# APPENDICES

# TRANSFUSION RELATED ACUTE LUNG INJURY AFTER RED BLOOD CELL, PLASMA, AND PLATELET ADMINISTRATION 2013-2015

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The Sentinel System is sponsored by the U.S. Food and Drug Administration (FDA) to proactively monitor the safety of FDA-regulated medical products and complements other existing FDA safety surveillance capabilities. The Sentinel System is one piece of FDA's Sentinel Initiative, a long-term, multi-faceted effort to develop a national electronic system. Sentinel Collaborators include Data and Academic Partners that provide access to healthcare data and ongoing scientific, technical, methodological, and organizational expertise. The Sentinel Coordinating Center is funded by the FDA through the Department of Health and Human Services (HHS) Contract number HHSF223201400030I. This project was funded by the FDA through HHS Mini-Sentinel contract number HHSF223200910006I.

# Appendices

## Transfusion Related Acute Lung Injury After Red Blood Cell, Plasma, And Platelet Administration 2013-2015

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## A. APPENDIX A: BLOOD COMPONENT/PRODUCT EXPOSURE DEFINITIONS

The National Healthcare Safety Network's (NHSN) variable of Prod_CDC[1] was used in combination with Codabar and ISBT-128 code systems to collapse lengthy code lists into blood component categories relevant to this study (Table A1). Categories included in the NHSN system are listed below. For Codabar codes which are no longer updated, we used the NHSN labels and categories exclusively. For ISBT-128 blood product codes, we used NHSN labels in combination with the ISBT-128 coding system which is updated monthly[2], to ensure that code lists were complete and up to date. The structure of the Sentinel Common Data Model (SCDM)[3] inpatient pharmacy and transfusion tables are also included in Tables A2 and A3.

**Table A 1. Method for categorizing blood products/components the National Healthcare Safety Network (NHSN): Variable Prod_CDC 1**

| Broad Categorization | Description |
|---|---|
| Plasma | APHPLASMA - Apheresis plasma |
| | WBDPLASMA - Whole blood derived plasma |
| Platelets | APHPLAT - Apheresis platelets |
| | IRAPHPLAT - Irradiated apheresis platelets |
| | IRRAPHPLAT - Irradiated leukocyte reduced apheresis platelets |
| | IRLRWBDPLAT - Irradiated leukocyte reduced whole blood derived platelets |
| | IRWBDPLAT - Irradiated whole blood derived platelets |
| | LRSPHPLAT - Leukocyte reduced apheresis platelets |
| | LRWBDPLAT - Leukocyte reduced whole blood derived platelets |
| | WBDPLAT - Whole blood derived platelets |
| Red Blood Cells | APHRBC - Apheresis red blood cells |
| | IRAPHRBC - Irradiated apheresis red blood cells |
| | IRLRAPHRBC - Irradiated leukocyte reduced apheresis red blood cells |
| | IRLRWBDRBC - Irradiated leukocyte reduced whole blood derived RBC |
| | IRWBDRBC - Irradiated whole blood derived red blood cells |
| | LRAPHRBC - Leukocyte reduced apheresis red blood cells |
| | LRWBDRBC - Leukocyte reduced whole blood derived red blood cells |
| | WBDRBC - Whole blood derived red blood cells |
| Whole Blood | WB - Whole blood |
| Other | CRYO – Cryoprecipitate |
| | GRAN – Granulocytes |
| | LEUK – Leukocytes |
| | LYMPH – Lymphocytes |
| | MNC - Mononuclear cells |
| | SERUM – Serum |

**Table A 2. Inpatient Pharmacy, HCA Healthcare (HCA) Table structure as of August 2017[3]**

| Variable Name | Variable Type and Length (Bytes)* | Values | Definition / Comments / Guideline |
|---|---|---|---|
| PatID* | Character(Site specific length) | Unique member identifier | Arbitrary person-level identifier. Used to link across tables. Derivative of HCA Patient Account Number. |
| EncounterID | Character(Site specific length) | Unique encounter identifier | A unique combination of PatID, ADate, Provider and EncType. Used to link the Encounter, Diagnosis, Procedure, Inpatient Pharmacy, and Inpatient Transfusion tables. |
| NDC | Character(11) | National Drug Code | Please expunge any place holders (e.g., '-' or extra digit) |
| RxID | Character(15) | Unique Rx administration identifier | For mapping back to source data |
| RxADate | Numeric(4) | SAS date value | Rx Administration date |
| RxATime | Numeric(4) | SAS time value HH:MM | Rx Administration time |
| RxRoute | Character(10) | Values as developed by HCA | Actual/administered |
| RxDose | Numeric(8) | Values as developed by HCA | Actual/administered. Format captures maximum # of whole and decimal digits allowed by software technology for numeric data. |
| RxUOM | Character(10) | Values as developed by HCA | Actual/administered--HCA to develop a standard list of values. |

**Technical note: These are attributes of SAS© variables. For numeric values, the number of storage bytes and the number of decimal digits in a value are not identical*

**Table A 3. Inpatient Transfusion, Hospital Corporation of America (HCA) Table structure as of August 2017[3]**

| Variable Name | Variable Type and Length (Bytes)* | Values | Definition / Comments / Guideline |
|---|---|---|---|
| PatID* | Character(Site specific length) | Unique member identifier | Arbitrary person-level identifier. Used to link across tables. Derivative of HCA Patient Account Number. |
| EncounterID | Character(Site specific length) | Unique encounter identifier | A unique combination of PatID, ADate, Provider and EncType. Used to link the Encounter, Diagnosis, Procedure, Inpatient Pharmacy, and Inpatient Transfusion tables. |

| Variable Name | Variable Type and Length (Bytes)* | Values | Definition / Comments / Guideline |
|---|---|---|---|
| TransID | Character(15) | Unique transfusion administration identifier | For mapping back to source data |
| TransCode | Character(15) | Code value for an infusion product | Must be paired with the correct TransCode_Type |
| TransCode_Type | Character(2) | Code type for the value in TransCode | Transfusion product code type. This variable combined with the TransCode variable should be used to capture any type of Inpatient Infusion product in the source data. Other code types will be added as new terminologies are used.<br>IS=ISBT<br>CD=CODABAR |
| Orig_TransProd | Character(Site specific length) | Original product name/mnemonic | Name of product within Data Partner |
| BloodType | Character(3) | Blood type: A, B, O, AB (upper case) with RH factor (+, -, or null only) | Blood type and Rh factors, left-justified. Convert any text Rh factor to symbols (e.g., “pos” to “+”, “negative” to “-“). Rh factor can be blank. |
| TDate_Start | Numeric(4) | SAS date value | Administration start date |
| TTime_Start | Numeric(4) | SAS time value HH:MM | Administration start time |
| TDate_End | Numeric(4) | SAS date value | Administration end date |
| TTime_End | Numeric(4) | SAS time value HH:MM | Administration end time |
| EncType | Character(2) | ED = Emergency Department | ED encounters only |
| | | IP = Inpatient Hospital Stay | Includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date. This also includes ED visits that become inpatient stays. |
| | | IS = Non-Acute Institutional Stay | Includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays. |
| | | OA = Other Ambulatory Visit | Includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, |

| Variable Name | Variable Type and Length (Bytes)* | Values | Definition / Comments / Guideline |
|---|---|---|---|
| | | | as well as telemedicine, telephone and email consultations. |

**Technical note: These are attributes of SAS© variables. For numeric values, the number of storage bytes and the number of decimal digits in a value are not identical*

## B. APPENDIX B: DIAGNOSIS CODES FOR TRANSFUSION-RELATED ACUTE LUNG INJURY (TRALI)

Below is a table displaying the details for the diagnosis codes for transfusion-related acute lung injury (TRALI) we used to identify potential cases of TRALI in this study. Table B2 includes the electronic criteria used for various TRALI definitions.

