



Variation in use of anti-SARS-CoV-2 monoclonal antibody therapies by social vulnerability and urbanicity

KEY POINTS

- Anti-SARS-CoV-2 monoclonal antibodies are an effective treatment to prevent progression to severe COVID-19 or hospitalization in high-risk individuals.
- Between November 2020 and March 2021, the number of monoclonal antibody doses administered per 100,000 COVID-19 diagnoses at the county level varied significantly across the country.
- Counties with high social vulnerability in terms of socioeconomic status, racial or ethnic minority population, or housing and transportation tended to use monoclonal antibodies at a lower rate during this period compared with other counties.
- Given the disproportionate impact of COVID-19 on specific populations, including racial and ethnic minorities, ensuring equitable distribution and accessibility of these drugs and other therapeutics is a critical tool in combatting COVID-19.

INTRODUCTION

As of December 6, 2021, over 780,000 Americans have lost their lives due to COVID-19. Despite the widespread availability of effective vaccines to prevent COVID-19, the emergence of variants and increasing case rates around the country demonstrate the continued need for effective therapeutics to treat COVID-19, particularly in high-risk patients. Although most therapeutic drugs have been developed for treatment of severely ill, hospitalized patients with COVID-19, anti-SARS-CoV-2 monoclonal antibody therapies have been developed for treatment in an outpatient setting to reduce the likelihood of severe disease in high-risk patients.¹ The FDA issued emergency use authorizations (EUAs) for two monoclonal antibodies in November 2020 for use in adults and children over the age of 12 with mild to moderate COVID-19 who are at risk of progressing to severe COVID-19 and/or hospitalization. The federal government initially distributed doses to states based on case burden and utilization, allowing state health departments to determine which sites within their states would receive the doses. As supply of monoclonal antibodies increased, the federal government shifted to a system that allowed

¹ There are a range of medical conditions and factors that might make an individual at high risk of severe COVID-19. These include, but are not limited to: aged ≥ 65 years, obesity, diabetes, cardiovascular disease, hypertension, and chronic lung diseases. Other risk factors that may warrant consideration of monoclonal antibody therapies are available at: <https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-mono-clonal-antibodies/>, last accessed August 31, 2021.

sites such as hospitals to order doses directly from the distributor.² Since the initial authorization of these therapeutics in November 2020, several additional monoclonal antibodies have received EUAs. Given the potential for monoclonal antibodies to prevent severe COVID-19 and progression to hospitalization, monoclonal antibody therapies have significant benefits for the individual as well as for reducing burden on the healthcare system.

The COVID-19 pandemic has also highlighted disparities in healthcare access and health outcomes. Non-Hispanic American Indian/Alaska Native, non-Hispanic Black, and Hispanic populations are 2-3 times more likely to be hospitalized with or die from COVID-19 compared to non-Hispanic White populations.³ Rural counties, counties with high social vulnerability, and counties that have high percent of population in poverty have the highest death rates per 100,000 population.⁴ These disparities highlight the importance of ensuring that therapeutics like monoclonal antibodies with the potential to keep people out of the hospital and prevent death from COVID-19 are equitably distributed and accessible to those at greatest risk or with limited access to healthcare.

Despite the benefits offered by monoclonal antibody treatment, early reports indicated that monoclonal antibodies were not being widely used.⁵ The COVID-19 surge in summer 2021 due to transmission of the Delta variant only underscores the importance of ensuring that effective therapeutics are available; however, a recent report shows that monoclonal antibodies continue to be underused.⁶ This brief explores variation in use of the first two monoclonal antibodies from November 2020 through March 2021, and identifies potential disparities in uptake by social vulnerability and urbanicity.

METHODS

The data for the study were drawn from November 2020-March 2021 IQVIA US Open Source Claims, a multi-payer pre-adjudicated health insurance claims database covering all 50 states and Washington, D.C. IQVIA US Open Source Claims includes professional claims generated by office-based physicians (CMS-1500), institutional claims generated by hospitals and other institutions (UB-04), and prescription claims. The version of the data used in this study contains information only on patients who were diagnosed with COVID-19, had a test for COVID-19, or exhibited COVID-19 symptoms such as fever, fatigue, shortness of breath, or cough. The dataset includes patient location at the ZIP3 level (first three digits of the patient's zip code, which covers a broader geographic area than a 5-digit ZIP code), gender, and age. Age was suppressed for patients over the age of 85 to minimize the risk of re-identification due to low patient counts.

Monoclonal antibody uptake was estimated by the number of unique patients with a medical claim for bamlanivimab or casirivimab/imdevimab, the first two therapeutics of this product type, divided by the number

² Due to increased demand, HHS returned to a state/territory-coordinated distribution system on September 13, 2021. For more details, see: <https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/Update-13Sept21.aspx>, last accessed September 15, 2021.

³ CDC. Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html>, last accessed August 22, 2021.

⁴ CDC. Trends in COVID-19 Cases and Deaths in the United States, by County-level Population Factors. Available at: https://covid.cdc.gov/covid-data-tracker/#pop-factors_7daynewcases, last accessed August 22, 2021.

⁵ CNN. Lifesaving COVID-19 antibody treatments are plentiful, but still sitting on the shelf. Available at: <https://www.cnn.com/2021/01/21/health/covid-19-monoclonal-antibody-treatment-neglected/index.html>, last accessed August 22, 2021.

⁶ The Washington Post. Monoclonal antibodies are free and effective against COVID-19, but few people are getting them. Available at: https://www.washingtonpost.com/health/covid-monoclonal-abbott/2021/08/19/a39a0b5e-0029-11ec-a664-4f6de3e17ff0_story.html, last accessed August 22, 2021.

of unique patients with medical claims containing a COVID-19 diagnosis code. Only claims for individuals over the age of 12 were included in the final dataset. The number of claims attributable to each county was estimated using a ZIP3 to county crosswalk. For more details about the data and methods, see the Appendix.

Variation in monoclonal antibody use by social vulnerability and urbanicity was explored at the county level. Social vulnerability was defined using the four themes of the CDC Social Vulnerability Index. These themes capture socioeconomic status, household composition and disability, minority status and language, and housing type and transportation. Together, these themes summarize the extent to which a community is socially vulnerable to disaster.⁷ Urbanicity was defined in this study using the NCHS Urban-Rural Classification Scheme for Counties.⁸ A multivariate linear regression model was also used to explore monoclonal antibody use, social vulnerability, and urbanicity, while controlling for potential confounding factors. Additional details about the variables used in the regression model can be found in the Appendix.

