Convalescent Plasma Utilization Among Inpatient U.S. Medicare Beneficiaries Ages 65 and Older Diagnosed with COVID-19 During 2020-2021

Authors: Mikhail Menis[1], Kushal Naik[2], Shreejaya Shrestha[2], Zhiruo Wan[2], Yeerae Kim[2], Sarah Barney[2], Mao Hu[2], Yoganand Chillarige[2], Jeffrey A. Kelman[3], Steven A. Anderson[1], Richard A. Forshee[1], Barbee I. Whitaker[1] (1. CBER, FDA; 2. Acumen LLC; 3. CMS)

This study was supported/funded by the U.S. Food and Drug Administration, Center for Biologics Evaluation and Research. There are no conflicts of interest for any parties involved in this research.

BACKGROUND

- In the U.S., COVID-19 convalescent plasma (CP) was available for use as of April 2020, first under individual patient Emergency Investigational New Drug (EINDs) applications and then under the national Expanded Access Protocol (EAP) sponsored by the Mayo Clinic;
- In August 2020, CP received the Emergency Use Authorization (EUA) by the U.S. FDA for the treatment of hospitalized patients with COVID-19;
- Adults ages 65+ and immunocompromised (IC) persons have multiple underlying comorbidities and are also at increased likelihood of blood component transfusions and severe COVID-19.

OBJECTIVES

- **To evaluate CP use among transfused inpatient fee-for-service Medicare beneficiaries age 65+ with COVID-19 during 2020-2021.**

METHODS

- **Study Design:** Retrospective claims-based study using large Medicare administrative databases;
- **Study Population:** Inpatient transfusion stays with recorded COVID-19 diagnosis among fee-for-service Medicare beneficiaries ages 65+, continuously enrolled in Part A (hospital insurance) and Part B (medical insurance) within 3 months prior to the index date (i.e., admission date), during April 2020-December 2021;
- **COVID-19, convalescent plasma (CP), and other transfused blood component ascertainment:**
  a. Revenue center and ICD-10-CM procedure codes were used to identify blood and blood components transfused, including CP, red blood cells, platelets, and plasma, among others;
  b. ICD-10-CM diagnosis code U07.1 was used to identify COVID-19 infection among inpatient transfusion stays.
- **IC status** was evaluated based on the presence of specific diagnosis or procedure codes for malignancies, chemotherapy, radiation or transplantation within 3 months prior to or on the index date;

Analytic Plan:

- Evaluate the use prevalence of CP only, CP in combination with other blood components (i.e. CP transfusion combination), and non-CP transfusions per 100 COVID-19 inpatient transfusion stays: overall, monthly, and by recipient characteristics, time since most recent COVID-19 diagnosis within 30 days prior to admission, and by COVID-19 severity measures (e.g., inpatient [IP] mortality, mechanical ventilation [MV], intensive care unit [ICU] admission, length of stay [LOS]);
- This study also evaluated mean units per stay for CP only, CP transfusion combination, and non-CP transfusion unit-quantifiable stays.

RESULTS

- **Among 1,569,398 inpatient transfusion stays during April 2020-December 2021, 183,335 (11.7%) had COVID-19;**
- **Among COVID-19 transfusion stays, 45.1% received CP only, 3.1% CP with other blood component(s), and 51.8% non-CP transfusion(s):**
  - ⇨Severity measures for CP only vs. CP transfusion combination vs. non-CP transfusion stays were:
    - LOS>10 days (41.7% vs. 75.3% vs. 57.4%), ICU admission (59.5% vs. 82.4% vs. 67.5%), mechanical ventilation (17.8% vs. 52.2% vs. 32.6%) and inpatient mortality (25.7% vs. 52.5% vs. 32.9%);
    - Mean units transfused of 1.82, 4.50, and 3.33, respectively;
- **Figure 1 shows CP prevalence by patient characteristics among COVID-19 transfusion stays;**
- **Figure 2 shows CP prevalence by U.S. Census Regions (Northeast, West, South, Midwest) and by rural vs. urban residence:**
  - ⇨For specific regions (data not shown), lowest CP only prevalence was for Northeast New England (26.7%) and for Northeast Middle Atlantic (30.8%), and highest for Midwest West North Central (57.4%);
- **Figure 3 shows any CP prevalence over time by hospital admission months, overall and by IC status among COVID-19 transfusion stays;**
- **Figure 4 shows CP use prevalence by severity measures for COVID-19 transfusion stays;**
- **Figure 5 shows CP use prevalence by time to most recent COVID-19 diagnosis, among COVID-19 transfusion stays:**
  - ⇨Much lower CP only prevalence for COVID-19 transfusion stays with COVID-19 diagnosis within 11-30 days prior to admission;
- **Figure 6 shows distribution (%) of COVID-19 severity measures by time to most recent COVID-19 diagnosis prior to hospitalization:**
  - ⇨Stays with COVID-19 diagnosis within 4-10 days prior to admission had the highest IP mortality;
- **Figure 7 shows IP mortality (%) by patient characteristics.**

