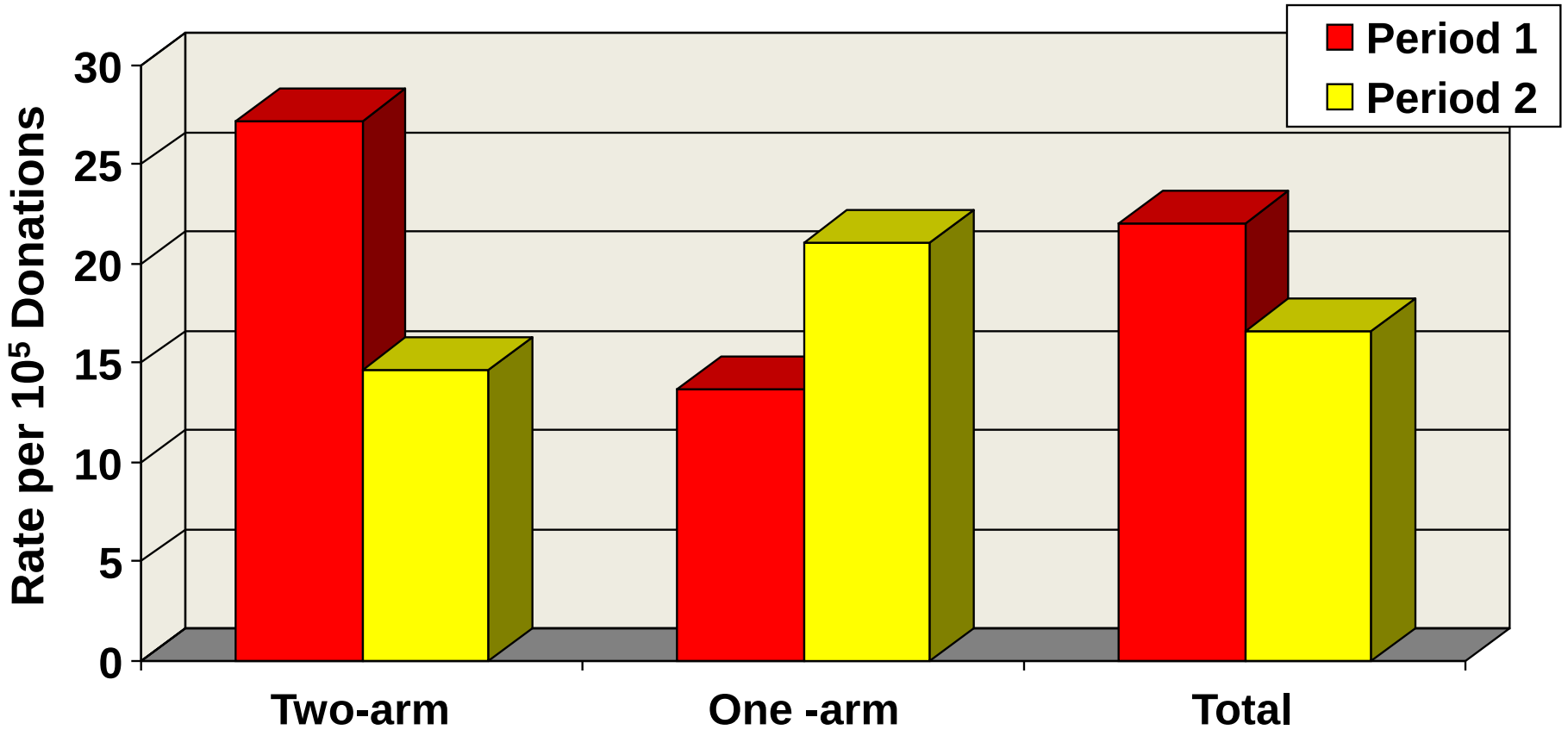
Increase culture sensitivity

- Increase volume inoculated into culture bottle (4ml vs 8ml)
- Predicted to increase bacterial detection rates

Compare **Period 1** (03/04-05/06; 1,004,206 donations)
to **Period 2** (12/06-07/08; 781,936 donations)