**Table B 1. Working list of diagnosis codes for Transfusion-related acute lung injury (TRALI) and transfused acute lung injury (ALI)**

| ICD-9-CM Code | Definition |
|---|---|
| 518.7 | Transfusion-related acute lung injury |
| 518.81 | Acute respiratory failure |
| 518.82 | Other pulmonary insufficiency, not elsewhere classified code in any position |
| 999.80 | Other infusion and transfusion reaction |
| 999.89 | Other transfusion reaction |
| E934.7 | Natural blood and blood products causing adverse effects in therapeutic use |

**Table B 2. Electronic criteria to identify potential cases of transfusion-related acute lung injury (TRALI)**

| Criteria | ICD-9-CM Code(s) |
|---|---|
| Criterion A | TRALI, ICD-9-CM code in any position (518.7) |
| Criterion B | Acute respiratory failure ICD-9-CM code in any position (518.81), WITH code for a blood transfusion reaction (999.80 or 999.89 or E934.7) |
| Criterion C | Other pulmonary insufficiency (518.82), WITH code for a blood transfusion reaction (999.80 or 999.89 or E934.7) |
| Any TRALI Criteria | Criteria A, and/or B, and/or C listed above |

## C. APPENDIX C: ADJUDICATION FORM

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

Sentinel

**CLINICAL ADJUDICATION FORM: Blood Safety Continuous Active-Surveillance Network**
**Transfusion-Related Acute Lung Injury Medical Record Review**

**Goals:**

- Determine through medical chart review the performance of an ICD-9-CM code based algorithm for identifying TRALI
- Determine the positive predictive value of reported transfused product exposure in potential TRALI cases
- Review of potential TRALI cases will be compared to information included in HCA's Sentinel database

**Instructions:**

- This form includes some information about transfusion exposures for potential TRALI cases extracted from HCA data.
- Please confirm or correct any information presented.
- If upon review, there were multiple possible TRALI events, please complete one form for EACH potential event
- If multiple transfusions, please extract information only for transfusions of interest:
  - Those that occurred <6 hours prior to ALI symptoms (Definitive TRALI) and transfusions that occurred >6 hours and ≤ 72 hours of the ALI symptoms (Delayed TRALI)
  - If no ALI symptoms exist within this chart, please provide case decision (Not a case of TRALI/ALI, or unable to determine), provide mechanical ventilation information (Q14), and complete transfusion information for the first observed transfusion in the chart.
- If you have any additional questions please call or email:

  Margaret Johnson, Project Coordinator, 617-867-4565, margaret_johnson@harvardpilgrim.org

  Adee Kennedy, Project Manager, 617-867-4241, adee_kennedy@harvardpilgrim.org

**Table 1: Transfusion Related Acute Lung Injury (TRALI) definitions**

| Definition | Clinical Description |
|---|---|
| Definitive TRALI | 1. No evidence of acute lung injury (ALI) prior to transfusion<br>AND<br>2. ALI onset during or within 6 hours of transfusion<br>AND<br>3. Hypoxemia defined by any of these methods:<br>•PaO2 / FiO2 ≤300 mm Hg<br>•Oxygen saturation is < 90% on room air<br>•Other clinical evidence<br>AND<br>4. Radiographic evidence of bilateral infiltrates<br>AND<br>5. No evidence of left atrial hypertension (i.e. circulatory overload)<br>AND<br>6. No temporal relationship to an alternative risk factor for ALI during or within 6 hours of completion of transfusion |
| Possible TRALI | Same as above EXCEPT there is a temporal relationship to a specific ALI risk factor (Table 2) |
| **Delayed TRALI definition, defined in critically ill patients** | |
| Delayed TRALI | Same as for possible TRALI except allows for symptom onset within 6 to 72 hours of blood transfusion |

**Table 2: Alternate risk factors for Acute Lung Injury (ALI)**

| Direct Lung Injury | Indirect lung injury |
|---|---|
| Aspiration | Severe sepsis |
| Pneumonia | Shock |
| Toxic inhalation | Multiple trauma |
| Lung contusion | Burn injury |
| Near drowning | Acute pancreatitis |
| | Cardiopulmonary bypass |
| | Drug overdose |

***Our primary diagnosis criteria for Acute Lung Injury (ALI) are:***

-Acute onset

-Presence of bilateral infiltrates on CXR consistent with edema

-PAWP < 18 mm Hg or clinical absence of left atrial hypertension

-Hypoxemia with Pa O 2 / FI O 2 < 40 PaO2/FiO2 ≤300 mm Hg (if Pa O 2 / FI O 2 < 27, ARDS)

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*Complete one form for EACH separate episode of possible TRALI event identified*
*Transfusions of interest include those that occurred <6 hours prior to ALI symptoms (Definitive TRALI) and transfusions that occurred >6 hours and ≤ 72 hours of the ALI symptoms (Delayed TRALI)*

## ALI Information

★ ☐ **Please check if no mention of transfusion documented anywhere in the medical record, STOP, adjudication complete.**

| *Dates and times of ALI and transfusion* | | *Additional Notes* |
|---|---|---|
| 1. Date of acute lung injury (ALI) onset. *If exact date is unavailable please use timing recorded for CT or CXR if available* | _____ MM/DD/YY ☐ Unknown/Not documented | |
| 2. Specify time of ALI onset. *If exact time is unavailable please use timing recorded for CT or CXR if available* | _____ ☐AM ☐PM HH:MM ☐ Unknown/Not documented | |
| 3. Date of transfusion associated with TRALI or ALI event | _____ MM/DD/YY ☐ Unknown/Not documented | |
| 4. Start time of transfusion associated with TRALI or ALI event | _____ ☐AM ☐PM HH:MM ☐ Unknown/Not documented | |
| 5. End time of transfusion associated with TRALI or ALI | _____ ☐AM ☐PM HH:MM ☐ Unknown/Not documented | |

**Additional Note:**

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

6. If specific transfusion dates and times are NOT In the medical record, please answer the following:

| | |
|---|---|
| A. In the medical record, was there mention of a transfusion <6 hours prior to the initiation of ALI symptoms? | ☐ Yes ☐ No/not documented<br>Note: |
| B. In the medical record, was there mention of a transfusion >6 hours and ≤ 72 prior to the initiation of ALI symptoms? | ☐ Yes ☐ No/not documented<br>Note: |

7. If ALI symptom dates and times are NOT in the medical chart, please answer the following:

| | |
|---|---|
| A. In the medical record, was there mention of ALI symptoms <6 hours after a transfusion? | ☐ Yes ☐ No/not documented<br>Note: |
| B. In the medical record, was there mention of ALI symptoms >6 hours and ≤ 72 after a transfusion? | ☐ Yes ☐ No/not documented<br>Note: |

★ ☐ **Please check if no mention of transfusion ≤ 72 hours of ALI symptoms noted anywhere in the medical record, please proceed to case decision (Not a case of TRALI/ALI, or Unable to determine, Q 12), extract mechanical ventilation (Q 14), extract the first transfusion observed in the chart (final pages of form), STOP.**

★ ☐ **If no ALI symptoms exist within this chart, please proceed to case decision (Not a case of TRALI/ALI, or Unable to determine, Q 12), extract mechanical ventilation (Q 14), extract the first transfusion observed in the chart (final pages of form), STOP.**

