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Does monoclonal antibody treatment for COVID-19 impact short and long-term outcomes in a large generalisable population? A retrospective cohort study in the USA

Daniel Griffin 1,2, Chace McNeil, 3 James Okusa, 3 Diana Berrent, 4 Yinglong Guo, 3 Sarah E Daugherty 3

ABSTRACT

Objectives To explore whether monoclonal antibodies (MAb) administered to high-risk patients with COVID-19 during the first week of illness prevent postacute sequelae of SARS-CoV-2 infection.

Design Retrospective cohort study.

Setting USA.

Participants A sample of 3809 individuals who received MAb and a matched one-to-one comparison group from a set of 327,079 eligible patients who did not receive MAb treatment were selected from a deidentified administrative data set from commercial and Medicare Advantage health plan enrollees in the USA, including claims and outpatient laboratory data.

Results Individuals who received MAb were 28% less likely to be hospitalised (HR=0.72, 95% CI 0.58 to 0.89) and 41% less likely to be admitted to the intensive care unit (HR=0.59, 95% CI 0.38 to 0.89) 30 days from SARS-CoV-2 diagnosis compared with individuals who did not receive MAb. A higher proportion of individuals given MAb therapy received care for clinical sequelae in the postacute phase (p=0.018).

Conclusions While MAb therapy was associated with benefits in the acute period, the benefit of therapy did not extend into the postacute period and did not reduce risk for clinical sequelae.

INTRODUCTION

The first cases of COVID-19 caused by SARS-CoV-2 were reported in late December 2019 and a number of interventions to address both acute and long-term consequences have been developed. 1 Vaccination has emerged as the most important and effective strategy; however, there are a number of individuals who remain at increased risk of poor outcomes due to choice, access issues, inability to tolerate vaccination or an impaired immune system limiting vaccination response. 2 Certain other vaccinated individuals remain at increased risk of poor outcomes despite vaccination due to advanced age or comorbidities such as obesity, diabetes mellitus, hypertension, malignancy, chronic renal disease, chronic cardiovascular or pulmonary disease. Monoclonal antibody (MAb) therapy emerged as a therapy that can provide passive immunity to these individuals who remain at high risk. 3 Although small-molecule antivirals such as remdesivir, nirmatrelvir-ritonavir and molnupiravir have been introduced, MAb therapy was a frequently used therapeutic in high-risk patients when still active against circulating strains.

A number of animal studies and prior experience with other diseases provided encouraging data, suggesting that treatment with SARS-CoV-2-specific antibody therapy might provide benefit in the treatment of COVID-19. 4-6 Several small randomised controlled studies provided evidence that MAb therapy was effective at reducing the risk of progression to hospitalisation and death if administered within the first 10 days of illness. 7-11 It is not clear whether MAb has the same impact on acute disease with real-world delivery and when different viral variants are prevalent. 12 There is less information on the longer term...
health outcomes among individuals with SARS-CoV-2 infection.

While most individuals infected with SARS-CoV-2 are able to avoid hospitalisation or death, some individuals are left with significant new clinical sequelae 30 days after acute infection.13-15 This can result in a number of disabling symptoms, an increased incidence of new medical diagnoses and, in some cases, a syndrome referred to as postacute sequelae of COVID-19 (PASC) or Long COVID, defined by WHO as COVID-19 symptoms that last for at least 3 months after diagnosis.16 While initially recognised by the Centers for Disease Control and Prevention and the National Institutes of Health, it is now clear to many that Long COVID or PASC is an important endpoint for COVID-19 therapeutics.17

We compared the risk of 30-day and 90-day hospitalisations and incident clinical sequelae among individuals aged 12 years and older who were and were not treated with MAb therapy after being diagnosed with SARS-CoV-2. This study provides real-world evidence of the benefits and limitations of MAb therapy from a large generalisable sample in the USA for both acute and postacute sequelae.

METHODS
Data source
We conducted a retrospective cohort analysis using OptumLabs’ deidentified administrative claims data from Medicare Advantage and commercially insured health plan enrollees in the USA. The database contains medical (emergency, inpatient and outpatient) and pharmacy claims for services submitted for third-party reimbursement, available as International Classification of Diseases, Tenth Revision (ICD-10), Clinical Modification and National Drug Codes claims, respectively. These claims are aggregated after completion of care encounters and submission of claims for reimbursement. We also included laboratory results, where available. Data are available on reasonable request.