RESULTS

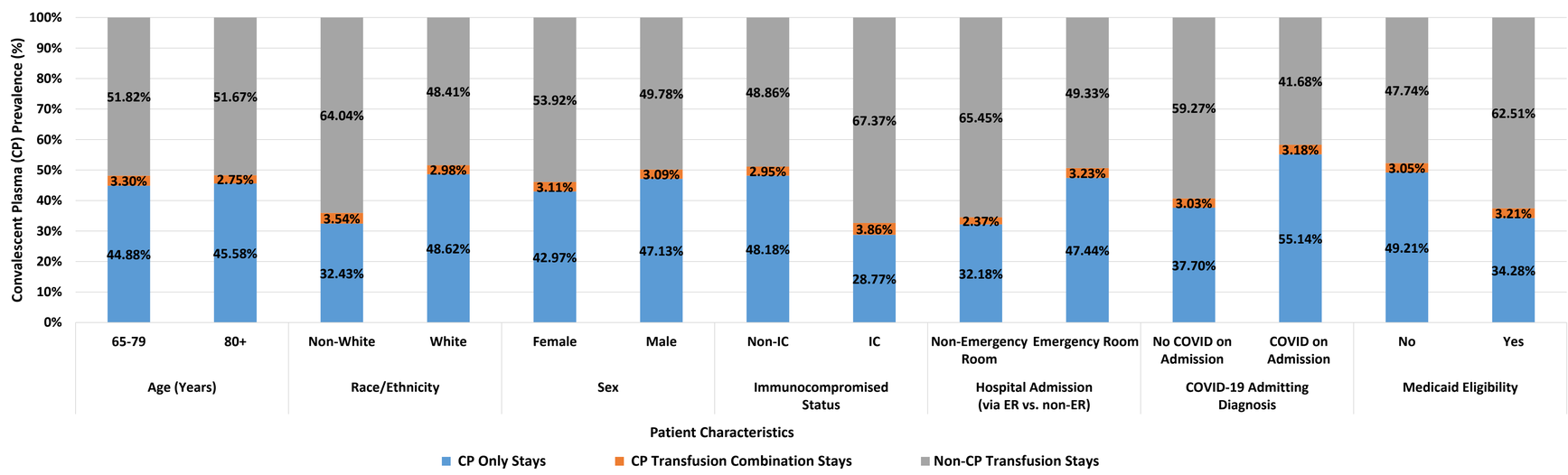

Figure 1. CP prevalence by patient characteristics among COVID-19 transfusion stays during 2020-2021

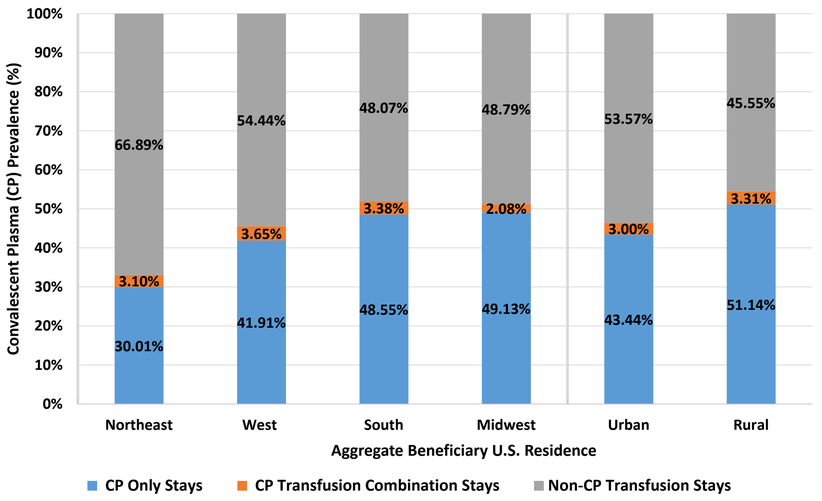

Figure 2. CP prevalence by U.S. Census Regions and urban vs. rural residence during 2020-2021

