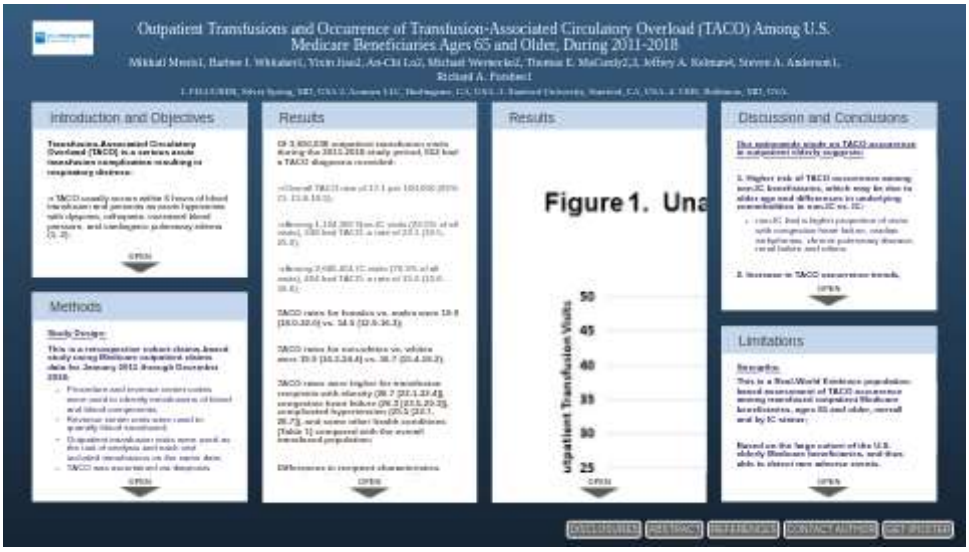
# Outpatient Transfusions and Occurrence of Transfusion-Associated Circulatory Overload (TACO) Among U.S. Medicare Beneficiaries Ages 65 and Older, During 2011-2018





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# INTRODUCTION AND OBJECTIVES

**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 (1, 2);

⇒TACO is one of the leading reported causes of transfusion-related fatalities in the United States (3);

⇒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 (1, 4-8).

**Study Objectives:**

**To assess TACO occurrence and evaluate recipient and transfusion characteristics among the U.S. Medicare population ages 65 and older transfused in the institutional outpatient setting, during 2011-2018.**

# METHODS

**Study Design:**

**This is a retrospective cohort claims-based study using Medicare outpatient claims data for January 2011 through December 2018:**

- Procedure and revenue center codes were used to identify transfusions of blood and blood components;
- Revenue center units were used to quantify blood transfused;
- Outpatient transfusion visits were used as the unit of analysis and each visit included 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 (i.e., different blood components transfused on the same visit);

**Analytic Plan:**

**1. Assess 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;**

**2. Compare IC vs. non-IC visits and IC vs. non-IC cases (i.e., visits with TACO): by demographics, health conditions, hospitalization, ICU/CCU admission, length of stay (LOS), and inpatient mortality.**

# 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 were 19.9 (18.0-22.0) vs. 14.5 (12.9-16.3);**

**TACO rates for non-whites vs. whites were 19.9 (16.2-24.4) vs. 16.7 (15.4-18.2)**;

**TACO rates were higher for transfusion recipients 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) compared with the overall transfused population;**

**Differences in recipient characteristics were identified when comparing IC vs. non-IC transfusion visits, and IC vs. non-IC cases:**

⇒Non-IC transfusion visits were more likely for:

- Females (58.7% vs. 44.4%);
- Aged ≥80 (50.3% vs. 34.3%);

⇒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 to have LOS of ≥7 days (26.8% vs. 14.3%) and higher inpatient mortality (4.5% vs. 3.4%), among hospitalized cases.

## Figures 1-5 show that:

**1. Annual TACO rates increased over time, overall and by IC status, during the study period (Figure 1):**

⇒The overall annual TACO rates varied between 10.7 (95% CI: 8.2-13.9) and 26.5 (95% CI: 22.1-31.8) during 2011-2018;

**2. TACO rates varied by blood component groups, overall and by IC status (Figure 2):**

⇒Higher TACO rates were identified for RBCs only (18.3, 95% CI: 16.8-19.8) and for multi-component visits (22.5, 95% CI: 17.1-29.5) comprised mostly of RBCs and platelets (>87%);

**3. TACO rates were higher with greater number of units transfused, overall and by IC status (Figure 3):**

⇒Overall TACO rates varied between 16.2 (95% CI: 14.1-18.7) and 21.7 (95% CI: 5.4-86.6) for 1 unit and ≥10 units, respectively.