Effect of Intervention

Bacterial Contamination, Period 2 vs. Period 1

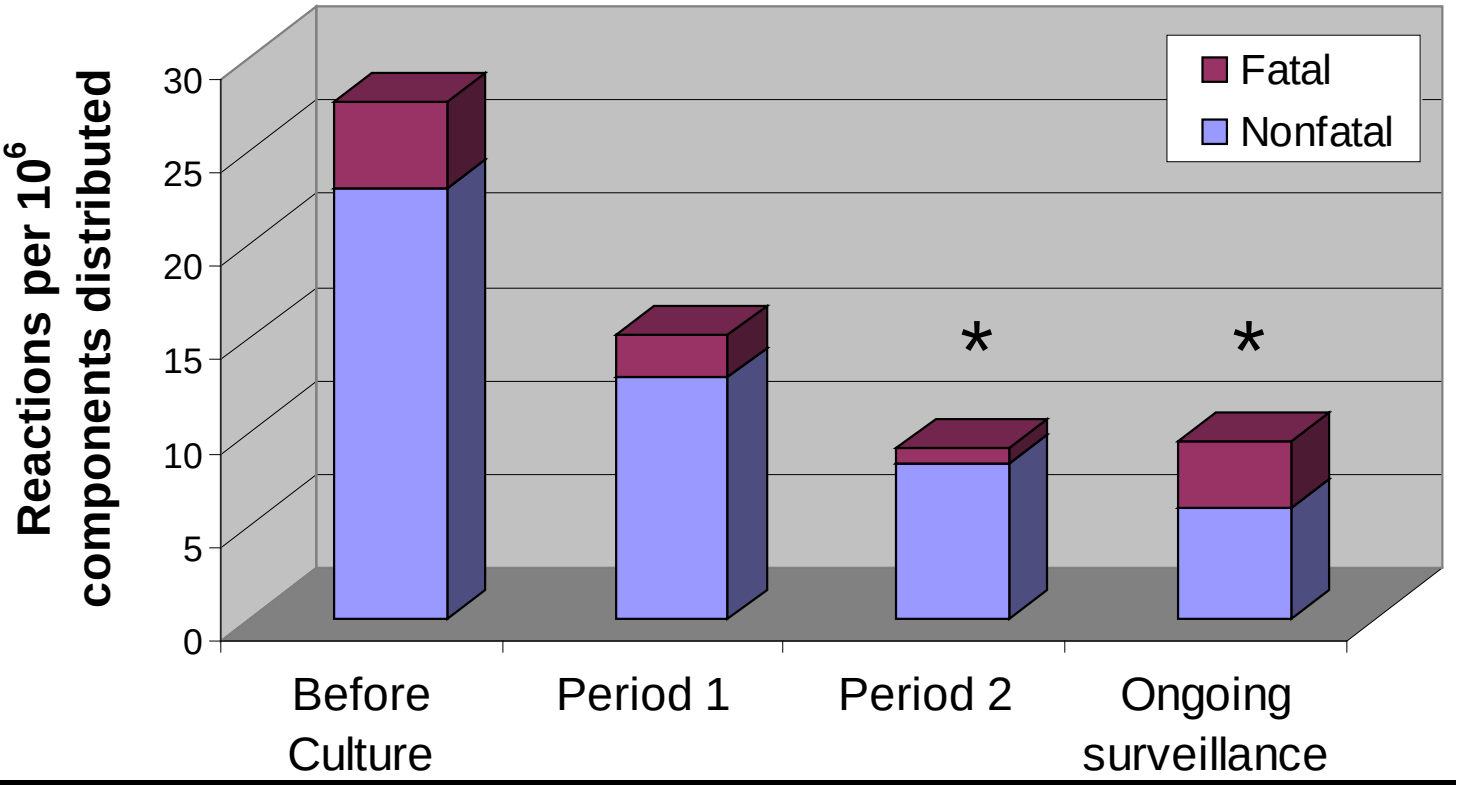


Period 2 v 1 OR 95% CI:	**0.54 (0.41-0.70)**	**1.54 (1.05-2.27)**	**0.76 (0.61-0.94)**

Eder et al Transfusion. 2009, 49:1554.

American Red Cross

Safety of Apheresis Platelets



Culture Volume	NA	4 mL	8 mL	8 mL
Diversion	NA	39%	100%	100%
Septic RATE	1:36,000	1:66,000	1:109,000	1:106,000

* Compared to Before Culture, $p < 0.05$

Period 1 & 2: Eder et al, Transfusion 2009, 49:1554.