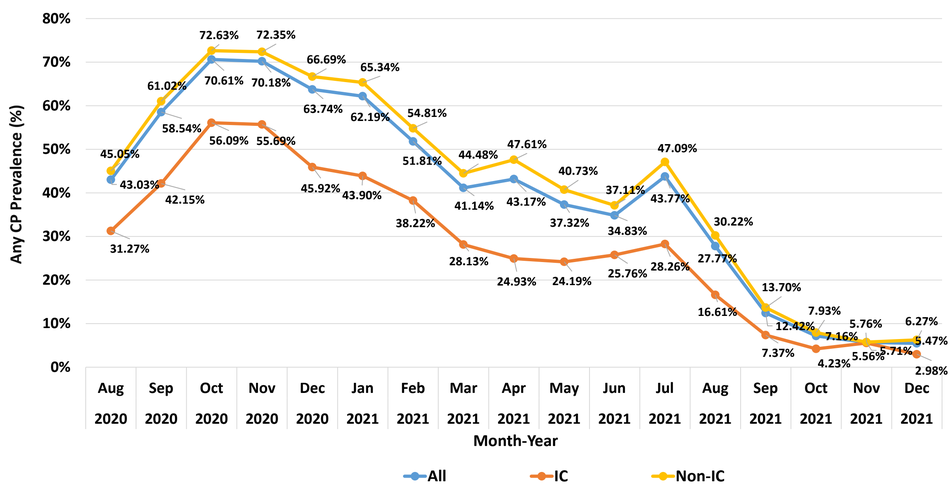

Figure 3. Any CP use prevalence by hospital admission months, overall and by IC status during 2020-2021

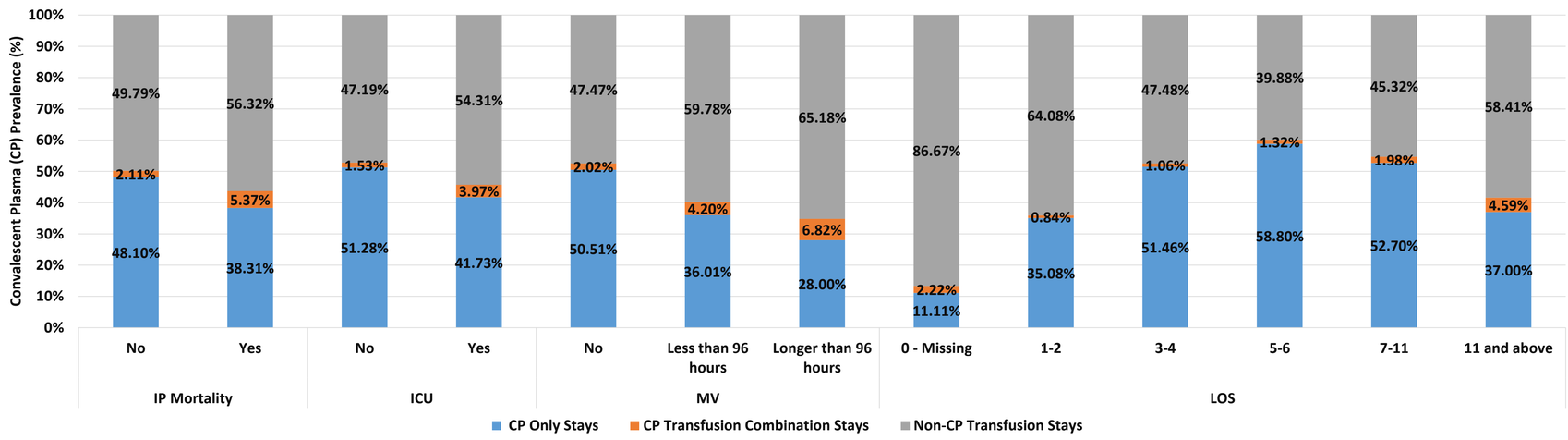

Figure 4. CP prevalence by COVID-19 severity measures among COVID-19 transfusion stays, during 2020-2021