**4. TACO rates varied with advancing age, overall and by IC status (Figure 4):**

⇒Higher overall TACO rates were identified for ages 80-84 and ≥85: 19.7 (16.6-23.3) and 20.5 (17.6-23.9), respectively;

⇒Among Non-IC, TACO rates were highest at ≥75;

⇒Among IC, TACO rates were highest at ≥80.

**5. Proportion of transfusion visits with specific underlying conditions varied by IC status (Figure 5).**

# RESULTS

**Figure 1. Unadjusted TACO Rates by Calendar Year: Overall and by IC status, During 2011-2018**

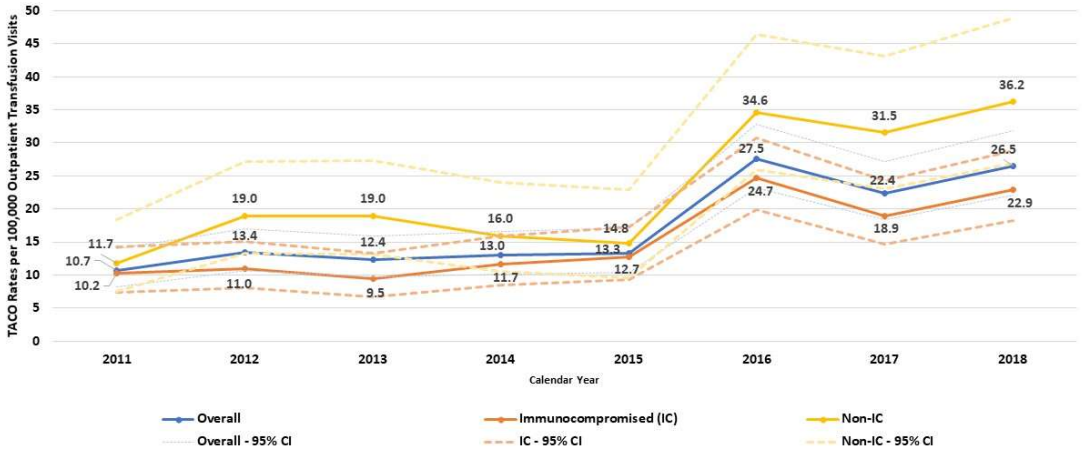


**Figure 2. Unadjusted TACO Rates by Blood Components: Overall and by IC status**

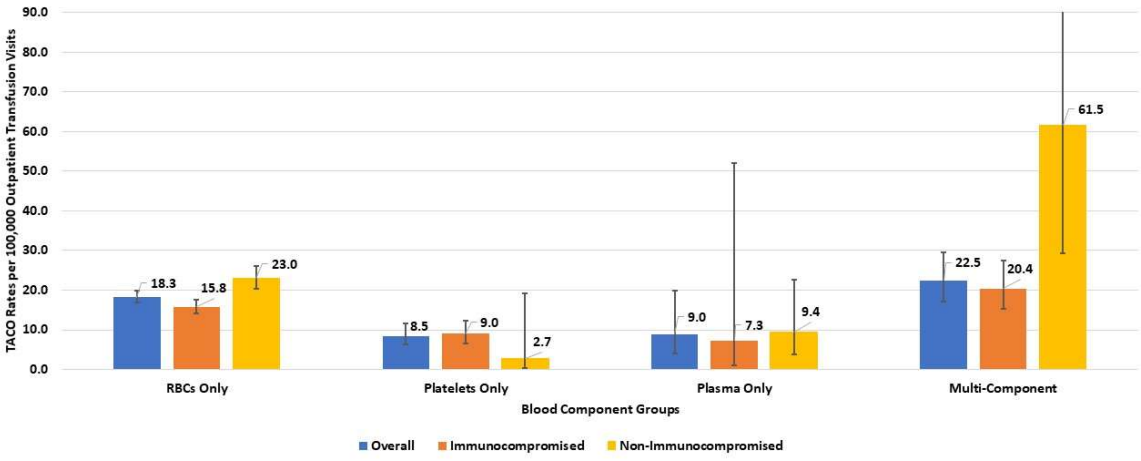

