Outcomes of Monoclonal Antibody Use in Patients with COVID-19

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Abstract

Background: Since early 2021, monoclonal antibody (mAb) therapy has emerged as an efficacious intervention for patients with mild-to-moderate COVID-19 infections, particularly those at high risk of progressing to more severe infections. With favorable results from clinical trials, the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorizations for a series of mAb treatments. As these therapeutic agents became readily available, clinicians and researchers embarked on comprehensive investigations into their impact on hospitalization rates and mortality outcomes.

Objective: This study delves deeper into the effectiveness of accessible mAb therapies and their synergistic interactions with COVID-19 vaccinations in mitigating rehospitalization and mortality over a span of 19 months, within the encompassing landscape of greater Seattle in western Washington.

Methods: We conducted an IRB-approved retrospective chart review of non-hospitalized adult patients who presented to emergency departments (ED) in the greater Seattle area from March 2021 through October 2022, exhibiting with mild-to-moderate COVID-19 infections and met eligibility criteria for monoclonal antibody therapy, having at least one of the following active comorbidities: arrythmia, cancer, cardiovascular dysfunction, diabetes, immunosuppression, obesity, renal dysfunction, a respiratory disorder, and/or tobacco use. We compared outcomes of patients who were treated with monoclonal antibodies to eligible patients who were not treated. Primary outcomes were rates of 28-day rehospitalization and all-cause hospital mortality. Secondary outcomes were rates of hospital inpatient admission, intensive care unit admission, and necessity for mechanical ventilation. We used propensity score matching and logistic regression models to isolate the effect of monoclonal antibody treatment on the outcome variables controlling for demographic characteristics and comorbidities. All statistical analyses were done in R Studio, and the MatchIt package was used for propensity score matching.

Results: A total of 21,139 patients were included in the analysis. In the matched cohorts (mAb treated: N = 1,349; untreated: N = 1,349), mAb treatment was associated with reduced significantly odds of 28-day rehospitalization (adjusted odds ratio [aOR] 0.66, [95% confidence interval (CI)] 0.49-0.87), P = 0.004), mortality (adjusted odds ratio [aOR] 0.32, [95% confidence interval (CI)] 0.19-0.51), P < 0.001), and inpatient admissions (adjusted odds ratio [aOR] 0.43, [95% confidence interval (CI)] 0.31-0.61), P < 0.001).

Conclusions: From March 2021 through October 2022, monoclonal antibodies emerged as a pivotal factor in significantly reducing the incidence of rehospitalization, mortality, and inpatient admission amongst patients with mild-to-moderate COVID-19 infections in western Washington. Our study contributes real-world evidence to the medical literature, reaffirming the efficacy of monoclonal antibodies as a therapeutic option for outpatients with mild-to-moderate COVID-19 who are at an increased risk of developing severe infection. In light of the evolving landscape of the COVID-19 pandemic, marked by changing variants, the efficacy of individual mAb agents should continue to be vigilantly evaluated.

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1. Introduction

Since early 2021, monoclonal antibody (mAb) therapy has emerged as an efficacious intervention for patients with mild-to-moderate COVID-19 infections, particularly those at high risk of progressing to more severe infections. With favorable results from clinical trials, the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorizations for a series of mAb treatments: casirivimab-imdevimab (REGEN-COV) in November 2020 [1, 2], bamlanivimab plus etesevimab (BAM+ETE) in February 2021 [3, 4], sotrovimab (SOT) in May 2021 [5, 6], then bebtelovimab (BEB) in February 2022 [7, 8].

As these therapeutic agents became readily available, clinicians and researchers embarked on comprehensive investigations into their impact on hospitalization rates and mortality outcomes. In spring 2021, bamlanivimab was associated with reduced rehospitalizations and, in most cases, mortality within 28 days [9, 10, 11, 12]. Later, in the fall of 2021, sotrovimab use also seemed to decrease odds of hospitalization and mortality [13, 14]. Later studies of bebtelovimab use, however, found mixed results [15, 16].

More recent studies have examined the effect of all available agents, along with COVID vaccinations, on patient outcomes over a longer period of the pandemic. These studies have also found decreased odds of rehospitalization and mortality in treated patients across phases of the pandemic [17, 18].