Study population
The study population consisted of individuals 12 years and older who were enrolled in either a commercial or Medicare Advantage plan and were diagnosed with SARS-CoV-2 between 9 November 2020 and 31 May 2021. The index date was the first date of either (1) a primary, secondary or tertiary clinical diagnosis of COVID-19 identified by ICD-10 code U07.1 in administrative claims; or (2) documentation of a positive PCR test in an outpatient laboratory data set. To identify comorbidities that would determine eligibility for MAb therapy and allow appropriate matching for controls, individuals were required to have at least 6 months of continuous enrolment in their health insurance plan prior to index date (n=184674 were excluded). Individuals who did not meet one of the Food and Drug Administration’s (FDA) Emergency Use Authorization (EUA) eligibility criteria16 for receipt of MAb therapy at index date were removed (n=104374). These criteria included those considered under the EUA at the time of study entry (see online supplemental table 1 for ICD-10 codes): age 65 or older, body mass index (BMI) of 35 or greater, type 1 or type 2 diabetes, chronic kidney disease, immunosuppressive disease, receiving immunosuppressive treatment, or age 55 or older and at least one of the following: heart disease, hypertension, chronic obstructive pulmonary disease, other chronic respiratory disease. Individuals were also excluded if they were on a special needs plan (n=46057) or had inconsistent or missing values for demographic variables (n=789) (figure 1).

MAb therapy administration
Individuals who received MAb therapy through intravenous administration were identified by Healthcare Common Procedure Coding System (HCPCS) procedure codes Q0239, M0239, Q0240, M0240, M0241, Q0243, M0243, Q0244, M0244, Q0245, M0245 and M0246. Individuals who received MAb treatment outside of the FDA EUA-specified 10-day window after initial diagnosis (n=146) were excluded from the analysis. Different formulas of MAb therapy were approved by the FDA at different time points depending on clinical trial evidence and variant circulation. Only individuals who received MAb therapy within the EUA window were included in the analysis (bamlanivimab only (9 November 2020 to 6 April 2021), casirivimab/imdevimab (21 November 2022 to end of study), bamlanivimab/etesevimab (4 February 2021 to end of study), resulting in n=79 being excluded. This meant that per the EUA limitations, <10% of circulating variants at the time in each region were resistant to the administered MABs. A sample of 3809 individuals were identified for the treatment arm of the analysis. There were 11 individuals in the treatment group for whom an adequate match (matching criteria described in the next section) could not be found. The final matched analytical sample was 3798 patients treated with MAB therapy.