**Figure 3. Unadjusted TACO Rates by Number of Blood Units Transfused: Overall and by IC status**

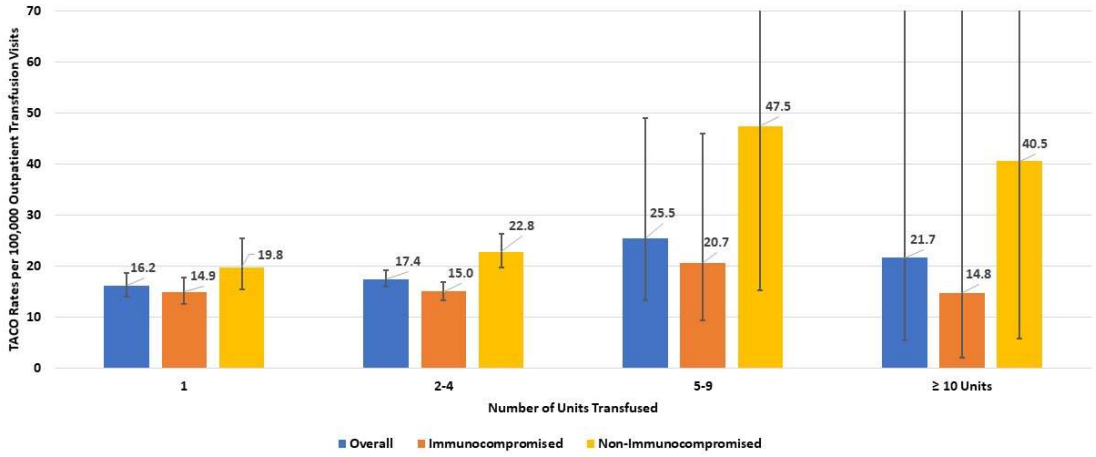


**Figure 4. Unadjusted TACO Rates by Age Groups: Overall and by IC status**

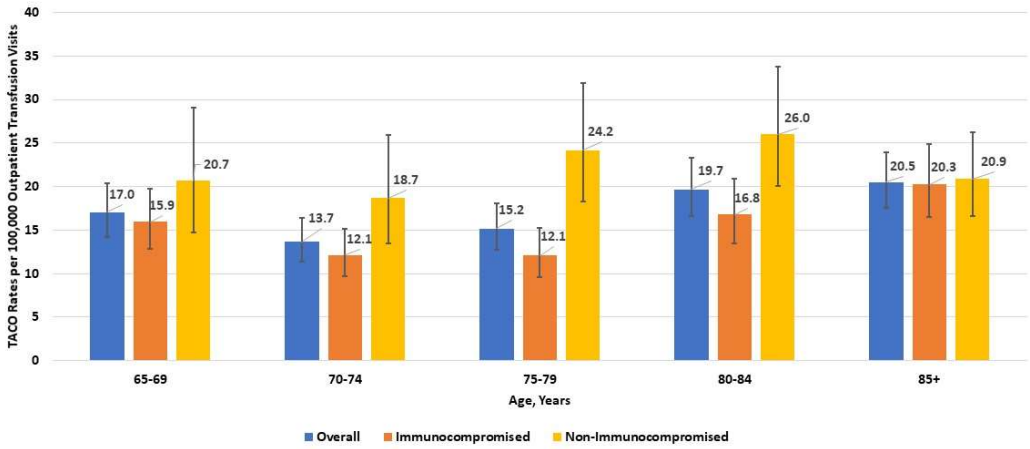

**Figure 5. Percentage of Transfusion Visits with Underlying Comorbidities: Overall and by IC status**

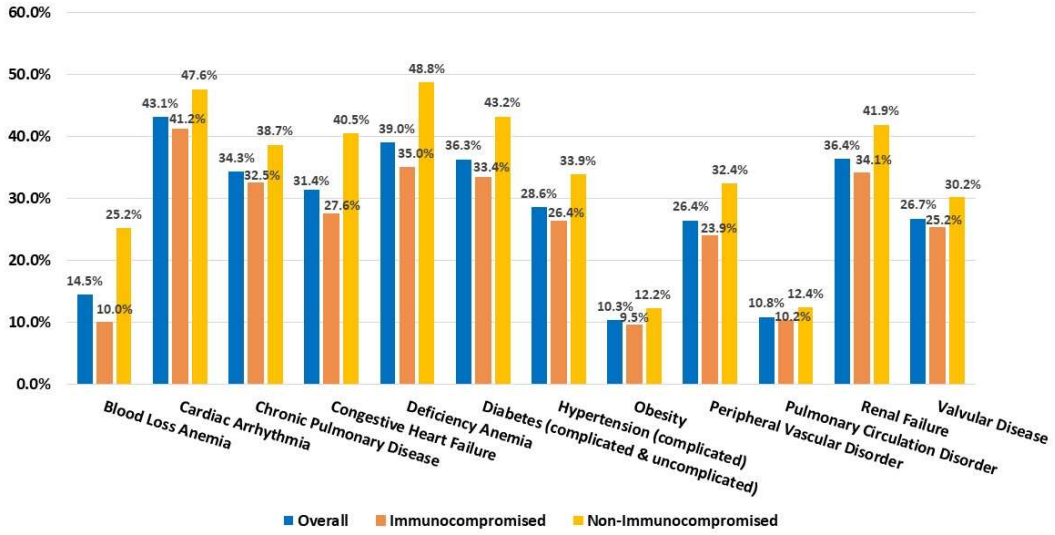


**Table 1. Unadjusted TACO Rates for Recipients with Different Health Conditions in the Prior 6 Months**

| 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. Health conditions were identified within 6 months prior to transfusion visits.*