RESULTS

This dataset was comprised of 57,659 claims for either bamlanivimab or casirivimab/imdevimab between November 2020 and March 2021. Claims for monoclonal antibody treatment peaked in January 2021 and declined in February and March 2021.

Table 1: Patients with claims of bamlanivimab and casirivimab/imdevimab, by month

Month	Number of claims (bamlanivimab)	Number of claims (casirivimab/imdevimab)	Total claims	Percent of COVID-19 diagnoses with claims for monoclonal antibodies
November 2020	1,399	1	1,400	0.15
December 2020	13,489	1,478	14,967	0.91
January 2021	21,714	3,866	25,580	1.68
February 2021	9,706	1,105	10,811	1.70
March 2021	4,223	678	4,901	1.01
Total (all months)	50,531	7,128	57,659	1.11

Note: November 2020 data represents only diagnosed COVID-19 cases between November 9-30, 2020, to match the dates during which monoclonal antibody therapies were available. If patients had more than one claim for a monoclonal antibody during the dataset period (including individuals who received both types of monoclonal antibodies), only the first is counted here.

Recipients of monoclonal antibodies and individuals with positive COVID-19 diagnoses had a similar gender distribution (Table 2), but recipients of monoclonal antibodies tended to be older than patients diagnosed with COVID-19. The median age of monoclonal antibody recipients was 64 years compared to 51 years for individuals diagnosed with COVID-19.

⁷ Social vulnerability refers to the potential negative effects on communities caused by external stresses on human health. The CDC/ATSDR Social Vulnerability Index (SVI) uses 15 U.S. census variables to help local officials identify communities that may need support before, during, or after disasters. SVI values range from 0 (least vulnerable) to 1 (most vulnerable). The 2018 SVI summary themes were used in this study. SVI data are available at: https://www.atsdr.cdc.gov/placeandhealth/svi/documentation/SVI_documentation_2018.html, last accessed August 25, 2021.

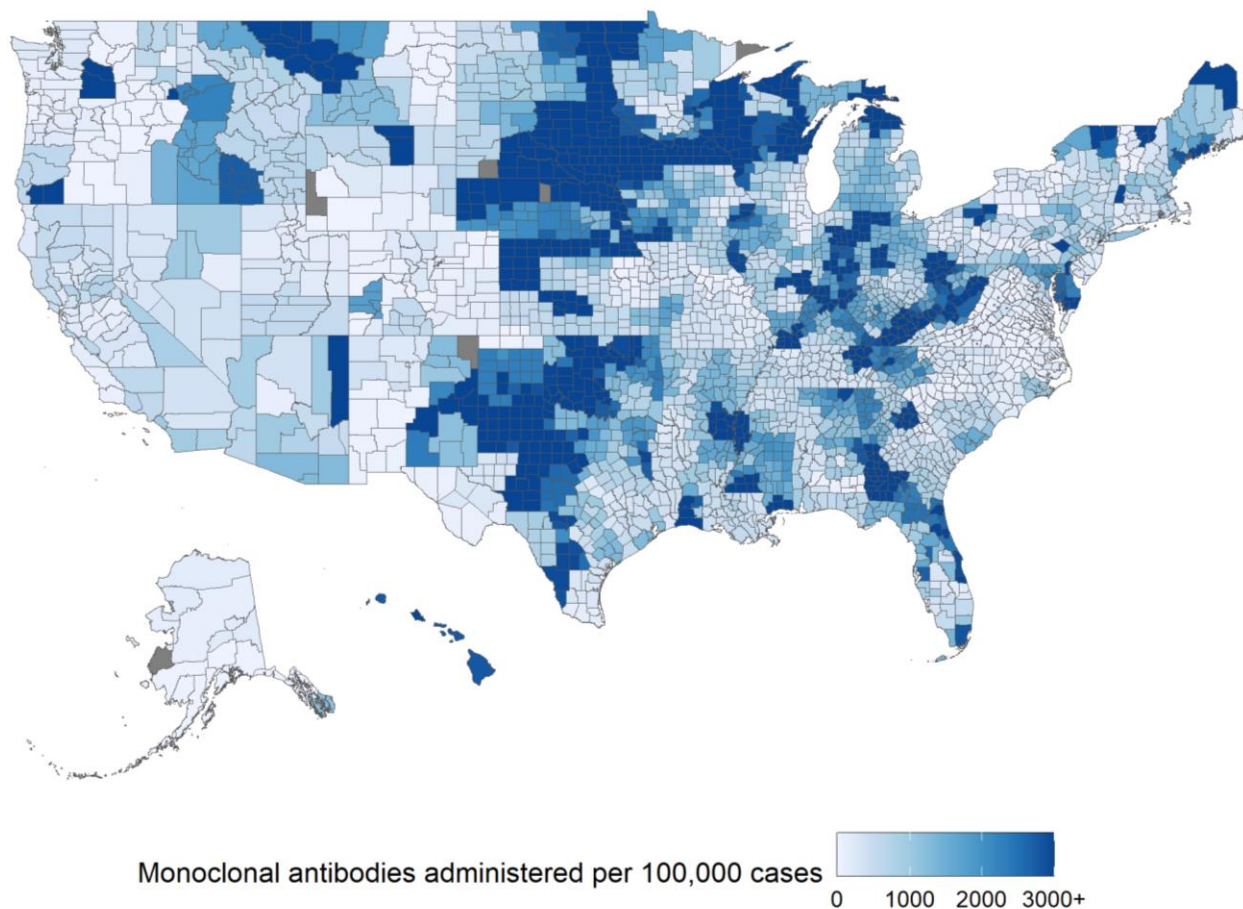
⁸ NCHS. Urban-Rural Classification Scheme for Counties (2013). Available at https://www.cdc.gov/nchs/data_access/urban_rural.htm, last accessed August 25, 2021.