Ongoing surveillance: August 2008 – Aug 2009

American Red Cross

Residual Risk

Septic Transfusion Reactions

Case #	Transfusion Date	Day of Transfusion	Organism	Probability
1	10/7/2007	5	S. aureus	Definite
2	2/15/2007	5	Staph, coag negative	Definite
3	3/27/2007	4	Staph, coag negative	Probable
4	2/17/2007	4	Klebsiella spp.	Probable
5	1/5/2007	5	Staph aureus	Probable
6	1/9/2008	4	Staph, coag negative	Probable
7	1/9/2008	4	Staph, coag negative	Probable
8	1/9/2008	4	Staph, coag negative	Probable
9	4/19/2008	5	Staph, coag negative	Definite
10	4/27/2008	5	Staph, coag negative	Definite
11	5/3/2008	5	Staph, coag negative	Definite
12	8/19/2008	4	Staph, coag negative	Definite
13	9/17/2008	2	Staph, coag negative	Probable
14	10/19/2008	4	Staph, coag negative	Probable
15	10/20/2008	5	Staph, coag negative	Probable
16	11/21/2008	4	Staph aureus	Definite
17	4/18/2009	5	Staph, coag negative	Definite
18	5/10/2009	5	Staph aureus	Definite
19	8/3/2009	4	Staph, coag negative	Definite
20	8/13/2009	5	Staph, coag negative	Definite
21	7/20/2009	5	Staph, coag negative	Definite
22	8/3/2009	5	Enterobacter cloacae	Probable
23	8/11/2009	4	Streptococcus, alpha hem.	Probable

The residual risk is still from skin organisms that escape detection with routine QC bacterial culture

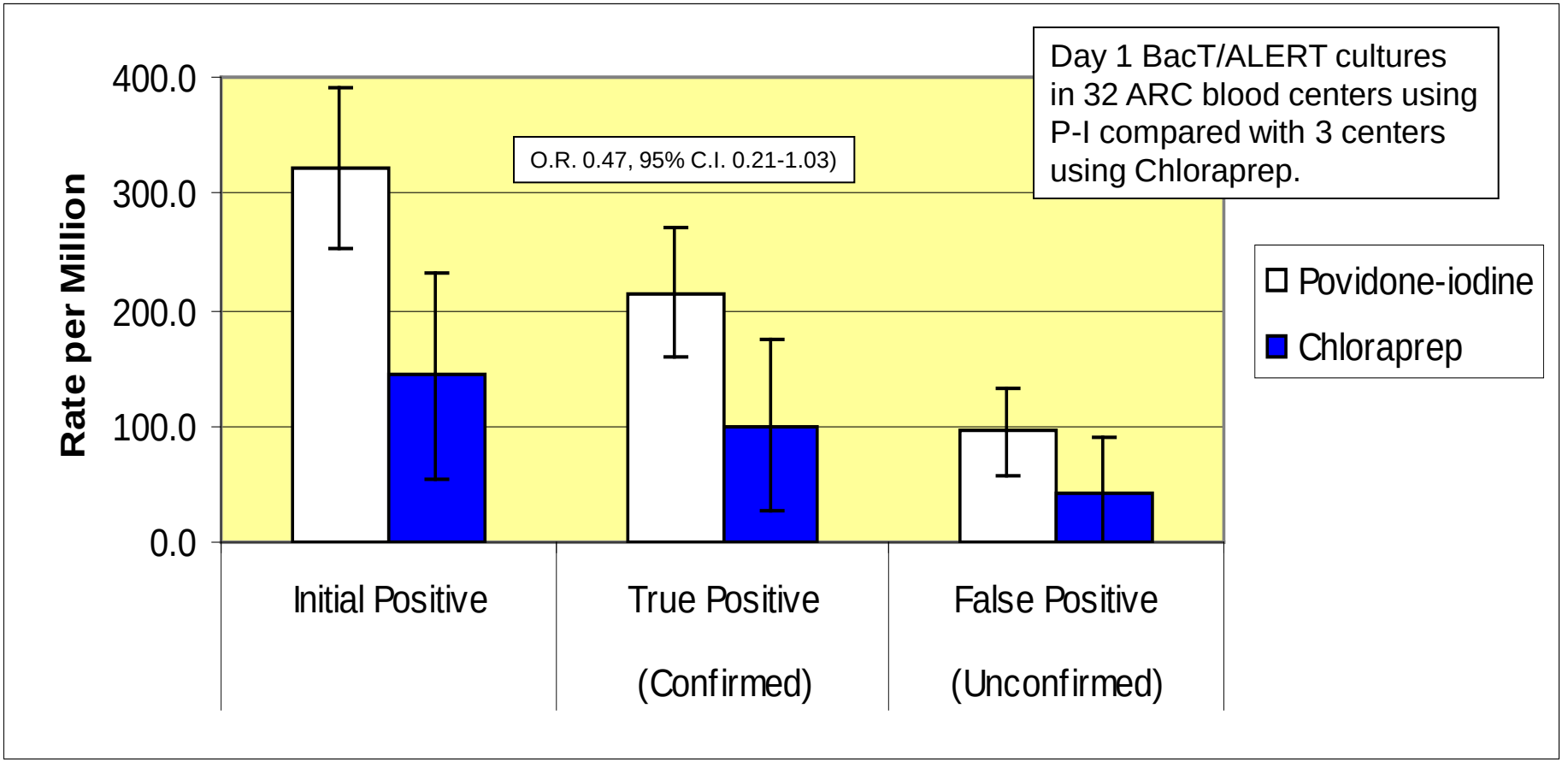
Eder AF et al, Transfusion 2009
Unpublished data, American Red Cross