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Data QC'd – Date/Initials: _____/_____

*The final page of this form includes questions about the blood transfusion, including blood components/ product transfused, number of units transfused, and processing method. Please complete this information if it is available.*

8. **Please document primary underlying reason for transfusion (if available in chart). Please select all that apply.**

RBC:

- ☐ Operative associated blood loss
- ☐ Trauma associated blood loss
- ☐ Low hemoglobin in patients with Heart failure, CAD, MI, or shock
- ☐ Low hemoglobin in patients with syncope or Hypotension/orthostatic hypotension not responsive to fluid resuscitation
- ☐ Chronic bone marrow failure (myelodysplasia, leukemia)
- ☐ Obstetric associated blood loss
- ☐ Other_____

**Platelets:**

- ☐ DIC (Sepsis, trauma, obstetrics)
- ☐ Immune thrombocytopenias (ITP, neonatal alloimmune thrombocytopenia)
- ☐ Disease associated marrow failure (leukemia, lymphoma, aplasia, myeloproliferative/myelodysplastic disorders, solid tumor metastases)
- ☐ Chemotherapy/radiation induced marrow failure
- ☐ Cardiac surgery associated bleeding
- ☐ Bleeding or anticipated surgery in patients on anti-platelet agents
- ☐ Trauma- or surgery associated massive transfusion
- ☐ Congenital thrombocytopenia/thrombocytopathy
- ☐ Other_____

**Frozen Plasma:**

- ☐ Abnormal coagulation studies and hemorrhage
- ☐ Prophylactic use for elevated PT/APTT
- ☐ Warfarin reversal
- ☐ Other_____

**Cryoprecipitate:**

- ☐ Fibrinogen deficiency
- ☐ Hemophilia A, von Willebrand disease, or F XIII deficiency
- ☐ Uremic coagulopathy
- ☐ Other_____

**Granulocytes:**

- ☐ Neutropenia
- ☐ Neonatal sepsis
- ☐ Hereditary neutrophil function defects
- ☐ Other_____

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

9. On evaluation of the medical chart, was there an alternative cause of ALI?

☐ Yes ☐ No

If yes, please describe:

10. Was there a temporal relationship to an alternate ALI risk factor present during or within 6 hours of completion of transfusion?

☐ Yes ☐ No

If yes, please check all that apply:

- ☐ Aspiration
- ☐ Pneumonia
- ☐ Toxic inhalation
- ☐ Lung contusion
- ☐ Severe sepsis
- ☐ Shock
- ☐ Multiple trauma
- ☐ Near drowning
- ☐ Acute pancreatic
- ☐ Cardiopulmonary bypass
- ☐ Drug overdose
- ☐ Burn injury
- ☐ Other ALI risk factor (Please describe)

11. **Principal ALI Criteria:** Were any of the following present?
*(Record any mention of ALI. Include reports by physicians, nurses, and parents/caregiver)*

Was evidence of ALI prior to transfusion noted? ☐ Yes ☐ No

Was ALI onset during or within 6 hours of transfusion noted? ☐ Yes ☐ No

Was ALI onset within 6 - 72 hours of transfusion noted? ☐ Yes ☐ No

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Data QC'd – Date/Initials: _____/_____

Was there evidence of **Hypoxemia?** ☐ Yes → **(PLEASE COMPLETE ALL ITEMS BELOW)**
☐ No

i. **PaO2/FiO2 ≤ 300 mm Hg** ☐ Yes → Please indicate: _____mm Hg
☐ No
☐ Not documented

ii. **pO2 < 60 mm Hg** ☐ Yes → Please indicate: _____mm Hg
☐ No
☐ Not documented

iii. **Oxygen saturation <90% on room air** ☐ Yes → Please indicate: _____%
☐ No
☐ Not documented

iv. **Other clinical evidence** ☐ Yes → Please describe:
☐ No
☐ Not documented

Evidence of **left atrial hypertension** (i.e. circulatory overload)
☐ Yes
☐ No **(PLEASE COMPLETE ALL ITEMS BELOW)**

i. **PAWP < 18 mm Hg or clinical absence of left atrial hypertension**
☐ Yes → Please indicate: _____mm Hg
☐ No
☐ Not documented

ii. **Echo done** ☐ Yes ☐ No

Date of Echo (MM/DD/YY) : _____

Was the Echo done before or after onset of ALI? ☐ Before ☐ After ☐ Unknown

LVEDP on Echo _____ or ☐ Not documented

LVEF on Echo _____ % or ☐ Not documented

iii. **Other clinical evidence** ☐ Yes ☐ No

Please describe:

Was there radiographic evidence of **bilateral infiltrates?**
☐ Yes → **(PLEASE COMPLETE ALL ITEMS BELOW)**
☐ No
☐ Not documented

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

i. **Primary CXR findings, bilateral infiltrates** ☐Yes ☐No ☐Not documented

ii. **Other clinical evidence** ☐Yes ☐No

Please describe:

**Temporal relationship to an alternative risk factor for ALI during or within 6 hours of completion of transfusion** Yes ☐ No ☐

**12. Case Adjudication Decision (CHECK ONE ONLY, specific definition page 1)**

- ☐ Definitive TRALI
- ☐ Possible TRALI
- ☐ Delayed TRALI
- ☐ Acute Lung Injury, ALI not associated with a transfusion
- ☐ Not a case of TRALI or ALI (Essential clinical information was available for review, and not a TRALI or ALI case. Describe in note field)
- ☐ Unable to determine (If clinical information essential to case determination was NOT available, please select unable to determine and describe in note field)

★ ☐ **Please check if this is a challenging case and you would like a second opinion on final decision.**

**Additional notes on case adjudication decision:**

**13. Severity of TRALI reaction (Only complete if TRALI case)**

- ☐ Mild (PaO2/FiO2 201 – 300)
- ☐ Moderate (PaO2/FiO2 101 – 200)
- ☐ Severe (PaO2/FiO2 <100)
- ☐ Not a case of TRALI or ALI (please describe in note field)
- ☐ Unable to determine

**Additional notes on TRALI severity:**

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

## *Treatment and/or risk information*

14. In the medical record, was there note of mechanical ventilation of this patient?
☐Yes
☐No/not documented

If yes, indicate date (s) and time (s) of mechanical ventilation. If there were multiple instances of mechanical ventilation, please only document mechanical ventilation prior to and immediately after the ALI event

| Date of mechanical ventilation (MM/DD/YY) | Time of mechanical ventilation (HH:MM) | Duration of mechanical ventilation (Hours) | Indicate timing of mechanical ventilation in relation to ALI event | Notes |
|---|---|---|---|---|
| _____ ☐Unknown | _____ ☐AM ☐PM ☐Unknown | _____ | ☐Prior to ALI ☐After ALI | |
| _____ ☐Unknown | _____ ☐AM ☐PM ☐Unknown | _____ | ☐Prior to ALI ☐After ALI | |
| _____ ☐Unknown | _____ ☐AM ☐PM ☐Unknown | _____ | ☐Prior to ALI ☐After ALI | |
| _____ ☐Unknown | _____ ☐AM ☐PM ☐Unknown | _____ | ☐Prior to ALI ☐After ALI | |

15. If there was another treatment noted in the record, please describe below

| |
|---|
| |

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

16. Did the patient die during this hospitalization?

- ☐ Yes → Specify date of death (MM/DD/YY): _____
- ☐ No
- ☐ Unknown/Not documented

Please record any additional details you think may be helpful:

| |
|---|
| |

## ***Hospital admission type, and unit information***

17. Specify admission type at time (if possible) of ALI or TRALI diagnosis

- ☐ Emergency room
- ☐ Elective
- ☐ Transfer
- ☐ Direct admission
- ☐ Other: _____
- ☐ Not Documented

18. Specify the hospital unit/level of care at time of ALI or TRALI diagnosis (please check all that apply)

- ☐ Intensive care unit (Medical, Surgical (non-Trauma), Cardiac)
- ☐ Floor (Non-telemetry)
- ☐ Emergency room
- ☐ Telemetry or step-down unit
- ☐ Other: _____
- ☐ Not Documented

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

## *Transfusion information*

**Please extract or confirm the following information about the transfusion associated with TRALI or ALI event from the patient chart.**
*Fill out one transfusion table for each blood component given during the transfusion of interest.