Table 2: Demographics of patients diagnosed with COVID-19 and recipients of monoclonal antibodies

Demographic characteristic	COVID-19 diagnoses	Monoclonal antibody recipients
Gender		
Female	55.1%	53.7%
Male	44.7%	46.2%
Unknown	0.2%	0.1%
Age Group		
Under 18	6.1%	0.5%
19-24	7.3%	1.0%
25-39	19.7%	6.3%
40-54	22.0%	16.4%
55-64	16.5%	25.0%
65+	28.3%	50.8%

Monoclonal antibody use varied significantly by geography, even when accounting for variation in local case rates (Figure 1 and Appendix Figure 2). The highest numbers of monoclonal antibodies administered per 100,000 COVID-19 cases were found in the Midwest and South, whereas the lowest rates were found in the West, and parts of the East and West coasts. However, within-state variation was also prevalent, indicating that use of monoclonal antibody therapies was not uniformly distributed based on case burden.

Figure 1: Monoclonal antibodies administered per 100,000 COVID-19 diagnoses at the county level



Notes: Dark blue denotes 3,000 or more monoclonal antibody claims per 100,000 COVID-19 diagnoses. Gray areas did not have any COVID-19 diagnoses in the IQVIA dataset during the time frame of this study.

A significant body of research has identified populations vulnerable to COVID-19 infection and disproportionate rates of deaths due to COVID-19: these include low income populations,⁹ racial and ethnic minority populations,¹⁰ people with disabilities,¹¹ as well as other underserved populations.¹² The CDC's Social Vulnerability Index (SVI)¹³ includes four indices for different themes of social vulnerability: socioeconomic status,¹⁴ household composition and disability,¹⁵ minority status and language,¹⁶ and housing type and transportation.¹⁷ Each of these indices is composed of several demographic factors that fall under each theme. To evaluate how monoclonal antibodies were utilized across counties with a range of social vulnerability, the average number of monoclonal antibodies administered per 100,000 COVID-19 diagnoses was calculated across each month for SVI quartiles (Figure 2). Counties with the lowest social vulnerability for socioeconomic status, minority status and language, and housing type and transportation tended to have the highest rates of monoclonal antibodies administered per COVID-19 diagnosis. The gaps in monoclonal antibody uptake were most stark for counties with high minority populations and non-native English speakers ("Minority status and language"). Among these counties, large gaps persisted between the highest and lowest social vulnerability counties from December 2020 through March 2021.

These results were further supported by linear regression analysis, after controlling for a number of potentially confounding factors.¹⁸ Counties with high social vulnerability in terms of socioeconomic status, minority status and language, or housing type and transportation used significantly fewer monoclonal antibodies per COVID-19 diagnosis than less socially vulnerable counties. Counties with high social vulnerability in terms of household composition and disability tended to have higher monoclonal antibody uptake; however, this is expected given that this SVI theme includes the size of the 65+ population in a county.

⁹ Miller, S., Wherry, L., Mazumder, B. (2021). Estimated mortality increases during the COVID-19 pandemic by socioeconomic status, race, and ethnicity. *Health Affairs* 40(8). doi: 10.1377/hlthaff.2021.00414

¹⁰ CDC. Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html>, last accessed August 26, 2021.

¹¹ Gleason, J., Ross, W., Fossi, A., Blonsky, H., Tobias, J., Stephens, M. (2021). The Devastating Impact of COVID-19 on Individuals with Intellectual Disabilities in the United States. Available at: <https://catalyst.neim.org/doi/full/10.1056/CAT.21.0051>, last accessed August 26, 2021.

¹² CDC. Trends in COVID-19 Cases and Deaths in the United States, by County-level Population Factors. Available at: https://covid.cdc.gov/covid-data-tracker/#pop-factors_7daynewcases, last accessed August 26, 2021.

¹³ Full documentation for the 2018 Social Vulnerability Index is available here: https://www.atsdr.cdc.gov/placeandhealth/svi/documentation/SVI_documentation_2018.html, last accessed August 26, 2021.

¹⁴ This theme index is calculated using variables from the American Community Survey addressing the following characteristics: below poverty, unemployed, income, no high school diploma. Values range from 0-1, with 0 being the least vulnerable and 1 being the most vulnerable.

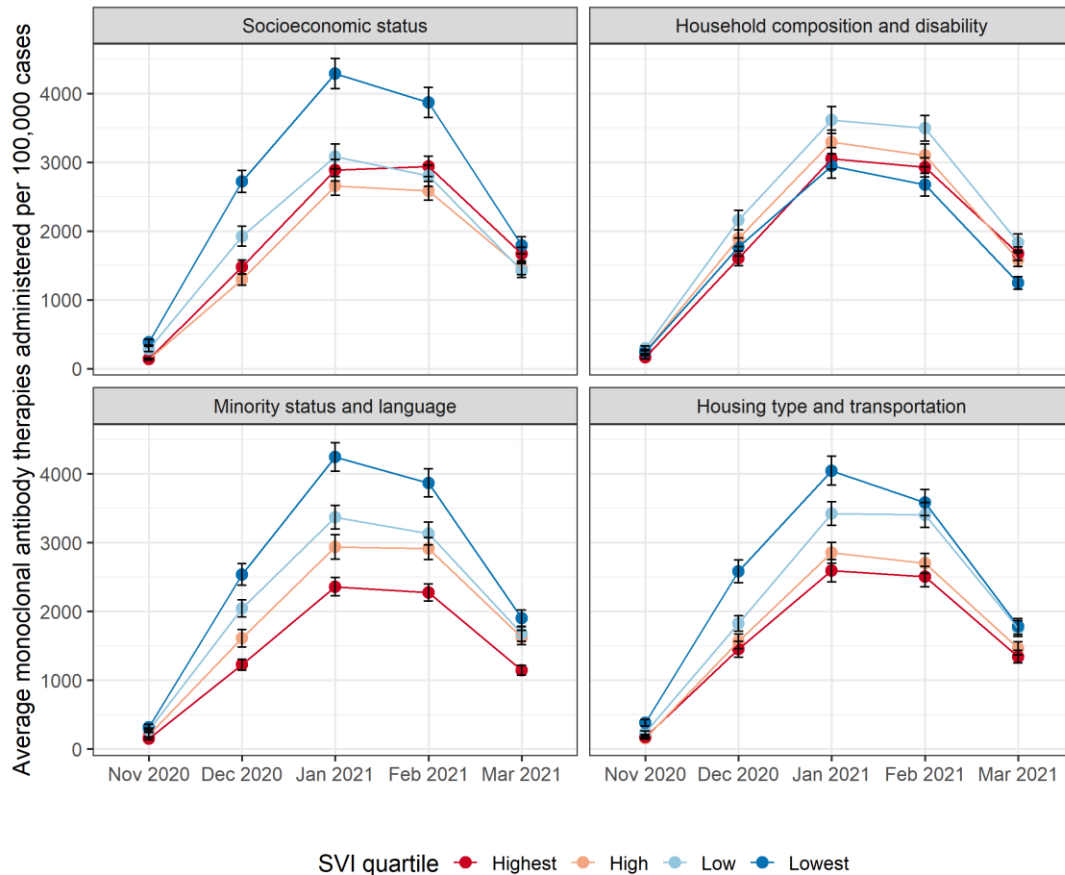
¹⁵ This theme index is calculated using variables from the American Community Survey addressing the following characteristics: aged 65 or older, aged 17 or younger, civilian with a disability, single-parent households. Values range from 0-1, with 0 being the least vulnerable and 1 being the most vulnerable.