Comparison group
From the set of 327079 eligible patients who did not receive MAB therapy, we created a one-to-one matched comparison group that did not receive MAB therapy (any COVID-19 treatment other than MAb therapy was allowed) using propensity score matching. During this period, there was still very limited access to Mabs such that the vast majority of acutely infected patients were not being treated with MABs. Individuals were required to have similar index dates (date±14 days) and similar ages (±5 years) and age buckets (<65 years or ≥65 years) (table 1). Additionally, because individuals were required by the EUA to not be hospitalised between the diagnosis and treatment date, to ensure similar health and hospitalisation status between those who received MAB therapy and those who did not, each individual in the comparison group was randomly assigned a “hypothetical” no-hospitalisation period drawn from the paired MAB therapy group, reflecting the period of time between index date.
Figure 1 Population sampling and exclusions for study comparison groups. EUA, Emergency Use Authorization; FDA, Food and Drug Administration; MAb, monoclonal antibody.
<table>
<thead>
<tr>
<th>Variable</th>
<th>MAb therapy matched group n (%)</th>
<th>Standard of care matched comparison group n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean (SD))</td>
<td>60.5 (13.4)</td>
<td>60.3 (13.3)</td>
<td>0.43</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1911 (50.3)</td>
<td>1871 (49.3)</td>
<td>0.36</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>1298 (34.2)</td>
<td>1288 (33.9)</td>
<td>0.81</td>
</tr>
<tr>
<td>Suburban</td>
<td>1366 (36.0)</td>
<td>1455 (38.3)</td>
<td>0.035*</td>
</tr>
<tr>
<td>Rural</td>
<td>1134 (29.9)</td>
<td>1055 (27.8)</td>
<td>0.045*</td>
</tr>
<tr>
<td>Census region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>333 (8.8)</td>
<td>380 (10.0)</td>
<td>0.064</td>
</tr>
<tr>
<td>Midwest</td>
<td>760 (20.0)</td>
<td>679 (17.9)</td>
<td>0.018*</td>
</tr>
<tr>
<td>South</td>
<td>2153 (56.7)</td>
<td>2221 (58.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>West</td>
<td>552 (14.5)</td>
<td>518 (13.6)</td>
<td>0.26</td>
</tr>
<tr>
<td>Business line</td>
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<tr>
<td>Commercial</td>
<td>2788 (73.4)</td>
<td>2764 (72.8)</td>
<td>0.53</td>
</tr>
<tr>
<td>Medicare</td>
<td>1015 (26.7)</td>
<td>1037 (27.3)</td>
<td>0.57</td>
</tr>
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<td>MAb eligibility criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥65</td>
<td>1380 (36.3)</td>
<td>1380 (36.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>BMI ≥35</td>
<td>758 (20.0)</td>
<td>657 (17.3)</td>
<td>0.0029*</td>
</tr>
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<td>Type 1 diabetes</td>
<td>1485 (39.1)</td>
<td>1473 (38.8)</td>
<td>0.78</td>
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<tr>
<td>Type 2 diabetes</td>
<td>170 (4.5)</td>
<td>144 (3.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>440 (11.6)</td>
<td>433 (11.4)</td>
<td>0.80</td>
</tr>
<tr>
<td>Immunosuppressive disease</td>
<td>2963 (78.0)</td>
<td>2886 (76.0)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Receiving immunosuppressive treatment</td>
<td>353 (9.3)</td>
<td>330 (8.7)</td>
<td>0.36</td>
</tr>
<tr>
<td>Age ≥55 and at least one of the following:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease</td>
<td>375 (9.9)</td>
<td>336 (8.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2713 (71.4)</td>
<td>2787 (73.4)</td>
<td>0.058</td>
</tr>
<tr>
<td>COPD</td>
<td>1062 (28.0)</td>
<td>1046 (27.5)</td>
<td>0.68</td>
</tr>
<tr>
<td>Other chronic respiratory disease</td>
<td>146 (3.8)</td>
<td>121 (3.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>Elixhauser Comorbidity Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality score (mean (SD))</td>
<td>3.3 (6.4)</td>
<td>3.1 (6.4)</td>
<td>0.32</td>
</tr>
<tr>
<td>Readmission score (mean (SD))</td>
<td>11.8 (14.6)</td>
<td>10.7 (14.6)</td>
<td>0.0011*</td>
</tr>
<tr>
<td>Claims-derived variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Care Provider (PCP) visits in 6 months prior to diagnosis (mean number of visits (SD))</td>
<td>3.1 (4.2)</td>
<td>2.9 (4.4)</td>
<td>0.093</td>
</tr>
<tr>
<td>Nephrologist visits in 6 months prior to diagnosis (mean number of visits (SD))</td>
<td>0.1 (0.9)</td>
<td>0.1 (0.8)</td>
<td>0.96</td>
</tr>
<tr>
<td>Cardiologist visits in 6 months prior to diagnosis (mean number of visits (SD))</td>
<td>0.4 (1.3)</td>
<td>0.4 (1.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>Inpatient hospital days in 6 months prior to diagnosis (mean number of days (SD))</td>
<td>0.3 (2.9)</td>
<td>0.3 (2.6)</td>
<td>0.88</td>
</tr>
<tr>
<td>Claims-derived variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bamlanivimab</td>
<td>2851 (75.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bamlanivimab-etesevimab</td>
<td>353 (9.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REGN-COV2</td>
<td>594 (15.6%)</td>
<td></td>
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</tbody>
</table>

Continued
and treatment date when no hospitalisation could occur. Individuals in the comparison group were not considered a match if they were hospitalised during this assigned no-hospitalisation period. The final matched comparison group contained 3798 patients who did not receive MAb therapy. The EUA for nirmatrelvir/ritonavir did not go into effect until December 2021 so no patients in the comparator group received this antiviral. Early outpatient remdesivir use has been very limited so it is unlikely that many in either group received this therapy.

