

# Outpatient Transfusions and Occurrence of Transfusion-Associated Circulatory Overload (TACO) Among U.S. Medicare Beneficiaries Ages 65 and Older, During 2011-2018



Mikhail Menis<sup>1</sup>, Barbee I. Whitaker<sup>1</sup>, Yixin Jiao<sup>2</sup>, An-Chi Lo<sup>2</sup>, Michael Wernecke<sup>2</sup>, Thomas E. MaCurdy<sup>2,3</sup>, Jeffrey A. Kelman<sup>4</sup>, Steven A. Anderson<sup>1</sup>, Richard A. Forshee<sup>1</sup>  
(1. FDA, CBER; 2. Acumen LLC; 3. Stanford University; 4. CMS)

## Abstract

**Background:** Transfusion-associated circulatory overload (TACO) is a leading cause of transfusion-related fatalities.

**Purpose:** The study aimed to assess TACO occurrence and potential risk factors among the U.S. Medicare population aged 65 and older transfused in the institutional outpatient setting.

**Methodology:** This retrospective claims-based study utilized Medicare databases for 2011-2018. Transfusions were identified by procedure and revenue center codes, and TACO via diagnosis code(s) recorded same or next day following outpatient transfusion visit. The study evaluated unadjusted TACO rates per 100,000 transfusion visits: overall and by year, immunocompromised (IC) status, demographics, 6-month history of health conditions, blood components, and number of units transfused.

**Results:** Of 3,810,038 outpatient transfusion visits, 652 had a TACO diagnosis recorded (17.1 per 100,000), with 70.5% of visits and 62.0% of cases for IC beneficiaries. The annual TACO rates ranged from 10.7 in 2011 to 26.5 in 2018 and varied by number of units from 16.2 for 1 unit to 24.7 for ≥5 units. Females and males had rates of 19.9 vs. 14.5. Higher rates were identified for ages 80-84 and >84: 19.7 and 20.5. TACO rates by blood components were 8.5 for platelets only, 9.0 for plasma only, 18.3 for RBCs only, and 22.5 for multi-component transfusions comprised mostly of RBCs and platelets. TACO rates were 15.0 for IC vs. 22.1 for non-IC beneficiaries. TACO rates were highest for beneficiaries with obesity (26.7), congestive heart failure (26.3), and complicated hypertension (25.5).

**Conclusion:** Our 8-year population-based study shows higher TACO rates in recent years, potentially due to increased provider awareness. The study suggests the importance of blood components, number of units transfused, demographic characteristics and underlying comorbidities. Although most outpatient transfusion visits and cases were IC, the study identified higher TACO risk among non-IC. This study highlights utility of real-world evidence and suggests the need for further investigations.

## Introduction

- **Transfusion-Associated Circulatory Overload (TACO) is a serious acute transfusion complication resulting in respiratory distress;**
- **TACO usually occurs within 6 hours of blood transfusion and presents as acute hypoxemia with dyspnea, orthopnea, increased blood pressure, and cardiogenic pulmonary edema;**
- **TACO is one of the leading reported causes of transfusion-related fatalities in the United States;**
- **Older and immunocompromised (IC) may be at an increased risk for TACO due to higher blood use and underlying health conditions affecting cardiac, pulmonary, and renal function.**

## Materials and Methods

- **This is a retrospective cohort claims-based study using Medicare 100% Outpatient Common Working Files for January 2011 through December 2018:**
  - Procedure codes and revenue center codes were used to identify transfusion of blood components, and revenue center units were used to quantify blood transfused;
  - Outpatient transfusion visits were used as the unit of analysis and each visit comprised transfusions on the same date;
  - TACO was ascertained via diagnosis code(s) recorded on the same or next day of outpatient transfusion visit;
  - Outpatient transfusion visits were grouped into mutually exclusive blood component categories: RBCs only, Platelets only, Plasma only, and Multi-Component transfusions.
- **We assessed unadjusted TACO rates per 100,000 outpatient transfusion visits: overall, by calendar year, IC status, demographics, 6-month history of health conditions (using Elixhauser Comorbidities), blood components, and number of units transfused; and**
- **Compared IC vs. non-IC visits and IC vs. non-IC cases (i.e., visits with TACO) by demographics (e.g., age, gender), health conditions, hospitalization, ICU/CCU admission, Length of Stay (LOS), and inpatient mortality.**