¹⁶ This theme index is calculated using variables from the American Community Survey addressing the following characteristics: minority and aged 5 or older who speaks English "less than well". Values range from 0-1, with 0 being the least vulnerable and 1 being the most vulnerable.

¹⁷ This theme index is calculated using variables from the American Community Survey addressing the following characteristics: multi-unit structures, mobile homes, crowding, no vehicle, group quarters. Values range from 0-1, with 0 being the least vulnerable and 1 being the most vulnerable.

¹⁸ The model controlled for the demographics of COVID-19 diagnosed patients in the county, obesity rate, primary care physicians per capita, COVID-19 case fatality rate, and new COVID-19 cases per capita. Additional details about the model can be found in the Appendix.

Figure 2: Monoclonal antibodies administered per 100,000 cases, by SVI and month

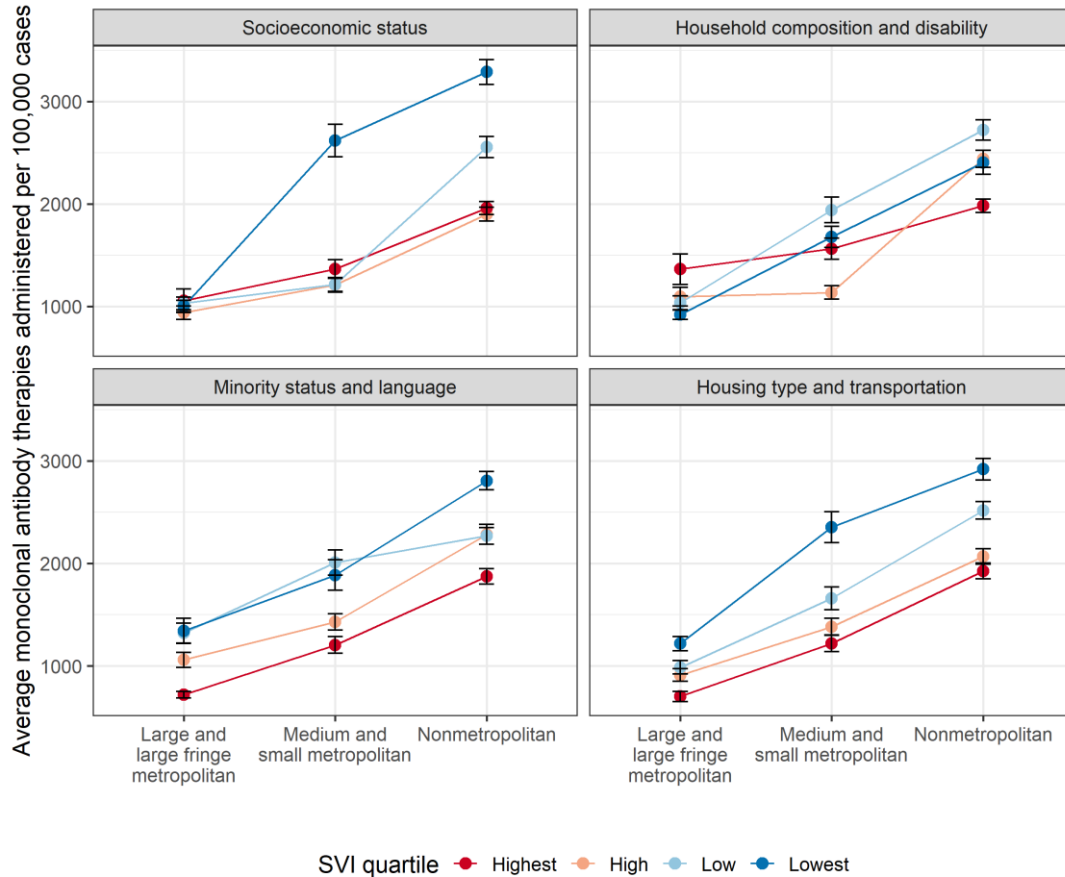


Notes: SVI quartiles were defined as follows: Highest (0.75-1), High (0.5-0.74), Low (0.25-0.49), and Lowest (0-0.24). Points represent the average number of monoclonal antibodies administered per 100,000 cases across all counties in an SVI quartile. Error bars represent standard error.

Monoclonal antibodies can reduce the likelihood of high-risk individuals progressing to severe illness or requiring hospitalization. Therefore, monoclonal antibodies would ideally be used in populations at high risk of severe COVID-19, or in areas where overburdening of the healthcare system might lead to considerable increases in mortality. In this dataset, monoclonal antibodies administered per 100,000 diagnoses tended to decrease with urbanicity (Figure 3), when not controlling for other factors.

When evaluating this relationship in the regression model, urbanicity was not significantly associated with monoclonal antibody uptake. This suggests that differences in urbanicity cannot explain variation in monoclonal antibody uptake, after controlling for other potentially confounding factors. Factors that also increase with decreasing urbanicity, such as obesity rates, may partially explain this relationship.

