



# UTILIZATION OF BLOOD COMPONENTS WITHIN THE BEST INITIATIVE EHR NETWORK, 2012–2018

## OBJECTIVE

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To identify and quantify transfused individuals, transfusion episodes, transfused units and processing methods on an annual basis during 2012-2018 within the BEST Initiative EHR network.

## BACKGROUND

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CBER is responsible for regulating how blood donations are processed; CBER also reviews and accepts the Circular of Information (labeling) regarding the use of blood for transfusion. Blood, in contrast to other drugs, is of human origin and there is no single manufacturer that can be held responsible for safety, effectiveness, and quality of the products. Instead, the production of blood components is carried out in a decentralized system of blood banks, some of which belong to the healthcare institutions where they are administered to patients with the medical need, and some of which are independent organizations focusing on collection, processing, or distribution. This system presents a challenge to systematic monitoring since data about blood component production and exposure are needed in the context of other patient data representing prior clinical constellation such as indication and comorbidities, and the outcome consequences.

To address these challenges, a network of databases in OMOP CDM was established for the BEST Initiative, allowing identification of patients with exposure to blood components. These databases are derived from these EHR databases:

- Columbia University Medical Center
- Regenstrief Institute
- Colorado UC Health System

This study is focused on using a labeling and identification system called Information Standard for Blood and Transplant (ISBT) 128. ISBT 128 codes are designed to make medical products of human origin collected at one facility easily managed and read by a different facility. Currently, in the U.S., the governing rules regarding labeling of blood and blood component products are in the Code of Federal Regulations. The FDA does not require ISBT 128 for blood and blood component product labeling in the U.S.; however, the FDA does require that certain information, typically included on ISBT 128 labels, such as the product code and the unique facility identifier, be included on blood and blood component labels. While the FDA does not require ISBT 128, the American Association of Blood Banks (AABB), a leader in the development of standards in blood and blood component collection, processing, and transfusion, does require that blood and blood components be labeled using ISBT 128 at AABB-accredited facilities in and outside of the U.S.<sup>1</sup> ISBT 128 codes summarize all information about the component's Class (e.g. red blood cells), Modifiers (e.g. thawed), and Attributes including Core Conditions (e.g. anticoagulant).<sup>2</sup>

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<sup>1</sup> "United States Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128." Version 3.0.0 (2013). <<https://www.iccbba.org/uploads/4a/e3/4ae3b3fd95bae57d4ee0f58ab6c5874f/IG-002-US-Consensus-Standard-Blood-v3.0.0.pdf>>.

<sup>2</sup> "Standard Terminology for Medical Products of Human Origin For Use with Product Description Code Database." Version 7.17 (2018). <<https://www.iccbba.org/uploads/b5/ad/b5ad322bf583e86dd877277c07cde231/Standard-Terminology-for-Medical-Products-of->

ISBT 128 records from blood banks have the potential to significantly improve the ability to define exposures and blood products for several reasons:

1. ISBT 128 allows studying blood components at greater detail than the rather generic procedure codes.
2. The procedure codes are subject to billing rules, which generally tend to suppress detailed activities that are part of larger procedures. For example, blood transfusions administered to patients receiving trauma care or large surgeries are generally not listed, even when such transfusions happened.<sup>3</sup>

## SPECIFICATIONS

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### Cohort Criterion

*All patients with at least one day of enrollment or at least one health encounter in each calendar year within the study period.*

### Data Sources

- Columbia University Medical Center
- Regenstrief Institute
- Colorado UC Health System

### Definitions

**Number of Transfused Patients:** Number of unique patients with at least one ISBT 128 code specific to the blood component of interest in a given year. The patient will be counted only once for a specific blood component. If transfusion of a specific blood component is given on day #1 (1 unit), day #45 (4 units) and day #46 (10 units), this counts as 1 patient with transfusion of specific blood component.

**Number of Patients with 1, 2-5, 6-11, or >12 Transfusion episodes:** Number of unique patients binned by number of transfusion episodes in a given year. Transfusion episode is defined as an occurrence of at least one ISBT 128 code specific to the blood component of interest per day, in a given year. If transfusion of a specific blood component is given on day #1 (1 unit), day #45 (4 units) and day #46 (10 units), this counts as 3 RBC transfusion episodes. For the patient level diagram, this patient will be categorized in the 2-5 transfusion episode bin. The patient will be counted only once for a specific blood component.