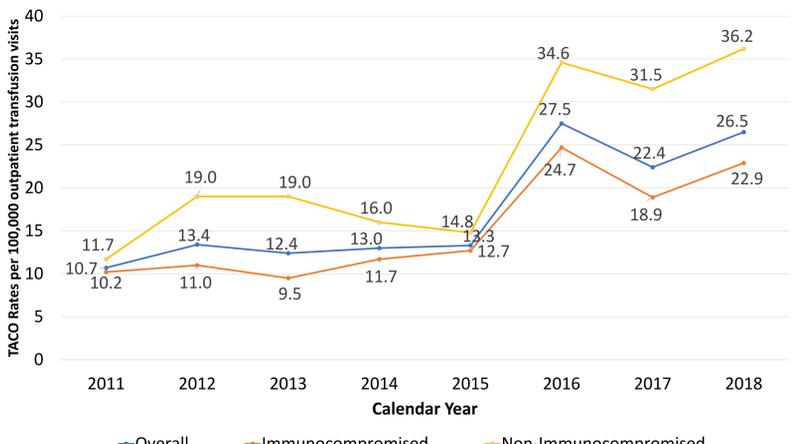


Figure 1. Unadjusted Annual TACO Rates, Overall and by IC Status, 2011-2018

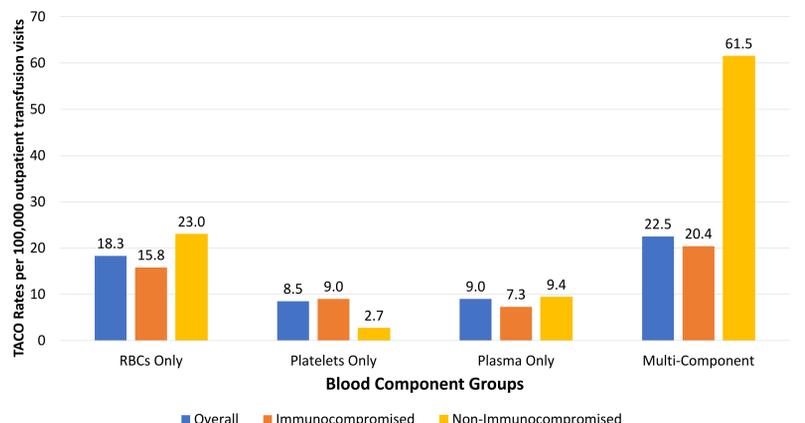


Figure 2. Unadjusted TACO Rates by Blood Components, Overall and by IC status

## Results

- **Of 3,810,038 outpatient transfusion visits during the 2011-2018 study period, 652 had a TACO diagnosis recorded:**
  - **Overall TACO rate of 17.1 per 100,000 (95% CI: 15.8-18.5):**
    - Among 1,124,387 Non-IC visits (29.5% of all visits), 248 had TACO: a rate of 22.1 (19.5-25.0);
    - Among 2,685,651 IC visits (70.5% of all visits), 404 had TACO: a rate of 15.0 (13.6-16.6);
  - **TACO rates for females vs. males: 19.9 (18.0-22.0) vs. 14.5 (12.9-16.3);**
  - **Rates for non-whites vs. whites: 19.9 (16.2-24.4) vs. 16.7 (15.4-18.2);**
  - **TACO rates were highest for beneficiaries with obesity (26.7 [22.1-32.4]), congestive heart failure (26.3 [23.5-29.3]), complicated hypertension (25.5 [22.7-28.7]), and some other health conditions (Table 1);**
- **Differences in recipient characteristics were identified when comparing IC vs. non-IC transfusion visits, and IC vs non-IC cases:**
  - **In comparison with IC visits, non-IC transfusion visits were more likely for:**
    - Females (58.7% vs. 44.4%);
    - Ages ≥80 (50.3% vs. 34.3%);
  - **In comparison with IC cases, non-IC TACO cases were more likely to be:**
    - Hospitalized (45.2% vs. 29.5%);
    - Admitted to ICU/CCU (58.0% of hospitalized non-IC cases vs. 51.3% of hospitalized IC cases); and have LOS ≥7 days (26.8% vs. 14.3%) and higher inpatient mortality (4.5% vs. 3.4%), among hospitalized cases.