Figure 3: Monoclonal antibodies administered per 100,000 cases, by SVI and urbanicity



Notes: SVI quartiles were defined as follows: Highest (0.75-1), High (0.5-0.74), Low (0.25-0.49), and Lowest (0-0.24). Points represent the average number of monoclonal antibodies administered per 100,000 cases across all counties in an SVI quartile and rural/urban category. Error bars represent standard error.

DISCUSSION

These results show that use of monoclonal antibodies for treatment of COVID-19 varied considerably across the United States between November 2020 and March 2021. This geographic variation is associated with disparities in monoclonal antibody use by certain county-level characteristics, particularly social vulnerability. Of particular concern, these results suggest that populations that have been disproportionately impacted by COVID-19, such as racial and ethnic minorities and low-income populations, received monoclonal antibodies at a lower rate during the studied period.

This analysis suggests that low-income counties and counties with a large racial and ethnic minority population used fewer monoclonal antibodies than higher-income or low-minority counties during the examined period. Since monoclonal antibodies have the potential to reduce the risk of hospitalization, it is particularly concerning that racial and ethnic minorities, who have a 2-3 higher risk of hospitalization compared with non-Hispanic Whites,¹⁹ may have been less likely to receive this treatment. We also observed lower uptake in counties with high social vulnerability in terms of housing type and transportation. This theme index includes variables that

¹⁹ CDC. Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html>, last accessed August 22, 2021.

account for COVID-19 risk factors such as crowding and group housing, as well as variables that may relate to access barriers such as having no vehicle. Together, these results suggest that although monoclonal antibodies are an effective treatment to prevent progression of COVID-19 to severe illness and hospitalization, the use of monoclonal antibodies may not have been distributed equally among vulnerable populations. The largest gaps in monoclonal antibody use between SVI groups were present in February 2021, but monoclonal antibody use in March 2021 was relatively similar between SVI groups. This may reflect a decreasing demand for monoclonal antibody treatment in low SVI counties due to higher vaccination coverage.²⁰ Although these results cannot point to reasons for these disparities, identifying barriers to accessing monoclonal antibodies is essential in the ongoing battle against COVID-19, particularly in the context of lower vaccination rates in rural,²¹ low-income,²² and socially vulnerable communities,²³ as well as in racial and ethnic minorities.²⁴ Future work should explore how these relationships may have changed with increasing vaccination rates since March 2021, as well as during the surge of COVID-19 cases driven by the Delta variant in fall 2021.

Although rural counties tended to have higher monoclonal antibody use than metropolitan counties during the examined period, urbanicity was not significantly associated with monoclonal antibody use after accounting for other factors in the regression model. However, density of primary care physicians was negatively correlated with monoclonal antibody uptake. This relationship was relatively small but suggests that areas with lower density of primary care physicians, and therefore potentially reduced access to healthcare, had slightly higher uptake of monoclonal antibodies. Reducing burden on the healthcare system by preventing hospitalizations in high-risk individuals, particularly in areas where healthcare resources are limited, is a key goal of monoclonal antibody treatment. However, this analysis shows that high SVI rural counties were still using monoclonal antibodies at lower rates than low SVI rural counties. This suggests that a targeted focus on ensuring that high SVI counties have access to monoclonal antibodies, regardless of urbanicity, may be necessary. These results also indicate that areas with higher proportions of certain at-risk populations recommended²⁵ for monoclonal antibody treatment, such as adults over the age of 65 or obese adults, were associated with higher uptake of monoclonal antibodies.

These results are consistent with a number of media reports indicating that monoclonal antibodies have not been used as widely as originally expected given the number of eligible COVID-19 patients.^{26,27} Low uptake has been attributed to a lack of awareness among physicians and the general public, as well as logistical challenges

²⁰ Hughes, M., Wang, A., Grossman, M. *et al.* (2021). County-level vaccination coverage and social vulnerability – United States, December 14, 2020–March 1, 2021. *MMWR Morb Mortal Wkly Rep* 70: 431-436. doi: 10.15585/mmwr.mm7012e1

²¹ Murthy, B., Sterrett, N., Weller, D. *et al.* (2021). Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties – United States, December 14, 2020 – April 10, 2021. *MMWR Morb Mortal Wkly Rep* 70: 759-764. doi: 10.15585/mmwr.mm7020e3

²² Barry, V., Dasgupta, S., Weller, D., *et al.* (2021). Patterns in COVID-19 Vaccination Coverage, by Social Vulnerability and Urbanicity – United States, December 14, 2020 – May 1, 2021. *MMWR Morb Mortal Wkly Rep* 70: 818-824. doi: 10.15585/mmwr.mm7022e1

²³ CDC. COVID-19 Vaccination Equity. Available at: <https://covid.cdc.gov/covid-data-tracker/#vaccination-equity>, last accessed August 26, 2021.

²⁴ CDC. COVID Data Tracker. Available at: <https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends>, last accessed August 26, 2021.

²⁵ NIH COVID-19 Treatment Guidelines: Anti-SARS-CoV-2 Monoclonal Antibodies. Available at:

<https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-mono-clonal-antibodies/>, last accessed August 26, 2021.

²⁶ The Washington Post. Monoclonal antibodies are free and effective against COVID-19, but few people are getting them. Available at: https://www.washingtonpost.com/health/covid-mono-clonal-abbott/2021/08/19/a39a0b5e-0029-11ec-a664-4f6de3e17ff0_story.html, last accessed August 22, 2021.

²⁷ CNN. Lifesaving COVID-19 antibody treatments are plentiful, but still sitting on the shelf. Available at:

<https://www.cnn.com/2021/01/21/health/covid-19-mono-clonal-antibody-treatment-neglected/index.html>, last accessed August 22, 2021.

of setting up sites to administer monoclonal antibodies.²⁸ Although primary care physicians are authorized to administer monoclonal antibodies, some may not have the resources to perform intravenous infusions, and as a result, patients are often referred to infusion centers or hospitals. However, hospitals dealing with large numbers of COVID-19 patients may not have the capacity to administer monoclonal antibodies.²⁹ Delays due to the challenges of finding appointments or sites administering monoclonal antibodies also present a significant barrier, as monoclonal antibodies are most effective if administered within 10 days of initial symptoms.³⁰ These challenges may disproportionately impact vulnerable populations, particularly those living in areas without easy access to healthcare facilities or without the means to identify and travel to an appropriate facility. One report indicated that as of August 2021, the monoclonal antibody treatment casirivimab/imdevimab was reaching only 30% of eligible patients. It is also not well known to what extent social or cultural factors may influence patient acceptance of monoclonal antibody therapies. One study conducted in late 2020 found several factors associated with higher acceptance of monoclonal antibody therapy, including being non-Hispanic White and English speaking.³¹ Variation in patient acceptance by demographic characteristics may also contribute to the differences observed in the present study. With continued disparities in vaccination rates by social vulnerability, ensuring equitable access to monoclonal antibodies continues to be critically important to reduce hospitalization and severe illness due to COVID-19.