**Number of Transfusion Episodes<sup>4</sup> having 1, 2-4, or >5 Transfused units/ Transfusion Episode:** Number of ISBT 128 code counts of the blood component of interest per transfusion episode bin in a given year. The patient will be

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Human-Origin-v7.17.pdf>.

<sup>3</sup> U.S. Centers for Medicare & Medicaid Services. National Correct Coding Initiative Edits - PTP Coding Edits. (2018). <<https://www.cms.gov/Medicare/Coding/NationalCorrectCodingInitiative/NCCI-Coding-Edits.html>>.

<sup>4</sup> A transfusion episode is defined as a transfusion of one or more specific blood component(s) on a single day, from 12AM to 11:59PM. All sites are asked to use the end date of the transfusion of the last unit of the specific blood component transfused in the day as the date of the transfusion episode. If the transfusion occurs across more than one day (e.g. 22:00h on Feb 12 to 00:30 on Feb 13, this should be counted as one transfusion episode ending on Feb 13 (and only being counted on Feb 13). If the transfusion includes two units, the first of them ending on Feb 12 at 21:50 and the second unit (from the previous example) ending at 00:30 on Feb 13, these would be counted as two transfusion episodes one on Feb 12 and one on Feb 13. If the transfusion end date is not available, sites will use the start date of the transfusion to mark a transfusion episode.

counted once for **EACH** episode for a specific blood component. If transfusion of a specific blood component is given on day #1 (1 unit), day #45 (4 units) and day #46 (10 units), this counts as 3 episodes: one in the 1 unit episode bin, one in the 2-4 units episode bin, and one in the >5 units episode bin (under the same 2-5 transfusion patient-episode bin).

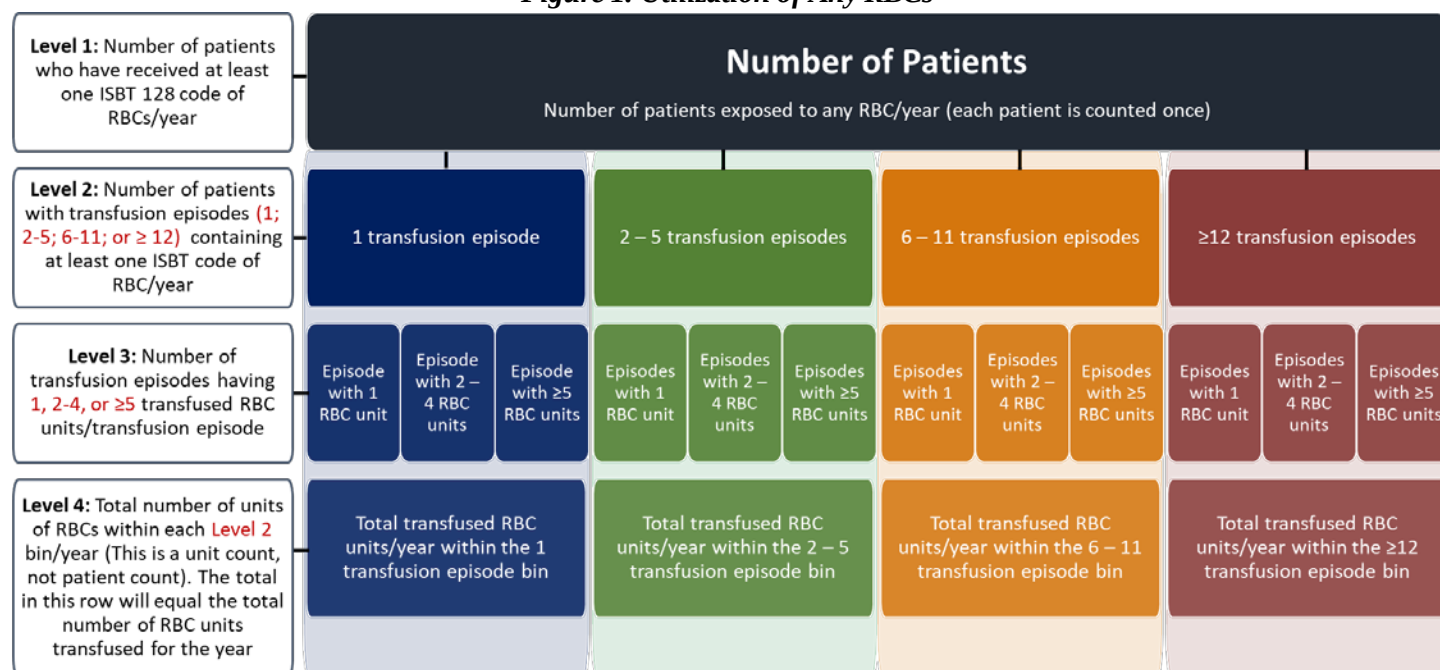
**Total Transfused units in each transfusion episode bin:** Number of ISBT 128 code counts of the blood component of interest within the transfusion episode bin in a given year. If transfusion of a specific blood component is given on day #1 (1 unit), day #45 (4 units) and day #46 (10 units), this counts as 15 transfused units of specific blood component within the 2-5 transfusion episode bin. This measurement is at the transfused unit level, it does NOT count patients.

