

Claims-based Study of Transfusion-Related Acute Lung Injury (TRALI) Among Inpatient U.S. Medicare Beneficiaries Ages 65 and Older, 2007-2021



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Abstract

Background: TRALI is a leading cause of transfusion-related fatalities presenting as respiratory distress with non-cardiogenic pulmonary edema.

Purpose: To assess TRALI occurrence, severity, and potential risk factors among inpatient Medicare Fee-for-Service beneficiaries, ages 65+, transfused during 2007-2021.

Methodology: This is a hypothesis-generating study that utilized large Medicare databases, with transfusions identified by recorded procedure and revenue center codes, and TRALI by diagnosis codes. Unadjusted TRALI rates per 100,000 inpatient transfusion stays were evaluated by demographic and transfusion characteristics. Severity measures included inpatient mortality, mechanical ventilation, length of stay (LOS), and Charlson Comorbidity Index (CCI) score. Fisher's exact tests compared rates and Cochran-Armitage tests ascertained trends by year, age, and units.

Results: Of 20,601,732 inpatient transfusion stays, 7,479 had a TRALI diagnosis, an overall rate of 36.3 per 100,000 stays, with 2-year pre- and pandemic rates of 57.9 and 54.2. Annual TRALI rates ranged from 14.3 in 2007 to 55.3 in 2021 ($p < 0.001$). Rates by units increased from 18.3 for 1 unit to 155.8 for >9 units ($p < 0.001$). Rates by blood components, included RBCs only: 26.2; plasma only: 36.1; COVID-convalescent plasma only: 37.4; platelets only: 49.0; RBCs and plasma: 78.0; platelets and plasma: 97.4; RBCs and platelets: 140.9; and RBCs, plasma, and platelets: 301.1. TRALI rates by age declined from 45.3 for 65-69 to 25.5 for ≥85 ($p < 0.001$). Rates among males and females were 38.1 and 34.9 ($p < 0.001$); whites and non-whites: 37.7 and 29.2 ($p < 0.001$); and for immunocompromised vs. non-immunocompromised: 60.0 and 31.0 ($p < 0.001$). Pandemic TRALI rates were 45.8 for with vs. 55.3 without COVID-19 ($p = 0.11$). TRALI cases with vs. without COVID-19 were immunocompromised: 29.8% vs. 33.5%; and had CCI≥3: 54.8% vs. 64.4%, mechanical ventilation: 54.8% vs. 40.8%, LOS≥11 days: 69.0% vs. 53.8%, and inpatient mortality: 58.3% vs. 31.6%.

Conclusion: Our 15-year population-based study showed increasing TRALI rates over time, except with lower TRALI rates during pandemic vs. 2-years pre-pandemic. Study found higher TRALI rates with platelet components transfused, greater numbers of units transfused, and for immunocompromised beneficiaries. Finally, our study identified an overall lower TRALI rate and greater case-severity in COVID-19 beneficiaries and requires further inferential investigations.

Introduction

Transfusion-related acute lung injury (TRALI) is defined as a new episode of acute lung injury (ALI) that occurs within 6 hours of blood transfusion;

TRALI is a rare adverse event, and one of the leading reported causes of transfusion-related fatalities in the U.S.;

It presents as acute hypoxemia, respiratory distress, and non-cardiogenic pulmonary edema;

Older adults and immunocompromised persons may be at increased risk for TRALI due to underlying comorbidities and higher blood use.

Materials and Methods

Study Design:

This is a retrospective cohort study using large Medicare databases from January 2007 through December 2021:

Procedure codes and revenue center codes were used to identify transfusion of blood components, and revenue center units were used to quantify blood transfused;

Inpatient transfusion stays were the unit of analysis;

TRALI was identified via diagnosis code(s) recorded on transfusion stays;

Transfusion stays were grouped into mutually exclusive blood component categories.