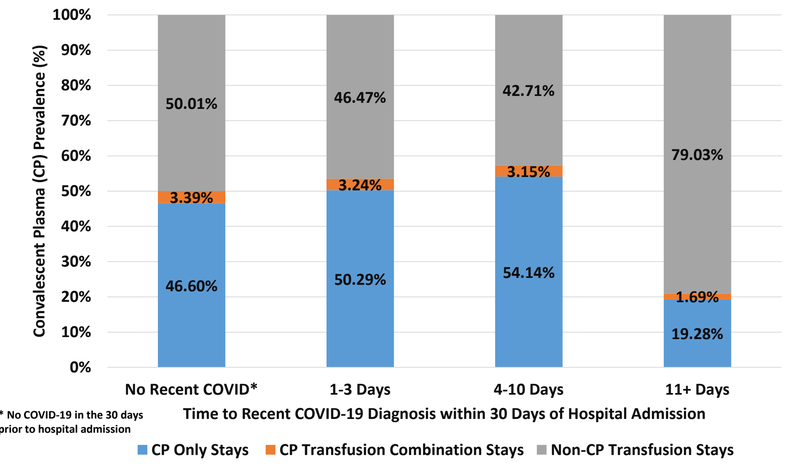

Figure 5. CP prevalence by time to most recent COVID-19 diagnosis during 2020-2021

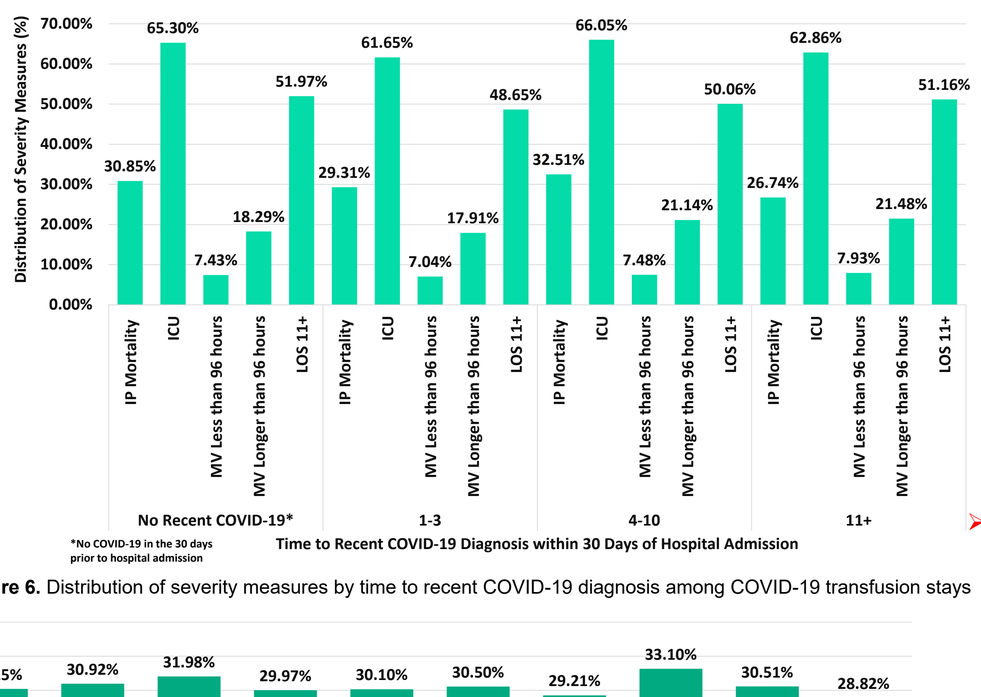

Figure 6. Distribution of severity measures by time to recent COVID-19 diagnosis among COVID-19 transfusion stays