January 2007-December 2009

American Red Cross

Skin Decontamination:

Chlorhexidine vs. Standard Povidone Iodine



Benjamin et al. Transfusion online early: 2010

American Red Cross

Summary

Bacterial Contamination of Apheresis Platelets

- Sepsis remains a risk of platelet transfusion
- Bacterial QC culture, improved skin preparation & diversion have reduced the risk of reported sepsis to ~1:106,000 distributed platelets
- The residual risk of bacterial sepsis from platelet transfusion is from skin flora that escape detection with routine QC testing with sampling on Day 1
- These data suggest that further interventions are needed to protect against bacterial contamination.
- Point-of-issue test (e.g., Verax) for bacterial detection are currently under evaluation in clinical practice

The Kansas City Star

KU patient's case highlights risk of tainted platelets

By ALAN BAVLEY
The Kansas City Star

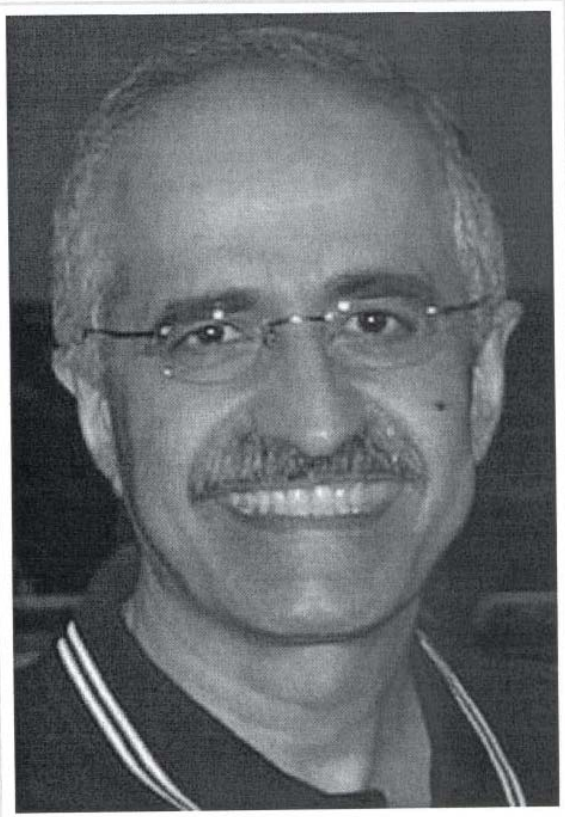
Hossein Novin tried to be a model cancer patient.

The 54-year-old engineer from Overland Park kept eating even when his mouth and throat were full of sores. He kept up his exercise, even when he was tired and nauseated.

But two weeks ago, he received a transfusion of platelets contaminated with staph that almost killed him. He spent days on a ventilator, his lungs bleeding. On Monday, he was in fair condition at the University of Kansas Hospital.

