Expansion of the US FDA Sentinel System to inpatient blood transfusion data from Hospital Corporation of America: new surveillance options

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Disclosure

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- The views expressed in this paper are those of the authors and are not intended to convey official U.S. Food and Drug Administration (FDA) policy or guidance
Background

- Sentinel System is the US Food and Drug Administration (FDA)’s active safety surveillance system to monitor medical products
- US FDA’s Center for Biologics Evaluation and Research (CBER) responsible for ensuring safety of blood & blood products/components
- Blood Safety Surveillance Continuous Active Network (BloodSCAN)
  - A subcomponent of the Sentinel System sponsored by CBER to monitor recipient safety of FDA-regulated blood components and blood-derived products
Background

- Hospital Corporation of America (HCA) became a full Sentinel data partner in 2016
  - Many blood transfusions occur in inpatient settings
  - Claims data often do not contain important transfusion details
  - Full-text electronic health records
    - Facilitate chart review and health outcomes of interest validation
  - Provides new safety surveillance potential for BloodSCAN
Hospital Corporation of America

~5% of all inpatient care delivered in USA

Objective

- To describe Sentinel’s HCA transfusion data expansion and characterize data elements with potential for conducting surveillance for adverse events after exposure to blood components and blood-derived products.
Methods

- Sentinel and HCA created an inpatient transfusion table and added it to the Sentinel Common Data Model (SCDM)
- As HCA worked to populate the SCDM with quality checked data from more than 165 facilities
  - A test database was provided for blood component characterization
- Using analytic programs we:
  - Described data elements relevant to BloodSCAN.
  - Mapped Codabar and ISBT-128 product codes in the HCA Sentinel database to blood components
Sentinel Common Data Model: HCA

Existing SCDM Tables

- **Demographic**
  - Person ID
  - Birth date
  - Sex
  - ZIP code
  - Etc.

- **Encounter**
  - Person ID
  - Service date(s)
  - Encounter ID
  - Encounter type & provider
  - Facility
  - Etc.

- **Diagnosis**
  - Person ID
  - Service date(s)
  - Encounter ID
  - Encounter type & provider
  - Diagnosis code & type
  - Principal discharge diagnosis
  - Etc.

- **Procedure**
  - Person ID
  - Service date(s)
  - Encounter ID
  - Encounter type & provider
  - Procedure code & type
  - Etc.

- **Vital Signs**
  - Person ID
  - Measurement date and time
  - Height and weight
  - Diastolic & systolic BP
  - Procedure code & type
  - Tobacco use & type

New SCDM Tables

- **Inpatient Pharmacy Dispensing**
  - Person ID
  - Encounter ID
  - NDC
  - Rx Administration date
  - Rx Administration time
  - Actual/administered route
  - Actual/administered dose
  - Etc.

- **Inpatient Transfusion**
  - Person ID
  - Encounter ID
  - Unique transfusion identifier
  - Product code and codetype
  - Blood type
  - Transfusion date/time start
  - Transfusion date/time end
  - Etc.
<table>
<thead>
<tr>
<th>Broad Categorization</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma</strong></td>
<td></td>
</tr>
<tr>
<td>APHPLASMA</td>
<td>Apheresis plasma</td>
</tr>
<tr>
<td>WBDPLASMA</td>
<td>Whole blood derived plasma</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td></td>
</tr>
<tr>
<td>APHPLAT</td>
<td>Apheresis platelets</td>
</tr>
<tr>
<td>IRAPHPLAT</td>
<td>Irradiated apheresis platelets</td>
</tr>
<tr>
<td>IRRAPHPLAT</td>
<td>Irradiated leukocyte reduced apheresis platelets</td>
</tr>
<tr>
<td>IRLRWBDPABLAT</td>
<td>Irradiated leukocyte reduced whole blood derived platelets</td>
</tr>
<tr>
<td>IRWBDBPLAT</td>
<td>Irradiated whole blood derived platelets</td>
</tr>
<tr>
<td>LRSHPBLAT</td>
<td>Leukocyte reduced apheresis platelets</td>
</tr>
<tr>
<td>LRWBDBPLAT</td>
<td>Leukocyte reduced whole blood derived platelets</td>
</tr>
<tr>
<td>WDBPLAT</td>
<td>Whole blood derived platelets</td>
</tr>
<tr>
<td><strong>Red Blood Cells</strong></td>
<td></td>
</tr>
<tr>
<td>APHRBC</td>
<td>Apheresis red blood cells</td>
</tr>
<tr>
<td>IRAPHRBC</td>
<td>Irradiated apheresis red blood cells</td>
</tr>
<tr>
<td>IRLRAHRBC</td>
<td>Irradiated leukocyte reduced apheresis red blood cells</td>
</tr>
<tr>
<td>IRLRWBDBRBC</td>
<td>Irradiated leukocyte reduced whole blood derived RBC</td>
</tr>
<tr>
<td>IRWBDBRBC</td>
<td>Irradiated whole blood derived red blood cells</td>
</tr>
<tr>
<td>LRAPHRBC</td>
<td>Leukocyte reduced apheresis red blood cells</td>
</tr>
<tr>
<td>LRWBDBRBC</td>
<td>Leukocyte reduced whole blood derived red blood cells</td>
</tr>
<tr>
<td>WBDBRBC</td>
<td>Whole blood derived red blood cells</td>
</tr>
<tr>
<td><strong>Whole Blood</strong></td>
<td>WB - Whole blood</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>CRYO</td>
<td>Cryoprecipitate</td>
</tr>
<tr>
<td>GRAN</td>
<td>Granulocytes</td>
</tr>
<tr>
<td>LEUK</td>
<td>Leukocytes</td>
</tr>
<tr>
<td>LYMPH</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>MNC</td>
<td>Mononuclear cells</td>
</tr>
<tr>
<td>SERUM</td>
<td>Serum</td>
</tr>
</tbody>
</table>
Results