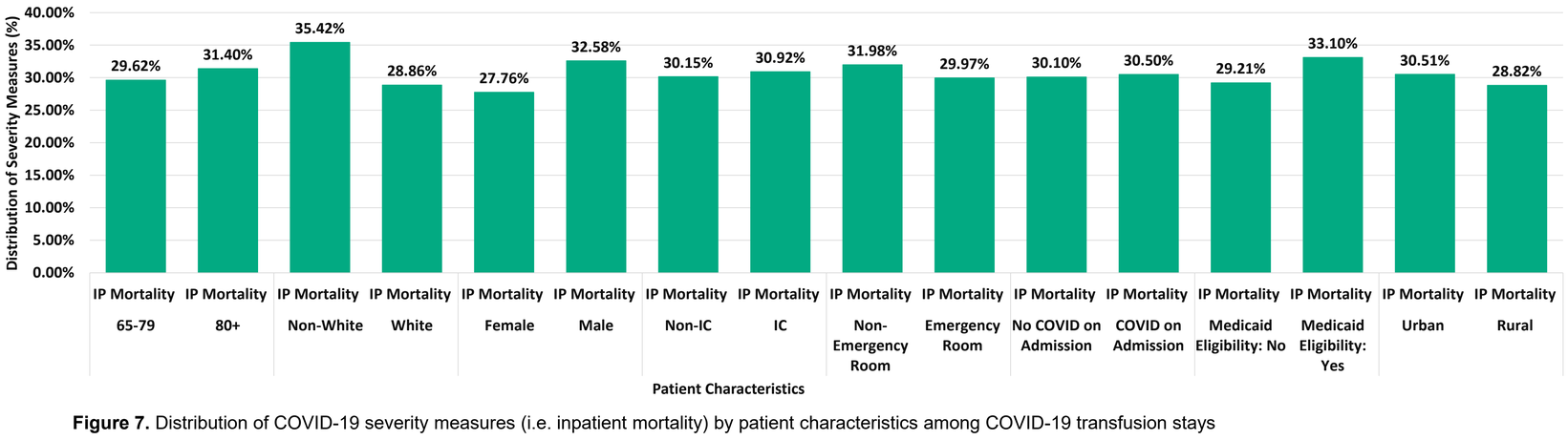

Figure 7. Distribution of COVID-19 severity measures (i.e. inpatient mortality) by patient characteristics among COVID-19 transfusion stays

DISCUSSION AND CONCLUSIONS

- **Our population-based nationwide study on CP utilization during pandemic among transfused inpatient U.S. Medicare beneficiaries ages 65+ with COVID-19 shows:**
  1. **Substantial use of CP (48.2%) among transfused inpatients aged 65+:**
     - ⇨Substantial proportion of COVID-19 transfusion stays received CP only;
     - ⇨CP only users had fewest mean units transfused and lowest severity measure rates suggesting lower COVID-19 severity as compared to the other transfusion groups;
  2. **CP prevalence was highest during October and November of 2020 with substantial decline through end of 2021, overall and by IC status:**
     - ⇨ Consistently higher CP prevalence was for non-IC vs. IC;
     - ⇨The findings could be related to increasing availability of vaccination and COVID-19 treatments, declining COVID-19 severity, and varying evidence on CP effectiveness;
  3. **CP only prevalence was higher for non-IC vs. IC, whites vs. non-whites, males vs. females, non- vs. Medicaid eligible, rural vs. urban, and residents of the South and Midwest vs. West and Northeast:**
     - ⇨IC, non-whites, and with Medicaid eligibility had among the lowest CP use prevalence;
  4. **CP prevalence was higher for stays with either no recent COVID-19 diagnosis or with COVID-19 diagnosed within 1-10 days prior to admission, and lowest for stays with COVID-19 diagnosed within 11-30 days prior to hospital admission:**
     - ⇨Findings generally support early CP administration guidelines;
  5. **The findings suggest an overall lower CP prevalence with higher COVID-19 severity:**
     - ⇨Those with IP mortality and longer mechanical ventilation and LOS had lower CP only and higher CP transfusion combination prevalence;
     - ⇨COVID-19 patients with greater disease severity (e.g., non-whites, Medicaid eligible, urban residents) had lower CP prevalence, with findings not consistent for others (e.g., gender, age) suggesting multiple factors at play that need further investigation.
  6. **The findings also compared COVID-19 severity measures by time since COVID-19 diagnosis:**
     - ⇨In the inpatient setting, COVID-19 severity does not appear to correlate with time since COVID-19 diagnosis, which could be related to differences in access to care and health-seeking behaviors.
- **Overall, differences identified in CP utilization may be due to variations in COVID-19 severity, time to recent COVID-19 diagnosis, underlying comorbidities, CP availability, prescribing patterns, access to care, and health-seeking behaviors and need future evaluation.**

STRENGTH AND LIMITATIONS

Strengths:

- **This is a real-world evidence population-based study of CP utilization during the COVID-19 pandemic and highlights the utility of large Medicare databases;**

Limitations:

- **The study was based on the administrative databases, and consequently:**
  - ⇨CP and other blood transfusions may be under- or mis-recorded (i.e., unknown sensitivity, specificity, and positive predictive value of the procedure and revenue codes in the claims data);
  - ⇨Inability to quantify units for all transfusion stays, especially for the CP only group, and lack of clinical detail to validate units transfused;
- **The conclusions are derived from unadjusted prevalence data and may not be applicable to the broader U.S. population. Further inferential analyses are needed to evaluate impact of potential factors on CP utilization in the study population, overall and by IC status.**