His case highlights the serious risk of infection from platelets, even when those collecting, storing and transfusing the blood product follow safety procedures. And it set off a flurry of local activity aimed at improving safety.

It is the second time in three years that a KU cancer patient has received tainted platelets from the Community Blood Center. In the first case, the patient died within 48 hours after receiving a transfusion laced with E. coli bacteria.



Novin

"Even though blood centers have been monitoring platelets since 2004,

their methods cannot catch every case."

"None of us knew there was this risk from transfusion," said his daughter

Young donor safety initiative

Photo credit: Pueblo Chieftain, Chris McLean,Sept 4, 2009

American Red Cross

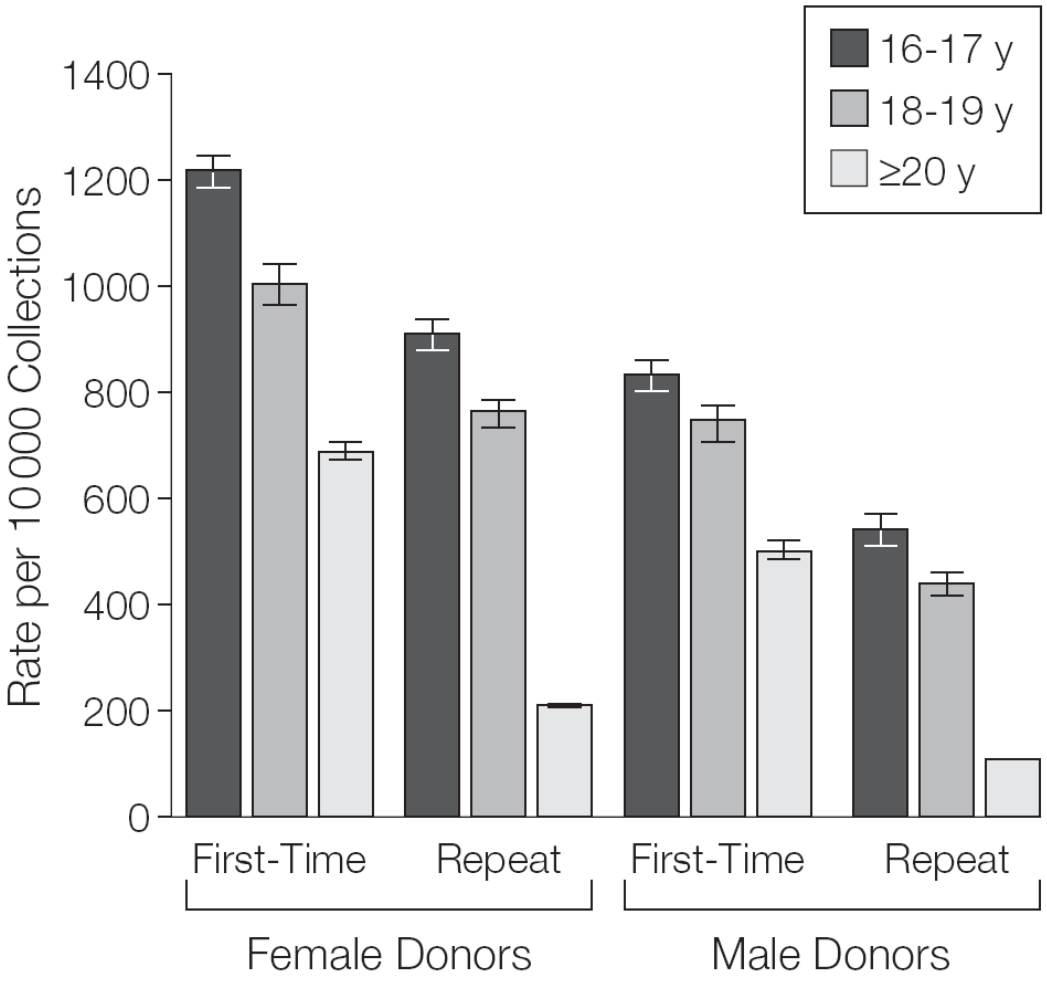
Background

16- to 18-year-old Whole Blood Donors

- Donors younger than 19 years contribute substantially to the blood supply
- 16 year olds are increasingly recruited as more States lower their minimum age for blood donation
  - In 2006: ~15 States
  - In 2010: ~34 States
  - Most states require parental permission
- 16-18 year olds account for ~16% of the whole blood donations in the American Red Cross

Syncope and related complications

Donor subgroups, by age



Eder et al, 2008 J Amer Med Assn 299(19):2279-2286.