Main outcomes
The primary outcome for this study was 30-day hospitalisation. Secondary outcomes included any hospitalisations out to 90 days but we also broke these 90 days down into those after 30 days but before 90 days for hospitalisations between 31 and 90 days after SARS-CoV-2 diagnosis; and similarly with intensive care unit (ICU) admissions within 30 days, within 90 days and then after 30 days but prior to the end of 90 days (the 31–90 days of ICU admissions). Exploratory analysis also evaluated diagnosis of postacute clinical sequelae including mental health conditions, Diabetes Mellitus Type-II (DM-II), hypertension, fatigue, hypercoagulability, renal, arrhythmia, amnesia, encephalopathy, respiratory and congestive heart failure known to be associated with SARS-CoV-2 in this adult population (see online supplemental table 2 for ICD-10 codes). Events were only ascertained on or after the treatment date (matched comparator was assigned a hypothetical ‘treatment date’ based on matched pair treatment date) through the end of the period of interest. All events that occurred prior to the treatment date were not included.

Hospitalisation events were identified in claims by indicating an inpatient stay. ICU admissions were identified by procedure codes 0200–0203, 0207–0212 and 0219.

Study variables
All variables used for analysis were derived from administrative claims and member characteristics associated with plan enrolment. The following variables were used to generate a propensity score: gender (male, female), geography (census region (Northeast, North Central, South, West)), locale (urban, suburban, rural), baseline Elixhauser Comorbidity Index with mortality and hospital readmission scores (both continuous), baseline chronic conditions (conditions used to determine MAb eligibility), measurements of healthcare utilisation (Primary care provider (PCP), nephrologist and cardiologist visits in 6 months prior to index date) and total number of inpatient days in 6 months prior to index date. Additional details on the propensity score are discussed in the Statistical methods section.

Statistical methods

Propensity score matching
The one-to-one matching process selected a comparator with the closest propensity score for each individual who received MAb therapy. Propensity scores were calculated using a logistic regression model predicting MAb treatment for the population of members diagnosed with COVID-19 within the study timeframe. Predictors for the model included demographics and clinical information, and matches were obtained using a calliper of 0.1. The balance between MAb therapy and comparator groups was assessed by comparing distributions of demographics and prevalence rates for common comorbidities. A plot of standardised mean differences was used to compare group balance before and after matching (see figure 2).

Data analysis

Demographic and clinical factors were evaluated using univariate t-tests for continuous variables, while percentages were compared using proportion z-tests. Differences in the number of clinical sequelae during 0–30 days, 31–90 days and then 0–90 days were evaluated using χ² tests. Any clinical diagnoses that occurred prior to the index date were not counted. Logistic regression was used to calculate ORs and 95% CIs for the main outcomes of 30-day and 90-day hospitalisations and ICU admissions. For each of the individual clinical sequelae, HRs and corresponding 95% CIs were calculated using a Cox proportional hazards model. Individuals were censored by event of interest, death, disenrollment from the insurance plan or end of 30-day or 90-day period.

Patient and public involvement
We partnered with the founder and senior leader of Survivor Corps, a US-based advocacy for patients with COVID-19 and non-profit organisation. As a coauthor on this paper, she provided substantive feedback on the analytical plan and draft manuscript.

RESULTS
Of the 330 888 eligible SARS-CoV-2-diagnosed individuals, 3809 (1.2% of the eligible population) underwent

<table>
<thead>
<tr>
<th>Variable</th>
<th>MAb therapy matched group n (%)</th>
<th>Standard of care matched comparison group n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median days to treatment (IQR)</td>
<td>1 (3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Difference when compared with treatment group is statistically significant (p<0.05).

BMI, body mass index; COPD, chronic obstructive pulmonary disease; MAb, monoclonal antibody.

