The impact of COVID-19 monoclonal antibodies on clinical outcomes: A retrospective cohort study

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**Purpose:** Despite progress in the treatment of coronavirus disease 2019 (COVID-19), including the development of monoclonal antibodies (mAbs), more clinical data to support the use of mAbs in outpatients with COVID-19 is needed. This study is designed to determine the impact of bamlanivimab, bamlanivimab/etesevimab, or casirivimab/imdevimab on clinical outcomes within 30 days of COVID-19 diagnosis.

**Methods:** A retrospective cohort study was conducted at a single academic medical center with 3 campuses in Manhattan, Brooklyn, and Long Island, NY. Patients 12 years of age or older who tested positive for COVID-19 or were treated with a COVID-19–specific therapy, including COVID-19 mAb therapies, at the study site between November 24, 2020, and May 15, 2021, were included. The primary outcomes included rates of emergency department (ED) visit, inpatient admission, intensive care unit (ICU) admission, or death within 30 days from the date of COVID-19 diagnosis.

**Results:** A total of 1,344 mAb-treated patients were propensity matched to 1,344 patients with COVID-19 patients who were not treated with mAb therapy. Within 30 days of diagnosis, among the patients who received mAb therapy, 101 (7.5%) presented to the ED and 79 (5.9%) were admitted. Among the patients who did not receive mAb therapy, 165 (12.3%) presented to the ED and 156 (11.6%) were admitted (relative risk [RR], 0.61 [95% CI, 0.50-0.75] and 0.51 [95% CI, 0.40-0.64], respectively). Four mAb patients (0.3%) and 2.64 control patients (0.2%) were admitted to the ICU (RR, 0.15; 95% CI, 0.45-5.09). Six mAb-treated patients (0.4%) and 3.37 controls (0.3%) died and/or were admitted to hospice (RR, 1.61; 95% CI, 0.54-4.83). mAb therapy in ambulatory patients with COVID-19 decreases the risk of ED presentation and hospital admission within 30 days of diagnosis.
Keywords: antibodies, monoclonal; bamlanivimab; casirivimab; COVID-19; imdevimab; SARS-CoV-2

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Key Points

• Ambulatory patients with COVID-19 treated with monoclonal antibodies (mAbs) were significantly less likely than those not treated with mAbs to present to the emergency department (ED) or be admitted to the hospital within 30 days.

• There was no significant difference in the risk of death or admission to the intensive care unit in ambulatory patients treated with mAbs as compared to those who were not treated with mAbs.

• Among patients who received mAb therapy for COVID-19, there was an increased protective effect against ED presentation and hospitalization when mAb therapy was given within 5 days of symptom onset.
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created a worldwide crisis and resulted in a global pandemic. Infections can range in severity from asymptomatic or mild disease to respiratory failure, hospitalization, and even death. The pandemic has stimulated research and development in the prevention and treatment of coronavirus disease 2019 (COVID-19). Major advancements have been made in the development of effective vaccines, new antiviral medications, and neutralizing monoclonal antibody (mAb) therapies.

Neutralizing antibodies are essential components to protective immunity for most viral diseases and may play a therapeutic and preventative role in the fight against COVID-19. Preclinical studies of neutralizing antibody treatments for SARS-CoV-2 infection in several animal models showed reductions in viral loads in the upper and lower respiratory tracts.\(^1\)

In late 2020, 2 mAb therapies were granted emergency use authorization (EUA) by the Food and Drug Administration (FDA)—bamlanivimab and casirivimab/imdevimab. Also granted EUA by FDA were sotrovimab (in May 2021) and bebtelovimab (in February 2022). These are mAbs against the spike glycoprotein that mediates viral cell entry.\(^2,3\) Antibodies to the viral spike protein prevent viral binding to the angiotensin-converting enzyme 2 on many cell types, thereby inhibiting viral entry.\(^4\) In March 2021, given an increased prevalence of variants with decreased susceptibility to bamlanivimab alone, the EUA for bamlanivimab was revoked and replaced with an EUA for a combination monoclonal antibody, bamlanivimab/etesevimab.\(^5\) And now, in areas with a high prevalence of the omicron BA2 variant, bebtelovimab is being used instead due to its greater capacity for neutralization of this variant.
According to the initial EUAs, these monoclonal antibodies are specifically indicated for patients 12 years of age or older at increased risk for severe COVID-19. They are not authorized for use in patients with increased oxygen requirements in the context of COVID-19 or in patients who are hospitalized due to COVID-19. However, the initial EUAs were expanded to also include postexposure prophylaxis in patients at risk for severe disease.\textsuperscript{6}