This study delves deeper into the effectiveness of accessible mAb therapies and their synergistic interactions with COVID-19 vaccinations in mitigating rehospitalization and mortality over a span of 19 months, within the encompassing landscape of greater Seattle in western Washington.

2. Methods

2.1 Patient population

We conducted a propensity-matched, retrospective, observational study using data from our

electronic medical record system (EHR; Epic). This study was approved by the institutional review board of Providence-St. Joseph Health Care, a large multistate healthcare organization. Individual patient consent was not required. The setting for this study was Providence Swedish Health Services, a regional healthcare network in the Puget Sound area of western Washington which includes approximately 1,570 licensed beds. The network includes seven emergency departments (ED's) that were host to 221,000 ED visits in 2022.

We identified a study population of adult patients who were eligible for monoclonal antibody therapy. Our inclusion criteria were adult outpatients who presented to an ED in the greater Seattle area from March 25, 2021 (the date of the first mAb administration) through October 31, 2022, exhibiting mild-to-moderate SARS-CoV-2 infections and met eligibility criteria for mAb therapy, having at least one of the following active comorbidities: arrythmia, cancer, cardiovascular dysfunction, diabetes, immunosuppression, obesity, renal dysfunction, a respiratory disorder, and/or tobacco use. We excluded patients who lacked all of the aforementioned comorbidities, who received oxygen therapy on their first ED visit, and/or who were admitted to the hospital on their first ED visit. Baseline demographic data we collected included age, sex, and race. We also collected acuity levels and dates of COVID-19 vaccinations.

2.2 Outcomes

Our two primary outcomes were 28-day rehospitalization and all-cause hospital mortality. Secondary outcomes were any days as a hospital inpatient, in intensive care, and/or on mechanical ventilation following discharge from their first ED visit.

2.3 Variable definitions

We defined our first primary outcome of 28-day rehospitalization as admission to an ED or an inpatient hospital admission for a COVID-19-related reason within 28 days of discharge from the first ED visit. We operationalized this outcome as a dichotomy in which 1 indicated readmission to an ED or hospital within 28 days and 0 all others. Our second primary outcome of mortality we

defined as all-cause hospital mortality, and this we measured as a dichotomy in which 1 indicated all-cause hospital mortality in the time between discharge from the ED visit and the end of the study period, and 0 all others. We defined a COVID-19-related reason as either (1) a positive SARS-CoV-2 lab test undertaken within the hospital encounter, (2) a SARS-CoV-2 infection documented in the ED infectious risk screening, and/or (3) a COVID-19-related ED encounter diagnosis using ICD10 codes (U00, U09, U49, U50, U85, J12.82, M35.81, Z20.822). To account for historical change in the pandemic, we calculated the time in months from the date of the first mAb approval (November 21, 2020) to the date of the hospital encounter (whether an ED visit or inpatient admission). Because our secondary outcomes (post-ED inpatient days as inpatient, days in ICU, and days on mechanical ventilation) were skewed, we measured these as dichotomies in which 1 indicated any inpatient days, ICU days, and/or mechanical ventilation days, and 0 all others.

Our covariates of interest included sex, race, age, comorbidities, mAb treatment status, acuity level, and number of vaccinations at the first ED visit. We coded sex as a dichotomy in which a value of 1 indicated male and 0 female, and race as a dichotomy in which 1 = nonwhite and 0 = white. We dichotomized age into patients below or at least 65 years of age at the time of the hospital encounter. For comorbidities we used ICD10 codes on the patient problem list. We coded each comorbidity as a dichotomy in which 1 indicated active presence within the study period and 0 nonpresence. We identified mAb-treated patients from documented administrations of mAb infusions on the first ED visit. Treatments included bamlanivimab, casirivimab + imdevimab, bamlanivimab + etesevimab, sotrovimab, and bebtelovimab. Acuity level we coded into the following 4-point ordinal scale of increasing urgency: 1 = Non-urgent, 2 = Less urgent, 3 = Urgent, 4 = Emergent or Immediate. Finally, we measured vaccination status as the cumulative count of documented COVID-19 vaccination dates received by the hospital encounter.

2.4 Statistical analysis

We first reported baseline characteristics and clinical indicators for the treated and untreated

patients both before and after propensity score matching. We reported as descriptive statistics means and standard deviations for continuous variables and frequencies and percentages for categorical variables.