## Exposure Ascertainment

Each transfused blood component unit was ascertained by the presence of a unique ISBT 128 code. Every transfused patient was first categorized according to the number of transfusion episodes per year (1, 2-5, 6-11, or  $\geq 12$  transfusion episodes) containing at least one blood component unit. Each transfusion episode was then categorized according to the number of units transfused (1, 2-4, or  $\geq 5$  units) during the episode. The total number of transfused units per year was determined within each transfusion episode by counting the number of units transfused. In addition, using the naming attributes from the ISBT 128 codes, the number of transfused units received by a patient in a given year was subcategorized according to the modification method (e.g., leukocyte reduction, irradiation). See figures and tables below for further specifications for each type of blood component.

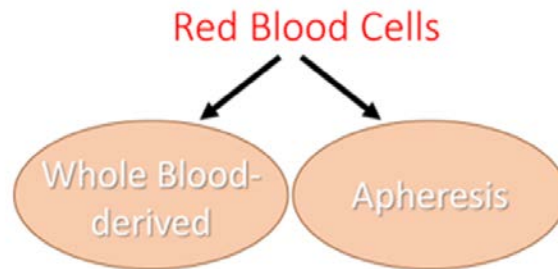
## Red Blood Cells (RBCs)

**Figure 1. Utilization of Any RBCs**





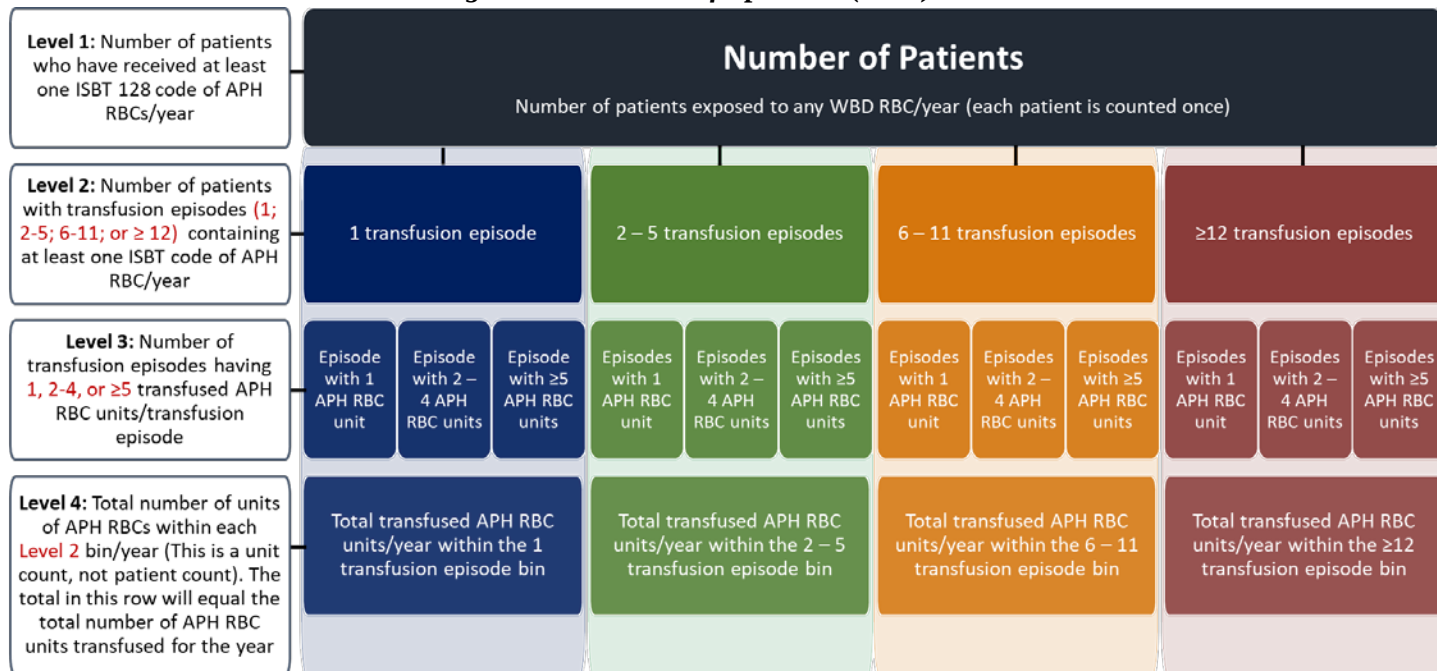
**Figure 2. Collection Method: Whole Blood Derived (WBD) and Apheresis (APH) RBCs**