# DISCUSSION AND CONCLUSIONS

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

**1. Higher risk of TACO occurrence among non-IC beneficiaries, which may be due to older age and differences in underlying comorbidities in non-IC vs. IC:**

- non-IC had a higher proportion of visits with congestive heart failure, cardiac arrhythmias, chronic pulmonary disease, renal failure and others.

**2. Increase in TACO occurrence trends, overall and by IC status, during 2011-2018;**

- Temporal trends are not linear.

**3. Higher TACO risk with greater number of units transfused, overall and by IC status;**

**4. 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;

**5. Demographic characteristics may be associated with TACO occurrence:**

- Higher TACO rates were identified with older age;

- Higher TACO rates were found in females vs. males, which requires further investigation;

**6. The need for investigation into the role of underlying health conditions in TACO occurrence, with higher hospitalization rates, longer LOS, and higher inpatient mortality for non-IC vs. IC cases.**

# LIMITATIONS

**Strengths:**

**This is a Real-World Evidence population-based assessment of TACO occurrence among transfused outpatient Medicare beneficiaries, ages 65 and older, overall and by IC status;**

**Based on the large cohort of the U.S. elderly Medicare beneficiaries, and thus able to detect rare adverse events.**

**Limitations:**

**Evaluation was based on the administrative databases and consequently:**

⇒TACO occurrence may be under- or misrecorded (i.e., unknown sensitivity and specificity of TACO code in the claims data);

⇒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 greater TACO diagnosis awareness during the study period.**

# DISCLOSURES

**This research is funded by CBER, FDA. The authors have no conflicts of interest.**

# ABSTRACT

## Abstract #109773

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

**Menis M**[1], Whitaker BI[1], Jiao Y[2], Lo AC[2], Wernecke M[2], MaCurdy TE[3], Kelman JA[4], Anderson SA[1], Forshee RA[1]
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**OBJECTIVES :** Transfusion-associated circulatory overload (TACO) is a leading cause of transfusion-related fatalities. 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.

**METHODS :** 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).

**CONCLUSIONS :** 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.

**Abstract ID#:**
109773

# REFERENCES


1. Wiersum-Osselton JC, Whitaker B, Grey S, et al. Revised international surveillance case definition of transfusionassociated circulatory overload: a classification agreement validation study. Lancet Haematol. 2019;6:e350-e358.

2. Andrzejewski C Jr, Casey MA, Popovsky MA. How we view and approach transfusion-associated circulatory overload: pathogenesis, diagnosis, management, mitigation, and prevention. Transfusion 2013; 53: 3037–47.

3. US Food and Drug Administration. Fatalities reported to FDA following blood collection and transfusion annual summary for FY2019. 2019. https://www.fda.gov/media/147628/download. Accessed May 10, 2021.

4. Karafin MS, Bruhn R, Westlake M, et al. Demographic and epidemiologic characterization of transfusion recipients from four US regions: evidence from the REDS-III recipient database. Transfusion 2017;57:2903-13.

5. Rogers MA, Blumberg N, Heal JM, Langa KM. Utilization of blood transfusion among older adults in the United States. Transfusion. 2011;51(4):710–718.

6. Menis M, Burwen DR, Holness L, Anderson SA. Blood use in the ambulatory setting among elderly in the United States. Transfusion 2009 Jun; 49(6): 1186-94.

7. Menis M, Anderson SA, Forshee RA, McKean S, Johnson C, Holness L, Warnock R, Gondalia R, Worrall CM, TE, Kelman JA, Ball R, Izurieta HS. Transfusion-Associated Circulatory Overload (TACO) and Potential Risk Factors Among the Inpatient U.S. Elderly as Recorded in Medicare Administrative Databases During 2011. Vox Sanguinis 2014; 106:144-152

8. Menis M, Whitaker BI, Jiao Y, Li Y, Storch E, Kwist A, Wernecke M, MaCurdy TE, Kelman JA, Anderson SA, Forshee RA. Transfusion-Associated Circulatory Overload Among Inpatient US Medicare Beneficiaries Ages 65 and Older, 2011-2019: A Claims-Based Study. Transfusion 2020;60(S5):257A.