

Impact of plasma collection date on antibodies to SARS-CoV-2 in intravenous immunoglobulin

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BACKGROUND

- Some patients with primary immunodeficiency (PI) fail to mount an immune response when faced with an infection or in response to immunization.
- Intravenous immunoglobulin (IVIG) products contain a broad spectrum of antibodies and provide protection for patients with PI against common infections. The antibody profile reflects that of the plasma donor population and donor exposure to viruses such as SARS-CoV-2, the virus responsible for the COVID-19 pandemic.
- It is critical that all IVIG preparations contain antibodies to viruses circulating in the general population, including the SARS-CoV-2 virus.
- In January 2024, there were more than 20,000 COVID-19-associated hospital admissions per week in the USA.¹
- Plasma donors' antibody levels against SARS-CoV-2 tend to decrease over time. This decline starts with the first donation (at least two weeks after recovery, following FDA guidelines) and continues up to at least 8 weeks after exposure (Figure 1).

PURPOSE

- This study was initiated to assess the impact of plasma collection during and after a pandemic such as the COVID-19 pandemic, on antibody levels in IVIG products and to provide some information on the criticality of plasma collection during a pandemic.

METHODS

- Gammaplex 5% (50 g/L) and Gammaplex 10% (100 g/L) are IVIG solutions licensed for the treatment of PI.
- Both products are manufactured exclusively from source plasma collected in the United States (US).
- A screening program for SARS-CoV-2 antibodies in commercial preparations of these IVIG 5% and IVIG 10% products was completed.
- Samples were assayed using the GenScript cPass surrogate virus neutralization test (sVNT).²
 - Immunoglobulin (IgG) was incubated with recombinant viral receptor binding domain (RBD) and binding to immobilized ACE2 receptors was monitored.
 - ACE2 acts as the receptor for the SARS-CoV-2 virus and allows it to infect the cell.³
 - The amount of RBD bound to the ACE2 receptors is inversely proportional to the neutralizing antibody concentration.
 - Neutralizing antibody concentrations were normalized to a 100 g/L solution.
 - Results are reported with reference to the WHO International Standard for antibodies to SARS-CoV-2.
- All IVIG batches tested were released between 2021 and 2023, and plasma used for the manufacture of the batches was collected before, during, and after the pandemic period.
- To define the amount of plasma collected during the pandemic period and used for fractionation, a cutoff was applied on July 15, 2020, as the date at which >1% of the population in the US had reported as COVID-19 positive according to the available Centers for Disease Control and Prevention (CDC) statistics (total case numbers exceeded 3.3 million)¹ (Figure 2).
- Plasma collected prior to July 15, 2020, was considered pre-COVID-19.
- The number of donations collected during the COVID-19 pandemic was estimated for all plasma pools contributing to the screened batches.

Detectable levels of SARS-CoV-2 antibodies in IVIG batches tested across all three years of the COVID-19 pandemic, with stabilization in the post-pandemic period (2023).

Figure 1. Amount of SARS-CoV-2 Antibody Levels Present in Plasma Relative to the First Donation