**Figure 3. Utilization of Whole Blood Derived (WBD) RBCs**

|                                                                                                                                                                                                                      |                                                                                                            |                                  |                               |                                                                              |                                   |                                |                                                                               |                                   |                                |                                                                            |                                   |                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|----------------------------------|-------------------------------|------------------------------------------------------------------------------|-----------------------------------|--------------------------------|-------------------------------------------------------------------------------|-----------------------------------|--------------------------------|----------------------------------------------------------------------------|-----------------------------------|--------------------------------|
| <b>Level 1:</b> Number of patients who have received at least one ISBT 128 code of WBD RBCs/year                                                                                                                     | <b>Number of Patients</b><br>Number of patients exposed to any WBD RBC/year (each patient is counted once) |                                  |                               |                                                                              |                                   |                                |                                                                               |                                   |                                |                                                                            |                                   |                                |
| <b>Level 2:</b> Number of patients with transfusion episodes (1; 2-5; 6-11; or ≥ 12) containing at least one ISBT code of WBD RBC/year                                                                               | 1 transfusion episode                                                                                      |                                  |                               | 2 – 5 transfusion episodes                                                   |                                   |                                | 6 – 11 transfusion episodes                                                   |                                   |                                | ≥12 transfusion episodes                                                   |                                   |                                |
| <b>Level 3:</b> Number of transfusion episodes having 1, 2-4, or ≥5 transfused WBD RBC units/transfusion episode                                                                                                     | Episode with 1 WBD RBC unit                                                                                | Episode with 2 – 4 WBD RBC units | Episode with ≥5 WBD RBC units | Episodes with 1 WBD RBC unit                                                 | Episodes with 2 – 4 WBD RBC units | Episodes with ≥5 WBD RBC units | Episodes with 1 WBD RBC unit                                                  | Episodes with 2 – 4 WBD RBC units | Episodes with ≥5 WBD RBC units | Episodes with 1 WBD RBC unit                                               | Episodes with 2 – 4 WBD RBC units | Episodes with ≥5 WBD RBC units |
| <b>Level 4:</b> Total number of units of WBD RBCs within each Level 2 bin/year (This is a unit count, not patient count). The total in this row will equal the total number of WBD RBC units transfused for the year | Total transfused WBD RBC units/year within the 1 transfusion episode bin                                   |                                  |                               | Total transfused WBD RBC units/year within the 2 – 5 transfusion episode bin |                                   |                                | Total transfused WBD RBC units/year within the 6 – 11 transfusion episode bin |                                   |                                | Total transfused WBD RBC units/year within the ≥12 transfusion episode bin |                                   |                                |