American Red Cross

AABB Safety Recommendations

August, 2008

Predonation education

Drive set-up and environment

Staff supervision and phlebotomist skills

Interventions

- Donor eligibility criteria –blood volume (Ht,Wt) restrictions
- Water ingestion before donation and within 10-20 min
- Distraction during phlebotomy
- Muscle tension during phlebotomy
- Automated red cell collection

Post-reaction instructions to donors and parents

AABB Bulletin # 08-04

American Red Cross

Background

Predictors of Reactions, 16-18 year olds

- Young age, first-time donations status, estimated total blood volume (TBV< 3.5L) are the strongest independent predictors of reactions
  - Wiltbank et al.Transfusion 2008;48:1799-1808
- AABB Standards for donor weight (≥ 110 lb) and collection volume (≤ 10.5 mL/kg) are intended to limit blood loss to ≤ 15% TBV with ~525 mL donation
- Multivariate logistic regression analysis of data from 2 ARC blood centers predicted that selecting donors with estimated TBV ≥ 3.5 L would prevent ~15% of vasovagal-type reactions
  - Rios et al for REDSII, Transfusion 2010;50:1265

High School Donors

11% (13%)*

17% (20%)*

Loss (% blood volume) with 525 mL whole blood donation

16 years old
5 ft, 9 in
65 kg
TBV = 4.7 L

16 years old
5 ft
50 kg
TBV = 3.1 L

Nadler et al. Prediction of blood volume in normal human adults, Surgery 1962; 51:224
* Holme et al Prediction BV: do current nomograms overestimate? Transf 2008; 48 910

American Red Cross

New Selection Criteria For Young Donors*

Boys:			
If you are	4’ 10”	4’ 11”	5’ or taller
You must weigh at least	120	115	110

Girls:						
If you are	5’ 1”	5’ 2”	5’ 3”	5’ 4”	5’ 5”	≥ 5’ 6”
You must weigh at least	133	129	124	118	115	110

Predicted to prevent ~15% of prefaint/faint reactions and identifies ~9% of current donors in this age group (16-18 yo). Recruitment strategies will likely compensate for donor “loss”

* All high school students and donors < 19 yrs; Effective, Fall 2009

American Red Cross

Young Donor Safety - Timeline

System-wide Interventions

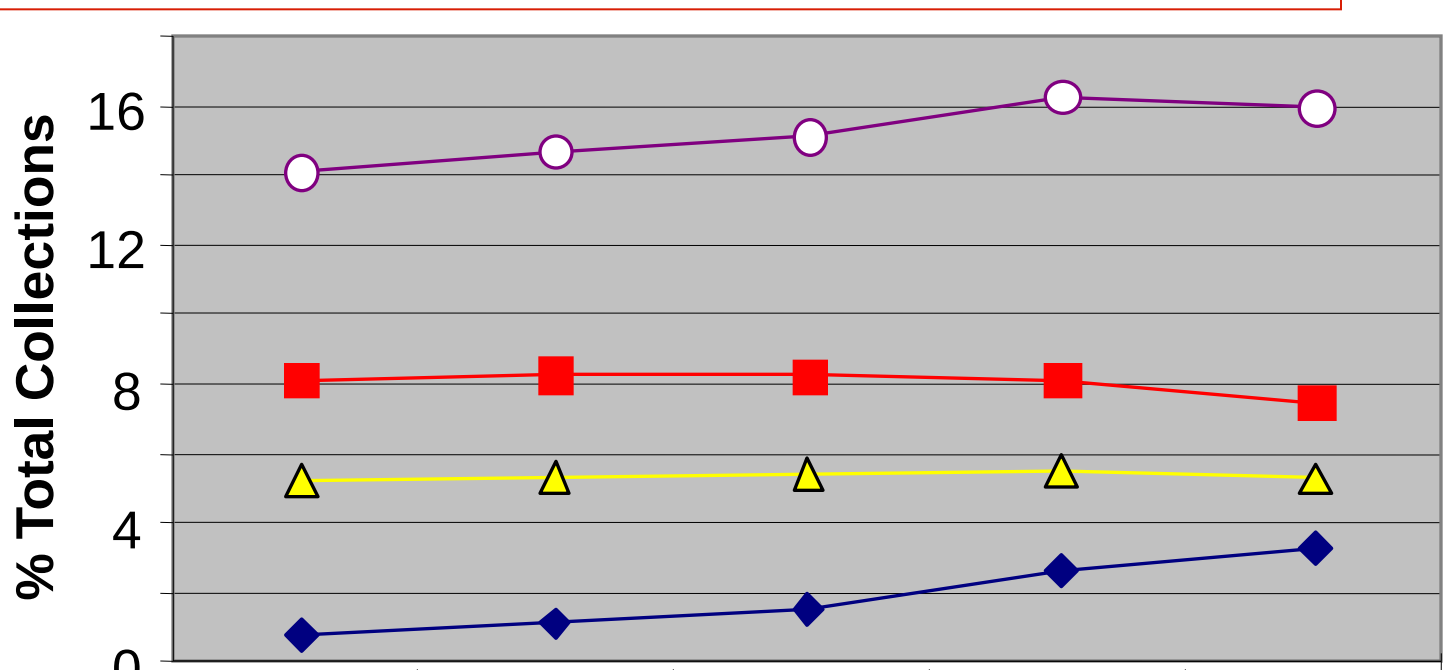
School Year (Sept to May)	Activity
Baseline 2005	• JAMA manuscript (CY2006 data) • Standard educational material for high school donors
2006	
2007	
Transition 2008	• Supervisor initiative (complete by Dec 31, 2008) • Standard drive guidance, pilot regions • Predonation hydration and muscle tension advice
2009	**• Height/Weight Selection Criteria**