Individuals who received MAb therapy were more likely than the total eligible population with SARS-CoV-2 to be younger, male, commercially insured, have BMI >35, have type 1 or type 2 diabetes, be receiving immunosuppressive treatment, have hypertension under age 55, have a lower risk of mortality and hospital readmission based on the Elixhauser Comorbidity Index, have slightly fewer PCP visits and have a shorter mean number of inpatient hospital days (online supplemental table 3). Few differences were seen in demographic and clinical factors within the analytical population between the matched MAb-treated individuals and the comparison group (all p>0.05), with the exception of living in suburban or rural areas (p=0.04), residing in the Midwest (p=0.018), having a BMI ≥35 (p=0.003), having immunosuppressive disease (p=0.036) and having Elixhauser Comorbidity Index scores for readmission (p=0.0011) (table 1). A total of 2851 individuals (75%) were treated with bamlanivimab, 594 (15.6%) were given REGEN-COV2, and 353 (9.3%) were given bamlanivimab/etesevimab (table 1).

In the first 30 days after SARS-CoV-2 diagnosis, 156 individuals (4.1%) were hospitalised due to COVID-19 after receiving MAb therapy versus 213 individuals (5.6%) in the comparison group (OR=0.72, 95% CI 0.58 to 0.89). In addition, individuals who received MAb therapy experienced a greater reduction in ICU admission (0.9%) than individuals in the comparison group (1.5%) (OR=0.59, 95% CI 0.39 to 0.91). No significant differences were seen by therapy status for hospitalisation (OR=1.19, 95% CI 0.84 to 1.69) or ICU admittance (OR=0.81, 95% CI 0.45 to 1.44) in the postacute period (31–90 days) (table 2).

While no differences were seen in the number of clinical sequelae during the first 30 days (p=0.50) (table 3),

Figure 2  Standardised mean differences for all matching variables before and after propensity score matching. AHRQ, Agency for Healthcare Research and Quality; BMI, body mass index; PCP, Primary Care Provider.
Table 2 ORs for 30-day and 90-day hospitalisations and ICU admittance comparing SARS-CoV-2-diagnosed individuals who received MAb therapy versus standard of care. OptumLabs’ deidentified administrative claims

<table>
<thead>
<tr>
<th></th>
<th>0-30 day from SARS-CoV-2 diagnosis</th>
<th>0-90 day from SARS-CoV-2 diagnosis</th>
<th>31-90 day from SARS-CoV-2 diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospitalisation</td>
<td>ICU</td>
<td>Hospitalisation</td>
</tr>
<tr>
<td></td>
<td>Events (%)</td>
<td>OR (95% CI)</td>
<td>Events (%)</td>
</tr>
<tr>
<td>MAb therapy (n=3798)</td>
<td>156 (4.1)</td>
<td>0.72 (0.58-0.89)*</td>
<td>34 (0.9)</td>
</tr>
<tr>
<td>Standard of care comparison group (n=3798)</td>
<td>213 (5.6)</td>
<td></td>
<td>77 (2.0)</td>
</tr>
</tbody>
</table>

*statistically significant difference in odds ratio (OR).

DISCUSSION

Principal findings

We conducted a large retrospective cohort analysis evaluating risk for hospitalisation, ICU admission and incident clinical sequelae during the acute and postacute periods among individuals 12 years and older who did and did not receive MAb therapy after SARS-CoV-2 diagnosis. We observed a 28% reduction in 30-day hospitalisation and a 41% reduction in 30-day ICU admittance, but no significant reduction in risk during the postacute period (31–90 days). We also observed a statistically significant elevation in the proportion of new clinical sequelae among individuals who were treated compared with those who were not treated with MAb in the postacute period, though no significant association by type of clinical sequelae was identified in either period. Our results suggest that MAb therapy does not likely provide protection from developing clinical sequelae due to SARS-CoV-2.

Comparison with other studies

Our results are consistent with several clinical trials and a small retrospective study that all demonstrate the efficacy of MAb therapy at reducing 29-day hospitalisation. The magnitude of the protective association observed in our study (28%), however, is smaller than what has been previously reported. The 30-day hospitalisation rate of our comparison group is lower (5.6%) than the 29-day hospitalisation rate (15%) observed in the placebo arm among a high-risk subset of individuals (BMI ≥ 35 years or ≥ 65 years) in the bamlanivimab trial, despite our population being selected based on EUA criteria and having a significant comorbidity profile. The hospitalisation rate of the comparison group was similar, however, to the placebo arm of all patients in the bamlanivimab trial (6.3%) and the prevalence of 29-day medically attended visits (6%) in the REGN-COV2 trial. This lower rate of hospitalisation may be partly explained by the comparison group being matched to the treatment group, which tended to be healthier than individuals in the general population who were MAb eligible (see online supplemental table 3).