**Figure 4. Utilization of Apheresis (APH) RBCs**



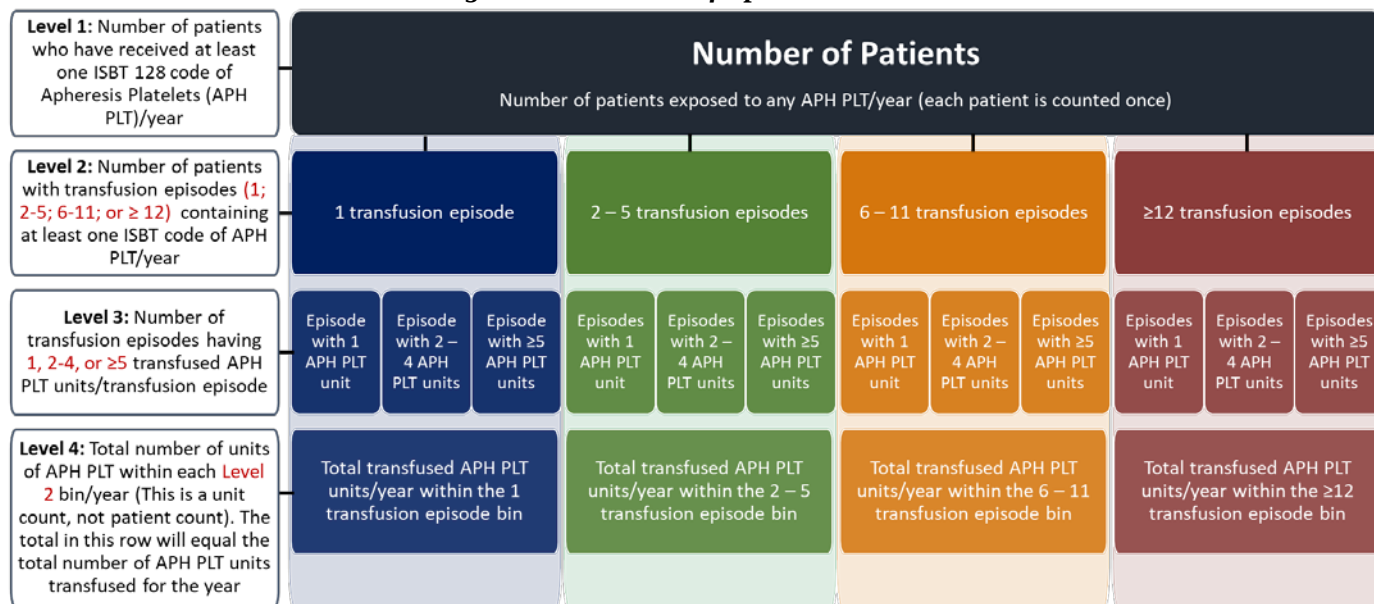
**Table 1. Modification Method RBCs**

| RBC Modification |                   | Number of unique patients with at least one ISBT code with the specified RBC modification (irrespective of all other products received) per year* | Number of transfused units/year with the specified modification (not patient level counts) |
|------------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Irradiation      | Leukocyte-reduced |                                                                                                                                                   |                                                                                            |
| No               | No                | That is <b>NOT</b> irradiated and <b>NOT</b> leukocyte-reduced (nIR/nLR)                                                                          | Total # of nIR/nLR RBC units                                                               |
| Yes              | No                | That is irradiated and <b>NOT</b> leukocyte-reduced (IR/nLR)                                                                                      | Total # of IR/nLR RBC units                                                                |
| No               | Yes               | That is <b>NOT</b> irradiated and is leukocyte-reduced (nIR/LR)                                                                                   | Total # of nIR/LR RBC units                                                                |
| Yes              | Yes               | That is irradiated and leukocyte-reduced (IR/LR)                                                                                                  | Total # of IR/LR RBC units                                                                 |

\*IR=Irradiated, LR=Leukocyte-reduced, nIR=Not Irradiated, nLR=Not Leukocyte-reduced

## Apheresis Platelets

**Figure 5. Utilization of Apheresis Platelets**



**Table 2. Modification Methods of Apheresis Platelets**

| Apheresis Platelets Modification |                   | Number of unique patients with at least one ISBT code with the specified apheresis platelet modification (irrespective of all other products received) per year* | Number of transfused units/year with the specified modification (not patient level counts) |
|----------------------------------|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Irradiation                      | Leukocyte-reduced |                                                                                                                                                                  |                                                                                            |
| No                               | No                | That is <b>NOT</b> irradiated and <b>NOT</b> leukocyte-reduced (nIR/nLR)                                                                                         | Total # of nIR/nLR RBC units                                                               |
| Yes                              | No                | That is irradiated and <b>NOT</b> leukocyte-reduced (IR/nLR)                                                                                                     | Total # of IR/nLR RBC units                                                                |
| No                               | Yes               | That is <b>NOT</b> irradiated and is leukocyte-reduced (nIR/LR)                                                                                                  | Total # of nIR/LR RBC units                                                                |
| Yes                              | Yes               | That is irradiated and leukocyte-reduced (IR/LR)                                                                                                                 | Total # of IR/LR RBC units                                                                 |
|                                  |                   | That is pathogen-reduced (PR & nPR)                                                                                                                              | Total # of PR & nPR units                                                                  |