Statistical Analysis:

Assessed unadjusted TRALI rates per 100,000 transfusion stays: overall, annually, by 2 years pre- (2018-2019) and during pandemic (April 2020-December 2021), by IC and COVID-19 status, and by demographics, blood components, and number of units transfused; and

Evaluated TRALI severity measures: inpatient mortality, ICU/CCU admission, mechanical ventilation, and length of stay (LOS);

Fisher's exact tests were performed to compare rates, and Cochran-Armitage tests to ascertain trends by year, age, and units transfused.

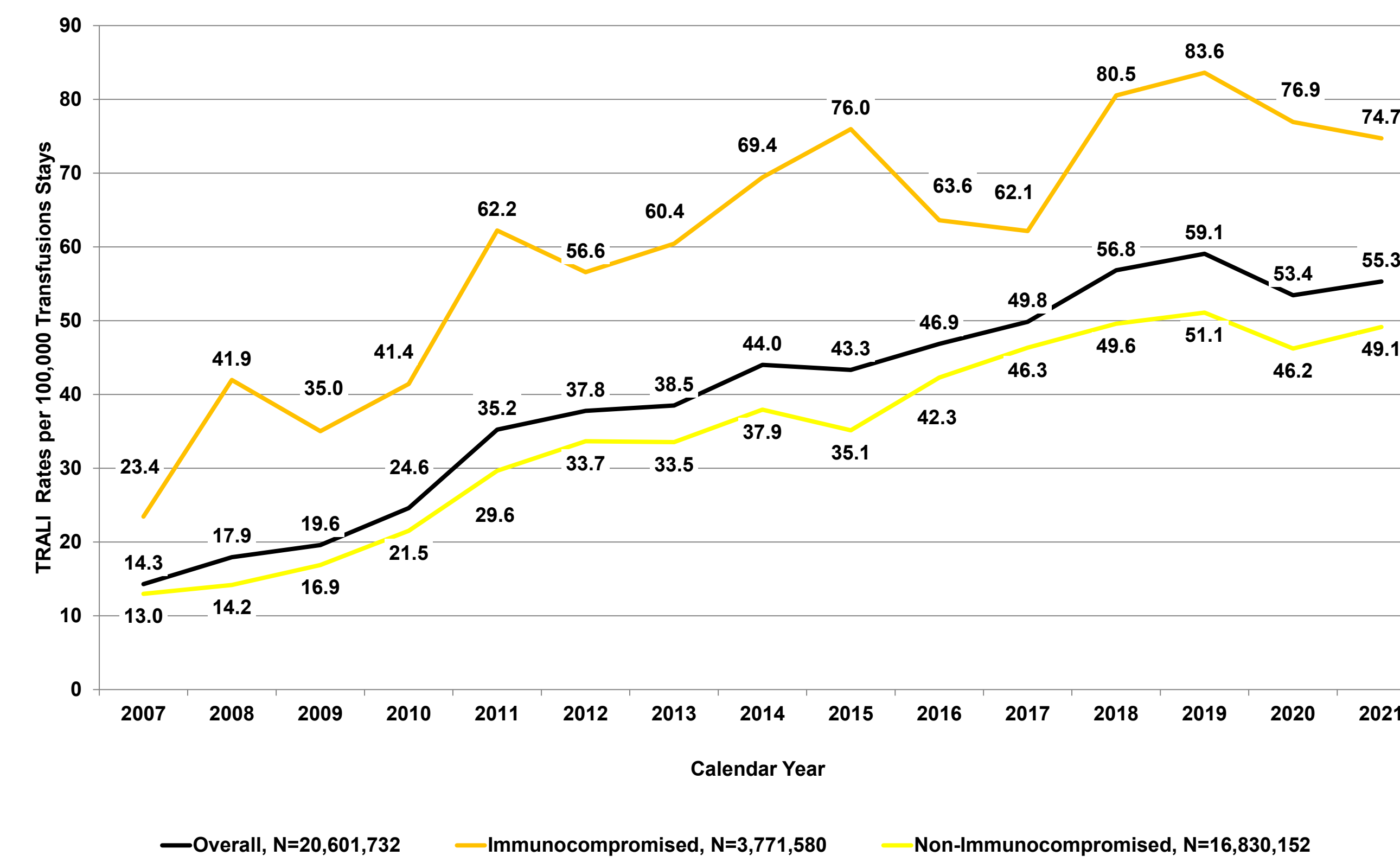


Figure 1. Unadjusted TRALI Rates by Calendar Year, Overall and by IC Status, During 2007-2021