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #Of units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br><br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br><br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br><br>☐ Not documented | ☐ Yes<br>☐ No<br><br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br><br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br><br>☐ Not documented | _____<br><br>☐ Not documented | _____<br><br>☐ AM<br>☐ PM<br><br>☐ Not documented | _____<br><br>☐ AM<br>☐ PM<br><br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br><br>If no, please estimate the number of units or mL<br>_____<br><br>Additional information: | _____<br><br>☐ Not documented | _____<br><br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

**Patient Case ID**_____

**Data Entry – Date/Initials:** _____/_____
**Data QC'd – Date/Initials:** _____/_____

***Fill out one transfusion table for each blood component given during the transfusion of interest**

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #f units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br>☐ Not documented | _____<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br>If no, please estimate the number of units or mL<br>_____<br>Additional information: | _____<br>☐ Not documented | _____<br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

**Patient Case ID**_____

**Data Entry – Date/Initials:** _____/_____
**Data QC'd – Date/Initials:** _____/_____

*Fill out one transfusion table for each blood component given during the transfusion of interest

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #f units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br>☐ Not documented | _____<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br>If no, please estimate the number of units or mL<br>Additional information: | _____<br>☐ Not documented | _____<br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

**Patient Case ID**_____

**Data Entry – Date/Initials:** _____/_____
**Data QC'd – Date/Initials:** _____/_____

***Fill out one transfusion table for each blood component given during the transfusion of interest**

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #f units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br>☐ Not documented | _____<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br>If no, please estimate the number of units) /mL<br>Additional information: | ☐<br>☐ Not documented | _____<br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

**Patient Case ID**_____

**Data Entry – Date/Initials:** _____/_____
**Data QC'd – Date/Initials:** _____/_____

***Fill out one transfusion table for each blood component given during the transfusion of interest**

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #f units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br>☐ Not documented | _____<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br>If no, please estimate the number of units or mL<br>Additional information: | _____<br>☐ Not documented | _____<br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

**Patient Case ID**_____

**Data Entry – Date/Initials:** _____/_____
**Data QC'd – Date/Initials:** _____/_____

***Fill out one transfusion table for each blood component given during the transfusion of interest**

| Transfusion environment (check all that apply) | Blood Components /Blood Product(s) Transfused | Select Processing Method (check all that apply) | Was this a whole blood derived blood product/ component | Select if blood product/ component was pooled or single donor | Select pathogen reduction method (if available) (check all that apply) | Date of transfusion (DD/MM/YY) | Time of transfusion (Start) (HH:MM) | Time of transfusion (End) (HH:MM) | Was entire volume transfused? | #f units transfused | Age of Product (days) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ☐ Intensive care unit<br>☐ Coronary care unit<br>☐ Surgical intensive care unit<br>☐ Surgery floor<br>☐ Medical floor<br>☐ Telemetry or step-down unit<br>☐ Trauma unit<br>☐ Neurological or Neurosurgical unit<br>☐ Emergency Department holding unit<br>☐ Other:<br>☐ Not documented | ☐ RBC<br>☐ Platelets<br>☐ Plasma<br>☐ Whole Blood<br>☐ Cryo-precipitated AHF<br>☐ Autologous transfusion<br>☐ Other:<br>☐ Not documented | ☐ Leukocyte reduced<br>☐ Irradiated<br>☐ Apheresis Derived<br>☐ Other:<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented | ☐ Pooled<br>☐ Single donor<br>☐ Not documented | ☐ No treatment<br>☐ Heat-treated<br>☐ Methylene blue-treated<br>☐ Psoralen-treated<br>☐ Riboflavin-treated<br>☐ Solvent detergent-treated<br>☐ Sterile filtered<br>☐ Other:<br>☐ Not documented | _____<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | _____<br>☐ AM<br>☐ PM<br>☐ Not documented | ☐ Yes<br>☐ No<br>☐ Not documented<br>If no, please estimate the number of units or mL<br>Additional information: | _____<br>☐ Not documented | _____<br>☐ Not documented |

**Please record any additional details about the relevant transfusion in chart, list all available information:**

Patient Case ID_____

Data Entry – Date/Initials: _____/_____
Data QC'd – Date/Initials: _____/_____

***Comments***

**Please record any additional details you may think may be helpful about the relevant transfusion in chart, list all available information:**

# D. APPENDIX D: CODES USED TO IDENTIFY TRALI PATIENT AND TRANSFUSION RISK FACTORS

## 1. List of potential TRALI patient and transfusion related factors

Below are tables displaying the details for the potential patient and transfusion (non-medication) related factors we considered for this study. Table D1 includes variables that were defined by specific variables in the Sentinel Common Data Model (SCDM), and were not defined by specific codes. Table D2 includes variables defined with specific codes and includes code type, and codes related to each variable.

**Table D 1. Demographic, calendar time, potential patient and transfusion related risk factors**

| Variable | Time to define |
|---|---|
| Age | At admission |
| Sex | At admission |
| Race | At admission |
| Calendar year | At admission |
| Discharge Disposition | At discharge (defined in the Sentinel Common Data Model) |
| Length of stay | Time between admission and discharge dates |
| Number of hospitalizations | By patient* during study period (September 2013-September 2015) |

**Please note, admissions to the same hospital can be tracked within the HCA Sentinel database, admissions across hospitals across the HCA network are not currently tracked within the HCA Sentinel database, and thus a patient admitted to two different hospitals in the HCA network may be counted as two separate patients. Thus we expect the number of hospitalizations per patient to be underrepresented.*