LIMITATIONS

This analysis is unable to capture the reasons why certain populations may have received fewer monoclonal antibodies than others. A range of factors, such as physician awareness, patient acceptance, allocation/distribution approach, and access to healthcare, may influence monoclonal antibody uptake. Future work should explore the extent to which these factors may have contributed to the geographic variation in monoclonal antibody uptake observed in this study.

The distribution process for monoclonal antibodies varied during the time period of this analysis. Between November 2020 and February 2021, the federal government distributed doses to states and state health departments determined how to allocate doses to sites within each state. In March 2021, which represents the final month of the analyzed dataset, sites could order doses directly from the distributor. This analysis cannot distinguish where variation in monoclonal antibody uptake may be due to allocation/distribution versus other factors, such as physician awareness. Furthermore, supply of monoclonal antibodies increased significantly during this time period, which may have further impacted how and where monoclonal antibodies were used. Future work should explore how uptake of monoclonal antibodies may have changed since March 2021. Monoclonal antibodies were widely available during the summer of 2021, but the surge of cases in the fall months led to a shortage of monoclonal antibodies.³² Evaluating the implications of these changes in supply and demand on use of monoclonal antibodies across a range of communities, including socially vulnerable and

²⁸ NPR. Demand For COVID Antibody Drugs Soars In Hard-Hit States. Available at:

<https://www.npr.org/2021/08/20/1029837227/demand-covid-antibody-drugs-soars-regeneron-florida>, last accessed September 14, 2021.

²⁹ The Washington Post. Monoclonal antibodies are free and effective against COVID-19, but few people are getting them. Available at: https://www.washingtonpost.com/health/covid-monoclonal-abbott/2021/08/19/a39a0b5e-0029-11ec-a664-4f6de3e17ff0_story.html, last accessed August 22, 2021.

³⁰ CDC. COVID-19: Treatments Your Healthcare Provider Might Recommend if You Are Sick. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/your-health/treatments-for-severe-illness.html>, last accessed September 14, 2021.

³¹ Bierle, D., Ganesh, R., Wilker, C., Hanson, S., Moehnke, D., Jackson, T., Ramar, P., Rosedahl, J., Philpot, L., Razonable, R. (2021). Influence of Social and Cultural Factors on the Decision to Consent for Monoclonal Antibody Treatment among High-Risk Patients with Mild-Moderate COVID-19. *Journal of Primary Care & Community Health* 12. doi: 10.1177/21501327211019282

³² The Washington Post. Biden administration moves to stave off shortages of monoclonal antibodies. Available at: <https://www.washingtonpost.com/health/2021/09/14/monoclonal-antibodies-shortage/>, last accessed September 15, 2021.

rural communities, will be important to ensure that monoclonal antibodies are reaching the people who need them the most.

These data do not directly assess the socioeconomic or demographic characteristics of monoclonal antibody recipients. Rather, this analysis uses geographic variables to assess whether uptake of monoclonal antibodies was similar across areas of different social vulnerability. Therefore, this analysis cannot definitively identify populations that have received monoclonal antibodies at a lower rate than other populations. Future work should directly evaluate monoclonal antibody uptake in racial and ethnic minorities, low-income individuals, and other populations.

This analysis uses medical claims data and does not capture claims from all insurance providers. We assume that any underestimation due to the sources of these medical claims would be evenly distributed across counties of a range of social vulnerabilities. Additionally, not all COVID-19 diagnoses are captured in medical claims; for example, individuals who were tested at sites that do not bill insurance will not be captured in this dataset. Therefore, the estimates of monoclonal antibodies administered per 100,000 COVID-19 diagnoses likely underrepresent COVID-19 diagnoses in a county. However, COVID-19 diagnoses associated with a clinical visit would be captured; we expect that this reflects the population of COVID-19 patients that may have been evaluated for monoclonal antibody treatment.

CONCLUSION

Monoclonal antibodies represent a critical tool in the fight against COVID-19. The disproportionate impact of COVID-19 on racial and ethnic minorities and low-income populations, as well as disparities in COVID-19 vaccination rates, indicate that it is critical to ensure monoclonal antibodies are available and accessible to these populations. These results highlight areas where future exploration is needed to identify populations that may benefit from monoclonal antibodies, but have not had equal access.

APPENDIX

Supplemental Methods

Data

Claims for anti-SARS-CoV-2 monoclonal antibodies were identified using the following codes: Q0239 and M0239 (bamlanivimab), and Q0243 and M0243 (casirivimab and imdevimab). For patients with more than one claim for monoclonal antibodies, including those treated with more than one type of monoclonal antibody, only the first claim (by date of service) was included in the final dataset. A COVID-19 diagnosis was identified with the following ICD-10 codes: U07.1 (COVID-19, lab-confirmed), U07.2 (COVID-19, clinically diagnosed), B97.29 (Other coronavirus as the cause of diseases classified elsewhere), and B34.2 (Coronavirus infection, unspecified). The codes B97.29 and B34.2 are not specific to COVID-19 and were therefore most frequently used prior to the introduction of COVID-19-specific codes; however, some limited use of these codes has continued and therefore is captured here. Bamlanivimab received an EUA on November 9, 2020; casirivimab and imdevimab received an EUA on November 21, 2020. The bamlanivimab EUA was revoked on April 16, 2021 due to declining effectiveness of the treatment against emerging variants of SARS-CoV-2.³³ As a result, the data pull from IQVIA for both COVID-19 diagnoses and monoclonal antibodies was restricted to November 9, 2020 through March 31, 2021. Children under the age of 12 were excluded from both datasets because they were not eligible to receive monoclonal antibody treatment under the EUAs.