Although the pharmaceutical randomized clinical controlled trials formed the basis for the FDA EUA,\textsuperscript{7-11} a recent Cochrane review of COVID-19 mAb therapies, which included 6 randomized controlled studies with over 17,495 participants, found the data available to be insufficient to draw meaningful conclusions about the SARS-CoV-2 monoclonal neutralizing antibodies.\textsuperscript{12} One retrospective study of bamlanivimab alone found that mAb-treated patients with COVID-19 had a statistically significant decrease in 28-day hospitalizations relative to propensity-matched controls.\textsuperscript{13} Similarly, another retrospective study of casirivimab/imdevimab with 696 treated patients found a significant decrease in hospitalization rates at 14, 21, and 28 days.\textsuperscript{14} Beyond these studies, data on clinical outcomes for bamlanivimab, bamlanivimab/etesevimab, casirivimab/imdevimab, sotrovimab, and bebtelovimab outside of the clinical trial setting are lacking.\textsuperscript{5,9,15} This study seeks to provide real-world data on outcomes with the use of bamlanivimab, bamlanivimab/etesevimab, and casirivimab/imdevimab during a study period prior to the emergence of the highly prevalent omicron variant.

\textbf{Methods}

The study was conducted within an academic medical center with 3 campuses in Manhattan, Brooklyn, and Long Island, NY.
Data collection. In this retrospective cohort study, study data were obtained from the electronic health record (Epic Systems, Verona, WI), which is an integrated electronic health record including all inpatient and outpatient visits in the health system that includes the study sites.

Patients older than 12 years old who tested positive for COVID-19 at the primary study site or were treated with COVID-19–specific therapy (inclusive of mAb therapy) at the study site between November 24, 2020, and May 15, 2021, were included. Patients who tested positive for COVID-19 but were not treated with mAb therapy comprised the control group.

Data were collected on the date of COVID-19 diagnosis and at subsequent emergency department (ED) visits, admissions, transfers to an intensive care unit (ICU) or hospice care and upon death within 30 days of the documented date of COVID-19 diagnosis. For patients in the mAb group, the date of symptom onset was collected in the electronic medication order in order to ensure mAb administration within the EUA guidelines. Adverse events were tracked through the institutional safety incident reporting system, which tracks medication-related adverse events. Other patient health data such as tobacco use, body mass index (BMI), comorbidities, insurance, the number of ambulatory visits, and utilization of the online patient portal were gathered from the electronic health record, including, when applicable, data entered during previous inpatient or outpatient visits. Patients in both groups were excluded from the analysis if they presented to the ED or were admitted within the median number of days between diagnosis and mAb infusion (2.5 days). This study was approved by the health system’s institutional review board.

Matching and statistical methods. Matching was based on age, gender, race, payer group, smoking status, body mass index (BMI), and comorbid conditions, including cardiac
and pulmonary disease as well as chronic kidney disease, diabetes, and cancer (Table 1). Patients were also matched by number of ambulatory visits at the health system as well as use of the patient-facing portal of the electronic health record, MyChart (Epic Systems), to control for connectivity to the health system. In order to control for the temporal confounders with changing variants, in this study patients in the mAb group were matched to patients who did not receive mAb therapy but tested positive within 7 days of the mAb patient’s positive test date. Of note, because of the weighted matching process, reported values for outcomes include fractions.