The hospitalisation rate among those who received MAb therapy in our study (4.1%) was higher than the rates reported in the treatment arm of the REGN-COV2 trial (3%), the bamlanivimab/etezolimab trial (2.1%) and a retrospective study evaluating REGN-COV2 within the Mayo healthcare system (1.6%), where care may have been more closely monitored. This may partially be explained by the increased effectiveness of REGN-COV2 and bamlanivimab-etezolimab across a wider variety of variants, but is more likely a result of the real-world

a significantly higher proportion of individuals who were given MAb treatment sought medical care for one or more clinical sequelae in the postacute phase (p=0.018) (table 4).

There were no significant interactions observed between therapy status and age or gender during either period (tables 3 and 4; all p>0.4). In an exploratory analysis evaluating types of clinical sequelae, no significant differences were observed in risk when comparing those who did and did not receive MAb therapy in either the acute or postacute period (figure 3, table 5).
nature of our data source collected across multiple health systems among high-risk individuals with multiple comorbidities.

**Strengths and limitations**

Few studies to date have evaluated the impact of MAb therapy on longer term hospitalisation and considered risk for incident clinical sequelae by therapy status in a large generalisable sample. Although we did not evaluate a long list of clinical sequelae and symptoms in our exploratory analysis, we considered the most significant clinical sequelae that required medical attention previously found to be elevated in this population of individuals diagnosed with SARS-CoV-2. Symptoms other than fatigue were not included because administrative claims do not allow for easy identification of these symptoms. Because our assessment of sequelae was claims based, our estimates could be impacted by care-seeking behaviours of patients as well as by the coding behaviour of providers. Providers may not have coded certain diagnoses due to lack of prioritisation of symptoms or diagnoses. Moreover, during the study period there were factors that may have limited access to care, such as lockdowns and risk avoidance behaviours, potentially leading to underascertainment of events and calculated risk. We were also not able to obtain reliable information on vaccination status using claims as going through insurance was not required for a large portion of individuals. Our study was done during the time period of 1 November 2020 through 31 May 2021 when vaccination was just becoming accessible to non-healthcare workers. Although this study was well powered to detect a difference in our primary outcome—30-day hospitalisation—it was underpowered to detect associations with individual clinical sequelae. Thus, we cannot rule out the possibility of small but important long-term differences due to MAb therapy that may have been missed. While inequities in administration were likely given the healthier status of individuals who received MAb therapy relative to the larger MAb-eligible population, we were not able to explore these socioeconomic inequities and their health implications in our data. We were also not able to evaluate racial differences because our commercial health plan data do not include...