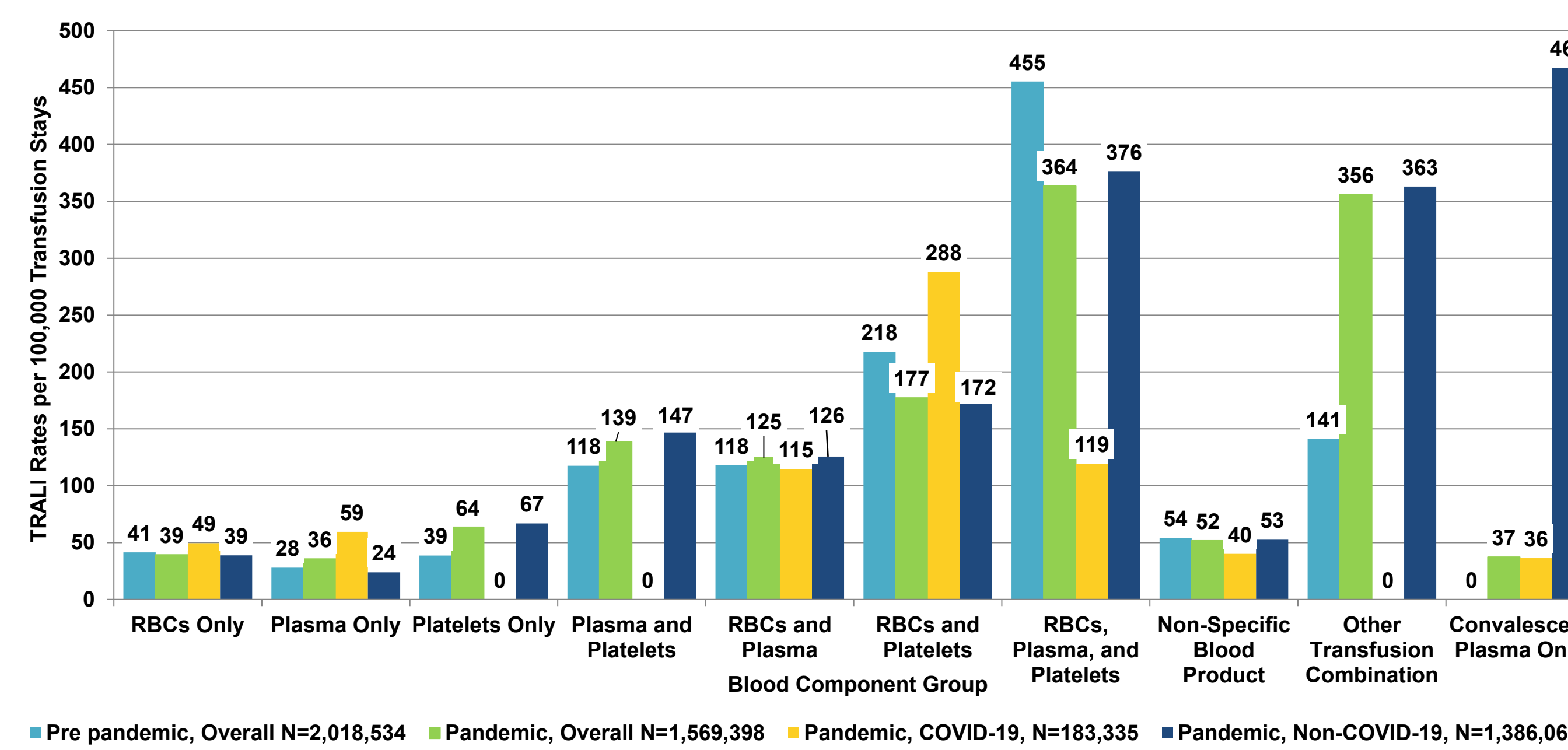


Figure 2. Unadjusted TRALI Rates by Blood Component Groups, by Pandemic and COVID-19 status