To minimize the impact of confounders of treatment, clustered propensity score matching based on the approach of Arpino and Cannas was used. First, a propensity score for receiving mAb therapy was developed using the eXtreme Gradient Boosting (xGBoost) algorithm. xGBoost was adopted after the more traditional logistic regression performed poorly for this task. Next, patients were matched, using 1-to-1 matching, to a similar patient (in terms of propensity score) within the same time period using the CMatching package of R statistical software (R Foundation for Statistical Computing, Vienna, Austria). The standardized mean difference (SMD) was used to assess the comparability of mAb and non-mAb groups for each variable. As is common practice, an SMD of <0.1 was considered a good match, and an SMD between 0.1 and <0.2 was considered a cautious match. Finally, in order to estimate the relative risk of the outcome for the mAb group versus the control group, a marginal structural model was developed for the risk of outcomes with a quasi-binomial transfer function. Weights for the model were supplied by the CMatching package.

Propensity score matching is only valid if the ignorability assumption holds, that is, if there are no unmeasured confounders. In any real-world observational study this
assumption is challenging to justify. Therefore, VanderWeele and Ding’s methodology \cite{23} was used to estimate the minimum strength of association that an unmeasured confounder (expressed as a relative risk [RR]) would need to have with both the treatment and the outcome to fully explain away a specific treatment-outcome association, conditional on the measured covariates. This measure is known as an E-value. A large E-value implies that considerable unmeasured confounding would be needed to explain away an effect estimate. While there are no formal thresholds for E-values, VanderWeele and Ding suggested that an E-value greater than 2 is robust and a value greater than 3 is very robust.

Results

A total of 1,628 patients with diagnosed COVID-19 were treated with mAb therapy. The 15,381 patients who tested positive for SARS-CoV-2 during the study period but did not receive mAb therapy were matched to the patients who tested positive for SARS-CoV-2 and received mAb therapy. Patients were excluded from the analysis if they presented to the ED or were admitted within 2.5 days of testing positive, the median number of days between diagnosis and mAb infusion. With this exclusion, there were 1,354 mAb-treated patients and 9,009 patients who did not receive mAb therapy. Ten patients who received mAb therapy were unable to be matched, and the remaining 1,344 patients were included in further analysis. As reported in Table 1, before matching all but one variable had an SMD of >0.2, indicating a poor match. The largest SMD was 0.986, for temperature. After the matching process, the largest SMD was 0.198, for both temperature and age. Fourteen variables where in the good-match range, and 4 variables were in the cautious-match range.

The mean age in the mAb group was 59.5 years. Patients who received mAb therapy were predominately non-Hispanic white (70.8%), but other represented races/ethnicities
included Asian, Hispanic, and African American. No race/ethnicity was recorded for 6.1% of the patients who received mAb therapy. The most common comorbidities in this population included hyperlipidemia (64.5%) and hypertension (63.1%); 40.6% of individuals were former or current smokers and 51.3% were overweight or obese. The median time from diagnosis to mAb infusion was 2.5 days. Notably, in this population no serious adverse events were reported in connection with mAb therapy. There were 6 reports of flushing or redness during or immediately after the mAb infusion, with none of these events requiring discontinuation of therapy.

Among patients who received mAb therapy, an ED visit or hospitalization admission was more likely in patients who received mAb therapy more than 5 days from symptom onset (P = 0.017; Figure 1). There were no statistical differences in rates of ED presentation or hospitalization within 30 days between patients who received mAb therapy at 1, 2, 3, or 4 days from symptom onset (P = 0.812 for all comparisons).

Within 30 days of diagnosis, among the patients who received mAb therapy, 101 (7.5%) presented to the ED and 79 (5.9%) were admitted. Among the patients who did not receive mAb therapy, 165 (12.3%) presented to the ED and 156 (11.6%) were admitted (RR, 0.61 [95% CI, 0.5-0.75] and 0.51 [95% CI, 0.4-0.64], respectively). Four mAb-treated patients (0.3%) and 2.64 control patients (0.2%) were admitted to the ICU (RR, 01.51; 95% CI, 0.45-5.09). Six mAb-treated patients (0.4%) and 3.37 controls (0.3%) died or were admitted to hospice care (RR, 1.61; 95% CI, 0.54-4.83) (Table 2). The E-values for ED presentation and admission were 2.66 and 3.55, respectively.
Discussion