ZIP3 to County Crosswalk

In order to compare with county-level metrics, a ZIP3 to county-level crosswalk was performed for (1) monoclonal antibody use and (2) COVID-19 diagnoses using the 2010 ZIP Code Tabulation Area (ZCTA) to County Relationship File,³⁴ as previously described in other research.³⁵ The gender ratio and age distribution of monoclonal antibody recipients and COVID-19 diagnoses at the county level were estimated using weighted means, with the weighting factor representing the proportion of claims in the ZIP3 that were crosswalked to a given county. The county-level estimates of monoclonal antibody uptake were then normalized by COVID-19 diagnoses (per 100,000 cases). Because this dataset represents medical claims, only positive diagnoses that were associated with a medical claim would be captured in this dataset. As a result, COVID-19 diagnoses were underestimated in the IQVIA dataset. However, COVID-19 diagnoses in the IQVIA dataset are correlated with actual COVID-19 cases at the county level (Appendix Figure 1).³⁶

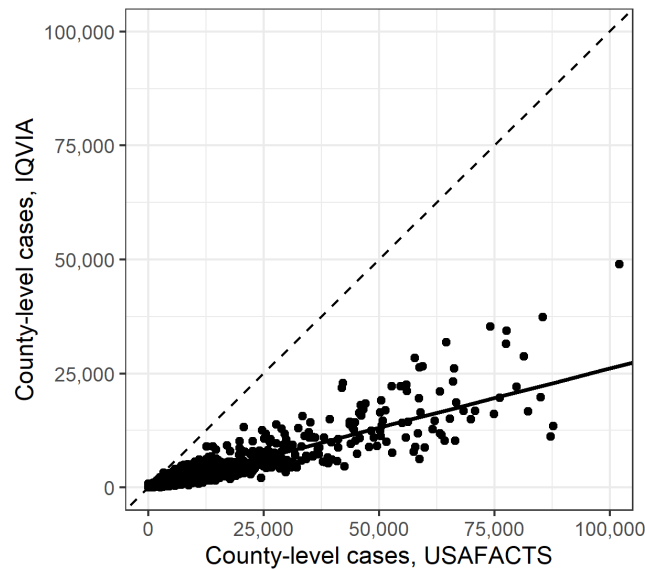
³³ FDA. Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Monoclonal Antibody Bamlanivimab. Available at: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab>, last accessed August 22, 2021.

³⁴ U.S. Census Bureau. 2010 ZIP Code Tabulation Area (ZCTA) Relationship File Record Layouts. Available at: <https://www.census.gov/programs-surveys/geography/technical-documentation/records-layout/2010-zcta-record-layout.html>, last accessed August 25, 2021.

³⁵ Sullivan, P., Mouhanna, F., Mera, R., Pembleton, E., Castel, A., Jaggi, C., Jones, J., Kramer, M., McGuinness, P., McCallister, S., Siegler, A. (2020). Methods for county-level estimation of pre-exposure prophylaxis coverage and application to the U.S. Ending the HIV Epidemic jurisdictions. *Annals of Epidemiology* 44, 16-30. <https://doi.org/10.1016/j.annepidem.2020.01.004>.

³⁶ The relationship between IQVIA COVID-19 diagnoses and reported COVID-19 cases was not significantly affected by social vulnerability or urbanicity; therefore, IQVIA COVID-19 diagnoses were assumed to capture a similar proportion of COVID-19 cases across all counties regardless of these factors.

Appendix Figure 1: COVID-19 diagnoses captured in IQVIA dataset versus actual reported



Notes: USAFACTS county-level COVID-19 case data were obtained from <https://usafacts.org/visualizations/coronavirus-covid-19-spread-map/>. Points represent the total number of cases in a county recorded between November 9, 2020 and March 31, 2021 in USAFACTS (x-axis) or as estimated by COVID-19 diagnosis codes in IQVIA (y-axis). Dashed line indicates the expected relationship if IQVIA captured 100% of COVID-19 diagnoses in a county. Solid line represents simple linear regression of these variables (slope = 0.26, p-value = $2e-16$, $R^2 = 0.91$).

Linear Regression

To further explore associations between monoclonal antibody use and county-level characteristics, a multivariate linear regression model was developed to predict county-level monoclonal antibody use per COVID-19 diagnosis. This model incorporated demographic information from IQVIA, estimated via the ZIP3 to county crosswalk as described above, and county-level variables. The model was run with month fixed effects. IQVIA demographic variables used in the model include the gender ratio of COVID-19 diagnoses in the county each month and the proportion of COVID-19 diagnoses in each of the following age groups each month: under 18, 19-24, 25-39, 40-54, 55-64, and 65+. Additionally, the model accounted for reported COVID-19 cases per month and the case fatality ratio in the county each month.³⁷ County-level characteristic variables included the four themes of the CDC Social Vulnerability Index - socioeconomic status, household composition and disability, minority status and language, and housing type and transportation - which together summarize the extent to which a community is socially vulnerable to disaster. Other county-level variables included urbanicity,³⁸ number of primary care physicians per 100,000 residents,³⁹ and the percent of the adult population that is obese.⁴⁰ These variables were chosen to represent priority populations for monoclonal antibody treatment: individuals at high risk due to comorbidities or age and individuals living in areas with limited access to healthcare. The

³⁷ Values calculated from USAFACTS county-level case and death data. Available at: <https://usafacts.org/visualizations/coronavirus-covid-19-spread-map/>, last accessed August 22, 2021.

³⁸ Urbanicity was defined using the NCHS Urban-Rural Classification Scheme for Counties (2013). Available at https://www.cdc.gov/nchs/data_access/urban_rural.htm, last accessed August 25, 2021.

³⁹ Calculated from Area Health Resources File (2019-2020 Release). Definition includes all M.D. and D.O. non-federal primary care physicians. Data are current as of 2018. Available at: <https://data.hrsa.gov/topics/health-workforce/ahrf>, last accessed August 25, 2021.