- HCA’s inpatient transfusion table captures administered transfusions including start and end times, product blood type, Rh factor
  - Number of units can also be derived

- ISBT-128 or Codabar codes assigned to each unit allow for identification of blood component and blood processing (eg, leukocyte reduction) methods
Results: HCA’s Sentinel database: Inpatient transfusions

- Provides information often not available in claims data
- Actual administered start/end transfusion dates AND times
- Blood type [A, B, O, AB, RH factor (+, -)]
- Information about transfused unit (can be used to identify blood component)
- # units, potentially large volume transfusion
Results: HCA’s Sentinel database:
Inpatient transfusions

- Captures transfused units, each labeled with code
- Two transfusion coding systems in use
  - >4,500 ISBT-128 codes
  - >1,500 Codabar codes
- Granular codes = new potential
  - Identification of blood components
  - Potential for identification of processing method (e.g., leukocyte-reduced, irradiated)
Results: HCA’s Sentinel database: Inpatient transfusions

- Although both Codabar and ISBT-128 systems are still in use at HCA, there has been an increased uptake in use of ISBT codes and a decrease in use of Codabar codes over time
  - By mid-2015 less than 1% of HCA transfusions were coded with a Codabar code
ISBT-128 product code, 5 digits in Sentinel Common Data Model

Source: ISBT-128 website, https://www.iccbba.org/
# Results: Sample Transfusion Codes at HCA

## CODABAR

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>18831</td>
<td>PLASMA IRRADIATED (from 250ml Whole Blood)(Storage -18 C or colder)</td>
</tr>
<tr>
<td>18901</td>
<td>LIQUID PLASMA IRRADIATED</td>
</tr>
<tr>
<td>31458</td>
<td>CPD WHOLE BLOOD LEUKOCYTES REDUCED^1 DIVIDED (Part H or 8)</td>
</tr>
<tr>
<td>31461</td>
<td>CPDA-1 WHOLE BLOOD LEUKOCYTES REDUCED^1 DIVIDED (Part A or 1)</td>
</tr>
<tr>
<td>35772</td>
<td>AS-3 Red Blood Cells leukocytes reduced^1 DIVIDED IRRADIATED (ACDA anticoagulant)(by pheresis)</td>
</tr>
<tr>
<td>35773</td>
<td>AS-3 Red Blood Cells leukocytes reduced^1 DIVIDED IRRADIATED (ACDA anticoagulant)(by pheresis)</td>
</tr>
</tbody>
</table>

## ISBT

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E0135</td>
<td>WHOLE BLOOD</td>
</tr>
<tr>
<td>E0154</td>
<td>RED BLOOD CELLS</td>
</tr>
<tr>
<td>E1146</td>
<td>Apheresis FRESH FROZEN PLASMA</td>
</tr>
<tr>
<td>E1149</td>
<td>Thawed Apheresis FRESH FROZEN PLASMA</td>
</tr>
<tr>
<td>E5326</td>
<td>Apheresis PLATELETS</td>
</tr>
<tr>
<td>E5329</td>
<td>PLASMA</td>
</tr>
<tr>
<td>Broad Categorization</td>
<td>Description</td>
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<tr>
<td>----------------------</td>
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</table>
| **Plasma**           | APHPLASMA - Apheresis plasma  
                        | WBDPLASMA - Whole blood derived plasma |
| **Platelets**        | APHPLAT - Apheresis platelets  
                        | IRAPPHPLAT - Irradiated apheresis platelets  
                        | IRRAPPHPLAT - Irradiated leukocyte reduced apheresis platelets  
                        | IRLRWBDBPLAT - Irradiated leukocyte reduced whole blood derived platelets  
                        | IRWBDPLAT - Irradiated whole blood derived platelets  
                        | LRSHPPLAT - 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  
                        | IRLRAPHRC - Irradiated leukocyte reduced apheresis red blood cells  
                        | IRLRWBDBRBC - 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  
                        | WBDRB - 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 |
# Results: Sample Transfusion Codes: With Prod_CDC