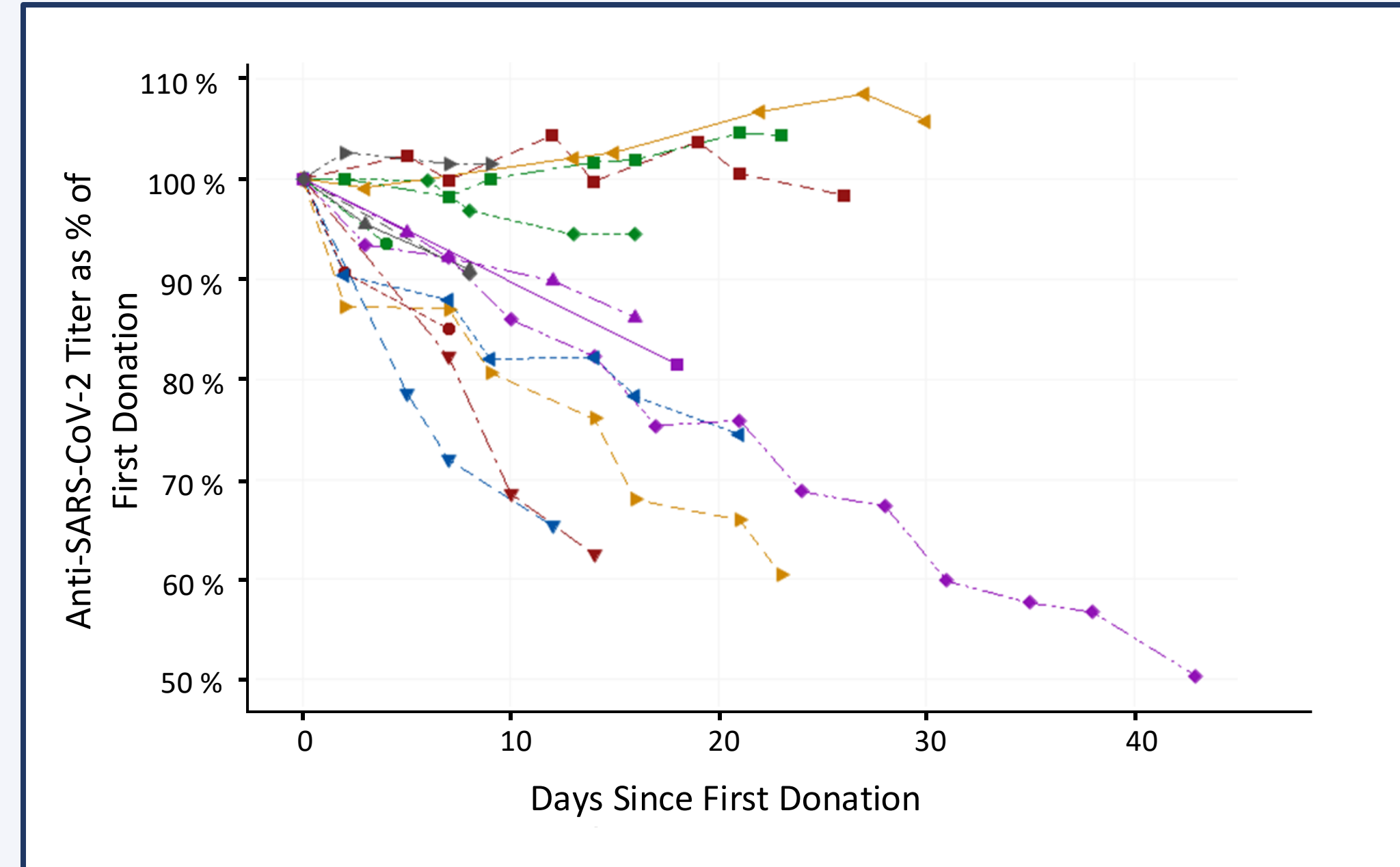


Figure 3. SARS-CoV-2 Antibodies in IVIG Expressed As IU/mg IgG in Batches Manufactured From 2021 to 2023