In this retrospective cohort study, we examined the impact of COVID-19 mAb therapy on presentation to the ED, hospital admission, ICU admission, and death or hospice admission within 30 days of diagnosis in a cohort of patients with a COVID-19 diagnosis or treated for COVID-19 at an academic medical center in New York. This study was limited to bamlanivimab, bamlanivimab/etesevimab, and casirivimab/imdevimab, as these were the mAbs used during the study period, prior to the omicron wave. We found that ambulatory patients with COVID-19 who were treated with mAbs were significantly less likely to present to the ED or to be admitted to the hospital than nontreated patients with COVID-19 matched on demographics, comorbidities, and timing of infection.

We found a 39% reduction in presentations to the ED and a 49% reduction in admissions in patients with COVID-19 treated with mAb therapy as compared to matched patients with COVID-19 who did not receive mAb therapy. Further supporting the significance of the study's results, the effect size in this study, as approximated by the E-values, suggests that a very strong confounder or bias in our study design would be required to reverse the significant findings in this study.

These results are consistent with data from randomized controlled trials. In a phase 3 study including 1,035 patients who were randomly assigned to receive bamlanivimab/etesevimab or a placebo, by day 29 there was a relative risk difference of 70% for hospitalization or death between those who did and those who did not receive mAb therapy ($P < 0.001$). In another randomized placebo-controlled trial of bamlanivimab/etesevimab in ambulatory patients with COVID-19, patients treated with mAb therapy had a significantly decreased rate of COVID-19–related hospitalization or any-
cause death. This is also consistent with the findings of a retrospective cohort study that found that patients with COVID-19 who received bamlanivimab had lower all-cause hospitalization rates than propensity-matched patients at days 14 (1.5% vs 3.5%; odds ratio [OR], 0.38), 21 (1.9% vs 3.9%; OR, 0.46), and 28 (2.5% vs 3.9%; OR, 0.61). Echoing the findings in this study, data from a randomized controlled study of casirivimab/imdevimab indicated a 71.3% relative reduction in hospitalization risk ($P < 0.0001$) and a shorter median time to symptom resolution in mAb-treated patients as compared to controls. A few uncontrolled retrospective studies have also shown some protective effect of casirivimab/imdevimab. In one study of 68 patients, 10% of patients treated with the mAb combination product re-presented to the ED and 2% were hospitalized for COVID-19 by 14 days. And a larger retrospective cohort study of 698 patients who received casirivimab/imdevimab found significant reductions in hospitalization at 14, 21 and 28 days.

The RR values for admission to the ICU and for death or hospice care were not statistically significant in our study, which may suggest that mAb therapy may be less effective in preventing progression to severe disease requiring ICU admission. That said, our study was likely underpowered to assess these rare outcomes, since ICU admission only occurred in 0.2% of the non-mAb group and 0.3% of the mAb group and death or hospice admission only occurred in 0.3% of the non-mAb group and 0.4% of the mAb group.

Additionally, the results of this study showed increased protective effect against ED presentation and hospitalization when mAb therapy was given within 5 days of COVID-19 symptom onset ($P = 0.017$). This suggests that despite possible challenges to obtaining mAb in a timely fashion and EUA authorizations within the first 7 days of symptom onset, it is advisable to treat as early as possible.
As COVID-19 variants evolve, SARS-CoV-2 virulence and susceptibility to neutralization by mAb therapy has also changed. For example, one study found that the mutations in the receptor binding domain in the South African (501Y.V2) and Brazilian (501Y.V3) variants abolished binding of bamlanivimab in vitro. Consequently, on the basis of variant prevalence, FDA briefly paused the EUA for bamlanivimab/etesevimab because more than 5% of reported strains were resistant to the combination. The EUA was later reinstated as bamlanivimab/etesevimab was found to be effective in neutralization of the delta variants (B.1.617.2, AY.1, and AY.2). Then, with the rise in the omicron variant, FDA recommended use of sotrovimab and, later, bebtelovimab rather than bamlanivimab/etesevimab or casirivimab/imdevimab in areas with high circulation of the omicron variant. While our study was performed before the emergence of the omicron variant, in order to attempt to control for the impact of changing COVID variants, patients in the mAb group were matched to those who did not receive mAb therapy but tested positive for COVID-19 within 7 days of the mAb-treated patient’s positive test date.