**Table D 2. Codes used to describe potential patient and transfusion related risk factors**

| Variable | Code type* | Codes |
|---|---|---|
| Acute pancreatitis | DX09 | 577.0 |
| Alcohol abuse[4] | DX09 | 265.2, 291.1, 291.2, 291.3, 291.5, 291.8*, 291.9 303.xx, 305.0x, 357.5, 425.5, 535.3x, 571.0, 571.1, 571.2, 571.3, 980.x, V11.3 |
| Aspiration, aspiration pneumonitis | DX09 | 507.x |
| Burn injury | DX09 | 947.1 |
| Cardiopulmonary bypass | PX09 | 39.61 |
| Cardiogenic shock | DX09 | 785.51 |
| Diabetes[5] | DX09 | 250.xx, 357.2, 362.01, 362.02, 362.04, 362.05, 363.03, 363.06, 363.07, 366.41 |
| Drowning | DX09 | 994.1 |
| Drug overdose[6] | DX09 | 960.x, 961.x, 962.x, 963.x, 964.x, 965.xx, 966.x, 967.x, 968.x, 969.xx, 970.xx, 971.x, 972.x, 973.x, 974.x, 975.x, 976.x, 977.x, 978.x, 979.x, 980.x, 981, 982.x, 983.x, 984.x, 985.x, 986, 987.x, 988.x, 989.xx, E850.x, E851, E852.x, E853.x, E854.x, E855.x, E856, E857, E858.x, E860.x, E861.x, E862.x, E863.x, E864.x, E865.x, E866.x, E867, E868.x, E869.x, E950.x, E951.x, E952.x, E962.x, E980.x, E981.x, E982.x |

| Variable | Code type* | Codes |
|---|---|---|
| End stage liver disease (Requires at least 1 code from each list)[7] | DX09 | Chronic liver disease: 020.22, 070.2x, 070.3x, 070.4x, 070.5x, 070.6x, 070.7x, 070.9, 273.4, 275.x, 453.0, 456.0 |
| | DX09 | Cirrhosis: 571.2, 571.5, 571.6 |
| | DX09 | Hepatic decompensation: 456.1, 456.2x, 567.0, 567.2x, 567.8, 567.89, 572.2, 572.4, 573.x, 576.1, 789.5, 789.59 |
| Liver transplant | DX09 | V42.7 |
| | PX09 | 00.9x, 50.5x |
| Lung contusion | DX09 | 861.21 |
| Mechanical ventilation | PX09 | 93.90, 96.0x, 96.7x |
| | PXHC | A7030 |
| Post-inflammatory pulmonary fibrosis | DX09 | 515, 516.31 |
| Pneumonia | DX09 | 480.x, 481, 482.xx, 483.x, 484.x, 485, 486, 997.3x |
| Sepsis broad[8] | DX09 | 038.x, 038.1x, 038.4x, 785.52, 995.91, 995.92 |
| Septic shock | DX09 | 785.52 |
| Severe sepsis[8-10] | DX09 | 785.52, 999.52 |
| Shock broad | DX09 | 785.5x |
| Smoking tobacco (comprehensive definition)[11] | DX09 | 305.1, 649.0x, 989.84, V15.82 |
| | PXC4 | 83887, 99406, 99407 |
| | PXHC | 1034F, 1035F, 4000F, 4001F, 4004F, C9801, C9802, G0375, G0376, G0436, G0437, G8093, G8094, G8402, G8403, G8453, G8454, G8455, G8456, G8688, G9016, S4990, S4991, S4995, S9075, S9453 |
| | NDC | See search strategy below |
| Anti-smoking medications only | NDC | See search strategy below |
| Toxic inhalation | DX09 | 987.9 |
| Trauma, multiple | DX09 | 800.xx, 801.xx, 802.xx, 803.xx, 804.xx, 805.xx, 806.xx, 807.xx, 808.xx, 809.x, 810.xx, 811.xx, 812.xx, 813.xx, 814.xx, 815.xx, 816.xx, 817.x, 818.x, 819.x, 820.xx, 821.xx, 822.x, 823.xx, 824.x, 825.xx, 826.x, 827.x, 828.x, 829.x, 830.x, 831.xx, 832.xx, 833.xx, 834.xx, 835.xx, 836.xx, 837.x, 838.xx, 839.xx, 840.x, 841.x, 842.xx, 843.x, 844.x, 845.xx, 846.x, 847.x, 848.xx, 850.xx, 851.xx, 852.xx, 853.xx, 854.xx, 860.x, 861.xx, 862.xx, 863.xx, 864.xx, 865.xx, 866.xx, 867.x, 868.xx, 869.x, 870.x, 871.x, 872.xx, 873.xx, 874.xx, 875.x, 876.x, 877.x, 878.x, 879.x, 880.xx, 881.xx, 882.x, 883.x, 884.x, 885.x, 886.x, 887.x, 890.x, 891.x, 892.x, 893.x, 894.x, 895.x, 896.x, 897.x, 958.xx, 959.xx, |

**Code type abbreviations: DX09 = ICD-9-CM diagnosis code, PX09 = ICD-9-CM procedure code, PXC4 = Current Procedural Terminology 4 (CPT-4) procedure code, PXHC = Healthcare Common Procedure Coding System (HCPCS) code*

## 2. Antismoking medication search strategy

Below is a table displaying the drug classes for the anti-smoking medication variable. Table D3 includes the classes, subclass1, and subclass2 (if applicable) associated with the medications we considered via NDC codes. We considered nicotine replacement, varenicline, and Zyban (brand only).

**Table D 3. Classes and subclasses of anti-smoking medication variable***

| Brand Name | Generic Name |
|---|---|
| Chantix | VARNICLINE TARTRATE |
| Zyban | BUPROPION HCL |
| Nicotine | NICOTINE |
| | NICOTINE BITARTRATE |
| | NICOTINE POLACRILEX |
| Nicorette | NICOTINE POLACRILEX |
| Nicorelief | NICOTINE POLACRILEX |

**Use defined through use of HCA's inpatient pharmacy table.*

# E. APPENDIX E: CODES USED TO IDENTIFY MECHANICAL VENTILATION IN THE SENTINEL DISTRIBUTED DATABASE

**Table E 1. Procedure codes used in the Sentinel database to define mechanical ventilation in potential transfusion-related acute lung injury (TRALI) cases**

| Outcome details | Code | Code Type | Description |
|---|---|---|---|
| Intubation | 96.0 | ICD-9 Procedure | Non-operative intubation of gastrointestinal and respiratory tracts |
| Intubation | 96.01 | ICD-9 Procedure | Insertion of nasopharyngeal airway |
| Intubation | 96.02 | ICD-9 Procedure | Insertion of oropharyngeal airway |
| Intubation | 96.03 | ICD-9 Procedure | Insertion of esophageal obturator airway |
| Intubation | 96.04 | ICD-9 Procedure | Insertion of endotracheal tube |
| Intubation | 96.05 | ICD-9 Procedure | Other intubation of respiratory tract |
| Invasive mechanical ventilation | 96.7 | ICD-9 Procedure | Other continuous invasive mechanical ventilation |
| Invasive mechanical ventilation | 96.70 | ICD-9 Procedure | Continuous invasive mechanical ventilation of unspecified duration |
| Invasive mechanical ventilation | 96.71 | ICD-9 Procedure | Continuous invasive mechanical ventilation for less than 96 consecutive hours |
| Invasive mechanical ventilation | 96.72 | ICD-9 Procedure | Continuous invasive mechanical ventilation for 96 consecutive hours or more |
| Non-invasive mechanical ventilation | 93.90 | ICD-9 Procedure | Non-invasive mechanical ventilation |
| Non-invasive mechanical ventilation | A7030 | HCPCS Code | Full face mask used with positive airway pressure device, each |