We estimated propensity scores for receipt of mAb therapy using the 1:1 nearest neighbor method without replacement with logistic regression. We matched on the factors shown in the descriptive analyses to be statistically significant differences between the treated and untreated patients in the full unmatched sample. These factors included age, race, immunosuppression, renal disorder, respiratory disorder, tobacco use, months into availability of mAb treatment, acuity level, and number of vaccinations. To estimate the treatment effect and its standard error, we fit logistic regression models for our outcomes on mAb treatment and any covariates remaining unbalanced after propensity score matching. We conducted all statistical analyses in RStudio [19]. For propensity score matching we used the MatchIt package [20].

3. Results

Between March 2021 and October 2022, a total of 21,139 patients met our inclusion criteria and were included the study. Upon propensity matching, 1,349 patients were included in the primary matched cohort (1,349 mAb-treated; 1,349 untreated). The propensity score matching diminished the imbalance in most of the key covariates, including age, race, immunosuppression, renal disorder, respiratory disorder, tobacco use, months into availability of mAb treatment, acuity level, and number of vaccinations. However, the propensity matched sample did differ significantly in months into mAb availability and number of COVID-19 vaccinations. Measures of association are available in Table 1.

Table 1

Patient Characteristics and Covariate Balance Before and After Propensity Matching

	Before propensity matching			After propensity matching		
Characteristic	Treated, N = 1,349[1]	Untreated, N = 19,790[1]	*p*-value[2]	Treated, N = 1,349[1]	Untreated, N = 1,349[1]	*p*-value[2]
Male	636 (47%)	8,273 (42%)	<0.001	636 (47%)	614 (46%)	0.400
Nonwhite	387 (29%)	7,743 (39%)	<0.001	387 (29%)	367 (27%)	0.400
Age 65+	805 (60%)	7,286 (37%)	<0.001	805 (60%)	839 (62%)	0.200
Arrythmia	305 (23%)	3,150 (16%)	<0.001	305 (23%)	296 (22%)	0.700
Cancer	186 (14%)	1,801 (9.1%)	<0.001	186 (14%)	174 (13%)	0.500
Cardiovascular disease	777 (58%)	8,965 (45%)	<0.001	777 (58%)	744 (55%)	0.200
Diabetes	250 (19%)	2,814 (14%)	<0.001	250 (19%)	233 (17%)	0.400
Immunosuppressed	136 (10%)	603 (3.0%)	<0.001	136 (10%)	140 (10%)	0.800
Obese	522 (39%)	8,679 (44%)	<0.001	522 (39%)	537 (40%)	0.600
Renal disease	275 (20%)	2,460 (12%)	<0.001	275 (20%)	255 (19%)	0.300
Respiratory disease	452 (34%)	7,040 (36%)	0.120	452 (34%)	412 (31%)	0.100
Tobacco user	47 (3.5%)	2,206 (11%)	<0.001	47 (3.5%)	34 (2.5%)	0.140
Months since mAb approval	15 (5)	13 (5)	<0.001	15 (5)	14 (5)	0.001
Acuity level			<0.001			0.130
Non-urgent	5 (0.4%)	179 (0.9%)		5 (0.4%)	14 (1.0%)	
Less urgent	173 (13%)	3,168 (16%)		173 (13%)	156 (12%)	
Urgent	923 (68%)	11,756 (59%)		923 (68%)	916 (68%)	
Emergent or Immediate	248 (18%)	4,687 (24%)		248 (18%)	263 (19%)	
COVID vaccinations			<0.001			0.040
0	1,298 (96%)	18,256 (92%)		1,298 (96%)	1,299 (96%)	
1	14 (1.0%)	420 (2.1%)		14 (1.0%)	19 (1.4%)	
2	4 (0.3%)	408 (2.1%)		4 (0.3%)	8 (0.6%)	
3	9 (0.7%)	489 (2.5%)		9 (0.7%)	14 (1.0%)	

	Before propensity matching			After propensity matching		
Characteristic	Treated, N = 1,349[1]	Untreated, N = 19,790[1]	*p*-value[2]	Treated, N = 1,349[1]	Untreated, N = 1,349[1]	*p*-value[2]
4	24 (1.8%)	217 (1.1%)		24 (1.8%)	9 (0.7%)	

[1] n (%/); Mean (SD)
[2] Pearson's Chi-squared test; Wilcoxon rank sum

3.1 Characteristics of the mAb patients in the primary cohort

In the propensity-matched cohort, mAb-treated patients reflected characteristics consistent with patients at high risk for progression to severe COVID-19 (Table 1). Among patients who received mAb therapy (n = 1,349), 805 (60%) were aged 65 years or older, 387 (29%) were nonwhite, 136 (10%) were immunosuppressed, 275 (20%) suffered from renal disorders, and 452 (34%) suffered from respiratory disorders.