While additional patient demographics were used for a rigorous matching process to control for confounders, one limitation in the study design is that we were unable to capture data on patients who may have presented to the ED, been admitted, or died outside of our hospital network. Although it may be assumed that patients who were receiving COVID-19 care at our medical center would receive follow-up care at one of our 3 hospital locations and that there was no a priori difference in likelihood of in-network follow-up between the groups, it is possible that based on patient geography or other factors, patients received follow-up care elsewhere. To account for this possible bias, patients were matched between the groups based on MyChart (online patient portal) utilization as well as number
of ambulatory care encounters to help to ensure that patients in the 2 groups were equally connected to the healthcare system.

We were unable to reliably obtain patients’ vaccination status in our data collection. Although vaccination may be a confounder since it mitigates the risk of hospitalization, we suspect the vast majority of our patient population in this study was not fully vaccinated. The study extended from November 2020 to April 2021. In New York, vaccination only became widely available to patients over 30 years of age on March 31, 2021, and to adults over 16 years of age on April 6. In January 2021, after the vaccination program was first launched, it was restricted to patients based on comorbidities and age, which were criteria for matching in our study protocol; this restriction may have contributed to controlling for vaccination status.

Additionally, we did not have data on the severity of patients’ COVID-19 at the time of testing, such as oxygen saturation data. It is possible that patients who were sicker at the time of diagnosis may have been more likely to get mAb therapy, which, if true, would only strengthen the protective effects found in this study. To further control for this, however, we excluded patients who were admitted or presented to the ED within 2.5 days of diagnosis, the median number of days in the mAb group between diagnosis and infusion, and matched the patients. This also helped to control for possible baseline differences in disease severity by eliminating patients who were quickly decompensating and may have, as a result, differentially sought out mAb therapy.

Notably, this study provides real-world data on clinical outcomes in ambulatory patients with COVID-19 treated with mAb medications, including bamlanivimab, bamlanivimab/etesevimab, and casirivimab/imdevimab, as compared to a matched cohort of patients who did not receive mAb therapy. Since this study combined the results for
multiple mAb products over an approximately 6-month period associated with changes in SARS-CoV-2 variants, specific conclusions about the relative efficacy of the specific antibodies cannot be made. However, the strong effect on ED presentation and hospitalization suggests that mAbs, as a therapeutic modality, may have an important role in our COVID-19 therapeutic armamentarium. As we have seen with the omicron variant, the specific mAb that is most effective in neutralizing SARS-CoV-2 will likely continue to change over time as variants shift and evolve. Nevertheless, the results of this study suggest that mAb therapy may have protective effects against SARS-CoV-2. In the setting of insufficient vaccination rates, breakthrough infections among the vaccinated, and the unclear future of SARS-CoV-2 variants, additional studies are needed to further understand the impact of mAb therapy in the treatment of COVID-19 in ambulatory patients.
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Table 1. Patient Characteristics Before and After Matching