Table 1. Unadjusted TACO Rates by 6-Month Histories of Health Conditions

Health Conditions	Unadjusted TACO Rate (95% CI)
Obesity	26.7 (22.1-32.4)
Congestive Heart Failure	26.3 (23.5-29.3)
Hypertension (complicated)	25.5 (22.7-28.7)
Paralysis	24.5 (14.5-41.4)
Pulmonary Circulation Disorder	24.0 (19.7-29.2)
Fluid and Electrolyte Disorder	23.9 (21.7-26.5)
Peripheral Vascular Disorder	23.1 (20.3-26.3)
Blood Loss Anemia	22.9 (19.2-27.2)
Depression	22.6 (19.3-26.4)
Valvular Disease	22.5 (19.8-25.6)

Note: this table displays the ten health conditions with highest TACO rates.

## Strengths and Limitations

- Strengths:**
- **This is a real-world population-based evaluation of TACO based on the large cohort of U.S. elderly Medicare beneficiaries, and thus able to detect rare adverse events;**
- Limitations:**
- **The evaluation was based on the administrative databases and consequently:**
    - TACO occurrence may be under- or misrecorded;
    - Potential under- or misrecording of transfusion procedures and number of units;
    - Lack of clinical detail to validate TACO diagnoses recorded;
  - **Unadjusted rate comparisons may yield biased results, and thus require further control for potential confounding, which is planned;**
  - **Our results could also be due to a potentially higher TACO diagnosis awareness during the study period.**

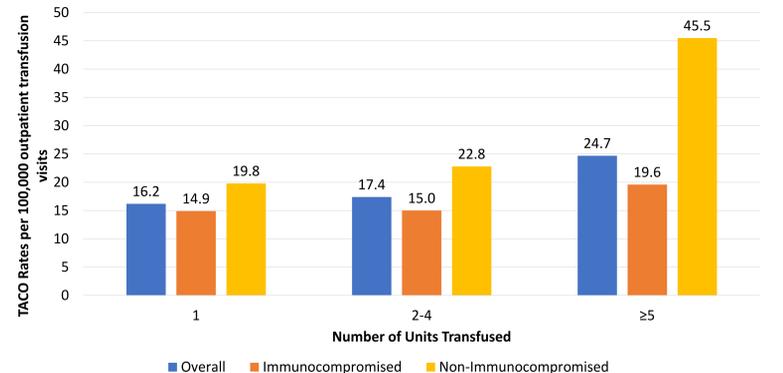


Figure 3. Unadjusted TACO Rates by Number of Units Transfused, Overall and by IC status

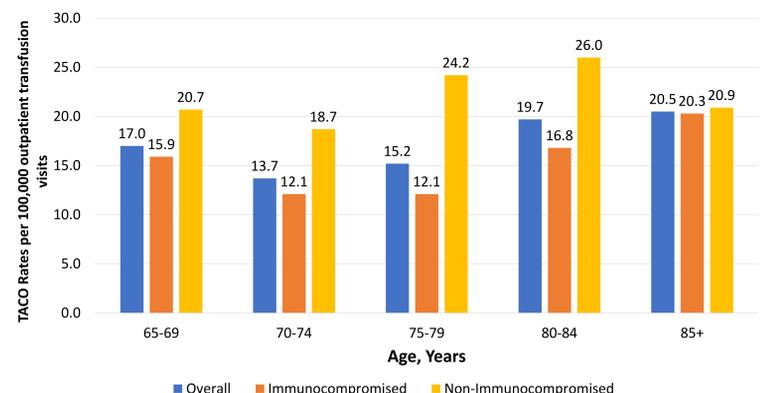


Figure 4. Unadjusted TACO Rates by Age Groups, Overall and by IC Status

## Conclusion

**Our population-based nationwide study on TACO occurrence in outpatient elderly suggests:**

- Higher risk of TACO occurrence among non-IC beneficiaries overall, by year, number of units, and other characteristics, which may be due to: Older age and differences in underlying comorbidities in non-IC vs. IC beneficiaries;**
- Increase in TACO occurrence trends, overall and by IC status, during 2011-2018;**
- Higher TACO risk with greater number of units transfused, overall and by IC status;**
- TACO risk may be related to the blood components transfused:**
  - Higher TACO rates for visits with RBCs, transfused either as a single component or in combination with platelets or plasma;
- Demographic characteristics may be associated with TACO occurrence:**
  - Higher TACO rates were identified with older age, overall and by IC status;
  - Higher TACO rates were found in females vs. males, which requires further investigation;
- The need for investigation into the role of underlying conditions in TACO occurrence, with higher hospitalization, longer LOS, and higher inpatient mortality for non-IC cases.**