Results and Discussion

Of 20,601,732 inpatient transfusion stays during the 2007-2021 study period, 7,479 had a recorded TRALI diagnosis, an overall TRALI rate of 36.3 per 100,000;

Figure 1 shows annual TRALI rates, ranging from 14.3 in 2007 to 55.3 in 2021 ($p < 0.001$);

2-year pre- (2018-2019) and during pandemic (Apr 2020-Dec 2021) rates of 57.9 vs. 54.2;

During the pandemic, TRALI rates were 45.8 for transfusion stays with vs. 55.3 without a recorded diagnosis code for COVID-19 [rate ratio 0.8 (95% CI 0.65-1.04)];

Table 1 compares overall unadjusted TRALI rates (per 100,000) by IC status, blood components, number of units and demographics;

Figures 2-5 show unadjusted TRALI rates by 2-year Pandemic and COVID-19 status.

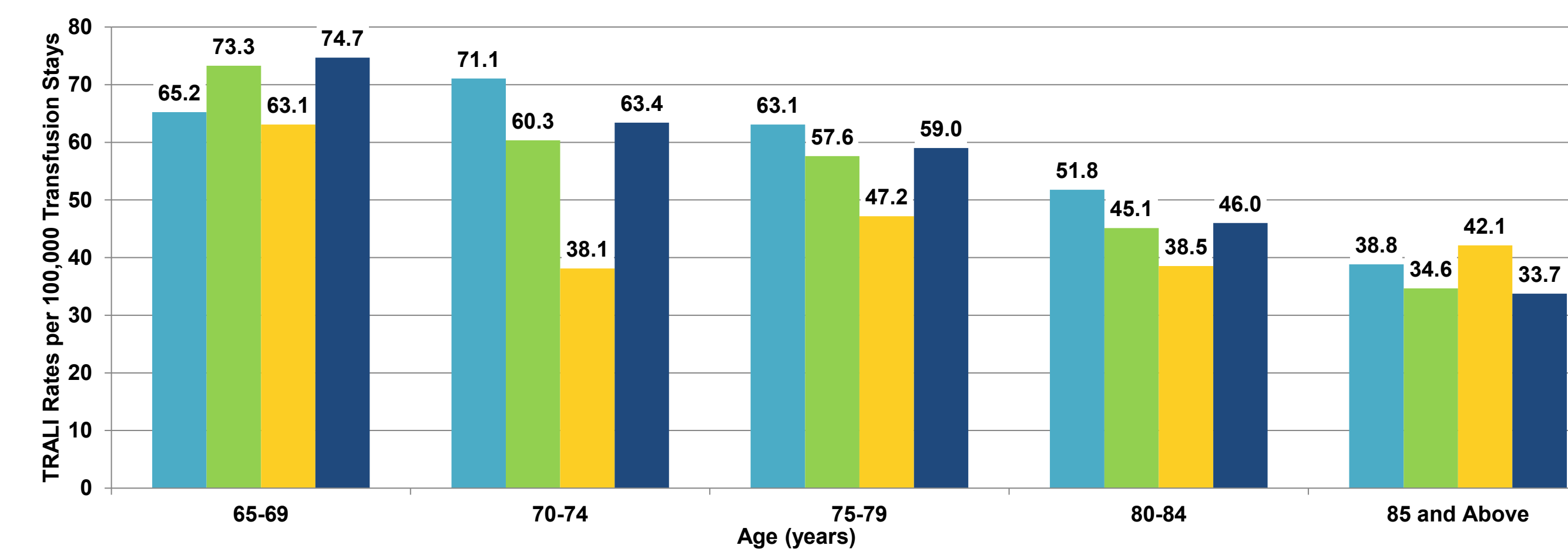


Figure 3. Unadjusted TRALI Rates by Age, by Pandemic and COVID-19 Status

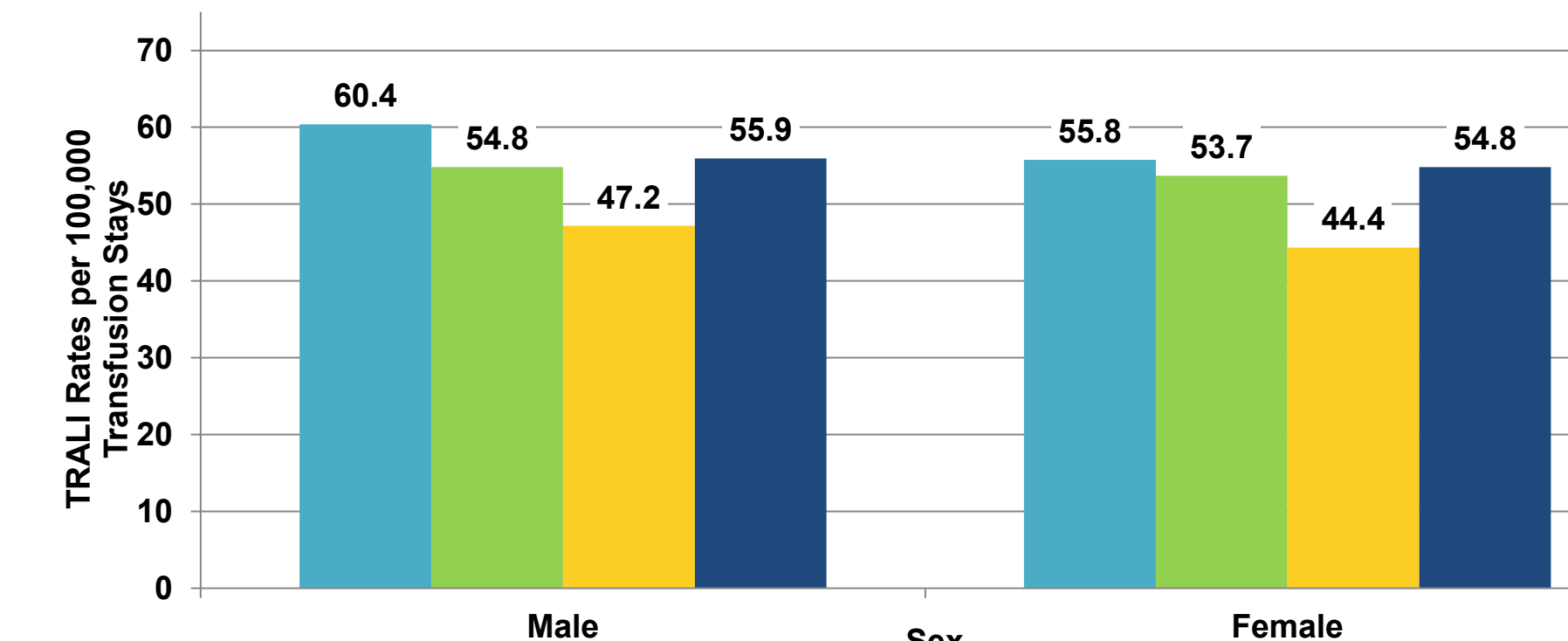


Figure 4. Unadjusted TRALI Rates by Sex and Race, by Pandemic and COVID-19 Status