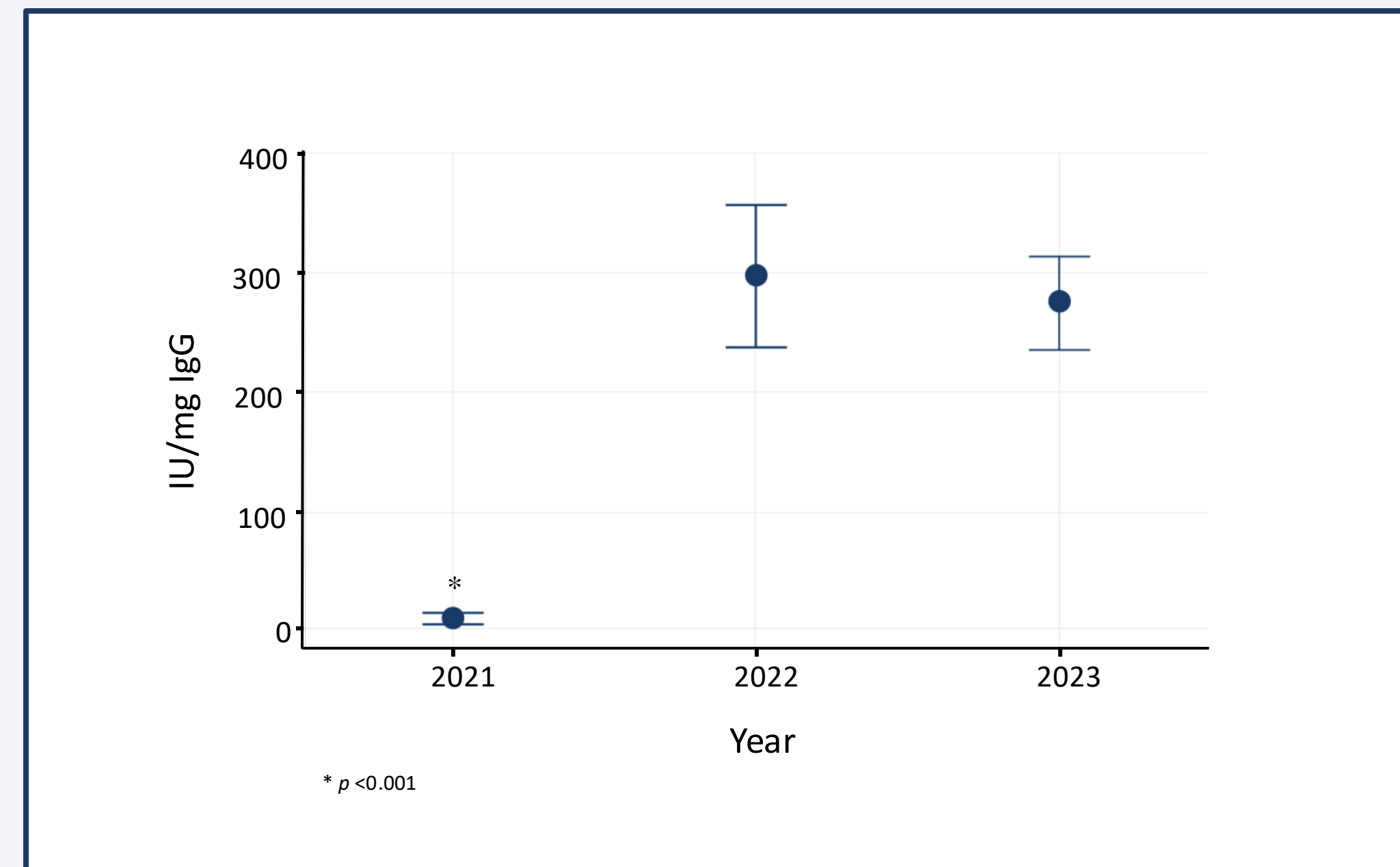


Figure 2. COVID-19 Cases Reported to the Centers for Disease