3.2 Primary and secondary outcomes

The crude rates of rehospitalization, mortality, and inpatient outcomes are shown in Table 2. During the study period, the incidence of 28-day hospitalization in our primary matched cohort was 9.4% (n = 127/1,349) for untreated patients compared to 6.3% (n = 85/1,349) among mAb-treated patients. The mortality rate for untreated patients was 5.3% (n = 41/1,349) compared to 1.7% (n = 23/1,349) for mAb-treated patients. The rate of inpatient admission for untreated patients was 8.6% (n = 116/1,349) compared to 3.8% (n = 51/1,349) for mAb-treated patients. Rates of ICU and mechanical ventilation did not differ significantly by treatment group.

In the adjusted analyses, treatment with mAb was associated with reduced odds of 28-day rehospitalization (adjusted odds ratio [aOR] 0.66, [95% confidence interval (CI)] 0.49-0.87), $P = 0.004$). Mortality rates also differed significantly between the two groups, with mAb treatment associated with reduced odds of mortality (adjusted odds ratio [aOR] 0.32, [95% confidence interval (CI)] 0.19-0.51), $P < 0.001$). mAb treatment was also associated with significantly reduced odds of inpatient admissions (adjusted odds ratio [aOR] 0.43, [95% confidence interval (CI)] 0.31-0.61), $P <$

0.001).

Table 2

Primary and Secondary Outcomes for Primary Matched Cohort

Characteristic	Treated	Untreated	*p*-value[2]	Adjusted odds ratio (95% confidence interval	*p*-value
Overall sample size	1,349[1]	1,349[1]			
Primary outcomes					
28-Day Readmission	85 (6.3%)	127 (9.4%)	0.003	0.66 (0.49 – 0.87)	0.004
Mortality	23 (1.7%)	71 (5.3%)	<0.001	0.32 (0.19 – 0.51)	<0.001
Secondary outcomes					
Any inpatient days	51 (3.8%)	116 (8.6%)	<0.001	0.43 (0.31 – 0.61	<0.001
Any ICU days	10 (0.7%)	20 (1.5%)	0.066		
Any ventilator days	4 (0.3%)	4 (0.3%)	>0.900		

[1] n (%)
[2] Pearson's Chi-squared test
Regression models adjusted for months since mAb approval at first ED visit and number of COVID vaccinations received by first ED visit.

4. Discussion

This study evaluated the effect of mAb therapy for outpatient use with mild-to-moderate COVID-19 on 28-day rehospitalization, all-cause hospital mortality, and inpatient admissions over a 19-month period in a major metropolitan area in western Washington. In a sample of propensity-matched treated and untreated patients, mAb treatment was associated with significantly reduced odds of 28-day rehospitalization, all-cause hospital mortality, and inpatient admissions. These findings are consistent with the literature on mAbs in real-world settings and contribute further real-world evidence of the effectiveness of mAbs in treating outpatients with mild-to-moderate COVID-19 infections.

While not the primary focus of this paper, it is illuminating to look at the initial differences between treated and non-treated patients with an eye to understanding physicians' decision making in

these cases. Conspicuously, patients who were immunosuppressed were roughly over four times more likely to receive monoclonal treatment. Additionally, treated patients were likely to be older, have cancer and cardiovascular disease more frequently, and had fewer vaccinations. So clearly physicians were targeting the most vulnerable ED patients for monoclonal antibody treatment.

Another thought-provoking aspect of this paper is our focus on patients with mild to moderate COVID-19 symptoms. While these patients had reported to an ED for treatment, they were not hospitalized. We can therefore assume that the treating physicians believed their patients had milder instances of COVID-19 infections. This would suggest that our results might underestimate monoclonal treatment benefits with more severe COVID-19 infections. Although plausible, we are unable to examine this possibility with this data set.