➢ Evaluated the effect on total collections and reactions among donors younger than 19 years

American Red Cross

Results

Denominators



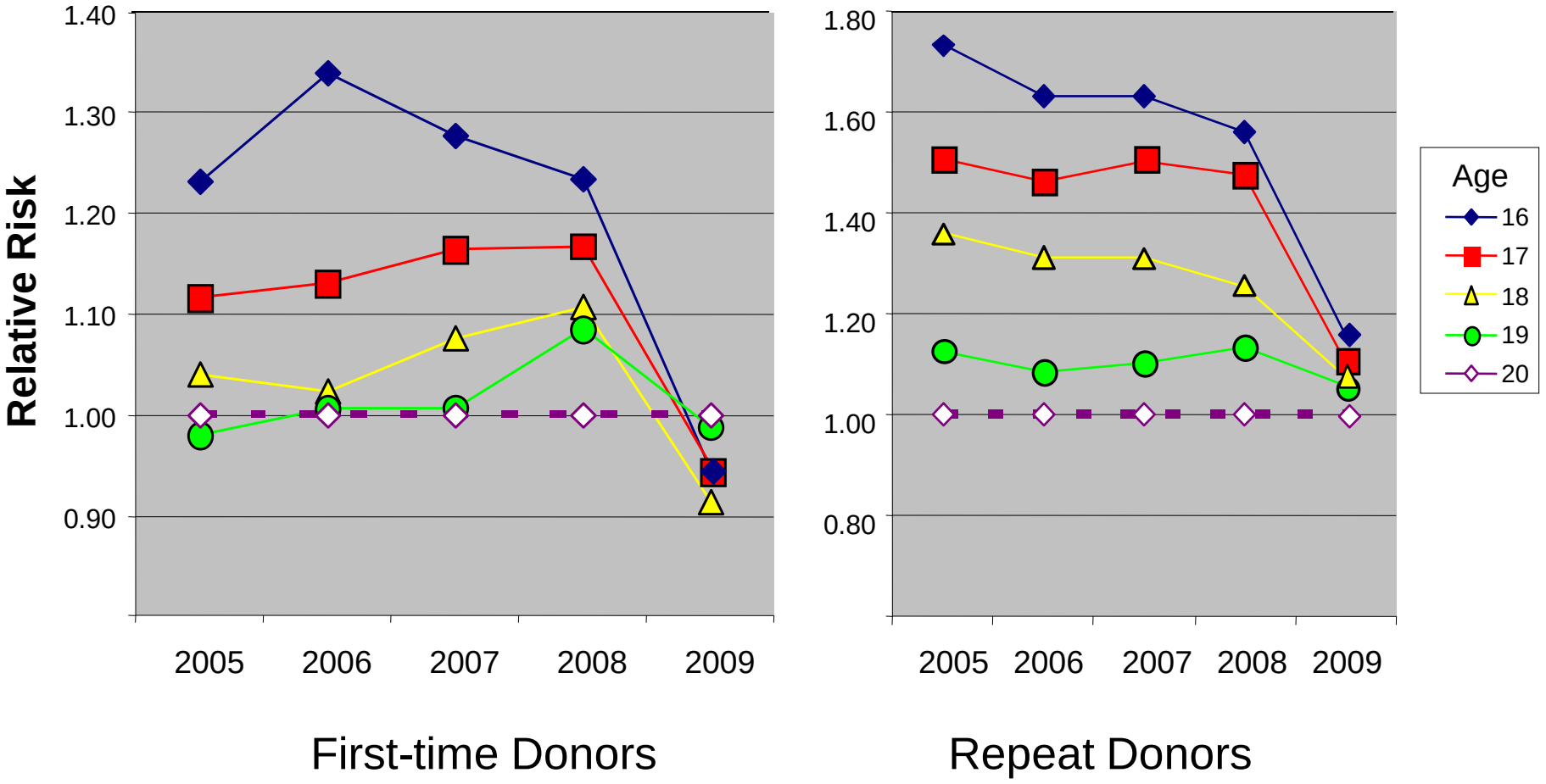
	2005	2006	2007	2008	2009
16	37,873	49,869	69,636	121,944	143,880
16-18	660,232	663,527	695,843	754,407	710,918
Total	4,685,490	4,518,033	4,593,177	4,638,754	4,451,933