\*IR=Irradiated, LR=Leukocyte-reduced, nIR=Not Irradiated, nLR=Not Leukocyte-reduced, PR=Pathogen-reduced, nPR=Not Pathogen-reduced



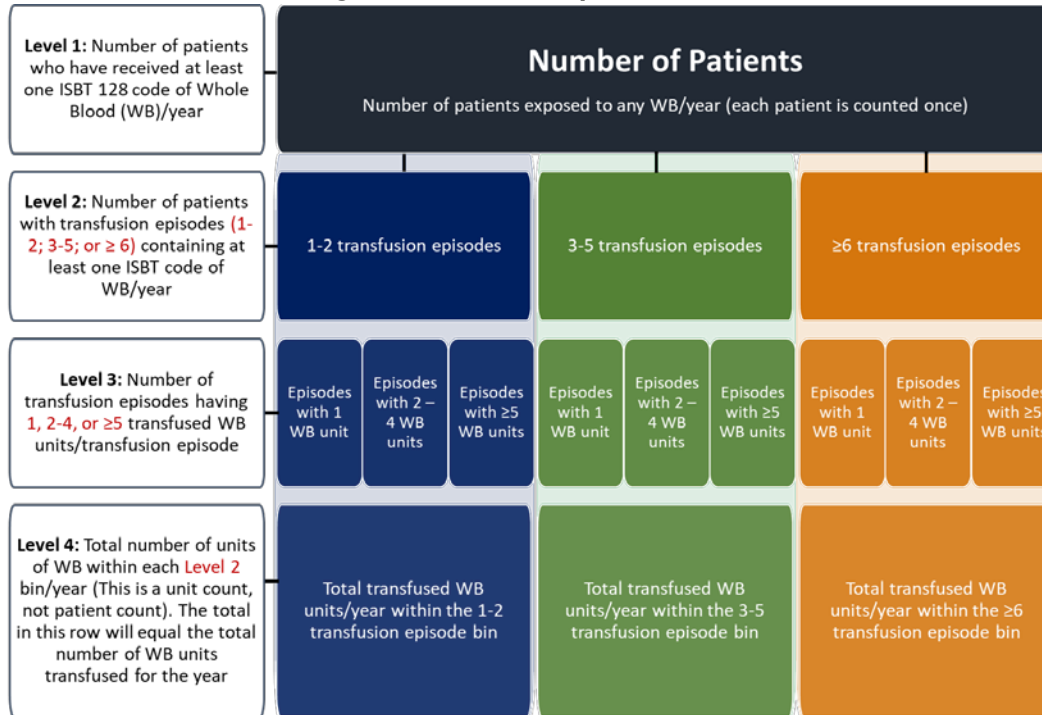
***Table 3. Additional Modification Method Combinations of Apheresis Platelets***

| Additional Modification Method Combinations       |                                                                                                                                                                                                                                                    |
|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Both, Leukocyte-reduced and Not Leukocyte-reduced | Unique patients who have received any leukocyte-reduced and not leukocyte-reduced platelets in a given year. These patients will be counted in the leukocyte-reduced and the not leukocyte-reduced bin. All three bins are not mutually exclusive. |
| Both, Irradiated and Not Irradiated               | Unique patients who have received any irradiated and not irradiated platelets in a given year. These patients will be counted in the irradiated and the not irradiated bin. All three bins are not mutually exclusive.                             |