4.1 Strengths

This study has several strengths by virtue of occurring within a single hospital system. All of the data are collected in a limited geographic area, thereby limiting regional differences, potential differences in strain exposure, differences in ED guidelines or hospital procedures, and differences in ED access to monoclonal treatment over the course of the pandemic. Additionally, propensity matching succeeded in rendering an untreated sample that was in many respects virtually identical to the treated sample.

4.2 Limitations

However, this study is limited in several notable ways. First, given the retrospective nature of this study, which relied entirely on pre-existing information documented in the electronic medical record, all eligibility for monoclonal antibodies were based on the provider who evaluated the patient and were there for not double checked for accuracy. Patients who may have qualified for a monoclonal antibody were not offered treatment based on the provider’s discretion.

5. Conclusion

From March 2021 through October 2022, monoclonal antibodies emerged as a pivotal factor

in significantly reducing the incidence of rehospitalization, mortality, and inpatient admission amongst patients with mild-to-moderate COVID-19 infections in western Washington. Our study contributes real-world evidence to the medical literature, reaffirming the efficacy of monoclonal antibodies as a therapeutic option for outpatients with mild-to-moderate COVID-19 who are at an increased risk of developing severe infection. In light of the evolving landscape of the COVID-19 pandemic, marked by changing variants, the efficacy of individual mAb agents should continue to be vigilantly evaluated.

Declaration of Competing Interests

The authors have no competing interests to declare.

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Ethical approval

The Providence-St. Joseph Health System Institutional Review Board approved this study with a waiver of written informed consent.

Author Contributions

DS and HB conceived the study. DS, HB, JH, and JS formulated the study design and methodology. JH collected and analyzed the data. DS and JH drafted the manuscript, and all authors contributed substantially to its revision. JH, HB, JS, and DS take responsibility for the paper as a whole.

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References

[1] O'Shaughnessy JA. Emergency use authorization 091. Accessed February 2, 2024. https://www.fda.gov/media/145610/download
[2] Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, Xiao J, Hooper AT, Hamilton JD, Musser BJ, Rofail D. REGEN-COV antibody combination and outcomes in outpatients with Covid-19. N Engl J Med. 2021 Dec 2;385(23):e81. https://doi.org/10.1056/NEJMoa2108163
[3] O'Shaughnessy JA. Emergency use authorization 094. Accessed February 2, 2024. https://www.fda.gov/media/145801/download
[4] Dougan M, Azizad M, Mocherla B, Gottlieb RL, Chen P, Hebert C, Perry R, Boscia J, Heller B, Morris J, Crystal C. A randomized, placebo-controlled clinical trial of bamlanivimab and etesevimab together in high-risk ambulatory patients with COVID-19 and validation of the prognostic value of persistently high viral load. Clin Infect Dis. 2022 Jul 1;75(1):e440-9. https://doi.org/10.1093/cid/ciab912
[5] O'Shaughnessy J. Emergency use authorization 100. Published online 2022. Accessed February 2, 2024: https://www.fda.gov/media/149532/download
[6] Gupta A, Gonzalez-Rojas Y, Juarez E, Casal MC, Moya J, Falci DR, Sarkis E, Solis J, Zheng H, Scott N, Cathcart AL. Effect of sotrovimab on hospitalization or death among high-risk patients with mild to moderate COVID-19: a randomized clinical trial. J Am Med Assoc. 2022 Apr 5;327(13):1236-46. https://doi:10.1001/jama.2022.2832
[7] O'Shaughnessy J. Emergency use authorization 111. Published online 2022. Accessed February 2, 2024: https://www.fda.gov/media/156151/download
[8] Lilly E. A study of immune system proteins in participants with mild to moderate COVID-19 illness. Accessed February 2, 2024: https://clinicaltrials.gov/study/NCT04634409
[9] Bariola JR, McCreary EK, Wadas RJ, Kip KE, Marroquin OC, Minnier T, Koscumb S, Collins K, Schmidhofer M, Shovel JA, Wisniewski MK. Impact of bamlanivimab monoclonal antibody treatment on hospitalization and mortality among nonhospitalized adults with severe acute respiratory syndrome coronavirus 2 infection. In Open Forum Infect Dis 2021 Jul 1 (Vol. 8, No. 7, p. ofab254). US: Oxford University Press. https://doi.org/10.1093/ofid/ofab254
[10] Ganesh R, Pawlowski CF, O'Horo JC, Arndt LL, Arndt RF, Bell SJ, Bierle DM, Borgen MD, Hanson SN, Heyliger A, Larsen JJ. Intravenous bamlanivimab use associates with reduced hospitalization in high-risk patients with mild to moderate COVID-19. J Clin Invest. 2021 Oct 1;131(19). https://doi.org/10.1172/JCI151697
[11] Iqbal L, Terlau TJ, Hernandez A, Woods K, Terlau T, Hernandez AT. Efficacy of bamlanivimab in reducing hospitalization and mortality rates in COVID-19 patients in a rural community. Cureus. 2021 Jul 19;13(7). https://doi.org/10.7759/cureus.16477
[12] Melton III JD, Wilson K, Blind F, Barbera A, Bhisitkul D, Hasara S, Homa K, Karp J, Escowitz H, Haber T, DeGroot D. Impact of early versus late administration of bamlanivimab on readmissions in patients with high-risk COVID-19. Amer J Emer Med. 2021 Dec 1;50:437-41. https://doi.org/10.1016/j.ajem.2021.08.032
[13] Aggarwal NR, Beaty LE, Bennett TD, Carlson NE, Davis CB, Kwan BM, Mayer DA, Ong TC, Russell S, Steele J, Wogu AF. Real-world evidence of the neutralizing monoclonal antibody sotrovimab for preventing hospitalization and mortality in COVID-19 outpatients. J Infect Dis. 2022 Dec 15;226(12):2129-36. https://doi.org/10.1093/infdis/jiac206
[14] Cheng MM, Reyes C, Satram S, Birch H, Gibbons DC, Drysdale M, Bell CF, Suyundikov A, Ding X, Maher MC, Yeh W. Real-world effectiveness of sotrovimab for the early treatment of COVID-19 during SARS-CoV-2 Delta and Omicron waves in the USA. Infect Dis Ther. 2023 Feb;12(2):607-21. https://doi.org/10.1007/s40121-022-00755-0
[15] Molina KC, Kennerley V, Beaty LE, Bennett TD, Carlson NE, Mayer DA, Peers JL, Russell S, Wynia MK, Aggarwal NR, Ginde AA. Real-world evaluation of bebtelovimab effectiveness during