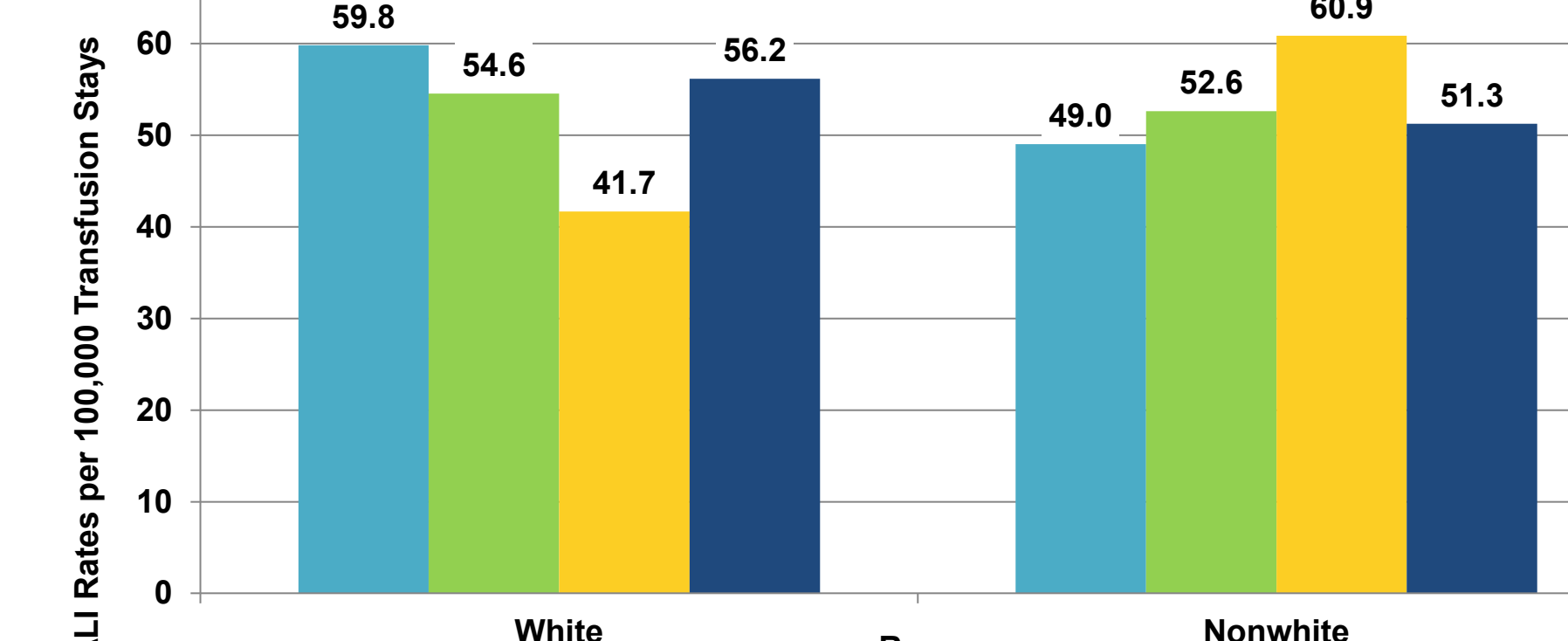


Figure 5. Unadjusted TRALI Rates by IC, Pandemic and COVID-19 Status

Table 1. Comparison of Unadjusted TRALI Rates by Transfusion and Recipient Characteristics Among Inpatient Medicare Beneficiaries Ages 65+ During 2007-2021