Whole blood donation, September – May (School Year)

American Red Cross

Results: Relative Risk

Female Donors



Results

Minor and Major Reaction Categories

Donor Age	Complication	Complication Rate per 10,000 donations		Odds Ratio	95% CI	Decrease (%)
		2008	2009			
16	Prefaint	876.7	732.3	**0.82**	**0.80-0.85**	**18%**
	LOC	43.3	37.1	**0.86**	**0.76-0.97**	**14%**
	Major	61.2	59.1	0.97	0.87-1.10	-
17	Prefaint	777.1	662.5	**0.84**	**0.83-0.86**	**16%**
	LOC	38.0	36.0	0.95	0.88-1.02	-
	Major	50.5	50.8	1.01	0.94 -1.10	-
18	Prefaint	655.6	600.3	**0.91**	**0.89-0.93**	**9%**
	LOC	30.9	30.4	0.98	0.89-1.09	-
	Major	39.6	41.4	1.05	0.96-1.14	-

LOC, loss of consciousness; CI, confidence interval
Major reactions include LOC, prolonged recovery, LOC with injury

American Red Cross

Summary

Young Donor Safety Initiative

- 16-18 year olds accounted for 16% of whole blood donations in the 2008 and 2009 school years
- Selecting donors with an estimated blood volume ≥ 3.5 L significantly decreased reactions among 16-18 year olds in 2009 compared to previous school years
- Benefit was most apparent in youngest age group
  - 16 year olds: 18% decrease in presyncopal symptoms
    14% decrease in syncope
  - 17 year olds: 14% decrease in presyncopal symptoms
  - 18 year olds: 9% decrease in presyncopal symptoms

Summary

Young Donor Safety Initiative

- For the first time in the ARC system, 16-year-olds were at the same risk as 20-year-olds in the analysis stratified for age and sex, after implementing the new selection criteria
- The reduced reaction rates may have contributed to improved operational efficiency (reduced QNS rates) and increased repeat donation rates among young donors

Conclusions

ARC Hemovigilance Program

Hemovigilance programs offer a means to identify and assess the current risks of transfusion and donation.

Data allows prioritization of effort to intervene and to measure the efficacy of a given intervention.

- Bacterial safety, apheresis platelets

  Improvements in limiting and detecting bacteria in apheresis platelets and associated reduction in septic transfusion reactions

- TRALI mitigation

  A significant reduction in TRALI from plasma transfusion with male-predominant plasma strategy

- Young donor safety initiative

  A significant reduction in donor reactions among young (16-18 year olds) donors

American Red Cross

Questions?

edera@usa.redcross.org