<table>
<thead>
<tr>
<th>CODABAR</th>
<th>Description</th>
<th>Prod_CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Code 18831</td>
<td>PLASMA IRRADIATED (from 250ml Whole Blood)(Storage - 18 C or colder)</td>
<td>Prod_CDC WBDPLASMA - Whole blood derived plasma</td>
</tr>
<tr>
<td>Code 35772</td>
<td>AS-3 Red Blood Cells leukocyteS reduced^1 DIVIDED IRRADIATED (ACDA anticoagulant)(by pheresis)(P...</td>
<td>Prod_CDC IRLRAPHRBC - Irradiated leukocyte reduced apheresis red blood cells</td>
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<tr>
<td>Code 35773</td>
<td>AS-3 Red Blood Cells leukocyteS reduced^1 DIVIDED IRRADIATED (ACDA anticoagulant)(by pheresis)(P...</td>
<td>Prod_CDC IRLRAPHRBC - Irradiated leukocyte reduced apheresis red blood cells</td>
</tr>
</tbody>
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</tr>
</thead>
<tbody>
<tr>
<td>Code E0135</td>
<td>WHOLE BLOOD</td>
<td>Heparin/450mL/refg</td>
</tr>
<tr>
<td>Code E1149</td>
<td>Thawed Apheresis FRESH FROZEN PLASMA</td>
<td>ACD-B/XX/refg</td>
</tr>
</tbody>
</table>
Results: Proportion of units attributed to each blood component (*March 2013-January 2015)*

<table>
<thead>
<tr>
<th>Blood product/component, units administered</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Blood Cells</td>
<td>62.8%</td>
</tr>
<tr>
<td>Plasma</td>
<td>13.4%</td>
</tr>
<tr>
<td>Platelets</td>
<td>9.2%</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other or unknown**</td>
<td>14.7%</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td></td>
</tr>
</tbody>
</table>

Learned:

• National Blood Collection and Utilization Survey 2011 Report: RBC, 63%, Plasma, 18%, Platelets, 15% Other or unknown***
• Underestimating plasma/platelets

*Analysis conducted on HCA Sentinel test database

**Other includes codes which could not be identified, along with other valid codes

Results

- HCA’s Sentinel database included consistently populated transfusion data starting in late 2013
Results: # Encounters in HCA Sentinel database with a recorded transfusion (June 2011-May 2015, HCA Sentinel database 1)

HCA began bringing transfusion data into Sentinel database in 2013

N= 373,743 encounters with transfusions October 2013-May 2015
Results: Variables for outcomes of interest

- Diagnosis and procedure codes could be used to define adverse events.

- Present-on-admission and principal discharge diagnosis flags
  - Provide further refinement potential

- Also available:
  - Admission and discharge dates
  - Discharge disposition (eg, expired)
  - Admitting source (eg, hospital transfer)
Results: What do we know about diagnoses?

ICD-9

ICD-10

Admission date

Principale

Discharge date

Present-on-admission

Secondary
Results: What do we know about procedures?

- 642 million observed procedures codes
  - 21 million ICD-9 procedure codes (typically describe surgical procedures)
  - Over 3 million drug administrations (injections)
Results: CBER test cases underway

- Evaluation of development of Transfusion–Related Acute Lung Injury (TRALI) after exposure to blood and blood products
  - Publically posted protocol, assessment underway, includes chart validation component
Limitations

- Current SCDM includes admission and discharge dates, no procedure or diagnosis dates or times
  - Transfusion administration dates and time are available, but temporality of exposures/outcomes may be difficult to capture
  - Data model expansion currently being evaluated
- Unit of analysis is a hospitalization
  - Limitations for tracking patients within HCA Sentinel data
- More evaluation of blood coding systems needed, including validation of blood product/component
Conclusions

- HCA’s inpatient transfusion data hold potential for BloodSCAN expansion, but need validation
  - Potential for identification of blood processing method
  - Dates/times of blood transfusions available
  - # units available
  - Full-text electronic health records, facilitate chart review/validation

- Identified red blood cell proportions were similar to those reported in national surveys, but those of plasma and platelets maybe under-identified
  - Examination of local hospital coding and additional blood component mapping systems needed
  - Test cases underway, 1 includes chart validation of transfusion exposure
Acknowledgements

- The authors also thank Adee Kennedy at SOC, as well as other contributors in CBER’s OBE for their assistance