## F. APPENDIX F: SUPPLMENTARY TABLES

### 1. Patient related tables for primary electronic analyses

**Table F 1. Description of potential transfusion-related acute lung injury (TRALI) and non-TRALI patients contributing to the inpatient analyses: *All Encounters, patients with inpatient stays***

| | Any TRALI, N | Any TRALI, % | No TRALI, N | No TRALI, % | p-value |
|---|---|---|---|---|---|
| **Patients: Total** | 207 | - | 2,956,472 | - | - |
| **Hospitalization Characteristics** | | | | | |
| Discharge Disposition: Discharged Alive | 164 | 79.23% | 2,913,731 | 98.60% | <.0001 |
| Discharge Disposition: Expired | 43 | 20.77% | 42,741 | 1.45% | <.0001 |
| Discharge Disposition: Unknown | 0 | 0.00% | 0 | 0.00% | |
| Patient Hospitalization, median (min, max, standard deviation) | 1 | (1,2, SD 0.07) | 1 | (1,430, SD 2.18) | <.0001 |
| **Patient Demographics** | | | | | |
| Age, median (min, max, standard deviation) | 63 | (0,97, SD 21.52) | 48 | (-1,165, SD 28.22) | 0.0002 |
| Age Group: 0-19 | 10 | 4.83% | 596,756 | 20.20% | <.0001 |
| Age Group: 20-34 | 21 | 10.14% | 535,747 | 18.10% | 0.0029 |
| Age Group: 35-49 | 32 | 15.46% | 383,037 | 13.00% | 0.2836 |
| Age Group: 50-64 | 46 | 22.22% | 533,144 | 18.00% | 0.117 |
| Age Group: 65-79 | 60 | 28.99% | 566,124 | 19.10% | 0.0003 |
| Age Group: 80+ | 38 | 18.36% | 341,647 | 11.60% | 0.0022 |
| Sex: Female | 111 | 53.62% | 1,744,941 | 59.00% | 0.1143 |
| Sex: Male | 96 | 46.38% | 1,211,068 | 41.00% | 0.1132 |
| Sex: Ambiguous | 0 | 0.00% | 0 | 0.00% | - |
| Sex: Unknown | 0 | 0.00% | 463 | 0.02% | - |
| Race: White | 149 | 71.98% | 2,073,957 | 70.10% | 0.5641 |
| Race: Black/African American | 26 | 12.56% | 422,464 | 14.30% | 0.4772 |
| Race: Other | <10 | 0.00% | 3,744 | 0.13% | NS* |
| | | | | | |
| | | | | | |
| Race: Unknown | 31 | 14.98% | 456,307 | 15.40% | 0.8552 |

** NS= not statistically significant at the p≤0.05 level, exact value not included due to small sample sizes for some demographic cells and to desire to prevent the ability to derive from other reported cells*

**Table F 2. Description of potential transfusion-related acute lung injury (TRALI) and non-TRALI patient contributing to the inpatient analyses: *All Encounters with transfusions, patients with inpatient stays***

| | Any TRALI, N | Any TRALI, % | No TRALI, N | No TRALI, % | p-value |
|---|---|---|---|---|---|
| **Patients: Total** | 191 | - | 285,583 | - | - |
| **Hospitalization Characteristics** | | | | | |
| Discharge Disposition: Discharged Alive | 149 | 78.01% | 266,627 | 93.40% | - |
| Discharge Disposition: Expired | 42 | 21.99% | 18,956 | 6.64% | - |
| Discharge Disposition: Unknown | 0 | 0.00% | 0 | 0.00% | - |
| Patient Hospitalization, median (min, max, standard deviation) | 1 | (1,2, SD 0.07) | 1 | (1,27, SD 0.76) | <.0001 |
| **Patient Demographics** | | | | | |
| Age, median (min, max, standard deviation) | | 63(0,97, SD 21.77) | | 66 (0,165, SD 21.27) | 0.0262 |
| Age Group: 0-19 | 9 | 4.71% | 11,494 | 4.02% | 0.6290 |
| Age Group: 20-34 | 21 | 10.99% | 24,139 | 8.45% | 0.2068 |
| Age Group: 35-49 | 29 | 15.18% | 30,717 | 10.80% | 0.0484 |
| Age Group: 50-64 | 44 | 23.04% | 64,124 | 22.50% | 0.8470 |
| Age Group: 65-79 | 53 | 27.75% | 91,806 | 32.10% | 0.1932 |
| Age Group: 80+ | 35 | 18.32% | 63,303 | 22.20% | 0.2013 |
| Sex: Female | 103 | 53.93% | 162,146 | 56.80% | 0.4266 |
| Sex: Male | 88 | 46.07% | 123,420 | 43.20% | 0.4257 |
| Sex: Ambiguous | 0 | 0.00% | 0 | 0.00% | - |
| Sex: Unknown | 0 | 0.00% | 17 | 0.01% | - |
| Race: White | 139 | 72.77% | 207,994 | 72.80% | 0.9860 |
| Race: Black/African American | 24 | 12.57% | 45,533 | 15.90% | 0.2023 |
| Race: Other | <10 | 0.00% | 359 | 0.13% | NS |
| | | | | | |
| | | | | | |
| Race: Unknown | 27 | 14.14% | 31,697 | 11.10% | 0.1817 |

** NS= not statistically significant at the p≤0.05 level, exact value not included due to small sample sizes for some demographic cells and to desire to prevent the ability to derive from other reported cells*

**Table F 3. Description of potential transfusion-related acute lung injury (TRALI) and non-TRALI patient contributing to the inpatient analyses: Patients with inpatient encounters including RBCs, platelets, or plasma**

| | Any TRALI, N | Any TRALI, % | No TRALI, N | No TRALI, % | p-value |
|---|---|---|---|---|---|
| **Patients: Total** | 185 | - | 271,156 | - | |
| **Hospitalization Characteristics** | | | | | |
| Discharge Disposition: Discharged Alive | 144 | 77.84% | 252,556 | 93.10% | <.0001 |
| Discharge Disposition: Expired | 41 | 22.16% | 18,600 | 6.86% | <.0001 |
| Discharge Disposition: Unknown | 0 | 0.00% | 0 | 0.00% | - |
| Patient Hospitalization, median (min, max, standard deviation) | 1 | (1,2, SD 0.07) | 1 | (1,27, SD 0.76) | <.0001 |
| **Patient Demographics** | | | | | |
| Age, median (min, max, standard deviation) | 58 | (0,97, SD 21.85) | 67 | (0,165, SD 20.71) | 0.001 |
| Age Group: 0-19 | 9 | 4.86% | 10,507 | 3.87% | 0.4856 |
| Age Group: 20-34 | 21 | 11.35% | 17,971 | 6.63% | 0.0098 |
| Age Group: 35-49 | 29 | 15.68% | 28,737 | 10.60% | 0.0249 |
| Age Group: 50-64 | 44 | 23.78% | 62,570 | 23.10% | 0.8191 |
| Age Group: 65-79 | 50 | 27.03% | 89,648 | 33.10% | 0.0811 |
| Age Group: 80+ | 32 | 17.30% | 61,723 | 22.80% | 0.0763 |
| Sex: Female | 102 | 55.14% | 150,781 | 55.60% | 0.8960 |
| Sex: Male | 83 | 44.86% | 120,359 | 44.40% | 0.8973 |
| Sex: Ambiguous | 0 | 0.00% | 0 | 0.00% | - |
| Sex: Unknown | 0 | 0.00% | 16 | 0.01% | - |
| Race: White | 133 | 71.89% | 196,874 | 72.60% | 0.8278 |
| Race: Black/African American | 24 | 12.97% | 44,056 | 16.20% | 0.2274 |
| Race: Other | <10 | 0.00% | 346 | 0.13% | |
| | | | | | - |
| | | | | | 0.0408 |
| Race: Unknown | 27 | 14.59% | 29,880 | 11.00% | 0.1206 |

** NS= not statistically significant at the p≤0.05 level, exact value not included due to small sample sizes for some demographic cells and to desire to prevent the ability to derive from other reported cells*

## 2. Sensitivity analyses associated with medical chart confirmed cases of transfusion-related acute lung injury (TRALI), including positive predictive values (PPVs) associated with inpatient diagnosis codes for TRALI