Control in the US¹

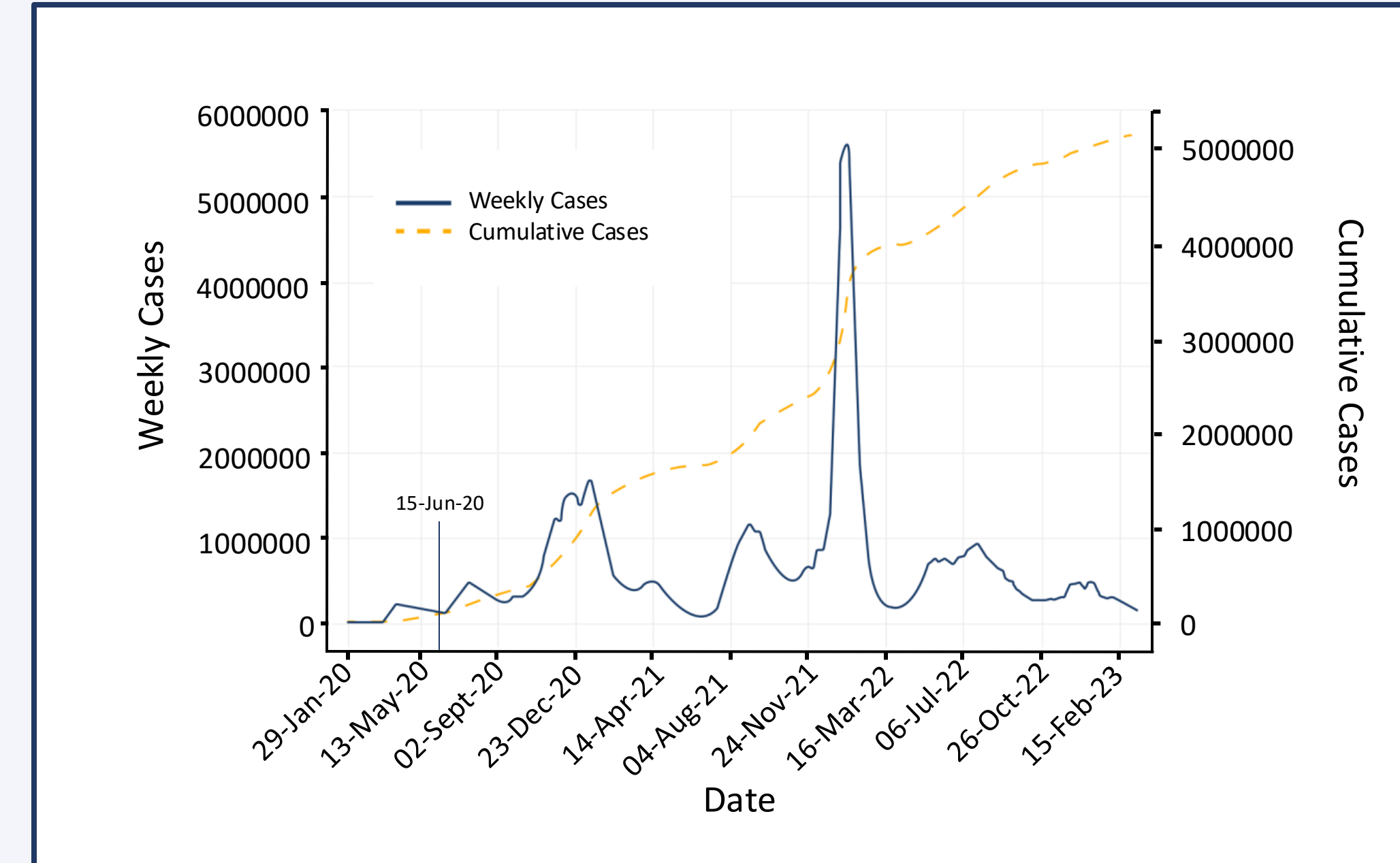
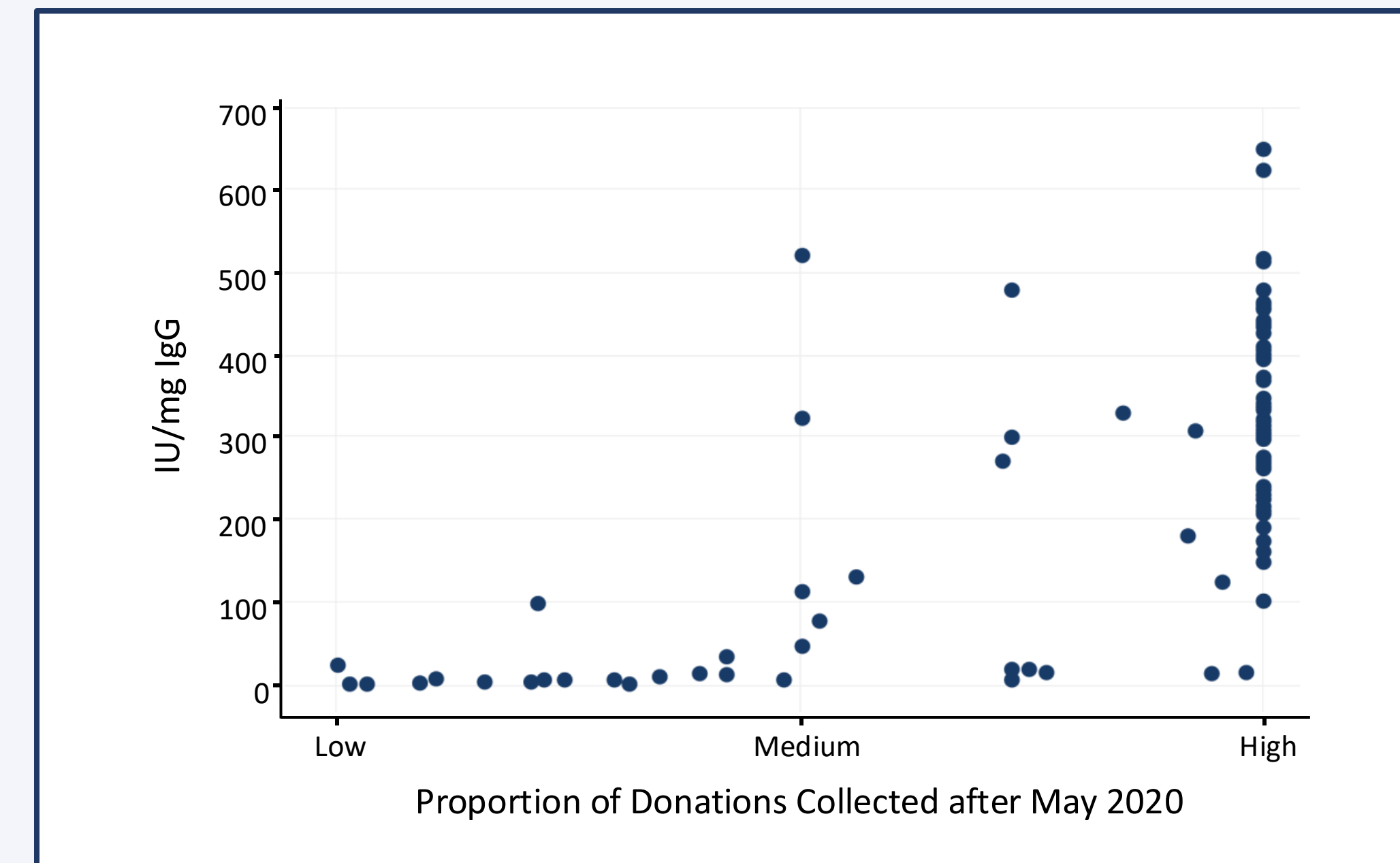