| Characteristic                  | Before matching | Post matching |
|--------------------------------|-----------------|---------------|
|                                | No mAb (n = 9,009) | mAb (n = 1,354) | SM D | No mAb (n = 1,344) | mAb (n = 1,344) | SM D |
| Age, mean (SD), years          | 41.44 (20.44)    | 59.52 (15.35) | 0.7 | 56.13 (18.71) | 59.52 (15.35) | 0.1 |
| Male gender                    | 4,269 (47.4)     | 650 (48)      | 0.0 | 629 (46.8) | 645 (48.0) | 0.0 |
| Race/ethnicity                 | 0.4             | 65            |     |                  | 0.0            | 93   |
| Asian                          | 517 (5.7)        | 85 (6.3)      | 73.5 | 84 (6.3) |
| Hispanic                       | 559 (6.2)        | 77 (5.7)      | 69.5 | 76 (5.7) |
| Non-Hispanic African American  | 915 (10.2)       | 94 (6.9)      | 89.3 | 93 (6.9) |
| Non-Hispanic white             | 4,724 (52.4)     | 958 (70.8)    | 1,000.6 | 952 (70.8) |
| Other/multiracial              | 649 (7.2)        | 58 (4.3)      | 49.6 | 58 (4.3) |
| Unknown                        | 1,645 (18.3)     | 82 (6.1)      | 61.5 | 81 (6.6) |
| Payer group                    | 0.5             | 0.0           | 52   | 44       |
| Commercial                     | 4,539 (50.4)     | 448 (33.1)    | 426.8 | 445 (33.1) |
| Medicaid                       | 1,209 (13.4)     | 104 (7.7)     | 106.2 | 103 (7.7) |
| Medicare                       | 1,130 (12.5)     | 362 (26.7)    | 348.4 | 359 (26.7) |
| Other                          | 27 (0.3)         | 1 (0.1)       | 1 (0.1) | 1 (0.1) |
| Condition                          | Value (Mean) | Value (SD) | Value (Mean) | Value (SD) | Value (Mean) | Value (SD) |
|-----------------------------------|--------------|------------|--------------|------------|--------------|------------|
| Uninsured/self-pay                | 212 (2.4)    | 5 (0.4)    | 5 (0.4)      | 5 (0.4)    |              |            |
| Unknown                           | 1,892 (21)   | 434 (32.1) | 456.6 (34)   | 431 (32.1) |              |            |
| Coronary artery disease           | 505 (5.6)    | 292 (21.6) | 0.4          | 79         | 267 (19.9)   | 290 (21.6) | 0.0         | 42         |
| Heart failure                     | 187 (2.1)    | 95 (7)     | 0.2          | 39         | 94.3 (7)     | 94 (7)     | <0.001      |            |
| Hyperlipidemia                    | 2,467 (27.4) | 874 (64.5) | 0.8          | 04         | 806 (60)     | 868 (64.6) | 0.0         | 95         |
| Hypertension                      | 2,052 (22.8) | 854 (63.1) | 0.8          | 91         | 800 (59.5)   | 848 (63.1) | 0.0         | 73         |
| Diabetes                          | 869 (9.6)    | 423 (31.2) | 0.5          | 56         | 384.1 (28.6) | 420 (31.3) | 0.0         | 58         |
| Pulmonary disease                 | 1,202 (13.3) | 379 (28)   | 0.3          | 68         | 307.7 (22.9) | 376 (28)   | 0.1         | 17         |
| CKD                               | 220 (2.4)    | 125 (9.2)  | 0.2          | 93         | 113.2 (8.4)  | 124 (9.2)  | 0.0         | 29         |
| Cancer                            | 614 (6.8)    | 222 (16.4) | 0.3          | 03         | 193.6 (14.4) | 220 (16.4) | 0.0         | 55         |
| Smoking status                    |              |            | 0.5          | 58         | 0.0          | 98         |
| Current                           | 635 (7)      | 161 (11.9) | 125.1 (9.3)  | 160 (11.9) |              |            |
| Former                            | 1,323 (14.7) | 389 (28.7) | 378.2 (28.1) | 386 (28.7) |              |            |
| Never, including passive exposure | 5,458 (60.6) | 748 (55.2) | 792.1 (58.9) | 742 (55.2) |              |            |
| Unknown                           | 1,593 (17.7) | 56 (4.1)   | 48.6 (3.6)   | 56 (4.2)   |              |            |
| BMI (kg/m²)                       |              |            |              |            | 0.7          | 0.0        | 87         |
| <30                               | 4,249 (47.2) | 566 (41.8) | 605.5 (45.1) | 562 (41.8) |              |            |
| ≥40                               | 401 (4.5)    | 168 (12.4) | 150.9 (11.2) | 167 (12.4) |              |            |
| 30 to <40                         | 1,858 (20.6) | 527 (38.9) | 516.2 (38.4) | 523 (38.9) |              |            |
| Unknown                           | 2,501 (27.8) | 93 (6.9)   | 71.5 (5.3)   | 92 (6.8)   |              |            |
| Temperature, °C | 0.9 | 0.1 |
|----------------|-----|-----|
|                | 86  | 98  |