## Whole Blood

**Figure 7. Utilization of Whole Blood**

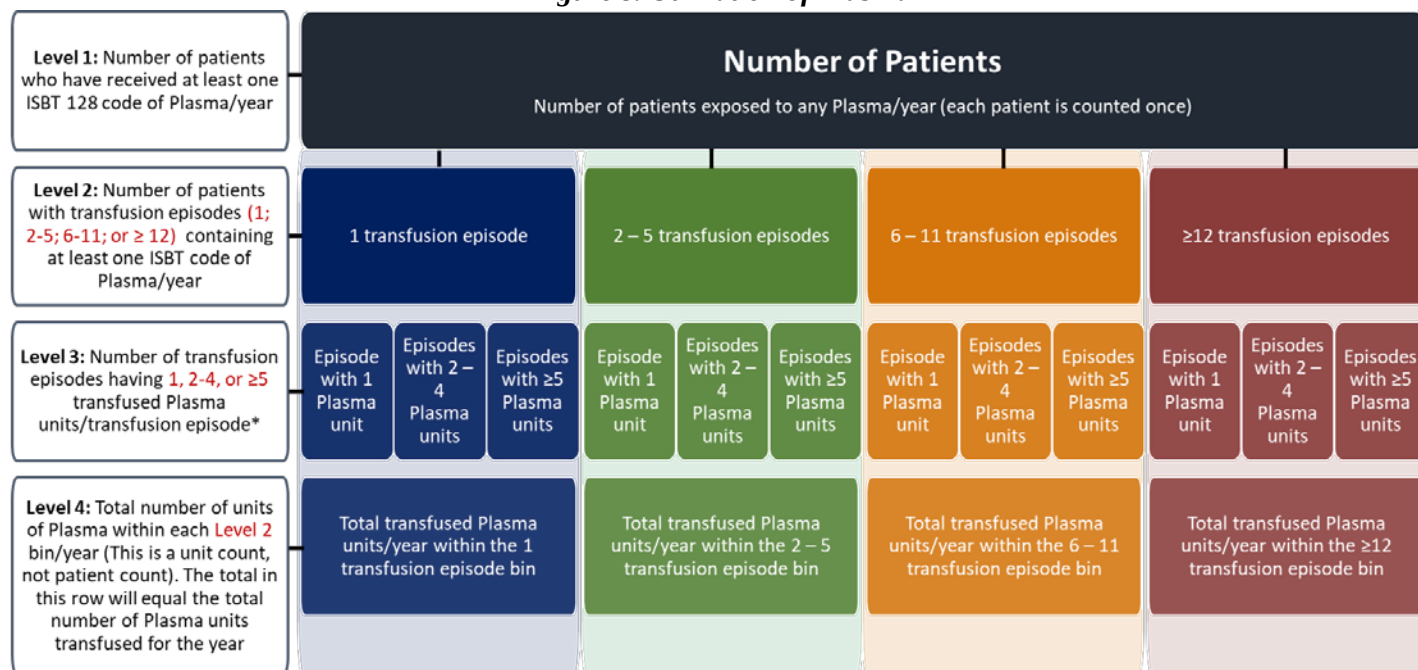


**Table 4. Modification Methods of Whole Blood**

| Number of unique patients with at least one ISBT code with the specified whole blood (WB) modification (irrespective of all other products received) | Number of transfused units/year with the specified whole blood (WB) modification (Not patient level count) |
|------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| That is Leukocyte-reduced                                                                                                                            | Total # of Leukocyte-reduced units                                                                         |
| That is <b>NOT</b> Leukocyte-reduced                                                                                                                 | Total # of <b>NOT</b> Leukocyte-reduced units                                                              |