### Table 3

<table>
<thead>
<tr>
<th>Cohort number of sequelae</th>
<th>MAb therapy group Events/total (%)</th>
<th>SOC comparison group Events/total (%)</th>
<th>Comparison of 90-day sequelae prevalence rates Diff % (95% CI)</th>
<th>P value for $\chi^2$ test</th>
<th>P value for interaction in ANOVA test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>3502/3798 (92.2)</td>
<td>3480/3798 (91.6)</td>
<td>0.6 (−0.6, 1.8)</td>
<td>0.50</td>
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<tr>
<td>1–2 sequelae</td>
<td>283/3798 (7.5)</td>
<td>300/3798 (7.9)</td>
<td>−0.4 (−1.6, 0.7)</td>
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<tr>
<td>≥3 sequelae</td>
<td>13/3798 (0.3)</td>
<td>18/3798 (0.5)</td>
<td>−0.1 (−0.4, 0.2)</td>
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<tr>
<td>Age (years)</td>
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</tr>
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<td>≥65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.49</td>
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<tr>
<td>No sequelae</td>
<td>1,246/1,380 (90.3)</td>
<td>1,228/1,380 (89.0)</td>
<td>1.3 (−1.0, 3.6)</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>1–2 sequelae</td>
<td>127/1,380 (9.2)</td>
<td>140/1,380 (10.1)</td>
<td>−0.9 (−3.1, 1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 sequelae</td>
<td>7/1,380 (0.5)</td>
<td>12/1,380 (0.9)</td>
<td>−0.4 (−1.0, 0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
</tr>
<tr>
<td>No sequelae</td>
<td>2256/2418 (93.3)</td>
<td>2252/2418 (93.1)</td>
<td>0.2 (−1.3, 1.6)</td>
<td>0.97</td>
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<tr>
<td>1–2 sequelae</td>
<td>156/2418 (6.5)</td>
<td>160/2418 (6.6)</td>
<td>−0.2 (−1.6, 1.2)</td>
<td></td>
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<tr>
<td>≥3 sequelae</td>
<td>6/2418 (0.2)</td>
<td>6/2418 (0.2)</td>
<td>0.0 (−0.3, 0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
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<td></td>
<td></td>
<td>0.59</td>
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<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>1763/1911 (92.3)</td>
<td>1709/1871 (91.3)</td>
<td>0.9 (−0.8, 2.7)</td>
<td>0.34</td>
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<td>1–2 sequelae</td>
<td>142/1911 (7.4)</td>
<td>151/1871 (8.1)</td>
<td>−0.6 (−2.3, 1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 sequelae</td>
<td>6/1911 (0.3)</td>
<td>11/1871 (0.6)</td>
<td>−0.3 (−0.7, 0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>1739/1887 (92.2)</td>
<td>1771/1927 (91.9)</td>
<td>0.3 (−1.5, 2.0)</td>
<td>0.95</td>
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</tr>
<tr>
<td>1–2 sequelae</td>
<td>141/1887 (7.5)</td>
<td>149/1927 (7.7)</td>
<td>−0.3 (−1.9, 1.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 sequelae</td>
<td>7/1887 (0.4)</td>
<td>7/1927 (0.4)</td>
<td>0.0 (−0.4, 0.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ANOVA, analysis of variance; MAb, monoclonal antibody; SOC, standard of care.
individual-level race variables. We limited our analysis to 90 days, so there is the possibility that significant differences by therapy status could occur with longer follow-up. Finally, our numbers did not allow for an evaluation of associations by type of MAb therapy or by timing of administration, though these factors would be important potential modifiers for future larger studies to consider. It is possible that we were not able to accurately gauge the 10-day treatment window using administrative claims. Claims can identify the date of SARS-CoV-2 diagnosis but not symptom onset, potentially causing us to include some individuals who were given MAb therapy after the 10-day window, reducing the effectiveness of the treatment. While we excluded many patients who were given MAbs outside of the EUA it is possible that we did not exclude all of these. It is also possible that there is a small impact on PASC and that a larger study or a different study design such as using a 1:2 or 1:3 could have increased the power to detect a statistically significant but perhaps not clinically relevant difference.

ICU admissions were identified through claims data, and we would expect some variability based on hospital thresholds for admission to the ICU, rather than a consistent level of required pulmonary support. While there are currently no available effective MAb therapy for COVID-19 as data become available on the impact of early small-molecule antiviral therapy this will be a relevant comparison.

**Policy implications**
Our findings could inform public health policy and the allocation of resources regarding how acute COVID-19 and the long-term sequelae are approached. As MAb therapy continues to be widely used for the treatment of acute COVID-19 and alternative therapies may have differential impacts on PASC or Long COVID this information is very timely for making decisions about different treatment choices. While hospitalisations, ICU admissions and deaths are a significant concern with SARS-CoV-2 infection, the number of people with postacute sequelae from COVID-19 may impact an even larger number of individuals for a greater period of time. If instead of measures to decrease case numbers, the use of MAbs is substituted, we may end up with more cases of Long

---

### Table 4
Proportion of clinical sequelae in 31–90 days comparing SARS-CoV-2-diagnosed individuals who received MAb therapy versus standard of care, OptumLabs’ deidentified administrative claims