**Table F 4. Description of transfusion-related acute lung injury (TRALI) patient demographics and other clinical information in chart confirmed TRALI cases (n=68)**

| | Definitive, N=26 N (%) | Possible, N=15 N (%) | Delayed, N=27 N (%) |
|---|---|---|---|
| **Race** | | | |
| White | 19 (73%) | 8 (53%) | 21 (78%) |
| Black/African American/Other | 3 (12%) | 3 (20%) | 3 (11%) |
| Other | - | - | |
| | | | |
| | | | |
| Unknown | 4 (15%) | 4 (27%) | 3 (11%) |
| **Ethnicity** | | | |
| Hispanic | 5 (19%) | 1 (7%) | 7 (26%) |
| Not Hispanic | 17 (65%) | 10 (67%) | 14 (52%) |
| Unknown | 4 (15%) | 4 (27%) | 6 (22%) |
| **Sex** | | | |
| Female | 21(81%) | 8 (53%) | 14 (52%) |
| Male | 5 (19%) | 7 (47%) | 13 (48%) |
| Unknown | - | | |
| **Age (years) at encounter admission or visit** | | | |
| 0-19 | - | - | 1(4%) |
| 20-34 | 2 (8%) | 3(20%) | 1(4%) |
| 35-49 | 2 (8%) | 2(13%) | 5 (19%) |
| 50-64 | 3 (11%) | 3(20%) | 11 (40%) |
| 65-79 | 13 (50%) | 3(20%) | 6 (22%) |
| 80+ | 6 (23%) | 4(27%) | 3 (11%) |
| **Year of encounter admission** | | | |
| 2013 | 3 (12%) | 2 (13%) | 6 (22%) |
| 2014 | 14 (54%) | 8 (53%) | 12 (44%) |
| 2015 | 9 (35%) | 5 (33%) | 9 (33%) |
| **Death** | | | |
| Alive at discharge | 23 (88%) | 13 (87%) | 19 (70%) |
| Expired in hospital | 3 (12%) | 2 (13%) | 8 (30%) |
| **Severity of TRALI reaction** | | | |
| Mild (PaO2/FiO2 201 – 300) | 4 (15%) | 2 (13%) | 4 (15%) |
| Moderate (PaO2/FiO2 101 – 200) | 9 (35%) | 3 (20%) | 5 (19%) |
| Severe (PaO2/FiO2 <100) | 7 (27%) | 3 (20%) | 12 (44%) |
| Unable to determine | 6 (23%) | 7 (46%) | 6 (22%) |
| **Temporally associated Acute Lung Injury risk factor*** | | | |

| | Definitive, N=26 N (%) | Possible, N=15 N (%) | Delayed, N=27 N (%) |
|---|---|---|---|
| Any | - | 15 (100%) | 10 (37%) |
| Aspiration | - | - | - |
| Pneumonia | - | 6 (40%) | 6 (22%) |
| Toxic inhalation | - | - | - |
| Lung contusion | - | 1 (17%) | 1 (4%) |
| Severe sepsis | - | 2 (13%) | 1 (4%) |
| Shock | - | 4(27%) | - |
| Multiple trauma | - | - | 1 (4%) |
| Near drowning | - | - | - |
| Acute pancreatic | - | - | - |
| Cardiopulmonary bypass | - | 2 (13%) | 1 (4%) |
| Drug overdose | - | - | - |
| Burn injury | - | - | - |
| Other ALI risk factor (Please describe)* *Other include: TACO (1), bleeding and required IABP for hemodynamic and BP support and heart failure (1), other hemolytic anemia, aortic dissection and pulmonary vascular congestion and fluid overload (1), cardiac arrest and respiratory arrest with PEA (1), and congestive heart failure (2) | - | 6 (40%) | - |
| **Admission type at time of ALI or TRALI diagnosis** | | | |
| Emergency room | 17 (65%) | 11 (73%) | 20 (77%) |
| Elective | 1 (4%) | 2 (13%) | 4 (15%) |
| Transfer | 2 (8%) | 1 (7%) | 2 (7%) |
| Direct admission | 4 (15%) | 1 (7%) | - |
| Other** **Other includes: direction admission for surgery (1), hemo oncology transfusion center (1), and SICU (1) | 2 (8%) | - | 1 (4%) |
| **Hospital unit/level of care at time of ALI or TRALI diagnosis** | | | |
| Intensive care unit (Medical, Surgical (non-Trauma), Cardiac) | 5 (19%) | 6 (40%) | 10 (37%) |
| Floor (Non-telemetry) | 6 (23%) | 3 (20%) | 6 (22%) |
| Emergency room | 1 (4%) | - | 1 (4%) |
| Telemetry or step-down unit | 5 (19%) | 5 (33%) | 2 (7%) |
| Other*** ***Other includes: oncology (3), infusion floor (1), post operative (1), interventional radiology lab (1), outpatient infusion center (1), OR (1), intermediate care (1), SICU (1), unsure (1), and trauma unit/ICU (2) | 6 (23%) | 3 (20%) | 4 (15%) |
| Not documented | 2 (8%) | | |
| **Transfusion indication*** | | | |
| **RBCs** | | | |
| Operative associated blood loss | 2 (8%) | 1 (7%) | 4 (15%) |

| | Definitive, N=26 N (%) | Possible, N=15 N (%) | Delayed, N=27 N (%) |
|---|---|---|---|
| Trauma associated blood loss | - | 3 (20%) | 1 (4%) |
| Low hemoglobin in patients with Heart failure, CAD, MI, or shock | 1 (4%) | 2 (13%) | 4 (15%) |
| Low hemoglobin in patients with syncope or Hypotension/orthostatic hypotension not responsive to fluid resuscitation | 2 (8%) | - | - |
| Chronic bone marrow failure (myelodysplasia, leukemia) | 4 (15%) | - | 3 (11%) |
| Obstetric associated blood loss | - | - | 1 (4%) |
| Other | 20 (77%) | 8 (53%) | 11 (40) |
| **Platelets** | | | |
| DIC (Sepsis, trauma, obstetrics) | - | - | - |
| Immune thrombocytopenias (ITP, neonatal alloimmune thrombocytopenia) | - | 1 (7%) | 2 (7%) |
| Disease associated marrow failure (leukemia, lymphoma, aplasia, myeloproliferative/myelodysplastic disorders, solid tumor metastases) | 3 (12%) | - | 2 (7%) |
| Chemotherapy/radiation induced marrow failure | 1 (4%) | - | - |
| Cardiac surgery associated bleeding | - | 2 (13%) | - |
| Bleeding or anticipated surgery in patients on anti-platelet agents | - | - | - |
| Trauma- or surgery associated massive transfusion | - | 1 (7%) | 3 (11%) |
| Congenital thrombocytopenia/thrombocytopathy | - | - | - |
| Other | 4 (15) | 1 (7%)- | 4 (15%) |
| **Plasma** | | | |
| Abnormal coagulation studies and hemorrhage | 2 (8%) | 2 (13%) | 3 (11%) |
| Prophylactic use for elevated PT/APTT | - | - | - |
| Warfarin reversal | 1 (4%) | - | 1 (4%) |
| Other | - | 1 (7%) | 8 (30%) |
| **Cryoprecipitate** | | | |
| Fibrinogen deficiency | - | 2 (13%) | 1 (4%) |
| Hemophilia A, von Willebrand disease, or F XIII deficiency | - | - | - |
| Uremic coagulopathy | - | - | - |
| Other | - | - | 4 (15%) |
| **Granulocytes** | | | |
| Neutropenia | - | - | - |
| Neonatal sepsis | - | - | - |
| Hereditary neutrophil function defects | - | - | - |
| Other | - | - | - |
| **Unknown** | | | |