## Plasma

**Figure 8. Utilization of Plasma**



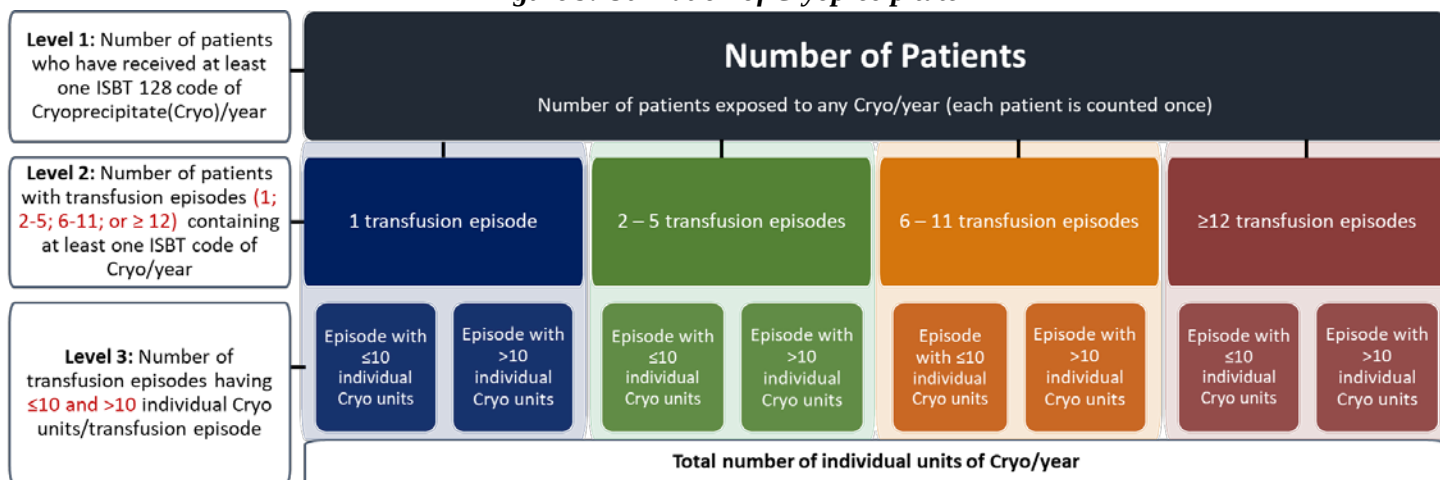
\*Note: In reference to collection method, level 3, transfusion episode number of units' stratification layer was modified to reflect 1 unit, 2-4 units, and 5 units, respectively. It was necessary to modify the query because following inspection of our data, the sites pooled plasma = 3-4 units, and all sites used either 1 unit or 2-4 units of plasma for most of their transfusions.

**Table 5. Modification Methods of Plasma**

| Number of unique patients with at least one ISBT code with the specified plasma modification (irrespective of all other products received) | Number of transfused units/year with the specified modification (Not patient level count) |
|--------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| That is Liquid Plasma                                                                                                                      | Total # Units of Liquid Plasma                                                            |
| That is Thawed Plasma                                                                                                                      | Total # Units of Thawed Plasma                                                            |
| That is Fresh Frozen Plasma, Thawed                                                                                                        | Total # Units of Fresh Frozen Plasma, Thawed                                              |
| That is Plasma Frozen within 24 Hrs, Thawed                                                                                                | Total # Units of Plasma Frozen within 24 Hrs, Thawed                                      |
| That is Plasma Frozen within 24 Hrs after Phlebotomy held at Room Temperature for 24 Hrs (PF <sup>24</sup> RT <sup>24</sup> )              | Total # Units of Plasma at Room Temperature                                               |

## Cryoprecipitate

**Figure 9. Utilization of Cryoprecipitate**



**Table 6. Counting of Cryoprecipitate Based on Data Source**

| Regenstrief                                                    | Regenstrief Individual Cryo Units* | Columbia                                           | Columbia Individual Cryo Units* | Colorado                                                               | Colorado Individual Cryo Units* |
|----------------------------------------------------------------|------------------------------------|----------------------------------------------------|---------------------------------|------------------------------------------------------------------------|---------------------------------|
| <b>E3591</b> , a pool of 5 cryo                                | 5                                  | <b>E5165</b> , Infants get 1 bag of cryo           | 1                               | <b>E3571, E5165</b> (Frozen Cryo)<br><b>E3581, E5256</b> (Thawed Cryo) | 1                               |
| <b>E5256</b> , a single cryo                                   | 1                                  | <b>E3587</b> , Adults get 1-2 pre-pooled bags of 5 | 5                               | <b>E3587</b> (Frozen Cryo)<br><b>E3591, E3592, E5284</b> (Thawed Cryo) | 5                               |
| <b>E3592</b> , a pooled product that could contain 3-10 donors | 6.5                                |                                                    |                                 |                                                                        |                                 |

\*Presence of each code will be multiplied by a factor of the corresponding number in this column. **Example:** Patient A receives 2 bags of cryoprecipitate. The bags of cryoprecipitate are coded as E3591. In this case, the presence of 2 E3591 codes should be counted as patient A receiving 10 individual cryoprecipitate units.