<table>
<thead>
<tr>
<th>Cohort number of sequelae</th>
<th>MAb therapy group</th>
<th>SOC comparison group</th>
<th>Comparison of 90-day sequelae prevalence rates</th>
<th>P value for proportions test</th>
<th>P value for interaction in ANOVA test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events/total (%)</td>
<td>Events/total (%)</td>
<td>Diff % (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>3488/3798 (91.8)</td>
<td>3547/3798 (93.4)</td>
<td>−1.6 (−2.7, −0.4)</td>
<td>0.018</td>
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<tr>
<td>1–2 sequelae</td>
<td>291/3798 (7.7)</td>
<td>241/3798 (6.3)</td>
<td>1.3 (0.2, 2.5)</td>
<td></td>
<td></td>
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<tr>
<td>≥3 sequelae</td>
<td>19/3798 (0.5)</td>
<td>10/3798 (0.3)</td>
<td>0.2 (−0.0, 0.5)</td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>1242/1380 (90.0)</td>
<td>1266/1380 (91.7)</td>
<td>−1.7 (−3.9, 0.4)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>1–2 sequelae</td>
<td>127/1380 (9.2)</td>
<td>106/1380 (7.7)</td>
<td>1.5 (−0.6, 3.6)</td>
<td></td>
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</tr>
<tr>
<td>≥3 sequelae</td>
<td>11/1380 (0.8)</td>
<td>8/1380 (0.6)</td>
<td>0.2 (−0.4, 0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>2246/2418 (92.9)</td>
<td>2281/2418 (94.3)</td>
<td>−1.4 (−2.8, −0.1)</td>
<td>0.035</td>
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</tr>
<tr>
<td>1–2 sequelae</td>
<td>164/2418 (6.8)</td>
<td>135/2418 (5.6)</td>
<td>1.2 (−0.2, 2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 sequelae</td>
<td>8/2418 (0.3)</td>
<td>2/2418 (0.1)</td>
<td>0.2 (−0.0, 0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>1771/1911 (92.7)</td>
<td>1769/1871 (94.5)</td>
<td>−1.9 (−3.4, −0.3)</td>
<td>0.042</td>
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<tr>
<td>1–2 sequelae</td>
<td>133/1911 (7.0)</td>
<td>94/1871 (5.0)</td>
<td>1.9 (0.4, 3.4)</td>
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</tr>
<tr>
<td>≥3 sequelae</td>
<td>7/1911 (0.4)</td>
<td>8/1871 (0.4)</td>
<td>−0.1 (−0.5, 0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sequelae</td>
<td>1717/1887 (91.0)</td>
<td>1778/1927 (92.3)</td>
<td>−1.3 (−3.0, 0.5)</td>
<td>0.017</td>
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<td>1–2 sequelae</td>
<td>158/1887 (8.4)</td>
<td>147/1927 (7.6)</td>
<td>0.7 (−1.0, 2.5)</td>
<td></td>
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</tr>
<tr>
<td>≥3 sequelae</td>
<td>12/1887 (0.6)</td>
<td>2/1927 (0.1)</td>
<td>0.5 (0.1, 0.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ANOVA, analysis of variance; MAb, monoclonal antibody; SOC, standard of care.
COVID and turn short-term gains into long-term losses. It may seem effective relative to short-term outcomes to focus on expanded access to MAbs, but a greater strain on our healthcare system and suffering resulting from failure to prevent Long COVID may result. It remains unclear if other therapies, such as antiviral medications, may have the ability to impact the risk for Long COVID but data, published and posted in preprint form, are emerging to suggest a potential impact.25 26 If newer antiviral therapies have the added impact of preventing Long COVID, they may end up being preferred on this basis. When comparing small-molecule antiviral agents and other COVID therapeutics, the impact on Long COVID should be studied and considered in treatment recommendations.

**CONCLUSION**

While used in high-resource settings, treatment of acute COVID-19 with MAb therapy does not appear to have a beneficial impact on the risk of clinical sequelae. Further studies with longer term follow-up should be performed to verify that there is not an impact that our study failed to identify. Other COVID therapeutics, such as the now available small-molecule antivirals, should undergo a similar study to determine their impact on the development of Long COVID.

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**Competing interests** None declared.
Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This research was determined to be exempt from human research regulations by the United Health Group Office of Human Research Affairs (Action ID: 2021-0057-01).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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REFERENCES