Figure 4. Correlation Between Donations Collected During the Pandemic and Potency of Gammaplex



RESULTS

- Screening was performed on a total of 82 batches: 21 batches filled in 2021, 35 batches filled in 2022, and 26 batches filled in 2023 (Table 1).
- Of the 82 batches tested, 77 were IVIG 10% and 5 were IVIG 5%.

Table 1. IVIG Batches Tested by Year of Collection

| Testing Period | 5% IVIG Batches Tested | 10% IVIG Batches Tested |
|----------------|------------------------|-------------------------|
| 2021 | 2 | 19 |
| 2022 | 2 | 33 |
| 2023 | 1 | 25 |

IVIG = intravenous immunoglobulin

- Neutralizing antibody potency of the tested IVIG batches ranged from 0 to 644 IU/mg IgG with a mean potency of 215 IU/mg IgG and a median potency of 213 IU/mg IgG.
- Comparison of the IVIG batches by year found a significant difference between 2021 and 2022 batches ($p < 0.001$) with a mean potency of 8.5 IU/mg IgG for 2021 batches compared to 296 IU/mg IgG for 2022 batches and 274 IU/mg IgG for 2023 batches (Figure 3).
- Of the 82 IVIG batches screened, there were 11 batches (13%) where less than 25% of the contributing donations were identified as having been collected after July 15, 2020.
- Eleven IVIG batches (13%) had 25% to 50% of the donated plasma collected after July 15, 2020.
- Seven IVIG batches (9%) had 50% to 75% of the donated plasma collected after July 15, 2020.
- Fifty-three IVIG batches (65%) had more than 75% of the donated plasma collected after July 15, 2020.
- There was a positive correlation between the neutralizing antibody potency of the finished IVIG product and the proportion of donations collected after July 15, 2020, during the pandemic period (Pearson correlation coefficient = 0.64) (Figure 4).

CONCLUSIONS

- IVIG batches collected in 2022 and 2023 contained significantly higher levels of SARS-CoV-2 antibodies compared to IVIG batches collected in 2021 (earlier in the COVID-19 pandemic).
- Levels in 2023 were slightly reduced from the peak in 2022, and this may show a stabilization of antibody levels associated with immunization amongst plasma donors.
- Safe plasma collection and processing from the start of a pandemic allows IVIG batches containing antibodies to circulating viruses to be made available to immune-deficient patients as soon as possible.



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