⁴⁰ Obtained from the CDC Diabetes Surveillance System. Data represent the age-adjusted percentage of adults over 20 years of age who are obese, as of 2017. Available at: <https://gis.cdc.gov/grasp/diabetes/diabetesatlas.html#>, last accessed August 25, 2021.

response variable (monoclonal antibodies administered per 100,000 cases) was transformed using a $\log(x+1)$ transformation to account for skew and large numbers of zeroes in the dataset. Appendix Table 1 shows the coefficients and p-values from the multivariate linear regression.

Appendix Table 1: Results from Multivariate Linear Regression

	Coefficient (95% confidence interval)	p-value
Social vulnerability: Socioeconomic status	-0.32 (-0.57, -0.08)	$p < 0.01$
Social vulnerability: Household composition and disability	0.26 (0.06, 0.46)	$p < 0.05$
Social vulnerability: Minority status and language	-0.52 (-0.69, -0.34)	$p < 0.001$
Social vulnerability: Housing type and transportation	-0.52 (-0.71, -0.32)	$p < 0.001$
Gender ratio of COVID-19 diagnoses	3.3 (2.3, 4.3)	$p < 0.001$
Proportion of COVID-19 diagnoses in each age group:		
Under 18	-3.9 (-7.1, -0.8)	$p < 0.05$
19-24	-16.6 (-19.9, -13.3)	$p < 0.001$
25-39	-9.9 (-13.1, -6.7)	$p < 0.001$
40-54	-10.1 (-13.2, -7.0)	$p < 0.001$
55-64	-5.6 (-8.7, -2.5)	$p < 0.001$
65+	-9.2 (-12.0, -6.3)	$p < 0.001$
Urbanicity⁴¹	-0.03 (-0.06, 0.005)	0.09 (ns)
New cases per month per 100,000 residents⁴²	0.00022 (0.00017, 0.00027)	$p < 0.001$
Case fatality rate per month⁴³	0.26 (-0.34, 0.87)	0.39 (ns)
Primary care physicians per 100,000 residents	-0.002 (-0.004, -0.001)	$p < 0.001$
Percent of population 20+ that is obese	0.03 (0.02, 0.04)	$p < 0.001$

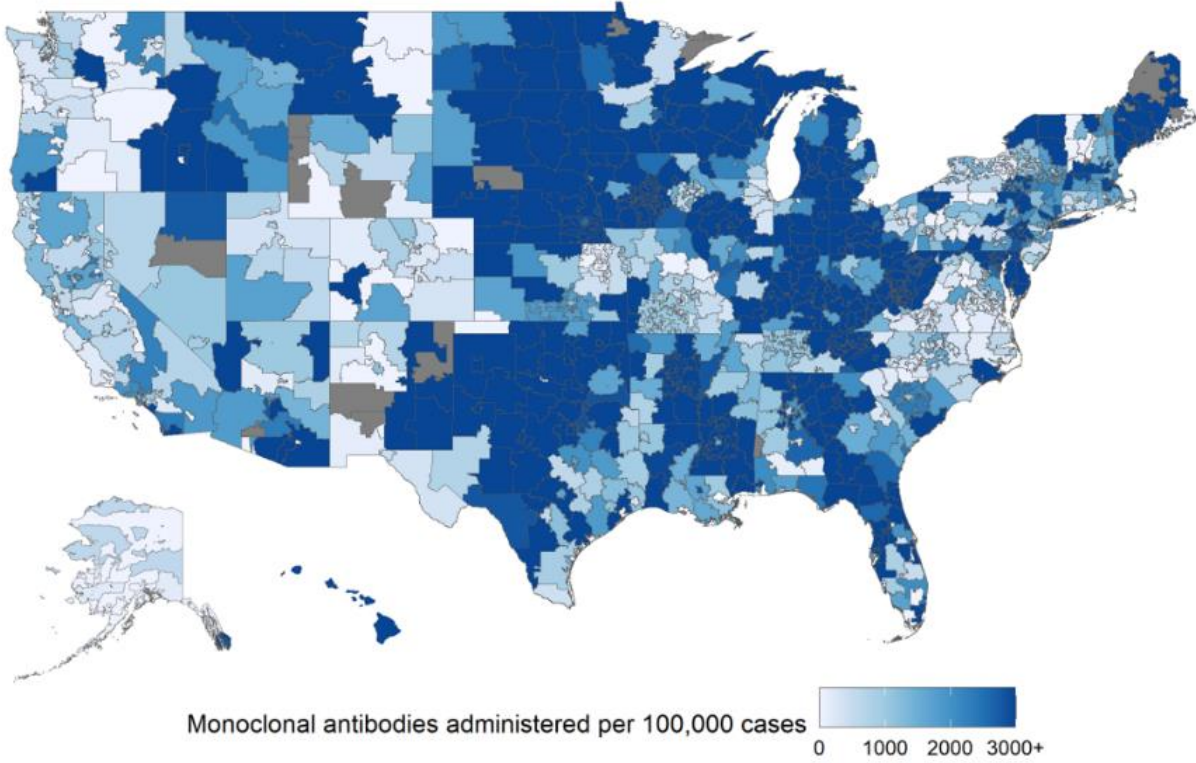
Notes: The response variable was log-transformed for this regression. Therefore, coefficients can be interpreted such that $(\exp(\text{coefficient}(x))-1)*100 = \text{the percent change in monoclonal antibodies administered per 100,000 COVID-19 cases per one unit change in variable } x$.

⁴¹ As defined by the NCHS Urban-Rural Classification Scheme for Counties (2013). Values range from 1 (counties in metro areas of population 1 million or more) to 9 (completely rural or less than 2,500 urban population, not adjacent to a metro area). Available at https://www.cdc.gov/nchs/data_access/urban_rural.htm, last accessed August 25, 2021.

⁴² COVID-19 case data were obtained from USAFACTS.

⁴³ COVID-19 case and death data were obtained from USAFACTS and used to calculate the case fatality rate for a given county and month.

Appendix Figure 2: Monoclonal antibody claims per 100,000 COVID-19 diagnoses at the ZIP3 level



Notes: Dark blue denotes 3,000 or more monoclonal antibody claims per 100,000 COVID-19 diagnoses. Gray areas did not have any COVID-19 diagnoses in the IQVIA dataset during the time frame of this study.

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SUGGESTED CITATION

Kolbe, A. Variation in use of anti-SARS-CoV-2 monoclonal antibody therapies by social vulnerability and urbanicity. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. December 2021.

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