**Note, many confirmed TRALI patients had multiple transfusion indications, and some had multiple temporally associated ALI risk factors*

**Table F 5. Positive predictive values (PPVs) associated with inpatient diagnosis codes for Transfusion-related acute lung injury (TRALI) (unable to determine excluded from denominators)**

| PPVs associated with inpatient diagnosis codes for TRALI, compared to chart review (N =183) | |
|---|---|
| All TRALI codes | 37% (68/183, 95% CI: 30-45%) |
| **By TRALI Criterion recorded in electronic data** | |
| $TRALI_A$* | 48% (49/102, 95% CI: 38-58%) |
| $TRALI_B$† | 24% (19/78, 95% CI: 15-35%) |
| $TRALI_C$‡ | - (0/3) |
| $TRALI_{B\ or\ C}$§ | 23% (19/81, 95% CI: 15-34%) |
| **By whether a transfusion was recorded in electronic data** | |
| Transfusion recorded in electronic data | 38% (66/174, 95% CI: 31-46%) |
| No transfusion recorded in electronic data | 22% (2/9, 95% CI: 3-60%) |
| **By sex in electronic data** | |
| Female | 43% (43/99, 95% CI: 34-54%) |
| Male | 30% (25/84, 95% 20-41%) |
| **By age category in electronic data** | |
| 0-19 years | 11% (1/9, 95% CI, 0.3-48%) |
| 20-34 years | 35% (6/17, 95% CI: 14-62%) |
| 35-49 years | 35% (9/26, 95% CI: 17-56%) |
| 50-64 years | 40% (17/42, 95% CI: 26-57%) |
| 65-79 years | 41% (22/54, 95% CI: 28-55%) |
| 80+ years | 37% (13/35, 95% CI: 21-55%) |
| **By TRALI Criterion recorded in electronic data as compared to definitive, possible, delayed clinical case definitions** | |
| All TRALI codes compared to definitive TRALI | 14% (26/183, 95% CI: 10-20%) |
| All TRALI codes compared to possible TRALI | 8% (15/183, 95% CI: 5-13%) |
| All TRALI codes compared to delayed TRALI | 15% (27/183, 95% CI: 10-21%) |
| $TRALI_A$ codes compared to definitive TRALI | 16% (16/102, 95% CI: 9-24%) |
| $TRALI_A$ codes compared to possible TRALI | 11% (11/102, 95% CI: 6- 18%) |
| $TRALI_A$ codes compared to delayed TRALI | 22% (22/102, 95% CI: 14-30%) |
| $TRALI_B$ codes compared to definitive TRALI | 13%, (10/78, 95% CI: 6-22%) |
| $TRALI_B$ codes compared to possible TRALI | 5% (4/78, 95% CI: 1-13%) |
| $TRALI_B$ codes compared to delayed TRALI | 6% (5/78, 95% CI, 2-14% |

**$TRALI_A$: TRALI, ICD-9-CM code in any position (518.7). See Final Report, Table 4.*

*† $TRALI_B$: Acute respiratory failure ICD-9-CM code in any position (518.81), WITH ICD-9-CM code for a blood transfusion reaction (999.80 or 999.89 or E934.7). See Final Report, Table 4.*

*‡ $TRALI_C$: Other pulmonary insufficiency (518.82), WITH IICD-9-CM code for a blood transfusion reaction (999.80 or 999.89 or E934.7). See Final Report, Table 4.*

*§$TRALI_{B\ or\ C}$: $TRALI_B$, or $TRALI_C$ as listed above. See Final Report, Table 4.*

## 3. Description of blood products and components, exploratory aims

**Table F 6. Description of blood products and components identified with ISBT-128 only in transfusion-related acute lung injury (TRALI) and non-TRALI inpatient stays in the Sentinel database, September 2013- September 2015**

| Blood product/component | **Inpatient** *encounters with evidence of transfusion and ANY TRALI (n=192)* | **Inpatient** *encounters without TRALI and evidence of transfusion (n=**353,557**)* |
|---|---|---|
| **Any Platelets** | 71 (37%) | 47,571 (13%) |
| Platelet units per encounter, median (min, max, Standard Deviation) | 2 (1,9, SD 1.7) | 1 (1,21, SD 1.27) |
| Apheresis platelets | 71 (99%) | 46,403 (97%) |
| Leukocyte reduced platelets | 69 (96%) | 47,102 (98%) |
| Irradiated platelets | 21(29%) | 14,939 (31%) |
| Whole blood derived platelets | 3 (4%) | 2,636 (5%) |
| Leukocyte reduced apheresis platelets | 69 (96%) | 45,929 (96%) |
| Irradiated apheresis platelets | 21 (29%) | 14,687 (31%) |
| Irradiated Leukocyte reduced | 19 (26%) | 14,763 (31%) |
| Irradiated Leukocyte reduced apheresis platelets | 19 (26%) | 14,514 (30%) |
| **Any Red Blood Cells (RBCs)** | 170 (89%) | 305,632 (86%) |
| RBC units per encounter, median (min, max, Standard Deviation) | 2 (1,14, SD 2.50) | 2 (1, 42, SD 1.43) |
| Irradiated RBCs | 30 (18%) | 29,386 (10%) |
| Leukocyte reduced RBCs | 163 (95%) | 292,603 (96%) |
| Apheresis derived RBCs | 87 (51%) | 124,428 (41%) |
| Whole blood derived RBCs | 60 (94%) | 268,281 (88%) |
| Irradiated apheresis RBCs | 14 (8%) | 11,224 (4%) |
| Leukocyte reduced apheresis RBCs | 86 (51%) | 121,322 (40%) |
| Irradiated leukocyte reduced RBCs | 30 (18%) | 28,435 (9%) |
| Irradiated Leukocyte reduced apheresis RBCs | 14 (8%) | 10,952 (4%) |
| **Any Plasma** | 64 (33%) | 50,440 (14%) |
| Plasma units per encounter, median (min, max, Standard Deviation) | 2 (1,7, SD 1.25) | 1 (1,33, SD 1.25) |
| Irradiated plasma | 2 (3%) | 1,521 (3%) |
| Leukocyte reduced plasma | 1 (2%) | 301 (1%) |
| Apheresis derived plasma | 24(37%) | 16,676 (33%) |
| Whole blood derived plasma | 58 (89%) | 45,056 (89%) |
| Irradiated apheresis plasma | 1 (2%) | 611 (1%) |
| Leukocyte reduced apheresis plasma | 0 | 182 (0%) |
| Irradiated leukocyte reduced plasma | 0 | 16 (0%) |
| Irradiated leukocyte reduced apheresis plasma | 0 | 5 (0%) |
| Cryoprecipitated AHF | 26 (14%) | 6,835 (2%) |

| Blood product/component | **Inpatient** *encounters with evidence of transfusion and ANY TRALI (n=192)* | **Inpatient** *encounters without TRALI and evidence of transfusion (n=**353,557**)* |
|---|---|---|
| Cryoprecipitated AHF units per encounter, median (min, max, Standard Deviation) | 1(1,3, SD 0.71) | 1(1,8, SD 1.46) |
| Number of encounters with transfusions with ALL ISBT or codabar codes that could not be mapped | 1 (1%) | 2736 (1%) |
| Number of encounters with transfusions with ANY (not all) ISBT or codabar codes that could not be mapped | 6 (3%) | 4221 (1%) |

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