Category	Number of transfusion stays	Number of stays with TRALI	TRALI rate (per 100,000)	Rate Ratio	95% CI	P-Value
Overall	20,601,732	7,479	36.3			
Blood Component Groups*						
RBC only (Reference)	9,239,823	2,419	26.2	1.0		
Plasma only	587,672	212	36.1	1.4	1.19-1.59	<0.001
Platelets only	249,133	122	49.0	1.9	1.55-2.24	<0.001
Plasma and Platelets	42,078	41	97.4	3.7	2.66-5.07	<0.001
RBCs and Plasma	613,155	478	78.0	3.0	2.69-3.29	<0.001
RBCs and Platelets	414,488	584	140.9	5.4	4.91-5.89	<0.001
RBCs, Plasma, and Platelets	177,029	533	301.1	11.5	10.45-12.64	<0.001
Non-specific Blood Product	8,895,037	2,982	33.5	1.3	1.21-1.35	<0.001
Other Transfusion Combination	75,616	53	70.1	2.7	2-3.51	<0.001
Convalescent Plasma (CP) Only	82,960	31	37.4	1.4	0.97-2.03	0.052
Age**						
65-69 (Reference)	3,665,521	1,660	45.3	1		
70-74	4,037,430	1,730	42.8	0.9	0.88-1.01	0.11
75-79	4,145,884	1,632	39.4	0.9	0.81-0.93	<0.001
80-84	3,889,430	1,218	31.3	0.7	0.64-0.75	<0.001
85+	4,863,467	1,239	25.5	0.6	0.52-0.61	<0.001
Sex						
Male (Reference)	9,060,534	3,451	38.1	1		
Female	11,541,198	4,028	34.9	0.9	0.88-0.96	<0.001
Race/Ethnicity						
Non-White (Reference)	3,375,457	986	29.2	1		
White	17,226,275	6,493	37.7	1.3	1.21-1.38	<0.001
Immunocompromised Status						
No (Reference)	16,830,152	5,215	31	1		
Yes	3,771,580	2,264	60	1.9	1.84-2.04	<0.001
Quantifiable Units Transfused**						
1 (Reference)	19,224,437	7,164	37.3	1		
2-4	4,281,645	782	18.3	0.5		
5-9	10,698,366	2,655	24.8	0.7	1.25-1.47	<0.001
>9	2,748,334	1,396	50.8	1.4	2.55-3.04	<0.001
>9	1,496,092	2,331	155.8	4.3	7.86-9.26	<0.001

* Blood component groups are mutually exclusive. Groups with less than 10 TRALI occurrences are excluded for data privacy.
** Cochran-Armitage tests for TRALI trend analyses: by age ($p < 0.001$), by calendar year ($p < 0.001$), and by units transfused ($p < 0.001$)
Highlighting indicates a statistically significant p-value.

Conclusion

Our population-based nationwide study on TRALI occurrence in U.S. Medicare beneficiaries ages 65+ suggests:

- Increasing TRALI occurrence over time, overall and by IC status, except with lower rates during 2-year pandemic vs. pre-pandemic periods:
 - Further studies are needed to better understand potential reasons (e.g., increased TRALI awareness, blood components utilization, and underlying comorbidities);
- Importance of transfusion and recipient characteristics, with higher TRALI risk for:
 - IC vs non-IC; males vs. females; and whites vs. non-whites;
 - Platelets transfused alone or in combination; and with
 - Greater number of units transfused;
- Declining TRALI risk with advancing age, overall and during the pre- and pandemic periods, but no significant age trend identified for patients with COVID-19;
- Generally lower TRALI risk during 2-year pandemic vs. pre-pandemic, except for:
 - Non-whites and age group 65-69;
 - Recipients of plasma only, platelets only, platelets and plasma, and RBCs and plasma components;
- Lower TRALI risk for COVID-19 vs. non-COVID-19 transfusion stays, except for:
 - Plasma only, RBCs only, and RBCs and platelets transfusion stays as well as for IC and non-whites;
 - The findings may be confounded by similarity in clinical respiratory presentation between TRALI and COVID-19, and/or due to differences in the COVID-19 severity, underlying comorbidities, blood components and amount transfused, and need further investigation;
- For COVID-19 patients transfused, the TRALI risk is lower for those receiving CP only, which could be related to lower COVID-19 severity and fewer units transfused (mean 1.82 per stay);
- Inpatient TRALI cases with COVID-19 were more likely to have severe outcomes than TRALI cases without COVID-19 (e.g., mechanical ventilation: 54.8% vs. 40.8%, LOS≥11 days: 69.0% vs. 53.8%, and inpatient mortality: 58.3% vs. 31.6%);
- Further inferential investigations using multivariate regression analyses are needed to better understand TRALI risk factors during the COVID-19 pandemic vs. pre-pandemic.