the period of COVID-19 Omicron variants, including BA. 4/BA. 5. Int J Infect Dis. 2023 Jul 1;132:34-9. https://doi.org/10.1016/j.ijid.2023.04.396
[16] Sridhara S, Gungor AB, Erol HK, Al-Obaidi M, Zangeneh TT, Bedrick EJ, Ariyamuthu VK, Shetty A, Qannus AA, Mendoza K, Murugapandian S. Lack of effectiveness of Bebtelovimab monoclonal antibody among high-risk patients with SARS-Cov-2 Omicron during BA. 2, BA. 2.12. 1 and BA. 5 subvariants dominated era. PloS One. 2023 Apr 28;18(4):e0279326. https://doi.org/10.1371/journal.pone.0279326
[17] Wynia MK, Beaty LE, Bennett TD, Carlson NE, Davis CB, Kwan BM, Mayer DA, Ong TC, Russell S, Steele JD, Stocker HR. Real-world evidence of neutralizing monoclonal antibodies for preventing hospitalization and mortality in COVID-19 outpatients. Chest. 2023 May 1;163(5):1061-70. https://doi.org/10.1016/j.chest.2022.10.020
[18] Kip KE, McCreary EK, Collins K, Minnier TE, Snyder GM, Garrard W, McKibben JC, Yealy DM, Seymour CW, Huang DT, Bariola JR. Evolving real-world effectiveness of monoclonal antibodies for treatment of COVID-19: a cohort study. Ann Intern Med. 2023 Apr;176(4):496-504. https://doi.org/10.7326/M22-1286
[19] RStudio Team. RStudio: Integrated development environment for R. Rstudio, PBC, Boston, MA. http://www.rstudio.com
[20] Stuart EA, King G, Imai K, Ho D. MatchIt: nonparametric preprocessing for parametric causal inference. J Stat Softw. 2011. https://doi.org/10.18637/jss.v042.i08