|                | 2.0 | 2.0 |
|                | 0.1 | 0.1 |

|                | 189.6 | 210 |
|                | 14.1  | 15.6 |

|                | 7.9   | 8.0  |
|                | 0.6   | 0.6  |

|                | 807.0 | 342  |
|                | 60.0  | 25.4 |

| No. of ambulatory care encounters, mean (SD) | 4.41 (8) | 9.23 (12.4) | 0.4 | 7.2 (11.68) | 9.23 (12.4) | 0.1 |
|---------------------------------------------|---------|-------------|-----|------------|-------------|-----|
|                                             | 61      | 66          |    |            |             |    |

| No. of MyChart sessions, mean (SD) | 2,768.15 | 5,963.58 | 0.2 | 4,534.6 | 5,963.58 | 0.0 |
|------------------------------------|----------|----------|-----|---------|----------|-----|
|                                    | (9,113.79) | (19,808.7) | 07 | (17,925.88) | (19808.6) | 76 |

| Date tested for COVID-19 | 0.8 | <0. |
|--------------------------|-----|-----|
|                          | 10  | 001 |

|                | 14 (1.0) | 14 (1) |
|                | 134 (10.0) | 134 (10) |
|                | 368 (27.4) | 368 (27.4) |
|                | 343 (25.5) | 343 (25.5) |
|                | 330 (24.6) | 330 (24.6) |
|                | 139 (10.3) | 139 (10.3) |
|                | 16 (1.2) | 16 (1.2) |

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; SMD, standardized mean difference.

*All values are No. (%) unless indicated otherwise.
Table 2. Results of Outcomes Sensitivity Analysis\textsuperscript{a}

| Outcome                              | Before matching and weighting | Post matching and weighting | E-value\textsuperscript{b} |
|--------------------------------------|------------------------------|-----------------------------|-----------------------------|
|                                      | No mAb (n = 9,009) | mAb (n = 1,354) | No mAb (n = 1,344) | mAb (n = 1,344) | Absolute difference, % | Relative risk (CI) | \( P \) value | Estimate | LC | I |
| ED presentation within 30 days        | 268 (3.0) | 101 (7.5) | 165 (12.3) | 101 (7.5) | -4.8 | 0.61 | <0.001 | 2.66 | 2.01 |
| Hospital admission within 30 days     | 190 (2.1) | 79 (5.8) | 156 (11.6) | 79 (5.9) | -5.7 | 0.51 | <0.001 | 3.35 | 2.51 |
| ICU admission within 30 days          | 28 (0.3) | 4 (0.3) | 2.64 (0.3) | 4 (0.3) | 0.1 | 1.51 | 0.5 | 0.04 | 0.05 |
| Death or hospice admission within 30 days | 14 (0.2) | 6 (0.4) | 3.73 (0.4) | 6 (0.4) | 0.2 | 1.61 | 0.3 | 0.54 | 4.83 |

Abbreviations: LCI, lower bound of CI; mAb, monoclonal antibody.

\textsuperscript{a}This analysis excluded mAb-treated patients with an outcome event between the date of a positive COVID-19 test and the mAb order date and non-mAb patients who experienced an outcome event within the median time to an event in the mAb group (2.5 days).

\textsuperscript{b}The E-value is the minimum strength of both the confounder associations that must be present, above and beyond the measured covariates, for an unmeasured confounder to explain an association. E-values were not calculated for estimates whose CI crossed 1.
**Figure 1.** Rate of emergency department (ED) visit or hospitalization admission by days from symptom onset to monoclonal antibody (mAb) administration in the study cohort. Error bars represent 95% CIs.